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Modeling Prevention Strategies for Gonorrhea and Chlamydia Using Stochastic Network Simulations

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A simulation model was used to study the spread of two sexually transmitted diseases (STDs), namely gonorrhea and genital infection with *Chlamydia trachomatis*. The model is based on a stochastic pair formation and separation process, which describes the underlying structure of the sexual contact pattern. It is implemented as a Monte Carlo simulation model. Spread of the STDs was modeled in an age-structured heterosexual population with a highly sexually active core group. Contact tracing strategies, screening of various subgroups, and the effect of condom use were compared. The authors conclude that contact tracing is very effective as a prevention strategy, that screening should be targeted to the highly active core group, that age is not sufficient as a determinant for high sexual activity to make screening of certain age groups useful, and, finally, that consistent condom use by a fraction of the population can contribute substantially to the prevention of STDs. All strategies proved more effective for gonorrhea than for chlamydia prevention, which may explain the relatively high prevalence of chlamydia found in many heterosexual populations. *Am J Epidemiol* 1996;144:306–17.

chlamydia infections; gonorrhea; models, stochastic; Monte Carlo method; sexually transmitted diseases

In decision making in public health policy, one usually has a limited budget that one would like to spend in such a way as to reach a maximal health benefit. Often, alternative prevention or intervention strategies are available for a disease and it is difficult to judge in advance which one will be most effective. Also, it may be impossible to evaluate different strategies in the same population.

A tool for dealing with this dilemma is offered by mathematical modeling. In a model, it is possible to change some parameters while keeping others constant and to perform a series of experiments with a model population. Whether this is useful depends on the kind of questions one wants to answer, the appropriateness of the model used, the availability of information on essential parameters, and the correct interpretation of the results obtained.

In the area of modeling sexually transmitted diseases (STDs), much theoretical work has been done in the last two decades, inspired largely by the acquired immunodeficiency syndrome (AIDS) epidemic. Pioneering work was done by Hethcote and Yorke (1) in regard to gonorrhea. Their work is exemplary in combining analytical work on mathematical models with data analysis, and in translating the results into conclusions for prevention strategies. Summaries of various aspects of STD modeling can be found in Anderson and May (2), Castillo-Chavez (3), and Kaplan and Brandeau (4).

In this article, we report on results obtained with a stochastic simulation model for the spread of STDs. The model is based on a discrete time stochastic process of pair formation and separation combined with a stochastic process of disease transmission analogous to deterministic models introduced by Dietz and Hadeler (5). It is implemented as a Monte Carlo simulation model. The technical details are not discussed (for these details, we refer the reader to references 6–8), but the main ideas of the model are summarized.

We used information on heterosexual behavior obtained in a sexual behavior survey of the general population in the Netherlands and on transmission parameters of gonorrhea and genital infection with *Chlamydia trachomatis* (which we refer to as chlamydia hereafter) in order to compare the prevalence and distribution of these STDs in an endemic situation. We also compared the effectiveness of different prevention and intervention scenarios, including contact

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Abbreviations: AIDS, acquired immunodeficiency syndrome; CV, coefficient of variation; STDs, sexually transmitted diseases.

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tracing, screening of various subgroups, and condom use in reducing the prevalences of these diseases.

Although neither gonorrhea nor chlamydia contribute to mortality and both can be treated easily, the high percentages of asymptomatically infected persons pose a problem for public health. Untreated infections in women may give rise to complications such as pelvic inflammatory disease, which in turn may lead to infertility and an increased risk of ectopic pregnancies. Treatment of these complications is connected with high costs for the health care system (9).

MATERIALS AND METHODS

Survey data

In 1989, a national survey was carried out in the Netherlands of the sexual behavior of Dutch adults (10). Detailed information was gathered on sexual practices and on the perception and prevention of human immunodeficiency virus (HIV)/AIDS. Using a multistage, stratified random sample, 1,001 adults were interviewed (net response rate, 58.3 percent). A "nonresponder" study confirmed that the population under study was satisfactorily represented in the sample.

Age is an important determinant of sexual behavior (11). The most sexually active age class was between 18 and 32 years. With increasing age, the respondents had fewer partners per unit time and the average duration of steady partnerships increased. Although in the older age classes most respondents had settled to a steady monogamous relationship, a remaining fraction had only casual relationships. In general, a small fraction of the population (often referred to as the core group) had many partners per year, while the majority had a low rate of partner change. The survey contains no information about the mixing between core and non-core groups.

Tables 1 and 2 refer to the 926 respondents who reported only heterosexual partnerships. Table 1 shows the distribution of the number of sex partners per person in the last year. A distinction was made between steady and casual partnerships. A steady partnership was defined as one that had lasted for at least one year at the time of the survey. Table 2 shows the percentage of the respondents that had no sex, only a steady relationship, only casual relationships, or both in the last year. In general, the behavior of the population can be described as sequentially monogamous. The duration of steady relationships at the time of the survey was age dependent (age 18–24 years, 4.0 years; age 26–33, 8.8 years; age 34–41, 14.1 years; and age 42–50 years, 22.4 years). The frequency of sexual intercourse in steady partnerships decreased slightly with age and with duration of the partnership; the average was 7 times per month (10).

Condoms were used consistently by 15 percent of those respondents who did not have a steady partnership and by 6 percent of respondents with a steady partnership. Condoms were sometimes used by 32 percent of respondents without a steady partnership and 15 percent of respondents who had a steady partnership (10).

For information about age mixing, we relied on observations from other studies (10, 12, 13) (table 3). Typically, most partnerships are within age classes with a slight tendency toward men being older than their female partners. Other variables, such as socioeconomic status, might also play a role with respect to mixing (14), but we did not take that into account.

To gain insight into the behavior of core group individuals, a study among STD clinic patients in Amsterdam in 1986–1988 was considered (unpublished data). Besides having more sexual partners than the average population, core group individuals often had concurrent partnerships, usually casual relationships simultaneously to one steady relationship. (For discussion about the core group concept and mixing patterns see references 15 and 16.)

