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Using infection prevalence, seroprevalence and case report data to estimate chlamydial infection incidence

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Abstract

Objectives—To measure the effectiveness of chlamydia control strategies, we must estimate infection incidence over time. Available data, including survey-based infection prevalence and case reports, have limitations as proxies for infection incidence. We therefore developed a novel method for estimating chlamydial incidence.

Methods—We linked a susceptible infectious mathematical model to serodynamics data from the National Health and Nutritional Examination Survey, as well as to annual case reports. We created four iterations of this model, varying assumptions about how the method of infection clearance (via treatment seeking, routine screening or natural clearance) relates to long-term seropositivity. Using these models, we estimated annual infection incidence for women aged 18–24 and 25–37 years in 2014. To assess model plausibility, we also estimated natural clearance for the same groups.

Results—Of the four models we analysed, the model that best explained the empirical data was the one in which longer-lasting infections, natural clearance and symptomatic infections

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Contributors PAC primarily built model, conducted analysis and wrote manuscript. IHS conceptualised project and gave input on model structure along with EDP. GEA, CMK, JH and DCD gave subject matter advice on chlamydia serology, lab testing methods and sampling statistics. CEC and GEA coordinated project. All authors contributed to editing the manuscript. PAC accepts full responsibility for the work and/or the conduct of the study, had access to the data, and controlled the decision to publish.

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all increased the probability of long-term seroconversion. Using this model, we estimated 5910 (quartile (Q)1, 5330; Q3, 6500) incident infections per 100 000 women aged 18–24 years and 2790 (Q1, 2500; Q3, 3090) incident infections per 100 000 women aged 25–37 years in 2014. Furthermore, we estimated that natural clearance rates increased with age.

Conclusions—Our method can be used to estimate the number of chlamydia infections each year, and thus whether infection incidence increases or decreases over time and after policy changes. Furthermore, our results suggest that clearance via medical intervention may lead to short-term or no seroconversion, and the duration of untreated chlamydial infection may vary with age, underlining the complexity of chlamydial infection dynamics.

INTRODUCTION

Chlamydia trachomatis infects more people in the USA than any other sexually transmitted bacterial pathogen, with >1.5 million cases annually reported since 2015.[1 2] Worryingly, chlamydial case report rates in the USA increased yearly from 2013 to 2019, suggesting that more women may be at risk of developing sequelae such as pelvic inflammatory disease and ectopic pregnancy over time. To assess the effectiveness of chlamydia control strategies, we must estimate national annual infection incidence (the number of individuals who contract chlamydia in a year).

Multiple approaches have been used previously to derive incidence estimates, varying in complexity and types of inputs (online supplemental table S1). First, case reports may be used as a direct proxy for incidence but miss many asymptomatic infections (eg, among those not covered by screening guidelines[3]) and infections in individuals without access to healthcare. Second, Satterwhite *et al*[4] estimated incidence by dividing the prevalence of positive nucleic acid amplification tests (NAAT) from the National Health and Nutrition Examination Survey (NHANES) by infection duration. However, infection duration is context-specific, depending on age, sex and access and utilisation of sexual health resources, and is particularly difficult to estimate for asymptomatic, untreated infections.[5 6] Third, Lewis and White[7 8] used the number of positive and negative NAAT across England to estimate infection prevalence and infection duration, putting them in a position to estimate incidence. Unfortunately, the number of negative tests is not reported along with case reports in the USA. Fourth, Ali *et al*[9] used a Bayesian decision tree model of infection and testing fit to Australian case report data and health insurance test rebates to estimate incidence. However, this model requires strong prior knowledge of the proportion of infections that are symptomatic and the proportion of infections that clear naturally. Both parameters rely on indirect estimates and likely vary between populations. Fifth, Woodhall *et al*[10] used serological surveys to estimate cumulative infection incidence, from which incidence rates can be derived. While this method can identify infections that were undiagnosed and thus previously absent from case data, it misses infections of individuals who do not seroconvert and reinfections of seropositive individuals. Finally, Kreisel *et al*[1] combined NAAT prevalence data from NHANES with case report data. NHANES tested asymptomatically infected individuals who otherwise would not have been tested, which the case report data missed. Likewise, the researchers did not have to estimate infection duration for reported cases, as these were assumed to occur in individuals who cleared their infection

via medical intervention. However, the method by Kreisel *et al* still requires estimates of infection duration for untreated individuals. We suggest that incorporating case reports, infection prevalence and serology data into incidence estimates will allow us to account for both diagnosed and undiagnosed infection while reducing the need to estimate difficult parameters.

