Epidemics 48 (2024) 100785

Contents lists available at ScienceDirect

Epidemics

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

Dynamics of *Neisseria gonorrhoeae* transmission among female sex workers and clients: A mathematical modeling study

Houssein H. Ayoub [a,*], Milan Tomy [b,c], Hiam Chemaitelly [b,c,d], Ryosuke Omori [e], Kent Buse [f], Nicola Low [g], Sarah Hawkes [h], Laith J. Abu-Raddad [b,c,d,i,j,**]

[a] *Department of Mathematics and Statistics, College of Arts and Sciences, Qatar University, Doha, Qatar*
[b] *Infectious Disease Epidemiology Group, Weill Cornell Medicine-Qatar, Cornell University, Doha, Qatar*
[c] *World Health Organization Collaborating Centre for Disease Epidemiology Analytics on HIV/AIDS, Sexually Transmitted Infections, and Viral Hepatitis, Weill Cornell Medicine–Qatar, Cornell University, Qatar Foundation – Education City, Doha, Qatar*
[d] *Department of Population Health Sciences, Weill Cornell Medicine, Cornell University, New York, NY, USA*
[e] *Division of Bioinformatics, Research Center for Zoonosis Control, Hokkaido University, Sapporo, Hokkaido, Japan*
[f] *Healthier Societies Program, The George Institute for Global Health, Imperial College London, London, United Kingdom*
[g] *Institute of Social and Preventive Medicine, University of Bern, Bern, Switzerland*
[h] *Centre for Gender Health and Social Justice, Institute for Global Health, University College London, London, United Kingdom*
[i] *Department of Public Health, College of Health Sciences, QU Health, Qatar University, Doha, Qatar*
[j] *College of Health and Life Sciences, Hamad bin Khalifa University, Doha, Qatar*

ARTICLE INFO

Keywords:
Neisseria gonorrhoeae
Sex work
Female sex workers
Sexual behavior
Epidemiology
Mathematical model

ABSTRACT

Background: This study aimed to examine the transmission dynamics of *Neisseria gonorrhoeae* (NG) in heterosexual sex work networks (HSWNs) and the impact of variation in sexual behavior and interventions on NG epidemiology.

Methods: The study employed an individual-based mathematical model to simulate NG transmission dynamics in sexual networks involving female sex workers (FSWs) and their clients, primarily focusing on the Middle East and North Africa region. A deterministic model was also used to describe NG transmission from clients to their spouses.

Results: NG epidemiology in HSWNs displays two distinct patterns. In the common low-partner-number HSWNs, a significant proportion of NG incidence occurs among FSWs, with NG prevalence 13 times higher among FSWs than clients, and three times higher among clients than their spouses. Interventions substantially reduce incidence. Increasing condom use from 10 % to 50 % lowers NG prevalence among FSWs, clients, and their spouses from 12.2 % to 6.4 %, 1.2 % to 0.5 %, and 0.4 % to 0.2 %, respectively. Increasing symptomatic treatment coverage among FSWs from 0 % to 100 % decreases prevalence from 10.6 % to 4.5 %, 0.8 % to 0.4 %, and 0.3 % to 0.1 %, respectively. Increasing asymptomatic treatment coverage among FSWs from 0 % to 50 % decreases prevalence from 8.2 % to 0.4 %, 0.6 % to 0.1 %, and 0.2 % to 0.0 %, respectively, with very low prevalence when coverage exceeds 50 %. In high-partner-number HSWNs, prevalence among FSWs saturates at a high level, and the vast majority of incidence occurs among clients and their spouses, with a limited impact of incremental increases in interventions.

Conclusion: NG epidemiology in HSWNs is typically a "fragile epidemiology" that is responsive to a range of interventions even if the interventions are incremental, partially efficacious, and only applied to FSWs.

1. Introduction

Gonorrhea is a common bacterial sexually transmitted infection (STI) caused by *Neisseria gonorrhoeae* (NG) (Unemo et al., 2019; Kirkcaldy et al., 2019). NG infects exposed urogenital, anorectal, or oropharyngeal mucosa, but the infection is typically asymptomatic and thus

* Correspondence to: Mathematics Program, Department of Mathematics and Statistics, College of Arts and Sciences, Qatar University, P.O. Box 2713, Doha, Qatar.
** Correspondence to: Infectious Disease Epidemiology Group, World Health Organization Collaborating Centre for Disease Epidemiology Analytics on HIV/AIDS, Sexually Transmitted Infections, and Viral Hepatitis, Weill Cornell Medicine - Qatar, Qatar Foundation - Education City, P.O. Box 24144, Doha, Qatar.
E-mail addresses: hayoub@qu.edu.qa (H.H. Ayoub), lja2002@qatar-med.cornell.edu (L.J. Abu-Raddad).

https://doi.org/10.1016/j.epidem.2024.100785
Received 8 May 2023; Received in revised form 12 July 2024; Accepted 29 July 2024
Available online 5 August 2024

undiagnosed and untreated, particularly in women (Unemo et al., 2019; Kirkcaldy et al., 2019; Neslon and Williams, 2007). Untreated infection can lead to a range of complications including vaginal discharge and bleeding, urethritis, cervicitis, pelvic inflammatory disease, ectopic pregnancy, and infertility (Unemo et al., 2019; Kirkcaldy et al., 2019; Chemaitelly et al., 2021). The World Health Organization (WHO) estimated that in 2016 the global prevalence of NG among adults 15–49 years of age was 0.9 % in women and 0.7 % in men (Rowley et al., 2019). Recent data suggest increasing incidence of NG infection in a number of countries (Fu et al., 2022; Centers for Disease Control and Prevention, 2019; Gonorrhoea European Centre for Disease Prevention and Control. Annual epidemiological report, 2018).

NG infection can be promptly and effectively treated and cured within just a few days using appropriate antibiotics administered orally or intramuscularly (World Health Organization, 2023a; Centers for Disease Control and Prevention, 2023). Leading health organizations, including the WHO and the Centers for Disease Control and Prevention, have established treatment guidelines for gonorrhea (World Health Organization, 2023a; Centers for Disease Control and Prevention, 2023). While these guidelines are widely recognized for their effectiveness in treating this infection, gonorrhea has become a significant global health concern due to widespread antimicrobial resistance (AMR) and the emergence of multiple extensively drug-resistant strains (Wi et al., 2017; Lewis, 2014; Bolan et al., 2012; Kirkcaldy et al., 2016). The treatment of this infection has become more challenging, and this has complicated efforts to control its spread.

The WHO declared NG (gonococcal) AMR a global high priority (World Health Organization, 2017) and launched a global action plan to control NG transmission (World Health Organization, 2023b). Additionally, WHO published a "Global Health Sector Strategy on STIs" to address the burden of STIs as a major public health issue (World Health Organization, 2022). The goal of this Strategy is to achieve a 90 % reduction in the incidence of NG infection worldwide by 2030 through evidence-based interventions and expanding access to quality preventive, diagnostic, and therapeutic services (World Health Organization, 2022). It is essential to address the problem of AMR in gonorrhea and to implement effective strategies to prevent and control its spread. Failure to do so could result in increased morbidity, higher healthcare costs, and a significant public health burden.

NG infection is often concentrated among specific populations, particularly female sex workers (FSWs) and their male clients (Brunham and Plummer, 1990), who define together a heterosexual sex work network (HSWN). This infection is commonly associated with recent unprotected sex with a new sexual partner (Rogers et al., 2002; Turner et al., 2002). However, the impact of sexual networks, whether HSWN or other sexual networks, on the epidemiology of NG infection and other STIs remains inadequately understood (Morris, 1997; Omori and Abu-Raddad, 2017). Various metrics of sexual networks seem to affect different STIs differently (Omori and Abu-Raddad, 2017). Therefore, developing a better understanding of NG transmission dynamics among populations most affected by this infection is critical to achieving global public health goals for it. According to the WHO Strategy mentioned above, achieving these goals will also require efforts to address discrimination, stigma, and criminalization of key populations, including sex workers and their clients, which exacerbate risk of infection and prevent the use of health services.

Building on a recently constructed and calibrated individual-based mathematical model for HSWNs and HIV transmission dynamics among FSWs and their clients in these networks (Chemaitelly et al., 2022), a model was developed to simulate the transmission dynamics of NG within these networks. The model was utilized to investigate the influence of sexual behavior summary measures on the spread of NG among FSWs, their clients, and the clients' stable sexual partners or spouses, referred to as client spouses. Additionally, the study investigated the effects of three interventions - condom use and the treatment of symptomatic and asymptomatic infections - on transmission dynamics.

The protracted armed conflicts, economic crises, and massive forced displacements that have affected the Middle East and North Africa (MENA) region have raised concerns about the transmission of STIs, particularly through commercial sex (Hankins et al., 2002; Mumtaz et al., 2022). The structural determinants of STI transmission disproportionately impact conflict-affected populations, with displaced women being vulnerable due to sexual violence, sex trafficking, and forced or transactional sex work (Hankins et al., 2002; Mumtaz et al., 2022; Yasmine and Moughalian, 2016; Charles and Denman, 2013). Given our broader research focus on the vulnerabilities of this region and the availability of current systematic data to inform model data inputs (Chemaitelly et al., 2019a, 2019b), MENA was selected as a primary regional focus for this study.

While we utilized data from the MENA region to parameterize certain model parameters, the study also aimed to generate generic theoretical results of relevance to the global epidemiology of NG infection, irrespective of the region. To achieve this objective, a range of analyses were conducted at diverse parameter values, extending well beyond those specific to MENA. By providing such a theoretical understanding of the epidemiology of this infection in HSWNs, this study aligns with the Global Health Sector Strategy on STIs, emphasizing the need for a better understanding of NG transmission dynamics among populations most affected by this infection (World Health Organization, 2022).

