## Web Material

Web Appendix 1: Literature identification

We sought prospective studies of women with CT including observational studies with or without a control group, and RCTs of screening interventions. We identified studies from recent review papers (1-4), reference searches of published economic and population transmission models (5-15) and as part of a wider review of the literature on the natural history of CT. Included among these was a recent systematic review instituted at an Expert Advisory Meeting of the Centers for Disease Control and Prevention (1). We exclude the study by Bachmann et al (16) because the follow-up time was not reported, the study by Stamm et al (17) because the patients were co-infected with gonorrhoea, and the study by Westergaard et al (18) because the patients were women who had just undergone an abortion, and this is a very unrepresentative population. The study by Morre et al (19) is excluded because of uncertainty about the adequacy of outcome assessment (20). Finally, four of the studies shown in table 1 are excluded from the modelling because of a lack of a control group (21-24). Web Appendix 2: Sensitivity analyses

We performed 3 sets of sensitivity analysis

First, the proportion of patients in the Scholes trial who were assumed to have been tested during the trial was lowered from 32% to 15%. This had no measurable effect on results of the final synthesis (results not shown).

The effect on key model results of changing the infection and reinfection rates for both the one and two rate models is shown in Web Table 1. The results show clearly that in the full synthesis the assumed infection/re-infection rates have a minimal impact on the results altering the estimates of  $\kappa$ , the probability that an incident CT episode causes PID, by at most a multiplicative factor of 4%.

In summary, we found that results from the full synthesis models were insensitive to these modelling assumptions.

Web Appendix 3. Development of functional relationships

Note that the notation used in the paper is extended here to facilitate a full mathematical description of the *non-homogenous* model.

1. Relationships between model parameters and data estimands.

Note: in our analyses the values of  $\lambda^{I}$ , u', u,  $\theta^{CT-}$  and hence any functions of them such as  $p_{ij}(t)$  are all study dependent but the *s* subscript has been dropped for ease of reading.

#### Expression in a homogenous model:

In a single rate model  $\theta^{CT+}$  is constant over time and the data from women who are CT+ and the women who are CT- at baseline in study *s* inform the transition probabilities  $p_{13}(t)$  and  $p_{23}(t)$  respectively where *t* is the mean follow-up time of the study. These transition probabilities are obtained by solving equation 2 numerically in each iteration of the MCMC simulation using the Runge-kutta method in WBDiff.

#### Expression in a two step piecewise homogenous model:

We use a 1 day discrete time approximation to the underlying continuous process to simplify the calculations. It is necessary to extend the notation used in the paper. Let  $\pi_{i,h}$  be the state occupancy proportion for state *i* in day *h* of the study. The proportion in state *i* = 1 is further subdivided into the proportion  $\pi_{i,h}^{hi}$  who are subject to developing PID caused by CT at rate  $\delta_1$ , and the proportion  $\pi_{i,h}^{low}$  who develop PID caused by CT at rate  $\delta_2$  where:

$$\pi_{1,h} = \pi_{1,h}^{low} + \pi_{1,h}^{hi}$$

Finally  $p_{ij}^{hi}$  and  $p_{ij}^{low}$  are the daily transition probabilities from state *i* to state *j*, for women who are subject to developing PID caused by CT at rates  $\delta_1$  and  $\delta_2$  respectively.  $p_{ij}^{hi}$  and  $p_{ij}^{low}$  are calculated using equation 2, and solved using WBDiff, with the appropriate expression for  $\theta_s^{CT+}$  substituted into equation 1. The observed data inform the proportions  $\pi_{3,H}$  calculated for each arm where *H* is equal to the follow-up period of the study in days. So  $\pi_{3,H}$  is the proportion of patients in state 3 at the end of the study which is the parameter in the Binomial likelihood. Equations for the state occupancy proportions on day *h* of the study can be written as follows:

$$\begin{split} \pi_{1,h} &= \pi_{1,h-1}^{low} \cdot p_{11}^{low} + \pi_{1,h-1}^{hi} \cdot p_{11}^{hi} + \pi_{2,h-1} \cdot p_{21}^{hi} \\ \pi_{2,h} &= \pi_{2,h-1} \cdot p_{22}^{hi} + \pi_{1,h-1}^{low} \cdot p_{12}^{low} + \pi_{1,h-1}^{hi} \cdot p_{12}^{hi} \\ \pi_{3,h} &= 1 - \pi_{2,h} - \pi_{1,h} \end{split}$$

Where  $\pi_{1,0} = \pi_{1,0}^{low} + \pi_{1,0}^{hi}$ ,  $\pi_{2,0} = 1 - \pi_{1,0}$ ,  $\pi_{3,0} = 0$ . It just remains to specify equations for  $\pi_{1,h}^{hi}$  and  $\pi_{1,h}^{low}$ , which depend on whether the study is clinic or screening based. To speed up the processing time the code is written in WBDev (27), an add-on package for WinBUGS that can be used to specify new functions using component Pascal.

