Online Supplemental Material for "Direct and indirect effects of screening for *Chlamydia trachomatis* on the prevention of pelvic inflammatory disease: mathematical modeling study"

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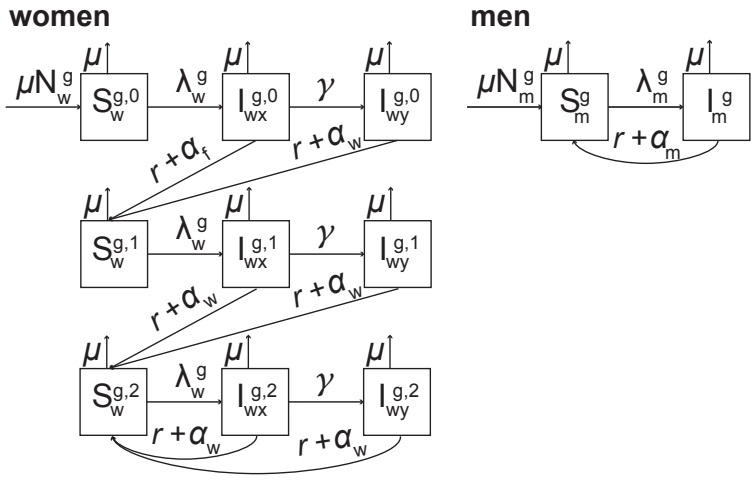
1 Description of the model

1.1 Schematic overview of the chlamydia infection process

eFigure **A1** is a schematic overview of the chlamydia infection process. The compartmental model has a susceptible-infected-susceptible (SIS) structure and stratifies the population by sex, using the labels w and m (woman, men) in the subscript. The population is also stratified by risk class, indicated with the label $g \in \{l, h\}$ in the superscript, which describe low risk and high risk groups, respectively.[1;2] It is assumed that the male and female populations are of equal size ($N_w = N_m$) and that a proportion ρ belongs to the high risk class ($N_w^h = \rho N_w = N_m^h = \rho N_m$). In the notation for women, the second superscript (k) defines the number of repeated chlamydia infections a woman has had $k \in \{0, 1, 2\}$. Note that the third layer ($k = 2$) also contains women with more than two repeated infections. Three layers for women allow us to vary the fraction of all infected women who progress to PID (f_k) depending on the number of repeated chlamydia infections. The infection in women is split into two stages. The transition from the first to the second stage defines the time point ($1/\gamma$) at which PID can develop. More details about the infection process, the incorporation of the progression from chlamydia to PID, and the screening intervention can be found in the main text and in chapters 1-3 of the eAppendix. The definitions of the the other parameters are given in Table 1 of the main text.



eFigure A1: Schematic overview of the chlamydia infection process.

1.2 Differential equations

The model is described by the following set of differential equations with $g \in \{l, h\}$. The definitions of the the other parameters are given in Table 1 of the main text.

$$\frac{dS_w^{g,0}}{dt} = \mu N_w^g - (\lambda_w^g + \mu) S_w^{g,0}$$
$$\frac{dI_{wx}^{g,0}}{dt} = \lambda_w^g S_w^{g,0} - (r + \alpha_w + \gamma + \mu) I_{wx}^{g,0}$$
$$\frac{dI_{wy}^{g,0}}{dt} = \gamma I_{wx}^{g,0} - (r + \alpha_w + \mu) I_{wy}^{g,0}$$

$$\frac{dS_w^{g,1}}{dt} = -(\lambda_w^g + \mu) S_w^{g,1} + (r + \alpha_w)\Big(I_{wx}^{g,0} + I_{wy}^{g,0} \Big)$$
$$\frac{dI_{wx}^{g,1}}{dt} = \lambda_w^g S_w^{g,1} - (r + \alpha_w + \gamma + \mu) I_{wx}^{g,1}$$
$$\frac{dI_{wy}^{g,1}}{dt} = \gamma I_{wx}^{g,1} - (r + \alpha_w + \mu) I_{wy}^{g,1}$$

$$\frac{dS_w^{g,2}}{dt} = -(\lambda_w^g + \mu) S_w^{g,2} + (r + \alpha_w)\Big(I_{wx}^{g,1} + I_{wy}^{g,1} + I_{wx}^{g,2} + I_{wy}^{g,2} \Big)$$
$$\frac{dI_{wx}^{g,2}}{dt} = \lambda_w^g S_w^{g,2} - (r + \alpha_w + \gamma + \mu) I_{wx}^{g,2}$$
$$\frac{dI_{wy}^{g,2}}{dt} = \gamma I_{wx}^{g,2} - (r + \alpha_w + \mu) I_{wy}^{g,2}$$

$$\frac{dS_m^g}{dt} = \mu N_m^g - (\lambda_m^g + \mu) S_m^g + (r + \alpha_m) I_m^g$$
$$\frac{dI_m^g}{dt} = \lambda_m^g S_m^g - (r + \alpha_m + \mu) I_m^g$$

1.3 Mixing matrix and the force of infection

The time dependent force of infection parameters $(\lambda_w^g, \lambda_m^g)$ are calculated, taking into account mixing between the risk groups, the number of infected persons of the opposite sex, and the transmission probability per partner. It is assumed that transmission probability per partner is independent of risk group. The risk group is indicated by the superscript $g \in \{l, h\}$ for low risk and high risk groups, respectively.

