

## Technical Appendix

### Effects of screening and partner notification on chlamydia positivity in the United States: a modelling study

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#### Model structure

We describe the model structure and assumptions, for more background information we refer the reader to earlier publications about our modeling approach (1-4). For modeling chlamydia transmission dynamics, a simulation model was used that describes pair-formation and -dissolution as well as transmission of infection as stochastic processes. The model describes a heterosexual population of 15 to 64 years. Individuals are characterized by age, sex, sexual activity (high/low), status of infection (not infected, symptomatic infection, asymptomatic infection), time since infection, number and identities of partners. A distinction was made between steady and casual relationships regarding the duration of the relationship and the frequency of sexual contacts during the relationship. In the younger age groups (15-34 years), a subset of the population is defined as the “core group” with higher numbers of partners. In the simulations reported here, the transmission probability of chlamydia infection is assumed to be equal between males and females. The recovery rate differs between the two sexes and depends on whether the infection is symptomatic or not.

More specifically, the model is an individual based stochastic simulation model with discrete time steps. The population is defined as an array of vectors, where the elements of the vector are variables keeping track of the status of the individual. In every time step events are generated according to probability distributions that define the probabilities of birth and death, formation and separation of partnerships, and disease transmission.

#### *Demography*

The population has a uniform age distribution in 1 year age classes in the age range 15-64 years. Once a year ages of individuals are increased by one year. Those who are then older than 64 are replaced by individuals aged 15. All partnerships of those individuals are then dissolved. The newly entering individuals have no partners and are uninfected.

#### *Partnership formation and separation*

The partnership formation process is based on the assumption that the overall number of partnerships in the model is in a stochastic steady state. The steady state value is based on the mean value computed from the input parameters  $p$  (the partnership formation rate) and the  $\sigma$ 's (the partnership separation rates). The partnership formation process forms new partnerships according to this steady state value. For every newly formed partnership two

random individuals are chosen from the population, one male and one female, and the probability of formation of the partnership then depends on the characteristics of that pair (e.g. ages, current partners, sexual activity level). This process is repeated until the partnership is formed. Separation of partnerships occurs according to constant rates  $\sigma_1$  for steady and  $\sigma_2$  for casual partnerships (1, 5).

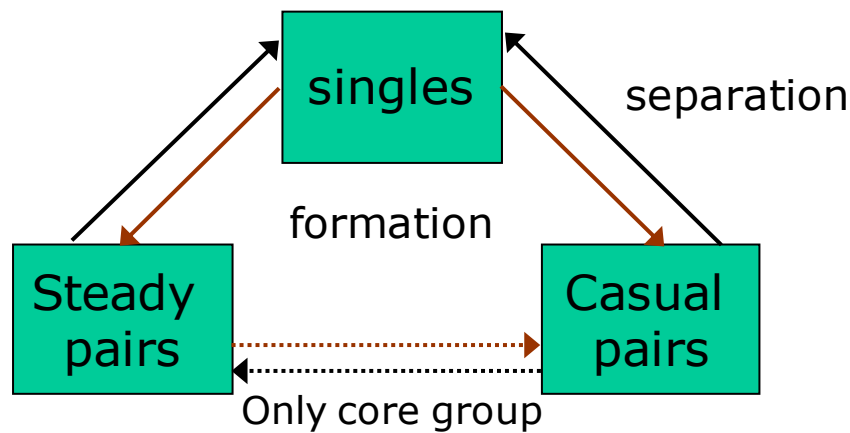


Figure A1: Flow diagram of the pair formation process.

#### *Transmission of infection*

Transmission of infection takes place within existing partnerships with a probability of 0.1 per day in casual partnerships and 0.025 per day in steady partnerships. The difference is based on the assumption that the frequency of sexual acts is higher in casual than in steady partnerships. We assume an average frequency of intercourse of 1 per day for casual and 0.25 per day for steady relationships.

#### *Screening, treatment and partner notification*

Screening in the model is implemented as follows. Every individual has a certain probability per day of seeking health care. If an individual seeks health care and belongs to the target group included in the screening program, he/she gets tested for chlamydia with probability  $p_t$ . If he/she tests positive, he/she accepts treatment with probability 95%. After a delay of 14 days he/she is treated effectively with probability 90%. The patients current partner(s) are notified with probability  $p_n$  and if notified get treated effectively with probability 90%.

The model was programmed in C and run on a Linux OS.

The model performs well in terms of summary parameters of sexual behavior and Chlamydia transmission (4). The model assumptions have been further scrutinized and we recently investigated how certain assumptions about individual sexual behaviour such as age at sexual debut influence summary measures such as the distribution of life time numbers of partners (Schmid & Kretzschmar; submitted manuscript). However, it should also be noted that the model was not built to reconstruct reality in all details or to make quantitative

predictions. Rather, our aim is to construct a simplified hypothetical population, in which chlamydial infections are transmitted and screening takes place. The aim is to understand better why various strategies have different effects and to compare their effects among each other. This means that we have calibrated the model to observed positivity before screening started, but we did not attempt to fit it to temporal trends of positivity or prevalence data that are subject to varying factors such as behavior change. One may use the model as an experimental reality, in which to observe the impact of various screening strategies in a controlled environment.

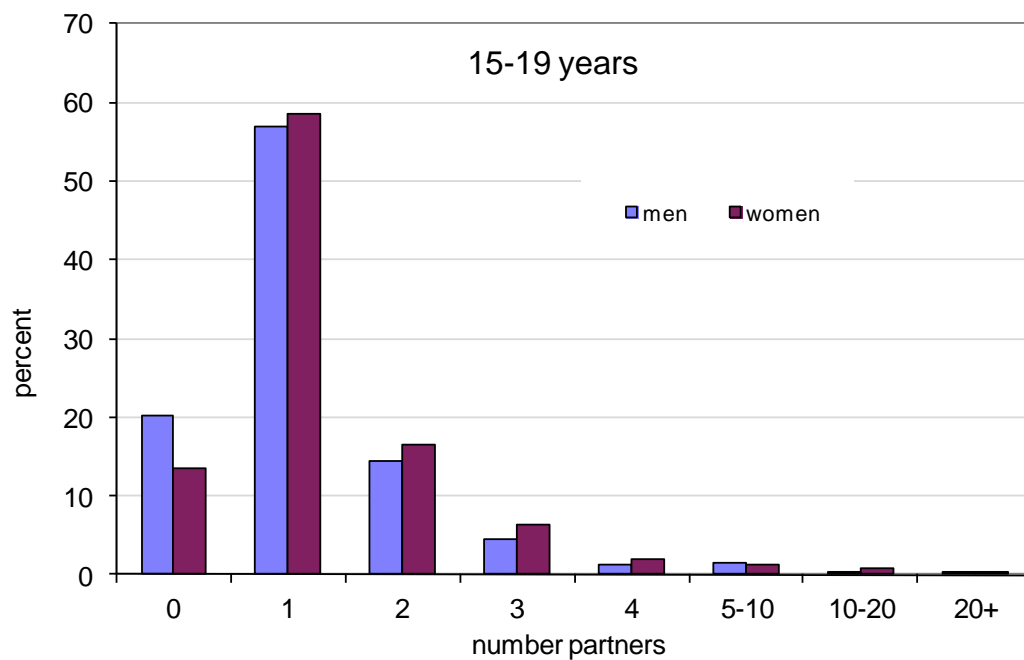
Table A1: Characteristics of individual-based stochastic simulation model of *C. trachomatis* transmission