## Clinic based studies:

$$\pi_{1,h}^{hi} = \pi_{1,h} \qquad \qquad \} h = 1, \dots, B$$
  
$$\pi_{1,h}^{hi} = \sum_{i=(h+1-B)}^{h} \left(\pi_{2,i-1} \cdot p_{21}^{hi}\right) p_{11}^{hi^{(h-i)}} \qquad \qquad \} h = B+1, \dots, H$$
  
$$\pi_{1,h}^{low} = \pi_{1,h} - \pi_{2,h}^{hi}$$

Recall from the main text that B is the number of days for which patients are subject to the rate  $\delta_1$  of PID caused by CT after entering state 1 if they don't leave during this period. So in clinic based studies all women in state 1 during the first B days are subject to the rate  $\delta_1$ . The second equation shows the proportion of women who are in state 1 and progress at rate  $\delta_1$  for each day h in the study after B days have elapsed. The equation sums over all patients who have moved to state 1 in the last B days multiplied by the probability they have remained there until day h. In the case arm  $\pi_{1,0}^{hi} = 1$  and,  $\pi_{1,0}^{low}$  and  $\pi_{2,0}$  equal 0. In the control arm  $\pi_{1,0}^{hi}$  and  $\pi_{1,0}^{low}$  equal 0, and  $\pi_{2,0}$  equals 1.

#### Screening based studies

In screened populations women who are CT+ have already been infected for a period of time before recruitment. We assume that a proportion,  $\phi$ , of incident CT cases are symptomatic and treated, clearing at rate  $\lambda^T$ , and the remaining infections, 1- $\phi$ , are asymptomatic and clear at rate  $\lambda^C$ . The probability  $w_b$  that a recruited patient was recruited exactly b days after infection is:

$$\omega_{b} = \varphi \cdot \left( \exp\left(-\lambda^{T} \cdot \frac{(b-1)}{365}\right) - \exp\left(-\lambda^{T} \cdot \frac{b}{365}\right) \right) + (1-\varphi) \cdot \left( \exp\left(-\lambda^{C} \cdot \frac{(b-1)}{365}\right) - \exp\left(-\lambda^{C} \cdot \frac{b}{365}\right) \right)$$

The proportions in the high and low rate groups are:

$$\pi_{1,h}^{hi} = \sum_{i=h}^{B} \omega_{B+1-i} \pi_{1,0} \cdot p_{11}^{\ h} + \sum_{i=1}^{h} \left( \pi_{2,i-1} \cdot p_{21}^{hi} \right) p_{11}^{hi^{(h-i)}} \quad \} h = 1, \dots, B$$
(A.1)

$$\pi_{1,h}^{hi} = \sum_{i=(h+1-B)}^{h} \left(\pi_{2,i-1} \cdot p_{21}^{hi}\right) p_{11}^{hi^{(h-i)}} \qquad \} h = B+1, \dots, H \qquad (A.2)$$
$$\pi_{1,h}^{low} = \pi_{1,h} - \pi_{2,h}^{hi}$$

Equation A.1 calculates the proportion of women who are in state 1 and subject to the first causal progression rate  $\delta_1$  on each day h of the study from 1 to B. The first term is the proportion of women who began the study as CT positive and were infected within 60 days of day h multiplied by the probability they have remained in state 1 until day h. This term is not included in A.2 because after B days all of the remaining patients move to the  $\delta_2$  rate. The second term sums over all patients who have moved to state 1 by day h multiplied by the probability they have remained that 1 by day h multiplied by the probability they have remained at the state 1 by day h multiplied by the probability they have remained there until day h. Equation A.2 is the same as for clinic based studies. In the CT positive group  $\pi_{1,0}^{hi} = \sum_{b=1}^{B} \omega_b$ ,  $\pi_{1,0}^{low} = 1 - \pi_{1,0}^{hi}$ , and  $\pi_{2,0}$  equals 0. In the CT negative group  $\pi_{1,0}^{hi}$  and  $\pi_{1,0}^{low}$  equal 0, and  $\pi_{2,0}$  equals 1.

## 2. Proportion of CT related PID that is prevented by screening

We consider an annual screening programme, in which women are screened at exactly 365day intervals. We derive an expression for the proportion of episodes of PID prevented by annual screening in women who become infected with CT. We assume that treatment is administered 14 days after testing (the results are fairly insensitive to different reasonable assumptions about this time period). Women are screened within a year of infection with each day having an equal probability (1/365) of this occurring. The expression differs between the one and two rate models.

## One rate model

The probability that an episode of PID is caused by a CT episode exactly b days after infection is:

$$\kappa_{b} = \varphi \cdot \left( \left( 1 - \exp\left(-\left(\lambda^{T} + \delta\right) \cdot t_{u_{0}u_{b}}\right) \right) - \left( 1 - \exp\left(-\left(\lambda^{T} + \delta\right) \cdot t_{u_{0}u_{(b-1)}}\right) \right) \cdot \frac{\delta}{\lambda^{T} + \delta} + \left( 1 - \varphi \right) \cdot \left( \left( 1 - \exp\left(-\left(\lambda^{C} + \delta\right) \cdot t_{u_{0}u_{b}}\right) \right) - \left( 1 - \exp\left(-\left(\lambda^{C} + \delta\right) \cdot t_{u_{0}u_{(b-1)}}\right) \right) \cdot \frac{\delta}{\lambda^{C} + \delta} \right)$$

