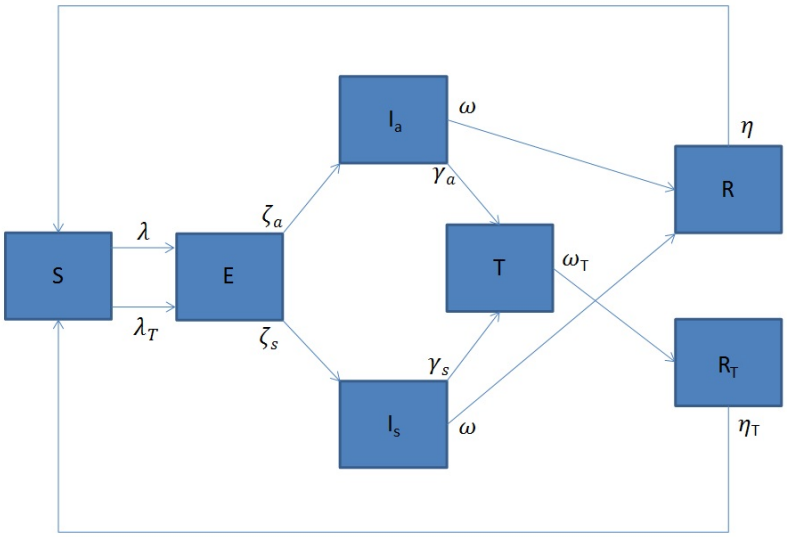
Modelling Chlamydia Transmission Dynamics in 20–24 Year Olds



Courtney Hamilton
Jonathan Kable
Jan Stellet

Abstract

In this report, a mathematical model is created to understand the dynamics of genital *Chlamydia trachomatis* infections. By understanding the dynamics of how the infection spreads, the effect of executing a screening program for 20–24 year olds in Australia can be investigated. One particular model developed by Regan et. al. [1] is taken and leads, together with simplifying assumptions, to a set of ordinary differential equations that constitutes the model. This forms the basis of this report. Further insight into the model is gained through sensitivity and uncertainty analyses. The effect of screening the potentially infected population was analysed and it was found that additional screening for *Chlamydia trachomatis* infections results in a marked reduction in the overall prevalence of the infection within the population. Screening just 5–10% of the potentially infected population could lead to a significant reduction in the incidence of *Chlamydia trachomatis* infections in the 20–24 year old population of Australia, suggesting that a screening program is a viable measure for controlling the spread of chlamydia.

Contents

List of Figures

List of Tables

1 Introduction

Genital *Chlamydia trachomatis* infection (chlamydia) is the most common curable sexually transmitted infection (STI) in Australia [2]. The increased incidence of chlamydia over the last decade has prompted the formation of numerous different models in an attempt to understand the dynamics of chlamydia transmission within populations. Another crucial objective is to assess the effectiveness of interventions such as screening regimes.

The experience of other countries who have already implemented screening programs may provide some valuable insight into how a screening program could be designed in Australia. In previous research [3, 4] the effects of proposed screening programs in the United States and United Kingdom have been analysed. Each takes a different approach to modelling the spread of chlamydia and each approach has its own benefits and drawbacks.

With the aid of a mathematical model adapted from Regan et. al. [1], this report investigates the effectiveness of a screening program targeted at 20–24 year olds on the prevalence of chlamydia within the population. First, the background of chlamydia along with a review on relevant research are presented in chapter 2. This then leads to a description of the model's concepts and underlying assumptions in section 2.3. Based on these considerations, the differential equations of the model are derived and a list of relevant parameter values is compiled in section 2.4.

Chapter 3 then focuses on analysing the model's properties by computer simulation. At first, section 3.1 details the transmission dynamics with and without screening measures. Apart from screening measures, changes in human behaviour or medical advancements may also pose changes to the model's parameters. Thus a sensitivity analysis is performed in section 3.2 in order to assess each parameter's impact on the outcome of the model. This main portion of the report concludes with an uncertainty analysis in part 3.3 which aims on investigating the effects of inaccuracies in the parameter values.

Finally the report concludes with a summary of all findings and an outlook on possible future work or enhancements to the model. This should allow an informed decision on whether or not the implementation of a screening program is an adequate measure to reduce the spread of chlamydia in Australia.