Characteristic	model
Stochastic, SIS	Yes
Programming language	C
Simulation method	Discrete time step simulation, 1 day time steps. Events occur each day with probabilities assigned or drawn from distributions
Model population size	40000
Model population age	15-65 years, uniform distribution, 50% females, heterosexual only
Sexual activity levels	Two activity groups Core (around 5% of 15-30 year old women and 15-35 year old men); Non-core (95% 15-30 year old women and 15-35 year old men, 100% 35+ year old men and 30+ year old women)
Partnership formation	Heterosexual only; determined by sexual activity group, existing partnership status, age difference
Partnership duration	Mean 17 days for casual partnerships, 3.04 years (1111 days) for steady partnerships; both exponentially distributed
Concurrent partnerships	Core group can have a casual concurrent partner at same time as one steady partner; Non-core group has only one casual or steady partner at a time
Partner notification modeled explicitly	Yes
Model calibration	Sexual behaviour data (numbers of partners in last year, fractions of casual and steady partnerships, age mixing); NSFG data and Seattle sex survey; Chlamydia positivity data, Region X

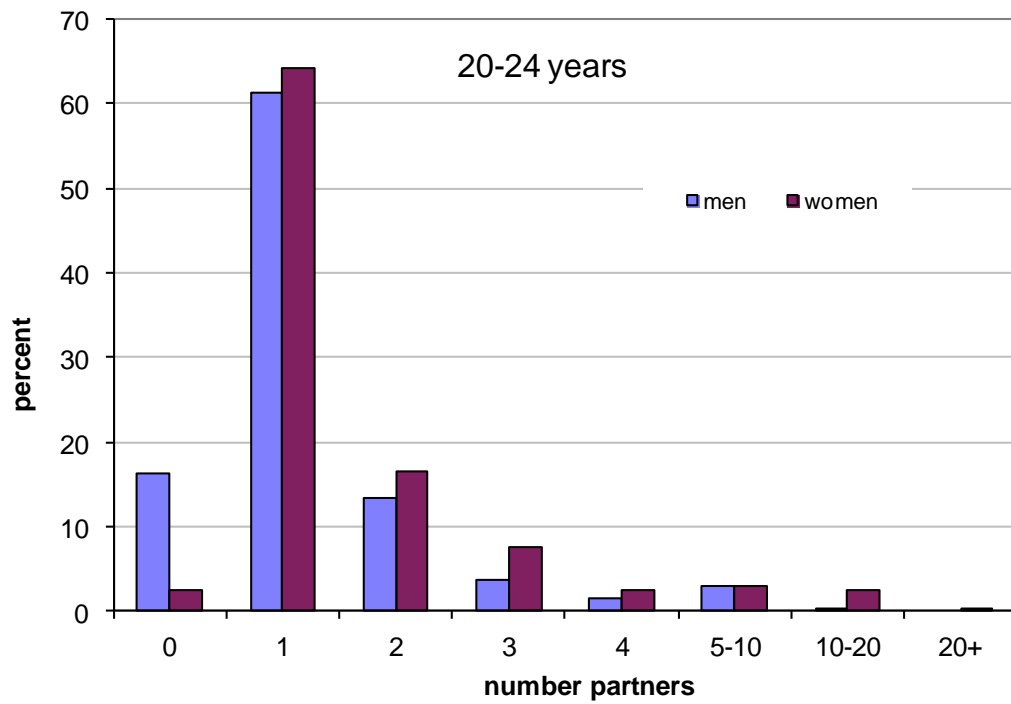
## Model parametrization

### *Numbers of partners*

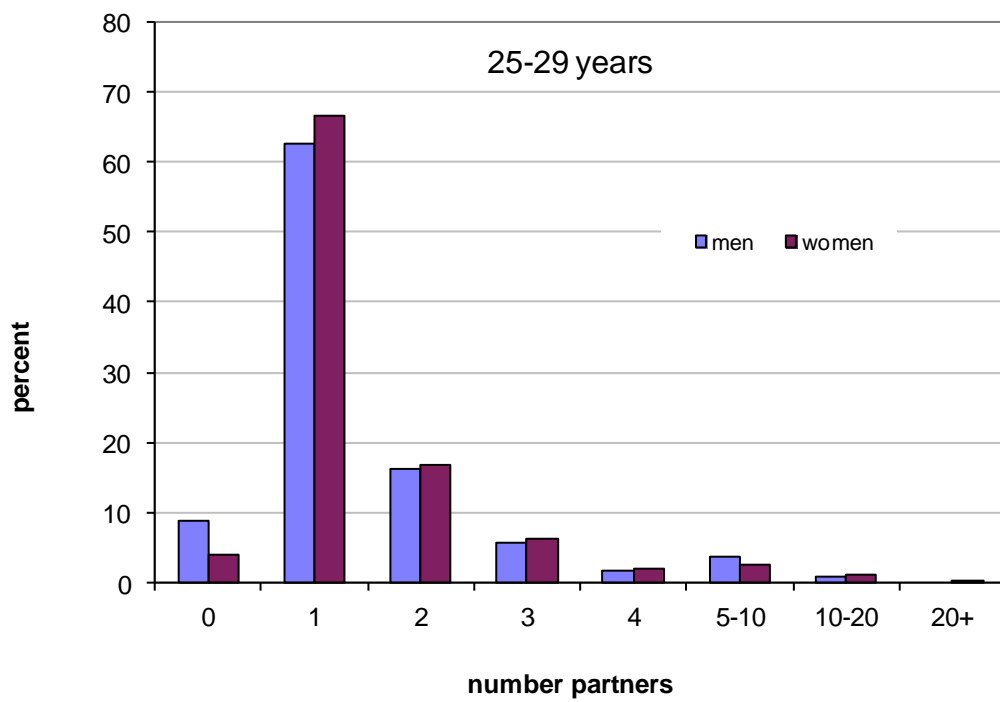
To parameterize the pair formation and separation process we used data from the National Survey of Family Growth (NSFG) a nationally-representative multistage area probability sample collected in 2002 (6). The survey data are based on 12,571 in-person interviews—4,928 with men and 7,643 with women. Participants were 15–44 years of age and in U.S. households. We used information about the number of (opposite-sex) sex partners in the last year stratified by age. We calibrated the model such that the numbers of partners in the last year in the model population reflected those of NSFG (Figure 1 of main text). The calibration was performed per 5-year age group (Figure A2). Numbers of partners fit well for each age group. Among 15-19 and 20-24 year olds, the fraction of persons with no partners is slightly higher in NSFG data than in the model. In the model population, age at first sex was lower than observed in the survey data, so the fraction of virgins in the younger age groups is much smaller. This does not impact our transmission dynamics, as prevalence in the sexually-active fraction of the population can easily be extrapolated to the total population.



