Technical appendix

1. Introduction

We developed an individual-based model of chlamydia transmission in a population of heterosexuals aged 14 to 60 years, with age, infection status, sexual partner history and sexual behaviour of individuals tracked and updated on a daily basis. See Section 2, “Modelled Population” for the age composition of the modelled population.

Each simulation run starts with a burn-in period of 150 years (consisting of 100 years with no infection, followed by the introduction of chlamydia and a further 50 years) to ensure chlamydia prevalence and the partnership network is well established and at equilibrium at the start of simulation runs.

Individuals enter the sexually active population at age 14 years and have no sexual partners. Individuals can then form partnerships with other individuals in the population, and multiple sexual acts can occur between partners until the partnership is dissolved. See Section 3, “Sexual Behaviour”, for descriptions of how partnerships and sexual acts are defined, and the process of formation and dissolution of partnerships.

Transmission of chlamydia can occur if a sexual act occurs between an infectious individual and a susceptible (i.e., uninfected with chlamydia) individual. Susceptible individuals who become infected will initially enter the ‘Exposed’ state and are not yet infectious. Following this period of latency, exposed individuals then become ‘Infectious’ either asymptomatically or symptomatically. Individuals recovering from infection naturally (i.e., without treatment) proceed to a short immunity period before returning to the susceptible state, while those who receive treatment return to the susceptible state immediately post treatment. See Section 4, “Transmission”, for a description of chlamydia transmission as defined in this model.

The results shown in the main text are presented as the median prevalence and interquartile range for 100 selected simulations under various scenarios. The 100 simulations are selected from 1000 simulations as those that most closely match the prevalences reported in the ACCEPt prevalence survey (see Table 2 in the main text). See Section 6, “Simulation Selection and Model Calibration”, for details on simulation selection and calibration process.

The model code is written in Java and is available on GitHub at the following address https://bbcbh@github.com/bbcbh/Package_ACCEPtPlus.git.

2. Modelled Population

The model population consists of 92000 heterosexual individuals. The population is comprised of an equal number of males and females aged 14 to 60 years, distributed uniformly across 1-year age-bands. When individuals exceed age 60 years, they are removed from the model. If the removed individual is in a partnership at the time they are removed, the partnership is maintained until the partnership is dissolved or the partner is also removed.

A removed individual is replaced by a new individual of the same gender aged 14 and will begin to seek partners at age 16. Individuals’ preferred partner age ranges are determined at an individual level and are assigned as they enter the population. The partner age preferences are based on partnership characteristics reported in Second Australian Study of Health and Relationships survey (ASHR2),(1) and are listed in Table A1.

Table A1: The preferred partner age range used in the model. Note the percentage used is slightly different to ASHR2 due to round-off and/or no response in ASHR2.

Will only accept partners that are …	Probability (male)	Probability (female)
More than 5 years older	2.9%	16.8%
1 to 5 years older	18.0%	46.6%
Of same age range (i.e., within ±1 year)	14.1%	15.5%
1 to 5 years younger	46.8%	16.7%
More than 5 years younger	18.2%	4.45

Overlapping (or concurrent) partnerships (i.e., more than one partnership at the same time) are allowed in the model. This behaviour is set at an individual level and is assigned as new individuals enter the population. The probability that an individual will have overlapping partnerships is 0.043 for males and 0.021 for females, based on the percentage of individuals who had extradyadic sex in the last year as reported in ASHR2.(2)

3. Sexual Behaviour

The formation and dissolution of sexual partnerships is governed by the partner acquisition rate. Initial values for age-specific partner acquisition rates are based on those reported in the ASHR2.(1) The model is calibrated by adjusting the partner acquisition rate, along with along with transmission probability, to match age- and gender-specific chlamydia prevalence reported in the ACCEPt prevalence survey (see Table 2, main text). The initial and inferred partner acquisition rates (given as the mean number of partners in the last 12 months) are given in Table A2 below.

Table A2: Inferred values for mean number of partners in last 12 months used in the model (inferred through calibration), and initial values from ASHR2.