2 Modelling Chlamydia Transmission Dynamics

2.1 Background

The notification rate for chlamydia has been steadily increasing over the past ten years from 88.4 notifications per 100,000 in 2000 to 332.7 notifications per 100,000 persons in 2010 [5]. This increase in the notification rate indicates that the current methods for detection and treatment are not sufficient to control the spread of chlamydia in Australia.

The prevalence of chlamydia is related to the high occurrence of asymptomatic cases, with up to 80% of chlamydia infections in men and women being asymptomatic. These can go undetected for months to years [6]. In women, if left untreated, chlamydia can lead to severe reproductive complications. Chlamydia contributes significantly to the development of pelvic inflammatory disease (PID) in women which is associated with a high risk of infertility, ectopic pregnancy, and chronic pelvic pain [6]. A screening program is a possible measure to control chlamydia prevalence in populations through detection and treatment of the infection before it becomes destructive.

The risk of infection varies considerably depending on the age of the population being studied [1]. People in the 20–24 years age group are considered to be at much higher risk of being infected because on average, they tend to be the most sexually active in a population. In 2010, the 20–24 years age group represented 36% of all reported cases which is the highest proportion among all age groups [5]. This would suggest that a screening program targeted at this age group would be more effective than targeting any other age group.

There is currently no screening program for chlamydia in Australia. However, other developed countries such as Sweden, Denmark and the United States had opportunistic screening programs introduced in 1980s [3]. Although opportunistic screening in these countries has not led to a sustained reduction in the prevalence of chlamydia, there is evidence that screening can reduce the incidence of complications such as PID [7].

2.2 Literature Review

Numerous approaches to modelling the effectiveness of a chlamydia screening program have been undertaken. Edmunds [4] developed a stochastic, individual based dynamic network model with three main strategies to explore the effectiveness of an opportunistic screening program in the United Kingdom. These strategies considered for <25 year olds were:

1. annual screening for women
2. annual screening for women or if changed partner within last 6 months
3. annual screening for men and women.

He concluded that the first strategy would be the most effective with a modelled reduction in prevalence of over 50% after five years.

Regan et. al. [1], which forms the basis of our report, developed a dynamic transmission model parameterized with Australian sexual behaviour and epidemiology data. By extending the standard Susceptible-Infected-Recovered (SIR) model to incorporate treatment and the asymptomatic or symptomatic path chlamydia can take, Regan et. al. [1] has aimed to incorporate all the characteristics of chlamydia transmission in populations. A similar approach was employed by Welte [7], however, one major difference was that he assumed all sexual contact was unprotected by condom use, effectively overestimating the number of infections in the population.

2.3 Assumptions and Compartment Diagram

This report presents a simplified model adapted from Regan et. al. [1] that integrates both the behavioural and biological factors of chlamydia in a population of 20–24 year olds. The model is used, in combination with uncertainty and sensitivity analyses, to predict the outcomes of the implementation of a continuous screening program. As this report deals only with the 20–24 year old age group, the term "population" henceforth refers to this subgroup.

The model describes the number of susceptible individuals (S), infected but not yet infectious (exposed, E), infectives (I), persons in treatment (T) and recovered (R). It is further differentiated between infectives with asymptomatic (I_A) and symptomatic infections (I_S) as well as recovery due to treatment (R_T) and the naturally recovered (R).

Therefore, five key aspects distinguish this model from one of the simplest infectious disease model, the Susceptible-Infected-Recovered (SIR) model:

1. A latent period after infection but before being infectious is considered (exposed state).
2. Two different characteristics (I_A and I_S) of the infection occur with different per-capita growth rates ζ_A and ζ_S.
3. While natural recovery at the same per-capita recovery rate ω is possible from both types of infection, the possibility of treatment with a deviant recovery process at rate ω_T is also considered.
4. The treatment state is reached either at a per-capita rate γ_S because symptoms occur and treatment is sought after or due to positive testing of asymptomatic infectives at rates γ_A and γ_{screen}. While in treatment (T), individuals are still infectious and still contribute to the spread of chlamydia but at a comparably smaller rate λ_T.
5. Furthermore, different time spans of immunity following natural recovery and recovery due to treatment are taken into account. This results in recovered individuals becoming susceptible again with different per-capita rates η and η_T respectively.

