Supplemental content for the manuscript: The use of mathematical models of chlamydia transmission to address public health policy questions: a systematic review

Table S1. Description of studies included in the review. Study designated as the main model paper is in bold, followed by further analyses of the model. The publications are ordered by the publication year of the main model.

Reference	Model framework	Reporting (items)	Setting and population	Intervention	Description of testing before intervention roll-out (baseline)	Summary of study findings
Mathematical models of screening published before 2009						
Kretzschmar (1996)[49s] /(2001)[50s] (RIVM model)	IBM, SIS, sequelae analyzed as a decision tree	1.5/3 (description of the IBM, sensitivity analysis[50s] but partially reported)	Heterosexual population in the Netherlands	Screening of women and men + PN[49s,50s], and condom use[49s]	At baseline no interventions,[49s] treatment of symptomatic[50s]	Yearly screening of women aged 15-24 reduced population prevalence from 4.07% to 2.49%. Increased condom use reduced prevalence further.
Welte (2000)[51s]	Decision analysis model of 2001[50s]	NA	"	Opportunistic screening of women and men + PN	Not reported, assumed the same as in 2001[50s] paper	Screening was cost-saving when evaluated in 10 year time horizon.
Welte (2005)[52s]	Comparing the dynamic model to a (static) decision analysis	NA	"	Screening women + PN	Not reported, assumed the same as in 2001[50s] paper	Static model estimated fewer prevented adverse health outcomes.
Andersen (2006)[53s]	Model calibrated for data in Denmark for decision analysis model	NA	Heterosexual population in Denmark	Opportunistic and home-based screening of women and men + PN	At baseline 24% and 5% of women and men, respectively, aged 15-24 tested yearly (for any reason)	Intervention can be cost-saving after 4 years, when including productivity costs associated with chlamydia.
Kretzschmar (2012)[54s]	Model calibrated to United States	1/3 (description of the IBM)	Heterosexual population in the US	Opportunistic screening of women and men+ PN	At baseline treatment of symptomatic, no PN	Screening women and providing PN had a notable effect on prevalence.

Townshend (2000)[20]	Compartmental $SI_1I_2I_3S$ model	0.5/3 (sensitivity analyses done, partially reported)	Heterosexual population in the UK	Screening of women + PN	Not reported	Screening reduced sequelae in all scenarios and would become cost-saving after 5 years.
Brunham (2005)[21]	Compartmental extended[a] SE I_1I_2 I_3RS model	0/3 (supplementary material not found)	General population[b] in Vancouver (Canada)	Screening (compared to 100% effective vaccine)	Not reported	Screening reduced prevalence followed by a rebound.
Turner (2006)[56s] **/ (2006)**[55s] **(HPA model)**	IBM, SIS	3/3 (description of the IBM, frequentist calibration of behavioral parameters, sensitivity analysis)	Heterosexual population in Britain	Screening of women and men + PN	At baseline few cases are tested due to active treatment seeking (model not stratified by symptom status), and 20% PN	With high coverage (and PN), opportunistic screening program can reduce prevalence.
Adams (2007)[57s]	Cost-effectiveness analysis using a decision tree	NA	Heterosexual population in England (UK)	Screening of women and men + PN	At baseline no screening	Offering annual screening to men and women aged <20 years was the optimal strategy.
Gillespie (2012)[58s]	Cost-effectiveness analysis using a decision tree	NA	Healthcare utilization adapted to Ireland	Annual opportunistic screening of women and men + PN	At baseline the current strategy in Ireland with no organized care	Opportunistic screening program was unlikely to be cost-effective in Ireland.
De Vries (2006)[23]	Compartmental SIS model, sequelae calculated in decision tree	1/3 (differential equations)	Heterosexual population in the Netherlands	Screening of women and men + PN compared to one-off screening	At baseline treatment of symptomatic cases, no PN	One-off screening was not cost-saving in base case, but net cost per MOA averted was deemed reasonable.
De Vries (2008)[22]	"	1/3 (differential equations)	"	Screening of women and men +PN	"	Screening intervals every 2 years, 5 years, or 10 years were deemed cost-effective.
Low (2007)[59s] **/ Roberts (2007)**[60s] **(ClaSS model)**	IBM, SEIS, sequelae (PID or epididymitis) incorporated in the model	1/3 (description of the IBM)	Heterosexual population in England (UK)	Active screening of women and men +PN	At baseline symptomatic are treated with a low level of background screening (between 7-13% per year in the	Screening was not cost-effective at coverage levels achieved in empirical studies and when assuming low incidence of sequelae.

