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The Impact of Screening and Partner Notification on Chlamydia Prevalence and Numbers of Infections Averted in the United States, 2000–2015: Evaluation of Epidemiologic Trends Using a Pair-Formation Transmission Model

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Population-level effects of control strategies on the dynamics of *Chlamydia trachomatis* transmission are difficult to quantify. In this study, we calibrated a novel sex- and age-stratified pair-formation transmission model of chlamydial infection to epidemiologic data in the United States for 2000–2015. We used sex- and age-specific prevalence estimates from the National Health and Nutrition Examination Surveys, case report data from national chlamydia surveillance, and survey data from the Youth Risk Behavior Survey on the proportion of the sexually active population aged 15–18 years. We were able to reconcile national prevalence estimates and case report data by allowing for changes over time in screening coverage and reporting completeness. In retrospective analysis, chlamydia prevalence was estimated to be almost twice the current levels in the absence of screening and partner notification. Although chlamydia screening and partner notification were both found to reduce chlamydia burden, the relative magnitude of their estimated impacts varied in our sensitivity analyses. The variation in the model predictions highlights the need for further data collection and research to improve our understanding of the natural history of chlamydia and the pathways through which prevention strategies affect transmission dynamics.

chlamydia; mathematical modeling; reproductive health; sexually transmitted infections; surveillance

Abbreviations: CDC, Centers for Disease Control and Prevention; CrI, credible interval.

Chlamydia, caused by *Chlamydia trachomatis*, is the most commonly reported sexually transmitted infection in the United States and the most prevalent bacterial sexually transmitted infection worldwide (1, 2). Chlamydia prevalence is typically highest among young adults, and asymptomatic infections are common. In women, chlamydial infections have been associated with pelvic inflammatory disease, which can cause ectopic pregnancy and tubal factor infertility. Repeated chlamydia diagnoses have been associated with an additional increase in the risk of pelvic inflammatory disease in studies using routinely collected data (3, 4). Chlamydial infection may be associated with an increase in the risk of acquiring human immunodeficiency virus by inducing inflammation at the site of infection (5, 6).

The US Preventive Services Task Force recommends chlamydia and gonorrhea screening (testing of asymptomatic individuals) for women who are sexually active and under age 25 years or for older women who are at increased risk of infection (7). In addition to screening of women, the Centers for Disease Control and Prevention (CDC) also recommends considering screening sexually active young men in high-prevalence settings (e.g., sexual health clinics, correctional facilities, adolescent clinics) when there are sufficient resources available (8). An aim of the National Center for HIV/AIDS, Viral Hepatitis, STD, and TB Prevention's Strategic Plan is to increase the proportion of young females screened for chlamydia (9).

Previous chlamydia modeling has suggested that increasing screening coverage in the general population should reduce chlamydial infection (10). In a review of chlamydia screening trials, Low et al. (11) found moderate evidence that screening reduced the risk of pelvic inflammatory disease and found

limited trial evidence on the impact of screening on chlamydia prevalence. In the United States, chlamydia trends are characterized by increasing numbers of case reports, while estimates of chlamydia prevalence have remained more stable over time (12, 13). There are several explanations for increasing rates of case reporting: Increasing screening frequency would detect more cases, as would use of more sensitive test diagnostics, and moving towards computerized surveillance systems improves the completeness of reporting of diagnosed chlamydia cases at the national level. How these factors affect chlamydia burden remains unclear. There are numerous uncertainties around chlamydia natural history, epidemiology, and control strategies. In the context of uncertainty and limitations in empirical data, mathematical modeling can provide useful insights into the effects of different prevention strategies on chlamydial infection. By combining different sources of data and incorporating the processes through which the data are generated, we may better understand how observed patterns and trends relate to the underlying dynamics of disease and intervention.

In this study, we developed a novel chlamydia transmission model and calibrated the model to multiple epidemiologic time-series data in order to explore uncertainties in the drivers of recent trends in chlamydial infection. We explored uncertainties in recent trends in the coverage of screening and the completeness of case reporting. The calibrated model was used to estimate the possible impact of screening and partner notification in the United States during the period 2000–2015.

METHODS

Mathematical model overview

We developed a deterministic compartmental heterosexual pair-formation model describing chlamydia transmission in a heterosexual age- and risk-stratified population. The use of pair-formation models to study sexually transmitted infections has been developed by Dietz and Hadeler (14), Waldstätter (15), and Kretzschmar and Dietz (16) and applied in a number of other mathematical models of sexually transmitted infections (17–20). In a pair-formation model, partnerships are explicitly represented as compartments, in contrast to traditional deterministic models of sexually transmitted infections, in which sexual contacts are modeled as instantaneous. The pair-formation framework allows modeling of differential infection risks among persons who are single or paired. Pairs in which both partners are susceptible are protected from infection and pairs in which both partners are infected are not transmitting the infection to others, unless there is concurrency. If one infected person in a pair is diagnosed and treated but their immediate partner is not, reinfection within the partnership is likely to occur (17, 21).