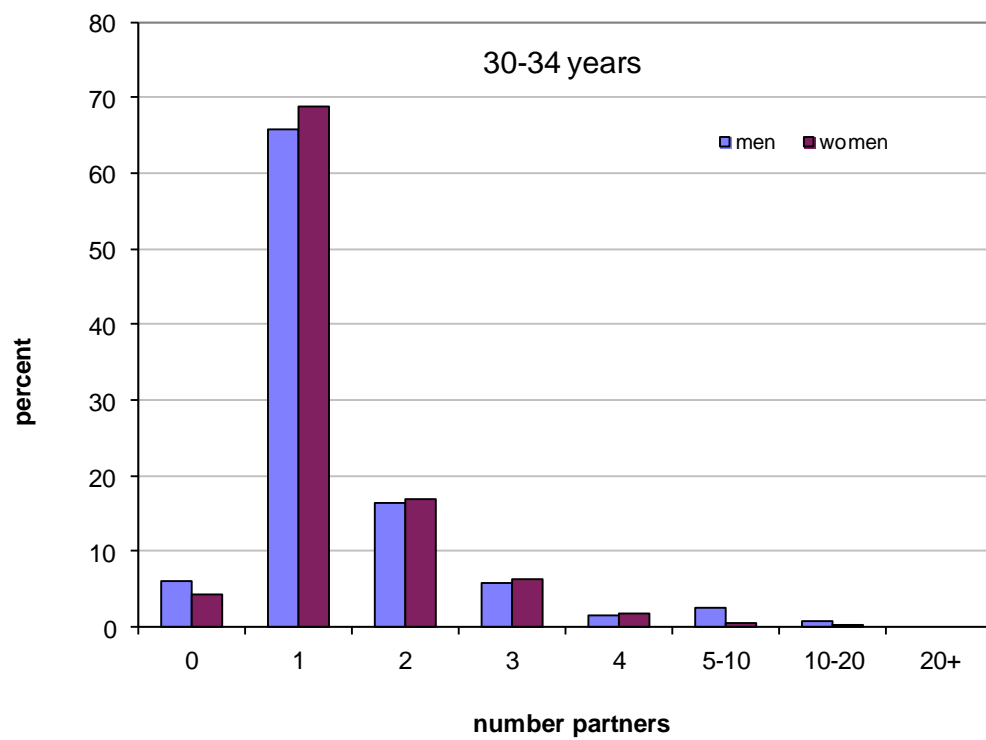
(a)



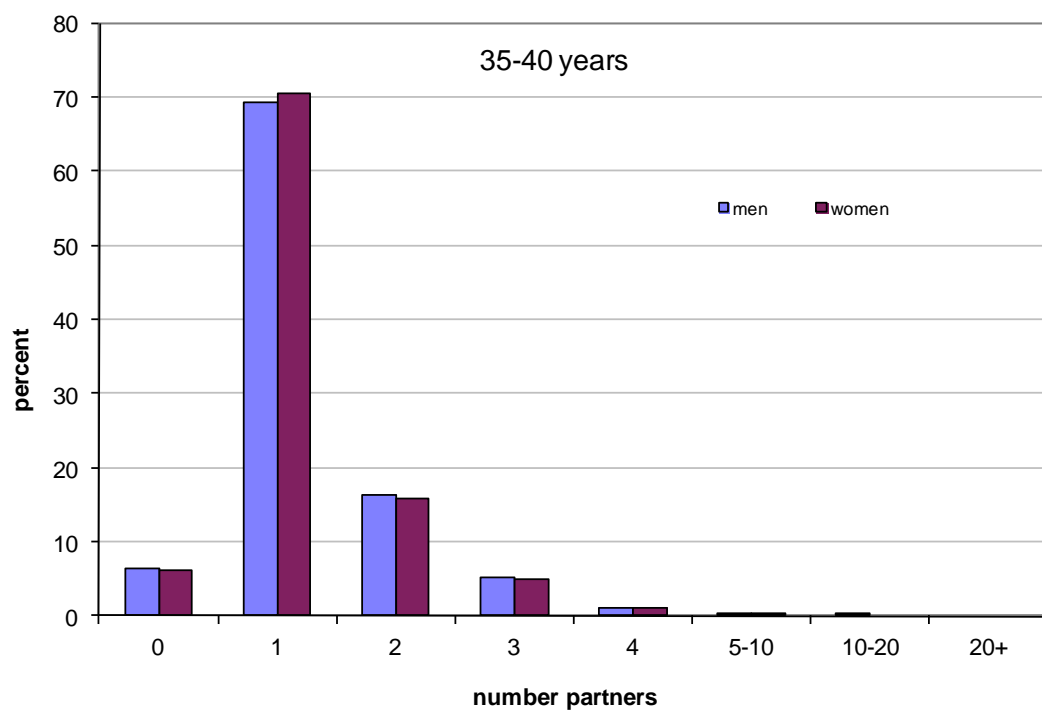
(b)



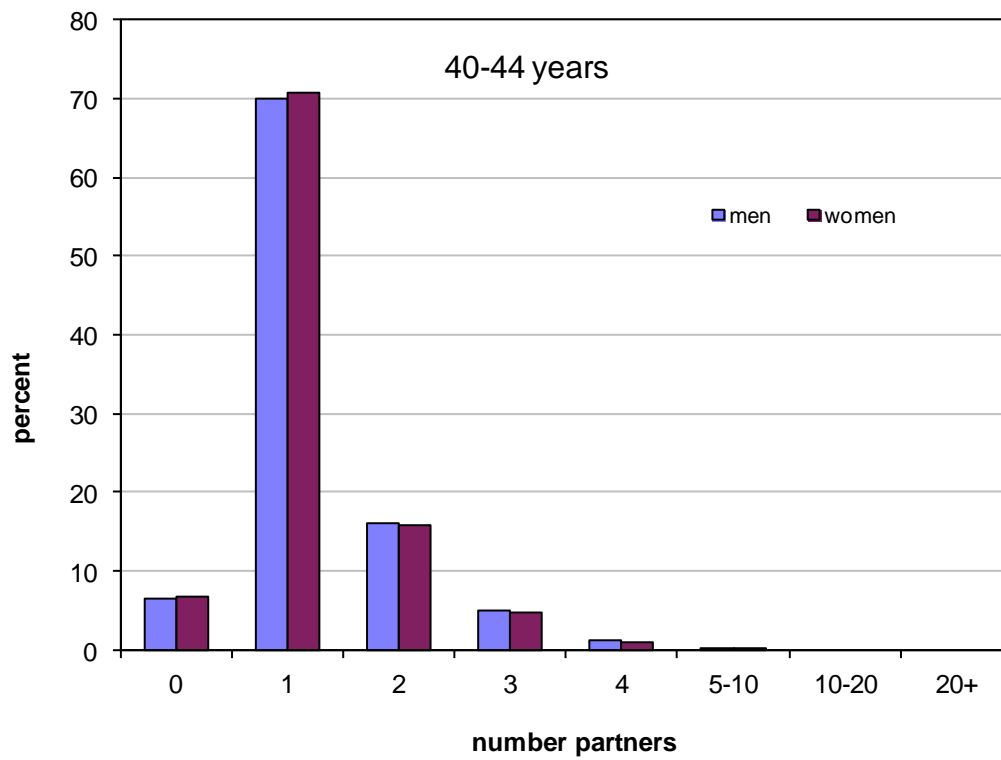
(c)