2. Materials and methods

2.1. Mathematical model for female sex workers and male clients

An individual-based Monte Carlo simulation model was developed to simulate sexual networks of FSWs and male clients, and to simulate the transmission of NG within these networks. The model was adapted from a recently published model that described HIV transmission dynamics in HSWNs (Chemaitelly et al., 2022). To represent the natural history of NG infection, the model was modified by changing the modeled HIV infection to match the progression of NG infection, as illustrated in Fig. 1. The NG model structure was developed using earlier STI models (Omori and Abu-Raddad, 2017; Johnson and Geffen, 2016; Ghani and Garnett, 2000) as a reference. A summary of the model description is provided below, while additional details can be found in the previous publication and its supplementary material (Chemaitelly et al., 2022).

The sexual network was constructed by simulating cohorts of FSWs and clients (regular and non-regular/one-time) who form and dissolve sexual partnerships, enter and exit the network, or acquire and transmit NG infection through sex at monthly time steps in each simulation run. The number of sexual partnerships formed by each client with FSWs followed a gamma distribution, as suggested by sexual network and behavioral studies (Omori and Abu-Raddad, 2017; Chemaitelly et al., 2019a; Hamilton et al., 2008; Handcock and Jones, 2004; Omori et al., 2015). Each month, every regular or non-regular client may form a new partnership with one or more FSWs, based on a random probability drawn from the gamma distribution. The mean and variance in the number of partnerships among clients (and consequently among FSWs) are determined from this distribution.

Existing partnerships dissolve stochastically assuming an exponential distribution at a rate that is inversely proportional to the duration of the partnership. Clients randomly selected FSW partners, but different clients had different propensities to form partnerships, a situation known as proportionate mixing (Omori and Abu-Raddad, 2017; Garnett and Anderson, 1993).

To reduce complexity, the individual-based model only accounted for sexual partnerships between clients and FSWs. Although clients and FSWs may have spouses and other sexual partners, these partners are more likely to acquire the infection from clients and FSWs, rather than bringing the infection into the HSWN, thus reducing their role in the

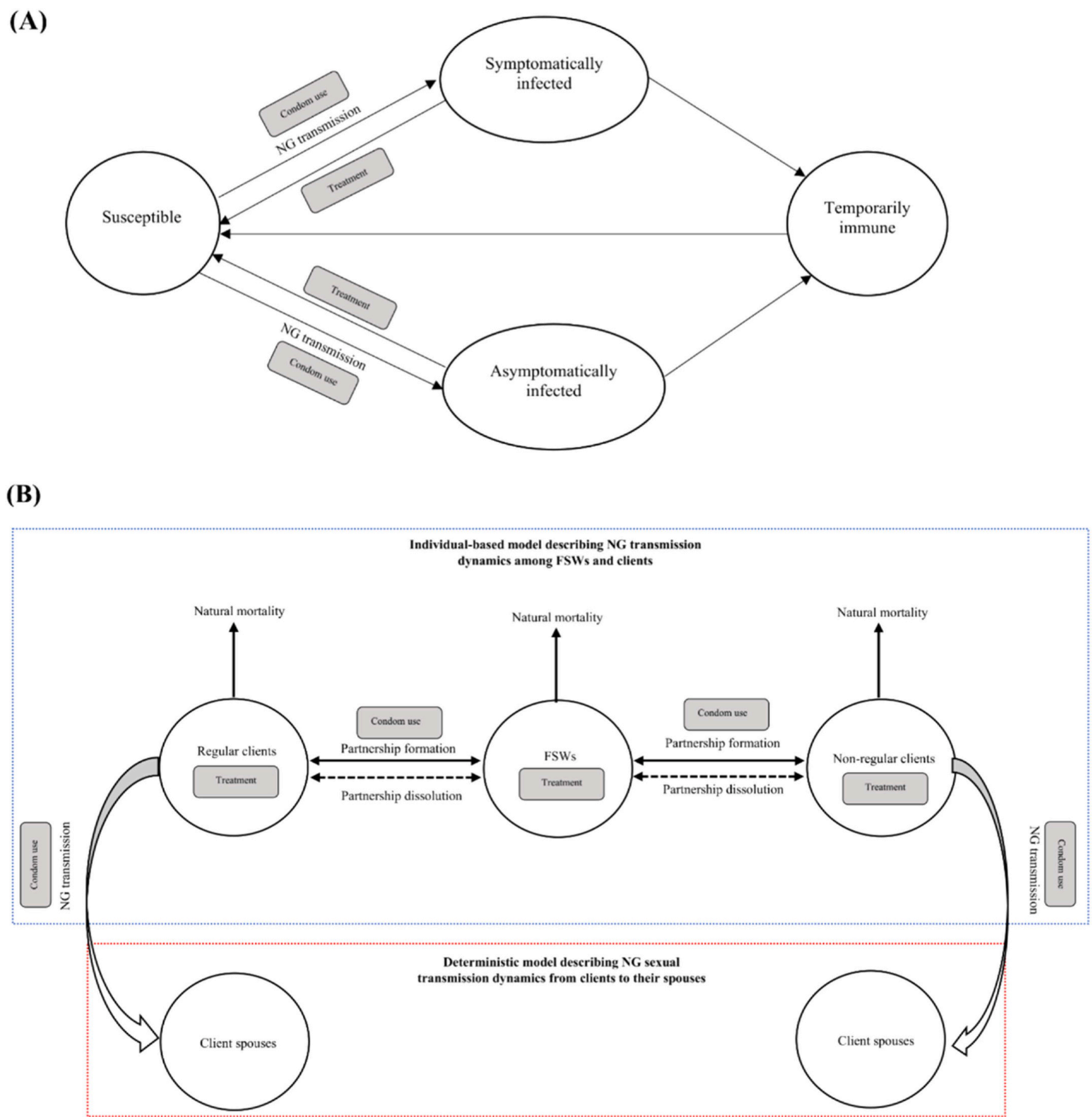

Fig. 1. Basic structure of the mathematical model. A) Schematic diagram describing the natural history of NG infection and effects of interventions on this natural history. B) Schematic diagram describing the modeled transmission dynamics in the heterosexual sex work network. Abbreviations: NG: *Neisseria gonorrhoeae*, FSW: female sex worker.

transmission dynamics (Chemaitelly et al., 2019a; Mumtaz et al., 2013; Kouyoumjian et al., 2018; Abu-Raddad et al., 2010a).

In the simulations, FSWs and clients exited the sexual network due to natural mortality or if the FSW ceased to practice sex work or if the client ceased to buy sex from FSWs (Fig. 1). Individuals who exited the network were replaced by new persons with no history of NG infection, thus maintaining a fixed cohort size for FSWs and clients.

The probability of NG transmission in a partnership between a client and a FSW was calculated using the binomial model (Chemaitelly et al., 2022; Røttingen and Garnett, 2002), which takes into account the probability of NG transmission per coital act and the number of coital acts per time step in this partnership. The probability of transmission per coital act varied depending on the sex of the infected partner and whether a condom was used during sex. Treated individuals were assumed to be non-infectious. The number of coital acts and duration of partnership varied based on whether the client was a regular or non-regular client.

The natural history of NG infection was modeled as a progression from a susceptible state to either symptomatic or asymptomatic infection, followed by a short-term temporary immunity (Fig. 1). Progression through the natural history was modeled stochastically following an exponential distribution, with a rate of the inverse of the duration of each stage.

Condom use, as well as screening and treatment for both symptomatic and asymptomatic infections, were randomly assigned based on the coverage of each intervention in the population at each given time step. For example, in the treatment intervention, a specific probability was assigned to screen and treat newly infected individuals, defining the intervention's coverage. A 50 % coverage indicated a 50 % probability of being screened and treated. Upon treatment, individuals were considered immediately non-infectious, with no alteration in their sexual behavior. Treated individuals who were not immune were assumed to be immediately (within the same time step) susceptible to reinfection.

At each time step in the model simulations, all variables were updated following a specific sequential order of events based on event probabilities and their occurrence. The order included updating deaths and births, followed by partnership dissolution and formation, infection transmission from FSWs to clients, infection transmission from clients to FSWs, recovery from infection through natural recovery or treatment, and lastly, waning of immunity. Notably, this is a two-sex model. If a client becomes infected at a given time step, their status changes to infected, immediately introducing the risk that their uninfected FSW partners may also become infected within the same time step. Therefore, it is possible for a client to become infected and subsequently infect FSWs within the same time step.

Similarly, if an individual's status changes to infected, there is an immediate likelihood of treatment within the same time step. Hence, an individual can be infected and treated within the same time step. After all events and variables are updated at each time step, the prevalence of infection among clients and FSWs, as well as other summary statistics, are calculated for that specific time step.

2.2. Mathematical model for clients and their spouses

To model NG transmission from clients to their spouses, a separate deterministic model was used, which took the output of the individual-based model for clients as input (Chemaitelly et al., 2022). The use of a deterministic model was motivated by computational efficiency and by the fact that the transmission in this case is one-directional and unlikely to be significantly affected by stochastic and non-linear effects. We assumed that all NG incidence among spouses occurred through transmission from an infected client, as the risk of infection from other sources should be minimal compared to the risk of infection from the client (Chemaitelly et al., 2019a; Mumtaz et al., 2013; Kouyoumjian et al., 2018; Abu-Raddad et al., 2010a).

This deterministic modeling component was included to investigate a critical aspect of NG and other STIs epidemiology, often overlooked (Smolak et al., 2019; Land and Ambrosino, 2019). While the core dynamics of NG transmission are among FSWs and their clients, a substantial portion of NG incidence can occur among spouses of clients who engage in no sexual risk behavior. These spouses are consequently affected by a range of adverse reproductive outcomes due to the infection's disproportionate disease burden among women (Unemo et al., 2019; Kirkcaldy et al., 2019; Chemaitelly et al., 2021; Smolak et al., 2019; Land and Ambrosino, 2019).