The original model proposed by Regan et. al. is based on several assumptions, some of which include:

1. Total population size is assumed to stay constant.
2. In order to calculate the rate of infection, numerous factors are taken into account. These include different sexual behaviour of different age groups and further differentiation of these into four risk groups. The number of sex acts per relationship per year and the use of condoms are also considered.

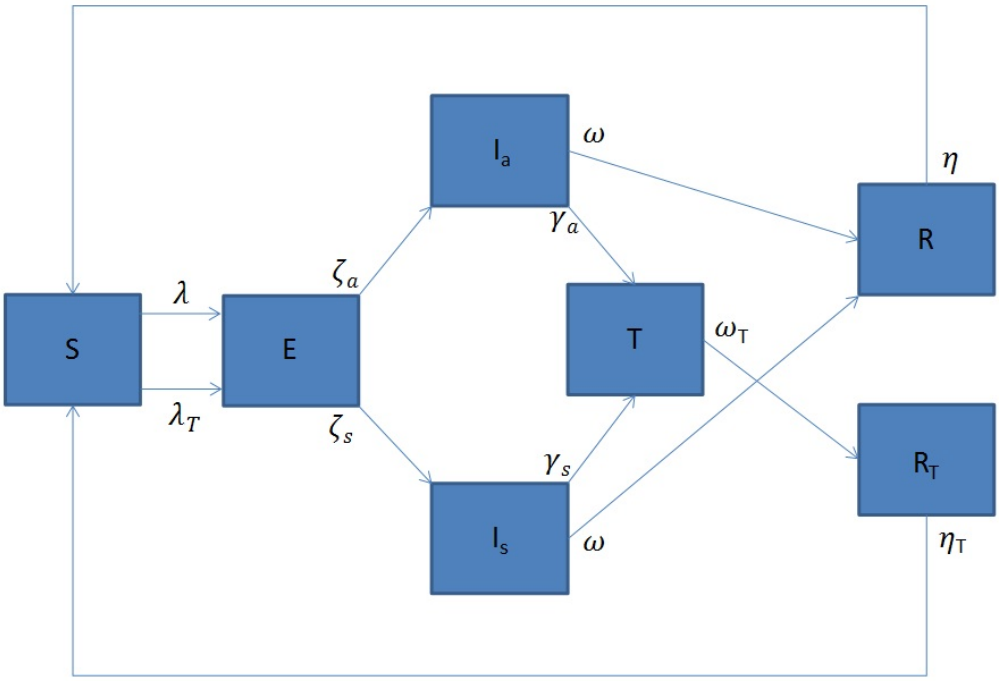


Figure 2.1: Compartment diagram of simplified model

3. Another assumption is that people with symptomatic infections will look for medical advice within 1-2 weeks and then receive treatment. Generally, all people who test positive are also assumed to receive treatment.

In addition to these it is assumed, for the simplified model, that asymptomatic individuals will not develop symptoms and symptomatic individuals will not cease to display symptoms. It is also assumed that fixed proportions of all infections either remain asymptomatic or develop symptoms. This report does not take different age and risk groups into account but focuses on the 20–24 age group with 2.83 new partners per year on average (weighted average over all risk groups from the original model). This alteration is a significant simplification as each age and risk group would otherwise require a separate model for interaction between the different groups. As a consequence of this, the influence of individuals from other age groups interacting with the 20–24 age group is neglected.

All relationships described in this section are visualized in a compartment diagram as shown in figure 2.1. This allows the formulation of the corresponding differential equations which will be, together with the parameter values, detailed in the following section.

2.4 Differential Equations and Parameter Values

The compartment diagram (figure 2.1) is a graphical representation of the simplified model. Shown below (equations (2.1)–(2.7)) is the set of ordinary differential equations that constitutes the model. Its main parameters are given in table 2.1.

The parameters γ_{screen} and λ_T have been added in this alteration to the original article's model, although γ_{screen} will take the value of 0 until population screening is introduced in 3.1. There is a full list of all the parameters and the expressions used to calculate them in section A.1 of the appendix.