To incorporate serology data into incidence estimates, we must understand the relationship between infection history and serostatus. Not all women seroconvert by the time they clear their infections.[11 12] Of women who seroconvert, not all maintain their seropositive status. Most women either serorevert within a few months, or they maintain their seropositive status for more than a decade.[13 14] If serostatus is a reliable signature of an active immune response, then one potential explanation for these patterns is the arrested immunity hypothesis, where the strength of the immune response of individuals postchlamydia is determined by whether individuals clear their infections medically (via antibiotics) or naturally.[15 16] However, no studies have mechanistically linked long-term serostatus to the method of recovery. Given this uncertainty, we consider multiple mechanisms for the development of long-term seropositivity so that serology data can inform incidence estimates.

In this manuscript, we develop methods for estimating infection incidence in women using a combination of infection prevalence, seroprevalence and case report data. We estimate incidence under various assumptions of how infection clearance relates to long-term serostatus. Finally, we compare our incidence estimates with case reports and examine estimates of the rate at which women clear infection with no medical intervention to assess the plausibility of these models.

METHODS

Our goal is to derive solutions for annual chlamydia incidence in women as a function of (a) infection prevalence and (b) seroprevalence data from NHANES,[17] (c) national case data reported to the CDC and (d) other observable parameters (eg, screening rate). Empirical data show that infected women generally do not seroconvert, seroconvert and then quickly serorevert or seroconvert and maintain their seropositive status for over a decade.[11 13 14 18] We assume in our model that women either do not seroconvert or develop long-lasting seropositivity (online supplemental appendix S6). We consider (1) a model where all women seroconvert after infection (all seroconversion model), (2) a model where women seroconvert after lengthy infections (long infection seroconversion model), (3) a model where women seroconvert if they clear their infection without medical intervention (natural clearance seroconversion model) and (4) a model where all clearance methods can lead to seroconversion, but the likelihood of seroconverting increases with infection duration, natural clearance or symptoms (mixed seroconversion model, table 1). Because to date NHANES specimens have not been tested for chlamydia serostatus in male-identified individuals (although we note that NHANES does not distinguish between male-identified individuals and individuals assigned male at birth), models presented here calculate infection incidence in women only.

See table 2 for parameter meanings and values for all models.

Models

All models begin with uninfected-seronegative women (U_0). These women acquire chlamydia at a rate, λ, and become asymptomatically infected (A) with a probability β, or become symptomatically infected (S) with a probability $1-\beta$. Infected women clear infections naturally at a rate ψ and clear infections due to routine screening at a rate σ. Symptomatic women additionally clear infections at a rate of treatment seeking, τ. Whether women return to the uninfected-seronegative state (U_0) or enter the uninfected-seropositive state (U_1) depends on the method of clearance (ψ, σ, τ), and symptom status (table 1). Uninfected-seropositive women can have decreased susceptibility to infection, and so become infected at a rate $\varepsilon\lambda$, where ε lies between 0 and 1. Seropositive women become symptomatic at the same probability as seronegative women when acquiring infection, although our model estimates do not change and we assume that seropositivity lowers the probability of symptom development (online supplemental appendix S5). Uninfected, seropositive women serorevert to U_0 at a rate ω. Population size increases at a rate γ. Finally, we introduce a variable R into equations, which prevents seropositive women from seroreverting due to clearing subsequent infections (online supplemental appendix S2). Model schematics are displayed in figure 1.

In the 'all seroconversion' model, all infections lead to seroconversion. Equations are given by:

$$\frac{dU_0}{dt} = -\lambda U_0 + \omega U_1 + \gamma\frac{U_0}{N} \tag{1}$$

$$\frac{dA}{dt} = \lambda\beta U_0 + \varepsilon\lambda\beta U_1 - (\psi+\sigma)A + \gamma\frac{A}{N} \tag{2}$$

$$\frac{dS}{dt} = \lambda(1-\beta)U_0 + \varepsilon\lambda(1-\beta)U_1 - (\psi+\sigma+\tau)S + \gamma\frac{S}{N} \tag{3}$$

$$\frac{dU_1}{dt} = -\varepsilon\lambda U_1 + (\psi+\sigma)A + (\psi+\sigma+\tau)S - \omega U_1 + \gamma\frac{U_1}{N} \tag{4}$$