To estimate the number of NG transmissions from clients to spouses, we used the proportion of clients who were in spousal partnerships, the NG prevalence among clients, and the probability of NG transmission per partnership. The probability of transmission per partnership was estimated using the binomial model (Chemaitelly et al., 2022; Røttingen and Garnett, 2002), which took into account the probability of transmission per coital act, the number of coital acts per partnership, and the coverage of condom use.

The models were coded and all analyses were conducted in MATLAB R2019a (The MathWorks and Inc, 2019). Simulations were conducted using the Red Cloud infrastructure of Cornell University (Red Cloud).

2.3. Model parameters and data sources

The model parameters were selected based on current knowledge and understanding of NG infection natural history and epidemiology. The sources used to determine the parameter values include a comprehensive study on STI models and parameters by Johnson and Geffen (Johnson and Geffen, 2016), the WHO STI estimation model (Rowley et al., 2019), and two systematic reviews on STI/HIV prevalence and sexual behavior among FSWs and clients in MENA (Chemaitelly et al., 2019a, 2019b). Table 1 provides a list of the model parameters and their corresponding references.

2.4. Model simulations

The model was initially run for 20 years without NG introduction to ensure the equilibrium of the sexual network structure. After that, NG infection was seeded, and the model was run for an additional 30 years as a "burn-in" period to ensure endemic equilibrium. To prevent stochastic extinction in the finite simulated network, one NG infection among FSWs was seeded every month. All analyses were implemented at endemic equilibrium to separate the epidemiological effects from the transient temporal effects.

The model was subsequently fitted to the pooled mean prevalence of current NG infection among FSWs in MENA (Chemaitelly et al., 2019b) to estimate the mean number of partnerships among clients per month. This MENA model was designated as the baseline model for this study. Nonlinear least-squares fitting using the Nelder-Mead simplex algorithm was implemented iteratively to generate a set of 50 best model fits (Chemaitelly et al., 2022; Lagarias et al., 1998). A best fit was defined by a relative error of less than 5 % between model prediction and empirical data. The final best model fit was determined as the most probable value for the mean number of partnerships among clients per month among these 50 best fits.

Subsequently, the mean number of partnerships among clients and the variance were sampled from plausible ranges (Table 1) to generate 100 distinct dynamic sexual networks. These networks were intended to represent the global variation in the epidemiology of NG within sexual networks. Each of the 100 dynamic networks maintained the same sampled parameters (mean number of partnerships among clients and variance) in the subsequent simulations described below.

Networks were classified as low-risk, intermediate-risk, or high-risk based on the mean number of partnerships among clients: <0.8, ≥ 0.8 but <1.5, and ≥ 1.5, per month, respectively. The MENA network is an example of a low-risk network (mean number of partnerships of 0.3 per month). A very low-risk network was defined as having a mean number of partnerships ≤ 0.1 per month. This classification was informed by the dependence of prevalence on the mean number of partnerships (Fig. 2). NG prevalence and incidence obviously increase with higher risk classification. Each of the 100 networks underwent 500 simulation runs to account for stochasticity, with each run using different random seeds. This simulation approach balanced computational efficiency with a thorough exploration of network variability.

To explore the impact of interventions, additional simulations were conducted by sampling condom use coverage, symptomatic treatment coverage among FSWs, and asymptomatic treatment coverage among FSWs from broad ranges (Table 1). Treatment coverage was increased by raising the probability of an infection being treated, which implicitly reduced the average duration of infection in the population. Each intervention was assessed separately using 500 simulation runs at different levels of coverage while keeping sexual behavior parameters at their MENA baseline values (a low-risk network). Similar analyses were conducted for a high-risk network. The objective was to examine the effects of condom use and symptomatic and asymptomatic treatment on NG transmission dynamics in the global context.

Table 1
Model parameters.

Parameter	Value	Justification/Source
Natural history and transmission parameters		
Proportion of infections that become symptomatic		
Women	34 %	Based on review of the literature and WHO STI estimation model (Rowley et al., 2019; Newman et al., 2015).
Men	64 %	Based on review of the literature and WHO STI estimation model (Rowley et al., 2019; Newman et al., 2015).
Average duration of natural (i.e. untreated) infection		
Women	6 months	Based on review of the literature and WHO STI estimation model (Rowley et al., 2019; Newman et al., 2015).
Men	5 months	Based on review of the literature and WHO STI estimation model (Rowley et al., 2019; Newman et al., 2015).
Average duration of natural temporary immunity		
Women	12 months	Based on review of the literature and Johnson and Geffen model (Johnson and Geffen, 2016).
Men	12 months	Based on review of the literature and Johnson and Geffen model (Johnson and Geffen, 2016).
Transmission probability per coital act		
From women to men	0.2	Based on empirical data and quantitative estimates (Johnson and Geffen, 2016; Platt et al., 1983; Lin et al., 1998; Orroth et al., 2007; Bracher et al., 2003; Korenromp et al., 2000; Ghani and Aral, 2005).
From men to women	0.4	Based on empirical data and quantitative estimates (Johnson and Geffen, 2016; Orroth et al., 2007; Bracher et al., 2003; Korenromp et al., 2000; Ghani and Aral, 2005; Holmes et al., 1970; Hooper et al., 1978).
Treatment-related parameters		
Duration of infection if treated		
FSWs	4 weeks	Based on review of the literature and WHO STI estimation model (Rowley et al., 2019; Newman et al., 2015).
Clients of FSWs	2 weeks	Based on review of the literature and WHO STI estimation model (Rowley et al., 2019; Newman et al., 2015).
Symptomatic treatment coverage		
FSWs	0–100 %	This parameter was varied to generate Fig. 5A−5 C and was set at 35 % for the baseline model for MENA based on WHO STI estimation model (Rowley et al., 2019; Newman et al., 2015).
Clients of FSWs	48 %	Based on WHO STI estimation model (Rowley et al., 2019; Newman et al., 2015).
Asymptomatic treatment coverage		
FSWs	0–100 %	This parameter was varied to generate Fig. 5D−5 F and was set at 3.5 % for the baseline model for MENA based on WHO STI estimation model (Rowley et al., 2019; Newman et al., 2015).
Clients of FSWs	4.8 %	Based on WHO STI estimation model (Rowley et al., 2019; Newman et al., 2015).
Proportion of infected immune after treatment cure	50 %	Based on Johnson and Geffen model (Johnson and Geffen, 2016).
Cohort size in the modeling simulations		
FSWs	600	Informed by HIV modeling work for MENA (Chemaitelly et al., 2022).
Clients of FSWs	6000	Assumed to be ten times larger than the size of the FSW population as informed by a systematic review of sexual behavior data among FSWs and clients in MENA (Chemaitelly et al., 2019a) and earlier modeling studies (Chemaitelly et al., 2022; Mumtaz et al., 2013; Kouyoumjian et al., 2018).
Sexual behavior parameters		
Number of coital acts with a FSW		
Regular clients	3 acts per month	Informed by a systematic review of sexual behavior data among FSWs and clients in MENA (Chemaitelly et al., 2019a).
One-time clients	1 act per month	Informed by a systematic review of sexual behavior data among FSWs and clients in MENA (Chemaitelly et al., 2019a).
Partnership duration with a FSW		
Regular clients	3 months	Informed by a systematic review of sexual behavior data among FSWs and clients in MENA (Chemaitelly et al., 2019a).
One-time clients	1 month	Informed by a systematic review of sexual behavior data among FSWs and clients in MENA (Chemaitelly et al., 2019a).
Proportion of clients in stable partnerships	56.4 %	Pooled estimate based on data of Demographic and Health Surveys for MENA countries (The United States Agency for International Development USAID, 2021).
Number of coital acts with spouses for regular and one-time clients	25 acts per year	Reasonable value informed by earlier modeling work (Chemaitelly et al., 2022; Mumtaz et al., 2013; Kouyoumjian et al., 2018).
Mean number of partnerships among clients per month	0.05–5.0	This parameter was varied to generate Fig. 2. The parameter was estimated in MENA by fitting model output to the pooled prevalence of current NG infection among FSWs (Chemaitelly et al., 2019b).
Variance in the number of partnerships among clients per month^2	0.01–5.0	This parameter was varied to generate Fig. 3. The parameter was set at 0.2 per month^2 for the baseline MENA model as informed by HIV modeling work for MENA (Chemaitelly et al., 2022).
Duration of practice of sex work	35 years	Informed by a systematic review of sexual behavior data among FSWs and clients in MENA (Chemaitelly et al., 2019a).
Duration of clients buying sex from FSWs	35 years	Reasonable assumption.
Intervention-related parameters		
Condoms		
Effectiveness in reducing NG transmission	80 %	Informed by findings of observational studies for protection against HIV infection (Weller, 2001; Hughes et al., 2012; Pinkerton et al., 1998).

(continued on next page)

Table 1 (*continued*)

Parameter	Value	Justification/Source
Coverage in commercial sex	0–100 %	This parameter was varied to generate Fig. 4. The parameter was set at 52.2 % for the baseline MENA model based on a systematic review of sexual behavior data among FSWs and clients in MENA (Chemaitelly et al., 2019a).
Coverage in spousal partnerships*	2.9 %	Pooled estimate based on data of Demographic and Health Surveys for MENA countries (The United States Agency for International Development USAID, 2021).

Abbreviations: FSW: female sex worker, MENA: Middle East and North Africa, NG: *Neisseria gonorrhoeae*, STI: sexually transmitted infection, WHO: World Health Organization.