Under the assumptions outlined above, the probability  $\kappa^{SCN}$  a CT infection causes an episode of PID in a woman who is screened at random annually is:

$$k^{SCN} = \sum_{b=1}^{14} \kappa_{b'} + \sum_{b=15}^{379} \kappa_{b'} \left( 1 - \frac{(b-14)}{365} \right)$$
(A.3)

And the proportion of PID episodes that are caused by CT, in women with CT, that are prevented by annual testing,  $\chi$ , equals:

$$\chi = 1 - \frac{\kappa^{SCN}}{\kappa} \tag{A.4}$$

## Two rate model

In a two rate model the probability that an episode of PID develops exactly *b* days after infection equals:

$$\varphi. \left( \exp(-\left(\lambda^{T} + \delta_{1}\right) t_{u_{0}u_{(b-1)}} - \exp\left(-\left(\lambda^{T} + \delta_{1}\right) t_{u_{0}u_{b}}\right) \right) \cdot \frac{\delta_{1}}{\lambda^{T} + \delta_{1}} + \left(1 - \varphi\right) \cdot \left( \exp(-\left(\lambda^{C} + \delta_{1}\right) t_{u_{0}u_{(b-1)}} - \exp\left(-\left(\lambda^{C} + \delta_{1}\right) t_{u_{0}u_{b}}\right) \right) \cdot \frac{\delta_{1}}{\lambda^{C} + \delta_{1}} \right\} b \leq B$$

$$\kappa_{b} = \left\{ \varphi. \left( \exp(-\left(\lambda^{T} + \delta_{2}\right) t_{u_{1}u_{(b-1)}} - \exp\left(-\left(\lambda^{T} + \delta_{2}\right) t_{u_{1}u_{b}}\right) \right) \cdot \frac{\delta_{2}}{\lambda^{T} + \delta_{2}} + \left(1 - \varphi\right) \cdot \left( \exp(-\left(\lambda^{C} + \delta_{2}\right) t_{u_{1}u_{(b-1)}} - \exp\left(-\left(\lambda^{C} + \delta_{2}\right) t_{u_{1}u_{b}}\right) \right) \cdot \frac{\delta_{2}}{\lambda^{C} + \delta_{2}} \right\} b > B$$

Where B = 30, 60, 90 days the proportion of PID cases prevented by screening is calculated from equations A.3 and A.4 as before.

# Web Appendix 4: Estimation

A 'burn-in' period of 50 000 iterations was used for the MCMC simulation and the Brooks-Gelman-Rubin statistic (28) demonstrated convergence of all parameters within a few thousand samples. The results reported in the paper are summary means and credible intervals of the marginal distributions from this joint posterior based on samples of 200 000. Web Appendix 5: Computer code