(d)



(e)



(f)  
Figure A2 (a-f): Number of partners in last 12 months for different age groups in the model population.

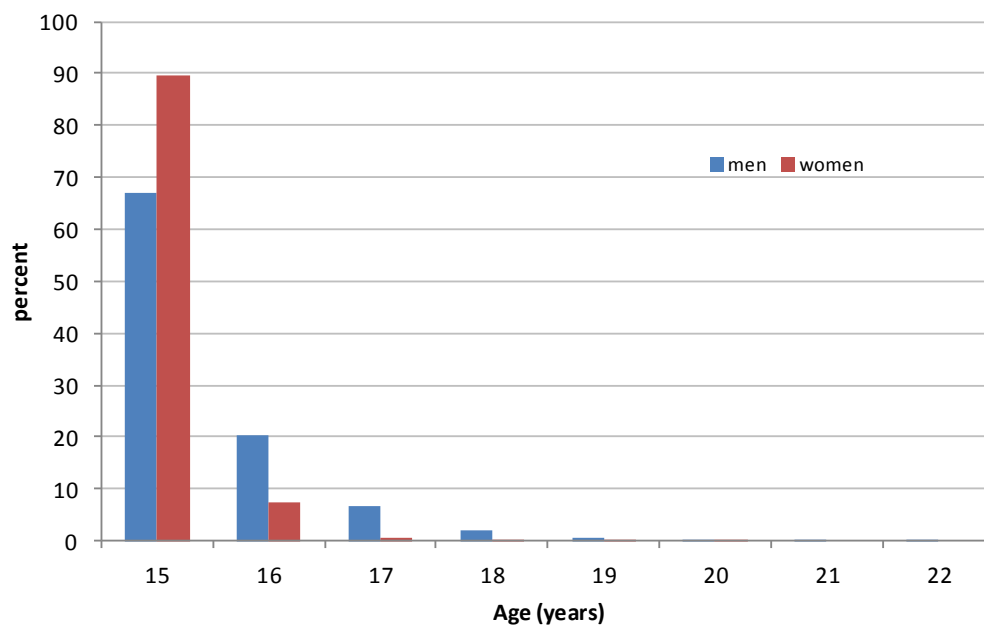


Figure A3: Age at first sex in the model population for males and females.

### Partnership duration

To estimate partnership durations, we used results from a telephone survey conducted in Seattle, Washington, in 2003-2004 (7). The fraction  $p(t)$  of partnerships surviving up to time  $t$  after partnership formation is calculated in the model as

$$p(t) = f \exp(-\sigma_1 t) + (1 - f) \exp(-\sigma_2 t)$$

with a fraction of steady partnerships  $f$ , a separation rate of steady partnerships  $\sigma_1$ , and a separation rate of short term partnerships  $\sigma_2$  (Table 1) (8). We fitted this function to the data shown in Figure 4 of (7) to obtain estimates for  $f$ ,  $\sigma_1$ , and  $\sigma_2$  (Figure A4).

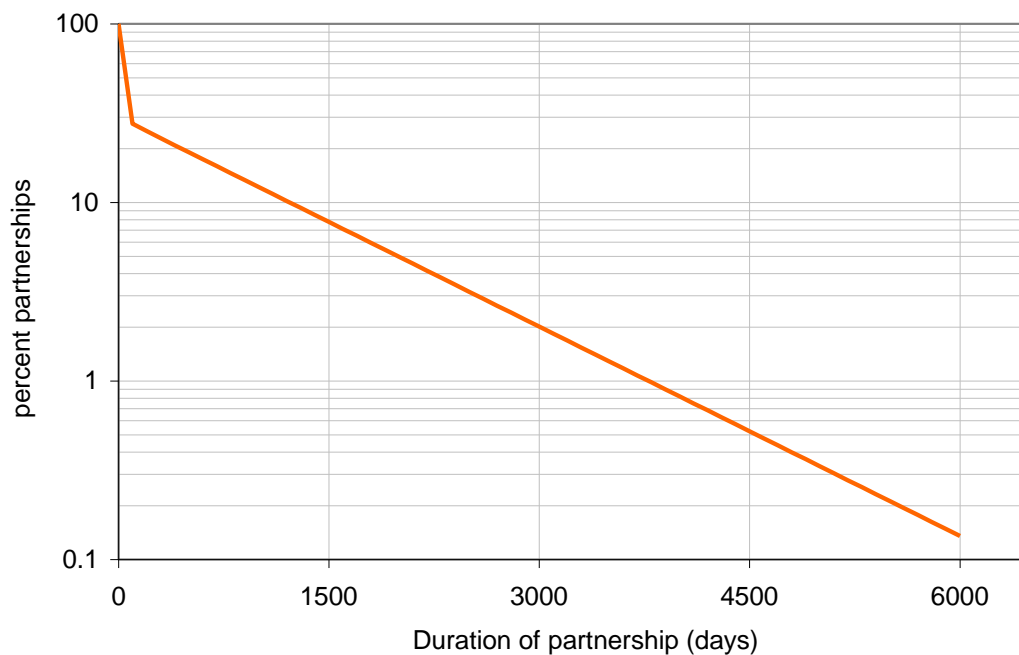


Figure A4: Survival distribution of partnerships with parameters as used in the model.

We also tried working with partnership durations depending on age at formation of partnership, but as the resulting distributions of number of partners led to a poorer fit of the NSFG data, we decided to stick with constant separation rates. Differences in partnership durations by age then arise naturally, because older individuals have had more time to spend in a partnership and therefore longer partnerships can only be observed in older individuals. This effect seems sufficient in the model to reflect observed partnership durations without an additional age dependent effect on separation rates. This decision is also supported by results in (9) showing little effect of age on formation and separation rates as estimated from the Seattle Sex Survey data.