Transmission and course of infection

Gonorrhea and chlamydia are both bacterial diseases with similar clinical symptoms and a similar

TABLE 1. Distribution of numbers of partners (in percent) in the past year for survey respondents (from van Zessen and Sandfort (10)) and model population (average over 10 runs)

No. of partners	Survey		Model			
	Men	Women	Men	Women	Men (core)	Women (core)
0	14.0	10.8	7.9	9.5	4.6	4.7
1	73.0	82.5	73.4	74.0	0.6	0.0
2	6.2	4.3	11.0	9.2	3.5	0.1
3	3.5	1.4	4.2	3.8	4.0	0.2
4	0.5	0.2	1.4	1.2	6.3	1.4
5–9	2.1	0.6	1.6	1.2	55.3	37.6
10–19	0.5	0.0	0.6	1.3	24.7	54.3
≥20	0.0	0.0	0.0	0.02	0.0	0.7

TABLE 2. Relational status in the past year (in percent) for survey respondents (from van Zessen and Sandfort (10)) and model population (average over 10 runs)

Relational status	Survey		Model	
	Men	Women	Men	Women
No sex	14.0	10.8	8.8	10.8
Steady	68.7	79.6	65.1	66.2
Both	5.7	3.8	10.2	9.8
Casual	11.6	5.8	16.0	13.2

TABLE 3. Mixing between age classes in the simulation model (average over 10 runs): percent of partnerships by ages of partners at the time of formation of the partnership

Age class (years), men	Age class (years), women				
	15–24	25–34	35–44	45–54	55–64
15–24	22.8	4.0	0.5	0.1	0.04
25–34	15.3	13.4	1.6	0.4	0.1
35–44	1.6	6.9	4.5	1.1	0.3
45–54	0.3	1.3	4.2	5.2	1.7
55–64	0.06	0.3	0.8	5.2	8.3

course of infection. Although gonorrhea has been studied for a long time, only in the last decade has chlamydia been recognized as an STD, and empirical knowledge on the transmission and the natural course of chlamydia infection is scarce (see references 17 and 18).

In order to model the transmission dynamics, we needed to specify

- the fraction of asymptomatic infections;
- the transmission probabilities per sexual contact from male to female and vice versa;
- incubation times and patient delays;
- the duration of the infectious period for symptomatic and asymptomatic males and females.

Although there is evidence for partial immunity for gonorrhea and chlamydia, we did not take that into account.

For gonorrhea, the transmission probability from man to woman is estimated at 0.5–0.7 per sexual contact, and that from woman to man at 0.2–0.3 (17, 19, 20). About 10 percent of infected men and 30–60 percent of infected women are asymptomatic. Symptoms appear about 2–5 days after infection for men, and around 10 days after infection for women. The duration of the infectious period is variable and not well known, although for symptomatic women, it is estimated at 3–45 days; for asymptomatic women, 3–12 months; for symptomatic men, 3–30 days; and for asymptomatic men, 3–6 months (17, 19). It is unclear whether these estimates include treatment effects. The patient delay, i.e., the time between first appearance of symptoms and treatment, is estimated at around 7 days for women and 4 days for men (H. J. A. van Haastrecht, unpublished data). Treatment takes one day to be effective.

For chlamydia, there are only rough estimates for these parameters. It is thought that the infectious period lasts longer than in gonorrhea, whereas the transmission probabilities per contact are lower (17, 20–22). In Severijnen (22), based on Lyck et al. (20), the following estimates were given: 0.5 for the transmission probability per sexual contact from man to woman, and 0.25 for transmission from woman to man. Katz (21) gave lower estimates for the transmission probabilities per contact. The incubation time is estimated to be 7–21 days. About 70 percent of infected women and 25 percent of infected men are asymptomatic (17, 22). In Fish et al. (23), 86 percent of infected partners of infected women who attended a gynecology clinic were found to be asymptomatic. Persons who are asymptomatically infected can be infectious for several years. Buhaug et al. (24) estimated the average duration of the infectious period for women at 1 year, while Rahm et al. (25) reported durations of up to 2 years. Patient delays are the same as for gonorrhea, but treatment takes about 7 days to be effective.

Incidence and prevalence

Notification of gonorrhea cases has been mandatory in the Netherlands since 1976. However, it was estimated that only one-third of all cases are registered. Since the early 1980s, incidence has been constantly declining from 104 cases per 100,000 inhabitants in 1981 to 12.2 cases per 100,000 inhabitants in 1993 (26; also data from the Medical Inspectorate of Health, Rijswijk, the Netherlands, 1993). This decline is partly ascribed to behavioral changes due to the AIDS epidemic and also to other control measures such as routine screening programs.

For chlamydia, registration data is fragmentary; there is no national reporting. Severijnen (9) estimated the national prevalence of chlamydia based on gonorrhea notification and on the ratio of chlamydia/gonorrhea in gynecologic practices, STD clinics, and other health services. Chlamydia is far more prevalent in the general population than is gonorrhea. Dekker and Boeke (27) found a prevalence of 7.9 percent among women who visited general practitioners for vaginal problems (see also reference 28). In addition, in women who visited an STD clinic in Amsterdam, chlamydia infections were more prevalent than was gonorrhea (29). The reasons for this higher prevalence are that diagnostic tools until recently were not well developed, many asymptomatic infections remain unnoticed due to lack of contact tracing, compliance with

the 7-day therapeutic scheme is not optimal, and chlamydia has been included in screening programs in only a few STD clinics in the Netherlands. The reporting system of the nursing staff in STD services showed no increase in the number of chlamydia infections since 1988 (30).

The model

The simulation model is a discrete time Markov model describing pair formation and separation and disease transmission as stochastic processes. Variants of this model and related deterministic models have been discussed (6–8, 31, 32).

The model population consisted of 10,000 individuals with a sex ratio of 1:1 and was assumed to be purely heterosexual. Steady and casual partnerships were distinguished; they differed in average duration (6.9 years for steady partnerships and 10 days for casual partnerships) and in the frequency of sexual contact during the partnership (0.25/day for steady partnerships and 1/day for casual partnerships).