WinBUGS program for the 2-rate model.

```
model {
# chlamydia informative priors
r.phi ~ dbin(phi,129)
lambda.c ~ dnorm(0.743, 193)
dur.symp ~ dunif(0.077, 0.15)
                                # 4 - 8 weeks
lambda.t <- 1 / cut(dur.symp)</pre>
# Prospective PID analysis constant progression rate
# Likelihood
for (s in 1:4) {
 for (i in 1:2) {
  r[s,i] \sim dbin(p[s,i],n[s,i])
  }
 }
# transistion probability calulations
for (s in 1:4) {
 for (i in 1:2) {
  for(j in 1:3) {
   theta[s,1,index[i,j]] <- lambda[s,1,i,j]</pre>
   theta[s,2,index[i,j]] <- lambda[s,2,i,j]</pre>
   }
  }
 lambda[s,1,1,1] <- - lambda[s,1,1,2] - lambda[s,1,1,3]</pre>
 lambda[s,1,1,3] <- theta.CTpos1[s]</pre>
 lambda[s,1,2,2] <- - lambda[s,1,2,1] - lambda[s,1,2,3]</pre>
 lambda[s,1,2,3] <- theta.CTneg[s]</pre>
 lambda[s,2,1,1] <- - lambda[s,2,1,2] - lambda[s,2,1,3]</pre>
 lambda[s,2,1,3] <- theta.CTpos2[s]</pre>
 lambda[s,2,2,2] <- - lambda[s,2,2,1] - lambda[s,2,2,3]</pre>
 lambda[s,2,2,3] <- theta.CTneg[s]</pre>
 }
# Infection rate
for (s in 1:2) {
 lambda[s,1,2,1] <- 0.0
 lambda[s,2,2,1] <- 0.0
 }
for (s in 3:4) {
 lambda[s,1,2,1] <- 0.0
 lambda[s,2,2,1] <- 0.0
 }
# Clearance + treatment rate
lambda[1,1,1,2] <- lambda.c + 0.64</pre>
lambda[1,2,1,2] <- lambda.c + 0.64</pre>
lambda[2,1,1,2] <- lambda.c + 0.43</pre>
lambda[2,2,1,2] <- lambda.c + 0.43
lambda[3,1,1,2] <- lambda.c + 0.32</pre>
lambda[3,2,1,2] <- lambda.c + 0.32</pre>
lambda[4,1,1,2] <- lambda.c + 0.32</pre>
lambda[4,2,1,2] <- lambda.c + 0.32
```

```
# Models for rates
for (s in 1:4) {
 theta.CTpos1[s] <- alpha[s] + delta[1]</pre>
 theta.CTpos2[s] <- alpha[s] + delta[2]</pre>
 theta.CTneg[s] <- alpha[s]</pre>
 }
# Other data
r.sch ~ dbin(pi.sch,n.sch) # Scholes - ct prevalence
r.ost ~ dbin(pi.ost,n.ost) # Ostergaard - ct prevalence
# Priors
delta[1] ~ dexp(0.00001)
delta[2] ~ dexp(0.00001)
for (s in 1:4) {
 alpha[s] ~ dexp(0.00001)
pi.sch ~ dbeta(1,1)
pi.ost ~ dbeta(1,1)
phi ~ dbeta(1,1)
# Calculation of parameters in the likekihood
for (s in 1:4) {
 solutionld[s,1,1:dim] <- three.state(init[1:dim],time,theta[s,1,1:n.par],</pre>
                                          origin, tol)
 solution1d[s,2,1:dim] <- three.state(init[1:dim],time,theta[s,2,1:n.par],</pre>
                                          origin, tol)
 for (i in 1:2) {
  for (z in 1:6) {
   vectorforwbdev[s,i,z] <- solution1d[s,1,z]</pre>
   vectorforwbdev[s,i,z+6] <- solution1d[s,2,z]</pre>
   }
  vectorforwbdev[s,i,13] <- round(t[s] * 365)</pre>
  vectorforwbdev[s,i,14] <- B</pre>
  vectorforwbdev[s,i,15] <- lambda.c</pre>
  vectorforwbdev[s,i,16] <- lambda.t</pre>
  vectorforwbdev[s,i,17] <- phi</pre>
  vectorforwbdev[s,i,18] <- clinorscreen[s]</pre>
  vectorforwbdev[s,i,19] <- caseprop[s,i]</pre>
  p[s,i] <- generatep(vectorforwbdev[s,i,1:19])</pre>
  }
 caseprop[s,2] <- 0</pre>
 }
caseprop[1,1] <- 1</pre>
caseprop[2,1] <- 1</pre>
caseprop[3,1] <- pi.sch</pre>
caseprop[4,1] <- pi.ost</pre>
clinorscreen[1] <- 0 # clinic based study</pre>
for (s in 2:4) {
 clinorscreen[s] <- 1 # screening studies</pre>
 }
# Residual Deviance
for (s in 1:4) {
 for (i in 1:2) {
  dev[s,i] <- 2 * (r[s,i] * log(r[s,i] / (p[s,i] * n[s,i])) +</pre>
                    (n[s,i] - r[s,i]) * log((n[s,i] - r[s,i]) /
                    (n[s,i] - (n[s,i] * p[s,i]))))
```

```
}
}
dev.sch <- 2 * (r.sch * log(r.sch / (pi.sch * n.sch)) +
               (n.sch - r.sch) * log((n.sch - r.sch) /
               (n.sch - (n.sch * pi.sch))))
dev.ost <- 2 * (r.ost * log(r.ost / (pi.ost * n.ost)) +
               (n.ost - r.ost) * log((n.ost - r.ost) /
               (n.ost - (n.ost * pi.ost))))
sumdev <- sum(dev[ , ]) + dev.sch + dev.ost</pre>
# Results
kappa <- (1 - phi) * (
          (1 - (exp( - (lambda.c + delta[1]) * (B / 365)))) *
           delta[1] / (lambda.c + delta[1]) +
           exp( - (lambda.c + delta[1]) * (B / 365)) *
           delta[2] / (lambda.c + delta[2])
           ) +
           phi * (
          (1 - (exp( - (lambda.t + delta[1]) * (B / 365)))) *
           delta[1] / (lambda.t + delta[1]) +
           exp( - (lambda.t + delta[1]) * (B / 365)) *
           delta[2] / (lambda.t + delta[2])
           )
# proportion of PIDs prevented by annual screening
# assumes two-week delay between test and treatment
for (i in 1:B) {
 temp1[i] <- phi * (
             ((1 - exp(-(lambda.t + delta[1]) * (i/365))) -
              (1 - exp(-(lambda.t + delta[1]) * ((i-1)/365)))) *
              (delta[1] / (lambda.t + delta[1])) *
              (1 - (max(0,(i-14)) / 365))) +
             (1 - phi) * (
             ((1 - exp(-(lambda.c + delta[1]) * (i/365))) -
              (1 - exp(-(lambda.c + delta[1]) * ((i-1)/365)))) *
              (delta[1] / (lambda.c + delta[1])) *
              (1 - (max(0,(i-14)) / 365)))
 }
for (i in B+1:379) {
 temp1[i] <- phi * (</pre>
             ((1 - exp(-(lambda.t + delta[2]) * (i/365))) -
              (1 - exp(-(lambda.t + delta[2]) * ((i-1)/365)))) *
              (delta[2] / (lambda.t + delta[2])) *
              (1 - (max(0, (i-14)) / 365))) +
             (1 - phi) * (
             ((1 - exp(-(lambda.c + delta[2]) * (i/365))) -
              (1 - exp(-(lambda.c + delta[2]) * ((i-1)/365)))) *
              (delta[2] / (lambda.c + delta[2])) *
              (1 - (max(0,(i-14)) / 365)))
 }
prop.prevent <- 1 - (sum(temp1[ ]) / kappa)</pre>
# Bayesian p-value
test <- delta[1] - delta[2]</pre>
B.p <- step(test)</pre>
}
```

```
# Data
list(
# PID (1 month) prospective
# 1. Rees
# 2. POPI
# 3. Scholes
# 4. Ostergaard
r=structure(.Data=c(
8,3,
7,1,
33,7,
20,9
),.Dim=c(4,2)),
n=structure(.Data=c(
67,62,
74,63,
1598,645,
487,443
),.Dim=c(4,2)),
t = c(0.125, 1, 1, 1),
B = 60, # If this were set above 365 WBDEV code would need changing
r.sch = 44,
n.sch = 645,
r.ost = 43,
n.ost = 867,
r.phi=30,
time = 0.00274,
# forward equations
dim=6,origin=0,tol=1.0E-4, init=c(1,0,0, 0,1,0),n.par=6,
index=structure(.Data=c(1,2,3,
                         4,5,6), .Dim=c(2,3))
)
# Initial values - 1
list(
# Prospective
phi = 0.23, lambda.c = 0.74, delta = c(0.2, 0.1),
alpha = c(0.01, 0.01, 0.01, 0.01),
pi.sch = 0.051, pi.ost = 0.07, dur.symp = 0.1
)
# Initial values - 2
list(
# Prospective
phi = 0.7, lambda.c = 2, delta = c(0.1, 0.6),
alpha = c(0.15, 0.15, 0.15, 0.15),
pi.sch = 0.2, pi.ost = 0.2, dur.symp = 0.145
)
```