We assume that women and men have the same proportion ρ of high risk members, and that there are equal proportions of men and women in the total population (N), i.e. $N^l = (1-\rho)N$ and $N^h = \rho N$, where N stands for the total population.

The 2×2 mixing matrix $M = (m_{ij})_{i,j \in \{l,h\}}$ is defined as follows

$$m_{ij} = \omega\Big(\frac{c_j N^j}{c_l N^l + c_h N^h}\Big) + (1 - \omega)\delta_{ij} \qquad \text{with } \delta_{ij} = \begin{cases} 1 \text{ for } i = j \\ 0 \text{ for } i \neq j \end{cases}$$

where the first index $i \in \{l, h\}$ represents the risk group of the susceptible person and the second index $j \in \{l, h\}$ represents the risk group of the infected person of the opposite sex.[1;2] The parameter ω is used to change from fully assortative mixing ($\omega = 0$) to fully proportionate mixing ($\omega = 1$).

The time dependent force of infection parameters (λ_w^g, λ_m^g) are calculated as follows with

$$\begin{aligned} \lambda_w^g &= c^g \beta m_{gl} \frac{I_m^l}{N_m^l} + c^g \beta m_{gh} \frac{I_m^h}{N_m^h} \\ \lambda_m^g &= c^g \beta m_{gl} \frac{\sum_{k=0}^{2} (I_{wx}^{l,k} + I_{wy}^{l,k})}{N_w^l} + c^g \beta m_{gh} \frac{\sum_{k=0}^{2} (I_{wx}^{h,k} + I_{wy}^{h,k})}{N_w^h} \end{aligned}$$

where c^g is the partner change rate in the risk group g, β the transmission probability per partner; m_{ij} the mixing between risk groups, $I_{wx}^{g,k}, I_{wy}^{g,k}$, and I_m^g the number of infected people, and N_w^g, N_m^g the total number of persons in risk group g for women and men, respectively. For example, λ_w^l is the force of infection which works on susceptible woman in the low risk group, see also eTable **A1** on p5.

eTable A1: Force of infection formula with the example λ_w^l

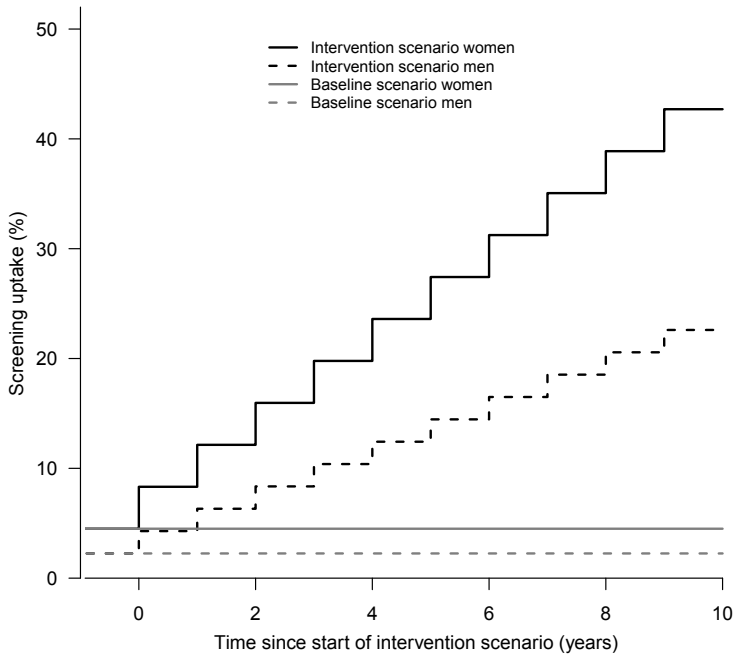
$\lambda_w^l = c^l \beta m_{ll} \frac{I_m^l}{N_m^l} + c^l \beta m_{lh} \frac{I_m^h}{N_m^h}$	
c^l	contact rate for woman in a low risk group
β	transmission probability per partner
m_{ll}	mixing of low risk susceptible with low risk infected
m_{lh}	mixing of low risk susceptible with high risk infected
I_m^l / N_m^l	proportion of infected men in low risk group (prevalence)
I_m^h / N_m^h	proportion of infected men in high risk group (prevalence)

2 Detailed description of screening interventions

For the baseline scenario we assumed constant coverage of chlamydia test uptake. We used an estimated proportion of women seeking treatment for chlamydia in the UK. This estimate (4.5%) was derived in a model by Turner et al.,[3] which was fitted to data from Natsal-2[I] and Adams et al.[4;5] Owing to a lack of data, we assumed that screening uptake in men would be half the screening uptake in women (2.25%).

For the intervention scenario, we assumed a stepwise increase over ten years from the baseline scenario level of test uptake, to the screening uptake in 2010/2011 based on the reports of the National Chlamydia Screening Programme in 15-24 year olds: women (42.7%); men (22.6%).[6] We applied these uptake levels to the model population aged 16-25 years, for whom we defined the behavioural parameters of the model, and assumed no difference in uptake between low risk and high risk groups. See eFigure **A2** on p6.