## Core group

We assumed that 5% of the population starts their sexual activity in the highly active core group. This means that these individuals can have casual partners in addition to their steady partner and that their propensity to form casual partnerships is higher than for individuals who are not in the core. Core group membership lasts at least up to the age of 25 years for women and 30 years for men; after that age, there is a probability of 0.2 per year to leave the core group and move into the low-activity population. For those >30 and 35 years, respectively, all remaining core group members move to the low-activity population. We assume that all individuals have at most one steady long term partner. During such partnerships, core group members can form concurrent casual partnerships. In the model population, women have a higher probability of forming a new partnership with an older man than with a younger man (see figure A5); most partnerships of women are with a partner of their own age group or with a partner of an older age group (10). Figure A6 shows the numbers of partners in the last year for the individuals in the core population. The asymmetry between men and women is apparent with core women having higher partner numbers than core men. This asymmetry is caused by the age mixing between men and women. It is possible that core group members have only few partners in a given year simply by chance.

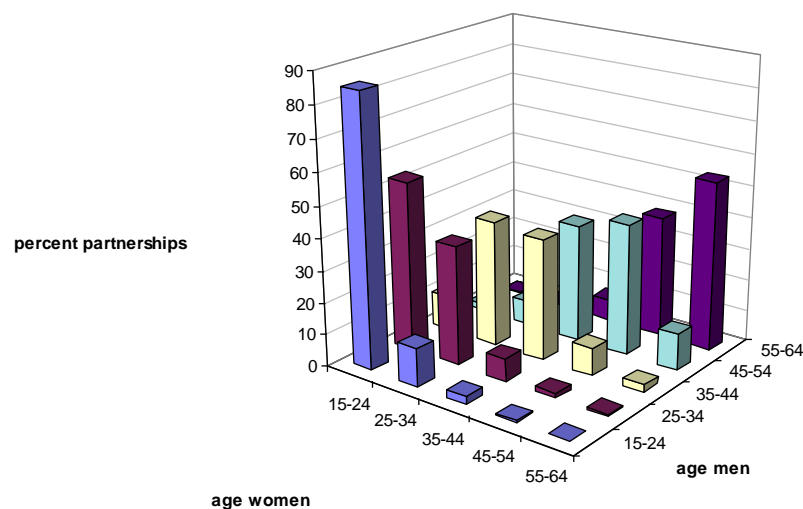


Figure A5: Mixing by age in the model population.

Parameter choices for the natural history of Chlamydia infection and transmission probabilities are shown in Table 2. The estimate for the transmission probability was taken from (2), the fraction of asymptomatic infections from (11), the duration of asymptomatic infections in women from (12). The durations of symptomatic infection were estimated based on information on latent period and patient delay (1). Given these parameter values Chlamydia infection will not remain restricted to the core group, but will be pervasive in the low risk population as well (1).

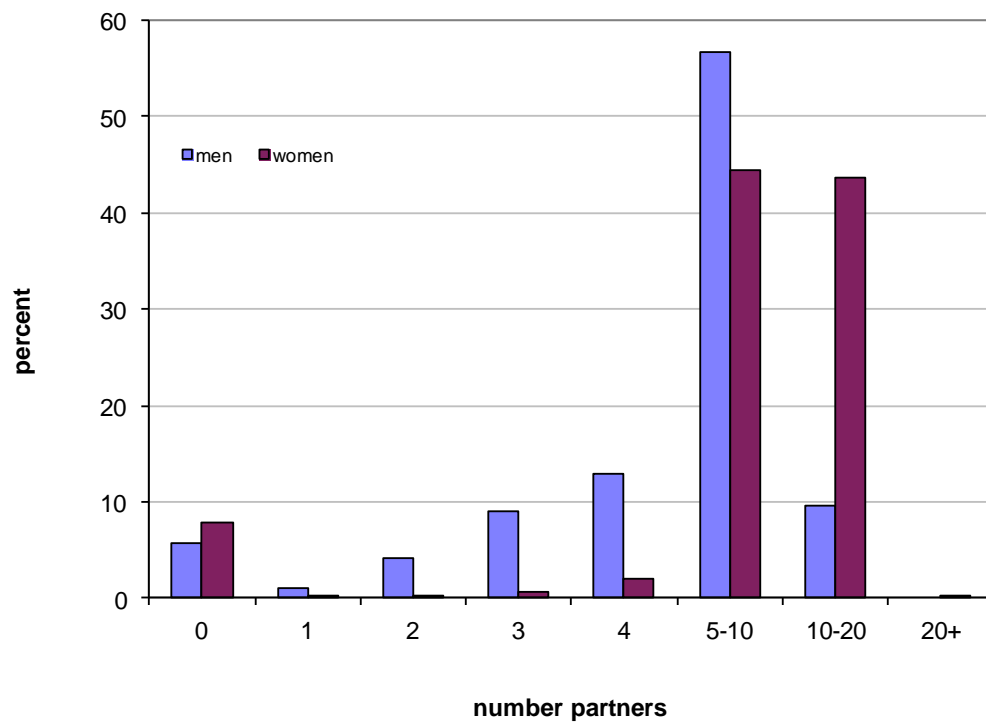


Figure A6: Number of partners in the last 12 months for men and women of the core group.

Table A2: Probabilities of heterosexual transmission of *C. trachomatis*, coital frequency, level of asymptomatic infection, and duration of infection (11, 12).

Parameter	Value
Male–Female, probability per sex act	0.1
Female–Male, probability per sex act	0.1
Frequency of sex acts	1/day casual; 0.25/day steady
Proportion with symptomatic infection	
Men	0.30
Women	0.15
Duration asymptomatic infection (mean in days)	
Men	200
Women	370
Duration symptomatic infection (mean in days)	
Men	33
Women	40

### ***Chlamydia positivity and prevalence***

We used positivity data collected from family planning clinics participating in the Infertility Prevention Project (IPP) (13). In view of the fact that the most complete set of information about a variety of parameters was available for Region X, we focused on positivity data from that area and compared model simulation results with estimates from that area. Positivity reflects the occurrence of chlamydia infections only in that part of the population that undergoes testing. Prevalence in the general population may differ substantially from positivity; however, we chose to model positivity rates instead of prevalence assuming that the population participating in screening does not change over the modeled time period. Therefore, in the model we equate positivity with prevalence. To obtain population prevalence from these positivity rates requires information about the population participating in the particular health care and family planning centers that provided the positivity data. We did not have this information for this study.

If we look at the distribution of numbers of partners of infected persons in the situation with baseline screening (figure A7), we see that clearly many infected persons have high numbers of partners (5+), but there is also a substantial fraction of infected persons with only 1 partner in the last year. This reflects the distribution of Chlamydia infections also in the low risk “general” population. In the uninfected part of the population the fraction of highly active individuals is small. Chlamydia prevalence increased with increasing number of partners (Figure A8).