One time step represents one day. At every time step t, a model individual is completely described by a state vector $(n, g, a, c, s, \tau, d, \mathcal{N})$,
where
n is a unique identifier or "name."
g is gender; either m (male) or f (female).
a is age ($15 \leq a \leq 64$); at the end of a simulation year $a \rightarrow a + 1$; at $a = 65$ replacement takes place. The age distribution of the population is uniform on the interval $15 \leq a \leq 64$. For some purposes, we distinguish five age classes numbered from 1 to 5 (i.e., 15–24, 25–34, 35–44, 45–54, and 55–64 years).
c is sexual activity, which takes the values 0 (low activity) or 1 (high activity). The core group is defined as the set of individuals with $c = 1$. Rules for assignment of activity status were as follows: 1) individuals with $15 \leq a \leq 34$ are assigned $c = 1$ with probability 0.05, otherwise $c = 0$; for $a \geq 35$, $c = 0$; 2) replacement: an individual entering the population ($a = 15$) is assigned $c = 1$ with probability 0.05, otherwise $c = 0$; 3) aging: c is set to 0 at $a = 35$.
s is disease status, which takes the values 0 (susceptible), 1 (symptomatically infected), or 2 (asymptomatically infected). Infection is a transition from $s = 0$ to $s = 1$ with disease and gender-specific probability, p, or to $s = 2$ with probability $1 - p$ (see table 4).
τ is time since infection; at transmission $\tau = 0$; for all infecteds, $\tau \rightarrow \tau + 1$ in every time step; $\tau = -1$ for susceptibles. We assume that the latent period equals the incubation time, i.e., that an infected individual is infectious and a symptomatically infected displays symptoms for $\tau >$ incubation time (see table 4).
d is the number of current partners of an individual ($0 \leq d \leq 5$); and
$\mathcal{N}$ is a set of names of current partners of an individual.

TABLE 4. Disease-specific parameter values used in the simulations

Parameter	Gonorrhea	Chlamydia
Transmission rate* male → female, steady partnerships (/day)	0.15	0.0385
Transmission rate female → male, steady partnerships (/day)	0.0625	0.0305
Transmission rate male → female, casual partnerships (/day)	0.6	0.154
Transmission rate female → male, casual partnerships (/day)	0.25	0.122
Asymptomatic men (%)	10	25
Asymptomatic women (%)	45	70
Incubation time men (days)	5	12
Incubation time women (days)	10	10
Patient delay + treatment men (days)	5	11
Patient delay + treatment women (days)	8	14
Recovery rate asymptomatic men (/day)	0.0074	0.005
Recovery rate symptomatic men (/day)	0.04	0.03
Recovery rate asymptomatic women (/day)	0.0044	0.0027
Recovery rate symptomatic women (/day)	0.03	0.025

* Transmission rates are composed of the transmission probability per sexual contact and the frequency of sexual contacts depending on the type of partnership.

Now we can define the transitions that take place per simulation time step.

1. Formation of partnerships
   a) Compute $n = N/2 - P(t)$, where $P(t)$ is the total number of partnerships.
   b) For $i = 1$ to n form a partnership with probability $\rho = 0.006$ (i.e., on average, $n\rho$ new partnerships will be formed per time step).
   c) For the formation of one partnership, the following rules apply:
      i. The partnership is assigned to be "steady" with probability $f = 0.2$, otherwise "casual."
      ii. A male y and a female x are drawn randomly from the population.
      iii. They form a partnership with probability $\phi(x, y)$ (see below).
      iv. Repeat ii and iii until a partnership has been formed.
2. Disease transmission. In every partnership of a susceptible ($s = 0$) and an infectious individual ($s = 1$ or $s = 2$; $\tau >$ incubation time), transmission takes place with disease- and gender-specific probabilities (see table 4).

3. Separation of partnerships. Steady partnerships separate with probability $\sigma_1 = 0.0004$, casual partnerships with probability $\sigma_2 = 0.1$. Separation results in transitions $d \rightarrow d - 1$ and $\mathcal{N} \rightarrow \mathcal{N}\backslash\{\text{name of partner}\}$ for both individuals.
4. Replacement. Every individual $(n, g, 65, c, s, \tau, d, \mathcal{N})$ is replaced by $(n, g, 15, c', 0, -1, 0, \emptyset)$ (including separation of all his/her partnerships; c' denotes the new activity status).
5. Recovery. Transition of infecteds ($s = 1$ or $s = 2$) to $s = 0$ with disease and gender-specific probabilities (see table 4).
6. Treatment (and contact tracing). Transition of symptomatically infecteds ($s = 1$) with $\tau =$ (incubation time + patient delay) to $s = 0$ with probability 1 (i.e., the effectivity of treatment is 100 percent). Contact tracing: at treatment of a symptomatically infected, all partners identified by $\mathcal{N}$ also return to disease status $s = 0$. There is no snowball tracing of partners of individuals in $\mathcal{N}$.
7. Screening. At given screening time steps $t = T_{sc}$ (e.g., once a year), a specified percentage of individuals is chosen at random from the subgroup to be screened. For those individuals, s is set to 0.

It remains to define the mixing probability $\phi(x, y)$ depending on type of the partnership to be formed, and on ages, activity levels, and numbers of current partners of the individuals x and y. Assume that x is described by the state vector $(x, f, a_x, c_x, s_x, \tau_x, d_x, \mathcal{N}_x)$ and y by $(y, m, a_y, c_y, s_y, \tau_y, d_y, \mathcal{N}_y)$. We define:

$$\phi^i(x, y) = \phi^i_a(j, k)\phi^i_{cd}(c_x, c_y, d_x, d_y),$$

where the superscript $i = 1,2$ refers to the type of partnership (1 = steady, 2 = casual), the subscripts refer to the state variable, and $j,k = 1, \ldots, 5$ refer to the female's and the male's age classes, respectively. For $i = 1, 2$, we take $\phi^i_a(j,k) = 1$ for $j = k$, and $\phi^i_a(j,k) = 0.2^{|j+1-k|}$ for $j \neq k$. The age mixing of the model population resulting from these mixing probabilities is shown in table 3. As observed in sexual behavior surveys, most partnerships are formed in younger ages and between individuals of the same or neighboring age classes, and there are more partnerships between men with somewhat younger women than vice versa.

