Epidemics 35 (2021) 100456

Contents lists available at ScienceDirect

Epidemics

journal homepage: www.elsevier.com/locate/epidemics

Using an agent-based sexual-network model to analyze the impact of mitigation efforts for controlling chlamydia

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ARTICLE INFO

Keywords:
Chlamydia
Agent based network model
Screening
Partner notification
Sexual network

ABSTRACT

Chlamydia trachomatis (Ct) is the most reported sexually transmitted infection in the United States, with a major cause of infertility, pelvic inflammatory disease, and ectopic pregnancy among women. Despite decades of screening women for Ct, rates increase among young African Americans (AA). We create and analyze a heterosexual agent-based network model to help understand the spread of Ct. We calibrate the model parameters to agree with survey data showing Ct prevalence of 12% of the women and 10% of the men in the 15–25 year-old AA in New Orleans, Louisiana. Our model accounts for both long-term and casual partnerships. The network captures the assortative mixing of individuals by preserving the joint-degree distributions observed in the data. We compare the effectiveness of intervention strategies based on randomly screening men, notifying partners of infected people, which includes partner treatment, partner screening, and rescreening for infection. We compare the difference between treating partners of an infected person both with and without testing them. We observe that although increased Ct screening, rescreening, and treating most of the partners of infected people will reduce the prevalence, these mitigations alone are not sufficient to control the epidemic. The current practice is to treat the partners of an infected individual without first testing them for infection. The model predicts that if a sufficient number of the partners of all infected people are tested and treated, then there is a threshold condition where the epidemic can be mitigated. This threshold results from the expanded treatment network created by treating an individual's infected partners' partners. Although these conclusions can help design future Ct mitigation studies, we caution the reader that these conclusions are for the mathematical model, not the real world, and are contingent on the validity of the model assumptions.

1. Introduction

Chlamydia trachomatis (Ct) is the most commonly notified bacterial sexually transmitted infection (STI) in the United States, with over 1.8 million cases each year (Torrone et al., 2014). It is a major cause of infertility, pelvic inflammatory disease (PID), and ectopic pregnancy among women (Cohen, 1998; Datta et al., 2012; Gottlieb et al., 2010a,b; Hillis and Wasserheit, 1996; Lan et al., 1995; Pearlman and Mcneeley, 1992), and is associated with increased HIV acquisition (Cohen, 1998; Gottlieb et al., 2010a; Lan et al., 1995; Pearlman and Mcneeley, 1992; Hillis and Wasserheit, 1996). Untreated, an estimated 14.8% of women with Ct will develop PID (Price et al., 2013), and 6% will have tubal infertility (Lan et al., 1995). In southern US cities, including New Orleans, there is an ongoing Ct epidemic in young African American (AA) adults. A pilot study in this community (Kissinger et al., 2014) found an average of 1.5 sexual partners per person per three months and approximately 11% prevalence of Ct infection, with a high acquisition of new sex partners in the month following treatment (24%). This high prevalence stresses the need for more effective mitigation efforts to bring the epidemic under control.

Further complicating the issue, some studies show that about 70%–95% of women and 90% of men infected with Ct are asymptomatic and still transmit the infection to others (Farley et al., 2003; Korenromp et al., 2002). When Ct prevalence is high, regular screening is a practical approach to identify and treat infected individuals. The US Preventive Services Task Force (USPSTF) recommends that sexually active women younger than 25 years old, or older if they have multiple sexual partners, be screened for Ct as part of their physical exam (LeFevre, 2014). However, untreated men may serve as a reservoir and reinfect treated women. We investigate the impact of

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https://doi.org/10.1016/j.epidem.2021.100456
Received 22 December 2019; Received in revised form 7 March 2021; Accepted 16 March 2021
Available online 24 March 2021

increased Ct screening of men in high prevalence areas such as New Orleans on the disease prevalence. Typically, when someone is known to be infected, they are urged to encourage their sexual partners to be tested for infection. Sometimes the partners are treated without first being tested for infection. If a partner is tested for infection and found to be infected, their partners can be notified and treated, identifying a chain of high-risk individuals who might be spreading Ct.

Transmission-based mathematical models create frameworks that capture the underlying Ct epidemiology and the heterosexual social structure underlying the transmission dynamics. Compartmental (Althaus et al., 2010; De Vries et al., 2008, 2006; Tuite et al., 2012; Townshend and Turner, 2000; Azizi et al., 2017, 2016; Boroojeni, 2018; Clarke et al., 2012) and agent-based (Adams et al., 2007; Andersen et al., 2006; Gillespie et al., 2012; Roberts et al., 2007; Low et al., 2007; Welte et al., 2005) mathematical models can help researchers to understand the transmission dynamics, and to analyze the efficiency and cost–benefit analysis of different intervention scenarios to control Ct infection in different regions. Althaus et al. (2010), and Clarke et al. (2012) used two different compartmental approaches to test the impact of screening programs on Ct infection. Both admitted that the prevalence of Ct is not effectively sensitive to this program alone. Althaus et al. (2010) identified the time to recovery from infection, and the duration of the asymptomatic period, as two essential model parameters governing the disease prevalence. When the underlying model is not static, Clarke et al. (2012) demonstrated that random screening, if coupled with partner notification, is a cost-effective mitigation approach.

