Dynamic sex roles among men who have sex with men and transmissions from primary HIV infection

Supplementary Material

eAppendix 1: Deterministic Compartmental Model for a MSM Population with Four Risk Categories

The deterministic compartmental model (DCM) is specified as a system of twelve differential equations for a MSM population, one for each compartment in the model. The compartments correspond to the four risk categories from Blower et al. [1995] and the stages of infection. The population is divided into four risk groups namely ‘dual-role’, ‘receptive-only’, ‘insertive-only’ and no-anal-sex or abstainers. Sexual acts in the model take place among the dual-role, receptive-only and insertive-only risk groups in the population. We assume instantaneous partnerships with one sex act for unidirectional and two sex acts for reciprocal partnerships. Other than in reciprocal partnerships, sex acts are assumed to be with independently encountered partners.

The sex act rates in the model correspond to the average number of sex acts per person per month. Our assumed values for the transmission probabilities for both receptive and insertive anal sex acts are similar to those reported by Varghese et al. [2002]. The analysis presented in eAppendix 2 explains the method used for distributing risk to the PHI and post-PHI stages of infection. Finally, the expected risk duration in the model, i.e. the average time spent by an individual making new sexual partnerships, is 40 years. A time step in the model corresponds to one month activity.

In this section, we first present the twelve differential equations in the compartmental model for a MSM population. We then present a list of the model’s parameters and their standard values. We then explain the incidence and risk groups’ transition flows in the model. Notice that we first present equations with general flows that will be specified differently for different model configurations.

The four risk groups, i.e. no-anal-sex, insertive-only, receptive-only and dual-role are denoted in the differential equations as $N$, $I$, $R$ and $D$. Subscripts $s$, $p$ and $c$ correspond to susceptible, primary HIV infection (PHI) and chronic (post-PHI) stages of infection. For example, the state variable $N_s$ denotes the no-anal-sex population that is susceptible. eTable 1 gives the list of all twelve state variables.
Table 1: State variables in the deterministic compartment model for the MSM case.

<table>
<thead>
<tr>
<th>State variable</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>$N_s$</td>
<td>Population in the no-anal-sex group that is susceptible</td>
</tr>
<tr>
<td>$N_p$</td>
<td>Population in the no-anal-sex group that is in PHI stage of infection</td>
</tr>
<tr>
<td>$N_c$</td>
<td>Population in the no-anal-sex group that is in post-PHI stage of infection</td>
</tr>
<tr>
<td>$I_s$</td>
<td>Population in the insertive-only group that is susceptible</td>
</tr>
<tr>
<td>$I_p$</td>
<td>Population in the insertive-only group that is in PHI stage of infection</td>
</tr>
<tr>
<td>$I_c$</td>
<td>Population in the insertive-only group that is in post-PHI stage of infection</td>
</tr>
<tr>
<td>$R_s$</td>
<td>Population in the receptive-only group that is susceptible</td>
</tr>
<tr>
<td>$R_p$</td>
<td>Population in the receptive-only group that is in PHI stage of infection</td>
</tr>
<tr>
<td>$R_c$</td>
<td>Population in the receptive-only group that is in post-PHI stage of infection</td>
</tr>
<tr>
<td>$D_s$</td>
<td>Population in the dual-role group that is susceptible</td>
</tr>
<tr>
<td>$D_p$</td>
<td>Population in the dual-role group that is in PHI stage of infection</td>
</tr>
<tr>
<td>$D_c$</td>
<td>Population in the dual-role group that is in post-PHI stage of infection</td>
</tr>
</tbody>
</table>

Let,

$I_{Total}$: Size of the insertive-only group in the population  
$R_{Total}$: Size of the receptive-only group in the population  
$D_{Total}$: Size of the dual-role group in the population  
$N_{Total}$: Size of the no-anal-sex (abstainers) group in the population

The differential equations for the DCM are given in the Equation Set 1 below.