[I] Britain's Second National Survey of Sexual Attitudes and Lifestyles



eFigure A2: Screening uptake in the baseline and intervention scenarios. Stepwise increase over ten years for the screening uptake in intervention scenario: women (black solid line) and men (black dashed line). Constant background chlamydia test uptake in the baseline scenario: women (grey solid line) and men (grey dashed line).

3 Progression from chlamydia infection to PID

We assumed that PID development becomes possible at a single timepoint after infection with chlamydia. This timepoint is not dependent on the number of repeated chlamydia infections (k) or on risk group membership (g).

3.1 Relation between the fractions f_k, $\tilde{f}_k$, and the scaling factor J

The difference between f_k and $\tilde{f}_k$ is that f_k is the fraction of all infected women in layer k who develop PID, whereas $\tilde{f}_k$ specifies the fraction of women who develop PID at the time point of possible PID occurrence. The relation between the two is

$$f_k = \tilde{f}_k \frac{\gamma}{(\gamma + r + \mu)}$$

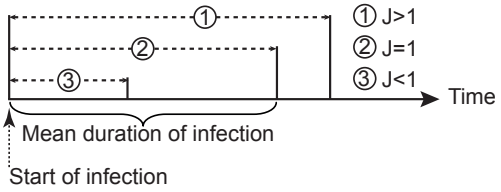
where $\frac{\gamma}{(\gamma+r+\mu)}$ is the probability of making the transition between the two infection stages, in absence of any screening uptake.

The mean time until point of possible PID occurrence $\frac{1}{\gamma}$ is regulated by the mean duration of infection $\frac{1}{r}$; the relation

$$\frac{1}{\gamma} = J\frac{1}{r}$$

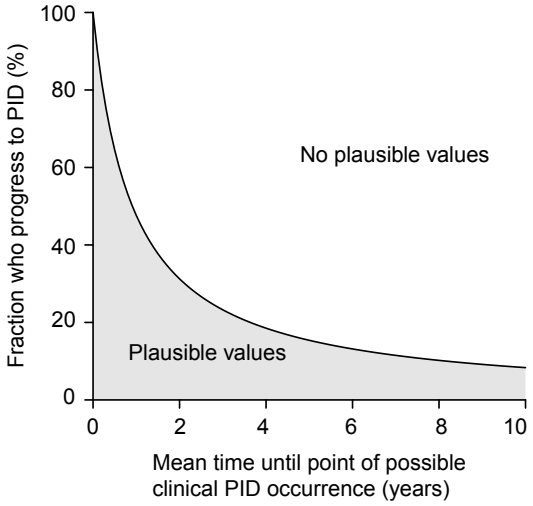
uses a scaling factor J (see eFigure **A3**). If development of PID happens close to the beginning of a chlamydia infection ($J \approx 0$), the fraction $\tilde{f}_k$ of women who develop PID at the time point of possible PID occurrence is almost equal to f_k. The later the time point of possible PID occurrence during the chlamydia infection, the bigger the fraction $\tilde{f}_k$, to guarantee that, overall, a fraction f_k will develop PID. This is necessary because there are more women able to clear

their infection before they are at risk of developing PID. For example, J=2, implies that the mean time until the point of possible PID occurrence is twice the mean duration of infection. In this situation, most infected women will have cleared the infection before this point, so only a small proportion will make the transition and be at risk of developing PID.



eFigure A3: Illustration of scaling factor J. Relationship between mean duration of infection $\frac{1}{r}$ and the mean time between start of infection and timepoint of possible clinical PID occurrence $\frac{1}{\gamma}$ using the scaling factor J. The three options indicated are that the mean time until the timepoint of possible clinical PID occurrence is longer than the mean duration of infection (1) with $J > 1$; is equal to the mean duration of the infection (2) with $J = 1$; or, is shorter than the duration of infection (3) $J < 1$.

eFigure **A4** shows the natural boundaries for the fraction (f) of infected women who progressed to PID for different mean times ($\frac{1}{\gamma}$) until the point of possible PID occurrence, using baseline values for all other parameters (Table 1 of the main text).



eFigure A4: Plausible values for the fraction of all women infected who develop PID for different mean time until progression to clinical PID becomes possible. The condition for the fraction of infected women who develop PID at time point when clinical PID becomes possible ($\tilde{f}$) is met, i.e. $\tilde{f} < 100\%$ (grey shaded area) and $\tilde{f} = 100\%$ (solid line), respectively.

There is only a small area of plausible combinations of the fraction (f) of all women infected with chlamydia who then progress to PID and the mean time until the point of possible PID occurrence. The range of plausible values for the fraction decreases with increasing mean time until point of possible PID occurrence because more women recover without making the transition to the second infection stage as the mean time increases. Therefore, the fraction $\tilde{f}$ of infected women who develop PID at the specific time point has to increase, but the condition $\tilde{f} \leq 100\%$ must be met simultaneously. The area with plausible combinations changes only marginally when the baseline value for the mean duration of infection is halved or doubled.