Age group	From ASHR2		Inferred values used in model	
	Male	Female	Male	Female

16 - 19	1.4	1.0	0.7	1.0
20 - 29	1.4	1.1	1.1	1.4
30 - 39	1.2	1.0	1.3	1.3
40 - 49	1.1	0.9	1.2	0.9
50 - 59	1.0	0.8	1.1	0.8

See Section 6, "Simulation Selection and Model Calibration", for a full description of the calibration process.

The partnership status of all individuals is updated daily. At each one-day cycle, the number of current partners of every individual aged >16 years is calculated, and the individual is then be placed into the following lists:

I. Those currently eligible to seek partners. This includes those who don't have a current partner, and those who do have a current partner and are permitted to have concurrent (overlapping) partnerships.

II. Those who currently have at least one partner.

Note that it is possible for an individual to be placed to both lists simultaneously.

At the same time, the number of partners acquired in the last 12 months for every individual aged >16 years is determined, which will then be used to calculate the mean number of partners in last 12 months for the modelled population under gender-age group defined in Table A2. The difference between the mean and the corresponding partner acquisition rate listed is then used to determine whether formation or dissolution of a partnership should occur for a given individual in a specific gender-age group. The calculation required for both processes is illustrated by the two examples below.

3.1. Example 1: partnership formation

For example, say at time step *t*, the mean number of partners in the last 12 months among males aged 20-29 years in the population is 0.9. This is lower than the (inferred) value of 1.1 defined for this group (see Table A2). Therefore, some males aged 20-29 years are required to form new partnerships to increase the mean to 1.1. The number of individuals required to form new partnerships is given by the difference between the means (i.e., 1.1 – 0.9 = 0.2 in this example) multiplied by the number of individuals in that gender-age group (i.e., the number of males aged 20-29). This number of individuals is then randomly selected from the list that contains all individuals eligible to seek partners in the current cycle (i.e., from List item I. described above). The process is repeated for all gender-age groups, which form a collection of individuals who will seek partners at time *t*.

Once the collection is established, individuals are then paired based on their pre-defined preferred partner age range (see Table A1). Note that preferred partner age range is strictly enforced in this model, such that an individual cannot form a partnership unless there is a potential partner of opposite gender that has age within the preferred age range.

Finally, partnerships are formed between paired individuals, and partnership specific behaviour is set. Refers to Section 3.3, “Setting Partnership” for more details.

3.2. Example 2: partnership dissolution

Alternatively, if at time step *t*, the mean number of partners in the last 12 months for a specific gender-age group in the population is greater than the value specified in Table A2, then some partnerships need to be dissolved in order to reduce the mean. The number of partnerships to be dissolved will again be the differences between the means multiplied by the number of individuals in that gender-age group. Individuals are then randomly selected from the list containing all individuals who have a current partner (i.e., List item II. described above). One partnership from each selected individual is then dissolved, with priority given to the partnerships with earliest expiry date (defined as the time when the partner is formed plus the duration of partnership, see Section 3.3, “Setting Partnership”) if the selected individual was in more than one partnership.

3.3. Setting Partnership Behaviour

The duration of a partnership is determined at the time of partnership formation. The duration is calculated as the average of two lengths (one from each gender) generated under the probabilities listed Table A3, which is based on the duration of partnerships reported in ASHR2.(2) Note, however, that the exact duration of partnerships is not strictly enforced in this model, as it is possible for a partnership to end prematurely under the partnership dissolution process described above.

Table A3: Distribution of the duration of partnerships at the formation of partnership, based on data from ASHR2

Duration of partnership	**Males**	**Females**
0 - 1 year	10.2%	8.4%
1 - 3 years	6.2%	7.3%
3 - 6 years	11.2%	11.2%
6 - 11 years	15.7%	15.8%
11 - 20 years	22.7%	22.9%
20 - 60 years	34.0%	34.4%

The probability of condom being used during sex is also determined at the formation of partnership. The probability varies based on the partners' age at the formation of partnerships, and corresponds to the condom usage reported by ASHR2 listed in Table A4.(3) For example, if a male of age 25 forms a partnership with a female of age 18, then the probability of condom being used in the partnership will be set to 73.4% or 85.0% (with equal probability).

Table A4: The proportion of sexual acts in which condoms are used, based on data from ASHR2.