**Equation Set 1. Risk Group Transition equations for the MSM Population Model**

For the no-anal-sex group ($N$), the corresponding equations are,

\[
\frac{dN_s}{dt} = \text{riskGroupTransition}_{N_s} + \mu e_N - \mu N_s
\]

\[
\frac{dN_p}{dt} = \text{riskGroupTransition}_{N_p} - \gamma_p N_p - \mu N_p
\]

\[
\frac{dN_c}{dt} = \text{riskGroupTransition}_{N_c} + \gamma_p N_p - \gamma_c N_c - \mu N_c
\]

where,

$\mu$ is the average risk duration  
$\gamma_p$ is the rate per month of advancing out of PHI to post-PHI  
$\gamma_c$ is the rate per month of advancing out of post-PHI to dying of AIDS  
$e_N$ is the equilibrium frequency of the no-anal-sex population in the absence of HIV  
$\text{riskGroupTransition}_{N_s}$ is the transition flow of the susceptible population in and out of the no-anal-sex group  
$\text{riskGroupTransition}_{N_p}$ is the transition flow of in an out of the no-anal-sex group in primary HIV (PHI) stage  
$\text{riskGroupTransition}_{N_c}$ is the transition flow of in an out of the no-anal-sex group in chronic or post-PHI stage
Notice that there is no incidence term for the no-anal-sex group and the prevalence of infection in this group is due to the transitions between the risk groups only. In our future work, there will be a risk from oral sex in this group in the model. Later in this section, we present the formulation for the transition flows for the four risk groups. \( eN \) is adjusted to keep the relative size of the receptive-only individuals fixed. The values are obtained by solving the equations numerically.

The differential equations for the other three risk groups contain incidence flows in addition to the transition, entry and exit flows in the no-anal-sex group. The equations for the insertive-only group \((I)\) is given as follows:

\[
\frac{dl_s}{dt} = \text{riskGroupTransition}_{ls} - \lambda_l \frac{l_s}{l_{Total}} + \mu e_I - \mu l_s
\]

\[
\frac{dl_p}{dt} = \text{riskGroupTransition}_{lp} + \lambda_l \frac{l_s}{l_{Total}} - \gamma_p l_p - \mu l_p
\]

\[
\frac{dl_c}{dt} = \text{riskGroupTransition}_{lc} + \gamma_p l_p - \gamma_c l_c - \mu l_c
\]

where,

\( e_I \) is the equilibrium frequency of the insertive-only population in the absence of HIV

\( \lambda_I \) is the force of infection for the insertive-only risk group

\( \text{riskGroupTransition}_{ls} \) is the transition flow of the susceptible population in and out of the insertive-only group

\( \text{riskGroupTransition}_{lp} \) is the transition flow of in and out of the insertive-only group in primary HIV (PHI) stage

\( \text{riskGroupTransition}_{lc} \) is the transition flow of in and out of the insertive-only group in chronic or post-PHI stage

Likewise, the equations for the other two groups, i.e. receptive only \((R)\) and dual-role \((D)\) are given as:

\[
\frac{dR_s}{dt} = \text{riskGroupTransition}_{Rs} - \lambda_R \frac{R_s}{R_{Total}} + \mu e_R - \mu R_s
\]

\[
\frac{dR_p}{dt} = \text{riskGroupTransition}_{Rp} + \lambda_R \frac{R_s}{R_{Total}} - \gamma_p R_p - \mu R_p
\]

\[
\frac{dR_c}{dt} = \text{riskGroupTransition}_{Rc} + \gamma_p R_p - \gamma_c R_c - \mu R_c
\]

where,

\( e_R \) is the equilibrium frequency of the receptive-only population in the absence of HIV