					youngest age groups) and PN	
Fisman (2008)[24]	Compartmental SIRS model	1.5/3 (differential equations, sensitivity analysis done, results not reported)	High-school heterosexual population in Philadelphia (US)	Screening of women and men	Baseline testing not reported	High-school based screening program was cost-effective.
Gift (2008)[25]	Compartmental SEIS model sequelae incorporated in the model	2/3 (differential equations, sensitivity analysis)	Heterosexual population in the US	Screening of men or expanding screening in women + PN	At baseline 35% of women are screened annually	Screening high-risk men can be cost-saving compared to screening of women.
Regan (2008)[26]	Compartmental SEITRS model	2/3 (differential equations, sensitivity analysis, calibration method not stated)	Heterosexual population in Australia	Annual screening strategies of women and men	At baseline 0.75-5% of asymptomatic and 75-85% of symptomatic tested	Systematic screening and treatment can reduce prevalence over 10 years.
Model comparison studies						
Kretzschmar (2009)[65s]	Comparison of three IBMs	NA	Heterosexual population in the UK and the Netherlands	Comparing model predictions under unified intervention scenarios	At baseline all models assumed treatment of symptomatic cases and differing levels of PN	Turner model predicted strongest impact of intervention, Low model showed limited impact whilst Kretzschmar was in between.
Althaus (2012)[66s]	"	NA	"	Harmonize natural history and intervention parameters	Not described, assumed the same as in 2009[65s] paper	Low and Kretzschmar models behaved similarly when parameters were harmonized.
Mathematical models of screening published after 2009						
Vickers (2010)[27]	Compartmental modified[c] SITRS model	3/3 (differential equations, frequentist calibration, sensitivity analysis)	General population[b] in Saskatchewan (Canada)	Using case data to explain observed trends in chlamydia transmission	Baseline testing assumptions not reported	Oscillating case trend was due to temporary immunity and increased reporting over time.
Althaus (2010)[28]	Compartmental SEIRS model	3/3 (differential equations, frequentist calibration, sensitivity analysis)	General population[b] in high-income country setting	Impact of disease-specific parameters on screening programs	At baseline no screening, treatment of symptomatic cases	Longer duration of immunity reduced, and longer duration of asymptomatic infection increased the screening

						impact.
Ong (2012)[29]	Compartmental SIS pair formation and frequency dependent models for chlamydia and gonorrhea; SI for HIV	1/3 (differential equations)	Heterosexual population, setting not specified	Increased condom use in different model structures	At baseline no screening, treatment of symptomatic cases	Pair formation model estimated a higher condom usage than the frequency dependent needed to bring R_0<1.
Tuite (2012)[30]	Compartmental SI_1I_2RS model, PID incorporated in the model	3/3 (differential equations, frequentist calibration, sensitivity analysis)	Heterosexual population in Canada	Increase in screening compared in historic case data	Low level of testing prior to 1991 (0.2% per year)	Expansion in testing as observed in Canada was deemed cost-effective. Increase in screening predicted to reduce PID and long-term sequelae.
Schmid (2012)[64s]**/ (2013)**[61s]	IBM, SIS	2/3 (description of the IBM, sensitivity analysis)	Heterosexual population in the Netherlands	Opportunistic and active screening of women and men compared + PN	Baseline health care seeking behavior of asymptomatic estimated from primary physician and STI clinic consultations (value not stated), baseline PN 40%	Screening women was about half as effective as screening both men and women. Screening can have a limited impact on prevalence level, which is dependent on achieving a sustained coverage over time. Retesting higher risk individuals and intensive PN may offer an alternative strategy.
de Wit (2015)[62s]	Cost-effectiveness analysis using a decision tree	NA	"	"	"	Screening was not cost-effective unless high uptake levels are achieved.
Owusu-Edusei (2013)[31s]	Compartmental SEIS model.	2/3 (differential equations, sensitivity analysis)	Heterosexual population in the US	Screening of inmates, and women in the community	At baseline screening coverage of 30% in women and treatment of symptomatic cases	Impact was higher in a population with higher prevalence and incarceration rates.
Clarke (2013)[44s]	IBM, SIS,compared (and later	2.5/3 (described IBM, but no given differential	General population[b] in	Screening + PN	At baseline 16% annual screening of	PN reduced prevalence and was an efficient use of