Furthermore, we define

$$\phi^1_{cd}(c_x, c_y, d_x, d_y) = \begin{cases} 1 & \text{if } d_x = 0 \text{ and } d_y = 0 \\ 0 & \text{otherwise} \end{cases}$$

$$\phi^2_{cd}(c_x, c_y, d_x, d_y) = \begin{cases} 1 & \text{if } c_x = c_y = 1 \\ 0.1 & \text{if } c_x = 1 \text{ and } c_y = d_y = 0 \\ 0.1 & \text{if } c_y = 1 \text{ and } c_x = d_x = 0 \\ 0.01 & \text{if } c_x = c_y = d_x = d_y = 0 \\ 0 & \text{otherwise.} \end{cases}$$

All other state variables did not influence the mixing probability.

The pair formation and separation process converges to a stationary process for the numbers of singles, steady partnerships, and casual partnerships, i.e., in the long run, the number of individuals who are single, and the numbers of steady and casual partnerships fluctuate around constant averages with a constant stochastic variability. To initialize the model, a pre-simulation was run until the pair formation process had reached its stationary state and a number of infections were introduced into the core group; then, the time t was set to 0 and the actual simulation phase started. All simulations covered a time span of $T = 20$ years.

With the above pair formation rate, 28.7 percent of the population was single, 71 percent had one partner, and 0.3 percent had more than one partner at a time. If disease transmission was allowed to proceed without intervention, changes of treatment, or behavior change, gonorrhea prevalence reached a stationary endemic state after 2–3 years, while chlamydia had established itself on a stable endemic level after about 8 years.

The distribution of numbers of partners in the last year is shown in table 1, columns 3 and 4. In the last two columns of table 2, the percentages of the model population are given that had no sex, a steady partnership, both steady and casual, and only casual relationships, respectively.

Comparison of the survey data and the simulation results presented in tables 1 and 2 demonstrates that the chosen parameter values resulted in a higher sexual activity than observed in the survey. The reason for choosing these values was that otherwise prevalences in the endemic state were too low to clearly distinguish between prevention scenarios, because stochastic influences and disease extinction prevailed. However, considering the concentration of STDs in urban areas with a higher sexual activity than the national average, this seems a valid choice of parameters.

Prevention scenarios

In the model population, as described above, various prevention scenarios were compared. As a reference scenario, we took the situation where the disease

spreads without intervention and an endemic equilibrium is established. The reference scenario cannot be compared with prevalence data from the Netherlands, because a combination of prevention and intervention measures are implemented at present. It is therefore a theoretical, but clearly defined, reference point. Furthermore, the prevalence depends on parameters of the contact process about which insufficient information was available such as the degree of mixing between the core and non-core population. We measured the effectiveness of prevention strategies in percent reduction of the prevalence in the reference scenario.

We considered three types of prevention strategies: contact tracing, screening, and condom use. The first two strategies aim at finding and treating asymptomatic infecteds, while the third strategy seeks to minimize transmission. The practical problems of implementing these strategies, such as how to reach relevant subgroups or how to conduct education campaigns, are not discussed here.

For each of the scenarios listed in table 5, 10 simulation runs were performed. In all scenarios except scenario 0, treatment of symptomatic infecteds was included as a basic service of health care. Consequently, scenario 1a serves as a scenario for comparing the effects of additional measures. Scenarios 1 and 2 started at $t = 10$ years, when a stable endemic situation had been reached for both diseases; scenario 3 started at $t = 0$, i.e., we did not consider behavior change, but assumed that there was a given level of condom use from the start.

We considered four scenarios involving only treatment (and contact tracing) effects: In the first scenario (1a), only symptomatic infecteds were treated; additionally, varying percentages of their current partners were treated in scenarios 1b–1d. Due to the short duration of casual partnerships, most of those are steady partners. We neglected the delay between treatment of an index patient and his or her partner and assumed that they are treated simultaneously.

In all screening scenarios, 2 percent of the population was screened per year at specified days of the year. We assumed 100 percent sensitivity, i.e., every infected individual is diagnosed and treated. The targeted subgroups differ among scenarios 2a–2e, while the time interval at which screening takes place differs in scenario 2f.

In the condom use scenarios, some specified core and non-core individuals were assumed to use condoms consistently in all their partnerships. In a partnership between a condom user and a non-condom user, condoms were always used. Condom use reduced transmission probability to 0. We did not consider gender differences in condom use.

RESULTS

To study the influence of parameters describing sexual activity and contact structure on the total prev-

TABLE 5. Definitions of prevention/intervention scenarios for simulations

Scenario	Prevention/intervention strategy
0	**Reference situation**
	No intervention or prevention, endemic equilibrium
1	**Contact tracing**
a	Treatment of symptomatically infected, but not partners
b	Treatment of symptomatically infected and 25% of partners
c	Treatment of symptomatically infected and 50% of partners
d	Treatment of symptomatically infected and 100% of partners
2	**Screening**
a	Treatment of symptomatically infected, and yearly screening of 100% of 20-year-old men and women
b	Treatment of symptomatically infected, and yearly screening of 10% of age class 15–24, men and women
c	Treatment of symptomatically infected, and yearly screening of 20% of women in age class 15–24
d	Treatment of symptomatically infected, and yearly screening of 20% of men in age class 15–24
e	Treatment of symptomatically infected, and yearly screening of 100% of core group
f	Treatment of symptomatically infected, and half-yearly screening of 50% of core group
3	**Condom use**
a	Treatment of symptomatically infected, and 15% of core and 6% of non-core individuals use condoms consistently
b	Treatment of symptomatically infected, and 47% of core and 21% of non-core individuals use condoms consistently

alence of gonorrhea and chlamydia, we recorded the prevalence in the endemic situation for different values of the pair formation rate ρ, the fraction of steady partnerships f, and the degree of assortative mixing between core and non-core individuals. Those parameters were varied independently and the resulting sexual activity level was then summarized in a quantity C, which is computed from the mean m and the variance v of the distribution of the number of partners in the last year by

$$C = \frac{v}{m} + m.$$

In figure 1, the total prevalences of both diseases are shown as a function of C. At approximately $C = 1.9$, the basic reproduction ratio R_0 becomes larger than 1 for both diseases. The prevalences then rise in an approximately hyperbolic fashion. The prevalence of chlamydia was consistently higher than the prevalence of gonorrhea. To give an indication of the magnitude of C, we computed it from the survey data (table 1) separately for men ($C = 2.93$) and for women ($C = 1.44$), because of the inconsistency of their responses. (The measure C is related to the "effective contact rate" introduced by Anderson and May (2). While those authors consider the number of new partners per person per year, we have taken the number of partners per person in the last year including an individuals' partnership at the beginning of the year.)

