**Supplementary Materials**

***Technical details of the transmission model for gonorrhoea with sexual mixing***

We constructed a deterministic compartmental model for the transmission of gonorrhoea. This model took into consideration the heterogeneity due to the sexual mixing of high-risk and low-risk subgroups of MSM. Based on the STIGMA guidelines, we defined ‘high-risk’ MSM as those having more than 10 partners in the past 6 months and the low-risk group as those who have 10 or less [1].

*Behaviour and disease progression data*

We conducted a literature review of sexual behaviour data for Australian MSM in the period 2004 to 2014, including the frequency of oral sex, anal sex, kissing, rimming [2-5]; the number of sexual partners in the past 12 months [6-19] and condom usage during anal sex [2, 5, 20-23] (Table S1). The main data sources were Gay Community Periodic Surveys, Health in Men study (HIM) and empirical studies published by Sydney and Melbourne Sexual Health Centres.

When untreated, oropharyngeal and rectal gonorrhoea lasts an average of 12 and 50 weeks [24], respectively. The duration of untreated urethral gonorrhoea was assumed to be similar to that of oropharyngeal infection [25]. However, in the Australian setting, most MSM with symptomatic urethral gonorrhoea seek treatment promptly and are rendered non-infectious within a week of the appearance of symptoms [26]. Asymptomatic gonorrhoea is assumed to remain infectious until it resolves spontaneously.

The duration of untreated oropharyngeal gonorrhoea of 3 months (that is, ~100 days) corresponds to a natural clearance rate of approximately ~1% per day. It is likely that mouthwash increases the rate of clearance. Several studies on the antibacterial mouthwash Listerine® have been conducted at MSHC. Alcohol-containing Listerine® products such as Cool Mint and Total Care were effective in clearing NG at oropharynx, but saline had no inhibitory effect against NG [27]. *In vivo,*a randomised controlled trial of a single use of Listerine® (Cool Mint) compared to saline among 58 MSM with oropharyngeal gonorrhoea at MSHC showed that 52% in the Listerine® group were culture positive *versus* 84% in the saline group at five minutes post rinsing and gargling the solution (*p*=0.013). While the exact efficacy of mouthwash remains unknown, these preliminary findings suggest that regular daily use of mouthwash among MSM may reduce the concentration of gonococci in the saliva and oropharynx, and hence the transmissibility and duration of infection. If mouthwash is able to reduce the duration of oropharyngeal gonorrhoea by half, this corresponds to a further reduction of 1% clearance each day in addition to the 1% spontaneous daily clearance rate. In our model, we allow the rate of gonorrhoea clearance due to mouthwash to vary between 0.5% and 1.5% per day.

**Table S1. Common biological and NG screening data in MSM.**

|  |  |  |
| --- | --- | --- |
| **Indicators** | **Value (uncertainty bounds)** | **References/Remarks** |
| Percentage of MSM having >10 sexual partners in the past 6 months | 18% (12-24%) | Partnership data were obtained from MSHC dataset and published literature. The 2015 MSHC CASI data indicates that 12% of 15,366 clients at its clinic have more than 20 partners in the past 12 months. This likely underestimates the actual number of partners in the past 6 months due to a longer recall period. We hence used it as a lower bound. Guy et.al. [28] reported 24% of MSM have six or more sexual partners in the past six months. We hence use this as the upper bound of the estimation. |
| Proportion of urethral infections that are asymptomatic (%) | 10% (0.1-20%) |  [29-31] |
| Infection duration of gonorrhoea at throat (asymptomatic, weeks) | 12 (10-19) |  [24, 32, 33].  |
| Infection duration of gonorrhoea at penis (symptomatic infection, weeks) | 1 (0.9-1.1) |  [26]. This is the duration from the time of infection to the time the symptomatic individual receive treatment.  |
| Infection duration of gonorrhoea at penis (asymptomatic infection, weeks) | 12 (10-20) |  Model assumption of 12 weeks [25].  |
| Infection duration of gonorrhoea at rectum (asymptomatic infection, weeks) | 49.43 (48-52) |  [24].  |
| Condom efficacy in preventing gonorrhoea transmission (%) | 87.5% (80-95%) |  [34] |
| Proportion of MSM received throat swab in the past 12 months | 40% |  [35] |
| Proportion of MSM received rectal swab in the past 12 months | 40% |  [35] |