The efficiency of screening and partner notification strategies highly depends on the constructed model; that is, the result of one strategy can be different in the individual and population-level models (Althaus et al., 2012). Kretzschmar et al. (1996) used a stochastic network model based on pair formation and separation process to evaluate different screening and partner referral methodologies in controlling STIs such as Ct. Their results for Ct show that treating at least 50% of partners of infected people can reduce the prevalence to a low level of 0.34%. They observed that the effectiveness of screening depends on the age, gender, and other characteristics of the targeted group. In related research, Kretzschmar et al. (2012) compared the impact of screening and partner notification for women with screening men for infection. They found out that partner notification for women increases Ct screening. The observed that tripling the number of women screened has the same impact as doubling their partner notification. Their model also predicted that increased screening of men or notifying their partners to the program was less effective than these approaches.

The heterosexual network impacts the transmission dynamics, and the effectiveness of different intervention approaches via capturing complex heterogeneous and biased mixing and sexual behavior of agents involved in the transmission process. Models must capture this underlying heterosexual network to predict how infections spread. The number of partners a person has (the degree distribution of the graph) and the number of partners their partners have (the joint-degree distribution of the graph) both impact this spread. We estimated the heterosexual degree and joint-degree distribution from the ongoing New Orleans *Check-it* of young AAs sexual behavior study (Kissinger et al., 2014) to generate a heterosexual network that resembles the sexual activity of this population. We use the B2K algorithm (Boroojeni et al., 2017) to generate an ensemble of heterosexual networks with the same joint-degree distribution for sexual partnerships in our New Orleans AA modeled population.

Heterosexual partnerships are divided into long-term (primary) and short-term (casual) relationships. The casual partners change after a time, ranging from a few weeks to more than a year, while primary partners are maintained throughout the simulation. When changing casual partnerships, the degree and joint-degree distribution of this dynamic network are preserved.

We model Ct transmission as a discrete-time Monte Carlo stochastic event on this dynamic network. The model is initialized to agree with the current New Orleans Ct prevalence. We use sensitivity analysis to quantify the effectiveness of different prevention and intervention scenarios, including screening men, partner notification, which includes partner treatment and partner screening (contact tracing), condom-use, and rescreening.

2. Materials and methods

After describing how we generate the synthetic heterosexual network, we review our Ct transmission model and approaches for mitigating the infection.

2.1. Generating synthetic sexual network

In 2016, two data sets were collected in studies for New Orleans, LA. We based our parameter estimates on a pilot study of community-based STI testing and treatment for AA men ages 15–25 (Kissinger et al., 2014), and an Internet-based study of unintended pregnancy prevention interventions for AA women ages 18–19 (Green et al., 2014). Both studies were reviewed and approved by the Tulane University Institutional Review Board. The 202 men and 414 women enrolled in these studies were asked how many different heterosexual partners they had in the past three months (for women) or two months (for men). Women were also asked to estimate the average number of partners that their partners have had in the past three months. Therefore, these survey data provide the number of partners for men and women and the number of partners of partners for women in the last three months (Kissinger et al., 2014; Green et al., 2014), see Supporting Information.

We used the survey results and B2K algorithm in Boroojeni et al. (2017) to generate an ensemble of the bipartite heterosexual networks of P^m men and P^w women. The B2K algorithm in Boroojeni et al. (2017) preserves the degree (number of partners) and joint-degree (number of partners of partners) distributions of nodes (individuals) estimated from the survey data. The resulting generated networks for the sexually active population preserve the distribution for the number of partners that men and women have had in the past three months. They also preserve the distribution for the number of partners of their partners (the joint-degree distribution) (Boroojeni et al., 2017).

Weighted bipartite network : Each node denoted by the index $\mathbf{i}$ in the network represents a person with a specified gender, and each edge $\mathbf{e_{ij}}$ represents a heterosexual partnership between two nodes $\mathbf{i}$ and $\mathbf{j}$. That is, we assume that men only have partners from the women pool and vice versa, and there is no contact between two men or between two women. Individuals have different sexual activities per day per partner. In the "You Geaux Girl" survey data, women were also asked about their total number of sexual acts per partner during the last three months. We used this data to make the underlying network as a weighted one, where the weight $0 < w_{\mathbf{ij}} \leq 1$ for edge $\mathbf{e_{ij}}$ is the probability of sexual activity between partners $\mathbf{i}$ and $\mathbf{j}$ on any specific day. We have explained the process in details in Supporting Information.

Dynamic sexual act network : The simulation network is dynamic in sexual act. That is, if for example $w_{\mathbf{ij}} = 1/7$, then the two partners $\mathbf{i}$ and $\mathbf{j}$ engage in a sexual act, on average, once a week. Thus, the edge between them is present, on average, once every seven days. This is implemented in the model as a stochastic process, that is, every day the edge $\mathbf{e_{ij}}$ will exist (turn on) with probability $w_{\mathbf{ij}}$, or will not exist (turn off) with probability $1 - w_{\mathbf{ij}}$.