* Proportion of women reporting condoms as current contraceptive method.

2.5. Outcome measures

The output of the simulations was used to estimate prevalence of current NG infection and NG incidence among FSWs, clients, and client spouses. The prevalence of current NG infection was defined as the proportion of the population currently infected with NG at each time step, while NG incidence was defined as the number of new infections per unit time. The population share of FSWs, clients, and client spouses in the total NG incidence, indicating the relative contribution of each group to the overall NG incidence within the HSWN, was also calculated.

The means of the distributions of outcome measures over 500 simulation runs were used for model predictions. This number of simulations was found to provide minimal variation in the mean and distribution of the outcome measures. For computational efficiency, after experimenting with different cohort sizes and for consistency with related published HIV analyses (Chemaitelly et al., 2022), simulations were performed using a cohort of 600 FSWs and 6000 clients (one-third of which are regular and two-thirds are non-regular/one-time clients), as informed by MENA data (Chemaitelly et al., 2019a, 2019b).

2.6. Sensitivity analyses

Sensitivity analyses were conducted to assess the impact of various parameters on the model's outcomes. These analyses covered: 1) the ratio of clients per FSW, 2) the number of coital acts per partnership between clients and FSWs, 3) the number of coital acts per partnership

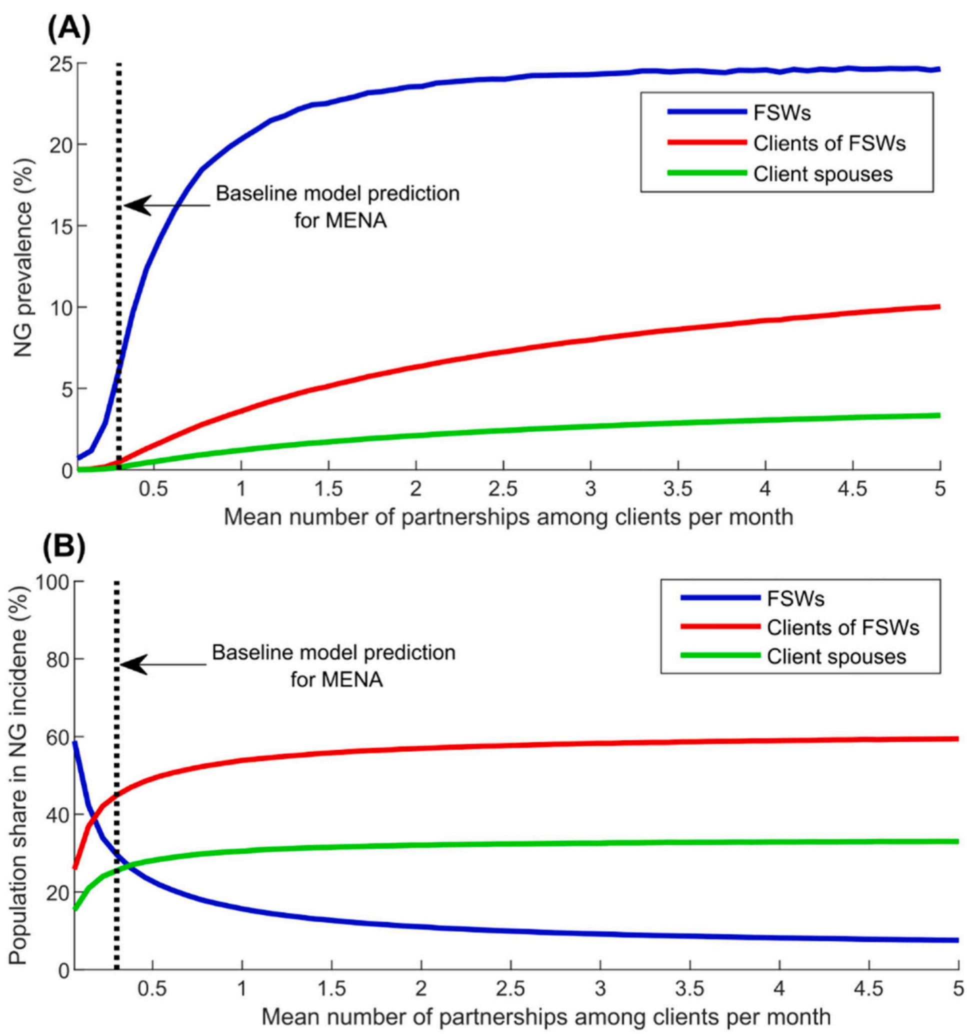

Fig. 2. Effect of mean number of partnerships among clients on NG epidemiology in HSWNs. A) NG prevalence among FSWs, clients, and client spouses as a function of mean number of partnerships among clients. B) Population share of FSWs, clients, and client spouses in the total NG incidence as a function of mean number of partnerships among clients. Abbreviations: FSW: female sex worker, HSWN: heterosexual sex work network, MENA: Middle East and North Africa, NG: *Neisseria gonorrhoeae*. Total NG incidence is defined as the sum of NG incidence among FSWs, clients, and client spouses. Variance in number of partnerships and intervention parameters are fixed at their MENA baseline values.

between clients and their spouses, 4) condom effectiveness, 5) sex work duration for FSWs, 6) duration of clients buying sex from FSWs, and 7) duration of natural immunity. Two additional sensitivity analyses were performed, introducing infection seeds among FSWs and clients from external sources. These external sources represented transmissions from regular partners of FSWs, spouses of clients, or other external contacts, aiming to indirectly assess the impact of transmissions from regular partners of FSWs to FSWs and from spouses of clients to clients on the model's outcomes. Throughout these sensitivity analyses, the non-variable parameters were kept fixed at their baseline MENA values.

3. Results

3.1. Effects of network properties on NG dynamics

Fig. 2 shows the effect of the mean number of partnerships among clients on NG epidemiology in HSWNs. Initially, the prevalence of NG among FSWs increased very rapidly with the mean number of partnerships, but eventually saturated at around 25 % (Fig. 2). On the other hand, the prevalence of NG among clients and their spouses also increased with the mean number of partnerships, but the increase was slow and lagged behind that for FSWs. At high mean numbers of partnerships, the prevalence of NG among clients and their spouses reached approximately 10 % and 3 %, respectively.

In terms of the population share in NG incidence, FSWs had a high contribution of 60 % when the mean number of partnerships was low, but this contribution steadily declined as the mean number of partnerships increased (Fig. 2). At a high mean number of partnerships, NG incidence among FSWs only accounted for approximately 10 % of the total incidence. In contrast, the population share of clients and their spouses in NG incidence increased with the mean number of partnerships and reached approximately 60 % and 30 %, respectively, at high mean numbers of partnerships.

The effect of the variance in the number of partnerships among

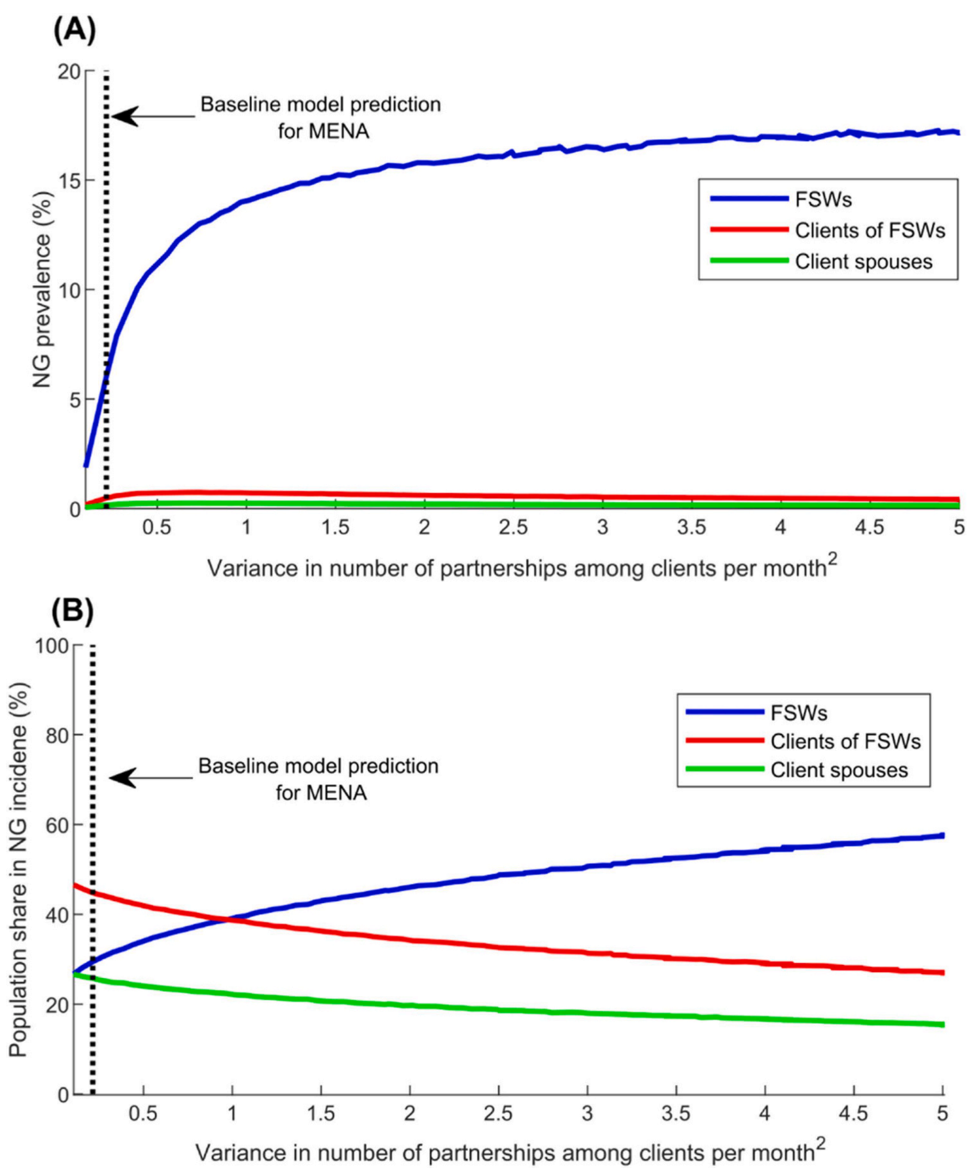

Fig. 3. Effect of variance in number of partnerships among clients on NG epidemiology in a low-risk HSWN. A) NG prevalence among FSWs, clients, and client spouses as a function of variance in number of partnerships among clients. B) Population share of FSWs, clients, and client spouses in the total NG incidence as a function of variance in number of partnerships among clients. Abbreviations: FSW: female sex worker, HSWN: heterosexual sex work network, MENA: Middle East and North Africa, NG: *Neisseria gonorrhoeae*. Total NG incidence is defined as the sum of NG incidence among FSWs, clients, and client spouses. Mean number of partnerships and intervention parameters are fixed at their MENA baseline values.