**Table S2 Prevalence of gonorrhoea and behavioural data among MSM, stratified by risk groups**

|  |  |  |
| --- | --- | --- |
| **Indicators** | **Value (uncertainty bounds)** | **References/Remarks** |
|  | **All MSM**  | **MSM with ≤10 sexual partners in the past 6 months** **(perc = 79%)** | **MSM with >10 sexual partners in the past 6 months (perc = 21%)** |  |
| Infection prevalence of gonorrhoea at oropharynx (%) | 8.6% (7.7-9.5%) | 8.1% (7.4-8.7%) | 10.6% (8.9-12.3) | Pharyngeal and rectal prevalence were obtained from 1,004 MSM individuals attending Melbourne Sexual Health Centre for gonorrhoea screening in 2015. Among the 1,004 MSM, 211 were considered ‘high-risk’, and 793 were ‘low-risk’. These prevalence levels were comparable with a separate publication by MSHC [36].  |
| Infection prevalence of gonorrhoea at rectum (%) | 8.3% (7.4-9.1%) | 8.0% (7.3-8.6%) | 9.2% (7.6-10.8%) |
| Infection prevalence of gonorrhoea at penis (%) | 0.20% (0.04-0.35%) | 0.21% (0.07-0.35%). | 0.25% (0.06-0.45%) | Symptomatic urethral positivity was found to be between 2.30% (2.02-2.58%) among MSM who attend Melbourne Sexual Health Centre in 2015 [37]. That is, out of 100 MSHC MSM attendees, 2.3 persons have symptomatic urethral infection. If this accounts for 80% of the urethral infected cases in the community, then the remaining 20% asymptomatic infections accounts for another 0.58 persons in the community. The symptomatic infection has a short infection period (present their clinical symptoms and receive treatment with a week) of about one week, whereas asymptomatic infection remains infected for 3 months before natural clearance. So, in a 12-month period, out of 100 community MSM, the total duration of infection is 2.3\*1/52 + 0.58\*1/4 = 0.2 years. This hence means, the urethral prevalence among community MSM is approximately 0.2% at any given time. We calculated the confidence intervals of this prevalence accordingly.  |
|  |  |  |  |  |
| Consistent condom usage in anal sex in past 12 months (%) | 46.9% (34.5-59.3%) | 60% (55-65%) | 40% (35-45%) | Condom use in all MSM is given in HIV Annual Surveillance Report  [35].We assumed condom use among ‘low-risk’ MSM is 60% (55-65%) in the model. Condom use among ‘high-risk’ MSM is calculated accordingly by weighting on the proportion of each risk groups, such that the overall condom use in MSM is identical to 46.9% [35]. |
| Frequency of kissing in the past 12 months  | 58 (0-183) | 41 (0-128) | 104 (0-328) | Clinical data based on 15,365 MSM individuals who attend Melbourne Health Sexual Centre in 2015 in indicates that the total number of sexual partners of these attendees was 11.8±24.6 in the past 12 months. Rosenberg et.al. reported that 72.7%, 37.2% and 25.5% of MSM have oral, anal and rimming partners [38], leading to estimates of 8.6±17.9, 4.4±9.2 and 3.0±6.3 for number of these partnerships in the past 12 months, respectively. Kissing happened more frequently (~1.5 times, unpublished MSHC data) than other sex types, indicating 17.7±38.4 kissing partners in the past 12 months. We further found that 31% of all partnerships were regular and each has approximately 8 partners a year on average, whereas casual partner only has one sexual act [39]. We hence estimated the frequency of sexual acts based on the number of partners and the number of sexual acts per partner. |
| Frequency of oral sex in the past 12 months | 27 (0-85) | 19 (0-60) | 49 (0 -153) |
| Frequency of rimming in the past 12 months  | 10 (0-30) | 7 (0-21) | 17 (0-54) |
| Frequency of anal sex in the past 12 months | 14 (0-44) | 10 (0-31) | 25 (0-78) |

*Site-specific model for gonorrhoea transmission among MSM*

We constructed a mathematical model to simulate the transmission of gonorrhoea across various anatomical sites among MSM (Figure 1). The model employed a simple susceptible-infected- susceptible (SIS) compartmental structure. The model thus has only two states, susceptible (S) and infected (I). At each anatomical site, susceptible individuals become infected through a ‘force of infection’ $Λ$ and clear infection at a rate γ. The force of infection is a function of infectivity of the bacteria, current infection status at transmitting and acquiring sites, the pattern of risk sexual practices of the modelled risk population (low-risk and high-risk) and the prevalence of gonorrhoea infection from the infected anatomical site in the risk population [40, 41]. To account for the different type of sexual practices among MSM, the overall transmission of gonorrhoea is calculated as the sum of ‘force of infection’ for each individual type of sexual practice. The clearance rate is inversely related to the duration of infection (Table S1). The clearance rate is inversely related to the anatomical site-specific duration of infection.