Parameter	Description	Value
η	Per-capita rate that natural immunity wears off	0.022222
η_T	Per-capita rate that treatment-induced immunity wears off	0.066666
λ	Transfer coefficient, the rate at which one infectious induvidual infects susceptibles	2.8477e-5
λ_T	Transfer coefficient during treatment	6.6256e-6
ζ_A	Per-capita rate that asymptomatic infections become infectious	0.053571
ζ_S	Per-capita rate that symptomatic infections become infectious	0.017857
γ_A	Per-capita rate that asymptomatic infections receive treatment	0.027094
γ_S	Per-capita rate that symptomatic infections receive treatment	0.064762
γ_{screen}	Per-capita rate of additional screening (analysis in section 3.1)	0
ω	Per-capita rate of natural recovery	0.020833
ω_T	Per-capita rate of treatment-induced recovery	0.142857

Table 2.1: List of main parameters.

$$\frac{dS}{dt} = \eta R + \eta_T R_T - \lambda S\left(I_A + I_S\right) - \lambda_T S T \tag{2.1}$$

$$\frac{dE}{dt} = \lambda S\left(I_A + I_S\right) + \lambda_T S T - \left(\zeta_A + \zeta_S\right) E \tag{2.2}$$

$$\frac{dI_A}{dt} = \zeta_A E - \left(\gamma_A + \gamma_{screen}\frac{I_A}{S + E + I_A} + \omega\right) I_A \tag{2.3}$$

$$\frac{dI_S}{dt} = \zeta_S E - \left(\gamma_S + \omega\right) I_S \tag{2.4}$$

$$\frac{dT}{dt} = \left(\gamma_A + \gamma_{screen}\frac{I_A}{S + E + I_A}\right) I_A + \gamma_S I_S - \omega_T T \tag{2.5}$$

$$\frac{dR}{dt} = \omega\left(I_A + I_S\right) - \eta R \tag{2.6}$$

$$\frac{dR_T}{dt} = \omega_T T - \eta_T R_T \tag{2.7}$$

The formulas for calculating these parameters are taken from the original article and adjusted to suit the simplified model. For instance, λ (the transfer coefficient) is no longer a sum of all the possible interactions between susceptible populations and infectious populations of all different age groups. It now merely represents interaction of susceptibles with two of the three infectious populations (asymptomatic and symptomatic infections) while λ_T represents interaction with the third (people receiving treatment).

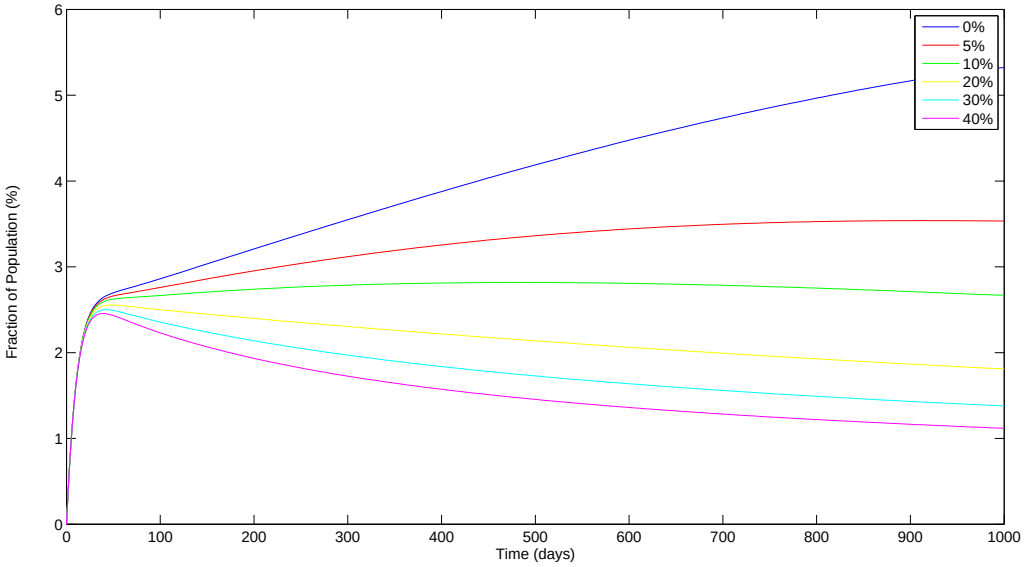


Figure 3.1: Six different values of screening resulting in six different population trends