clients in a low-risk HSWN is illustrated in Fig. 3. NG prevalence among FSWs was found to be sensitive to the variance among clients (Fig. 3), with an increase that was very rapid at first, but eventually saturated at around 20 %. On the other hand, NG prevalence among clients and their spouses increased very slowly with the variance, but then decreased at a similarly slow rate. The peak NG prevalence among clients and their spouses reached only approximately 0.7 % and 0.2 %, respectively, and was always much lower than that among FSWs in these simulations. It is worth noting that the variance in the number of partnerships among FSWs remained largely stable with increasing variance in the number of

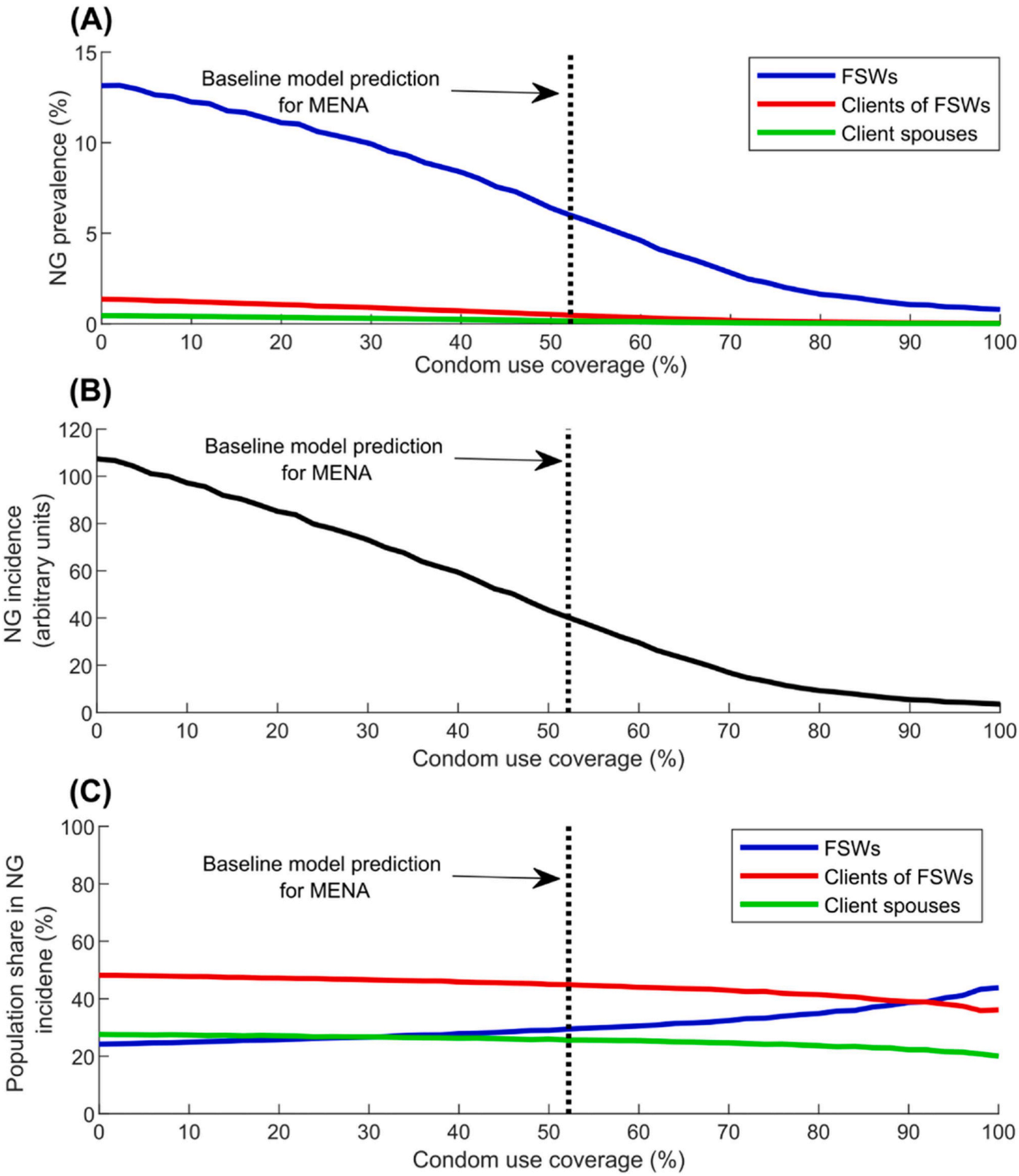

Fig. 4. Effect of condom use on NG epidemiology in a low-risk HSWN. A) NG prevalence among FSWs, clients, and client spouses as a function of condom use coverage. B) Total NG incidence in the HSWN as a function of condom use coverage. C) Population share of FSWs, clients, and client spouses in the total NG incidence as a function of condom use coverage. Effectiveness of condom use against NG transmission was assumed at 80 % (Weller, 2001; Hughes et al., 2012; Pinkerton et al., 1998). Abbreviations: FSW: female sex worker, HSWN: heterosexual sex work network, MENA: Middle East and North Africa, NG: *Neisseria gonorrhoeae*. Total NG incidence is defined as the sum of NG incidence among FSWs, clients, and client spouses. Mean and variance in number of partnerships and other intervention parameters are fixed at their MENA baseline values.

partnerships among clients (see Figure S1 of the Supplementary Material), because of the small number of FSWs compared to the number of clients.

The population share of FSWs in NG incidence increased with the variance among clients and reached approximately 60 % (Fig. 3). In contrast, the population share of clients and their spouses in NG incidence decreased with the variance and reached approximately 25 % and 15 %, respectively. The effect of the variance on NG epidemiology was further investigated in a high-risk HSWN as shown in Figure S2. Here, both the prevalence and population share in incidence among FSWs, clients, and their spouses did not vary considerably with the change in variance.

3.2. Effects of condom intervention

The effect of condom use in a low-risk HSWN is illustrated in Fig. 4. NG prevalence and incidence among FSWs, clients, and their spouses declined rapidly as condom use was increased. When condom use