#### WBDiff Program to calculate the transition probabilities

MODULE WBDiffThreeState;

```
IMPORT
WBDiffODEMath,
Math;
```

TYPE Equations = POINTER TO RECORD (WBDiffODEMath.Equations) END; Factory = POINTER TO RECORD (WBDiffODEMath.Factory) END;

CONST

nEq = 6; nSt = 4; (\* one higher as arrays start at zero\*)

VAR

fact-: WBDiffODEMath.Factory;

PROCEDURE (e: Equations) Derivatives (IN theta, C: ARRAY OF REAL; n: INTEGER; t: REAL; OUT dCdt: ARRAY OF REAL);

VAR

index: ARRAY nSt, nSt OF INTEGER;

BEGIN

(\* define index of parameters (look-up table) \*)

index[1,1] := 0; index[1,2] := 1; index[1,3] := 2; index[2,1] := 3; index[2,2] := 4; index[2,3] := 5;

(\* define system of nEq Differential Equations \*)

 $dCdt[index[1,1]]:= C[index[1,1]]*theta[index[1,1]] + C[index[1,2]]*theta[index[2,1]]; \\ dCdt[index[1,2]]:= C[index[1,1]]*theta[index[1,2]] + C[index[1,2]]*theta[index[2,2]]; \\ dCdt[index[1,3]]:= C[index[1,1]]*theta[index[1,3]] + C[index[1,2]]*theta[index[2,3]]; \\ dCdt[index[1,3]]:= C[index[1,3]] + C[index$ 

$$\label{eq:conditional} \begin{split} & dCdt[index[2,1]] \coloneqq C[index[2,1]] \\ & dCdt[index[2,2]] \coloneqq C[index[2,1]] \\ & theta[index[1,2]] + C[index[2,2]] \\ & theta[index[2,2]] \\ & dCdt[index[2,3]] \\ & = C[index[2,1]] \\ & theta[index[1,3]] + C[index[2,2]] \\ & theta[index[2,3]] \\ & theta[index[3,3]] \\ &$$

END Derivatives;

PROCEDURE (equations: Equations) SecondDerivatives (IN theta, x: ARRAY OF REAL; numEq: INTEGER; t: REAL; OUT d2xdt2: ARRAY OF REAL);

BEGIN HALT(126) END SecondDerivatives;

PROCEDURE (equations: Equations) Jacobian (IN theta, x: ARRAY OF REAL; numEq: INTEGER; t: REAL; OUT jacob: ARRAY OF ARRAY OF REAL);
BEGIN HALT(126) END Jacobian;
PROCEDURE (f: Factory) New (option: INTEGER): WBDiffODEMath.GraphNode; VAR equations: Equations;

node: WBDiffODEMath.GraphNode; BEGIN NEW(equations); node := WBDiffODEMath.New(equations, nEq); **RETURN** node END New;

PROCEDURE Install\*; BEGIN WBDiffODEMath.Install(fact) END Install;

PROCEDURE Init; VAR f: Factory; BEGIN NEW(f); fact := f END Init;

BEGIN Init END WBDiffThreeState.