3 Simulation Results and Further Analysis

3.1 Analysis of Simulation Results with and without Screening

Screening for and treating chlamydia in 20–24 year olds could result in a significant reduction in the occurrence of chlamydia as seen in figure 3.1 and table 3.1. In our model, screening is conducted on a fixed percentage of the potentially infected population. The potentially infected population includes those who are susceptible, exposed or asymptomatic as it is assumed that symptomatic individuals will not be chosen for screening due to already having the symptoms. The model was run with 0%, 5%, 10%, 20%, 30% and 40% screening to determine the degree of success that a potential screening program could have.

The percentage of asymptomatic cases that are detected without any kind of screening (κ_{pre}^{A}) is 3.1875%. This means that even with 0% additional screening, a proportion of the asymptomatic infections are being detected and treated. This level of detection arises from routine tests performed at general practitioners such as sexual health check-ups and pap smears identifying the infection in asymptomatic individuals.

From figure 3.1, if no screening program was introduced the prevalence of chlamydia would continue to rise to over 6% after 10 years. By screening 5% of the potentially infected population, it is possible to prevent a chlamydia epidemic and reduce the prevalence to below 3% in 10 years. Any additional screening results in a faster rate of reduction in incidences. As a consequence, the overall prevalence after 10 years is reduced. However, the reduction in prevalence due to increasing screening from 30% to

Proportion of potential infected screened	Prevalence after 2 years	Prevalence after 4 years	Prevalence after 6 years	Prevalence after 8 years	Prevalence after 10 years
0%	4.03%	5.66%	6.08%	6.16%	6.17%
5%	3.31%	3.47%	3.04%	2.60%	2.25%
10%	2.82%	2.54%	2.12%	1.77%	1.51%
20%	2.18%	1.68%	1.37%	1.16%	1.00%
30%	1.78%	1.27%	1.04%	0.89%	0.78%
40%	1.51%	1.03%	0.84%	0.73%	0.65%
original article: 40%	2.8%	1.8%	1.2%	0.8%	0.5%

Table 3.1: Approximate effectiveness of different screening proportions

40% is not as dramatic as when screening is increased from 10% to 20%.

The results obtained from our model are very similar to those Regan et. al. produced using their more complex model for of all age groups. A higher reduction in prevalence is seen in our model when compared to Regan et. al.'s model at 2 year intervals after the implementation of the screening program. However, ten years after implementing a screening program covering 40% of the potentially infected population, our model shows the prevalence of chlamydia to be 0.65% which is slightly higher than the 0.5% obtained by Regan et. al. The difference in results of these two models is most likely due to our model only considering the 20-24 years age group which shows the highest chlamydia prevalence of all age groups. Regan et. al. on the other hand consider all age groups and assume that sexual activity also occurs between people from different age groups.

3.2 Sensitivity Analysis of Model Parameters

One of the practical benefits of developing a model such as this is that we can predict how the prevalence of chlamydia will change in the real population based on how it changes in the model when certain parameters are varied. To this end, a sensitivity analysis was conducted on any parameters that humans have some level of control over; e. g. higher test accuracy could be achieved in the future, or the reduction factor due to treatment could vary depending on what specific medications or treatments the patient is receiving. A sensitivity analysis requires that each parameter is increased or decreased by some small percentage (in this case 5%) and then the corresponding percent shift in the resulting prevalence of infection is recorded. Table 3.2 below shows the results of this sensitivity analysis measured in "percent shift in prevalence of chlamydia after 300 days".

According to these results, the most effective measures that Australia can take to reduce the prevalence of chlamydia are decreasing sexual activity which includes the frequency of sex acts and the number of new parters per year, improving the accuracy of screening tests and increasing the proportion of asymptomatic infections that are detected. The latter two options fit into enhanced screening efforts, a concept that is discussed both in the previous section of this report and in the original paper by Regan et. al. [1].