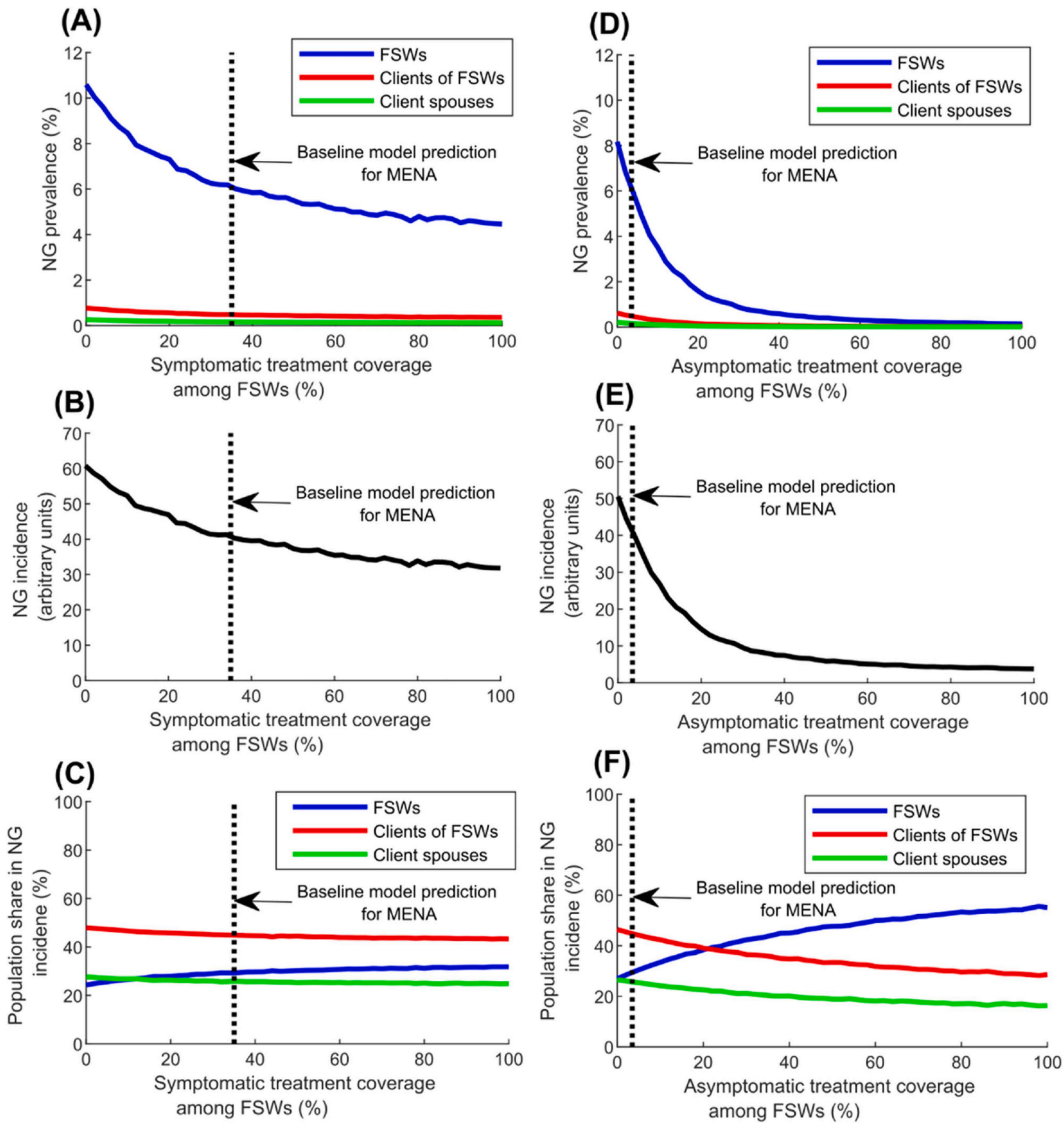

Fig. 5. Effect of symptomatic and asymptomatic infection treatment on NG epidemiology in a low-risk HSWN. NG prevalence among FSWs, clients, and client spouses as a function of A) symptomatic treatment coverage and D) asymptomatic treatment coverage. Total NG incidence as a function of B) symptomatic treatment coverage and E) asymptomatic treatment coverage. Population share of FSWs, clients, and client spouses in the total NG incidence as a function of C) symptomatic treatment coverage and F) asymptomatic treatment coverage. Abbreviations: FSW: female sex worker, HSWN: heterosexual sex work network, MENA: Middle East and North Africa, NG: *Neisseria gonorrhoeae*. Total NG incidence is defined as the sum of NG incidence among FSWs, clients, and client spouses. Mean and variance in number of partnerships and other intervention parameters are fixed at their MENA baseline values.

coverage was increased from 10 % to 50 %, NG prevalence decreased from 12.2 % to 6.4 % among FSWs, 1.2–0.5 % among clients, and 0.4–0.2 % among their spouses.

As condom use coverage increased further, the population share of FSWs in incidence increased, while that of clients and their spouses decreased. It is worth noting that, since the condom effectiveness against NG transmission was 80 %, incidence did not vanish even at 100 % condom use coverage. In a high-risk HSWN, the changes in prevalence and incidence were much slower as condom use was increased (Figure S3).

3.3. Effects of treatment interventions

The effect of symptomatic treatment among FSWs in a low-risk HSWN is illustrated in Fig. 5. NG prevalence (and incidence) among FSWs, clients, and their spouses decreased but slowly with increasing symptomatic treatment coverage. When coverage was increased from 0 % to 100 %, NG prevalence decreased from 10.6 % to 4.5 % among FSWs, 0.8–0.4 % among clients, and 0.3–0.1 % among their spouses. The population share of FSWs, clients, and their spouses in the total incidence remained largely stable with increasing treatment coverage. In a high-risk HSWN, the changes in prevalence and incidence were slower as treatment coverage was increased (Figure S4).

The effect of asymptomatic treatment among FSWs in a low-risk HSWN is also illustrated in Fig. 5. NG prevalence (and incidence) among FSWs, clients, and their spouses declined rapidly with increasing asymptomatic treatment coverage. When coverage was increased from 0 % to 50 %, NG prevalence among FSWs, clients, and their spouses decreased from 8.2 % to 0.4 %, 0.6–0.1 %, and 0.2–0.0 %, respectively. Prevalence reached very low levels when treatment coverage exceeded 50 %. As treatment coverage increased, the population share of FSWs in the total incidence increased, while that of clients and their spouses decreased. However, the changes in prevalence and incidence were slower in a high-risk HSWN as treatment coverage was increased (Figure S4).

3.4. Effect of stochasticity

To better understand the effect of stochasticity on model outcomes, Figure S5 shows the NG prevalence among FSWs in the above analyses for all 500 simulation runs. These results illustrate the considerable influence of stochasticity on NG transmission. For instance, the 500 simulation runs at the MENA baseline parameter values yielded an NG prevalence among FSWs with a mean of 6.1 %, yet with a relatively wide 95 % uncertainty interval spanning from 3.0 % to 9.3 %.

3.5. Sensitivity analyses

Figures S7-S10 present the results of the sensitivity analyses. As expected, the ratio of clients per FSW, numbers of coital acts, condom effectiveness, and natural immunity duration influenced NG prevalence and/or the population share in incidence. Conversely, the duration of sex work for FSWs and the duration of clients buying sex from FSWs had minimal or negligible effects on NG prevalence and the population share in incidence. The sensitivity analyses examining the effects of NG transmissions from external sources indicated a small impact for these infections, even under extreme assumptions regarding the proportion of exogenous infections among both FSWs and clients.

4. Discussion

NG epidemiology in HSWNs exhibits two distinct patterns, depending on the overall "risk of infection" in the network. The risk of infection can be seen as a concept to describe the ease of NG transmission in the HSWN. Low-risk networks are those in which the incidence of infection is low, and the likelihood of infection is relatively low. High-risk networks, on the other hand, are networks where the incidence of infection is high, and the likelihood of infection is relatively high. The risk of infection is ultimately determined by the confluence of the mean and variance in the number of partnerships and the coverage of interventions.

In low-risk HSWNs, such as those found in MENA, a significant proportion of NG incidence occurs among FSWs. Even small increases in the risk of infection can substantially increase NG prevalence among FSWs. NG prevalence among FSWs is 13-fold higher than among clients, while prevalence among clients is 3-fold higher than among their spouses. Incremental increases in the coverage of interventions targeted at FSWs can significantly reduce total NG incidence since these interventions are focused on the population most heavily affected by NG. Given the large contribution of HSWNs to NG incidence in the wider population (Lowndes et al., 2002), interventions targeted at FSWs are also likely to substantially reduce NG incidence in the broader population.

Meanwhile, in high-risk HSWNs, NG prevalence among FSWs saturates at high levels regardless of further increases in the risk of infection. The vast majority of NG incidence occurs among clients and their spouses, and only a small proportion occurs among FSWs. NG prevalence among FSWs is only 4-fold higher than among clients, while prevalence among clients remains 3-fold higher than among their spouses. Incremental increases in coverage of interventions among FSWs, such as condom use and treatment, have a limited effect on NG prevalence and incidence. However, very high coverage of interventions can transform a high-risk network into a low-risk network. Of note that NG epidemiology in intermediate risk HSWNs bridges the distinct low-risk and high-risk epidemiologies.

Based on the observed NG prevalence among FSWs worldwide (Chemaitelly et al., 2019b; Whelan et al., 2021), it is likely that most HSWNs are low-risk networks that are sensitive to interventions targeting FSWs, even if clients and their spouses are not directly targeted. This highlights the epidemiology of NG infection in HSWNs as "fragile epidemiology," which can respond to interventions, even if they have low coverage and are incremental. With the increasing availability of intervention modalities against NG infection, such as potentially vaccination (Petousis-Harris et al., 2017; Edwards et al., 2018; CROI, 2023) and post-exposure prophylaxis with doxycycline (DoxyPEP) (Lewis, 2022), in addition to condom use and treatment, even if these interventions are only partially efficacious, there is an opportunity to control better NG transmission and gonococcal AMR globally.

NG incidence among FSWs is typically a minority of the overall incidence in HSWNs, with the majority occurring among clients and their spouses who are less likely to access STI services. A significant proportion of incidence occurs among female spouses of clients, who may not engage in sexual risk behavior, but are exposed to the infection through their husbands. The epidemiology of NG among spouses of clients represents an immediate spill-over of NG epidemiology among clients and is critical given the extent of infection among spouses.

Interventions targeted at FSWs can have a significant impact in indirectly reducing NG incidence among clients and their spouses. However, it is important to consider the potential negative externalities of STI public health control interventions that focus solely on women selling sex rather than also targeting men who buy sex. Such interventions can perpetuate gendered inequalities and reinforce stigmatization of women in relation to STIs. It is important to adopt a gender-sensitive approach in STI control programs that avoids placing disproportionate blame on women.

Treatment of symptomatic NG infections has a modest impact on transmission because most infections are asymptomatic, but treating asymptomatic infections has a substantial impact. Regular screening for this infection and DoxyPEP (indirectly as a "presumptive treatment") can be seen as potential public health interventions, where asymptomatically infected individuals are treated, leading to a significant impact on the onward transmission of this infection. The proportion of asymptomatic infections that can be treated would depend on the frequency of using DoxyPEP and regular screening. Given that NG infection is more asymptomatic among women (Rowley et al., 2019; Newman et al., 2015), the treatment of asymptomatic infections holds particular significance for FSWs.

Heterogeneity in the number of sexual partners (i.e., larger variance in the number of partnerships) can effectively create a high-risk core of intense NG transmission in the network. Transmission becomes concentrated in this core, which comprises, in addition to FSWs, a small proportion of clients. Targeted interventions by risk group were not implemented in this study. The model's structure accounts for continuous and stochastic risk variations as the number of partners is modeled using a gamma distribution. Consequently, defining fine-grained core groups based on partner change rates demands careful consideration and necessitates a significant extension of the existing model. An in-depth exploration of the concept of targeted interventions by risk group is warranted and should be pursued in a dedicated study.