Age group	**Male**	**Female**
16 - 19	86.5%	85.0%
20 - 29	73.4%	62.4%
30 - 39	47.6%	37.7%
40 - 49	26.7%	22.7%
50 - 59	16.8%	8.1%

3.4. Sexual Acts

Sexual acts (required for transmission of infection) occur between two individuals within an existing partnership. In the model, the frequency of acts is based on the number of sexual acts per week reported in ASHR2,(1) and as listed in Table A5.

Table A5: Frequency of sexual acts per week, from ASHR2

Age group	**Male**	**Female**
16 - 19	1.97	1.88
20 - 29	2.16	1.99

30 - 39	1.39	1.43
40 - 49	1.36	1.37
50 - 59	1.15	1.20

The likelihood of a sexual act occurring within a partnership is based on the age and gender of those involved. For example, in a partnership between a male of age 25 and female of age 18, the per-day probability of a sexual act occurring is 2.16/7 = 0.309 for the male partner and 1.88/7 = 0.269 for the female partner. Two random numbers are generated by sampling from a uniform distribution in the range [0,1], and a sexual act occurs if the first number is less than 0.309, or if the second number is less than 0.269.

Finally, a third uniformly distributed random number (range [0,1]) is generated, and a condom is used for that act if that number is less than the partnership-specific condom usage assigned at formation of the partnership. We assume condoms are 100% effective at preventing transmission/acquisition of infection.

4. Transmission

Infection parameters are sampled from probability distributions as listed in Table A6. For example, the per-act probability of transmission from an infectious male to a susceptible female is sampled from a beta distribution with mean of 0.16 and standard derivation of 0.1. The transmission probability is sampled and assigned on a per-simulation basis, such that the same transmission probability is used for all sexual acts within a single simulation but is resampled for each simulation (and thus will vary between simulations).

When a sexual act occurs between an infectious individual and a susceptible individual, a random number (from uniform range [0,1]) is generated, and transmission of infection to the susceptible individual is deem successful if that number is less than the transmission probability assigned for the simulation. Similarly, the probability of developing symptoms is assigned on a per-simulation basis by sampling from the respective probability distributions for males and females. Conversely, the duration of each of the stages of infection (latent, infected, and immune) is sampled from the respective distributions and assigned on a per-infection basis.

Table A6: Chlamydia transmission and infection parameters and their respective sampling distributions. U (l, u) denotes a uniform distribution with lower limit of l and upper limit of u; β (m, σ) denotes a beta distribution with mean of m and standard deviation of σ; Γ (m, σ) denotes a gamma distribution with mean of m and standard deviation of σ.

Parameter	**Distribution**	**Source**
Probability of developing symptoms		
Male	β (0.30,0.15)	(4, 5)
Female	β (0.15,0.08)	(4, 5)
Duration of latent period (days)	U (12,28)	(5-7)
Duration of asymptomatic infection in the absence of treatment (days)	Γ (433,7)	(8)
Duration of symptomatic infection in the absence of treatment (days)	Γ (433,7)	(8)
Duration of immunity following recovery (days)	Γ (45, 15)	Assumption
Proportion immune after cure	0.5	(4)
Transmission probability per sexual act		

Male to Female	β (0.16, 0.10)	Calibrated based on (4)
Female to Male	β (0.12, 0.04)	Calibrated based on (4)

It was reported in ACCEPt 5% and 9% of participating non-virgin boys and girls aged 16 years, respectively, were infected with chlamydia, and that 40% of population has sexual experience at or before age 16. In our model it is assumed that 2% (40% of 5%) of males and 4% (40% of 9%) of all females will already be infected by the age of 16 years.

5. Chlamydia Testing Coverage

All scenarios investigated in this study assume that a proportion of the population will be tested annually for chlamydia. Testing coverages are set to match with the testing coverage achieved in the ACCEPt control arm in Scenario A, and to match with the testing coverage achieved in the ACCEPt intervention arm in Scenario B, C and D.(9) The testing coverage achieved in ACCEPt, as well as the scenarios for which they are applied, are listed in Table A7. For all scenario, testing coverage beyond fourth year is the same as the coverage at the fourth year.

Table A7: Annual chlamydia testing coverage for all the scenario included in the manuscript.