\( \lambda_R \) is the force of infection for the receptive-only risk group
$riskGroupTransition_{Rs}$ is the transition flow of the susceptible population in and out of the receptive-only group
d
$riskGroupTransition_{Rp}$ is the transition flow of in and out of the receptive-only group in primary HIV (PHI) stage
d
$riskGroupTransition_{Re}$ is the transition flow of in and out of the receptive-only group in chronic or post-PHI stage
d
\[
\frac{dD_s}{dt} = riskGroupTransition_{Ds} - \lambda_{D,U} \frac{D_s}{D_{Total}} + \lambda_{D,H} D_{Total} + \mu e_D - \mu D_s
\]

\[
\frac{dD_p}{dt} = riskGroupTransition_{Dp} + \lambda_{D,U} \frac{D_s}{D_{Total}} + \lambda_{D,H} D_{Total} - \gamma_p D_p - \mu D_p
\]

\[
\frac{dD_c}{dt} = riskGroupTransition_{Dc} + \gamma_p D_p - \gamma_c I_c - \mu D_c
\]

where,
e_D is the equilibrium frequency of the dual-role population in the absence of HIV
\[
\lambda_{D,U} \text{ is the force of infection for the unidirectional sex acts in the dual-role risk group}
\]
\[
\lambda_{D,H} \text{ is the force of infection for the reciprocal sex acts in the dual-role risk group}
\]
$riskGroupTransition_{Ds}$ is the transition flow of the susceptible population in and out of the dual-role group
$riskGroupTransition_{Dp}$ is the transition flow of in and out of the dual-role group in the primary HIV (PHI) stage
$riskGroupTransition_{Dc}$ is the transition flow of in and out of the dual-role group in chronic or post-PHI stage

The equilibrium frequencies for the four risk groups in the above differential equations match the observed proportions from the Blower et al. [1995] at equilibrium. These proportions are produced based on the transition rates, which are described in the subsequent section. In our model, we assume that the dynamics of switching sex roles (including abstinence) does not depend upon the prevalence of infection in the population.

Before describing the setup for the initial conditions, risk group transitions and incidence flows for the model compartments, we first introduce the model parameters and their standard values in eTable 2 below.
Table 2: Model parameters for deterministic compartmental model of MSM population

<table>
<thead>
<tr>
<th>Symbol</th>
<th>Description</th>
<th>Std value</th>
</tr>
</thead>
<tbody>
<tr>
<td>$\gamma_p$</td>
<td>The rate per month of advancing out of PHI to post-PHI stage</td>
<td>0.85</td>
</tr>
<tr>
<td>$\gamma_c$</td>
<td>The rate per month of dying from AIDS for the population in the post-PHI stage</td>
<td>0.00694444</td>
</tr>
<tr>
<td>$\mu$</td>
<td>The average time spent in the sexually active MSM population in months</td>
<td>$1/(40*12)$</td>
</tr>
<tr>
<td>$t$</td>
<td>Initial infection levels at time zero</td>
<td>0.01</td>
</tr>
<tr>
<td>$\beta$</td>
<td>Average transmission probability across all stages of infection during an insertive and receptive symmetric encounter</td>
<td>0.01</td>
</tr>
<tr>
<td>$\xi$</td>
<td>The ratio of transmissibility during PHI compared to post-PHI</td>
<td>60</td>
</tr>
<tr>
<td>$\tau$</td>
<td>Transmission fraction of insertive sex acts over the total of insertive and receptive sex acts.</td>
<td>0.07</td>
</tr>
<tr>
<td>$\chi$</td>
<td>The baseline average unidirectional (receptive) sex act rate per month in the segment of the population having receptive sex</td>
<td>4</td>
</tr>
<tr>
<td>$SCP$</td>
<td>Symmetric Contact Proportion: The fraction of receptive sex acts in dual-role group that are symmetric (i.e., both insertive and receptive)</td>
<td>1</td>
</tr>
<tr>
<td>$\chi_{ID}$</td>
<td>The sex act rate ratio for sex acts of insertive only (I) individuals compared to dual-role (D) individuals</td>
<td>1</td>
</tr>
<tr>
<td>$IRSwitch$</td>
<td>Directly related to flows between insertive-only and receptive-only individuals</td>
<td>1</td>
</tr>
</tbody>
</table>

Transitions between the Four Risk Groups

In this section, we present the transition rates responsible for the flows between the model compartments. eTable 3 presents the default rates of transition per month from a risk group to another is adapted from Blower et al. [1995].

eTable 3: Default rates per month of transition for the flows into or out of each compartment based on Blower et al. [1995] for the four risk behavior groups.