STIs have historically been overlooked by policymakers in the MENA region, primarily due to the complexities involved in addressing them, exacerbated by prevailing socio-cultural sensitivities surrounding sexuality (Abu-Raddad et al., 2010a; Smolak et al., 2019; Land and Ambrosino, 2019; Abu-Raddad et al., 2013, 2010a, 2010b). Limited access to and utilization of STI screening and treatment services are widespread challenges across the region (Abu-Raddad et al., 2010a; Smolak et al., 2019; Land and Ambrosino, 2019; Abu-Raddad et al., 2013, 2010a, 2010b). Therefore, we investigated the impact of interventions across a broad spectrum of coverages to provide a comprehensive understanding of their potential impact. The results underscore the importance of expanding STI screening and treatment services as well as sexual health programs throughout the region.

The introduced model and presented results establish the groundwork for dedicated modeling studies addressing various research questions, encompassing both theoretical explorations and practical applications. These practical applications may involve designing specific interventions in particular locations, where available costing and programmatic data enable the conduct of cost-effectiveness analyses and investigation of different programmatic considerations.

This study has limitations. Firstly, the estimates generated are based on current understanding of the natural history of NG infection, which is still inadequately understood, including the immunity effects of prior infections on subsequent ones. Similarly, the specifics of sexual networking in HSWNs remain inadequately understood. To address these limitations, we conducted various sensitivity analyses with respect to different model parameters. These analyses reinforced the main findings and also yielded additional results and insights, enhancing the depth of our understanding.

Secondly, the model did not simulate NG transmission beyond FSWs, male clients, and client spouses, potentially underestimating the true extent of NG infection arising from HSWNs. The model also did not account for transmissions from outside the HSWN. However, we addressed the latter limitation through sensitivity analyses examining the effects of NG transmissions from external sources. These analyses indicated a minimal impact for these infections, even under extreme assumptions regarding the proportion of exogenous infections among both FSWs and clients.

Thirdly, interventions were applied randomly, whereas in reality, people who adopt one intervention may also be more likely to adopt others—people who use condoms might be more likely to seek prompt treatment when they have symptoms, or to attend for regular testing if asymptomatic. Fourthly, the deterministic model used to estimate outcomes for spouses of clients does not capture stochasticity effects.

Fifthly, we analyzed low-risk and high-risk HSWNs separately. However, real-world networks on a large scale are likely to consist of subnetworks comprising both low-risk and high-risk HSWNs, as well as potentially a spectrum between these. Despite this, the presented results should remain applicable, as the connections between these subnetworks may not be strong enough to alter the inherent dynamics within each subnetwork.

Sixthly, due to computational limitations, the simulations were performed using sub-cohorts of FSWs and clients that are representative of the full cohorts, which may affect the results due to finite-network effects and a higher likelihood of stochastic fade-out. Seventhly, a one-month time step was used in the simulations without investigating time-step numerical convergence to optimize this choice. While a one-month time step could be relatively long for NG dynamics, potentially causing quantitative shifts in outcomes, it should not affect the qualitative results generated by the simulations. Despite these limitations, this study provided important insights into the dynamics of NG transmission in HSWNs and the potential impact of interventions.

In summary, NG epidemiology in HSWNs shows two patterns: low-risk HSWNs have a large proportion of NG incidence among FSWs, and interventions targeted at FSWs can substantially reduce NG incidence in the whole network. High-risk HSWNs have NG prevalence saturating among FSWs and the vast majority of incidence occurs among clients and their spouses. Incremental interventions in high-risk HSWNs have only a modest effect on transmission. Most HSWNs are low-risk, making the typical NG epidemiology in HSWNs a "fragile epidemiology" that is responsive to even partially efficacious interventions with small coverage and incremental increases.

Funding

This publication was funded by the Wellcome Trust grant (208712/Z/17/Z). HHA acknowledges the support of Qatar University internal grant QUCG-CAS-23/24-114. LJA and HHA acknowledge the support of the Qatar Research Development and Innovation Council [ARG01-0522-230273]. The content is solely the responsibility of the authors and does not necessarily represent the official views of Qatar Research Development and Innovation Council. The authors are also grateful for infrastructure support provided by the Biostatistics, Epidemiology, and Biomathematics Research Core at Weill Cornell Medicine-Qatar.

CRediT authorship contribution statement

Houssein H. Ayoub: Conceptualization, Data curation, Formal analysis, Funding acquisition, Investigation, Methodology, Project administration, Resources, Software, Supervision, Validation, Visualization, Writing – original draft, Writing – review & editing. **Milan Tomy:** Data curation, Formal analysis, Investigation, Methodology, Software, Validation, Visualization, Writing – review & editing. **Hiam Chemaitelly:** Data curation, Formal analysis, Investigation, Methodology, Software, Validation, Visualization, Writing – review & editing. **Ryosuke Omori:** Software, Validation, Visualization, Writing – review & editing, Resources. **Laith Abu-Raddad:** Conceptualization, Data curation, Formal analysis, Funding acquisition, Investigation, Methodology, Project administration, Resources, Software, Supervision, Validation, Visualization, Writing – original draft, Writing – review & editing. **Sarah Hawkes:** Funding acquisition, Resources, Validation, Visualization, Writing – review & editing. **Kent Buse:** Funding acquisition, Validation, Visualization, Writing – review & editing, Resources. **Nicola Low:** Funding acquisition, Resources, Validation, Visualization, Writing – review & editing.

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.

Data availability

Data will be made available on request.

Acknowledgements

We thank the administrators of the Red Cloud infrastructure at Cornell University for their support in running the simulations.

Authors' contributions

HHA, MT, and HC designed, parametrized, and coded the mathematical model. HHA generated simulations and wrote the first draft of the article. MT generated simulations. RO contributed to the model development. LJA conceived and led the design of the study and model, analyses, and drafting of the article. All authors contributed to discussion and interpretation of the results and to writing of the manuscript. All authors have read and approved the final manuscript.

Appendix A. Supporting information

Supplementary data associated with this article can be found in the online version at doi:10.1016/j.epidem.2024.100785.