In the simulations described in the following, performed with the parameter values from section named "The model," $C = 2.85$. For this value of C, the prevalence curves rise steeply and are well above 0, so that differences in effects of prevention measures are likely to be observed without driving the disease to extinction.

Reference scenario

Both gonorrhea and chlamydia established themselves as endemic diseases in the model population. The average prevalences (averaged over 10 simulation runs and over time) are shown in the first rows for gonorrhea and chlamydia in table 6. For gonorrhea, the prevalence was 2.84 percent and for chlamydia it was 4.07 percent of the population. While the prevalence of symptomatic infecteds was somewhat lower for chlamydia than for gonorrhea for both men and women, the contrary was true for asymptomatic infecteds. The number of asymptomatic infecteds with chlamydia is about three times as much in men and twice as much in women than the number of asymptomatic infecteds with gonorrhea. The coefficient of variation (CV) (ratio of standard deviation to mean) was used as a measure for the variability among sim-

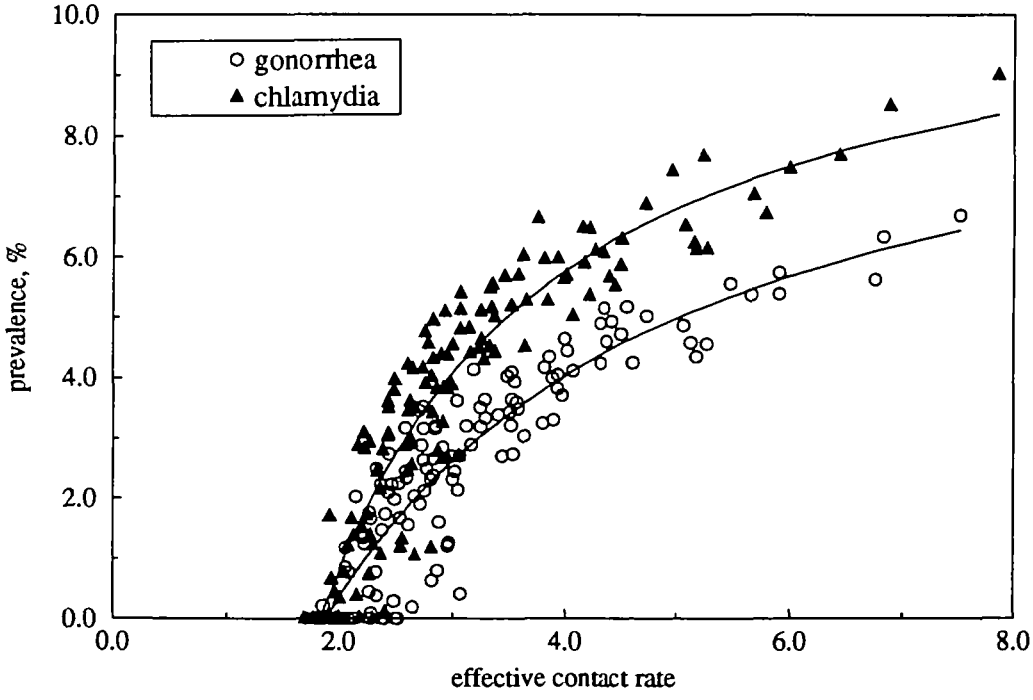

FIGURE 1. The prevalence of gonorrhea and chlamydia in percent of the model population as a function of the effective contact rate as defined in equation 1. Each data point represents one simulation run. The pair formation rate, the fraction of steady partnerships, and the probability of mixing between the core and non-core population was varied independently. The solid lines represent hyperbolic functions of the form, $y = [a_0(x - a_1)]/[a_2 + (x - a_1)]$, which were fitted to the data points with a nonlinear curve fitting program. The resulting parameter values were: gonorrhea, $a_0 = 10.08$, $a_1 = 1.89$, $a_2 = 3.18$; chlamydia, $a_0 = 11.12$, $a_1 = 1.85$, $a_2 = 2.0$.

TABLE 6. Average gonorrhea and chlamydia prevalence (cases per 10,000) in the simulations. For the reference scenario, the time average was taken over the last 10 years, and for intervention/prevention strategies, the time averages were taken for the last simulation year

Scenario	Men		Women	
	Asymptomatic	Symptomatic	Asymptomatic	Symptomatic
	Gonorrhea			
0*	44 (6.8)†	74 (9.5)	137 (14.5)	25 (5.1)
1a	19 (11.9)	10 (6.7)	41 (23.4)	3 (2.6)
b	0 (0)	0 (0)	0 (0)	0 (0)
c	0 (0)	0 (0)	0 (0)	0 (0)
d	0 (0)	0 (0)	0 (0)	0 (0)
2a	10 (7.4)	6 (4.1)	24 (14.5)	2 (1.7)
b	16 (9.3)	8 (5.2)	34 (20.5)	3 (2.4)
c	16 (7.7)	9 (5.1)	37 (15.7)	3 (2.2)
d	14 (7.0)	8 (4.4)	32 (14.9)	2 (1.8)
e	1 (1.1)	0 (0.7)	1 (2.2)	0 (0.2)
f	1 (1.1)	0 (0.9)	2 (2.5)	0 (0.3)
3a	5 (3.2)	3 (2.2)	11 (6.0)	1 (0.9)
b	0 (0)	0 (0)	0 (0)	0 (0)
	Chlamydia			
0*	120 (13.9)	60 (8.6)	217 (21.1)	10 (3.1)
1a	98 (15.0)	25 (5.3)	161 (22.4)	3 (1.8)
b	35 (12.5)	10 (4.6)	59 (19.6)	1 (1.4)
c	13 (8.6)	3 (2.3)	18 (11.9)	0 (0.7)
d	1 (1.2)	0 (0.3)	1 (1.9)	0 (0.1)
2a	93 (15.4)	24 (6.2)	154 (24.9)	3 (1.8)
b	97 (13.5)	25 (5.3)	158 (19.3)	4 (1.9)
c	88 (14.0)	23 (5.0)	135 (15.6)	3 (1.7)
d	95 (11.0)	25 (5.1)	156 (20.8)	3 (1.8)
e	12 (6.6)	3 (2.3)	22 (12.5)	0 (0.8)
f	18 (8.3)	4 (2.9)	27 (13.3)	1 (0.9)
3a	62 (11.9)	16 (4.5)	100 (20.4)	2 (1.2)
b	3 (4.5)	1 (1.3)	4 (6.9)	0 (0.3)