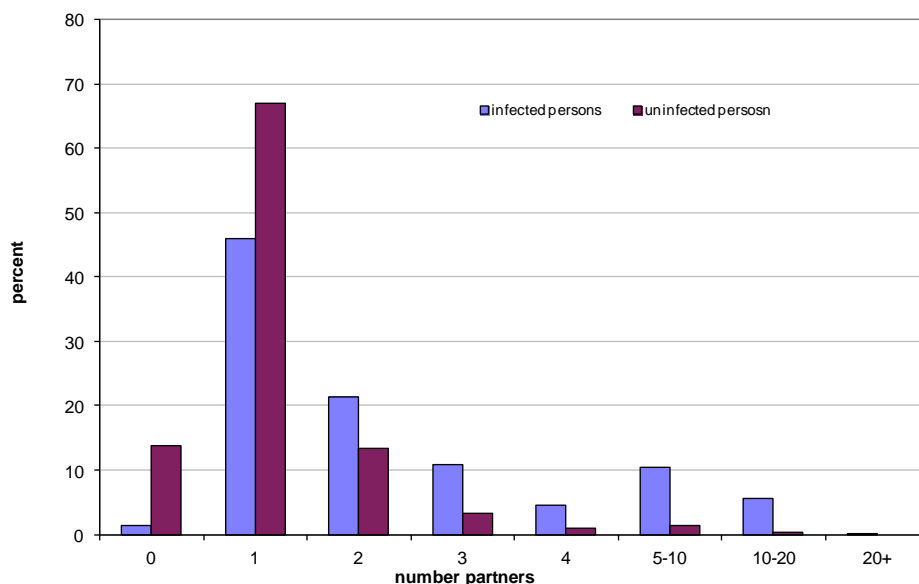


Figure A7: Numbers of partners in last 12 months for infected and uninfected individuals at the end of the simulation period in the baseline scenario..

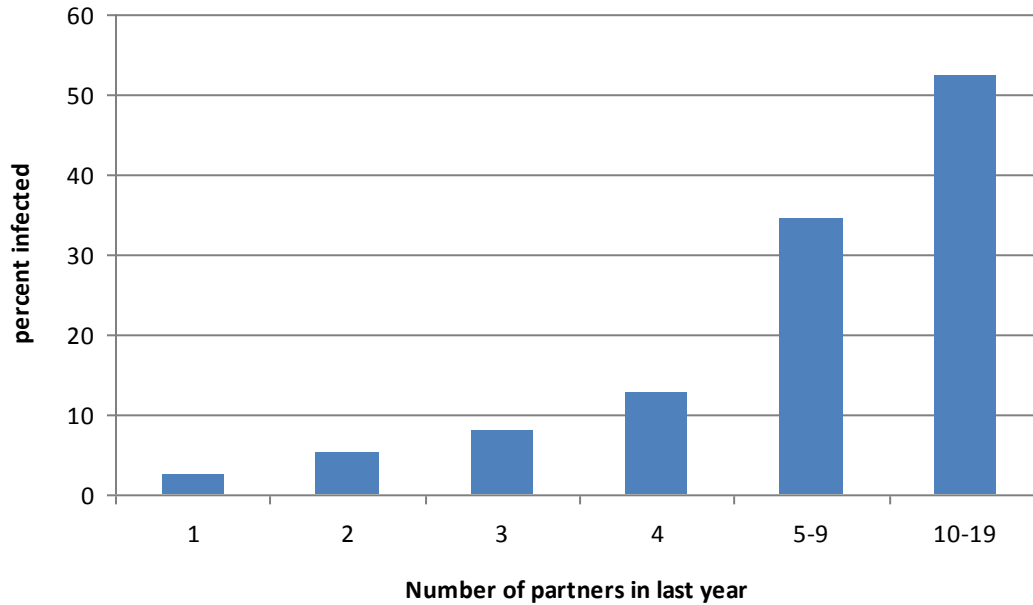
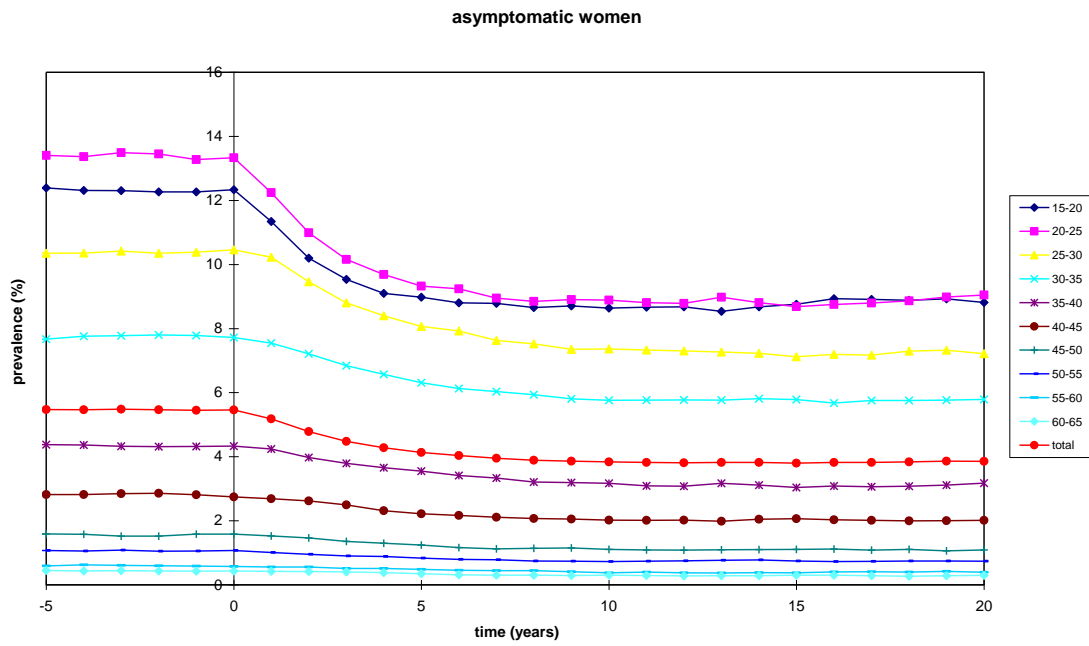


Figure A8: Prevalence by number of partners in last 12 months.