3.2 Direct and indirect effect of screening on PID incidence

The overall cumulative incidence of PID cases ($C[t]$) at time point t is the sum of the cumulative incidence $C^{g,k}[t]$ in the different risk groups g and layers k and is described by the following equation:

$$C[t] = \sum_{g \in \{l,h\}} \sum_{k=0}^{2} C^{g,k}[t] \quad \text{with} \quad \frac{dC^{g,k}[t]}{dt} = \tilde{f}_k \gamma I_{fx}^{g,k}[t]$$

where $\tilde{f}_k$ specifies the fraction of women who develop clinical PID at the time point of possible PID occurrence, $\frac{1}{\gamma}$ is the mean time between start of infection and time point of possible PID occurrence, and $I_{fx}^{g,k}[t]$ is the number of infected women in the first infection stage of risk class g and layer k at time point t.

Total prevented PID cases The total number of cumulative prevented PID cases ($P_{tot}[t]$) at time point t equals the difference between the cumulative PID incidences in the intervention scenario ($C_I[t]$) and the baseline scenario ($C_B[t]$).

$$P_{tot}[t] = C_B[t] - C_I[t]$$

Directly prevented PID The cumulative number of directly prevented PID cases ($P_d[t]$) at time point t is derived by keeping track of the number of women who leave the first infection stage through screening who would have developed PID in the absence of screening, i.e. women who receive a test and treatment who would otherwise have progressed to PID.

$$P_d[t] = \sum_{g \in \{l,h\}} \sum_{k=0}^{2} P_d^{g,k}[t] \quad \text{with} \quad \frac{dP_d^{g,k}[t]}{dt} = \tilde{f}_k \frac{\gamma}{\gamma + r + \mu} \alpha_f I_{fx}^{g,k}[t]$$

where $\alpha_f I_{fx}^{g,k}$ are the women who leave the first infection stage through screening, $\frac{\gamma}{\gamma+r+\mu}$ is the probability that they would have made the transition to the second infection stage in absence of screening, and $\tilde{f}_k$ is the fraction of those who would have developed PID.

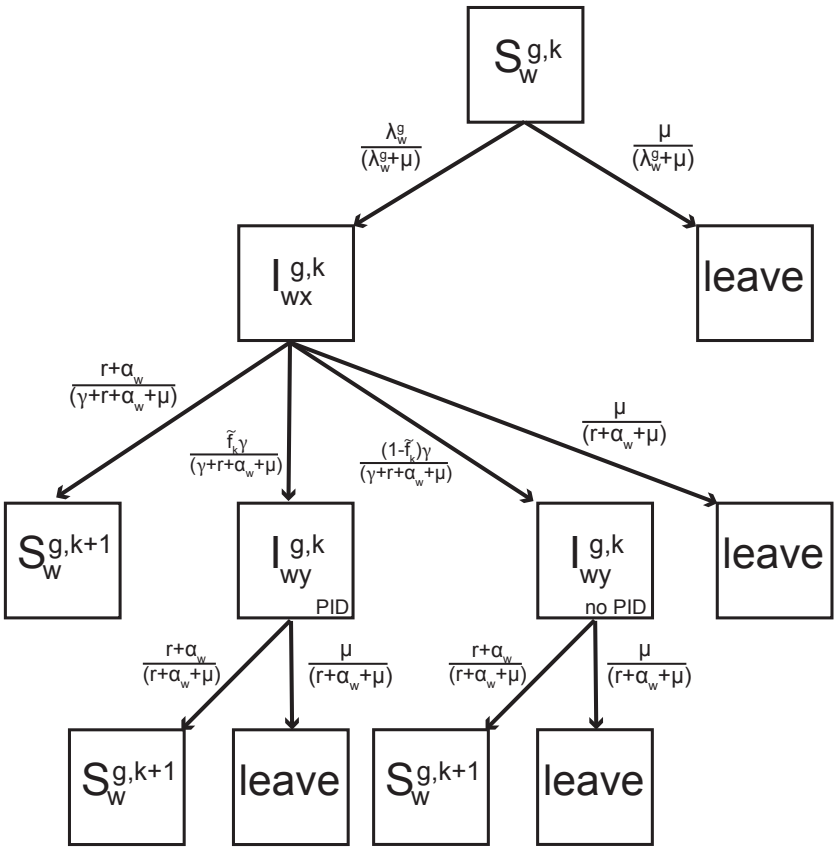
Indirectly prevented PID cases The cumulative number of indirectly prevented PID cases ($P_i[t]$) is derived from the difference between the total and the number of directly prevented PID cases, i.e. the change in the number of PID cases that results from infected women being treated and becoming susceptible and reducing the force of infection

$$P_i[t] = P_{tot}[t] - P_d[t].$$

All cumulative incidences are set to zero at start of the intervention scenario at time point $t = 0$.

3.3 Probability of experiencing a certain number of PID episodes

The probability that a woman will experience a certain number of clinical PID episodes during her sexual life time in the model can be calculated for a given constant force of infection ($\lambda_w^g[t] = \text{const}$). In the main text we use $n = 3$ layers, i.e. $k \in \{0, 1, 2\}$. eFigure **A5** shows the possibilities and corresponding probabilities that a woman who enters the k^{th} layer will proceed to the next layer or leaves the system.



eFigure A5: Possibilities and corresponding probabilities that a woman who enters the k^{th} layer proceeds to the next layer or leaves the system. See eTable **A2** for the explanation of the parameters.