Dynamic partnership network : Depending on the level and the time of partnership, partners of a person are categorized as primary (long-term) and casual (short-term) ones. Because of frequent changes in casual partners, we should make our network dynamic by first assigning the partnership level for individuals. Lescano et al. (2006) observed

that partners of individuals with many partners are most likely casual partners. On the other hand, individuals with few partners are more likely to be in a serious relationship. Based on this study and the fact that, on average, men have more partners than women, we assume that every man has one primary partner maintained for the entire simulation; all his other partners are causal. We randomly select his primary partner from his partners within two years of his age and have the fewest other partners. We assume that these primary female partners also consider the male as their primary partner (Lescano et al., 2006). The structure of the underlying weighted network changes every T days when people change their casual partners. The updated underlying network with the new casual partners has the same degree and joint-degree distributions as the original network. To change the casual partners, we use the subgraph of primary partnership as an initial sexual network and use the B2K algorithm in Boroojeni et al. (2017) to generate a set of networks. We define T as the time between changing casual partners. Every T days, we update the network by randomly choosing one network from this set.

2.2. Modeling spread of Ct on the network

In our stochastic Susceptible–Infectious–Susceptible (SIS) model, a person **i** at day t is either infected with Ct, $I_{\mathbf{i}}(t)$, or susceptible to being infected, $S_{\mathbf{i}}(t)$. During the day t, an infected person, $I_{\mathbf{j}}(t)$, can infect any of their susceptible sexual partners, $S_{\mathbf{i}}(t)$. We define λ_{ij} as the probability that $S_{\mathbf{i}}(t)$ will be infected by $I_{\mathbf{j}}(t)$ by the end of the day, $S_{\mathbf{i}}(t) \overset{\lambda_{ij}}{\rightarrow} I_{\mathbf{i}}(t+1)$. Similarly, we define $\gamma_{\mathbf{j}}$ as the probability that an infected person, $I_{\mathbf{j}}(t)$, will recover by the end of the day, $I_{\mathbf{j}}(t) \overset{\gamma_{\mathbf{j}}}{\rightarrow} S_{\mathbf{j}}(t+1)$.
The force of infection : $\lambda_{\mathbf{ij}}(t)$ is the probability that a susceptible person $S_{\mathbf{i}}$ becomes infected on day t by $I_{\mathbf{j}}$. The infection transmission depends on the probability of a sexual act between person **i** and **j** on a typical day, as defined by edge weight, $w_{\mathbf{ij}}$, in the model. We define β_{nc} as the probability of transmission per sexual act when a condom is not used, and β_c as the reduced probability of transmission per sexual act when a condom is used. The forces of infection between **i** and **j** for when condom is not used, $\lambda^{nc}_{\mathbf{ij}}$, and for when condom is used, $\lambda^{c}_{\mathbf{ij}}$, are defined by

$$\lambda^{nc}_{\mathbf{ij}} = \begin{cases} \beta_{nc} & \text{with probability } w_{\mathbf{ij}} \\ 0 & \text{with probability } 1 - w_{\mathbf{ij}}, \end{cases}$$
$$\lambda^{c}_{\mathbf{ij}} = \begin{cases} \beta_{c} & \text{with probability } w_{\mathbf{ij}} \\ 0 & \text{with probability } 1 - w_{\mathbf{ij}} \end{cases} . \tag{1}$$

We assumed that condom is $\epsilon = 90\%$ effective in preventing the infection from being transmitted. That is, condom sensitivity is 90% or $\beta_c = (1-\epsilon)\beta_{nc} = 0.1\beta_{nc}$ (Trussell and Guthrie, 2007). We assume that the effectiveness of condoms is independent of the gender of donors and recipients. We define β^{m2w} and β^{w2m} as the probabilities of transmission from men to women and from women to men. When condoms are used, these parameters are reduced by the factor $(1-\epsilon)$. We also assume that casual partners use condoms a fraction, κ, of the time. That is, if there is a sexual act between a man node and his casual partner, then they use a condom with probability κ. The fraction is estimated from the study byCooper and Orcutt (2000) who observed that condom use was more common with casual partners than with long-term sexual partners.
Recovery from infection : The model accounts for infected people recovering through natural recovery or via treatment. All infected people, if not seeking for treatment, eventually recover and return to susceptible status. The time for **natural (untreated) recovery** has an exponential distribution with an average time of infection of $\tau_n = 1/\gamma_n$ days, where index n refers to natural recovery. When a person is infected, the duration of their infection is determined by a random sample from this exponential distribution. The case that infected individuals become recovered through treatment is part on intervention program, explained in details in the next Subsection.

