

Coverage Is the Key for Effective Screening of *Chlamydia trachomatis* in Australia

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Background. The rate of diagnosis of *Chlamydia trachomatis* (chlamydia) infection has risen dramatically in Australia. In response, the Australian government is planning to implement systematic screening and testing. Several decisions must be made, including whom to screen.

Methods. To inform decisions surrounding screening, a dynamic transmission model of the chlamydia epidemic was developed and parameterized with Australian sexual behavior and epidemiology data. A range of screening strategies and coverage rates were evaluated targeting various groups based on age and sex. Rigorous uncertainty and sensitivity analyses were undertaken.

Results. The model predicts that even moderate screening coverage in young adults (<25 years old) will reduce prevalence rapidly. The absolute numbers of people screened, rather than the sex targeted, is the key determinant in reducing prevalence. Sensitivity analysis determined that chlamydia transmission is strongly related to 2 biological parameters (the proportion of infections that are asymptomatic in women and the duration of infection in men) and 2 behavioral parameters (the frequency of sex acts for 20–24-year-olds and the level of condom usage).

Conclusions. The model predicts that routine annual screening can significantly reduce the prevalence of chlamydia within 10 years, provided that adequate screening coverage is achieved. The most effective screening strategies will be those that target 20–24-year-olds.

Infection with *Chlamydia trachomatis* (chlamydia) is a significant health problem in Australia. The notification rate has increased ~5-fold in recent years, from 47.4 notifications per 100,000 population in 1997 to 247.1 per 100,000 in 2007 (in total, there were 51,935 notifications in 2007) [1]. Australian data show that young women aged 15–24 years bear the greatest burden of chlamydia infection, with more than two-thirds of notifications for women occurring in this age group. The prevalence of chlamydia infection is also highest among young women [2]. The number of notifications among men has also been steadily increasing each year [1]. The rise in notifications is of concern because chlamydia in-

fection can cause significant morbidity, particularly in women; up to two-thirds of cases of tubal infertility and one-third of cases of ectopic pregnancy may be directly attributable to chlamydia infection [3].

Because up to 80% of chlamydia infections are asymptomatic [3], screening is the only effective way to detect the majority of cases and to provide treatment. Noninvasive testing (first-pass urine samples) and highly effective single-dose antibiotic treatment now make widespread screening feasible [3, 4]. Screening programs for chlamydia are being adopted in many parts of the developed world. Scandinavian countries have had them in place for some years [5–7], and, more recently, the United Kingdom has implemented a chlamydia screening program targeting women and men aged 16–24 years [8].

The Australian government has recently announced plans for a chlamydia screening pilot program in Australia [9]. It is anticipated that screening will be offered opportunistically through general practice clinics and other primary care clinics. The primary aim of screening is to detect and treat infected individuals to reduce the morbidity of sequelae in infected females. A secondary but important aim is to reduce the number of incident

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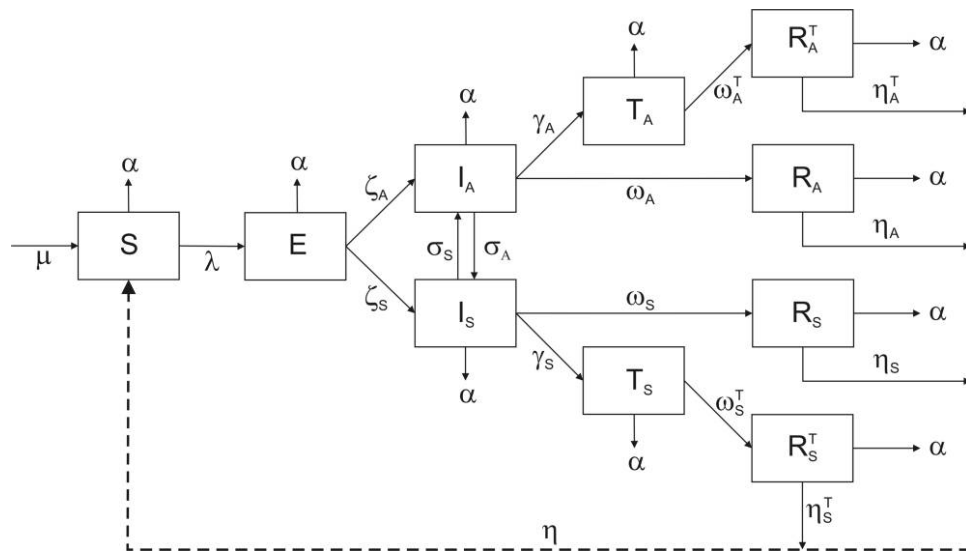


Figure 1. Schematic diagram of the structure of the model. The boxes represent the various disease states, and the arrows (and accompanying variables, which are defined in Appendix A) represent the rates of flow between the states. The model states are as follows: susceptible to infection (S), newly infected but not infectious (E), infected/infectious with asymptomatic (I_A) or symptomatic (I_S) infection, individuals receiving treatment (T_A and T_S), and individuals who have recovered and are temporarily immune from infection (R_A^T , R_A , R_S , and R_S^T).