The model includes compartments that stratify the population by age, sex, partnership status, sexual risk behavior, and chlamydial infection status. Age is divided into 4 categories: 15–18 years, 19–24 years, 25–39 years, and 40–54 years (Figure 1). Transmission of chlamydia in the model occurs via unprotected sex in heterosexual partnerships. The model is described in detail in Web Appendix 1 (which includes Web Figures 1–5 and Web Tables 1–4), and the model is operationalized using difference equations described in Web Appendix 2. The mathematical model was coded in R and C++ software, utilizing the "Rcpp" package (R Foundation for Statistical Computing, Vienna, Austria) (22).

Partnership dynamics

In the model, there are 3 partnership statuses that are mutually exclusive. In the 2 youngest age groups, there are people who have not yet become sexually active ("non–sexually active" in Figure 1). We assume that by age 25 years, everyone is sexually experienced. Once people become sexually active, they become part of the unpaired ("single") population, who can have casual partners at age-specific rates ("sexually active" in Figure 1). Casual partners represent short-term relationships, and they are modeled as instantaneous partnerships. Pairs are formed from the unpaired, sexually active people. The model specifies preferential formation of pairs within the same age group, with the possibility that women may form partnerships with older men. The pairs describe long-term partnerships such as cohabiting or marital partnerships. Heterogeneity in sexual risk behavior at the partnership level is modeled with pairs' being predominantly monogamous, with a low frequency of concurrency. Concurrency is modeled in the same fashion as casual partners among unpaired single people: There is a short-term instantaneous partnership from the casual partners pool. When a pair dissolves, the former members of the pair return to the unpaired state. At the population level, there is additional risk heterogeneity, with 10% of the population assumed to belong to the higher-risk group (with a higher rate of casual and concurrent partners), while 90% of the population have fewer casual and concurrent partners.

Natural history and time-varying parameters

Natural history is represented using a susceptible-infected-susceptible structure (Figure 2), further differentiating asymptomatic and symptomatic infections, as well as first infection from subsequent infections. Infection risk comes from the main partner in a pair and from any casual partners that unpaired or paired people have. Subsequent infections are added for later analysis. Testing of symptomatic people occurs at sex-specific rates, while screening of asymptomatic people varies by sex and age. There is a background natural recovery rate for chlamydia. Partner notification is modeled explicitly in the long-term partnerships ("pairs" in Figure 1), and partner notification is stratified by sex and age; however, in the absence of data on changes in this prevention strategy, the parameters are kept time-invariant. The different outcomes resulting from testing an index case in a long-term partnership are described in Web Appendix 1, Web Figure 2.

We included time-varying parameters in the model to reproduce the changes seen in the epidemiologic data. For healthcare–related parameters, we incorporated increasing sensitivity of chlamydia diagnostic tests, age-specific changes in screening due to increasing adherence to CDC and US Preventive Services Task Force recommendations, and adoption of nucleic acid amplification tests (Web Appendix 3, Web Figures 6 and 7). We also incorporated an increase in the completeness of reporting diagnosed cases to the CDC. The average sensitivity of chlamydia tests and probabilities of reporting a chlamydia