$$N = U_0 + A + S + U_1 \tag{5}$$

In the ‘long infection seroconversion’ model, we assume that infections with long duration lead to seroconversion. We thus assume that naturally cleared infections lead to seroconversion as no intervention shortens their duration. We assume that infections cleared via treatment seeking do not lead to seroconversion as individuals are on average infected for <2 months before being treated for symptomatic chlamydia (table 2). Routine screenings likely generate both long and short infection durations, depending on when individuals are screened during their infection. However, average time between screenings is 2–3 times longer than the average duration of untreated chlamydia (table 2[1]), and therefore unlikely to catch chlamydia shortly after infection. For this reason, we assume that infections cleared due to routine screening are of long duration and lead to seroconversion. See the ‘mixed seroconversion’ model for testing of this assumption. Equations are given by:

$$\frac{dU_0}{dt} = -\lambda U_0 + (1-R)\tau S + \omega U_1 + \gamma\frac{U_0}{N} \tag{6}$$

$$\frac{dA}{dt} = \lambda\beta U_0 + \varepsilon\lambda\beta U_1 - (\psi+\sigma)A + \gamma\frac{A}{N} \tag{7}$$

$$\frac{dS}{dt} = \lambda(1-\beta)U_0 + \varepsilon\lambda(1-\beta)U_1 - (\psi+\sigma+\tau)S + \gamma\frac{S}{N} \tag{8}$$

$$\frac{dU_1}{dt} = -\varepsilon\lambda U_1 + (\psi+\sigma)(A+S) + R\tau S - \omega U_1 + \gamma\frac{U_1}{N} \tag{9}$$

$$R = \frac{\varepsilon U_1}{U_0 + \varepsilon U_1} \tag{10}$$

In the ‘natural clearance seroconversion’ model, we assume women who clear their infections via antibiotics do not seroconvert. Equations are given by:

$$\frac{dU_0}{dt} = -\lambda U_0 + (1-R)(\sigma(A+S)+\tau S) + \omega U_1 + \gamma\frac{U_0}{N} \tag{11}$$

$$\frac{dA}{dt} = \lambda\beta U_0 + \varepsilon\lambda\beta U_1 - (\psi+\sigma)A + \gamma\frac{A}{N}$$

(12)

$$\frac{dS}{dt} = \lambda(1-\beta)U_0 + \varepsilon\lambda(1-\beta)U_1 - (\psi+\sigma+\tau)S + \gamma\frac{S}{N}$$

(13)

$$\frac{dU_1}{dt} = -\varepsilon\lambda U_1 + (\psi)(A+S) + R(\sigma(A+S)+\tau S) - \omega U_1 + \gamma\frac{U_1}{N}$$

(14)

$$R = \frac{\varepsilon U_1}{U_0 + \varepsilon U_1}$$

(15)

In the ‘mixed seroconversion’ model, we assume the likelihood of seroconversion increases with duration of infection, clearing infections without antibiotics or symptomatic infections. This model thus allows for every clearance mechanism to generate some seropositive individuals and some seronegative individuals. Equations are given by:

$$\frac{dU_0}{dt} = \begin{aligned} &-\lambda U_0 + (1-R)((\psi(1-\chi_{A,\psi}) \\ &+\sigma(1-\chi_{A,\sigma}))A + (\psi(1-\chi_{S,\psi}) \\ &+\sigma(1-\chi_{S,\sigma}) + \tau(1-\chi_{S,\tau}))S) + \omega U_1 + \gamma\frac{U_0}{N} \end{aligned}$$

(16)

$$\frac{dA}{dt} = \lambda\beta U_0 + \varepsilon\lambda\beta U_1 - (\psi+\sigma)A + \gamma\frac{A}{N}$$

(17)

$$\frac{dS}{dt} = \lambda(1-\beta)U_0 + \varepsilon\lambda(1-\beta)U_1 - (\psi+\sigma+\tau)S + \gamma\frac{S}{N}$$

(18)

$$\frac{dU_1}{dt} = \begin{aligned} &-\varepsilon\lambda U_1 + R((\psi\chi_{A,\psi} + \sigma\chi_{A,\sigma})A \\ &+(\psi\chi_{S,\psi} + \sigma\chi_{S,\sigma} + \tau\chi_{S,\tau})S) - \omega U_1 + \gamma\frac{U_1}{N} \end{aligned}$$

(19)

$$R = \frac{\varepsilon U_1}{U_0 + \varepsilon U_1}$$

(20)

Where $\chi_{i,}$ represents the probability of seroconverting depending on symptomatic status i and method of clearance j (online supplemental appendix S3).