cases and the overall prevalence of infection in the population. Before the development of a chlamydia screening program in Australia, several decisions must be made regarding the target groups (age and sex) and the frequency of screening. Mathematical models of chlamydia transmission, parameterized with Australian data, will help to inform these decisions. In the present study, we develop an age-structured heterosexual transmission model for the spread of chlamydia infection in Australia and, in conjunction with uncertainty and sensitivity analyses, use the model to assess the impact of different screening and treatment scenarios on age-dependent chlamydia incidence and prevalence. A wide range of coverage rates (from 20% to 80% per year) and age- and sex-specific strategies are evaluated. The primary research aims of this study are (1) to establish predictions for comparison of the impact of numerous screening strategies on reducing the incidence and prevalence of chlamydia infection and (2) to identify the most important factors contributing to the transmission and reduction of infection.

METHODS

Model formulation. A compartmental model was developed to simulate the transmission dynamics of the chlamydia epidemic in the Australian heterosexual population. It was formulated as a system of ordinary differential equations describing the change in the numbers of people in different disease and treatment states. Figure 1 illustrates the structure of the model schematically, and a full mathematical description is given in Appendix A, which appears only in the electronic edition of the *Journal*. An SEIR (susceptible, exposed, infectious, removed/immune)

framework [10–12] was adopted with the addition of treatment (T) states to capture screening and treatment. The model allows for symptomatic (I_S) or asymptomatic (I_A) infection and for the progression from these infected states to the treated and recovery states to occur independently. The model stratifies the population by sex and age. The male and female populations are assumed to be of equal size. Selection of new sex partners is assumed to commence at age 15 and to cease at age 50; within this range, the population ages through seven 5-year age bands. Sexual behavior, including age- and sex-specific rates of partner acquisition and numbers of sex acts per partnership, is captured in the model using data from the most recent and comprehensive survey of sexual behavior conducted in Australia [13]. The size of the population is assumed to not change over the time span simulated (10 years from the initiation of systematic screening). This is a reasonable assumption, given the short time frame and that mortality is not associated with chlamydia infection. A complete listing of model parameters, definitions, and ranges is presented in table 1.

In this model, it is assumed that treatment is always administered if infection is detected through screening and that the test sensitivity is 80%–90% [24]. We assume that people with symptomatic infection seek health care and are treated within 1–2 weeks after the onset of symptoms (table 1) [16, 26], whereas those with asymptomatic infection (70%–80% of infections [3, 18–20]) receive treatment only through opportunistic (e.g., when visiting a general practitioner for other reasons) or systematic screening. Little has been published about naturally acquired immunity after chlamydia infection. It is hypothesized that antibiotic treatment of chlamydia infection would reduce

the duration of natural acquired immunity after infection [27]. We assume the existence of short-term immunity after natural recovery from infection (1–2 months) and that treated individuals have shorter immunity (2–4 weeks). Our model is structured to accommodate different rates of recovery and immunity for symptomatic and asymptomatic infections, but, in the absence of data, we assume that these rates are the same for both types of infections.

The Australian National Sexually Transmissible Infections Strategy specifies that young adults are a priority target for chlamydia control [28]. On this basis, a wide range of potential screening strategies were simulated for evaluation, including targeting those <30 years old, those <25 years old, those <20 years old, those 15–19 years old, those 20–24 years old, and those 25–29 years old. Screening coverage was varied between 20% and 80% (in 10% increments) and was targeted at either females and males at equal coverage, females and males at 4:1 coverage, females only, or males only. For each of these target age groups and coverage levels, we performed 10,000 model simulations over the range of parameter values. That is, we performed a total of 1,960,000 model simulations—7 coverage rates times 4 sex targets times 7 age bands times 10,000 parameter sets. For each simulation, initial conditions were derived from the steady-state solution of the model before the introduction of screening, and then the model was run for 10 years with the implementation of the specific screening strategy.

Uncertainty, sensitivity, and statistical analysis. The model was parameterized to reflect the demography of Australia and the known sexual mixing patterns and was calibrated to obtain age-specific prevalence estimates consistent with published data (figure 2) [2, 29]. Uncertainty analysis was performed by defining a probability distribution for each input parameter (table 1), on the basis of published clinical and epidemiological studies. The distributions were then sampled 10,000 times (using Latin hypercube sampling [30]) for each screening strategy under investigation. For a given screening strategy, a simulation involved iterating over each parameter set to calculate the time-dependent prevalence over 10 years for each set. The main outcome variable of interest was the overall percent reduction in prevalence after 10 years of screening.

The variability in the input parameters generated distributions in the outcomes. Sensitivity analyses were performed by calculating partial rank correlation coefficients (PRCCs) [30] and using response hypersurface methodologies to clearly demonstrate and rank the importance of the biological and behavioral parameters in reducing prevalence. Because the overall population prevalence of chlamydia in Australia is relatively low (~2%), it was found that some parameter sets did not give rise to steady-state endemic equilibria—that is, an epidemic could not be sustained under these conditions. These ($n = 1245/10,000$) were removed by Monte Carlo filtering [31, 32] before implementing screening on the remaining ($n = 8755$) parameter sets. However, before removal this information was used in logistic

regression analysis to determine which parameters were the most influential in contributing to the establishment of epidemics (table 2).