2.3. Intervention strategies

Each year, some of the population is tested for Ct infection through a routine medical exam (random screening), after observing symptoms, or after being notified by one of their previous infected partners. We introduce a list of intervention strategies implemented in our model, that are random screening, partner notification, and rescreening.
Random Screening: We define random screening as testing for infection when there are no compelling reasons to suspect a person is infected. For example, random screening might be part of a routine physical exam and is an effective mitigation policy to identify asymptomatic infections. We assume that the σ_y fraction of people are randomly screened each year. Therefore, each day individuals are screened with probability $\sigma_d = 1-(1-\sigma_y)^{\frac{1}{365}}$. It is relatively rare for the Ct screening test to give a false negative result- the male screening sensitivity is higher than 94% (Gaydos et al., 2008). Therefore, for simplicity we assume that screening sensitivity is 100%.
Partner Notification: We assume that an infected person encourages some of their partners to be treated or tested for infection. We define θ_n as the fraction of their partners who are notified, which θ_t fraction of these notified partners follow treatment, and the rest ($\theta_s = 1-\theta_t$ fraction of notified partners) test for the infection. Therefore, a *notified partner* is the partner of an infected person who seeks treatment or testing as a direct result of the screening. We can divide all partners of person as follow:

(1) Partner Treatment: $\theta_n\theta_t$ fraction of all partners that are notified and treated, without first testing for infection.
(2) Partner Screening: $\theta_n\theta_s = \theta_n(1-\theta_t)$ fraction of all partners are notified and screened for infection and then start treatment if they are infected.
(3) Do nothing: $1-\theta_n = 1-\theta_n\theta_t - \theta_n\theta_s$ fraction of all partners are neither tested nor treated.

The model includes a time-lag of τ_n days between the day a person is found to be infected and the time their partners are notified and take action. The selected partners for notification are from the pool of partners in τ_n days after the infected person was tested.
Rescreening: People previously infected are more likely to be reinfected in the future. Repeated Ct infection can result from sexual activity with a new partner or reinfected by a previously infected partner. We assume that a fraction σ_r of the treated people return for retesting after τ_r days. The time τ_r between treatment and rescreening should be long enough so that it is likely that the person would be reinfected if one of their partners is still infected. If τ_r is too long, then a reinfected person could infect others. The current CDC guidelines recommend that people are rescreened for infection three months after treatment (Peterman et al., 2006). We use the model to compare the reinfection rates to help optimize the time from treatment to rescreening, τ_r. The Fig. 1 represents the schematic of intervention strategies.

Aside from intervention strategy, we assume the time to recover after treatment is a log-normal distribution with the parameters of $\tau_t = 1/\gamma_t$ days, where index t stands to recovery via treatment and $\sigma^2 = 0.25$. The reason for selecting log-normal distribution is the shape of distribution, which is non-monotonic. Unlike exponential distribution, log-normal distribution guarantees that only a few people quickly recover. Therefore, the duration of infection for a treated infected person is defined by a random number chosen from a log-normal distribution, $\log\mathcal{N}(\tau_t, 0.25)$, rounded to the nearest day. In the model, if that number of days is smaller than the duration remaining for naturally clearing the disease, then the shorter time is used for the recovery period.

2.4. Model initialization

The initially infected people are not randomly distributed among the susceptible population. They are distributed as they would be in an emerging epidemic that started sometime in the past. We call these

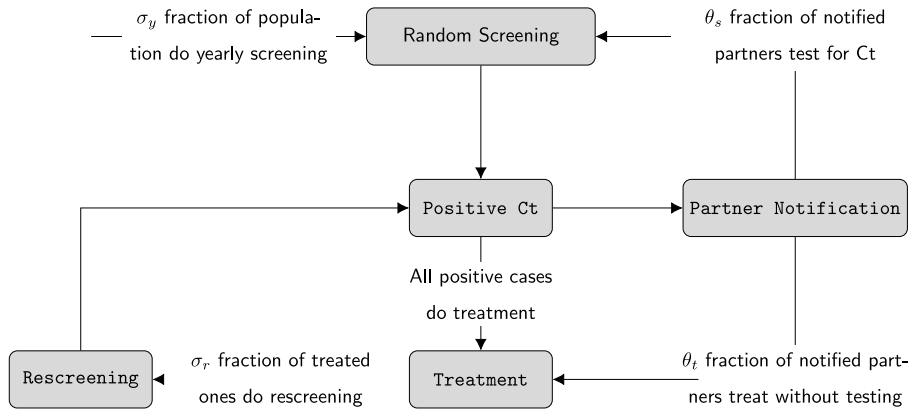


Fig. 1. Flowchart for Ct intervention strategies: These current interventions include screenings, partner notification (including partner treatment and partner screening), and rescreening.

Table 1
Parameter definitions and values: Whenever possible, the model parameters describing the transmission of Ct infection, the time to recover from infection, the screening rates, and partner notifications were estimated from the literature. When the estimates were not available, then the parameters were calibrated so that the biological, behavioral, and epidemiological model predictions were consistent with the heterosexual AA population being modeled in New Orleans. The probability of transmission per act was calibrated to a baseline prevalence of 12% among women and 10% among men.