S

I

$Λ$·S

γ·I

At each site:

where $Λ$ is force of infection and γ is the rate of infection clearance.

*Sexual Mixing Matrix*

As gonorrhoea is transmitted across risk populations, it is important to include sexual mixing as a part of the force of infection in the model. Based on the STIGMA guidelines, we defined ‘high-risk’ MSM as those having more than 10 partners in the past 6 months, and the low-risk group as those who do not [1]. A sexual mixing matrix represents the pattern of sexual ‘assortativity’ and interaction between risk subgroups. In our case, given there are only two risk populations, it is a 2x2 matrix denoted by *a, b, c, d*, which represent the percentage of sexual partnerships within or across risk populations (*a=*percentage of sexual partners of high-risk MSM that is high-risk; *b=*percentage of sexual partners of high-risk MSM that is low-risk; *c=*percentage of sexual partners of low-risk MSM that is high-risk; *d=* percentage of sexual partners of low-risk MSM that is low-risk). A ‘mixing index’ (α) denotes the level of mixing and is often represented as the ratio of the sum of the off-diagonal entries in the mixing matrix and the sum of diagonal entries ((b+c)/(a+d), [42]). The mixing index approach to zero when there is no sexual mixing between the subgroups and increases to an asymptotic value when the subgroups are ‘well-mixed’. In our model, the sexual mixing matrix satisfies three constraints:

* the overall percentage of partnerships in the high-risk and low-risk populations adds up to 100%, respectively;
* the sexual mixing index is 0.5. Notably, the choice of α relies on empirical data that informs the mixing of sexual partnerships in and between risk groups. This data is not available to us and we assume α = 0.5 [42].
* the number of partnerships with low-risk partners in high-risk MSM is identical to the number of partnerships with high-risk partners in low-risk MSM.

We estimate the sexual mixing matrix for partnerships among Australian MSM as follows.

|  |  |  |
| --- | --- | --- |
|  | High-risk MSM | Low-risk MSM |
| High-risk MSM | a=78.6% | b=21.4% |
| Low-risk MSM | c=45.2% | d=54.8% |

. This matrix has been integrated in the model to calculate the number of partnerships and frequency of sexual acts within and between risk groups, which inform the force of infection.

*Force of infection*

Taking into consideration the sexual mixing matrix, the force of infection $Λ$ takes the following explicit form:

$$Λ\_{ij}^{m}=\sum\_{i,j=o,r,u}^{m,n=h,l}λ\_{ij}^{mn}∙P\_{i}^{m}$$

$λ\_{ij}^{mn}=(1-\left(1-β\_{ij}∙(1-ε\_{c}∙C\_{mn})\right)^{\frac{f\_{ij}^{mn}}{2}})$,

where $P\_{i}$ represents the prevalence of gonorrhoea at the anatomical sites where gonorrhoea is transmitted from; $β\_{ij}$ represents the per-act transmission of gonorrhoea from site *i* to *j*; $C\_{mn}$is the percentage of condom use in anal intercourse among between risk populations in MSM (*m* is the risk group the infection is transmitted from and *n* is the risk group being infected); $ε\_{c}$ is the efficacy of condom in preventing transmission of sexually transmitted infections and $f\_{ij}^{mn}$ is the frequency of sexual acts in the past 12 months (including kissing) that may facilitate gonorrhoea transmission from site *i* in risk population *m* to *j* in risk population *n* (Table S1). $f\_{ij}^{mn}$ is calculated based on frequency of sexual acts data (Table S1) and the estimated sexual mixing matrix. In general, the anatomical sites (*i* and *j*) can be any of oropharynx (*o*), urethra (*u*) and rectum (*r*), and the risk groups (*m* and *n*) can be high-risk (*h*) and low-risk (*l*).