RESULTS

Systematic screening for chlamydia infection and treating infected individuals could result in a considerable reduction in prevalence among women in Australia (figures 2 and 3). The model predicts that if 40% of men and women under the age of 25 years are screened annually, the prevalence of chlamydia infection will decrease rapidly over 10 years in all age groups, with >50% of the reduction being achieved during the first 4 years (figure 2). Under this strategy, prevalence continues to decline after 10 years of screening, and the general age-specific prevalence profile is maintained. The modeled prevalence is lower in males than females in the younger age groups but is higher in the older age groups, which mirrors Australian data [33]. Although prevalence levels can be substantially reduced, the degree of reduction is dependent on the level of coverage (figure 3A). Our results provide estimates of the reductions attainable under a wide variety of screening strategies. For example, a 50% reduction in the overall prevalence of chlamydia infection in the population within 10 years can be achieved by various means: annually screening ~80% of females <20 years old, 30% of females <25 years old, 20%–30% of females <30 years old, 60% of males and females <20 years old, 20% of males and females <25 years old, or <20% of males and females <30 years old (figure 3A). The percent reduction in prevalence increases approximately linearly with coverage, until the reduction saturates at very high coverage rates (figure 3A). However, the reduction in prevalence does not increase linearly with the age groups targeted for screening. The increase in the reduction in prevalence attained by screening those <25 years old relative to screening only those <20 years old is considerably greater than that attained by screening those <30 years old (figure 3A). This is further elucidated in figure 3B, where we present the reduction in prevalence due to screening targeted specifically at the 5-year age groups 15–19 years old, 20–24 years old, or 25–29 years old. Here, targeting 20–24-year-olds has a much greater (~2-fold) impact on prevalence than targeting 15–19-year-olds or 25–29-year-olds. Targeting 15–19-year-olds is slightly more effective at reducing prevalence than targeting 25–29-year-olds. The relative importance and impact of targeting these age groups is directly reflected by the current age-specific prevalence profile of chlamydia infection in Australia [2, 29, 34]. Because prevalence is greatest in 20–24-year-olds (figure 2), the overall prevalence can be reduced most effectively by screening and treating this age group (figure 3A and 3B). Additional results, including reduction in prevalence in males, male-only screening, and differential sex-targeted screening, are presented in Appendix A. We found that targeting only men for screening and treatment yields ap-

Table 1. Parameters, definitions, ranges, and sources for the association between sexual behavior and the chlamydia epidemic in Australia.