<table>
<thead>
<tr>
<th>Symbol</th>
<th>Description</th>
<th>Std value</th>
</tr>
</thead>
<tbody>
<tr>
<td>$\phi_{ND}$</td>
<td>The rate per month of transition from no-anal-sex to dual role.</td>
<td>0.0138</td>
</tr>
<tr>
<td>$\phi_{DN}$</td>
<td>The rate per month of transition from dual role to no-anal-sex</td>
<td>0.03106</td>
</tr>
<tr>
<td>$\phi_{NI}$</td>
<td>The rate per month of transition from no-anal-sex to insertive role</td>
<td>0.0213</td>
</tr>
<tr>
<td>$\phi_{IN}$</td>
<td>The rate per month of transition from insertive role to no-anal-sex</td>
<td>0.0594</td>
</tr>
<tr>
<td>$\phi_{NR}$</td>
<td>The rate per month of transition from no-anal-sex to receptive role</td>
<td>0.0121</td>
</tr>
<tr>
<td>$\phi_{RN}$</td>
<td>The rate per month of transition from receptive role to no-anal-sex</td>
<td>0.0643</td>
</tr>
<tr>
<td>$\phi_{DI}$</td>
<td>The rate per month of transition from dual role to no insertive role</td>
<td>0.0291</td>
</tr>
<tr>
<td>$\phi_{ID}$</td>
<td>The rate per month of transition from insertive role to dual role</td>
<td>0.0311</td>
</tr>
<tr>
<td>$\phi_{DR}$</td>
<td>The rate per month of transition from dual role to receptive role</td>
<td>0.0176</td>
</tr>
<tr>
<td>$\phi_{RD}$</td>
<td>The rate per month of transition from receptive role to dual role</td>
<td>0.0331</td>
</tr>
<tr>
<td>$\phi_{IR}$</td>
<td>The rate per month of transition from insertive role to receptive role</td>
<td>0.0068</td>
</tr>
<tr>
<td>$\phi_{RI}$</td>
<td>The rate per month of transition from receptive role to insertive role</td>
<td>0.00855</td>
</tr>
</tbody>
</table>

From the above rates of transition, we can derive the transformations (see Equation Set 1) for the twelve compartments in our model in the Equation Set 2. The first subscript denotes the risk groups, i.e. no-anal-sex (N), insertive-only (I), receptive-only (R) and dual-role (D). The second subscript corresponds to the infection status, i.e. susceptible (s), primary HIV infection stage or PHI (p) and finally, chronic infection stage or post-PHI (c).
\[ \text{riskGroupTransition}_{Ns} = -N_s (\varphi_{NI} + \varphi_{ND} + \varphi_{NR}) + I_s \varphi_{IN} + R_s \varphi_{RN} + D_s \varphi_{DN} \]

Likewise, the remaining transitions for other compartments are given as follows:

\[ \text{riskGroupTransition}_{Np} = -N_p (\varphi_{NI} + \varphi_{ND} + \varphi_{NR}) + I_p \varphi_{IN} + R_p \varphi_{RN} + D_p \varphi_{DN} \]

\[ \text{riskGroupTransition}_{Nc} = -N_c (\varphi_{NI} + \varphi_{ND} + \varphi_{NR}) + I_c \varphi_{IN} + R_c \varphi_{RN} + D_c \varphi_{DN} \]

\[ \text{riskGroupTransition}_{Is} = -I_s (\varphi_{IN} + \varphi_{ID} + \varphi_{IR}) + N_s \varphi_{NI} + R_s \varphi_{RI} + D_s \varphi_{DI} \]

\[ \text{riskGroupTransition}_{Ip} = -I_p (\varphi_{IN} + \varphi_{ID} + \varphi_{IR}) + N_p \varphi_{NI} + R_p \varphi_{RI} + D_p \varphi_{DI} \]