For the women leaving the system from the k^{th} layer we determined the probabilities both for having had a PID episode in the k^{th} layer and for not having had a PID episode in the k^{th} layer. Similarly for the women progressing to the $(k+1)^{th}$ layer we determined the probabilities for having and not having had a PID episode in the k^{th} layer.

$$A_k = P\Big[S_f^{g,k} \to \text{leave with PID}\Big] = \frac{\lambda_w^g}{(\lambda_w^g + \mu)} \tilde{f}_k \frac{\gamma}{(\gamma + r + \alpha_w + \mu)} \frac{\mu}{(r + \alpha_w + \mu)}$$

$$B_k = P\Big[S_f^{g,k} \to S_f^{l,k+1} \text{with PID}\Big] = \frac{\lambda_w^g}{\lambda_w^g + \mu} \tilde{f}_k \frac{\gamma}{(\gamma + r + \alpha_w + \mu)} \frac{r + \alpha_w}{(r + \alpha_w + \mu)}$$

$$C_k = P\Big[S_f^{g,k} \to S_f^{l,k+1}\text{no PID}\Big] = \frac{\lambda_w^g}{\lambda_w^g+\mu}\left[\frac{r+\alpha_w}{\gamma+r+\alpha_w+\mu} + \frac{(1-\tilde{f}_k)\gamma}{(\gamma+r+\alpha_w+\mu)}\frac{r+\alpha_w}{(r+\alpha_w+\mu)}\right]$$

$$D_k = P\Big[S_f^{g,k} \to \text{leave no PID}\Big] = \frac{\mu}{\lambda_w^g+\mu} + \frac{\lambda_w^g}{\lambda_w^g+\mu}\left[\frac{\mu}{(\gamma+r+\alpha_w+\mu)} + \frac{(1-\tilde{f}_k)\gamma}{(\gamma+r+\alpha_w+\mu)}\frac{\mu}{(r+\alpha_w+\mu)}\right]$$

where it holds that $A_k + B_k + C_k + D_k = 1$ and A_k, B_k, C_k, D_k are all smaller than one if $\mu \neq 0$ for $\forall k \in \{0, 1, \ldots, n-1\}$. See eTable **A2** for the explanation of the parameters.

eTable A2: Definition of the parameters in eFigure **A5**

Symbol	Definition
$S_f^{g,k}$	Susceptible women in risk group g having had k repeated infections
$I_{fx}^{g,k}$	Infected women in 1^{st} infection stage in risk group g having had k repeated infections
$I_{fy}^{g,k}$	Infected women in 2^{nd} infection stage in risk group g having had k repeated infections
λ_w^g	Force of infection on women in risk group g
r	Clearance rate of infection
α_w	Screening and effective treatment rate of women
$1/\mu$	Mean duration of sexual activity
γ	Rate of transition from $I_{f,x}^{g,k}$ to $I_{f,y}^{g,k}$
$\tilde{f}_k$	Fraction of those women moving from $I_{f,x}^{g,k}$ to $I_{f,y}^{g,k}$ who develop PID after k repeated infections (in absence of intervention, $\alpha_w = 0$)

The probability that a woman will experience a certain number of clinical PID episodes is described below for the situation in the main text where there are three layers ($n = 3$). Notation: $P\Big[k = m_1, k = m_2\Big]$ is the probability that a woman experiences one PID episode in layer m_1 and one in layer m_2; and $P\Big[k = 2(j^{th})\Big]$ is the probability that a woman experiences one PID episode when in layer $k = 2$ for the j^{th} time.

$$\begin{aligned}\mathbf{P}\Big[\textbf{no PID episode}\Big] =& D_0 + C_0(D_1 + C_1(D_2 + C_2(D_2 + C_2(D_2 + \ldots \\ =& D_0 + C_0D_1 + C_0C_1\Big[D_2\sum_{i=0}^{M} C^i\Big] \overset{M\to\infty}{=} D_0 + C_0D_1 + C_0C_1\Big[\frac{D_2}{1-C_2}\Big]\end{aligned}$$

$$
\begin{aligned}
\mathbf{P}\Big[\textbf{1 PID episode }\Big] =& P\Big[k=0\Big] + P\Big[k=1\Big] + P\Big[k=2(1^{st})\Big] + P\Big[k=2(2^{nd})\Big] + \dots \\
=& A_0 + B_0 D_1 + B_0 C_1 \Big[\frac{D_2}{1-C_2}\Big] \quad k=0 \\
&+ C_0\Big(A_1 + B_1\Big[\frac{D_2}{1-C_2}\Big]\Big) \quad k=1 \\
&+ \frac{1}{1-C_2}\Big\{C_0 C_1\Big(A_2 + B_2\Big[\frac{D_2}{1-C_2}\Big]\Big)\Big\} \quad k=2
\end{aligned}
$$