* Reference situation: no intervention or prevention, endemic equilibrium.

† The time averages of the standard deviations among the 10 runs are shown in parentheses.

TABLE 7. Distribution of numbers of partners in percent in the past year for the infected population in scenario 0 (average over 10 runs)

No. of partners	Gonorrhea	Chlamydia
0	0.3 (0.5)*	0.8 (0.3)
1	40.0 (2.7)	45.7 (2.1)
2	13.6 (2.3)	15.4 (1.4)
3	9.8 (2.3)	9.0 (1.7)
4	5.3 (1.5)	4.2 (1.1)
5–9	14.3 (1.3)	12.7 (1.8)
10–19	16.6 (2.5)	11.9 (1.4)
≥20	0.1 (0.2)	0.2 (0.4)

* Standard deviations among the simulation runs are shown in parentheses.

ulation runs; we found that, for all groups of infecteds, the CV lies around 0.1, except for symptomatic women where the small means lead to a higher CV.

Due to the asymmetric age mixing between men and women, the peak of the age distribution of infecteds for both diseases lies in the youngest age class 15–24 years for women and in age class 25–34 years for men. This agrees with the age distribution of infecteds observed for gonorrhea in the Netherlands (19).

To see whether the diseases remained concentrated in the core group, we considered the number of partners in the last year for infected individuals (table 7). The infected population clearly consisted of two subgroups, namely a group with many partners (≥5) and a second group with only 1–2 partners in the last year. The fact that there were infected individuals with no partners in the last year was only due to the long duration of the infection. The fraction of individuals who had only one partner in the last year was somewhat higher for chlamydia (46 percent) than for gonorrhea (40 percent); on the other hand, a higher percentage of gonorrhea infecteds than chlamydia infecteds had more than 5 partners in the last year. Therefore, chlamydia had spread to a larger extent into the low activity population than had gonorrhea.

Prevention scenarios

To compare effects on prevalence of prevention/intervention strategies with the prevalence in the reference scenario, we defined a measure r as the ratio of post-intervention to pre-intervention total prevalence. As post-intervention prevalence, the average total prevalence in the last simulation year was taken. The effects of prevention/intervention on prevalence are shown in tables 6 and 8, and figures 2 and 3.

First, consider scenario 1a where only symptomatic infecteds were treated. For gonorrhea, the prevalence was reduced to 0.7 percent ($r = 0.26$), while for chlamydia, it was reduced to 2.9 percent ($r = 0.71$). In both cases, a new endemic equilibrium was reached 10 years after introduction of treatment.

As expected, the reduction in prevalence was more effective in the symptomatically infected group for both men and women. In gonorrhea, prevalence of symptomatically infected men and women was reduced to about 13 percent of the pre-intervention prevalence, while for asymptomatic infecteds the reduction was less effective (for men to 42.2 percent and for women to 29.5 percent). Chlamydia prevalences of symptomatic infecteds were reduced to 41.7 percent and 30.0 percent for men and women, respectively, of the pre-treatment level; for asymptomatic infecteds, the reduction was only to 81.7 percent in men and 74.2 percent in women.

The situation changed dramatically for contact tracing strategies, which proved highly efficient in reduc-

TABLE 8. Effectivity of prevention measures. The measure *r* is defined as the ratio of pre-intervention prevalence to post-intervention prevalence

Scenario	Gonorrhea		Chlamydia	
	Prevalence (%)	*r*	Prevalence (%)	*r*
0*	2.84	1	4.07	1
1a	0.73	0.26	2.87	0.71
b	0.0	0.0	1.05	0.26
c	0.0	0.0	0.34	0.08
d	0.0	0.0	0.02	0.0
2a	0.42	0.15	2.74	0.67
b	0.61	0.21	2.84	0.7
c	0.65	0.23	2.49	0.61
d	0.56	0.20	2.79	0.69
e	0.02	0.01	0.37	0.09
f	0.03	0.01	0.5	0.12
3a	0.2	0.07	1.8	0.44
b	0.0	0.0	0.08	0.02

* Reference situation: no intervention or prevention, endemic equilibrium.

ing prevalence. For gonorrhea, contacting and treating 25 percent of all current partners of symptomatic infecteds was sufficient to eradicate the disease after 10 years. With a higher percentage of contact tracing, time to extinction was reduced and was about 3 years if 100 percent of the current partners were treated. For chlamydia, contact tracing was less effective at lower percentages of partners treated ($r = 0.26$ for strategy 1b), but with increasing levels of contact tracing it was also a highly effective intervention strategy ($r = 0.08$ for strategy 1c and $r = 0.0$ for strategy 1d).

In general, all screening strategies were more effective in reducing gonorrhea prevalence than in reducing chlamydia prevalence.

First, consider strategies 2a–2e, for which the target group varied according to age and gender. For gonorrhea, the most effective of these strategies was 2a, where 20-year-old men and women were screened yearly. Prevalence was reduced to 0.4 percent ($r = 0.15$). Screening of broader age groups, whether it was men and women or only women, improved the situation somewhat compared with treating only symptomatic infecteds, but with r around 0.22 it was less effective than strategy 2a.