\[ \text{riskGroupTransition}_{Ic} = -I_c (\varphi_{IN} + \varphi_{ID} + \varphi_{IR}) + N_c \varphi_{NI} + R_c \varphi_{RI} + D_c \varphi_{DI} \]

\[ \text{riskGroupTransition}_{Rs} = -R_s (\varphi_{RN} + \varphi_{RD} + \varphi_{RI}) + I_s \varphi_{IR} + N_s \varphi_{NR} + D_s \varphi_{DR} \]

\[ \text{riskGroupTransition}_{Rp} = -R_p (\varphi_{RN} + \varphi_{RD} + \varphi_{RI}) + I_p \varphi_{IR} + N_p \varphi_{NR} + D_p \varphi_{DR} \]

\[ \text{riskGroupTransition}_{Rs} = -R_s (\varphi_{RN} + \varphi_{RD} + \varphi_{RI}) + I_s \varphi_{IR} + N_s \varphi_{NR} + D_s \varphi_{DR} \]

\[ \text{riskGroupTransition}_{Ds} = -D_s (\varphi_{DN} + \varphi_{DR} + \varphi_{DI}) + I_s \varphi_{ID} + N_s \varphi_{ND} + R_s \varphi_{RD} \]

\[ \text{riskGroupTransition}_{Ds} = -D_p (\varphi_{DN} + \varphi_{DR} + \varphi_{DI}) + I_p \varphi_{ID} + N_p \varphi_{ND} + R_p \varphi_{RD} \]

\[ \text{riskGroupTransition}_{Ds} = -D_s (\varphi_{DN} + \varphi_{DR} + \varphi_{DI}) + I_c \varphi_{ID} + N_c \varphi_{ND} + R_c \varphi_{RD} \]

**Incidence Flows in the Model**

In this section, we first present the formulation of the unidirectional and reciprocal sex acts between the risk groups in the model. We then present the incidence flows for the differential equations given in Equation Set 1. Finally, we describe the formulation for the transmission rates of infection.

The sex act rates in the model are formulated so as to allow us to keep certain totals constant while varying their distributions across the population. For example, our formulation keeps the total average transmission probability across both stages of infection constant as we changed the relative transmission probability of PHI as compared to the post-PHI period. Likewise, we keep the rate of receptive sex acts constant for an individual. We vary the distribution of these sex acts, first between the two risk groups who perform such acts and second between the complementary insertive partners. We first present the model equations without the formulations that allowed us to keep such constancy and then we present the formulations we used to maintain such constancy. The dual-role group is versatile in the sense that the sexual encounters can be exclusively receptive, exclusively insertive or both. That is, the dual-role population in the model is split into those participating in directional sex (exclusively with an insertive or receptive role) and those who take part in a symmetric sex act (both insertive and receptive roles). The proportion of the symmetric sex encounters is defined by the parameter \( SCP \) (see eTable 2) in the
model. Notice that we find that HIV transmission is not sustained for smaller values of the baseline sex act ratio \( \chi \) (eTable 2) such as 1 or 2. Notice that in reality, one may expect many more sex acts per partnerships, whereas in our case we are modeling instantaneous sex acts. The default value for the sex act ratio (i.e. 4) splits the difference between the true sex act rate and the new partnership formation rate.