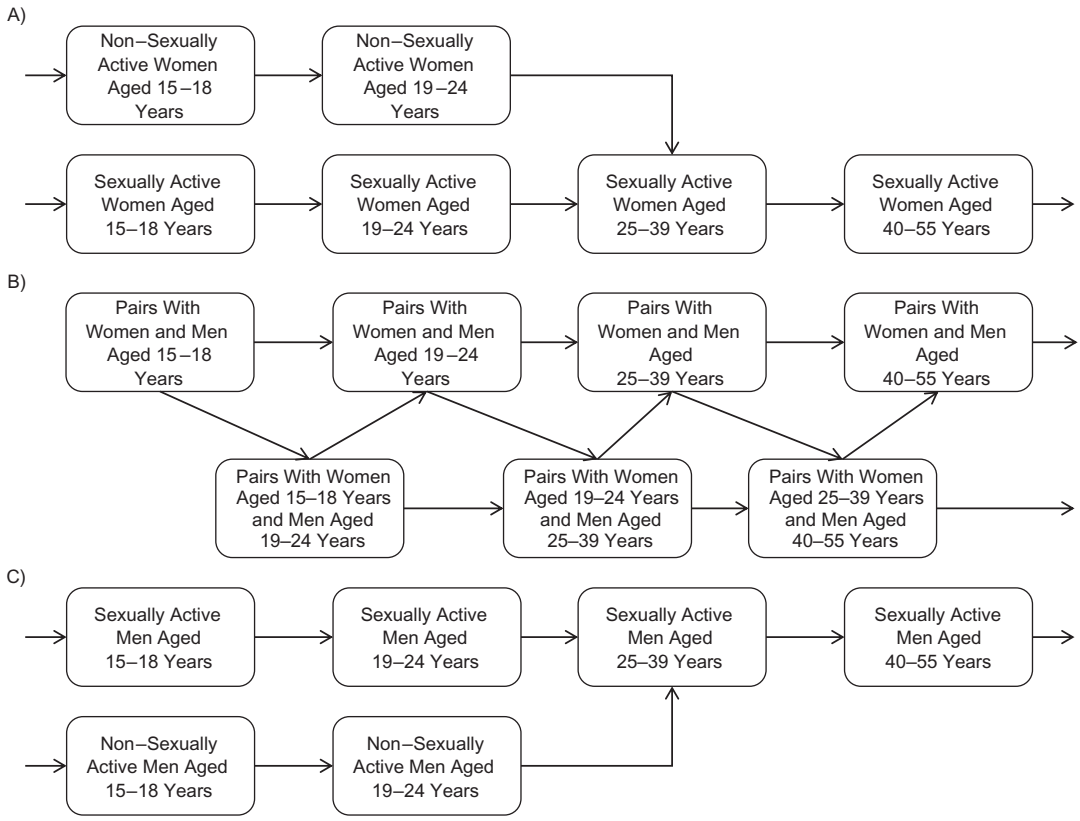

Figure 1. Schematic of the simulated model population and the pair formation process used to simulate chlamydia transmission, with arrows reflecting the aging of the population. A) Unpaired women; B) pairs of men and women, which represent long-term partnerships; C) unpaired men.

diagnosis to the CDC were modeled using a logistic function, constraining trends to increase over time. Time-varying changes in the frequency of screening were modeled with a more flexible function operationalized as a Bezier curve, allowing screening to increase or decrease at different time points. The time-varying parameters governing screening were specific by age and sex with parameters set for women aged 15–18, 19–24, and 25–39 years, and the screening for men was constrained by a multiplier (<1) applied to corresponding rates for women.

We also allowed time-varying trends for the initiation of sexual activity (moving from "non–sexually active" to the "sexually active" compartment) in the youngest age group (15–18 years), governed by monotonic functions describing time trends in both the proportion entering the group at age 15 years as sexually experienced and the rate of sexual initiation in the 15- to 18-year-old population.

Data

We calibrated the model to age- and sex-specific estimates of prevalence and case reports. Prevalence estimates for persons aged 15–39 years were obtained from the National Health and

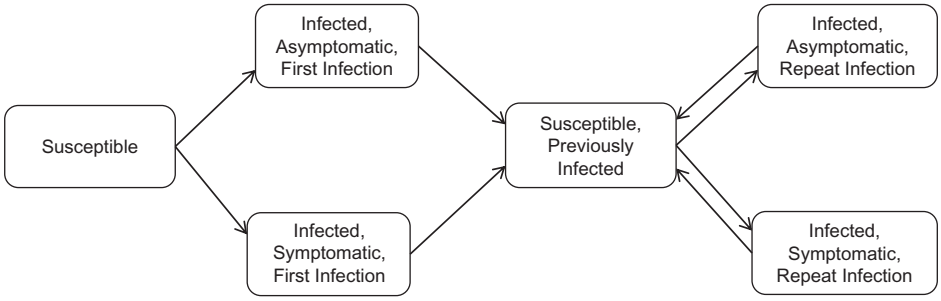

Figure 2. Natural history of chlamydia transmission, with arrows showing the transitions between health states.

Nutrition Examination Survey (23), pooled over 4-year intervals between 1999 and 2014 for each age group in the model up to age 39 years to reduce sampling variance in the estimates. National case reports for persons aged 15–54 years were obtained from CDC data for the years 2000–2015 (24). Chlamydia case report data rarely include information on the sex of sexual partners; to estimate diagnoses among heterosexual men, we assumed that 10% of reported male cases were in men who had sex with men and that 3% of the male population between the ages of 15 and 54 years were men who had sex with men (25). Using Youth Risk Behavior Survey data for 1999–2015 (26), we calibrated the model to the proportion of 15- to 18-year-olds who reported ever having had sex, which represents the age group with the most sizeable population of people who are not sexually active. Behavioral parameters were informed by the National Survey of Family Growth (27) and the Youth Risk Behavior Survey (26). Parameters and their prior distributions are shown in Web Appendix 1, Web Table 1.