## WBDEV code to calcuate the Binomial likelihood probabilities of PID for the 2-rate model

MODULE WBDevgeneratep;

IMPORT WBDevScalar, Math;

TYPE

Function = POINTER TO RECORD (WBDevScalar.Node) END; Factory = POINTER TO RECORD (WBDevScalar.Factory) END;

VAR

fact-: WBDevScalar.Factory;

PROCEDURE (func: Function) DeclareArgTypes (OUT args: ARRAY OF CHAR); BEGIN args := "v"; END DeclareArgTypes;

PROCEDURE calculation (func: Function; OUT output: REAL); VAR term1, term2, omega, omega cum,pi hi, pi low: ARRAY 366 OF REAL: ARRAY 4,366+1 OF REAL; pi: ARRAY 3,4 OF REAL; p\_hi, p\_low: H,B,h,i,b: INTEGER: Hin, Bin, lambdaC, lambdaT, phi, clinicorscreen, caseprop: REAL; BEGIN (\* Read in the parameter values \*) p\_hi[1,1] := func.arguments[0][0].Value(); p\_hi[1,2] := func.arguments[0][1].Value(); p hi[1,3] := func.arguments[0][2].Value(); p\_hi[2,1] := func.arguments[0][3].Value(); p\_hi[2,2] := func.arguments[0][4].Value(); p\_hi[2,3] := func.arguments[0][5].Value(); p\_low[1,1] := func.arguments[0][6].Value(); p\_low[1,2] := func.arguments[0][7].Value(); p low[1,3] := func.arguments[0][8].Value(); p low[2,1] := func.arguments[0][9].Value();

p low[2,2] := func.arguments[0][10].Value(); p low[2,3] := func.arguments[0][11].Value(); Hin := func.arguments[0][12].Value(); Bin := func.arguments[0][13].Value(); lambdaC := func.arguments[0][14].Value(); lambdaT := func.arguments[0][15].Value(); phi := func.arguments[0][16].Value(); clinicorscreen := func.arguments[0][17].Value(); caseprop := func.arguments[0][18].Value(); (\* Converts H and B to integer format \*) FOR i:= 1 TO 5000 DO IF (Hin = i) THEN: H := i: END; END: FOR i:= 1 TO 5000 DO IF (Bin = i) THEN; B := i; END; END: (\* Sets B to equal H if follow-up time is shorter than B - Note the program would need changing if a screening study with a follow-up time shorter than B was included \*) IF (H < B) THEN; B := H; END; (\* Calculates the proportion of cases in screening studies infected in the last c = 1 to C days \*) IF (clinicorscreen = 1) THEN: omega cum[0] := 0;FOR b := 1 TO B DO omega[b] := phi \* (Math.Exp( - lambdaT \* (b - 1) / 365) - Math.Exp( - lambdaT \* b / 365)) + (1 - phi) \* (Math.Exp( - lambdaC \* (b - 1) / 365) - Math.Exp( - lambdaC \* b / 365)); omega\_cum[b] := omega\_cum[b-1] + omega[b]; END; (\* specifies the proportion of women in each state at time zero \*) pi\_hi[0] := caseprop \* omega\_cum[B]; ELSE pi\_hi[0] := caseprop; END: pi[1,0] := caseprop;pi[2,0] := 1 - pi[1,0];pi[3,0] := 0;pi\_low[0] := pi[1,0] - pi\_hi[0]; (\* main analysis \*) FOR h := 1 TO B DO; pi[1,h] := pi\_low[h-1] \* p\_low[1,1] + pi\_hi[h-1] \* p\_hi[1,1] + pi[2,h-1] \* p\_hi[2,1]; pi[2,h] := pi[2,h-1] \* p\_hi[2,2] + pi\_low[h-1] \* p\_low[1,2] + pi\_hi[h-1] \* p\_hi[1,2]; pi[3,h] := 1 - pi[2,h] - pi[1,h];IF (clinicorscreen =0) THEN; pi hi[h] := pi[1,h]; $pi_low[h] := 0$ END; IF (clinicorscreen =1) THEN;

term1[h] := 0;FOR i := h TO B DO term1[h] := term1[h] + omega[B+1-i] \* pi[1,0] \* Math.Power(p\_hi[1,1],h); END: term2[1] := 0;IF (h >= 2) THEN; FOR i := 1 TO h DO term2[h] := term2[h-1] + (pi[2,i-1] \* p\_hi[2,1]) \* Math.Power(p\_hi[1,1],h-i); END; END; pi hi[h] := term1[h] + term2[h];pi low[h] := pi[1,h] - pi hi[h];END: END: IF (H > B) THEN; FOR h := B+1 TO H DO pi[1,h] := pi\_low[h-1] \* p\_low[1,1] + pi\_hi[h-1] \* p\_hi[1,1] + pi[2,h-1] \* p\_hi[2,1]; pi[2,h] := pi[2,h-1] \* p\_hi[2,2] + pi\_low[h-1] \* p\_low[1,2] + pi\_hi[h-1] \* p\_hi[1,2]; pi[3,h]:= 1 - pi[2,h] - pi[1,h]; term1[h] := 0;FOR i := h+1-B TO h DO term2[h] := term2[h-1] + (pi[2,i-1] \* p\_hi[2,1]) \* Math.Power(p\_hi[1,1],h-i); END:  $pi_h[h] := term1[h] + term2[h];$ pi\_low[h] := pi[1,h] - pi\_hi[h]; END; END; output := pi[3,H]; END calculation; PROCEDURE (func: Function) Evaluate (OUT value: REAL); VAR output: REAL; BEGIN calculation(func, output); value := output; END Evaluate; PROCEDURE (f: Factory) New (option: INTEGER): Function; VAR func: Function; BEGIN NEW(func); func.Initialize; RETURN func; END New; PROCEDURE Install\*; BEGIN WBDevScalar.Install(fact); END Install: **PROCEDURE** Init; VAR f: Factory; BEGIN

