Supplemental materials for Spicknall *et al.*: "Assessing uncertainty in an anatomical site-specific gonorrhea infection transmission model of men who have sex with men"

1 Model equations

We explicitly show equations for each modeled compartment below where compartments are defined by infection status at each site, where the first, second, and third letters refer to the infection status at the oropharynx, urethra, and rectum respectively. So, the ISI compartment is for people who have infection at the oropharynx, no infection at the urethra, and infection at the rectum. Because we modeled symptomatic and asymptomatic urethral infection, these compartments are further subdivided by the letters a and b for symptomatic and asymptomatic urethral infection(e.g., SISa and SISb are for people who only have infection at the urethra who are symptomatic and asymptomatic respectively). Supplemental Table 1 describes parameters and symbols used in model equations.

$$\begin{aligned}
 \dot{SSS} &= \gamma_0(SSI + ISS + ISI + SISa + SIIa + IISa + IIIa + SISb + SIIb + IISb + IIIb) + \\
 &\quad \gamma_1 ISS + \gamma_{2a}(SISa + SIIa + IISa + IIIa) + \gamma_{2b}SISb + \gamma_3 SSI - (\lambda_1 + \lambda_2 + \lambda_3)SSS \\
 \dot{SSI} &= \gamma_1 ISI - (\gamma_0 + \gamma_3)SSI + \gamma_{2b}SIIb - (\lambda_1 + \lambda_2)SSI + \lambda_3 SSS \\
 \dot{SISa} &= \gamma_1 IISa - (\gamma_0 + \gamma_{2a})SISa + \gamma_3 SIIa - (\lambda_1 + \lambda_3)SISa + \lambda_2 \sigma SSI \\
 \dot{SIIa} &= \gamma_1 IIIa - (\gamma_0 + \gamma_{2a} + \gamma_3)SIIa - \lambda_1 SIIa + \lambda_3 SISa + \lambda_2 \sigma SSI \\
 \dot{SISb} &= \gamma_1 IISb - (\gamma_0 + \gamma_{2b})SISb + \gamma_3 SIIb - (\lambda_1 + \lambda_3)SISb + \lambda_2(1 - \sigma)SSS \\
 \dot{SIIb} &= \gamma_1 IIIb - (\gamma_0 + \gamma_{2b} + \gamma_3)SIIb - \lambda_1 SIIb + \lambda_3 SISb + \lambda_2(1 - \sigma)SSI \\
 \dot{ISS} &= -(\gamma_0 + \gamma_1)ISS + \gamma_{2b}IISb + \gamma_3 ISI + \lambda_1 SSS - (\lambda_2 + \lambda_3)ISS \\
 \dot{ISI} &= -(\gamma_0 + \gamma_1 + \gamma_3)ISI + \gamma_{2b}IIIb + \lambda_1 SSI + \lambda_3 ISS - \lambda_2 ISI \\
 \dot{IISa} &= -(\gamma_0 + \gamma_1 + \gamma_{2a})IISa + \gamma_3 IIIa + \lambda_1 SISa - \lambda_3 IISa + \lambda_2 \sigma ISS \\
 \dot{IIIa} &= -(\gamma_0 + \gamma_1 + \gamma_{2a} + \gamma_3)IIIa + \lambda_1 SIIa + \lambda_3 IISa + \lambda_2 \sigma ISI \\
 \dot{IISb} &= -(\gamma_0 + \gamma_1 + \gamma_{2b})IISb + \gamma_3 IIIb + \lambda_1 SISb - \lambda_3 IISb + \lambda_2(1 - \sigma)ISS \\
 \dot{IIIb} &= -(\gamma_0 + \gamma_1 + \gamma_{2b} + \gamma_3)IIIb + \lambda_1 SIIb + \lambda_3 IISb + \lambda_2(1 - \sigma)ISI
 \end{aligned} \tag{1}$$

where forces of infection to each site (λ_1 , λ_2 , and λ_3) are given by:

$$\begin{aligned}
\lambda_1 &= \lambda_{toOfromO} + \lambda_{toOfromU} + \lambda_{toOfromR} \\
\lambda_2 &= \lambda_{toUfromO} + \lambda_{toUfromR} \\
\lambda_3 &= \lambda_{toRfromO} + \lambda_{toRfromU}
\end{aligned} \tag{2}$$

Forces of infection can be further decomposed as:

$$\begin{aligned}
\lambda_{toOfromO} &= \lambda \rho_{kiss} \pi_{o2o} I_o \\
\lambda_{toOfromU} &= \lambda \rho_{oralSex} \pi_{o2u} I_u \\
\lambda_{toOfromR} &= \lambda \rho_{rimming} \pi_{o2r} I_r \\
\lambda_{toUfromO} &= \lambda \rho_{oralSex} \pi_{u2o} I_o \\
\lambda_{toUfromR} &= \lambda \rho_{analSex} \pi_{u2r} I_r \\
\lambda_{toRfromO} &= \lambda \rho_{rimming} \pi_{r2o} I_o \\
\lambda_{toRfromU} &= \lambda \rho_{analSex} \pi_{r2u} I_u
\end{aligned} \tag{3}$$

where the proportion of infection at each anatomical site (i.e., I_o , I_u , and I_r) are given by:

$$\begin{aligned}
I_o &= IIIa + IIIb + IISa + IISb + ISI + ISS \\
I_u &= IIIa + IIIb + SIIa + SIIb + IISa + IISb + SISa + SISb \\
I_r &= IIIa + IIIb + SIIa + SIIb + ISI + SSI
\end{aligned} \tag{4}$$

Force of infection to each site is a function of the overall sexual activity rate (λ), proportion of each type of activity (parameterized from behavioral data) (ρ parameters for kissing, oral sex, anal sex, and rimming), and per act transmission probability for each act for each infection direction (the seven π parameters). Incidence is a function of each force of infection and the probability of infection discordant contact for each type of sex.