Connecting models to data

To help connect model dynamics to data, we introduce summary state variables in all models N represents the total population size, P represents infection prevalence, Q represents prevalence of seropositive and/or infected individuals and K represents case reports, given by the rate of diagnosis and subsequent medical clearance multiplied by the reporting percentage, ρ:

$$P = \frac{A + S}{N} \tag{21}$$

$$Q = \frac{A + S + U_1}{N} \tag{22}$$

$$K = \rho(\sigma A + (\sigma + \tau)S) \tag{23}$$

NHANES measures infection prevalence and for some years seroprevalence[17] across 2-year periods. We assume that the data in NHANES represent population summaries at the midpoint of each cycle. We then estimate annual infection incidence between the midpoints of sequential NHANES cycles.

We set P equal to the proportion of specimens in an NHANES cycle that are NAAT positive, and Q equal to the proportion of specimens in an NHANES cycle that are NAAT positive and/or have a positive Pgp3-MBA test. We set U_0 and U_1 equal to the proportion of women in NHANES who are uninfected and seronegative or seropositive, respectively, multiplied by census population size estimates, N. We set $A + S$ equal to the proportion of women in NHANES who are infected, multiplied by N. Rates of change for state variables $\left(\frac{dU_0}{dt}, \frac{dU_1}{dt}, \frac{d(A+S)}{dt}\right)$ are then set as the change in the number of individuals in NHANES categories between cycle midpoints (online supplemental appendix S4).

The change in population size (γ) is set to the change in the weighted number of individuals in a cohort between NHANES cycles. Finally, we set K equal to the number of annually reported chlamydia cases.

Solutions for incidence

For each model, we simultaneously solved for infection incidence (λ), natural clearance rate (ψ), proportion of infections without symptoms (β), the number of individuals in each infection category (U_0, A, S, U_1) and the proportion of infections coming from seropositive individuals (R), as a function of all other parameters and state variables, using the SymPy package in Python. If λ is a yearly rate, annual infection incidence for a given year is then given by substituting the solution for λ into

$$\lambda(U_0 + \varepsilon U_1) \tag{24}$$

We were also able to find solutions for the natural clearance rate (ψ). We use our model to estimate infection incidence in 2014, for illustrative purposes using publicly available data. We then examine the plausibility of the estimates of each model by comparing them with case reports, and by examining the natural clearance rate that accompanies each incidence estimate. See online supplemental appendix S5 for all solutions.

RESULTS

Incidence estimates

Our ‘natural clearance seroconversion’ model estimates the most incident infections for women aged 18–24 years, while our ‘mixed seroconversion’ model estimates the most incident infections for women aged 25–37 years. Our ‘all seroconversion’ model estimates the fewest incident infections for both age groups (figure 2A,B). All models estimate that women aged 18–25 years have more incident infections per capita than women aged 25–37 years. At $\varepsilon = 1$ (ie, when seropositivity does not confer protection from reinfection) our ‘all seroconversion’ model estimates incidence rates (per 100,000) of 1,850 (quartile (Q)1, 1,700; Q3, 1,990) for those aged 18–24 years and 1,440 (Q1, 1,320; Q3, 1,550) for those aged 25–37 years. Our ‘long infection seroconversion’ model estimates incidence rates of 4,190 (Q1, 3,790; Q3, 4,600) for those aged 18–24 years and 2,170 (Q1, 2,020; Q3, 2,310) for those aged 25–37 years. Our ‘natural clearance seroconversion’ model estimates incidence rates of 5,900 (Q1, 5,760; Q3, 6,050) for those aged 18–24 years and 2,380 (Q1, 2,270; Q3, 2,500) for those aged 25–37 years. Finally, our ‘mixed seroconversion’ model estimates incidence rates of 5,430 (Q1, 4,990; Q3, 5,870) for those aged 18–24 years and 2,510 (Q1, 2,310; Q3, 2,700) for those aged 25–37 years.

Decreasing the susceptibility of seropositive women relative to seronegative women decreased the estimated infections for all models. For all models except the ‘mixed seroconversion’ model, as ε decreased from 1 to 0, annual incidence linearly decreased by 455 infections per 100 000 women aged 18–24 years, and linearly decreased by 437 infections per 100 000 women aged 25–37 years. For the ‘mixed seroconversion’ model as ε decreased from 1 to 0, estimated annual incidence linearly decreased by 641 infections per 100 000 women aged 18–24 years, and linearly decreased by 595 infections per 100 000 women aged 25–37 years (figure 2A,B).