**Table 4: Description of the derived parameters in the deterministic compartmental model**

<table>
<thead>
<tr>
<th>Symbol</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>( RRCR )</td>
<td>Receptive sex rate of the receptive-only individuals</td>
</tr>
<tr>
<td>( DRCR )</td>
<td>Unidirectional receptive sex rate of the dual-role individuals</td>
</tr>
<tr>
<td>( FC_{IR} )</td>
<td>Fraction of non-symmetric insertive sex acts in the population that are made by insertive-only individuals</td>
</tr>
<tr>
<td>( FC_{DR} )</td>
<td>Fraction of non-symmetric insertive sex acts in the population that are made by the dual-role individuals with receptive-only individuals</td>
</tr>
<tr>
<td>( FC_{DD} )</td>
<td>Fraction of non-symmetric sex acts that are made by dual-role individuals within their own risk group</td>
</tr>
<tr>
<td>( \beta_{p,i} )</td>
<td>Transmission probability from a partner in PHI stage to an insertive partner</td>
</tr>
<tr>
<td>( \beta_{c,i} )</td>
<td>Transmission probability from a partner in post-PHI (chronic) stage to an insertive partner</td>
</tr>
<tr>
<td>( \beta_{p,r} )</td>
<td>Transmission probability from a partner in PHI stage to a receptive partner</td>
</tr>
<tr>
<td>( \beta_{c,r} )</td>
<td>Transmission probability from a partner in post-PHI (chronic) stage to a receptive partner</td>
</tr>
</tbody>
</table>

From the parameters in eTable 2 and eTable 4, the force of infection for the insertive-only group is given as,

\[
\lambda_I = D_{Total} DRCR (1 - SCP) FC_{IR} \left( \frac{\beta_{p,i} D_p + \beta_{c,i} D_c}{D_{Total}} \right) + R_{Total} RRCR FC_{IR} \left( \frac{\beta_{p,i} R_p + \beta_{c,i} R_c}{R_{Total}} \right)
\]

Likewise, the force of infection for the receptive-only group is given as,

\[
\lambda_R = R_{Total} RRCR \left[ FC_{IR} \left( \frac{\beta_{p,r} I_p + \beta_{c,r} I_c}{I_{Total}} \right) + FC_{DR} \left( \frac{\beta_{p,r} D_p + \beta_{c,r} D_c}{R_{Total}} \right) \right]
\]

Finally, the force of infection for the unidirectional encounters of the dual-role group (\( D \)) is given as,

\[
\lambda_{D_{-U}} = D_{Total} DRCR (1 - SCP) FC_{DD} \left( \frac{D_p (\beta_{p,i} + \beta_{p,r}) + D_c (\beta_{c,r} + \beta_{c,x})}{D_{Total}} \right)
+ R_{Total} RRCR FC_{DR} \left( \frac{\beta_{p,i} R_p + \beta_{c,i} R_c}{R_{Total}} \right)
+ D_{Total} DRCR (1 - SCP) FC_{IR} \left( \frac{\beta_{p,c,i} I_p + \beta_{c,c,i} I_c}{I_{Total}} \right)
\]

and the force of infection for the reciprocal sex encounters of the dual-role group (\( D \)) is given as,
\[ \lambda_{D,B} = DRCR SCP \left( \frac{D_p(\beta_{p,I} + \beta_{p,R}) + D_c(\beta_{c,I} + \beta_{c,R})}{D_{Total}} \right) \]

For the receptive-only group, sexual encounters with insertive are split between the insertive-only and the dual-role groups. The receptive-only group’s preference for a sex act with an insertive role is defined by the sex act rate ratio of partnerships with insertive-only individuals over the dual-role individuals \( (\chi_{ID}) \); a model parameter.

The fraction of non-symmetric insertive sex acts in the population that are made by insertive-only individuals with receptive-only individuals \( (FC_{IR}) \) is given as,

\[ FC_{IR} = I_{Total} \left( \frac{\chi_{ID}}{I_{Total} \chi_{ID} + D_{Total} (1 - SCP)} \right) \]

where, the parameter \( \chi_{ID} \) determines the number of sex acts between the insertive-only and receptive-only groups.

Similarly, the fraction of non-symmetric insertive sex acts in the population that are made by the dual-role individuals with receptive-only individual \( (FC_{DR}) \) is given as,

\[ FC_{DR} = D_{Total} \left( \frac{\chi_{ID}}{I_{Total} \chi_{ID} + D_{Total} (1 - SCP)} \right) \]

Receptive individuals in the dual-group role have sex encounters with insertive partners from within their group. For a resulting sex act between two individuals, this type of sex act is non-symmetric like in the other cases mentioned above. The fraction of non-symmetric sex act that are made by dual-role individuals within their own risk group \( (FC_{DD}) \) is given as,

\[ FC_{DD} = \frac{D_{Total} (1 - SCP)}{I_{Total} \chi_{ID} + D_{Total} (1 - SCP)} \]

Notice that other approaches such as the one used by Goodreau and Golden [2007] exist in maintaining the balance between the insertive and receptive acts. We have adopted the above approach for simplicity and focused on the dynamics of switching sexual roles in the population.