NEW(f); fact := f; END Init;

BEGIN Init; END WBDevgeneratep. Web References

1. Haggerty C, Gottlieb S, Taylor B, et al. Risk of Sequelae after Chlamydia trachomatis Genital Infection in Women. *J Infect Dis* 2010;201(S2):134-155.

2. Risser WL, Risser JMH. The incidence of pelvic inflammatory disease in untreated women infected with Chlamydia trachomatis: a structured review. *Int J STD AIDS* 2007;18(11):727-731.

3. Gottlieb S, Berman S, Low N. Screening and Treatment to Prevent Sequelae in Women with Chlamydia trachomatis Genital Infection: How Much Do We Know? *J Infect Dis* 2010;202(S2):S156-S167.

4. Land JA, van Bergen JEAM, Morre SA, et al. Epidemiology of Chlamydia trachomatis infection in women and the cost-effectiveness of screening. *Hum Reprod Update* 2010;16(2):189-204.

5. Roberts TE, Robinson S, Barton PM, et al. Cost effectiveness of home based population screening for Chlamydia trachomatis in the UK: economic evaluation of chlamydia screening studies (ClaSS) project. *BMJ* 2007;335(7614):291-294A.

6. Adams EJ, Turner KME, Edmunds WJ. The cost effectiveness of opportunistic chlamydia screening in England. *Sex Transm Infect* 2007;83(4).

7. Ginocchio RHS, Veenstra DL, Connell FA, et al. The clinical and economic consequences of screening young men for genital chlamydial infection. *Sex Transm Dis* 2003;30(2):99-106.

8. Goeree R, Jang D, Blackhouse G, et al. Cost-effectiveness of screening swab or urine specimens for Chlamydia trachomatis from young Canadian women in Ontario. *Sex Transm Dis* 2001;28(12):701-709.

9. Hu D, Hook EW, Goldie SJ. Screening for Chlamydia trachomatis in women 15 to 29 years of age: A cost-effectiveness analysis. *Ann Intern Med* 2004;141(7):501-513.

10. Mehta SD, Bishai D, Howell R, et al. Cost-effectiveness of five strategies for gonorrhea and chlamydia control among female and male emergency department patients. *Sex Transm Dis* 2002;29(2):83-91.

11. Townshend JRP, Turner HS. Analysing the effectiveness of Chlamydia screening. *Journal of the Operational Research Society* 2000;51(7):812-824.

12. Turner KME, Adams EJ, LaMontagne DS, et al. Modelling the effectiveness of chlamydia screening in England. *Sex Transm Infect* 2006;82(6):496-502.

13. Turner KME, Adams EJ, Gay N, et al. Developing a realistic sexual network model of chlamydia transmission in Britain. *Theor Biol Med Model* 2006; 3:3.

14. Wang LY, Burstein GR, Cohen DA. An economic evaluation of a school-based sexually transmitted disease screening program. *Sex Transm Dis* 2002;29(12):737-745.

15. Welte R, Kretzschmar M, Leidl R, et al. Cost-effectiveness of screening programs for Chlamydia trachomatis - A population-based dynamic approach. *Sex Transm Dis* 2000;27(9):518-529.

16. Bachmann LH, Richey CM, Waites K, et al. Patterns of Chlamydia trachomatis testing and follow-up at a university hospital medical center. *Sex Transm Dis* 1999;26(9):496-499.

17. Stamm WE, Guinan ME, Johnson C, et al. Effect of Treatment Regimens for Neisseria-Gonorrhoeae on Simultaneous Infection with Chlamydia-trachomatis. *N Eng J Med* 1984;310(9):545-549.

18. Westergaard L, Philipsen T, Scheibel J. Significance of Cervical Chlamydia-trachomatis Infection in Post-Abortal Pelvic Inflammatory Disease. *Obstet Gynecol* 1982;60(3):322-325.

19. Morre SA, van den Brule AJC, Rozendaal L, et al. The natural course of asymptomatic Chlamydia trachomatis infections: 45% clearance and no development of clinical PID after one-year follow-up. *Int J STD AIDS* 2002;13(Supp 2):12-18.

20. Simms I, Hornert P. Has the incidence of pelvic inflammatory disease following chlamydial infection been overestimated? *Int J STD AIDS* 2008;19(4):285-286.