Calibration and uncertainty analysis for reporting and screening

We calibrated the model and its parameters to the epidemiologic data using a Bayesian framework, which was operationalized with incremental mixture importance sampling (28). We defined prior probability distributions for the parameters that were varied, which reflected our prior information on their plausible values (Web Appendix 4, Web Table 5). The incremental mixture importance sampling algorithm iteratively explores parameter regions with the highest likelihood of the epidemiologic data given the model and the prior probability distributions for the parameters varied. The Bayesian approach yields joint-posterior probability distributions for the parameter values. These posterior probability distributions are used in the model simulations to produce model estimates, which are presented as mean values and 95% credible intervals for the model outputs. For each calibration scenario, we calibrated the model using the same prior distributions for parameters varied except for differing assumptions made for reporting and screening as described in Table 1. Parameter identifiability can be an issue with complex models. We were less interested in inferring the precise values of individual parameters than in capturing the epidemiologic trends produced by the joint probability distribution of the parameters varied as part of the calibration. We characterized correlation between parameters with a Pearson correlation matrix (Web Appendix 4, Web Figures 8–11). Each model simulation was initially run to equilibrium using time-invariant parameters, and time-varying parameters were introduced for the calibration period corresponding to the period 2000–2015.

To explore the impact of uncertainty regarding trends in screening and reporting, we calibrated the model under 4 discrete scenarios (Table 1), which are referred to henceforth as the "calibration scenarios."

Scenario 1: more constrained priors on reporting and screening. In scenario 1, screening was assumed to remain stable or increase during the 2000–2015 period, consistent with trends in health-care performance measures and claims data (Web Appendix 3, Web Figure 7). We assumed that reporting had increased from the year 2000 from a minimum level of 50%.

Scenario 2: less constrained priors on reporting and more constrained priors on screening. In scenario 2, we allowed reporting in the year 2000 to be less than 50%, while screening assumptions were the same as those in scenario 1.

Scenario 3: more constrained priors on reporting and less constrained priors on screening. In scenario 3, we also allowed screening to decline towards the end of the period 2000–2015, while assumptions for reporting were the same as those in scenario 1.

Scenario 4: less constrained priors on reporting and screening. In scenario 4, screening was also allowed to decline (as in scenario 3), and reporting in 2000 was allowed to be less than 50% (as in scenario 2).

Table 1. Calibration Scenarios Investigated as Part of a Sensitivity Analysis of Chlamydia Transmission, United States, 2000–2015[a]

Calibration Scenario	Prior Assumptions on Reporting[b] of Cases	Prior Assumptions on Screening[c]
Scenario 1: more constrained priors on reporting and screening	Reporting was assumed to be at least 50% in 2000, and it was constrained to increase over time from 2000 to 2015.	Screening was allowed to remain stable or to increase from one year to the next from 2000 to 2015.
Scenario 2: less constrained priors on reporting and more constrained priors on screening	Reporting was not constrained as in scenario 1, but it was only allowed to increase over time from 2000 to 2015.	Same as scenario 1
Scenario 3: more constrained priors on reporting and less constrained priors on screening	Same as scenario 1	Screening was allowed to decrease, remain stable, or increase from 2000 to 2015.
Scenario 4: less constrained priors on reporting and screening	Same as scenario 2	Same as scenario 3

Abbreviation: IQR, interquartile range.

[a] We examined the impact of prior assumptions on screening and reporting, which were implemented as time-varying parameters.

[b] The reporting probability of a diagnosed case was modeled as a logistic function. The prior parameter for reporting in 2000 was estimated as (Beta(7, 3)/2 + 0.5), with a median reporting probability of a diagnosed case of 86% (IQR, 80–90), in scenarios 1 and 3 and estimated as Beta(7, 3), with a median reporting probability of 71% (IQR, 61–80), in scenarios 2 and 4. The beta distribution is defined by shape parameters (α, β).

[c] Screening is modeled as a Bezier function with 4 control points to allow for more flexible time trends (see Web Appendix 1, section 1.8). Changes implemented in the screening priors in the calibration scenarios apply to the age groups 15–18 years and 19–24 years.

Table 2. Calibrated Model and 4 Counterfactual Scenarios Used to Investigate the Impact of Screening and Partner Notification in a Retrospective Analysis of Chlamydia Transmission, United States, 2000–2015

Scenario	Screening Parameters	PN Parameters
Current level (calibrated model)[a]	Screening from 2000 to 2015 was as estimated in the calibrated model.	PN from 2000 to 2015 was as estimated in the calibrated model.
Counterfactual[b]		
At 2000 level[c]	Screening was kept constant from 2000 to 2015 at the coverage estimated by the model for 2000.	Same as current level (calibrated model)
No PN	Same as current level (calibrated model)	PN set to 0 for 2000–2015
No screening	Screening set to 0 for 2000–2015	Same as current level (calibrated model)
No PN or screening	Screening set to 0 for 2000–2015	PN set to 0 for 2000–2015

Abbreviation: PN, partner notification.

[a] The calibrated model aimed to reflect the likely levels of screening and partner notification from 2000 to 2015 through calibration to a range of time-series data, including chlamydia prevalence estimates and case report data.