References

Abu-Raddad, L.J., et al., 2010a. Epidemiology of HIV infection in the Middle East and North Africa. AIDS 24 (Suppl 2), S5–S23.
Abu-Raddad, L.J., et al., 2010b. Policy Notes. Characterizing the HIV/AIDS epidemic in the Middle East and North Africa: Time for Strategic Action. Middle East and North Africa HIV/AIDS Epidemiology Synthesis Project. World Bank/UNAIDS/WHO Publication. The World Bank Press, Washington DC.
Abu-Raddad, L.J., et al., 2010a. Characterizing the HIV/AIDS epidemic in the Middle East and North Africa: Time for Strategic Action. Middle East and North Africa HIV/AIDS Epidemiology Synthesis Project. World Bank/UNAIDS/WHO Publication. The World Bank Press, Washington DC.
Abu-Raddad, L.J., et al., 2013. HIV and other sexually transmitted infection research in the Middle East and North Africa: promising progress? Sex. Transm. Infect. 89 (Suppl 3), iii1–iii4.
Bolan, G.A., Sparling, P.F., Wasserheit, J.N., 2012. The emerging threat of untreatable gonococcal infection. N. Engl. J. Med. 366 (6), 485–487.
Bracher, M., Santow, G., Watkins, S., 2003. "Moving" and Marrying: Modelling HIV Infection among Newly-weds in Malawi. Demogr. Res. 1, 207–246.
Brunham, R.C., Plummer, F.A., 1990. A general model of sexually transmitted disease epidemiology and its implications for control. Med. Clin. North Am. 74 (6), 1339–1352.
Centers for Disease Control and Prevention, *Gonorrhea treatment and care. Accessed on October 19, 2023.* 〈https://www.cdc.gov/std/gonorrhea/treatment.htm〉. 2023.
Centers for Disease Control and Prevention. Sexually Transmitted Disease Surveillance, 2019. Atlanta, GA: Department of Health and Human Services; April 2021. https://www.cdc.gov/std/statistics/2019/std-surveillance-2019.pdf. Accessed 30 March 2023.
Charles, L., Denman, K., 2013. Syrian and palestinian syrian refugees in lebanon: the plight of women and children. J. Int. Women's Stud. *14* (5), 96–111.
Chemaitelly, H., et al., 2019b. Epidemiology of Treponema pallidum, Chlamydia trachomatis, Neisseria gonorrhoeae, Trichomonas vaginalis, and herpes simplex virus type 2 among female sex workers in the Middle East and North Africa: systematic review and meta-analytics. J. Glob. Health 9 (2), 020408.
Chemaitelly, H., et al., 2019a. HIV epidemiology among female sex workers and their clients in the Middle East and North Africa: systematic review, meta-analyses, and meta-regressions. BMC Med. 17 (1).
Chemaitelly, H., et al., 2021. Global epidemiology of Neisseria gonorrhoeae in infertile populations: systematic review, meta-analysis and metaregression. Sex. Transm. Infect. 97 (2), 157–169.
Chemaitelly, H., et al., 2022. HIV incidence and impact of interventions among female sex workers and their clients in the Middle East and north Africa: a modelling study. Lancet HIV 9 (7), e496–e505.
CROI 2023: Vaccine and doxycycline PEP both cut gonorrhoea rates, Tuesday 21 February 2023. https://www.aidsmap.com/bulletin/conference-news/croi-2023/21-february-2023.
Edwards, J.L., Jennings, M.P., Seib, K.L., 2018. Neisseria gonorrhoeae vaccine development: hope on the horizon? Curr. Opin. Infect. Dis. 31 (3), 246–250.
Fu, L., et al., 2022. Incidence Trends of Five Common Sexually Transmitted Infections Excluding HIV From 1990 to 2019 at the Global, Regional, and National Levels: Results From the Global Burden of Disease Study 2019. Front. Med. (Lausanne) 9, 851635.
Garnett, G.P., Anderson, R.M., 1993. Factors controlling the spread of HIV in heterosexual communities in developing countries: patterns of mixing between different age and sexual activity classes. Philos. Trans. R. Soc. Lond. B Biol. Sci. 342 (1300), 137–159.
Ghani, A.C., Aral, S.O., 2005. Patterns of sex worker–client contacts and their implications for the persistence of sexually transmitted infections. J. Infect. Dis. 191 (Supplement_1), S34–S41.
Ghani, A.C., Garnett, G.P., 2000. Risks of acquiring and transmitting sexually transmitted diseases in sexual partner networks. Sex. Transm. Dis. 27 (10), 579–587.
Gonorrhoea European Centre for Disease Prevention and Control. Annual epidemiological report 2018. *Stockholm: European Centre for Disease Prevention and Control.* https://www.ecdc.europa.eu/en/all-topics-zgonorrhoeasurveillance-and-disease-data/annual-epidemiological-reports-gonorrhoea. Accessed 30 March 2023.
Hamilton, D.T., Handcock, M.S., Morris, M., 2008. Degree distributions in sexual networks: a framework for evaluating evidence. Sex. Transm. Dis. 35 (1), 30–40.
Handcock, M.S., Jones, J.H., 2004. Likelihood-based inference for stochastic models of sexual network formation. Theor. Popul Biol. 65 (4), 413–422.
Hankins, C.A., et al., 2002. Transmission and prevention of HIV and sexually transmitted infections in war settings: implications for current and future armed conflicts. Aids 16 (17), 2245–2252.
Holmes, K.K., Johnson, D.W., Trostle, H.J., 1970. An estimate of the risk of men acquiring gonorrhea by sexual contact with infected females. Am. J. Epidemiol. 91 (2), 170–174.
Hooper, R., et al., 1978. Cohort study of venereal disease. I: the risk of gonorrhea transmission from infected women to men. Am. J. Epidemiol. 108 (2), 136–144.
Hughes, J.P., et al., 2012. Determinants of per-coital-act HIV-1 infectivity among African HIV-1-serodiscordant couples. J. Infect. Dis. 205 (3), 358–365.
Johnson, L.F., Geffen, N., 2016. A comparison of two mathematical modeling frameworks for evaluating sexually transmitted infection epidemiology. Sex. Transm. Dis. 43 (3), 139–146.
Kirkcaldy, R.D., et al., 2016. Neisseria gonorrhoeae Antimicrobial Susceptibility Surveillance - The Gonococcal Isolate Surveillance Project, 27 Sites, United States, 2014. MMWR Surveill. Summ. 65 (7), 1–19.
Kirkcaldy, R.D., et al., 2019. Epidemiology of gonorrhoea: a global perspective. Sex. Health 16 (5), 401–411.
Korenromp, E.L., et al., 2000. Model-based evaluation of single-round mass treatment of sexually transmitted diseases for HIV control in a rural African population. Aids 14 (5), 573–593.
Kouyoumjian, S.P., et al., 2018. Mapping of new HIV infections in Morocco and impact of select interventions. Int J. Infect. Dis. 68, 4–12.
Lagarias, J.C., et al., 1998. Convergence properties of the Nelder–Mead simplex method in low dimensions. SIAM J. Optim. 9 (1), 112–147.
Land, J.A., Ambrosino, E., 2019. Prevalence of Chlamydia trachomatis infections in the Middle East and north Africa, what next? Lancet Glob. Health 7 (9), e1152–e1153.
Lewis, D.A., 2014. Global resistance of Neisseria gonorrhoeae: when theory becomes reality. Curr. Opin. Infect. Dis. 27 (1), 62–67.
Lewis, D., 2022. Push to use antibiotics to prevent sexually transmitted infections raises concerns. Nature 612 (7938), 20–21.
Lin, J.-S.L., et al., 1998. Transmission of Chlamydia trachomatis and Neisseria gonorrhoeae among men with urethritis and their female sex partners. J. Infect. Dis. 178 (6), 1707–1712.
Lowndes, C.M., et al., 2002. Role of core and bridging groups in the transmission dynamics of HIV and STIs in Cotonou, Benin, West Africa. Sex. Transm. Infect. 78 (Suppl 1), i69–i77.
Morris, M., *Sexual networks and HIV.* Aids, 1997. 11: p. S209-S216.
Mumtaz, G.R., et al., 2013. The distribution of new HIV infections by mode of exposure in Morocco. Sex. Transm. Infect. 89 (Suppl 3), iii49–iii56.
Mumtaz, G.R., et al., 2022. Status of the HIV epidemic in key populations in the Middle East and north Africa: knowns and unknowns. Lancet HIV 9 (7), e506–e516.
Neslon, K.E., Williams, C.M., 2007. Infectious disease Epidemiology: Theory and Practice, Second Edition. Jones and Bartlett Publishers, Sudbury, Massachussets.
Newman, L., et al., 2015. Global estimates of the prevalence and incidence of four curable sexually transmitted infections in 2012 based on systematic review and global reporting. PloS One 10 (12), e0143304.
Omori, R., Abu-Raddad, L.J., 2017. Sexual network drivers of HIV and herpes simplex virus type 2 transmission. AIDS 31 (12), 1721–1732.
Omori, R., Chemaitelly, H., Abu-Raddad, L.J., 2015. Dynamics of non-cohabiting sex partnering in sub-Saharan Africa: a modelling study with implications for HIV transmission. Sex. Transm. Infect. 91 (6), 451–457.
Orroth, K.K., et al., 2007. Understanding the differences between contrasting HIV epidemics in east and west Africa: results from a simulation model of the Four Cities Study. Sex. Transm. Infect. 83 (suppl 1), i5–i16.
Petousis-Harris, H., et al., 2017. Effectiveness of a group B outer membrane vesicle meningococcal vaccine against gonorrhoea in New Zealand: a retrospective case-control study. Lancet 390 (10102), 1603–1610.
Pinkerton, S.D., Abramson, P.R., Turk, M.E., 1998. Updated estimates of condom effectiveness. J. Assoc. Nurses AIDS Care 9 (6), 88–89.
Platt, R., Rice, P.A., McCormack, W.M., 1983. Risk of acquiring gonorrhea and prevalence of abnormal adnexal findings among women recently exposed to gonorrhea. Jama 250 (23), 3205–3209.
Red Cloud. Cornell University. https://www.cac.cornell.edu/services/cloudservices.aspx.
Rogers, S.M., et al., 2002. NAAT-identified and self-reported gonorrhea and chlamydial infections: different at-risk population subgroups? Sex. Transm. Dis. 29 (10), 588–596.
Røttingen, J.A., Garnett, G.P., 2002. The epidemiological and control implications of HIV transmission probabilities within partnerships. Sex. Transm. Dis. 29 (12), 818–827.
Rowley, J., et al., 2019. Chlamydia, gonorrhoea, trichomoniasis and syphilis: global prevalence and incidence estimates, 2016. Bull. World Health Organ. 97 (8), 548.
Smolak, A., et al., 2019. Epidemiology of Chlamydia trachomatis in the Middle East and north Africa: a systematic review, meta-analysis, and meta-regression. Lancet Glob. Health 7 (9), e1197–e1225.

The MathWorks and Inc. MATLAB, The language of technical computing. 2019, The MathWorks, Inc.
The United States Agency for International Development (USAID). *The Demographic and Health Surveys Program. Available from: https://dhsprogram.com/data/available-datasets.cfm. Accessed on: August 26, 2021*. 2021.
Turner, C.F., et al., 2002. Untreated gonococcal and chlamydial infection in a probability sample of adults. JAMA 287 (6), 726–733.
Unemo, M., et al., 2019. Gonorrhoea. Nat. Rev. Dis. Prim. 5 (1), 79.
Weller, S., Davis, K., 2001. Condom effectiveness in reducing heterosexual HIV transmission. Cochrane Database Syst. Rev. (3), CD003255
Whelan, J., et al., 2021. Gonorrhoea: a systematic review of prevalence reporting globally. BMC Infect. Dis. 21 (1), 1152.
Wi, T., et al., 2017. Antimicrobial resistance in Neisseria gonorrhoeae: Global surveillance and a call for international collaborative action. PLoS Med 14 (7), e1002344.
World Health Organization, *Gonorrhoea. Fact sheet on gonorrhoea. Accessed on October 19,* 2023. https://www.who.int/news-room/fact-sheets/detail/gonorrhoea-(neisseria-gonorrhoeae-infection). 2023a.
World Health Organization. *Global action plan to control the spread and impact of antimicrobial resistance in Neisseria gonorrhoeae.* 2012 [cited 2023b January 19,]; Available from: ⟨https://apps.who.int/iris/bitstream/handle/10665/44863/9789241503501_eng.pdf?sequence=1⟩.
World Health Organization. *Global health sector strategies on, respectively, HIV, viral hepatitis and sexually transmitted infections for the period 2022-2030*. 2022 [cited 2023 January 19,]; Available from: ⟨https://www.who.int/publications/i/item/9789240053779⟩.
World Health Organization. *Global priority list of antibiotic-resistant bacteria to guide research, discovery, and development of new antibiotics.* Geneva: World Health Organization 2017 [cited 2023 January 19,]; Available from: http://remed.org/wp-content/uploads/2017/03/lobal-priority-list-of-antibiotic-resistant-bacteria-2017.pdf.
Yasmine, R., Moughalian, C., 2016. Systemic violence against Syrian refugee women and the myth of effective intrapersonal interventions. Reprod. Health Matters 24 (47), 27–35.