	ACCEPt control arm (Scenario A)		**ACCEPt intervention arm (Scenario B, C, D)**	
Year	**Male (%)**	**Female (%)**	**Male (%)**	**Female (%)**
0-1	8.2	18.0	8.7	17.7
1-2	5.8	15.2	8.4	18.5
2-3	6.6	15.5	12.4	24.3
3-4	7.3	17.0	12.6	25.5

6. Simulation Selection and Model Calibration

The model is calibrated to age-specific chlamydia prevalence data by adjusting partner acquisition rates (with initial value based on those reported in ASHR2 (1) (see Table A2), and gender-specific per-act transmission probabilities (see Table A6).

Calibration was carried out by adjusting the mean partner acquisition rate (as described by the mean number of partners in last 12 months for each age group, see Table A2) and the mean transmission probability (see Table A6), with the aim of matching the output from model simulations with the prevalence observed in the ACCEPt baseline prevalence survey (see Table 2 in the main text). A brief description of the process follows.

We define the objective function, $f(\mathbf{x})$, as the sum of squared differences between the gender and age-specific prevalences produced by 32 model simulations under parameters x and the prevalences measured in the ACCEPt.

Using a Nelder–Mead simplex algorithm as described by Lagarias et al.(10), we adjust $\mathbf{x}$ accordingly with the aim of reducing $f(\mathbf{x})$ toward zero.
Model calibration stops when the differences in prevalences between the current and previous generation of parameter fits is less than the differences in prevalences generated by the model in the previous generation of parameter fits.

Note that the inferred parameter values (i.e., $\mathbf{x}$ as described above) do not represent the values used in the selected simulations. Instead, they serve as the target values to which the model aims towards (the mean number of partners in the last 12 months), or the scalar representations of the distribution of which simulation parameters are drawn from (the mean transmission probability).

For the scenarios describing ACCEPt control and intervention arms (i.e., Scenario A and B in the main text), the results of 100 simulations were to be included in this study. The simulations were selected from 1000 simulations generated that have the chlamydia prevalence amongst sexually active individuals (defined as having at least one sexual partner in lifetime) of aged 16-29 years matching closest (defined as having smallest square differences) to the prevalence reported in survey 1 and 2 from of ACCEPt.(9) The non-scenario specific parameters (e.g. the seed for the random number generator that govern partnership formations) from selected simulations from Scenario B were then reused to generate simulations for other scenarios. Note that as the simulation selection process will prioritise simulations that best match the baseline prevalence estimated from the control and intervention arms of ACCEPt, simulations that mirror the decline in in prevalence in both arms of ACCEPt are more likely to be included in the final results.

While the focus of this study is to examine the impact of the interventions, selected outputs were extracted from the base model to enable comparison with other models, or to compare with relevant data should they become available. As suggested by Althaus et al.,(11) we have generated the Lorenz curve and associated Gini coefficient from the base model, which is shown in Figure A1. While equivalent data is not available through ASHR2, our estimates are consistent with those estimated from other models and data as described in Althaus et al. The estimated value of the Gini coefficient in our model is 0.34, which is similar to the value of 0.38 estimated from a population-based survey of sexual attitudes and lifestyles in Britain (Natsal 2000).(12)