*The governing system of differential equations*

Transmission of N. Gonorrhoea in both high-risk and low-risk MSM was governed by the following system of ordinary differential equations.

$$\frac{dS\_{o}}{dt}=-\left(λ\_{oo}P\_{o}+λ\_{ro}P\_{r}+λ\_{uo}P\_{u}\right)∙\left(1-P\_{o}\right)∙N\_{o}+γ\_{o}∙I\_{o}$$

$$\frac{dI\_{o}}{dt}=\left(λ\_{oo}P\_{o}+λ\_{ro}P\_{r}+λ\_{uo}P\_{u}\right)∙\left(1-P\_{o}\right)∙N\_{o}-γ\_{o}∙I\_{o}$$

$$\frac{dS\_{r}}{dt}=-\left(λ\_{or}P\_{o}+λ\_{ur}P\_{u}\right)∙\left(1-P\_{r}\right)∙N\_{r}+γ\_{r}∙I\_{r}$$

$$\frac{dI\_{r}}{dt}=\left(λ\_{or}P\_{o}+λ\_{ur}P\_{u}\right)∙\left(1-P\_{r}\right)∙N\_{r}-γ\_{r}∙I\_{r}$$

$$\frac{dS\_{u}}{dt}=-\left(λ\_{ou}P\_{o}+λ\_{ru}P\_{r}\right)∙\left(1-P\_{u}\right)∙N\_{u}+γ\_{u}∙I\_{u}$$

$$\frac{dI\_{u}}{dt}=\left(λ\_{ou}P\_{o}+λ\_{ru}P\_{r}\right)∙\left(1-P\_{u}\right)∙N\_{u}-γ\_{u}∙I\_{u}$$

Where the *Si* and *Ii* represent the number of susceptible and infected individual respectively at each anatomical site. *Ni* is the number of individuals and sum of *Si* and *Ii*. Based on this system of equation, the prevalence levels of gonorrhoea at pharynx, urethra and rectum, $P\_{o}=I\_{o}/(S\_{o}+I\_{o})$, $P\_{u}=I\_{u}/(S\_{u}+I\_{u})$ and $P\_{r}=I\_{r}/(S\_{r}+I\_{r})$, were obtained in the following form,

$$\frac{dP\_{o}}{dt}=\left(λ\_{oo}P\_{o}+λ\_{ro}P\_{r}+λ\_{uo}P\_{u}\right)∙\left(1-P\_{o}\right)-γ\_{o}∙P\_{o}$$

$$\frac{dP\_{r}}{dt}=\left(λ\_{or}P\_{o}+λ\_{ur}P\_{u}\right)∙\left(1-P\_{r}\right)-γ\_{r}∙P\_{r}$$

$$\frac{dP\_{u}}{dt}=\left(λ\_{ou}P\_{o}+λ\_{ru}P\_{r}\right)∙\left(1-P\_{u}\right)-γ\_{u}∙P\_{u}$$

With this set of equations, we allowed the system to reach equilibrium, whereby $dP\_{o}/dt$, $dP\_{r}/dt$ and $dP\_{u}/dt $are equal to zero. The model was calibrated by adjusting transmission probability $λ\_{ij}$ in each type of sex acts such that prevalence at equilibrium matched empirical findings. However, the calibration was conducted on gonorrhoea prevalence at each independent anatomical sites. We assumed that the sites are independent and were not connected to specific individuals. Therefore, we did not include co-infection of gonorrhoea at multiple sites in our model. Notably, condom use for oral sex is very low and assumed to be zero in our model. The general form of the system of differential equations in both risk groups were hence presented as follows,

$$\frac{dP\_{j}^{k}}{dt}=\left(\sum\_{i,j=o,u,r}^{k=h,l}λ\_{ij}^{k}∙P\_{i}^{k}\right)∙\left(1-P\_{j}^{k}\right)-γ\_{j}∙P\_{j}^{k}$$

The prevalence *P*, clearance rate *γ* are defined in the same way previously. The subscript *i* and *j* denotes the anatomical sites that gonorrhoea transfer from and to, respectively, whereas *k* can be *h* and *l* that denote high- and low-risk, respectively.

*Model Calibration*

For each simulation, the rates of transmission were randomly sampled from the interval [0 1] using Latin hypercube sampling, and all biological, epidemiological and behavioural parameters were also sampled with the same approach from their corresponding confidence intervals (Table S1). The set of sampled indicators were input to the system of differential equations to generate a theoretical equilibrium prevalence, which was then calibrated to the corresponding empirical prevalence at each anatomical site in both risk subgroups and also the prevalence in the overall population. The difference between the theoretical and empirical data was measured by the sum of the least-squares. This process was repeated for 10,000 times, and the top 1% best-fit simulations were used to obtain the best estimate and confidence intervals of the transmission probabilities.

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