[b] Counterfactual scenarios in which screening and/or partner notification activities were changed but all other model parameters from the calibrated model were preserved.

[c] Screening was held at the level estimated for the year 2000.

Estimated impact of screening and partner notification

The calibration scenarios represent our estimation of chlamydia burden under the current prevention efforts for 2000–2015 given the uncertainty in screening and reporting coverage. We developed 4 counterfactual analyses to estimate the impact of screening and partner notification during this period in a retrospective analysis. The counterfactual analyses preserved the joint-posterior parameter estimates from the calibration, except for selected parameters governing screening and partner notification, as described in Table 2. For quantification of the overall impact of screening between 2000 and 2015, the first counterfactual analysis held screening constant at 2000 levels. The second counterfactual analysis assumed that there was no partner notification for the time period; the third counterfactual analysis assumed that there was no screening (across sex and age groups) during 2000–2015; and the fourth counterfactual analysis assumed no screening and no partner notification. We assume in the counterfactual scenarios that in the absence of prevention efforts the estimated sexual-risk and health-care–seeking behaviors would remain unchanged in the population. Results from the counterfactual analyses were summarized in terms of chlamydia prevalence in 2015 (allowing for comparison between the calibrated "current" estimate and a counterfactual) and averted infections for 2000–2015 (computing the difference in cumulative chlamydia incidence between the counterfactual analysis and the current estimate).

RESULTS

We calibrated the pair-formation model to prevalence, case report data, and the proportion of persons aged 15–18 years who reported ever having had sex. Each of the 4 calibration scenarios produced joint-posterior estimates of the model consistent with the observed epidemiologic data (Web Appendix 4, Web Figure 12). The calibration scenarios reflect uncertainty around trends in screening and completeness of reporting that cannot be resolved by fitting the model to data on prevalence, case reports, and sexual behavior; parameter values estimated by the model are described in Web Appendix 4, Web Table 6 and Web Figures 13–16. In the United States, there has been a steady increase in rates of chlamydia case reporting. The calibration scenarios were able to capture the changes in case report data and the sex- and age-specific difference in case report data, with younger women aged 15–24 years having the highest reported case rate and women over age 24 years and men in all age groups having fewer cases detected and reported across the time series. For the same time period, national prevalence estimates from the National Health and Nutrition Examination Survey lacked a clear trend, and the estimates were characterized by wide confidence intervals. The calibrated model suggested that there may have been a downward trend in chlamydia prevalence for 2000–2015. The Youth Risk Behavior Survey data on 15- to 18-year-olds' reporting of ever having had sex have remained relatively stable, with some indication that there may have been a decline in the average age of sexual debut in recent years (29).

Figure 3 presents mean values and 95% credible intervals for model-estimated chlamydia prevalence in 2015 given current prevention efforts for 2000–2015 and the estimated chlamydia prevalence in 2015 under 4 counterfactual scenarios: 1) no increase in screening since 2000; 2) no partner notification services during 2000–2015; 3) no screening during 2000–2015; and 4) no screening and no partner notification during 2000–2015. Prevalence estimates for 2000–2015 under each scenario are given in Web Appendix 4, Web Figures 17 and 18. The 4 calibration scenarios produced similar estimates for the retrospective analyses, with estimated 2015 prevalence estimates that were higher in the absence of prevention strategies for all counterfactuals and calibration scenarios.

Absence of both screening and partner notification had the largest impact on estimated prevalence across scenarios for both sexes and across age groups. Among women, absence of screening and partner notification was estimated to result in an approximate doubling of chlamydia prevalence in 2015 in comparison with the base case scenario reflecting current prevention efforts: For example, in calibration scenario 1 (with more constrained priors for reporting and screening), among women aged 15–24 years, the 2015 prevalence under current prevention efforts was