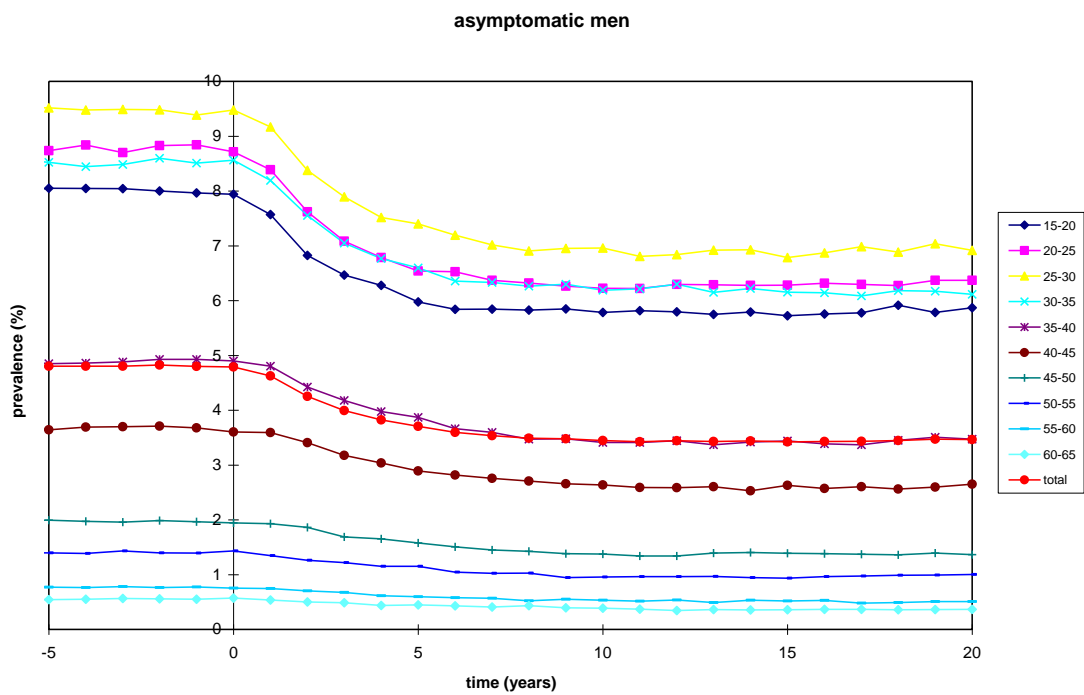
Parameter choices for screening parameters are shown in table A3, where the testing probability and partner notification rates are given for the baseline scenario. All other parameters remain unchanged in all simulations shown here. Figure A9 shows the prevalence in different age groups for the baseline screening scenario for women and men, respectively. Before screening the highest prevalence is observed in women aged 20-24, later on prevalence in the youngest age group 15-19 is at the same level. In men, prevalence peaks at somewhat older age of 25-30 years.

Table A3: Parameters associated with screening and treatment for *C. trachomatis*

Parameter	Baseline value
Probability per year of getting tested $p_t$	20%
Test sensitivity	90%
Compliance with treatment	95%
Effectiveness of treatment	90%
Partner notification in individuals identified through screening (% of current partners) after introduction of intervention	
Partners of women $p_n$	25%
Partners of men $p_n$	25%
Notified partners treated effectively	90%



(a)



(b)

Figure A9: (a) Prevalence of asymptomatic infection in women in all age groups for the baseline screening scenario. (b) Prevalence of asymptomatic infection in men in all age groups for the baseline screening scenario.

### Effects of decreasing coverage or partner notification

To investigate what the effects would be of a diminishing effectiveness of the present screening program we performed simulations in which either coverage or partner notification rate or both changed to less favorable values after 10 years of baseline screening. For both decreasing coverage and decreasing partner notification Chlamydia prevalence increased again in the second decade of screening. The increase was stronger for decreasing partner notification rate. If coverage increased to 35% but the rate of partner notification decreased to 10% the overall result was still a loss in effectiveness of the baseline screening program and increasing chlamydia prevalence.

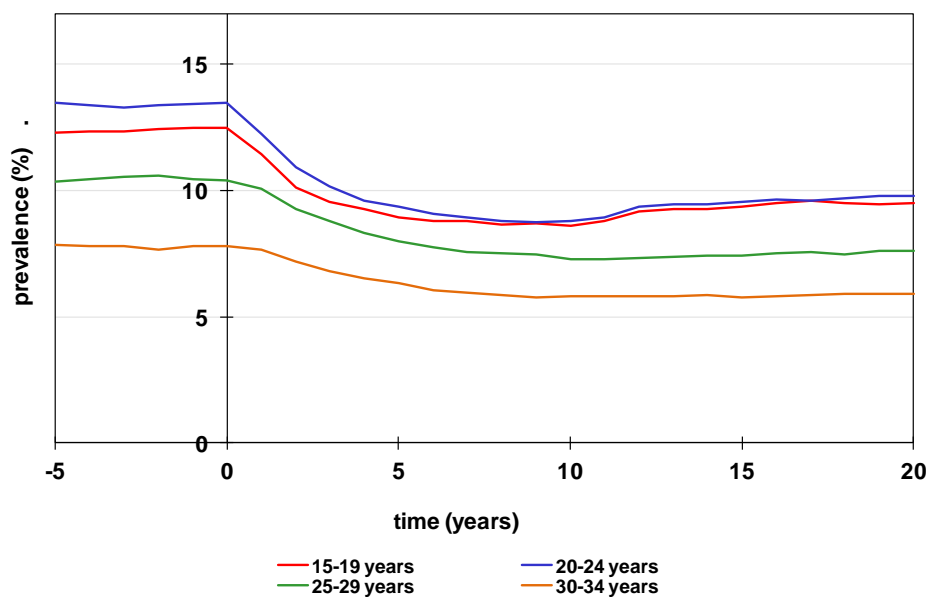


Figure A10: After 10 years of screening with a coverage of 20% the coverage drops to 10%. As a result the prevalence of chlamydia starts rising, especially in the two youngest age groups that are targeted by screening.

A general observation is that while the gains of introducing screening and partner notification and treatment at first have a large impact on Chlamydia prevalence, changing the parameters of screening after 10 years has only marginal impact. As we lack specific information about the distribution of Chlamydia infection before the introduction of large scale testing and treatment, it is also difficult to assess how well the model describes that prescreening situation. Age-prevalence distributions as observed in recent studies may not reflect distributions of 20 years ago as screening and treatment obviously impacts on those distributions. Observing different positivity rates in different age groups is also a result of differential screening uptake rates in different age groups. Here we are mainly interested in possible changes of positivity or prevalence after increasing or decreasing coverage and/or partner notification during an ongoing screening program. We do not aim at predicting the absolute impact of the complete screening program conducted over several decades.