For chlamydia, it was most effective to screen only women in the age class 15–24 years (strategy 2c). Prevalence could be reduced to 2.5 percent ($r = 0.61$). However, most of this reduction was due to the treatment of symptomatic infecteds. In comparison with strategy 1a, not much was gained. For strategies 2a and 2b, no effect was reached compared with strategy 1a.

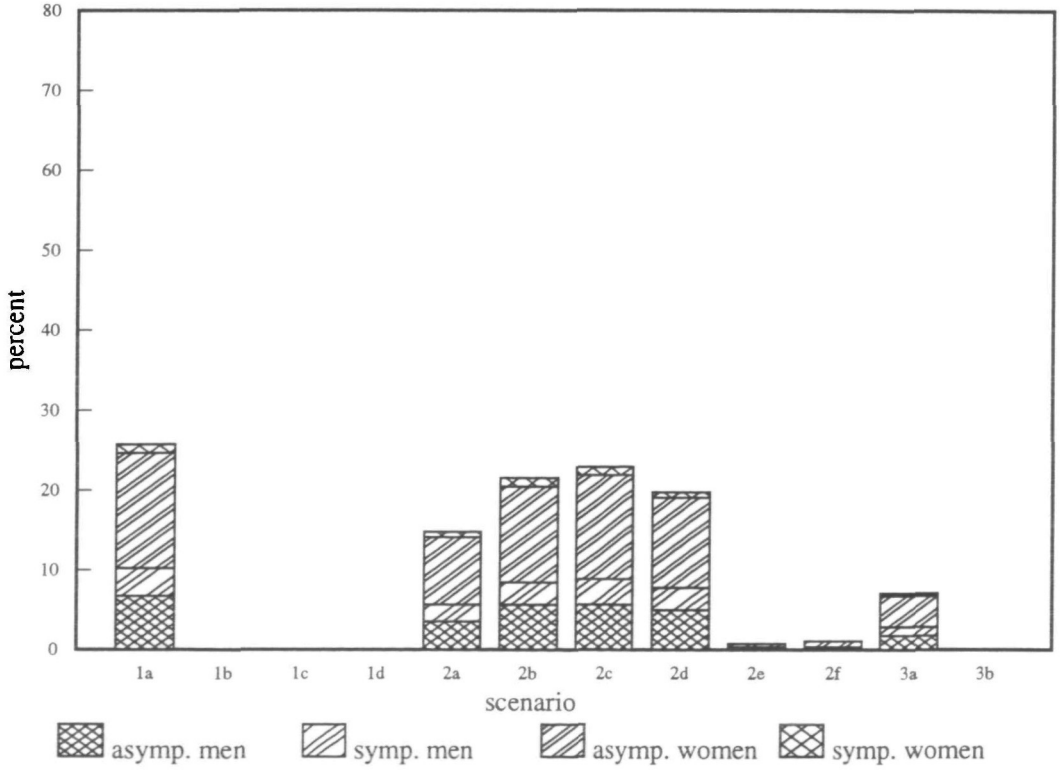

FIGURE 2. The effectiveness of different prevention strategies for gonorrhea among asymptomatic (asymp.) and symptomatic (symp.) men and women. The prevalence of the diseases in the last year of the simulation is shown compared with the prevalence in the endemic equilibrium of the reference scenario (100% = total prevalence in scenario 0).

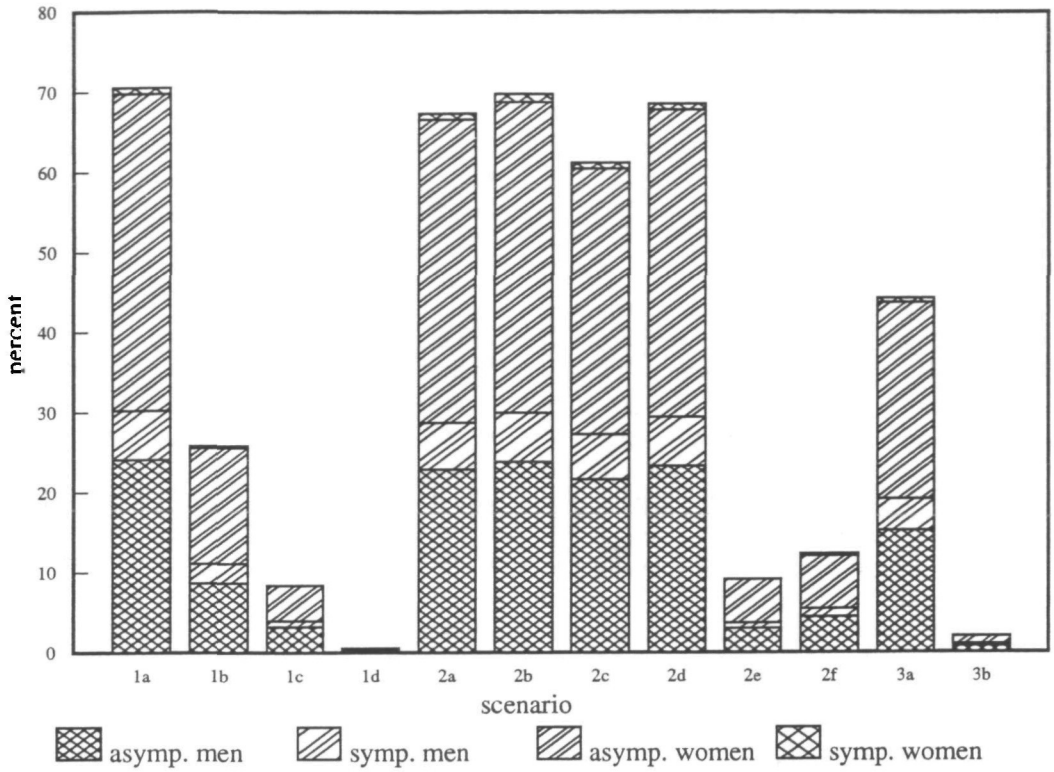

FIGURE 3. The effectiveness of different prevention strategies for chlamydia among asymptomatic (asymp.) and symptomatic (symp.) men and women. The prevalence of the diseases in the last year of the simulation is shown compared with the prevalence in the endemic equilibrium of the reference scenario (100% = total prevalence in scenario 0).