	approximated) to a compartmental model .	equations, frequentist calibration, sensitivity analysis)	England (UK)		women aged 16-24 and 45% PN (model not stratified by symptom status)	resources. Limits on maximum PN coverage achievable in the real world, require ongoing screening.
Xiridou (2013)[32s]	Compartmental model for chlamydia (SIS) and HIV (SI)	3/3 (differential equations, frequentist calibration, sensitivity analysis)	MSM in the Netherlands, some who are living with HIV	Screening HIV-diagnosed MSM; opportunistic screening in the community	At baseline opportunistic testing of low-risk men every 2.5-3.5 years and high-risk men depending on HIV-diagnosis (every 1-2.5 years)	Screening HIV-diagnosed MSM can reduce chlamydia and HIV in the general MSM population.
Vriend (2013)[33s]	Cost-effectiveness analysis.	NA	"	"	"	Intervention was cost-effective, particularly if men were not screened elsewhere.
Regan (2013)[34s]	Compartmental SITRS model.	1/3 (differential equations)	Heterosexual population in Australia	Screening of women and men with possible treatment failure	At baseline 8% of women and men are screened, and symptomatic cases are treated	Increase in treatment failure required longer time or a greater screening coverage to achieve prevalence reduction. In the most extreme case, 16% increase in annual screening rate was required to counterbalance the impact if 23% treatment failure.
Herzog (2013)[35s]	Compartmental SIS model for men; SI_1I_2S for women, PID in the model	2/3 (differential equations, sensitivity analysis)	Heterosexual population in the UK	Screening[b.]	At baseline 4.5% of women and 2.25% of men were screened yearly (model not stratified by symptom status)	The later that progression to PID occurred, the greater the impact of screening on PID.
Tuite (2014)[46s]	IBM, SIRS, PID in the model	2/3 (description of the IBM, sensitivity analysis)	Heterosexual high-risk groups in	Screening + PN or EPT	At baseline treatment of symptomatic cases	No intervention strategy was more cost-effective than treating only

			Canada			symptomatic cases. In high-risk population screening without PN resulted in rapid re-infection.
Looker (2015)[36s]	Compartmental $S_1I_1S_2I_2S_2$ model, sequelae (PID and TFI) included in the model	2/3 (differential equations, frequentist calibration)	Heterosexual population in Scotland (UK)	Screening of women + PN	Baseline testing coverage was 16.8% and PN 40% (model not stratified by symptom status)	Current testing strategy was not cost-effective in Scotland, but lowering coverage resulted in more PID and TFI cases. With less conservative estimates, screening could be cost-effective.
Teng (2015)[37s]	Compartmental SEIRS model	2/3 (differential equations, frequentist calibration, sensitivity analysis not presented)	General population[b] in a Midwest city in the US	Increased screening in different age groups of women and men	Model calibrated to optimal screening, and baseline prevention methods are not applicable	Age-dependent screening rate was found to be the optimal strategy: screening should be most frequent for 16-18 year-old women for whom the infection risk is highest.
Mathematical models focusing on partner notification						
Armbruster (2007)[63s]	Static sexual network with SIRS structure (removed only for the duration of treatment)	1/3 (description of the IBM, sensitivity analysis not done for chlamydia case study)	Small heterosexual population in the US	Increasing the rate of PN	No testing and treatment measures were defined at baseline	PN can reduce prevalence, but with diminishing returns as PN rate increases.
Heijne (2011)[38s]	Compartmental SIRS pair formation model compared to frequency dependent model	2/3 (differential equations, sensitivity analysis)	Heterosexual population, setting not specified	Screening of women and men + PN in different model structures	Not reported	Pair model gave more conservative estimates of the effect of the screening than a standard SIRS model, as it accounts for reinfection.
Heijne (2012)[45s]	Extended to include repeat infection, and treatment failure in a subgroup of women	2/3 (differential equations, sensitivity analysis)	Heterosexual population in the US	Screening of women + PN and repeat testing.	At baseline testing 10% of women per year (model not stratified by symptom status)	Repeat testing had less effect on prevalence than testing and treating current sex partners. Risk of repeat infection was