Parameter	Description	Baseline	Unit	Reference
Δt	Time step	1	day	–
$P^m(P^w)$	Population of men (women)	2000(3000)	people	Assumed
β^{m2w}	Probability of transmission per act from men to women	0.10	–	Calibrated
β^{w2m}	Probability of transmission per act from women to men	0.04	–	Calibrated
κ	Fraction of times that condoms are used during sex	0.58	–	Kissinger et al. (2014)
ϵ	Condom effectiveness	0.90	–	Trussell and Guthrie (2007)
$1/\gamma^n$	Average time to recover without treatment	365	days	Molano et al. (2005) and Althaus et al. (2010)
$1/\gamma^t$	Average time to recover with treatment	7	days	Morre et al. (1998)
σ_y^m	Fraction of men randomly screened per year	0.05	–	Kissinger et al. (2014)
σ_y^w	Fraction of women randomly screened per year	0.45	–	Kissinger et al. (2014)
σ_r	Fraction of infected people return for rescreening	0.10	–	Assumed
Sensitivity	Screening sensitivity	100%	–	Assumed
θ_n	Fraction of the partners of an infected person who are notified and do test or treated for infection	0.26	–	Kissinger et al. (2014)
θ_t	Fraction of notified partners of an infected person who are treated without testing	0.75	–	Kissinger et al. (2014)
θ_s	Fraction of notified partners of an infected person who are tested and treated for infection	0.25	–	Kissinger et al. (2014)
τ_n	Time lag of partner notification	5	days	Assumed
τ_R	Time lag of re-screening	100	days	Calculated
T	Time period for casual partner change	60	days	Assumed

initial conditions *balanced* because when the simulation starts, the infected and susceptible populations, along with the duration of infection, are in balance with the distributions for an emerging epidemic (Hyman et al., 2001). When the initial conditions are not naturally balanced, a rapid (nonphysical) initial transient of infections quickly settles down as the infected and susceptible populations transition to a realistic infection network.

To define the balanced initial conditions, we start an epidemic in the past by randomly infecting a few high degree individuals. We then advance the simulation until the epidemic grows to the prevalence of i_0. We then reset the time clock to zero and use this distribution of infected people, complete with their current infection timetable, as our initial conditions. Because these are stochastic simulations, we reinitialize each simulation by seeding different initial infected individuals when doing an ensemble of simulations.

3. Results

We define the local sensitivity analysis of different mitigations on Ct prevalence at a quasi-stationary state. The figures show the average of 50 independent stochastic simulations. All of the realizations start at the same initial point obtained with the model baseline parameters in Table 1, unless stated otherwise.

3.1. Model initialization

We initialize our model based on estimates for the current Ct epidemic of 11% among AA young adults residing in New Orleans. These estimates have a standard error of about 1% and are based on the current *Check it* survey data of 1084 AAs in New Orleans (Kissinger et al., 2014). The $i_0 = 8\%$ balanced initial infected individuals are randomly distributed in an otherwise susceptible population.

There is a wide range of reported values for the probability of transmission per sexual act from woman to man, β^{w2m}, or from man to woman, β^{m2w}, ranging from 0.04 to 0.16 (Low et al., 2007; Welte et al., 2005; Adams et al., 2007; Andersen et al., 2006; Gillespie et al., 2012; Roberts et al., 2007). In order to estimate these unknown parameters, we calibrate them to the current Ct prevalence using Method of Simulated Moments (MSM) (McFadden, 1989). We choose the unknown parameter as β^{m2w} and β^{w2m} and the first moment, mean of the prevalence at quasi-stationary state, as 11% of infected individuals. The Fig. 2 illustrates the typical progression of the epidemic to reach this 11% current Ct prevalence.

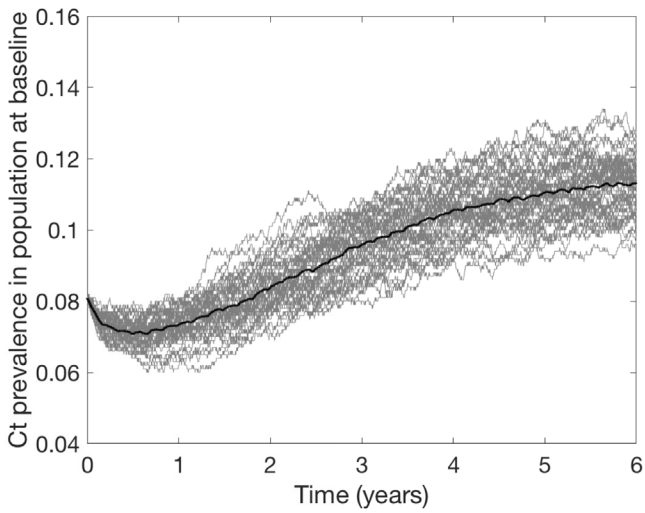


Fig. 2. Prevalence increases to reach the current quasi-stationary state: The light areas are the result for 50 different stochastic simulations, and the dark curve is the mean value of those simulations. About 11% of the population are infected at the quasi-stationary state for the baseline model parameters. The standard deviation for the prevalence is approximately 1%. This is in agreement with the current prevalence in New Orleans 15–25 year-old AA population.