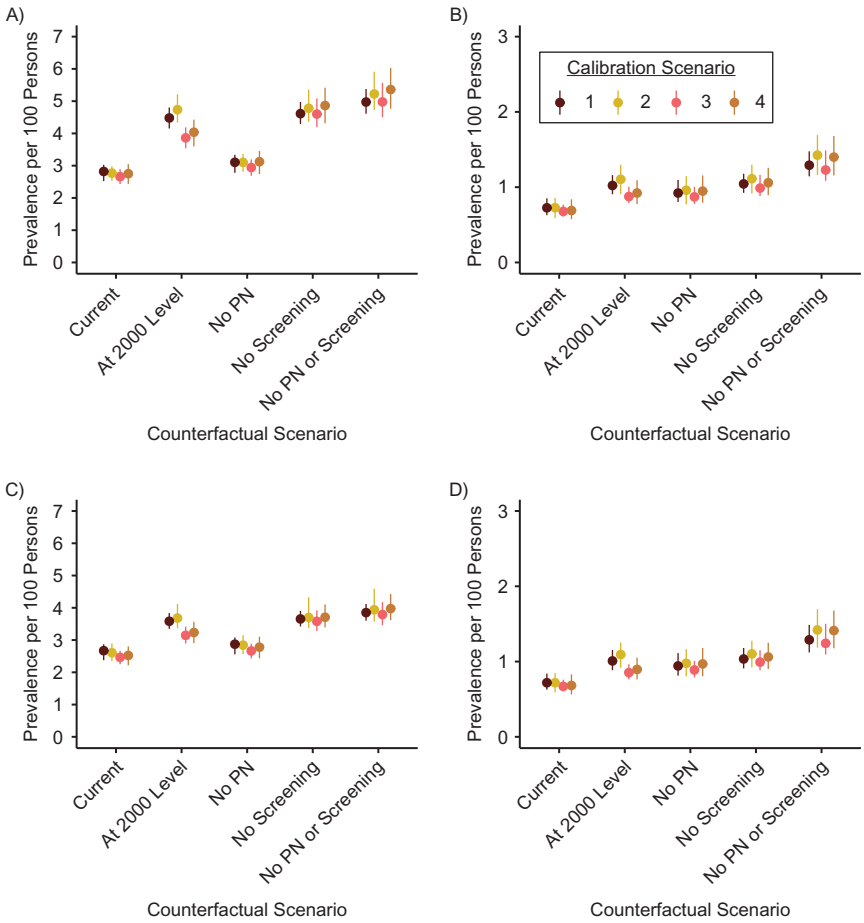

Figure 3. Model-estimated prevalence of chlamydia infection (mean values (circles) and 95% credible intervals (bars)) in the United States in 2015 in a calibrated model (current level) and in 4 counterfactual scenarios: 1) keeping screening at the year 2000 level, 2) no partner notification (PN), 3) no screening, and 4) no screening or PN. Results are presented for women aged 15–24 years (A), women aged 25–54 years (B), men aged 15–24 years (C), and men aged 25–54 years (D). Calibration scenario 1: more constrained priors on reporting and screening; calibration scenario 2: less constrained priors on reporting and more constrained priors on screening; calibration scenario 3: more constrained priors on reporting and less constrained priors on screening; calibration scenario 4: less constrained priors on reporting and screening.

estimated as 2.8% (95% credible interval (CrI): 2.5, 3.0) and predicted prevalence in the absence of partner notification and screening was 5.0% (95% CrI: 4.6, 5.4). Mean prevalence was 1.8–2.0 times that of the current level for both women aged 15–24 years and women aged 25–54 years across the 4 calibration scenarios. Among men, it was 1.4–1.6 times that of the current level for men aged 15–24 years and 1.8–2.1 times that of the current level for men aged 25–54 years. Holding screening at year 2000 coverage was estimated to result in prevalences that were 1.5–1.7 times and 1.1–1.3 times the current levels for women aged 15–24 years and women aged 25–54 years, respectively, while the absence of partner notification had a more modest impact, with a mean prevalence 1.1–1.4 times that of the current level for women aged 15–24 years and 1.3–1.4 times that of the current level for women aged 25–54 years. We also compared the predicted case report rates in 2015 under the different counterfactual scenarios. In Web Appendix 4, Web Figure 19, the case report rates varied most across counterfactual scenarios among women aged 15–24 years, given that this is the group targeted by screening guidelines. Because there is considerably less screening among heterosexual men, their case report rates remained relatively stable across the counterfactual scenarios.

All calibration scenarios predicted that chlamydia screening together with partner notification have averted chlamydial infections. There was substantial variation in estimated numbers of infections averted across the calibration scenarios and counterfactual analyses. Figure 4 shows the cumulative numbers of infections averted in 2000–2015. Screening and partner notification were estimated to have had the largest impact across the scenarios and for all age groups, with a mean of 0.9–2.3 million infections being averted among women aged 15–24 years and a mean of 2.5–3.6 million infections being averted among women aged 25–54 years across the counterfactual analyses. Holding screening at the year 2000 coverage level illustrates the incremental benefits derived from increased screening since 2000. This varied between the calibration scenarios, demonstrating the underlying uncertainty in how screening coverage