2 Relative weights of sexual activity

Using behavioral data from Zhang et al., we estimate 4 values of ρ in Supplemental Table 1, as the proportion of all activity represented by each activity type. Thus, these values of ρ sum to 1. This allows us to vary the overall rate of sexual activity, while holding constant the relative weights of each type of activity.

Symbol	Description	Notes
γ_0	Screening rate	static
γ_1	Innate recovery rate (oropharynx)	static
γ_{2a}	Treatment induced recovery rate (symptomatic urethra)	static
γ_{2b}	Innate recovery rate (asymptomatic urethra)	static
γ_3	Innate recovery rate (rectum)	static
λ_1	Force of infection to the oropharynx	composite
λ_2	Force of infection to the urethra	composite
λ_3	Force of infection to the rectum	composite
σ	Proportion of urethral infections that are symptomatic	static
λ	Overall sexual activity rate	static
$\rho_{kissing}$	Proportion of sexual activity that is kissing	static
$\rho_{oralSex}$	Proportion of sexual activity that is oral sex	static
$\rho_{rimming}$	Proportion of sexual activity that is rimming	static
$\rho_{analSex}$	Proportion of sexual activity that is anal sex	static
π_{o2o}	Per act transmission probability–kissing (oropharynx to oropharynx)	Fit
π_{o2u}	Per act transmission probability–oral sex (oropharynx to urethra)	Fit
π_{u2o}	Per act transmission probability–oral sex (urethra to oropharynx)	Fit
π_{o2r}	Per act transmission probability–rimming (oropharynx to rectum)	Fit
π_{r2o}	Per act transmission probability–rimming (rectum to oropharynx)	Fit
π_{u2r}	Per act transmission probability–anal sex (urethra to rectum)	Fit
π_{r2u}	Per act transmission probability–anal sex (rectum to urethra)	Fit

Table 1: Parameter symbols and descriptions. Refer to Table 1 in main text for associated values

3 Intervention supplemental information

We implement contagiousness interventions as a percent reduction in contagiousness from a given anatomical site. Thus, there is a separate intervention for each site.

3.1 Contagiousness intervention implementation

Model equations and implementation are unchanged except for the following. Contagiousness intervention for the urethral site affects the urethra-to-oropharynx and urethra-to-rectum transmission probabilities (π_{u2o} and π_{u2r} respectively) as:

$$\begin{aligned}\pi_{u2o}^* &= \pi_{u2o}(1 - \delta) \\ \pi_{u2r}^* &= \pi_{u2r}(1 - \delta)\end{aligned}\tag{5}$$

Contagiousness intervention for the rectal site affects the rectum-to-oropharynx and rectum-to-urethra transmission probabilities (π_{r2o} and π_{r2u} respectively) as:

$$\begin{aligned}\pi_{r2o}^* &= \pi_{r2o}(1 - \delta) \\ \pi_{r2u}^* &= \pi_{r2u}(1 - \delta)\end{aligned}\tag{6}$$

Contagiousness intervention for the oropharyngeal site affects the oropharynx-to-oropharynx, oropharynx-to-rectum, and oropharynx-to-urethra transmission probabilities (π_{o2o} , π_{o2r} , and π_{o2u} respectively) as:

$$\begin{aligned}\pi_{o2o}^* &= \pi_{o2o}(1 - \delta) \\ \pi_{o2r}^* &= \pi_{o2r}(1 - \delta) \\ \pi_{o2u}^* &= \pi_{o2u}(1 - \delta)\end{aligned}\tag{7}$$

For all analyses, we assume $\delta=20\%$. Thus, each transmission probability only has 80% of its original magnitude from the initial parameterization.

3.2 Intervention analysis

The same 10,000 parameterizations used in all earlier analyses are also used here. Each parameterization has an original prevalence value (i.e., without intervention). Here, prevalence of infection refers to having any of the three sites infected; a person infected at more than one site does not contribute more to prevalence than a person infected at only one site. For each parameterization, each of the three interventions is applied, yielding three intervention-prevalence values (i.e., one for each site-specific intervention). We calculate the effect of each intervention as the percent reduction in prevalence as:

$$\frac{Original - Intervention}{Original}\tag{8}$$

This allows us to describe the effect of each intervention at each parameterization. In other words, each one of the 10,000 parameterizations can be characterized by how strong each intervention would be against equilibrium prevalence. Then in Manuscript-Figure 5, these three effects are normalized, showing their effects relative to one another; this summarizes where intervention against one site would be heavily favored (i.e., if its effect is much greater than others), and where no specific intervention would be favored over another (i.e., when they all have similar effect strengths).

Figure 1: Trace of oropharynx-to-oropharynx transmission probability (y-axis) across 100,000 chains (x-axis). Green dots represent sub-sampled points used in our analysis (every 500th point).

4 Model fitting supplemental materials

To generate 10,000 parameterizations, we ran 100 separate seeds on separate clusters. Each seed used a random starting point. Each seed was ran to find 50,000 chains. In total, this leads to 5 million chains. We sub-sampled every 500th chain from the 5 million to achieve 10,000 for all our subsequent analysis. A trace of this sub-sampling is show in Supplemental Figure 1. This figure shows the parameter value for the oropharynx-to-oropharynx transmission probability when all routes may transmit; thus this is only one of the seven dimensions of parameter space being sampled. The figure shows the parameter value for 100,000 chains (2 consecutive seeds); thus, this only shows 2% of the trace for this one parameter. Green dots represent sampled points used in our subsequent analyses and red represent points that were adequate fits but not used, in order to avoid auto-correlation.