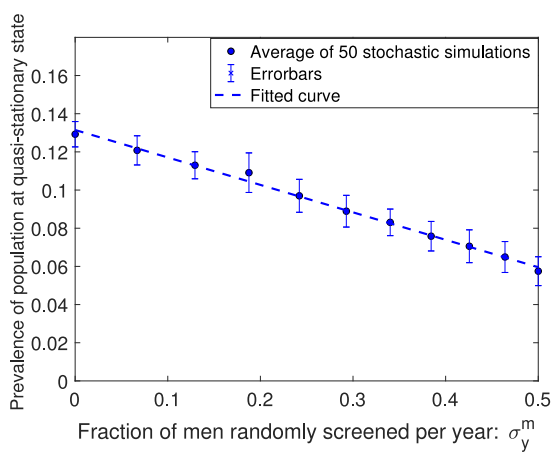


Fig. 3. Sensitivity analysis for screening men: The circles are the average of 50 different stochastic simulations, and the error bars are 95% confidence intervals. Screening men randomly by 50% reduces prevalence by 7%, which is not effective enough to implement as a sole intervention.

3.2. Sensitivity analysis of intervention strategies

To determine the effectiveness of each intervention strategy, we compare the quasi-stationary state prevalence by varying the intervention parameter while freezing other parameters fixed at their baseline value.

Screening Men: Fig. 3 shows a reduction in the overall Ct prevalence as the number of men randomly screened for Ct increases from 0 to 50%, $0 \leq \sigma_y^m \leq 0.5$. The least-square linear fit suggests that the quasi-stationary state Ct prevalence will decrease by 1.4% for every additional 10% of the men screened during a year. Though a drop of seven percent in prevalence is an admirable decrease, increased screening alone would not be sufficient to control Ct.

Partner Notification: We first evaluate the efficiency of partner notification under two scenarios: partner treatment only and partner screening only. We then compare partner treatment and partner screening for different levels of partner notification. To evaluate the impact of partner notification, we have simulated two scenarios:

- **Partner Treatment Only**: The Fig. 4a shows the impact of partner notification under the assumption that all the notified partners treat themselves, that is, $\theta_t = 1$. The least-square linear fit suggests that the quasi-stationary state Ct prevalence decreases by 0.07 for every 10% increment in the fraction of notified partners.
- **Partner Screening Only**: The Fig. 4b shows the impact of partner notification under the assumption that all the notified partners do screening, that is, $\theta_s = 1$, for several time period for casual partner change: when $T = 60$ days (black line), $T = 365$ days (blue curve), and $T = 730$ days (red curve). The simulations predict that partner notification and partner screening are more effective when men keep their casual partnerships for longer times. This is expected since when a partner is identified as being infected, and this partner's other (long-term) partners are tested, then the contact tracing is a branching process and is more likely to identify and treat the underlying infected sexual network. The resulting nonlinear effect is evident in the logistic-shaped curve θ_n when the casual-partners change less often or never change, Fig. 4c.

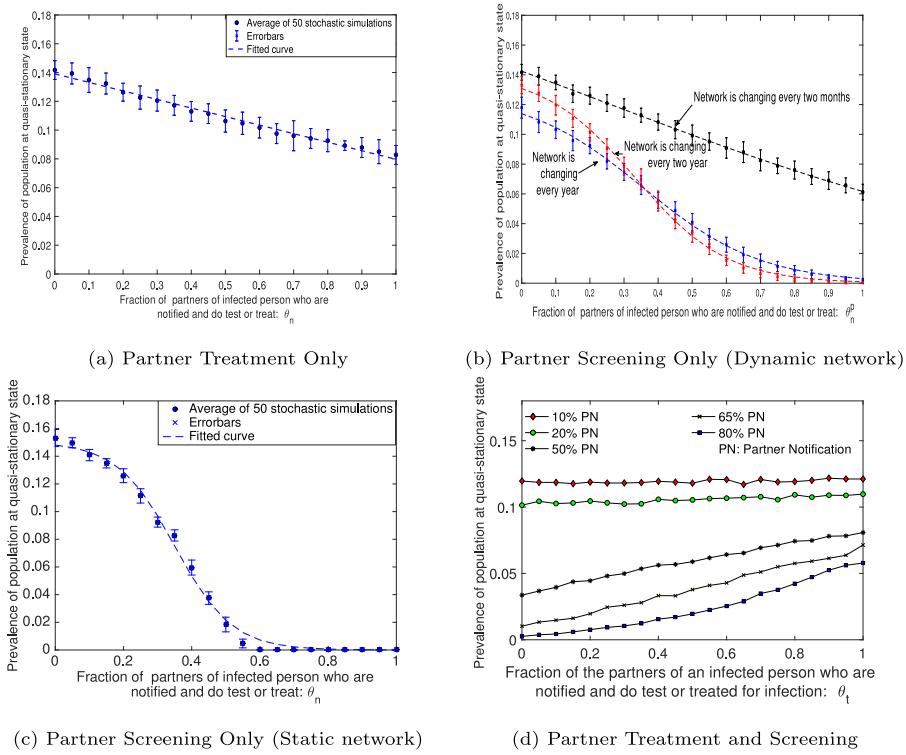
The Fig. 4d compares the impact of partner treatment and partner screening on quasi-stationary state prevalence in the whole population for various levels of partner notification changing from 0.1 to 0.8. For small values of θ_n, that is, when few partners are notified and take action, partner treatment and partner screening have almost the same impact on controlling the prevalence. For example, for $\theta_n = 0.10$ or 0.20, the prevalence versus $\theta_t = 1 - \theta_s$ is flat. For big values of θ_n, that is, when most of the partners are notified and take action, the partner screening becomes a highly successful mitigation policy. For example take the case $\theta_n = \theta_t = \theta_s = 0.5$, thus, the prevalence reduction is 6%. Compared with all notified partners following treatment without testing, $\theta_t = 1$, which reduces the prevalence by only 1%, conditional percolation is more effective. But compared to all notified partners following test and treat if necessary, $\theta_s = 1$, which reduces the prevalence by 11%, this combined scenario is not the one to select.