The original paper conducts its own sensitivity analysis, with ψ and ϕ being the two most sensitive parameters that also appear here. While the highest ranked parameter in their analysis was div_A (the

Rank	Parameter	Definition	+5%	-5%	Rank in original article
1	n	Number of new partners per year	+0.2447	-0.2055	-
2	ψ	Number of sex acts per couple per year	+0.2442	-0.2052	3
3	θ	Test accuracy	-0.1676	+0.1998	-
4	κ_{pre}^{A}	Proportion of asymptomatic infections screened	-0.1477	+0.1722	-
5	τ_A	Number of days between a positive test and the beginning of treatment	+0.1634	-0.1549	-
6	κ_{pre}^{S}	Proportion of symptomatic infections screened	-0.0222	+0.0248	-
7	τ_S	Number of days between first showing symptoms and the beginning of treatment	+0.0236	-0.0233	16
8	ϕ	Proportion of sex acts using condoms	-0.0220	+0.0224	2
9	ε	Efficacy of condoms	-0.0218	+0.0222	-
10	ζ	Proportion of people abstinent during treatment	-0.0081	+0.0081	-
11	ρ	Reduction factor for transfer due to treatment	-0.0038	+0.0038	-

Table 3.2: Results of Sensitivity Analysis

chance of an infection being asymptomatic), this parameter is not tested here as it is assumed to be an inherent characteristic of the infection. Aside from these few similarities, the original article does not state results for the rest of these parameters.

3.3 Uncertainty Analysis of Model Parameters

To assure the validity of the model's results, it is a crucial step to determine the model's parameter values. This is usually a task of measurement, estimation and assumption. Any measurement is, however, affected by uncertainty.

As it has been indicated in the previous chapter's sensitivity analysis, even small changes of parameter values can have significant effects on the outcome of the model. In order to estimate the effect of any parameter's uncertainty, an uncertainty analysis is performed.

This work is almost entirely based on parameter values which have been obtained by Regan et. al. [1] (see appendix A.1). Regan et. al. suggest that these values with their upper and lower boundaries should be considered as stochastic variables with a triangular probability density function. All analyses in previous sections are based on the mean values of the upper and lower boundary as stated in appendix (A.1).

In order to incorporate the stochastic nature of these values we now assume them to be independently distributed with a triangular probability density function and perform multiple simulation runs. Each simulation run results in a different value for the quantity "proportion of individuals with chlamydia after 300 days". Taking into account the results of all simulation runs, a histogram can be generated. Essentially this gives an idea about the underlying probability distribution. Therefore, further insight

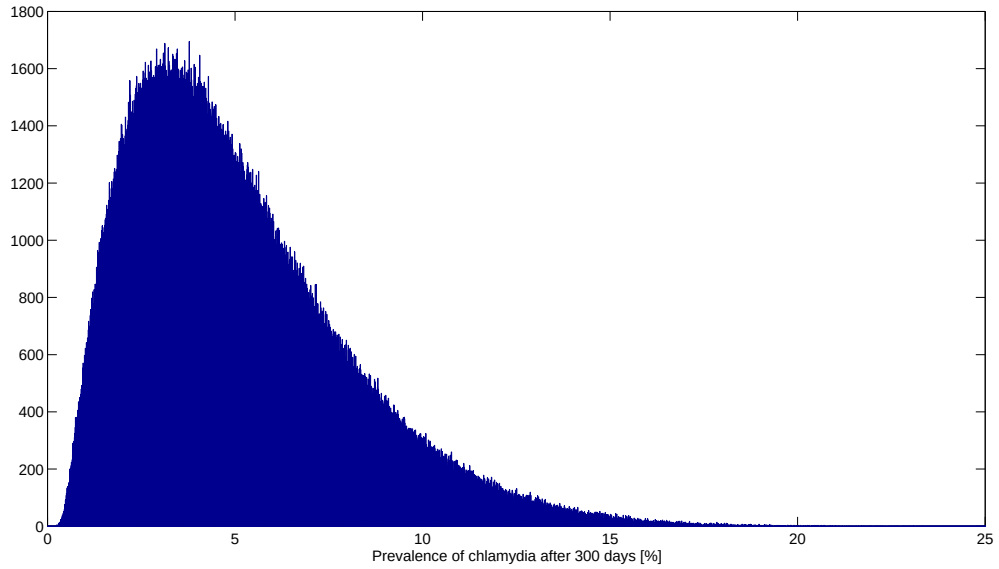


Figure 3.2: Results of uncertainty analysis $\left(n = 10^6\right)$. The histogram is based on classes with a size of 0.01%.

into the model and likely deviations from real world observations can be gained.