						highest 2-5 months after infection.
Althaus (2012)[39s] **(Rstisim model)**	IBM, SIS, implemented as frequency dependent, pair formation and triple model	2/3 (description of the IBM, sensitivity analysis)	Heterosexual population, setting not specificed	Screening of women and men + PN in different model structures	Screening of women and men every 10 years at baseline	Screening reduced prevalence more in instantaneous contact than in pair and triple models. Screening up to 3 partners from the 18 months prior can find new cases. PN of current partners was most effective at limiting transmission at population level.
Althaus (2014)[47s]	IBM with chlamydia and gonorrhea (SIRS) with shorter immunity for the latter. STI cofactor for the two STIs.	2/3 (description of the IBM, sensitivity analysis)	Heterosexual population in Britain	Comparing APT to traditional PN+ screening of women and men	No interventions at baseline	APT reduced chlamydia and gonorrhea prevalence more than standard PN by reducing reinfection rate from untreated partners (reinfection for 14, 3 and 1 days was 7.6%, 2.3% and 0.8%, respectively).
Models focusing on hypothetical vaccine						
Gray (2009)[48s]	IBM, SIRS, PID included in the model.	2/3 (description of the IBM, sensitivity analysis)	Heterosexual population in Australia	Impact of hypothetical vaccine for women and men + treatment seeking if symptomatic	At baseline testing of most symptomatic, low level of asymptomatic testing (4% women, 2.5% men)	Vaccines with full efficacy and immunity >10 years could lead to elimination, but vaccines can reduce prevalence even with <100% efficacy and waning immunity. Vaccination programs should focus on women in the first instance.
Owusu-Edusei (2015)[40s]	Compartmental heterosexual SEIRS model.	2/3 (differential equations, sensitivity analysis)	Heterosexual population in the US	Prophylactic hypothetical vaccine for women compared to screening of women	At baseline screening 30% per year in women 15-24	Vaccination led to reductions in chlamydia prevalence, and was a cost-effective addition to

						screening alone. Chlamydia could be eliminated with high efficacy vaccine with >75% coverage.
Models outside high income economies						
Vickerman (2009)[41s]	Compartmental SIRS model with HIV (SI), chlamydia, gonorrhea (SIS), and *Haemophilus duceryi* (SIS) STI cofactor for HIV	3/3 (differential equations, frequentist calibration, sensitivity analysis)	FSW and their clients in Johannesburg, Free State (South Africa), Cotonou (Benin) and Laos	Periodic presumptive antimicrobial treatment (PPT) of STIs	Calibrated to STI prevalence among in FSW with baseline PPT coverage and frequency (10% every 2 months)	PPT reduced STI prevalence in FSW >50% with a coverage >30% PPT monthly.
Johnson (2011[43s]/2011[42s])	Compartmental HIV model including chlamydia, gonorrhea, and trichomoniasis (SIS or SIRS)	2/3 (Bayesian calibration, sensitivity analysis)	Heterosexual population in South Africa, FSW included in the model	Improved STI management and condom use with different natural history assumptions	80% and 29% of health care workers in public and private sector, respectively, apply syndromic management correctly;[42s] symptomatic individuals tested and treated[43s]	Increased condom use had a significant impact on chlamydia prevalence whilst sydromic management is unlikely to have a large impact on chlamydia.

Footnote for table S1:
All IBM's are stochastic simulations, all compartmental models in this review are deterministic. IBMs simulate interacting individuals within populations, model events as stochastic, and typically require extensive data for parameterization. Deterministic models represent behaviors of the population average, and heterogeneity in population characteristics is created by dividing compartments into further subgroups (based on factors known to be important for epidemiology) with each person in a given compartment having identical characteristics.

We defined reporting score based on a crude scoring method with one point given for reporting of each: differential equations for deterministic models, or detailed description of the individual based model; sensitivity analysis of one or more key parameters excluding the intervention and outcome parameters; calibration used a statistical methods (least squares, maximum likelihood or other frequentist method, or Bayesian framework).

[a] Separated by re-infections with increasing immunity after each infection.
[b] One sex model approximating heterosexual population.
[c] Removed includes naturally recovered and those with reduced risk behavior after chlamydia diagnosis.

Abbreviations

Model structure: **S**-susceptible to infection, **E**-exposed (infected but not yet infectious), I-infected and infectious (I_1, I_2, I_n infectious disease stages separated to distinguish early infection from late infection), **R**-"removed" (immune to infection), **T**-duration of testing and treatment modeled explicitly. **APT**: accelerated partner therapy; **EPT**: expedited partner therapy; **FSW**: female sex worker; **MOA**: major outcome averted; **MSM**: men who have sex with men; **PID**: pelvic inflammatory disease; **PPT**: periodic presumptive treatment; $\mathbf{R_0}$: Basic reproductive number (measure of transmission potential; transmission cannot be sustained when $R_0<1$); **TFI**: tubal factor infertility