$$
\begin{aligned}
P\Big[1 \text{ PID episode in } k=2\Big] =& C_0 C_1\Big(A_2 + B_2\Big[\frac{D_2}{1-C_2}\Big]\Big) + C_0 C_1 C_2\Big(A_2 + B_2\Big[\frac{D_2}{1-C_2}\Big]\Big) \\
&+ \dots + C_0 C_1 C_2^{j-1}\Big(A_2 + B_2\Big[\frac{D_2}{1-C_2}\Big]\Big) + \dots \\
=& \sum_{j=0}^{M} C_0 C_1\Big(A_2 + B_2\Big[\frac{D_2}{1-C_2}\Big]\Big) C_2^j \\
\overset{M\to\infty}{=}& \frac{1}{1-C_2}\Big\{C_0 C_1\Big(A_2 + B_2\Big[\frac{D_2}{1-C_2}\Big]\Big)\Big\}
\end{aligned}
$$

$$
\begin{aligned}
\mathbf{P}\Big[\textbf{ 2 PID episodes}\Big] =& P\Big[k=0, k=1\Big] + P\Big[k=0, k=2(1^{st})\Big] + P\Big[k=0, k=2(2^{nd})\Big] + \dots \\
&+ P\Big[k=1, k=2(1^{st})\Big] + P\Big[k=1, k=2(2^{nd})\Big] + \dots \\
&+ P\Big[k=2(1^{st}), k=2(2^{nd})\Big] + \dots \\
=& B_0\Big(A_1 + B_1\Big[\frac{D_2}{1-C_2}\Big]\Big) + \frac{B_0 C_1}{1-C_2}\Big(A_2 + B_2\Big[\frac{D_2}{1-C_2}\Big]\Big) \quad k=0\text{+other} \\
&+ \frac{C_0 B_1}{1-C_2}\Big(A_2 + B_2\Big[\frac{D_2}{1-C_2}\Big]\Big) \quad k=1\text{+other} \\
&+ \frac{C_0 C_1 B_2}{1-C_2}\Big(A_2 + B_2\Big[\frac{D_2}{1-C_2}\Big]\Big) \quad 2\times \text{ in } k=2
\end{aligned}
$$

$$
\begin{aligned}
P\Big[k=0\text{+other}\Big] =& P\Big[k=0, k=1\Big] + P\Big[k=0, k=2(1^{st})\Big] + \dots + P\Big[k=0, k=2(j^{th})\Big] + \dots \\
=& B_0\Big\{A_1 + B_1\Big[\frac{D_2}{1-C_2}\Big]\Big\} + \dots + B_0 C_1 C_2^{j-1}\Big\{A_2 + B_2\Big[\frac{D_2}{1-C_2}\Big]\Big\} + \dots \\
=& B_0\Big\{A_1 + B_1\Big[\frac{D_2}{1-C_2}\Big]\Big\} + \frac{B_0 C_1}{1-C_2}\Big\{A_2 + B_2\Big[\frac{D_2}{1-C_2}\Big]\Big\}
\end{aligned}
$$

$$
\begin{aligned}
P\Big[k = 1\text{+other}\Big] =& P\Big[k = 1, k = 2(1^{st})\Big] + \ldots + P\Big[k = 1, k = 2(j^{th})\Big] + \ldots \\
=& \ldots + C_0 B_1 C_2^{j-1}\Big\{A_2 + B_2\Big[\frac{D_2}{1 - C_2}\Big]\Big\} + \ldots \\
=& \frac{C_0 B_1}{1 - C_2}\Big\{A_2 + B_2\Big[\frac{D_2}{1 - C_2}\Big]\Big\}
\end{aligned}
$$

$$
\begin{aligned}
P\Big[2 \times k = 2\Big] =& \sum_{j=2}^{M} C_0 C_1 C_2^{j-2} B_2\Big\{A_2 + B_2\Big[\frac{D_2}{1 - C_2}\Big]\Big\} \\
=& \sum_{j=0}^{M-2} C_0 C_1 C_2^{j} B_2\Big\{A_2 + B_2\Big[\frac{D_2}{1 - C_2}\Big]\Big\} \\
\overset{M\to\infty}{=}& \frac{C_0 C_1 B_2}{1 - C_2}\Big\{A_2 + B_2\Big[\frac{D_2}{1 - C_2}\Big]\Big\}
\end{aligned}
$$

$$
\mathbf{P}\Big[\geq \mathbf{3\ PID\ episodes}\Big] = 1 - \Big(P\Big[\text{no PID}\Big] + P\Big[1\text{ PID}\Big] + P\Big[2\text{*PID}\Big]\Big)
$$

Note, if we assume that all n layers are the same, i.e. $\tilde{f} = \tilde{f}_k$ and therefore $A = A_k, B = B_k, C = C_k$ and $D = D_k$, the probability that a woman will experience exact $s \geq 1$ episodes of PID can be calculated with

$$
\mathbf{P}\Big[\mathbf{exact\ s\ PID\ episodes}\Big] = \Big[A + BD\frac{1}{1 - C}\Big] \sum_{j=s-1}^{M} \Big[\binom{j}{s-1} B^{s-1} C^{j-(s-1)}\Big], \text{ for } M \to \infty
$$