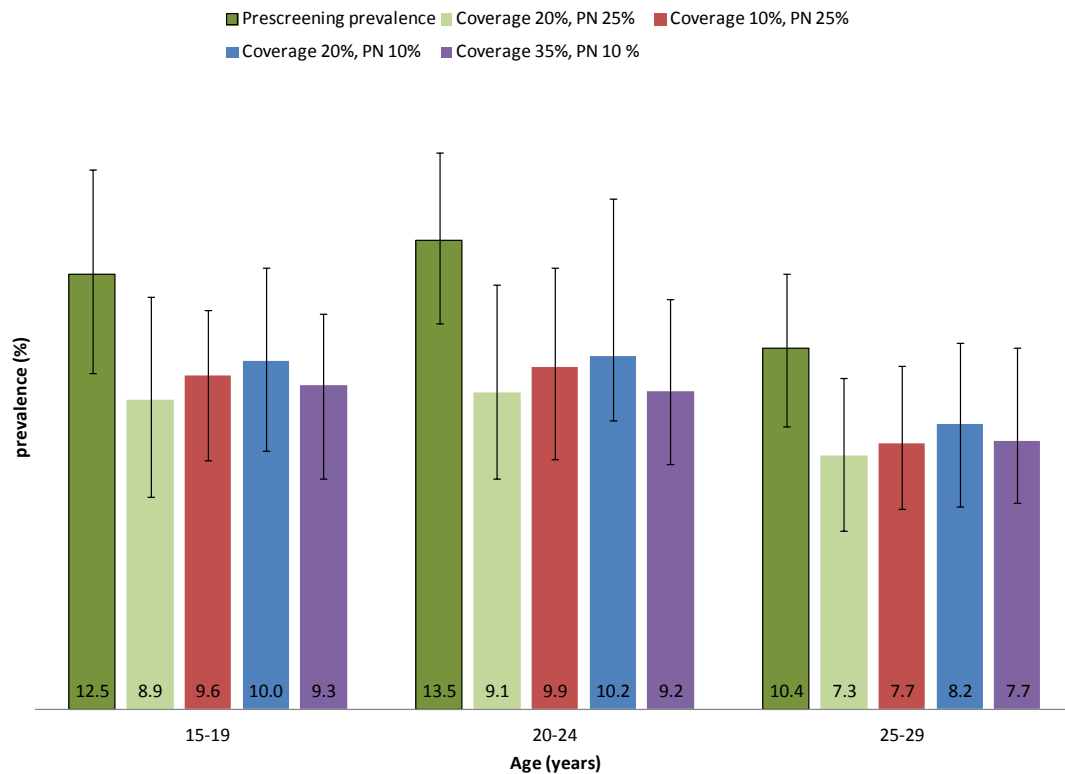


Figure A11: The light green bar shows the prevalence after 20 years of baseline screening. The other bars show the results of the screening becoming less effective after 10 years. The largest increase is seen if partner notification drops from 25% to 10% after 10 years.

### Alternative simulations

To see the impact of different baseline assumptions on partner notification and treatment rates, we present results of a similar set of simulations based on another choice of parameter values. We assumed here that 70% of infections in women and 50% infections in men are asymptomatic (so fewer asymptomatic infections than in the results in the main text). Screening is continued for 20 years and as before, prevalence levels at the end of 20 years screening are compared with pre-screening levels. Here we start with a baseline screening coverage of 35% and partner notification levels of 10% and 50%. In both sets of simulations one observes that increasing coverage has marginal effects, while increasing partner notification rates is more effective in reducing prevalence.

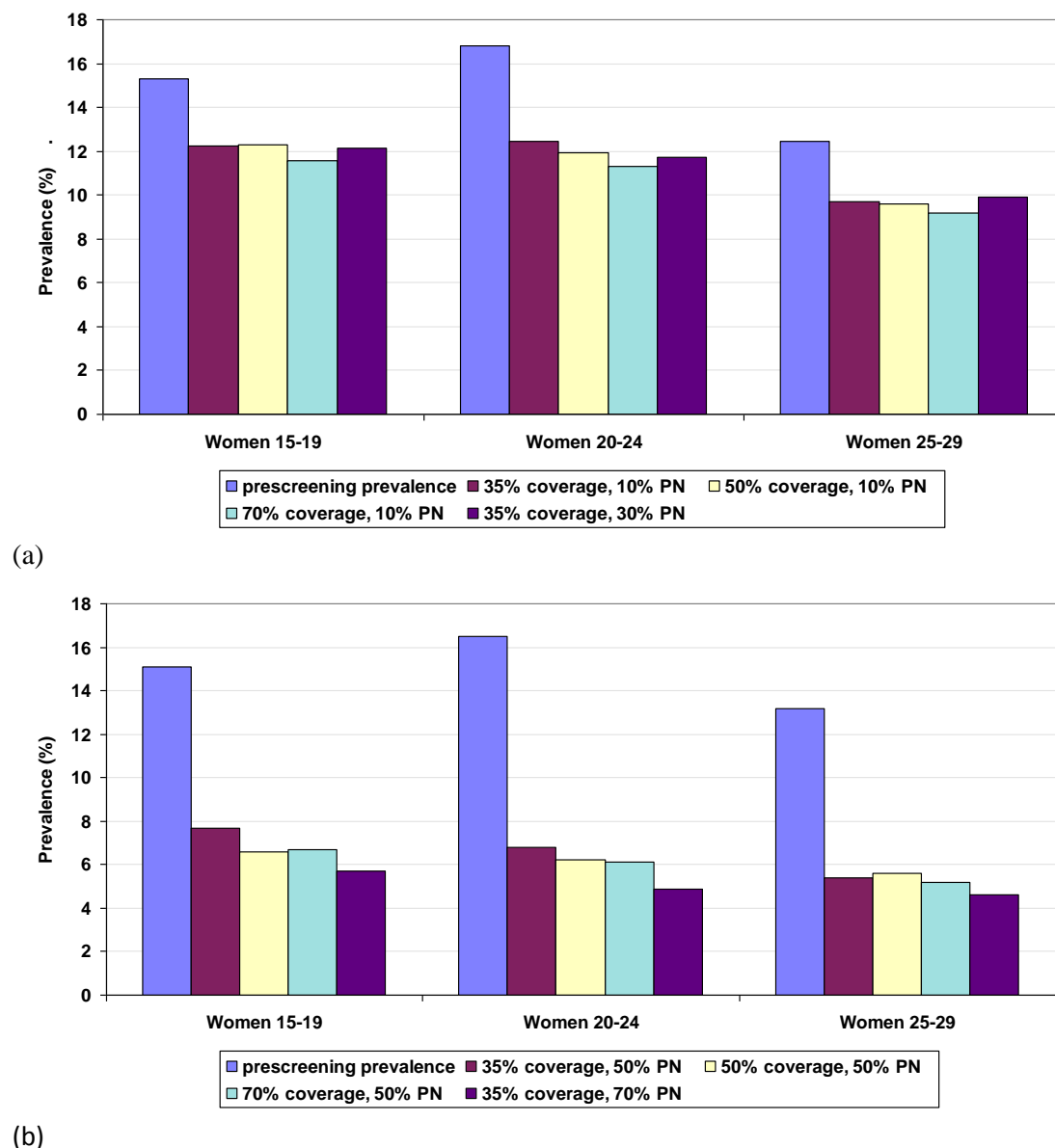


Figure A12: In these two sets of simulations the baseline rate of partner notification is varied. In (a) the partner notification rate in baseline is 10%; in (b) it is 50%.



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