Parameter	Description	Range ^a	Source																																																																
P_f	Proportion of the entire population who are female	50% (age 15–49 years)	[14]																																																																
$P_{m,gsy}$	Proportion of the male population who are homosexual	1.5% (age 15–49 years)	[13]																																																																
Risk group definitions	Average no. of new partners per year for 4 risk groups	$R_1 = 0, R_2 = 1.5, R_3 = 4, R_4 = 8$	[13]																																																																
Risk group allocation	Proportion of females in each age group who are in each risk group	<table border="1"> <thead> <tr> <th></th> <th>A1</th> <th>A2</th> <th>A3</th> <th>A4</th> <th>A5</th> <th>A6</th> <th>A7</th> </tr> </thead> <tbody> <tr> <td>R1</td> <td>30%–32%</td> <td>33%–35%</td> <td>26%–28%</td> <td>100% – (R2 + R3 + R4)</td> <td>18%–20%</td> <td>14%–16%</td> <td>10%–12%</td> </tr> <tr> <td>R2</td> <td>20%–22%</td> <td>23%–25%</td> <td>18%–20%</td> <td>23%–25%</td> <td>10%–12%</td> <td>9%–10%</td> <td>6%–7%</td> </tr> <tr> <td>R3</td> <td>14%–16%</td> <td>16%–18%</td> <td>12%–14%</td> <td>10%–12%</td> <td>7%–8%</td> <td>5%–6%</td> <td>4%–5%</td> </tr> <tr> <td>R4</td> <td>55.1%</td> <td>33.4%</td> <td>6.5%</td> <td>2.0%</td> <td>0.1%</td> <td>0.1%</td> <td>0.1%</td> </tr> </tbody> </table>		A1	A2	A3	A4	A5	A6	A7	R1	30%–32%	33%–35%	26%–28%	100% – (R2 + R3 + R4)	18%–20%	14%–16%	10%–12%	R2	20%–22%	23%–25%	18%–20%	23%–25%	10%–12%	9%–10%	6%–7%	R3	14%–16%	16%–18%	12%–14%	10%–12%	7%–8%	5%–6%	4%–5%	R4	55.1%	33.4%	6.5%	2.0%	0.1%	0.1%	0.1%	[13]																								
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Sexual mixing matrix	Proportion of female partnerships (for females in a given age group (rows)) with males of each age group (columns)	<table border="1"> <thead> <tr> <th></th> <th>A1</th> <th>A2</th> <th>A3</th> <th>A4</th> <th>A5</th> <th>A6</th> <th>A7</th> </tr> </thead> <tbody> <tr> <td>A1</td> <td>2.5%</td> <td>56.5%</td> <td>32.8%</td> <td>7.8%</td> <td>0.2%</td> <td>0.1%</td> <td>0.1%</td> </tr> <tr> <td>A2</td> <td>0.9%</td> <td>8.6%</td> <td>45.5%</td> <td>35.1%</td> <td>6.7%</td> <td>1.6%</td> <td>1.6%</td> </tr> <tr> <td>A3</td> <td>0.3%</td> <td>1.2%</td> <td>12.7%</td> <td>40.7%</td> <td>25.3%</td> <td>9.9%</td> <td>9.9%</td> </tr> <tr> <td>A4</td> <td>0.1%</td> <td>0.3%</td> <td>1.6%</td> <td>12.0%</td> <td>33.6%</td> <td>26.2%</td> <td>26.2%</td> </tr> <tr> <td>A5</td> <td>0.1%</td> <td>0.3%</td> <td>0.8%</td> <td>2.8%</td> <td>10.6%</td> <td>42.7%</td> <td>42.7%</td> </tr> <tr> <td>A6</td> <td>0.1%</td> <td>0.3%</td> <td>0.8%</td> <td>2.8%</td> <td>10.6%</td> <td>42.7%</td> <td>42.7%</td> </tr> <tr> <td>A7</td> <td>80–120</td> <td>80–120</td> <td>60–100</td> <td>50–90</td> <td>30–80</td> <td>20–60</td> <td>20–50</td> </tr> </tbody> </table>		A1	A2	A3	A4	A5	A6	A7	A1	2.5%	56.5%	32.8%	7.8%	0.2%	0.1%	0.1%	A2	0.9%	8.6%	45.5%	35.1%	6.7%	1.6%	1.6%	A3	0.3%	1.2%	12.7%	40.7%	25.3%	9.9%	9.9%	A4	0.1%	0.3%	1.6%	12.0%	33.6%	26.2%	26.2%	A5	0.1%	0.3%	0.8%	2.8%	10.6%	42.7%	42.7%	A6	0.1%	0.3%	0.8%	2.8%	10.6%	42.7%	42.7%	A7	80–120	80–120	60–100	50–90	30–80	20–60	20–50	[13]
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A7	20–50	20–50	20–50	20–50	20–50	20–50	20–50																																																												
β	Transmission probability per act	0.0165–0.17	[15]																																																																
ε	Efficacy of condoms	0.85–0.95	...																																																																
ϕ	Proportion of acts in which condoms are used	5%–15%	[13]																																																																
τ	Duration of latency	F: 0–28 days M: 0–28 days	[16, 17]																																																																
div_A	Proportion of infected individuals who remain asymptomatic	F: 70%–80% M: 70% – div_A	[3, 18–20]																																																																
div_S	Proportion of infected individuals who become symptomatic	100% – div_A	...																																																																

ω_A	Average total time for individuals with asymptomatic infection to recover in the absence of treatment	F: 44–52 weeks M: 44–52 weeks	[21, 22]																								
ω_S	Average total time for individuals with symptomatic infection to recover in the absence of treatment	F: 44–52 weeks M: 44–52 weeks	Assumed to be the same as for asymptomatic infection																								
ω_A^I	Average time for individuals with asymptomatic infection to clear infection from the start of treatment	F: 5–9 days M: 5–9 days	[23]																								
ω_S^I	Average time for individuals with symptomatic infection to clear infection from the start of treatment	F: 5–9 days M: 5–9 days	[23]																								
ρ	Reduction factor in transmission due to treatment during dosing course	0.7–0.75	Assumption																								
ζ	Proportion of people who abstain from sex during treatment period	80%–90%	Assumption																								
imm_N	No. of days immune after natural infection	30–60 days	Assumption																								
imm_T	No. of days immune for individuals who clear infection due to treatment	0–0.5 × imm_N days	Assumption																								
θ	Test sensitivity (proportion of infected who test positive)	80%–90%	[24]																								
κ_{pre}^A	Proportion of asymptomatic individuals screened each year before screening intervention	<table border="1"> <thead> <tr> <th></th> <th>A1</th> <th>A2</th> <th>A3</th> <th>A4</th> <th>A5</th> <th>A6</th> <th>A7</th> </tr> </thead> <tbody> <tr> <td>F</td> <td>4%–5%</td> <td>3.5%–4%</td> <td>3%–3.5%</td> <td>2%–3%</td> <td>1.5%–2%</td> <td>1%–1.5%</td> <td>0.75%–1%</td> </tr> <tr> <td>M</td> <td>2%–2.5%</td> <td>2.5%–2.75%</td> <td>2.25%–2.5%</td> <td>2%–2.25%</td> <td>1.25%–1.5%</td> <td>1%–1.25%</td> <td>0.75%–1%</td> </tr> </tbody> </table>		A1	A2	A3	A4	A5	A6	A7	F	4%–5%	3.5%–4%	3%–3.5%	2%–3%	1.5%–2%	1%–1.5%	0.75%–1%	M	2%–2.5%	2.5%–2.75%	2.25%–2.5%	2%–2.25%	1.25%–1.5%	1%–1.25%	0.75%–1%	[25]
	A1	A2	A3	A4	A5	A6	A7																				
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κ_{pre}^S	Proportion of symptomatic individuals screened each year before screening intervention	F 75%–85% M 75%–85%	75%–85% 75%–85% 75%–85% 75%–85%	[25]																							
τ	Average time for symptomatic individuals to be screened	7–14 days	[16, 26]																								
γ	Rate of treatment for infected individuals (transition from the I to the T compartment in our model)	$\gamma = \kappa \cdot \theta \cdot \frac{1}{\tau}$... ^b																								