Rescreening: Past studies have observed that about 25% of the rescreened people are again infected by three months. We plot the cumulative distribution of time between screening and reinfection events in Fig. 5a. The Figure demonstrates that our model predicts that about 25% of treated individuals are again infected after 100 days. The model also shows that the treated population's Ct prevalence exceeds the prevalence for the whole population after two months and suggests that the CDC guidelines for rescreening could be shortened slightly, Fig. 5a.

We varied the fraction of treated individuals who return for rescreening at 100 days after being treated to study if increasing the rate that people return for rescreening would have a significant impact on Ct prevalence, The Fig. 5b quantifies Ct's prevalence at quasi-stationary state dependent on rescreening rate σ_r: there is a negative correlation between the quasi-stationary state prevalence and σ_r. If σ_r fraction of screened individuals follow screening again, then the prevalence reduces roughly by $0.02\sigma_r$ ($SI = 2\%$). We observe that this rescreening result is insensitive to partner change in the network.

4. Discussion

Using a heterosexual behavior survey and Ct prevalence data for the sexually active young AA population in New Orleans, we created an agent-based dynamic network model to understand how the infection spreads and what mitigation approaches can slow it down. In the model, men and women are represented by the network nodes, and edges between the nodes characterize the sexual partnerships. The edges between partners in the network dynamically appear and disappear each day, depending on if the individuals engage in sex on that day. Men's partners are divided into primary and casual ones, and their casual partners are changing over time. One novel property of our model is that the network's joint-degree distribution, which captures



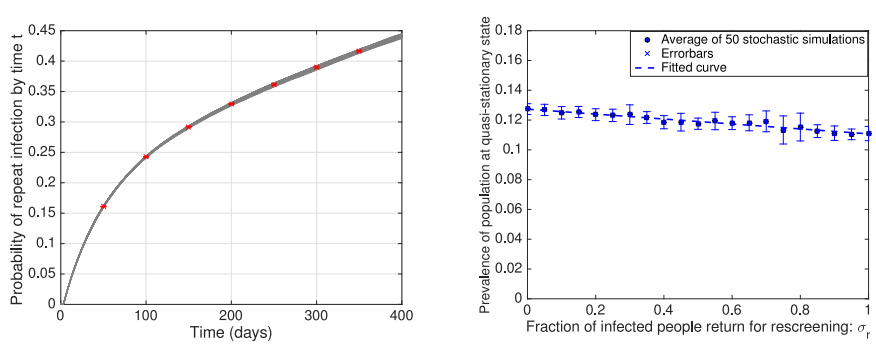
(a) Partner Treatment Only

(b) Partner Screening Only (Dynamic network)

(c) Partner Screening Only (Static network)

(d) Partner Treatment and Screening

Fig. 4. Sensitivity analysis for partner notification: The circles are the mean of 50 different stochastic simulations, and error bars are 95% confidence intervals. (4a): Partner notification for partner treatment only scenario is only mildly effective, and the prevalence remains high (8%), even when all the partners of treated people are treated. (4b): The figure illustrates how the effectiveness of partner notification increases as casual partners are changed less often from every 60 days (black line), every year (blue curve), and every two years (red curve). Partner notification for the partner screening only scenario is more effective in situations where the casual partners less often. (4c): Partner notification for the partner screening only scenario and for the static network is highly effective when θ_n is big enough, that is, when $\theta_n \geq 0.4$ and $\theta_s = 1$, the Ct prevalence rapidly decays to zero. (4d): When only a few partners of an infected person are notified, then partner treatment and partner screening have a similarly small impact on Ct prevalence. When more partners of infected people get notified, θ_n increases, then the partner screening strategy is more effective in controlling the infection.



(a) Cumulative probability distribution of τ_r

(b) Quasi-stationary state prevalence vs σ_r

Fig. 5. Sensitivity analysis for rescreening: The circles are the mean of 50 different stochastic simulations, and error bars are 95% confidence intervals. (5a): Truncated cumulative probability distribution of time between treatment and reinfection with Ct shows that about 25% of the treated people are again infected after 100 days. (5b): Rescreening all the infected people reduces the prevalence by only 2%.

the correlation of an individual's risk (their number of partners) with their partner's risk (number of partners of their partners), is preserved while changing casual partners. That is, the new network preserves the underlying sexual network structure while the topology changes to capture the impact of people changing their casual partnerships.