Model plausibility

We find that our ‘natural clearance seroconversion’ and ‘mixed seroconversion’ models give plausible estimates of incidence relative to case report data (figure 2A,B). The number of chlamydia cases reported to the Nationally Notifiable Disease Surveillance System was 3,800 per 100,000 women aged 18–24 years in 2014; since not all incident cases are diagnosed and false positives are low, this number should represent the minimum number of incident infections, with the actual number of incident infections being higher. However, estimated infections are equal to or lower than reported cases for our ‘long infection seroconversion’ model and our ‘all seroconversion’ model, indicating that these model incidence estimates are implausibly low.

In addition to solving for incidence (λ), we also solved for the natural clearance rate (ψ) (see online supplemental appendix S7 and S8 for solutions). We find that our ‘all seroconversion’ model estimates negative clearance rates, and thus we have additional evidence that estimates from this model are implausible. For our models with plausible clearance rate estimates, models estimate that women aged 25–37 years have a higher clearance rate than women aged 18–24 years (figure 2C,D).

DISCUSSION

In this manuscript, we join serology and infection data to develop an improved method of estimating annual chlamydial infection incidence that relies on fewer data-free inputs than previous methods. We analysed four models, two of which gave plausible incidence estimates. These methods estimate lower infection incidence for women aged 18–24 years, and higher infection incidence for women aged 25–37 years than prior methods that incorporate case reports and NHANES NAAT prevalence, but not serology.[1] Furthermore, we estimate that women aged 25–37 years take a shorter time to clear infections naturally than do women aged 18–24 years, possibly due to an increase in the lifetime number of chlamydia exposures with age, and the subsequent priming of the immune system. Ultimately, we recommend using the methods developed here for future chlamydia incidence estimates for women, especially if future studies can extend longitudinal studies of postinfection serostatus or can test the relationship between serostatus and susceptibility to reinfection.

Our ‘mixed seroconversion’ model is the best model for estimating chlamydia incidence. Only it and our ‘natural clearance seroconversion’ model make plausible estimates, defined as infection incidence estimates with IQRs greater than case reports, and positive clearance rate estimates. Our ‘natural clearance seroconversion’ model gives plausible incidence and clearance estimates but violates more empirical observations. This model assumes that individuals who clear their infections medically do not seroconvert. However, individuals who tested positive for chlamydia in clinical settings, indicating that they likely cleared their infection via medical intervention, can show long-term seropositivity.[13] In contrast, the assumptions in our ‘mixed seroconversion’ model, that likelihood of long-term seroconversion increases with duration of infection, natural clearance and symptoms are supported by empirical evidence. Specifically, infected individuals with multiple blood samples taken over a year, indicating frequent testing and thus short infection duration,[11]

have a lower seropositive prevalence than infected individuals in a cross-sectional non-clinical setting, who likely had been infected for a longer period.[12] While not a controlled comparison, these data indicate that infection duration may play a role in long-term seropositivity. Furthermore, women who naturally clear their infection have a lower likelihood of reinfection than women who clear their infection via medical intervention.[15 16] If this decreased susceptibility is due to an active immune response, and seropositive status is an indicator of immune activity, then this indicates that natural clearance will lead to seroconversion. Finally, many symptoms of bacterial infection are a sign of an active immune response,[19] and thus symptoms might accompany seroconversion.

We estimate that natural clearance is faster in the older age group. Older women have had more time to contract chlamydial infection than younger women. Repeat chlamydial infections increase the chance of women developing long-term seropositive status,[11 13] suggesting that repeated chlamydial infections generate a strong immune response, leading to more rapid clearance. An alternate hypothesis is that women physiologically change as they age in ways that reduce the severity of chlamydial infection.[20] Regardless of the mechanism, our models suggest that there are differences in how chlamydia is cleared in different age groups. We are unable to compare the consistency of this finding with prior work, as prior studies measuring natural chlamydia clearance rates have either not reported the impact of age on clearance rates,[21–26] or have enrolled too few individuals over the age of 25 years to measure the impact of age on clearance rates.[27] However, we note that our natural clearance rate estimates for younger women (~1 year) are comparable to clearance rate estimates from bootstrapping the data from these prior studies.[1]