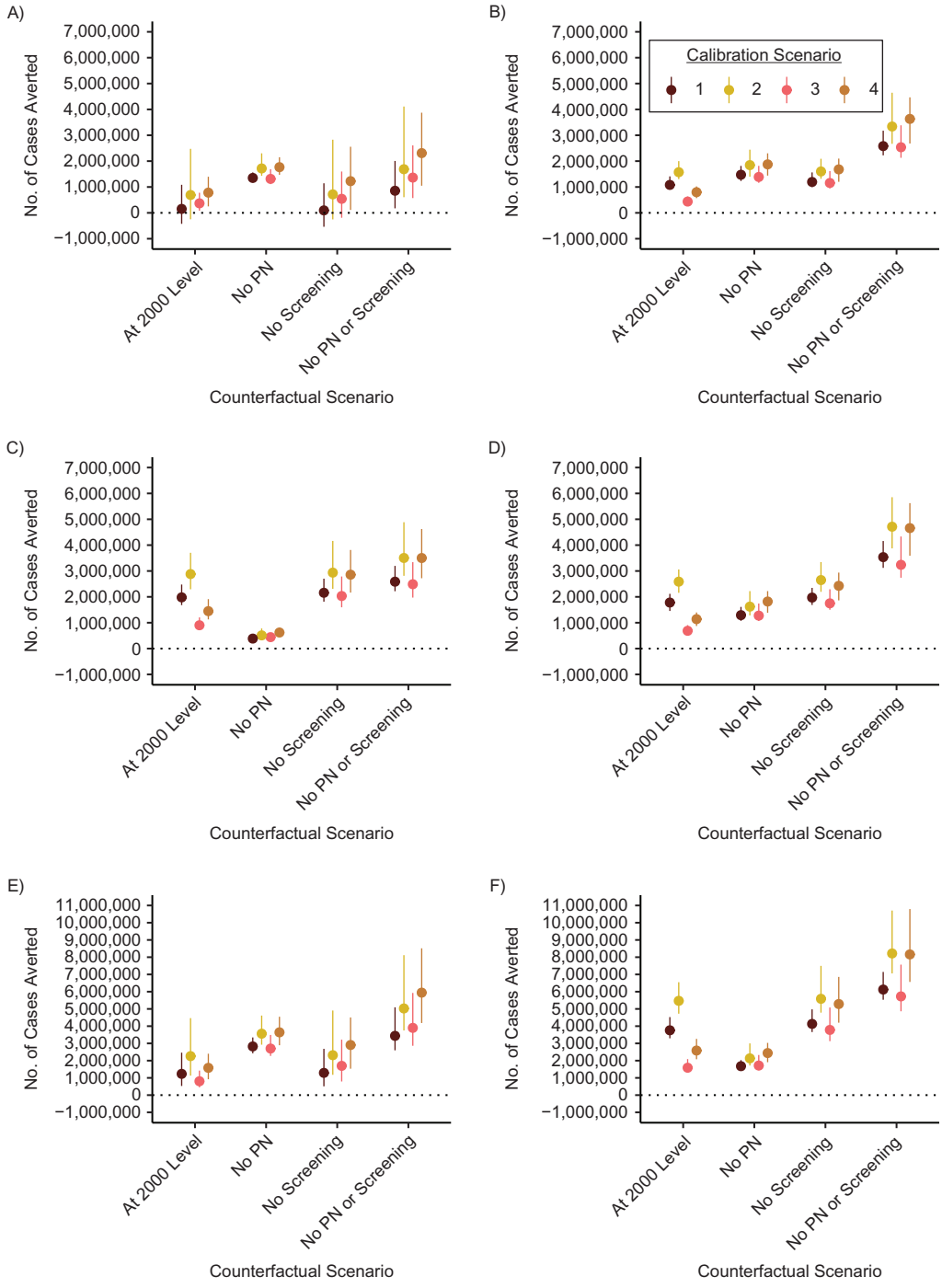

Figure 4. Model-estimated cumulative numbers of chlamydia cases averted (mean values (circles) and 95% credible intervals (bars)) in the United States during 2000–2015 when comparing 4 counterfactual scenarios with a calibrated model (current level). Results are presented for women aged 15–24 years (A), women aged 25–54 years (B), men aged 15–24 years (C), men aged 25–54 years (D), women aged 15–54 years (E), and men aged 15–54 years (F). Calibration scenario 1: more constrained priors on reporting and screening; calibration scenario 2: less constrained priors on reporting and more constrained priors on screening; calibration scenario 3: more constrained priors on reporting and less constrained priors on screening; calibration scenario 4: less constrained priors on reporting and screening. PN, partner notification.

has changed since 2000. The number of infections averted because of partner notification was estimated to be larger for women than for men (among persons aged 15–54 years, mean = 2.7–3.6 million infections averted for women and 1.7–2.4 million infections averted for men), which was due to rapid reinfection in long-term partnerships in the presence

of screening only, which the model structure enabled us to capture.

DISCUSSION

In this study, we first set out to reconcile observed chlamydia trends from national prevalence estimates and case reports. By including both prevalence estimates and case reports in our calibration, we gained a better understanding of the underlying epidemiology that would maintain fairly stable prevalence estimates at the same time as case report rates are increasing. This in turn allowed for more robust estimates of the impact of prevention efforts. We additionally calibrated the model to reported measures of sexual debut. Our model included the primary components thought to influence risk of chlamydia acquisition: age, sex, and sexual risk heterogeneity. It also included time-varying parameters for screening, test sensitivity, reporting of diagnosed cases, and sexual debut for the youngest age group. For time-varying parameters, we allowed for uncertainty in the level, direction, and shape of the change.