For both diseases, a screening strategy targeted at the sexually highly active core group was the most effective. Screening all core group members once a year reduced gonorrhea prevalence to 0.02 percent ($r = 0.01$), which in due course led to extinction of the disease in the stochastic setting. Chlamydia prevalence was reduced to 0.4 percent ($r = 0.09$). Half-yearly screening of 50 percent of the core group was as effective for gonorrhea as was the yearly scheme, whereas for chlamydia it was slightly less effective.

Both scenarios implementing condom use resulted in a large reduction of the prevalences of both diseases. Prevalence of gonorrhea was reduced to 0.2 percent ($r = 0.07$) in scenario 3a, and gonorrhea was eradicated in scenario 3b. For chlamydia, prevalence decreased to 1.8 percent ($r = 0.44$) in scenario 3a, while it almost disappeared in scenario 3b (prevalence = 0.08 percent; $r = 0.02$).

DISCUSSION

Our results show that differences in the prevalences of gonorrhea and chlamydia, as well as in their patterns of spread among the core group and the general population, can be explained on the basis of disease-specific parameters such as the differing fractions of asymptomatic infecteds and differences in the duration of the infectious period. Also, there are differences in the effectiveness of prevention and intervention strategies for the two diseases.

For the prevalence levels in the model, gonorrhea was easier to prevent than chlamydia. All strategies had higher values of effectiveness for gonorrhea than for chlamydia as measured by the ratio r of post-intervention to pre-intervention prevalence. Only extensive contact tracing and consistent condom use reduced chlamydia prevalence to levels comparable with that of gonorrhea.

For both diseases, treatment of symptomatic infecteds combined with contact tracing and treatment of infected partners was extremely effective in reducing prevalence. Gonorrhea disappeared if only 25 percent of partners were treated; for chlamydia, treatment of 50 percent of partners was necessary to reduce the prevalence to a very low level with good probability of extinction.

In designing a screening strategy, decisions have to be made about gender, age, and other characteristics of the subgroup to be targeted. Different diseases may demand targeting of different subgroups. In our model, gonorrhea screening of men and women at age 20

years was superior to screening a larger age interval, whether it was men and women or women only. For chlamydia, targeting women in age class 15–24 years was a better strategy than screening men and women of that age class or age 20 years. This conclusion also holds for the aim of only reducing the prevalence among women.

Effectiveness of screening was greatly increased for strategies targeted to the core group of highly sexually active individuals. Of course, the strategies considered here are highly unrealistic, because it is impossible to identify and screen all core group individuals. Nevertheless, this result shows that the effectiveness of a screening strategy depends greatly on how the subgroup to be targeted is chosen. Here, sociologic and epidemiologic research is needed to investigate the determinants of core group membership. Although age is one determinant, comparison with age-related screening strategies show that age alone is a poor marker for core group membership. Possibly there are other strategies that would make it possible to focus screening more precisely on the high-risk groups. The fact that targeting to the core group was more effective for gonorrhea than for chlamydia again reflects that chlamydia penetrated to a larger extent into the general population.

The effectiveness of condom use in reducing prevalence is striking. One should keep in mind that although the percentages of condom use in our scenarios were based on results from the behavior survey, we made two optimistic assumptions: one was that condom users were consistent in their behavior by always using condoms in all their partnerships; the other assumption, which was even more influential, was that in a partnership between a condom user and a noncondom user the behavior of the condom user was dominant, i.e., condoms were always used. This emphasizes the importance of educating high-risk groups in consistent condom use, and also of especially educating women in insisting on condom use when their partner is unwilling to do so.

Although we cannot make a quantitative comparison between screening and other types of strategies, because we do not have a measure for the effort or costs connected with each strategy, we want to address the question of why screening seems to be inferior to other prevention strategies in reducing prevalence. The essential difference between screening and the other types of strategies is that screening is directed to the individual, whereas contact tracing as well as condom use are directed to the partnership as the unit in which transmission takes place. If one thinks in terms of the sexual network, one could say that screening strategies target nodes of the network, while contact tracing and condom use target links. If individuals are treated regardless of the status of their partner, infected partners will act as a reservoir and quickly reinfect their partners. However, if both partners are treated, in general, formation of a new partnership is required before one of the partners is again at risk of becoming infected. Similarly, if an individual blocks the path of transmission by consistent condom use, all his or her links with other individuals are lost as transmission routes for the disease.

The differences in prevalence that are observed in reality between gonorrhea and chlamydia can be explained on the basis of disease-specific parameters and resulting differences in the effectiveness of prevention strategies applied at present. Treatment of symptomatic infecteds, less extensive use of condoms than defined in scenario 3a, and a moderate level of contact tracing all serve to amplify the difference in prevalence between gonorrhea and chlamydia, leading as observed to a much higher prevalence of chlamydia. If chlamydia is to be targeted specifically by prevention measures, one either has to make an effort to increase the level of contact tracing, increase consistent condom use, or introduce extensive screening of women in younger age classes, preferably targeted to highly sexually active women.

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ERRATUM

Re: "Amount and Intensity of Physical Activity, Physical Fitness, and Serum Lipids in Men"

The *Journal* is notified by Drs. Jaume Marrugat and Roberto Elosua of two errors in table 5 of their recently published paper (1).

The authors point out that in the published version of table 5, the β coefficients for VO_2max and for the constant are misaligned. In the published table, the row of β coefficients for VO_2max appears incorrectly opposite the caption "EEPA (100 kcal/day)" but should have appeared one line above this, opposite "VO_2max (ml/kg/minute)." Similarly, the published table shows the row of β coefficients for the constant incorrectly opposite "(yes = 1/no = 0)" under "Current smoking" instead of one line lower, opposite "Constant."

The authors and the *Journal* regret these errors.

REFERENCE

1. Marrugat J, Elosua R, Covas M-I, et al. Amount and intensity of physical activity, physical fitness, and serum lipids in men. Am J Epidemiol 1996;143:562–9.