Our ‘mixed seroconversion’ model predicts lower infection incidence for women aged 18–24 years than do methods developed by Kreisel *et al*, and higher incidence for women aged 24–39 years. These differences come about because of differing assumptions about steady state dynamics, and different sources for natural clearance rates. Kreisel *et al* calculates infection incidence as case reports plus prevalent infections multiplied by the natural clearance rate. This assumes that the number of women infected with chlamydia is steady over time. Furthermore, Kreisel *et al* estimates the natural clearance rate by bootstrapping observational data from prior studies. This generates an estimate of approximately 13 months until clearance; an estimate that is longer than our estimate for women aged 25–37 years. We find that if we assume steady state dynamics in our model, solve for incidence and clearance and then use our estimates of the natural clearance rate to calculate incidence using the method derived by Kreisel *et al*, then the estimated incidence of the two approaches agree with one another. This indicates that the methods used here can be used in conjunction with those developed by Kreisel *et al* to further constrain parameters for both models.

Ultimately, by employing more data sources than prior studies, we offer a robust method for estimating chlamydia incidence without relying on data-hungry time series analysis. Future research can apply the methods developed in this paper to measure trends in US chlamydia incidence over time, as long as NHANES or other data sources continue to publish paired cross-sectional NAAT and serology data. However, the true test of whether this is a superior estimation method compared with prior methods would be to compare various model

estimates of chlamydia incidence to direct measurements of chlamydia incidence. These direct measurements could be collected by intensive longitudinal NAAT sampling of study cohorts.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Data availability statement

No data are available. All data used in this publication are publicly available from the National Health and Nutrition Examination Survey, the National Survey of Family Growth, CDC STI surveillance reports and US census data.[28–31]

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WHAT IS ALREADY KNOWN ON THIS TOPIC

- The first step in understanding chlamydia dynamics is estimating chlamydia incidence.
- Available data, including survey-based infection prevalence and case reports, have limitations as proxies for infection incidence.

WHAT THIS STUDY ADDS

- By using both nucleic acid amplification test and serology data, we have developed an improved method for estimating chlamydia incidence.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

- By improving our ability to estimate changes in chlamydia incidence over time, this method improves our ability to measure the impact of chlamydia control strategies.