Performing an uncertainty analysis on the model of chlamydia transmission dynamics with 10^6 simulation runs yields the results shown in figure 3.2. The mean value can be calculated as 5.0806% and a standard deviation is found to be 2.9196%. One key finding is that the parameter uncertainties can lead to relatively large deviations from the mean value. As the histogram suggests, any result between 0.5% and 10% should be considered a plausible outcome. With lower likelihood, but still possible, are results in the region of 10% and higher.

Although the parameter uncertainty is assumed as being distributed with a triangular probability density function, the resulting histogram resembles a skewed normal probability distribution. This can be related to the non-linear dynamics of the model.

In conclusion, the uncertainty analysis clearly shows the implications of model parameters being known only to a certain precision. One way of improving the expected results is to improve the precision of the parameters, for instance through further research and more reliable statistical data.

4 Conclusion

This report identified a model for the transmission dynamics of *Chlamydia trachomatis* infection. The model allows the exploration of the effectiveness of screening regimes and the influence of parameter changes on the spread of the disease.

The model was derived on the basis of a more complex model by Regan et. al. [1]. In order to limit the scope of our analysis to the age group of 20–24 year olds as well as to simplify the model, several adaptations were made to the original design, which covers the entire population. The simplified model was then calculated using the same parameters and formulae given in the original article.

At first, the future development of chlamydia prevalence was simulated and the effects of screening on its spread were analysed. The results show that screening is a suitable means of reducing prevalence among 20–24 year olds. Screening just 5–10% of the potentially infected population yields a significant reduction in the long term projection of prevalence. In general, the results obtained from our simplified model correspond well to the ones obtained by Regan et. al. [1].

Secondly, the effects of parameter changes were analysed through a sensitivity analysis. It was found that decreasing the number of new partners, reducing the frequency of sex acts and improving the test accuracy have the highest influence on reducing the spread of chlamydia. These results indicate that apart from establishing a screening regime, an increased awareness, and thus changes in human behaviour, as well as advancements in testing provide further potential.

Finally, an uncertainty analysis was used to gain an idea of how the model is affected by random variation in parameter values. It was found that the calculated mean value complies with previous results but deviations have to be considered. This is especially important if decisions are made on the basis of a model's predictions. Further research and improved parameter estimation could lead to reduced uncertainty.

Overall, the original article by Regan et. al. [1] concludes that a screening regime is the best way to avoid an epidemic and our model provides evidence to support this conclusion. Furthermore, this report has shown that the significantly simplified model yields similar results to those stated in the original article. Therefore, the reduced form of the model may be used as a starting point that allows easier implementation and enhanced clarity before considering the more complex original model.

This report only covers the biological part of chlamydia infections and screening. However, the decision regarding the implementation of a screening program also depends on economic considerations, as discussed in [8]. Extending the model to gain an understanding of the net economic impact could be realised by incorporating the costs of each treatment, screening and possibly the loss of productivity during hospital stays.

A Appendix

A.1 Complete List of Model Parameter Values

Parameter	Description	Expression[1]	Value
η	Per-capita rate that natural immunity wears off	$\frac{1}{imm_N}$	0.022222
η_T	Per-capita rate that treatment-induced immunity wears off	$\frac{1}{imm_T}$	0.066666
λ	Transfer coefficient, the rate at which one population infects another	$n\left(1-(1-\beta)^{\psi(1-\phi)}\left(1-(1-\varepsilon)\beta\right)\right)$	2.8477e-5
λ_T	Transfer coefficient during treatment	$n\left(1-(1-(1-\rho)\beta)^{\psi\xi(1-\phi)}\left(1-(1-\varepsilon)(1-\rho)\beta\right)^{\psi\phi\xi}\right)$	6.6256e-6
ζ_A	Per-capita rate that asymptomatic infections become infectious	$div_A \frac{1}{0\ldots28}$	0.053571
ζ_S	Per-capita rate that symptomatic infections become infectious	$div_S \frac{1}{0\ldots28}$	0.017857
γ_A	Per-capita rate that asymptomatic infections receive treatment	$\kappa^A_{pre}\theta\frac{1}{\tau_A}$	0.027094
γ_{screen}	Per-capita rate of additional screening	$s\theta\frac{1}{\tau_A}$	
γ_S	Per-capita rate that symptomatic infections receive treatment	$\kappa^S_{pre}\theta\frac{1}{\tau_S}$	0.064762
ω	Per-capita rate of natural recovery	$\frac{1}{44\ldots52}$	0.020833
ω_T	Per-capita rate of treatment-induced recovery	$\frac{1}{5\ldots9}$	0.142857
ψ	Number of sex acts per couple per year	$70\ldots105$	87.5
n	Number of new partners per year	$25\%\cdot 0 + 34\%\cdot 1.5 + 24\%\cdot 4 + 17\%\cdot 8$	2.83