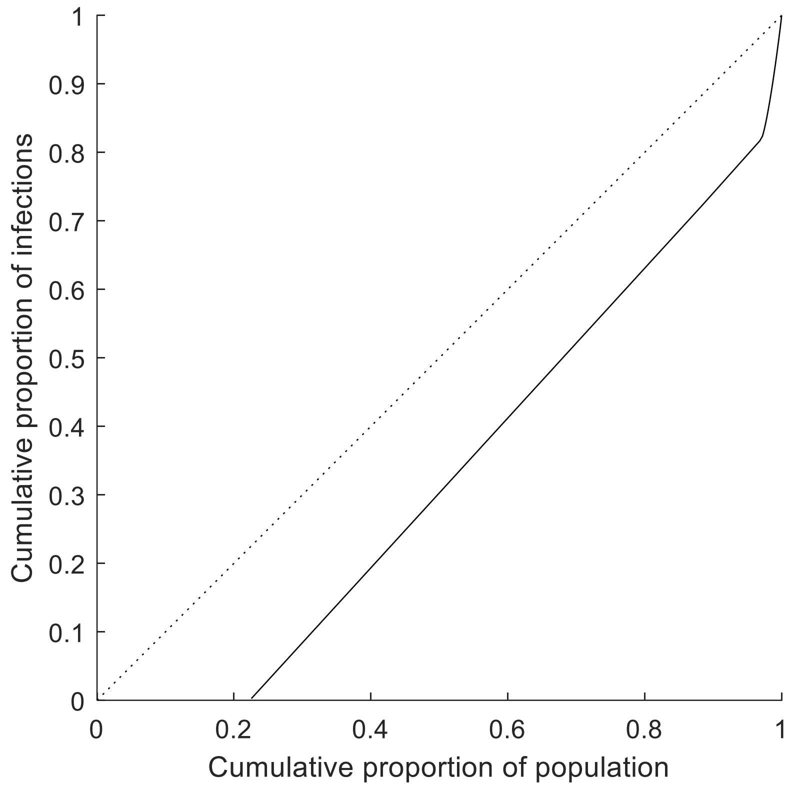

Figure A1: Lorenz curve representing the cumulative proportion of infections as a function of the cumulative proportion of the population, after individual are ranked based on their number of sexual partners in last 12 months. The dotted line is the line of equality. The Gini coefficient is 0.34.

7. References

1. Rissel C, Badcock PB, Smith AMA, Richters J, de Visser RO, Grulich AE, et al. Heterosexual experience and recent heterosexual encounters among Australian adults: the Second Australian Study of Health and Relationships. Sexual health. 2014;11(5):416-26.

2. Badcock PB, Smith AMA, Richters J, Rissel C, de Visser RO, Simpson JM, et al. Characteristics of heterosexual regular relationships among a representative sample of adults: the Second Australian Study of Health and Relationships. Sexual health. 2014;11(5):427-38.

3. de Visser RO, Badcock PB, Rissel C, Richters J, Smith AMA, Grulich AE, et al. Safer sex and condom use: findings from the Second Australian Study of Health and Relationships. Sexual Health. 2014;11(5):495-504.

4. Johnson LF, Alkema L, Dorrington RE. A Bayesian approach to uncertainty analysis of sexually transmitted infection models. Sexually Transmitted Infections. 2010;86:169-74.

5. Korenromp EL, Sudaryo MK, De Vlas SJ, Gray RH, Sewankambo NK, Serwadda D, et al. What proportion of episodes of gonorrhoea and chlamydia becomes symptomatic? International Journal of STD & AIDS. 2002;13(2):91-101.

6. Kretzschmar M, Satterwhite C, Leichliter J, Berman S. Effects of screening and partner notification on Chlamydia positivity in the United States: a modeling study. Sex Transm Dis. 2012;39(5):325-31.

7. Regan D, Wilson DP, Hocking JS. Coverage is the key for effective screening of Chlamydia trachomatis in Australia. Journal of Infectious Diseases. 2008;198(3):349-58.

8. Althaus CL, Turner KME, Schmid BV, Heijne JCM, Kretzschmar M, Low N. Transmission of Chlamydia trachomatis through sexual partnerships: a comparison between three individual-based models and empirical data. Journal of Royal Society Inferface. 2011.

9. Hocking JS, Temple-Smith M, Guy R, Donovan B, Braat S, Law M, et al. Population effectiveness of opportunistic chlamydia testing in primary care in Australia: a cluster-randomised controlled trial. Lancet. 2018;392(10156):1413-22.

10. Lagarias JC, Reeds JA, Wright MH, Wright PE. Convergence properties of the Nelder-Mead simplex method in low dimensions. Siam J Optimiz. 1998;9(1):112-47.

11. Althaus CL, Turner KM, Schmid BV, Heijne JC, Kretzschmar M, Low N. Transmission of Chlamydia trachomatis through sexual partnerships: a comparison between three individual-based models and empirical data. Journal of the Royal Society, Interface / the Royal Society. 2012;9(66):136-46.

12. Johnson AM, Mercer CH, Erens B, Copas AJ, McManus S, Wellings K, et al. Sexual behaviour in Britain: partnerships, practices, and HIV risk behaviours. Lancet. 2001;358(9296):1835-42.