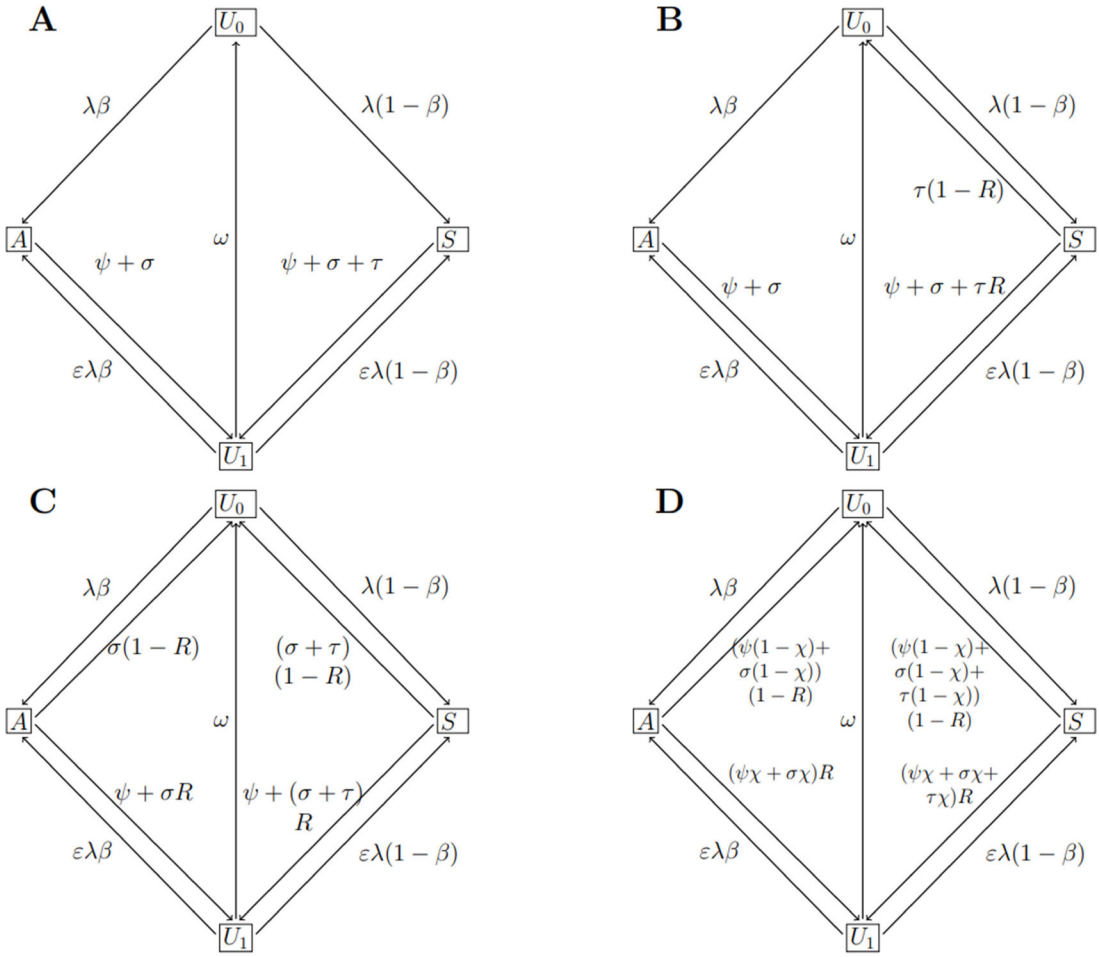

Figure 1.

Schematics of four models used to estimate chlamydia incidence in women under different assumptions about seroconversion: (A) all seroconversion model, (B) long infection seroconversion model, (C) natural clearance seroconversion model, (D) mixed seroconversion model. At any given time, women can be uninfected-seronegative (U_0), asymptomatically infected (A), symptomatically infected (S) or uninfected-seropositive (U_1). Note that for (D) values of χ differ depending on whether it is applied to symptomatic or asymptomatic infections and which mode of clearance it is attached to. See table 1 for a description of the parameters and see the text and online supplemental appendix for model details.

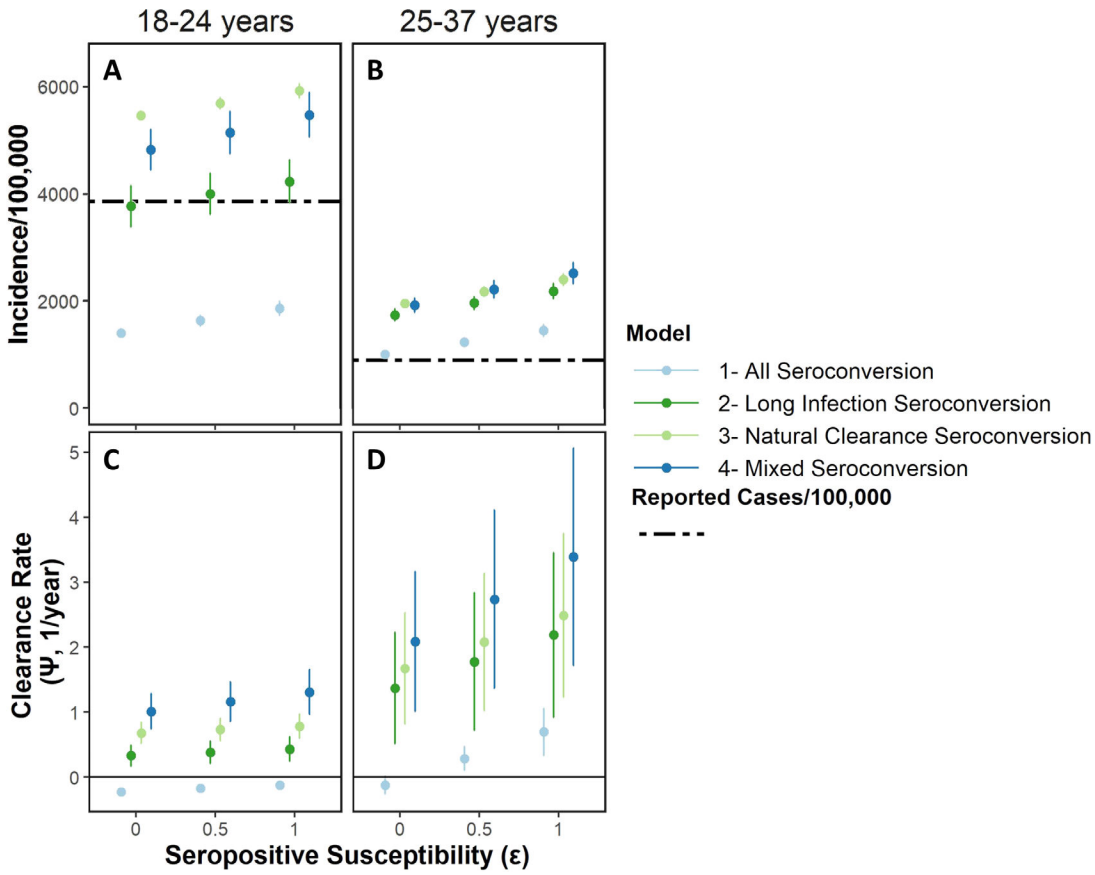

Figure 2.