To our knowledge, this is the first modeling exercise that has calibrated a chlamydia transmission model to sex- and age-specific time series for case reports and prevalence at the national level. By combining multiple sources of epidemiologic data, we gained a better understanding of the overall epidemiologic trends. There may have been a modest decline in chlamydia prevalence that was not captured by national estimates as predicted by the mathematical model. The increasing case report rates are a complex phenomenon, which can be explained in a number of different ways.

We examined the role of case reporting and screening over time in 4 calibration scenarios, and we used the calibrated model to retrospectively estimate the potential impact of screening and partner notification in the United States. The counterfactual scenarios suggested that screening and partner notification reduced the burden of chlamydial infection during the years 2000–2015 by averting infections and reducing prevalence.

Our analyses further suggested that prevalence estimates are fairly robust against different a priori assumptions for reporting and screening. While all of the calibration scenarios estimated that partner notification and screening have reduced prevalence, the full impact of these prevention strategies was difficult to gather from prevalence alone. This was seen in the variation in model predictions across the different calibration scenarios for infections averted in Figure 3.

The modeling results suggested that the greatest impact in chlamydia prevention in the United States has come from combining screening with partner notification. This is in accordance with other chlamydia modeling, where the largest gains have been predicted to come from high screening coverage combined with partner notification (10). Partner notification and screening are inherently linked, although they can be analyzed independently. In the absence of screening, there are a number of index cases whose partners will not be reached, and in the absence of partner notification, there are a number of index cases who will be screened but whose ongoing sexual partners will remain untreated, putting the index case at risk of fast reinfection. However, in the absence of data on patterns of partner notification for chlamydia, there remains uncertainty about the benefits attributed to partner notification. Based on the data we have used for calibration, the model is unable to differentiate between pathways leading to chlamydia diagnosis (screening of index case vs. partner notification). Our model assumed that there was some screening in place before 2000. Prior models that investigated screening impact and assumed no or little baseline screening identified a larger impact of screening intervention (10, 30).

This study highlights the benefit of gathering multiple epidemiologic data when the epidemiologic trends can be explained in a number of ways. We chose country as the level of analysis; therefore, this analysis could not capture local-level variation but rather was intended to provide insight on the impact of chlamydia prevention efforts at the national level. Whereas population-representative laboratory-based measures of prevalence are available at the national level for multiple time points via the National Health and Nutrition Examination Survey, analogous data are not available at the subnational level. Furthermore, guidelines for chlamydia screening are made at the national level.

Despite the added benefits brought in by model calibration, our pair-formation model had a number of limitations. First, the model may underestimate the heterogeneity in chlamydia acquisition and transmission risk and therefore overestimate the impact of screening and partner notification: Although we incorporated initiation of sexual activity as one type of sexual behavior change, accounting for changes in the sexually active population at a crucial time point for acquisition risk, we did not account for possible increases in incidence due to other changes in sexual risk behavior, such as changes in sexual mixing patterns. Second, we did not model chlamydia transmission among nonheterosexual partnerships. There is no evidence to date to suggest that chlamydia transmission among men who have sex with men would substantially influence the heterosexual chlamydia epidemic. More research is needed on health-care–seeking behaviors among men who have sex with women and the impact that screening for this group might have on chlamydia in the United States. Third, we assumed that treatment ensued immediately following identification of chlamydial infection, although this may not always happen in practice (31, 32). If treatment delays contribute to a number of onward transmissions, this would not have been captured in this study. Fourth, our model does not include ethnicity or measures of urbanicity and therefore cannot account for these sources of heterogeneity in chlamydia epidemiology that exist regionally in the United States (33, 34). Instead, it offers an overview of chlamydia prevention across the country. Fifth, we assumed no immunity to chlamydial infection at a population level. There is an ongoing debate about the role of natural immunity for chlamydia and whether it is sufficient to protect people from repeat infections. There are limited data available with which to draw inferences on natural immunity, and the existing body of work on chlamydial immunity at the population level has relied on case report rates (35) or short-term reinfection patterns among patients (36). Given that repeat infections are observed, it is likely that any immunity garnered is partial (37). Increasing the complexity of the model to incorporate the above factors would require a study or data set that could differentiate natural immunity from other phenomena and measure its impact on risk of reinfection.

In this modeling study, we have shown that chlamydia prevention efforts may be having a population-level impact despite a lack of decline in reported numbers of chlamydia cases. The model results suggest that chlamydia prevalence in 2015 would be notably higher had there been no chlamydia screening and partner notification activities from 2000 to 2015. However, the magnitude of the impact of prevention efforts on the burden of chlamydia is difficult to quantify precisely in the absence of further data on chlamydial infection.

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