We use this model to quantify the impact of increasing screening of men for infection, partner notification, and rescreening of treated individuals on reducing Ct prevalence. We observed that increasing Ct screening of men has a modest impact on reducing Ct prevalence in the young adult AA in New Orleans, Fig. 3. Our model predicts that starting at a baseline assumption of 11% prevalence and 45% of the women are being screened each year for Ct, then increasing the screening of men from 0% to 50% would reduce the overall Ct prevalence to 8%. Our observation that partner positivity is insensitive to screening is consistent with previous studies such as Clarke et al. (2012) and Kretzschmar et al. (2012). Kretzschmar also observed adding men screening does not show an effective result in reducing Ct positivity.

In evaluating the effectiveness of partner notification, we assumed some of the partners of an infected person would seek treatment without testing, (partner treatment) or be screened for infection, (partner screening). We observed that treating the notified partners without testing has only a modest impact on Ct prevalence. This practice, although common in disease control today, is not as effective as partner screening. When individuals change their partner less frequently, and the partners of an infected person were tested before treatment, then there will be a tipping point within which partner screening would

bring the epidemic under control. For example, when casual partners do not change very often, then when over 40% of notified partners of all the infected people are screened for infection, the Ct prevalence rapidly decreased to very low levels, Fig. 4c. This critical threshold represents the partner screening level, where a contact tracing tree can spread through the heterosexual network to identify and treat most of the infected people. Our model indicates that this is by far the most effective approach for bringing the epidemic under control.

However, partner screening is more expensive than partner treatment. The partner treatment and screening suggests that when the fraction of partners took action (θ_n is small), then partner screening may not be a good strategy compared to partner treatment. However, if a large enough fraction of an infected person's partners are notified, then either testing and treating (partner screening) can effectively control the spread of Ct. These results of the impact of partner notification are close to results from Kretzschmar et al. (1996) who found for Ct, contact tracing is less effective at lower percentages when partners are treated, but with increasing levels of contact tracing, it will be a highly effective intervention strategy.

Via rescreening, infected individuals return for testing a few months after being treated. We used the model to estimate the probability that a treated person would be reinfected as a function of the time since they were treated. We observed that for the case of 13% infected population, about 25% of the treated population were reinfected three months after treatment. Although the rescreening has only a small impact on the overall Ct prevalence, it is an effective way of identifying reinfection. Even though there is a high chance of reinfection when the individual's behavior does not change, we do not observe an effective impact on the prevalence of Ct by monitoring infected individuals. Similar to screening, rescreening program is not effective as sole intervention because it is not able to find the chain of infection like partner screening. On the other hand, the sensitivity of prevalence to rescreening is less than that of screening, indicating the fact that for a limited budget, the idea of finding more people to screen, random screening, is more effective than frequent screening for fewer people.

Although our model considers different important factors of Ct transmission and assesses the relative impact of different mitigation approaches, it is still too simplistic to be used for quantitative predictions. Our current model preserves the underlying statistical properties of the heterosexual network by retaining the same joint degree distribution for the network while changing casual partners. In our future models, we will focus on improving the heterosexual network dynamics as people change their partners. One of the most important behaviors to capture in the model is how often condoms are used in long-term and casual partnerships. Our model includes condom use, but it does not account for behavior changes, such as increased condom use after being treated for the infection. Our future research will improve the model by relaxing joint-degree distribution up to some error and then quantify the impact of counseling and behavioral changes such as increasing condom use or partner notification rates.

Our bipartite heterosexual network model was constructed based on the correlations between the number of partners a person has and their partners' number of partners. For our future work, we will extend our assortative mixing model to improve our assumptions where sexual partnerships are better characterized by their ages, ethnicity, social groups, economic status, and geographic location. We will focus on validating the model predictions and identifying which trends and quantities can and cannot be predicted within the model uncertainty limits. Our preliminary studies indicate that this paper's qualitative findings are relatively insensitive to adding these additional mixing constraints. Although the model is still too simple to directly guide mitigation efforts, the qualitative trends predicted by these simulations can help design studies to quantify the effectiveness of different mitigation efforts.

CRediT authorship contribution statement

Asma Azizi: Design of the mathematical model, Data analysis, Undertook numerical simulations and visualisation, Interpreted results, Wrote the first draft of the article, Writing and review of the draft. **Jeremy Dewar:** Reviewed the model design and interpretation, Writing and review of the draft. **Zhuolin Qu:** Reviewed the model design and interpretation, Writing and review of the draft. **James Mac Hyman:** Contributed to the study, Reviewed the model, Data analysis and results interpretations, Oversaw and coordinated the investigation, Writing and review of the draft.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Acknowledgment

All authors approved final manuscripts. This work was supported by the endowment for the Evelyn and John G. Phillips Distinguished Chair in Mathematics at Tulane University and grants from the National Institutes of Health National Institute of Child Health and Human Development (R01HD086794) and Office of Adolescent Health (TP2AH000013) and the National Institute of General Medical Sciences program for Models of Infectious Disease Agent Study (U01GM097658).

Appendix A. Supplementary data

Supplementary material related to this article can be found online at https://doi.org/10.1016/j.epidem.2021.100456.

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