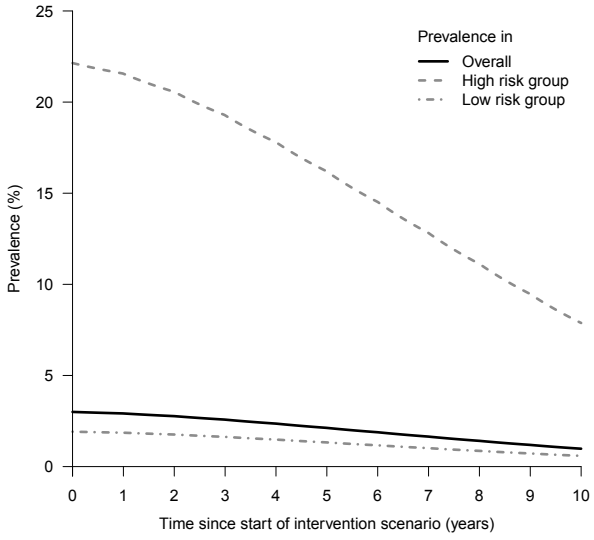
4 Additional results

4.1 Probabilities of clinical PID episodes during a woman's sexual life time in the model

eTable A3: Probabilities of clinical PID episodes during a woman's sexual life time in the model, in the absence of screening and using baseline values for all other parameters.

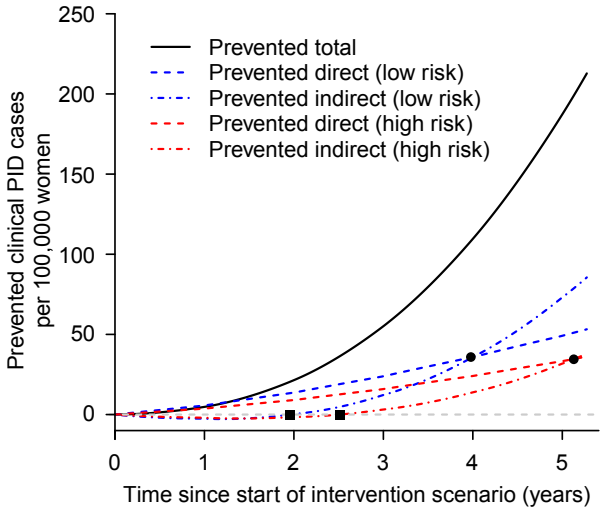
Risk group	**Probability of experiencing clinical PID episodes (%)**				
	None	**Any**	**One**	**Two**	≤ 3
Low risk	97.96	2.04	2.00	0.04	$< 10^{-4}$
High risk	80.17	19.83	16.24	2.23	1.36
Overall	97.01	2.99	2.76	0.15	0.07

4.2 Change in chlamydia prevalence



eFigure A6: Change in chlamdiya prevalence with intervention scenario, overall and by risk group. The implementation of the intervention scenario reduced chlamydia prevalence from 3.0% to 1.0% after ten years. The prevalence in the high risk group decreased from 22.1% to 7.9% and in the low risk group from 1.9% to 0.6%.

4.3 Cumulative incidences of prevented PID cases by risk group



eFigure A7: Cumulative incidences of prevented PID cases by risk group, using baseline values. The total number of prevented clinical PID cases per 100,000 women (solid line) is split by direct effect (dashed line) and indirect effect (dashed-dotted line), and by low-risk group (blue) and high-risk group (red). In women in the high-risk group, the time at which direct and indirect effects contribute equally to PID prevention occurs later than in low risk women (circles). The net increase of PID cases resulting from indirect screening is larger and lasts longer in women in the high risk group compared to the low risk group (squares).

4.4 Multivariable uncertainty analysis for the time point of equal contribution and duration of net increase of PID cases from the indirect effect

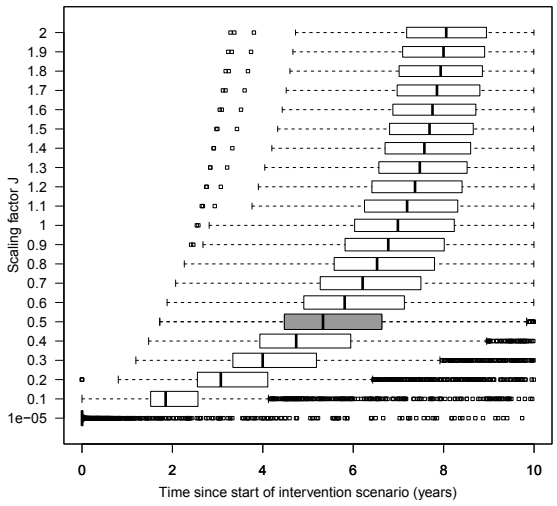
Of the sampled 3,000 parameter sets for the multivariable uncertainty analysis, 273 parameter combinations could not be used. This was because the transmission probability per partner must be ≤ 1 (6/273) and at the same time the prevalence drawn from the uniform distribution (described in Table 1 from the main text) must be achieved. An additional restriction is that in both risk groups the prevalence has to be more than 0.1% to ensure infection exists in both risk groups (267/273).