NOTE. Distributions of all parameters are triangular, peaking at the interval midpoint. We assume that, if an individual (of either sex and of any age group) is screened, then the person will be screened once in any given year, such that

$$p_{it} = 1 - \sum_{j=1, j \neq i}^5 p_{ij}.$$

^a The modeled population was stratified into seven 5-year age groups, as follows: A1, 15–19 years; A2, 10–24 years; A3, 25–29 years; A4, 30–34 years; A5, 35–39 years; A6, 40–44 years; A7, 45–49 years.

^b The rate per year that treatment is received is given by the proportion of people screened per year multiplied by the sensitivity of the screening test.

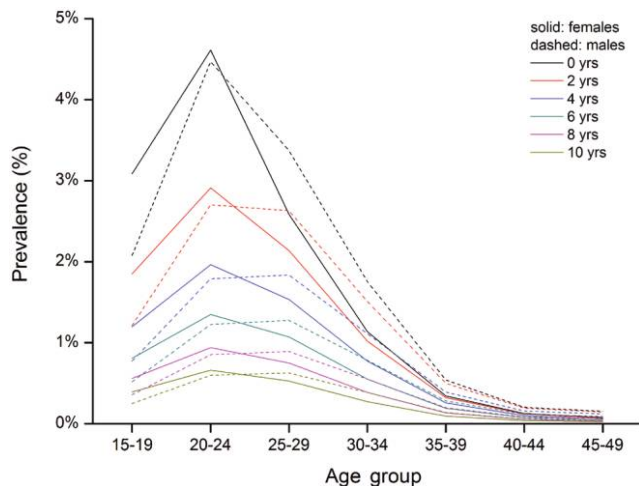


Figure 2. Age-specific prevalence in males (*dashed lines*) and females (*solid lines*) at 0, 2, 4, 6, 8, and 10 years after the introduction of screening, when 40% of both males and females are screened annually.

proximately the same overall reduction in prevalence in women as the reduction attained in men. But targeting only women for screening and treatment yields slightly greater reductions in overall prevalence in women than in men (see Appendix A).

Although the level of coverage is clearly the most important factor contributing to the outcome of screening, other biological

and behavioral parameters influence the outcome. Parameters that affected whether or not an epidemic occurred (that is, whether $R_0 > 1$ or $R_0 < 1$) were evaluated by logistic regression analysis on the prescreening data (table 2). PRCCs between the output prevalence and the input parameters were calculated. The dominant parameters in determining the overall population prevalence of chlamydia infection were also among the most important parameters in affecting whether an epidemic ensued and the reduction in prevalence (table 2), and they did not substantially differ between screening strategies or sex or age group. Therefore, for illustration purposes, we present a sensitivity analysis for one likely strategy: screening 40% of 15–24-year-old females each year (table 2). The sensitivity analyses revealed that reduction in prevalence is mostly a function of 2 biological parameters (the proportion of infections that are asymptomatic in women and the duration of infection in men) and 2 behavioral parameters (the frequency of sex acts for 20–24-year-olds and the level of condom usage). Response surfaces were generated to illustrate the relative importance of these parameters in influencing the reduction in prevalence attained (figure 4A and 4B).

DISCUSSION

The results from our model indicate that screening should be effective in reducing chlamydia prevalence in Australia. We have

Table 2. Results of sensitivity analysis.

Parameter	Rank of importance (no epidemic)	PRCC for prevalence (overall)	PRCC for reduction in prevalence
Proportion of infections that are asymptomatic in females	1	0.91	−0.90
No. of sex acts in partnerships in which females and males are both 20–24 years old	3	0.83	−0.81
Proportion of sex acts in which condoms are used	2	−0.77	0.78
Proportion of infections that are asymptomatic in males	8	0.75	−0.75
Average time to clear natural infection in males	5	0.69	−0.76
Average time to clear natural infection in females	4	0.67	−0.56
No. of sex acts in partnerships in which females and males are both 15–19 years old	7	0.59	−0.49
No. of sex acts in partnerships of 15–19-year-old females and 20–24-year-old males	6	0.58	−0.51
Proportion of women 20–24 years old who are in the highest risk group (average 8 partners per year)	9	0.56	−0.55
Proportion of women 20–24 year old who are in the second highest risk group (average 4 partners per year)	12	0.56	−0.30
No. of sex acts in partnerships of 20–24-year-old females and 25–29-year-old males	10	0.53	−0.11
Proportion of women 15–19 years old who are in the highest risk group (average 8 partners per year)	11	0.51	−0.44
Transmission probability per act	13	0.32	−0.33
No. of sex acts in partnerships in which females and males are both 25–29 years old	14	0.32	−0.47
Proportion of women 25–29 years old who are in the lowest risk group (no change in partners)	15	0.29	−0.05
Average time for someone with symptomatic infection to be screened and receive treatment	16	0.25	−0.26