[1] "$A\ldots B$" means "ranging from A to B"

ρ	Reduction factor for transfer due to treatment	$0.7 \ldots 0.75$	0.725
ζ	Proportion of people abstinent during treatment	$80\% \ldots 90\%$	0.85
ξ	Proportion of people not abstinent during treatment	$1 - \zeta$	0.15
β	Chance of infection	$1.65\% \ldots 1.7\%$	0.01675
ε	Efficacy of condoms	$85\% \ldots 95\%$	0.9
ϕ	Proportion of sex acts using condoms	$5\% \ldots 15\%$	0.1
κ^A_{pre}	Proportion of asymptomatic infections screened	$\frac{3.5+4+2.5+2.75}{4}$	0.031875
s	Screening percentage (of potentially infected population)	s	0%, 5%, 10%, 20%, 30%, 40%
κ^S_{pre}	Proportion of symptomatic infections screened	$75\% \ldots 85\%$	0.8
θ	Test accuracy	$80\% \ldots 90\%$	0.85
τ_S	Number of days between first showing symptoms and the beginning of treatment	$7 \ldots 14$	10.5
τ_A	Number of days between a positive test result and the beginning of treatment	$1 \ldots 2$	1.5
imm_N	Number of days immune naturally	$30 \ldots 60$	45
imm_T	Number of days immune due to treatment	$(0 \ldots 0.5)\ imm_N$	21
div_A	Chance of an infection being asymptomatic	$70\% \ldots 80\%$	0.75
div_S	Chance of an infection being symptomatic	$1 - div_A$	0.25

Table A.1: Full list of model parameters

Bibliography

[1] D. G. Regan, D. P. Wilson, and J. S. Hocking, "Coverage is the key for effective screening of chlamydia trachomatis in australia." *The Journal of infectious diseases*, vol. 198, pp. 349–358, August 2008.

[2] (2010, December) Chlamydia. Australian Government. [Online]. Available: http://www.health.gov.au/internet/sti/publishing.nsf/Content/chlamydia

[3] S. D. Hills, A. Nakashima, L. Amsterdam, J. Pfister, M. Vaughn, D. Addiss, P. A. Marchbanks, L. M. Owens, and J. P. Davis, "The impact of a comprehensive chlamydia prevention program in wisconsin," *Family Planning Perspectives*, vol. 27, no. 3, pp. 108–111, 1995.

[4] W. J. Edmunds, "Modelling the effectiveness of chlamydia screening in england," *Sexually transmitted infections*, vol. 86, no. 6, p. 496ff, 2006.

[5] (2011) National notifiable diseases surveillance system. Australian Government Department of Health and Ageing. [Online]. Available: http://www9.health.gov.au/cda/Source/CDA-index.cfm

[6] J. F. Peipert, "Genital chlamydial infections," *New England Journal of Medicine*, vol. 349, no. 25, pp. 2424–2430, 2003. [Online]. Available: http://www.nejm.org/doi/full/10.1056/NEJMcp030542

[7] R. Welte, "Comparative model-based analysis of screening programs for chlamydia trachomatis infections," *American journal of epidemiology*, vol. 153, no. 1, p. 90ff, 2001.

[8] D. Hu, E. W. H. III, and S. J. Goldie, "Screening for chlamydia trachomatis in women 15 to 29 years of age: A cost-effectiveness analysis," *Ann Intern Med.*, vol. 141, pp. 501–513, 2004.