**Transmission Probabilities for Unidirectional and Reciprocal Sex Acts**

We now present the derived parameters related to the transmission rates for the type of sex acts described earlier. We model two stages of infection: primary HIV infection (PHI) and the chronic stage (post-PHI). In the model, we assume a short period of high infectivity for the primary stage of infection; approximately 35 days. In case of the chronic or post-PHI infection stage, we assume that on average individuals spend 12 years before dying of AIDS. eTable 2 gives the rates of progression of the natural history of infection in the model for both the stages as \( \gamma_p \) and \( \gamma_c \) respectively.
Transmission probability per sex act from an infected partner depends upon the stage of infection of the infected partner and the role assumed by the susceptible partner in the sex act. For an insertive-only susceptible having a sex act with an individual in the post-PHI stage, the risk for getting infected is lowest. On the other hand, in our model, highest risk is associated with the reciprocal sex, which occurs within the dual-role population. As discussed before, duration of risk in the model is set as 40 years as the period of sexual activity of the individuals.

The expected lifetime in the PHI and post-PHI infection stage respectively is given as,

\[
E_p = \frac{1}{\gamma_p + 1/\mu} \quad (I)
\]

\[
E_c = \frac{\gamma_p}{(\gamma_p + 1/\mu)(\gamma_c + 1/\mu)} \quad (II)
\]

where,

- \(E_p\) is the expected lifetime in primary (PHI) infection stage in months
- \(E_c\) is the expected lifetime in chronic (post-PHI) infection stage in months
- \(\gamma_p\) is the rate per month of advancing out of PHI to post-PHI stage
- \(\gamma_c\) is the rate per month of dying from AIDS for the population in the post-PHI stage
- \(\mu\) is the average time spent in the sexually active MSM population (see eTable 2)

Given \(\beta\) as the average transmission probability across the two infection stages with a calculated value of 0.01 (see eTable 2). This is calculated from the method described in eAppendix 2.

Transmission probability in the post-PHI or chronic stage is given as:

\[
\beta_c = \frac{\beta (E_p + E_c)}{\xi E_p + E_c} \quad (III)
\]

where,

- \(\beta\) is the average transmission probability across the two infection stages
- \(\xi\) is the ratio of transmissibility during PHI compared to post-PHI

The numerator on the right hand side of the above equation is the total risk for an expected period of infection. We derive this by assuming that the average transmissibility across all the stages times the period of infectivity equals the sum of transmissibility times the duration of all stages. We obtain the \(\beta_p\) by dividing the total risk to the transmissibility that is split between PHI and post-PHI. In this paper, we have use the value for the ratio \(\xi\) as 60, which is derived from the method described in eAppendix 2. For \(\xi = 1\), the risk across the two infection stages is distributed evenly.

Based on the values for the parameters \(\beta\) and \(\xi\) and equations I, II and III, we can calculate the transmission probability for PHI (\(\beta_p = \beta\)) and post-PHI (\(\beta_c = \beta\)) to be 0.01 and 0.00617265 respectively.
For the transmission probabilities with respect to the infection stage and sex role of the susceptible partner in a sex act, we introduce the transmission fraction of insertive sex acts over the total of insertive and receptive sex acts ($\tau$; see eTable 2).

Transmission probability from a PHI stage receptive-only individual to an insertive-only individual ($\beta_{p,i}$) is given as,

$$\beta_{p,i} = \xi \beta_c \tau \quad (IV)$$

In equation IV, the product $\xi \beta_p$ gives the probability of transmission for the primary HIV infection stage (PHI). For a unidirectional or non-symmetric sex act, the transmission probability depends upon the transmission fraction ($\tau$), which is multiplied to get the probability of transmission for an individual in PHI to his insertive partner. For the case where a PHI individual encounters a receptive partner in a unidirectional sex act, ($\xi \beta_p$) is multiplied to the remainder of the fraction, i.e. $(1 - \tau)$ as shown in Equation (V) below.