21. Geisler WM, Wang C, Morrison SG, et al. The natural history of untreated Chlamydia trachomatis infection in the interval between screening and returning for treatment. *Sex Transm Dis* 2008;35(2):119-123.

22. Hook EW, Spitters C, Reichart CA, et al. Use of Cell-Culture and A Rapid Diagnostic Assay for Chlamydia-trachomatis Screening. *JAMA* 1994;272(11):867-870.

23. Paavonen J, Kousa M, Saikku P, et al. Treatment of Non-Gonococcal Urethritis with Trimethoprim-Sulfadiazine and with Placebo - A Double-Blind Partner-Controlled Study. *Br J Vener Dis* 1980;56(2):101-104.

24. Rahm VA, Belsheim J, Gleerup A, et al. Asymptomatic Carriage of Chlamydiatrachomatis - A Study of 109 Teenage Girls. *Eur J Sex Transm Dis* 1986;3(2):91-94.

25. Grimmett GDR, Stirzaker DR. *Probability and Random Processes*. Oxford, UK: Oxford University Press; 1992.

26. Welton NJ, Ades AE. Estimation of Markov Chain Transition Probabilities and Rates from Fully and Partially Observed Data: Uncertainty Propagation, Evidence Synthesis and Model Calibration. *Med Decis Making* 2005;25(6):633-645.

27. Lunn, D. WinBUGS Development Interface (WBDEV) 2004. <u>http://www.winbugs-development.org.uk/wbdev.html</u>. (Accessed March 21, 2013).

28. Brooks SP, Gelman A. General methods for monitoring convergence of iterative simulations. *Journal of Computational and Graphical Statistics* 1998;7(4):434-455.

Infection rate (Scholes, Ostergaard)	Re-infection rate (POPI, Rees)	Mean Residual Deviance	Causal rate Of PID	Probability CT causes clinical PID	Proportion prevented by screening
One-Rate model – All controlled studies					
0	0	10.8	0.19 (0.06,0.36)	0.16 (0.06,0.26)	0.61 (0.55,0.67)
0	0.05	10.7	0.19 (0.06,0.36)	0.16 (0.06,0.26)	0.61 (0.55,0.67)
0	0.1	10.6	0.19 (0.06,0.35)	0.16 (0.06,0.26)	0.61 (0.55,0.67)
0.05	0.1	10.6	0.19 (0.06,0.35)	0.16 (0.06,0.26)	0.61 (0.55,0.67)
0.05	0.15	10.7	0.19 (0.06,0.34)	0.16 (0.06,0.25)	0.61 (0.55,0.68)
0.05	0.20	10.8	0.19 (0.06,0.34)	0.15 (0.06,0.25)	0.61 (0.55,0.68)
0.1	0.15	10.6	0.18 (0.06,0.31)	0.15 (0.05,0.24)	0.61 (0.56,0.68)
0.1	0.20	10.7	0.18 (0.05,0.31)	0.15 (0.05,0.24)	0.62 (0.56,0.68)
Two-Rate models All controlled studies – 60 days					
0	0	10.3	$\delta_1$ 0.74 (0.07,1.72)	0.20 (0.09,0.31)	0.40 (0.13,0.68)

Web Table 1 – Effect on Key Results of Altering the Assumed Infection and Reinfection Rates

			$\delta_{\scriptscriptstyle 2}$ 0.16 (0.03,0.33)		
0	0.05	10.4	$\delta_{_{1}}$ 0.62 (0.05,1.46)	0.19 (0.09,0.30)	0.43 (0.16,0.69)
			$\delta_2$ 0.17 (0.03,0.34)		
0	0.1	10.8	$\delta_{_{1}}$ 0.48 (0.03,1.18)	0.18 (0.08,0.28)	0.48 (0.20,0.70)
			$\delta_2$ 0.17 (0.04,0.34)		
0.05	0.1	10.6	$\delta_{_{1}}$ 0.32 (0.02,0.68)	0.16 (0.07,0.26)	0.54 (0.30,0.72)
			$\delta_{\scriptscriptstyle 2}$ 0.18 (0.04,0.35)		
0.05	0.15	10.9	$\delta_{ m l}$ 0.29 (0.02,0.64)	0.16 (0.07,0.26)	0.55 (0.32,0.72)
			$\delta_{\scriptscriptstyle 2}$ 0.18 (0.05,0.35)		
0.05	0.20	11.2	$\delta_{\scriptscriptstyle 1}$ 0.25 (0.01,0.60)	0.16 (0.07,0.25)	0.57 (0.34,0.72)
			$\delta_{\scriptscriptstyle 2}$ 0.18 (0.05,0.35)		
0.1	0.15	11.0	$\delta_{\scriptscriptstyle 1}$ 0.18 (0.01,0.38)	0.15 (0.06,0.25)	0.61 (0.43,0.73)
			$\delta_{\scriptscriptstyle 2}$ 0.19 (0.05,0.36)		
0.1	0.20	11.1	$\delta_{\scriptscriptstyle 1}$ 0.17 (0.01,0.37)	0.15 (0.06,0.24)	0.61 (0.44,0.73)
			$\delta_2^{}$ 0.19 (0.05,0.36)		