Y-axis shows (A, B) incidence estimates per 100 000 women in 2014, (C, D) estimates of natural clearance rates for women in 2014 and x-axis shows relative susceptibility of seropositive women compared with seronegative women (ε). High values of ε indicate that seropositive and seronegative women are equally susceptible to infection, while low values of ε indicate that seropositive women are less susceptible than seronegative women. Left panel shows incidence for women aged 18–24 years, while right panel shows incidence for women aged 25–37 years. Points show mean estimates, with vertical lines showing IQRs. The black dashed line in panels A and B indicate case reports per 100 000 women. When $\varepsilon = 1$, models differ in incidence estimates because models differ in the proportion of infected individuals that become seropositive. Thus, models must invoke various incidence estimates to generate a proportion of the population that is seropositive that matches the proportion in the National Health and Nutrition Examination Survey.

Table 1

Difference in assumptions between models

Model	Natural clearance (A)	Natural clearance (S)	Screening (A)	Screening (S)	Treatment seeking (S)
All seroconversion	1.0	1.0	1.0	1.0	1.0
Long infection seroconversion	1.0	1.0	1.0	1.0	0.0
Natural clearance seroconversion	1.0	1.0	0.0	0.0	0.0
Mixed seroconversion	(0.6, 0.8)	(0.8, 1.0)	(0.4, 0.6)	(0.6, 0.8)	(0.0, 0.4)

For each model, table indicates the proportion, or range of proportions, of individuals who develop long-term seropositive serostatus based on method of clearance and symptom status.

A, asymptomatic infection; S, symptomatic infection.

Table 2

Parameters in models used to estimate chlamydia incidence: descriptions, mean values and sources

Parameter	Meaning	Mean value	Source
U_0	Uninfected, seronegative	State variable	NHANES, ACS
A	Asymptomatically infected	State variable	NA
S	Symptomatically infected	State variable	NA
$S + A$	Total infected	State variable	NHANES, ACS
U_1	Uninfected, seropositive	State variable	NHANES, ACS
N	Population size	State variable	Census
P	Prevalence of those infected	State variable	NHANES
Q	Prevalence of those who are infected and/or seropositive	State variable	NHANES
K	Annual case reports	State variable	CDC
λ	Infection rate	Model output * (1/year)	Estimated
β	Proportion asymptomatic	Removed from solution †	Estimated
ψ	Natural clearance rate	Model output * (1/year)	Estimated
σ	Screening rate	0.354/year (aged 18–24 years) 0.301/year (aged 25–37 years)	NSFG
T	Symptomatic treatment rate	1/49.4 days	Kreisel *et al*[1]
ω	Seroreversion rate	1/30 years	Max value from Horner *et al*,[14] sensitivity explored in online supplemental appendix S9
ε	Proportional susceptibility due to seropositive status	(0, 1)	NA
γ	Change in population size	Time varying (1/year)‡	NHANES
$\chi_{A,\psi}$	Probability seroconversion after natural clearance of asymptomatic individuals	(0.6, 0.8)	Horner *et al*[14] paired with assumptions based on expert opinion
$\chi_{S,\psi}$	Probability seroconversion after natural clearance of symptomatic individuals	(0.8, 1.0)	
$\chi_{A,\sigma}$	Probability seroconversion after screening of asymptomatic individuals	(0.4, 0.6)	
$\chi_{S,\sigma}$	Probability seroconversion after screening of symptomatic individuals	(0.6, 0.8)	
$\chi_{S,\sigma}$	Probability seroconversion after symptomatic treatment seeking	(0.0, 0.4)	

*These variables are the output for the solved system of equations.

†In solving the system of equations, we removed β from the solutions for incidence and clearance rates, and thus do not need a value of β for this analysis.

‡Varies annually based on immigration, emigration, birth and death rates.

ACS, American Community Survey; CDC, Centers for Disease Control and Prevention; NA, not applicable; NHANES, National Health and Nutrition Examination Survey; NSFG, National Survey of Family Growth.