NOTE. Listed are the most important parameters in determining whether an epidemic is established (as determined by the coefficients generated by logistic regression analysis), in contributing to the prevalence of the epidemic, and in the reduction in prevalence due to screening. The parameters are ordered by the magnitude of partial rank correlation coefficients (PRCCs) for prevalence (second column; only parameters with $|PRCC| > 0.2$ are presented).

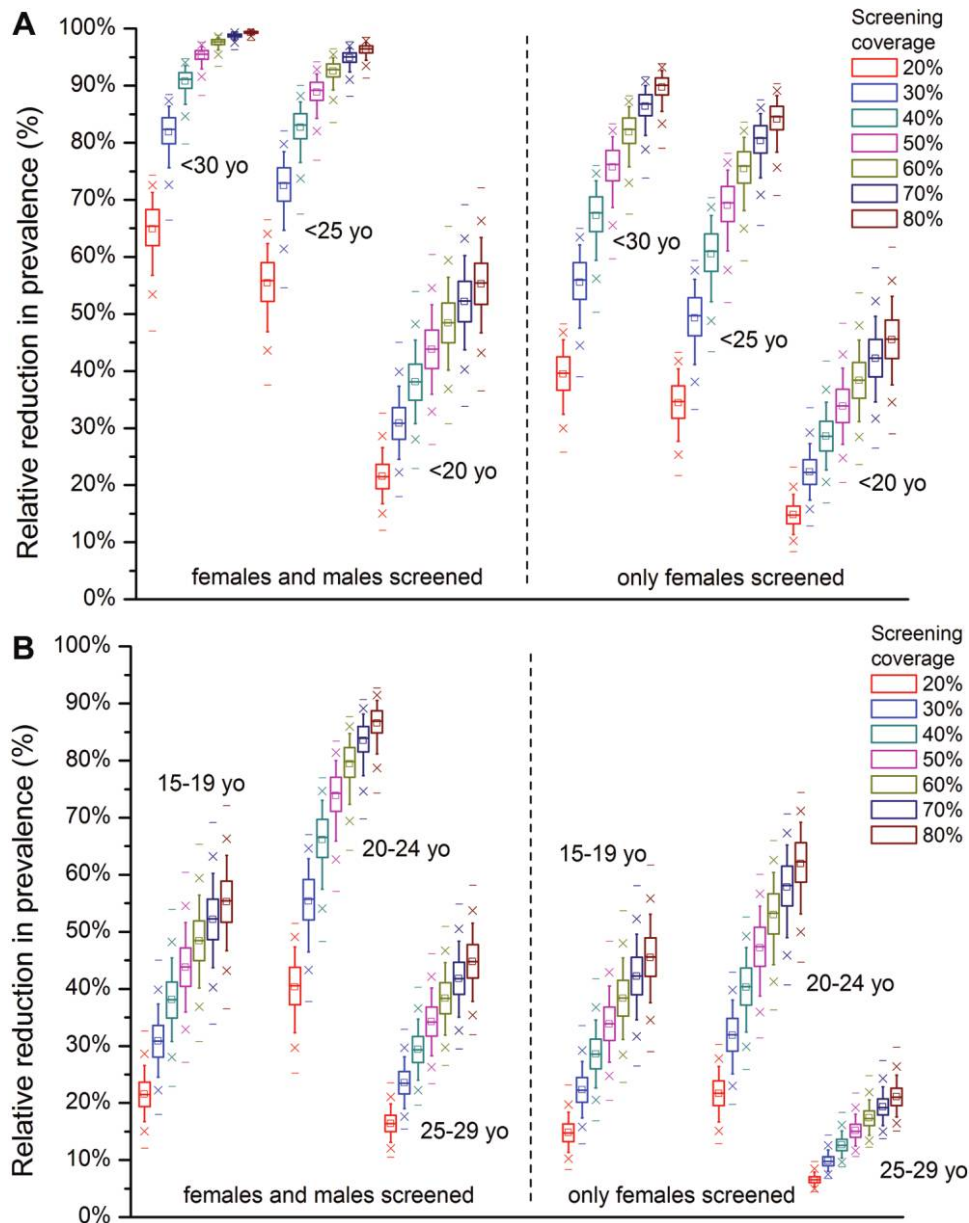


Figure 3. Relative reductions in prevalence in females, when females and males are screened or when females only are screened. These were calculated as 1 minus the ratio of the post- and prescreening prevalence after 10 years of screening. Panel A shows reductions for screening strategies targeted at the <30-year-old, <25-year-old, and <20-year-old populations. Panel B shows reductions for screening strategies targeted at the 15–19-year-old, 20–24-year-old, and 25–29-year-old groups. These are presented as box-and-whisker plots, which illustrate the degree of uncertainty in the output of the model. Each individual (age- and sex-specific) strategy was simulated over 10,000 parameter sets, and the interquartile range, mean (\square), median (*line within box*), and 5th–95th percentile range (*whiskers*) are indicated in the standard way. The 1st–99th percentile range (\times) and the minimum and maximum values ($-$) are also indicated.