We obtained the median and the interquartile range for the time points 'equal contribution' (eFigure **A8**) and the time point 'end of net increase of PID cases due to the indirect effect' (eFigure **A9**) by varying the scaling factor J for the mean time until point of possible PID occurrence from 10^{-5} to 2 (2,727 parameter combinations used).

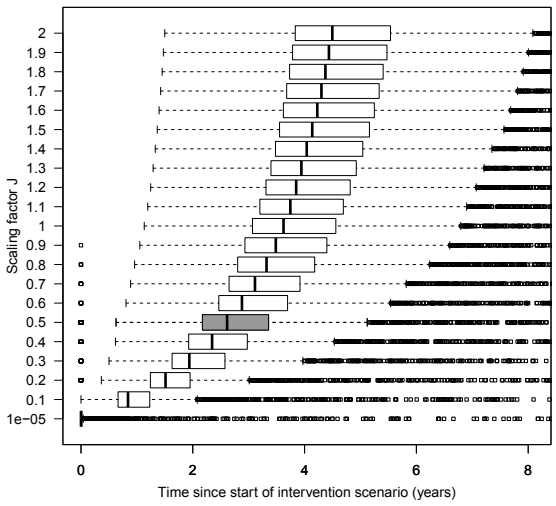
The range for the mean duration of infection in the 2,727 parameter sets was 117-600 days, i.e. with the scaling factor $J = 0.5$ (grey shaded box in eFigures **A8** and **A9**) the mean time until point of possible PID occurrence ranged from 58.5-300 days. Note that in each parameter set the mean time until point of possible PID occurrence is always 0.5 times the mean duration of infection.

If the scaling factor is increased there are fewer parameter sets in which the time points 'equal contribution' and 'end of net increase of PID cases due to the indirect effect' are within the ten years of the intervention scenario (shown in the eFigures with decreasing heights of boxes).

Therefore, time points of equal contribution, and the end of net increase of PID cases due to the indirect effect are right censored. However, the median of the two time points correspond closely with the values from the univariable uncertainty analysis.



eFigure A8: Equal contribution of direct and indirect effect (multivariable uncertainty analysis). In this analysis the 2,727 parameter sets are used and the scaling factor J (the mean time until point of possible PID occurrence) is varied. For each value of J, the time points at which there is a equal contribution of the direct and indirect effects are summarized over all parameter sets. The vertical line indicates the median and the width corresponds to the interquartile range. The whiskers extend to the most extreme data point, which is no more than 1.5 times the interquartile range from the box. Outliers are indicated with squares. The grey shaded box corresponds to the baseline value for scaling factor $J = 0.5$. Boxes are drawn with heights proportional to the square-roots of the number of observations in the groups.



eFigure A9: Duration of net increase of PID cases due to the indirect effect of screening (multivariable uncertainty analysis). In this analysis the 2,727 parameter sets are used and the scaling factor J (the mean time until point of possible PID occurrence) is varied. For each value of J, the duration of net increase of PID cases due to the indirect effect of screening are summarized over all parameter sets. The vertical line indicates the median and the width corresponds to the interquartile range. The whiskers extend to the most extreme data point, which is no more than 1.5 times the interquartile range from the box. Outliers are indicated with squares. The grey shaded box corresponds to the baseline value for the scaling factor $J = 0.5$. Boxes are drawn with heights proportional to the square-roots of the number of observations in the groups.

References

[1] H. W. Hethcote and J. A. Yorke. *Gonorrhea transmission dynamics and control: Lecture notes in biomathematics*. Springer, Berlin, 1984.

[2] G. P. Garnett, K. J. Mertz, L. Finelli, W. C. Levine, and M. E. St Louis. The transmission dynamics of gonorrhoea: modelling the reported behaviour of infected patients from Newark, New Jersey. *Philos T Roy Soc B*, 354(1384):787–797, 1999.

[3] K. M. E. Turner, Elisabeth J Adams, D. S. Lamontagne, L. Emmett, K. Baster, and W. J. Edmunds. Modelling the effectiveness of chlamydia screening in England. *Sex Transm Infect*, 82(6):496–502, 2006.

[4] K. A. Fenton, C. Korovessis, A. M. Johnson, A. McCadden, S. McManus, K. Wellings, C. H. Mercer, C. Carder, A. J. Copas, K. Nanchahal, W. Macdowall, G. Ridgway, J. Field, and B. Erens. Sexual behaviour in Britain: reported sexually transmitted infections and prevalent genital Chlamydia trachomatis infection. *The Lancet*, 358(9296):1851–1854, 2001.

[5] E. J. Adams, A. Charlett, W. J. Edmunds, and G. Hughes. Chlamydia trachomatis in the United Kingdom: a systematic review and analysis of prevalence studies. *Sex Transm Infect*, 80(5):354–362, 2004.

[6] National Chlamydia Screening Programme. England Quarters 1-4 April 2010 - March 2011. National Chlamydia Screening Programme, 2011. Available at: http://www.chlamydiascreening.nhs.uk/ps/assets/pdfs/data/sha_presentations11/Q1-4%202010-11%20ENGLAND.pdf (accessed 12.04.2012).