shown that large reductions in prevalence are possible but that the degree of reduction is highly dependent on the proportion of the eligible population screened. Our results suggest that it is most effective to screen 20–24-year-old men and women. The further screening of males and females 15–19 years old will also substantially affect the reduction in prevalence. Given that nearly 90% of women and 70% of men <25 years old visit a general practitioner for their own health each year, offering

screening through general practice clinics would give a large proportion of this age group the opportunity to be screened each year [35]. Our results suggest that, in terms of reduction in prevalence in females, it does not matter greatly which sex is screened; for a given overall coverage, virtually the same reduction in prevalence in both sexes will be obtained whether screening is targeted at males, females, or both. This suggests that the absolute number of people screened is the important factor.

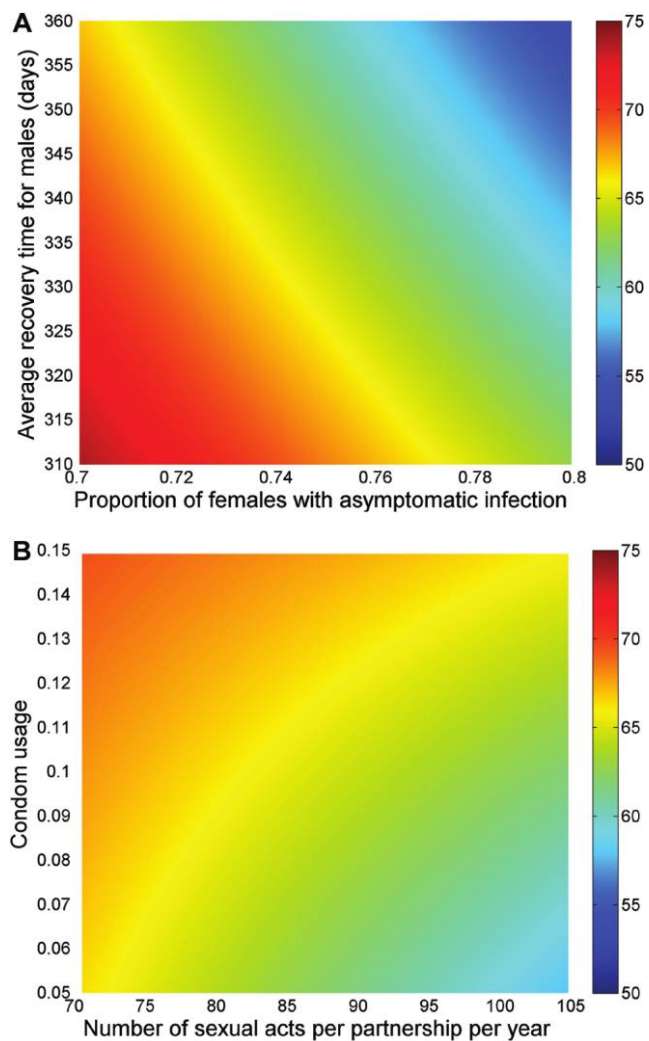


Figure 4. Response hypersurfaces showing the relative reduction in prevalence as a function of the average recovery time in males and the proportion of females with asymptomatic infections (*A*) and as a function of condom usage and the no. of sex acts per partnership per year (*B*).

It is interesting to note that the model predicts that chlamydia prevalence is higher in men than in women in the >25-year-old bracket, is nearly equivalent for the 20–24-year-olds, and is lower for those <20 years old (figure 2). This finding is consistent with Australian surveillance [1] and prevalence [2] data as well as with population sexual behavioral data that show that men are more likely to have younger sex partners than women [13].

Our analysis provides valuable information on the likely epidemiological impact of different screening strategies in Australia. Screening ~30% of 15–24-year-old males and females each year will reduce chlamydia prevalence among women by >70%. The greater the coverage, the more beneficial the intervention will be. Increasing the coverage will continue to be highly efficient until at least 50%–60% coverage is attained (at which point

the approximately linear “curve” starts to become nonlinear due to some saturation) (figure 3A). However, given that <50% of 20–24-year-old women participate in the biennial Pap-smear-screening program [36], the Australian government will need to invest in methods to encourage participation to achieve the coverage rates necessary to lower chlamydia prevalence.

Other mathematical modeling studies of the impact of screening on chlamydia prevalence have reported similar results, predicting that prevalence would be reduced if women 15–24 years old are screened annually in The Netherlands [16] and in the United Kingdom [37]. However, in Sweden for example, where opportunistic screening has been in place since the mid-1980s, the initial decline in chlamydia prevalence observed in the 1980s and early 1990s has reversed, with a steady increase since the mid-1990s despite screening ~25% of females 15–24 years old each year [38]. It is unclear why the prevalence has increased in the presence of screening in Sweden, but some have suggested inadequate coverage of those <25 years old, failure to comprehensively target young men, changing sexual behavior, or difficulties in maintaining adherence to an annual screen [37–39]. This observation, together with the differences in underlying chlamydia prevalence, sexual behavior, and health care access between countries, highlights the need for Australia to develop models parameterized with Australian data.

The most important public health outcome of a chlamydia-screening intervention campaign would be a reduction in the sequelae associated with chlamydia infection. However, since this develops over many years, the reduction in prevalence is the most important proxy for the overall effectiveness of the public health intervention. Our model is one of the first to show that chlamydia transmission is strongly related to 2 biological parameters (the proportion of infections that are asymptomatic in women and the duration of infection in men) and 2 behavioral parameters (the frequency of sex acts for 20–24-year-olds and the level of condom usage). It is evident that the biological parameters are considerably more important than the behavioral parameters in influencing the reduction in prevalence attained (table 2 and figure 4A compared with 4B). Screening will have the effect of indirectly changing the biological attributes— asymptomatic infections in women will be detected by screening, and the recovery time in men will be considerably reduced if they are screened; hence, the potential for screening to be so effective for chlamydia. Health-promotion strategies could be adopted to target behavioral factors, such as promoting condom use. Our model is also one of the first chlamydia transmission models to include immunity as a state variable. In the absence of published data, we assumed a short-term immunity of 30–60 days and that treatment will reduce the duration of immunity. However, the sensitivity analysis found that duration of immunity was only a moderately important factor in determining the reduction in chlamydia prevalence.

Our model considers only annual screening for 2 reasons. First, the screening interval should not be longer than the duration of infection; given that the duration of chlamydia infection is assumed to be 9–12 months in the model, a longer screening interval would not be appropriate. Second, several studies have demonstrated high reinfection rates for chlamydia, suggesting that at least annual screening may be necessary to interrupt transmission [40].

It is important that we acknowledge some of the limitations of our model. The model did not evaluate the impact of partner notification (tracing and testing sex partners of infected individuals) on chlamydia prevalence, and it has been shown that population prevalence is sensitive to the extent that partner notification is undertaken [16]. By definition, partner notification is associated with a network of individuals, and to model this intervention accurately it is necessary to develop an individual-based model of chlamydia transmission. We chose to develop a population-level model, which is most appropriate for exploring the dynamics of transmission in large populations in which an infection is endemic. Models of this type are not able to capture events that occur at the level of the individual. We have focused on the impact of screening, which will be the primary intervention in Australia, and on identifying the key determinants for reducing prevalence when screening is implemented. The model provides a conservative estimate of the impact of screening, and future work will involve the development of an individual-based model to address such questions as the potential added benefit of partner notification. We assumed that sexual risk behavior is not related to whether a person will be screened. This is a reasonable assumption, given that the vast majority of young adults visit a general practitioner each year and will be presented with the opportunity to be screened. Furthermore, in Australia there are many outreach screening programs targeting the homeless and marginalized populations as well as specialist youth, family planning, and sexually transmitted infection clinics. These services currently undertake widespread chlamydia testing, and it is likely that they will continue to do so in the future [41–43]. We assumed that men and women with symptomatic infection seek health care and are treated within 1–2 weeks after the onset of symptoms. There is evidence to support this for men, but few data are available for women. It is possible that, because symptoms in females are often nonspecific, they may delay seeking health care. In the absence of available data on women, we assumed the same time period for both men and women; this is consistent with other published models [16, 17]. Our sensitivity analysis determined that this parameter was not among the most important in determining chlamydia prevalence. In any model, there is some uncertainty about the data used for parameterization. However, unlike for other published chlamydia models, we have undertaken a comprehensive uncertainty analysis to capture how this uncertainty may affect the impact of chlamydia screening on the prevalence in Australia.

The hypothesis put forward by Brunham et al. [27] that early antibiotic treatment of chlamydia infection may inhibit the development of acquired immunity motivated us to include an immune state in our model. This theory is intuitively attractive despite a lack of solid evidence from human studies to support the notion of acquired immunity and model parameterization. In contrast to Brunham et al., our results suggest that the duration of immunity only modestly affects chlamydia prevalence. However, we note that Brunham et al. include an immune state that confers complete and lifelong protection from reinfection, whereas in our model immunity after infection lasts between 0 and 60 days depending on whether recovery is natural or due to early treatment (see table 1). Clearly, the assumption of Brunham et al. will have a stronger impact than our more conservative assumption.

Our model has been parameterized to capture the current sexual behavior and the current testing and treatment practices in order to track chlamydia transmission dynamics in Australia. It will help Australian policy makers design the most effective chlamydia screening program for Australia—particularly in determining the target population and screening coverage at which to aim (including in the upcoming pilot studies of systematic chlamydia screening in Australia). It also identifies key parameters for measurement and monitoring. Furthermore, the output from this model can be used to inform economic analyses of the cost-effectiveness of chlamydia screening in Australia. Our model suggests that an opportunistic screening program in Australia could reduce chlamydia prevalence, provided adequate screening coverage of the target population is achieved.

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