Transmission probability from a PHI stage insertive-only individual to a receptive-only individual ($\beta_{p,r}$) is,

$$\beta_{p,r} = \xi \beta_c \frac{(1 - \tau)}{\tau + (1 - \tau)} = \xi \beta_c (1 - \tau) \quad (V)$$

Note that we have formulated the transmission fraction in a way so as the total equals to 1 as shown in Equations (IV) and (V).

Likewise, transmission probability from a post-PHI (chronic) stage receptive-only individual to an insertive-only individual ($\beta_{c,i}$) is given as,

$$\beta_{c,i} = \beta_c \tau \quad (VI)$$

and the transmission probability from a post-PHI (chronic) stage insertive-only individual to a receptive-only individual ($\beta_{c,r}$) is given as,

$$\beta_{c,r} = \beta_c (1 - \tau) \quad (VII)$$

From the above equations, the ratio of transmissibility between the insertive and receptive sex acts for the PHI stage is given as,

$$\omega = \frac{\tau}{(1 - \tau)} \quad (VIII)$$

Finally, in case of reciprocal sex, we assume that the transmission probabilities for the primary and chronic stages of infection are given as ($\beta_{p,i} + \beta_{p,r}$) and ($\beta_{c,i} + \beta_{c,r}$) respectively.
Table 5 gives the numerical values for the above four derived transmission probabilities used in the paper. As discussed before, the chance for transmission of infection is highest when an infected partner in a reciprocal sex act is in the primary (PHI) infection stage. On the other hand, minimum risk is associated in for an insertive-only individual in a unidirectional sex act.

**Table 5: Numerical values of the per act transmission probabilities per act calculated based on the standard values of the model parameters.**

<table>
<thead>
<tr>
<th>Transmission probability per act</th>
<th>Symbol</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Transmission probability from a partner in PHI stage to an insertive partner</td>
<td>$\beta_{p,i}$</td>
<td>0.0259252</td>
</tr>
<tr>
<td>Transmission probability from a partner in post-PHI (chronic) stage to an insertive partner</td>
<td>$\beta_{c,i}$</td>
<td>0.0004321</td>
</tr>
<tr>
<td>Transmission probability from a partner in PHI stage to a receptive partner</td>
<td>$\beta_{p,r}$</td>
<td>0.344434</td>
</tr>
<tr>
<td>Transmission probability from a partner in post-PHI (chronic) stage to a receptive partner</td>
<td>$\beta_{c,r}$</td>
<td>0.0057406</td>
</tr>
</tbody>
</table>

The transmission probabilities estimates used in this paper are derived from the study by Wawer et al. [2005], which focused on a heterosexual cohort in Rakai, Uganda. For a MSM population, on which, our model is based, Wawer et al. [2005] like studies are not available. Nevertheless the calculated transmission probabilities used in our analysis are not significantly different from previous estimates (c.f. Verhagese et al. [2001]; Vittinghoff et al. [1999]).

**Analyzing fluctuation between the ‘dual-role’ and the ‘no-anal-sex’ groups**

In further examining the effect of fluctuation between the risk groups (see panels A and B of Figure 4 in the main article), we consider case where everyone is either in the dual role or in no-anal-sex (no risk) risk group as shown in eFigure 1. We examine the endemic prevalence and the fraction of transmission from PHI, varied over the rate of fluctuation between these two risk groups. The average time spent in either the no-anal-sex or dual-role group varies from 2 months to 20 years. Here we see that the fraction of transmissions from PHI is always considerably above the baseline transmission potential and is at its highest when the time spent in the high risk is close to the duration of PHI. When this figure is carried out to its two extremes of infinitely fast switching such that the population essentially behaves as a homogeneous unit or absolutely no switching, the 42% value of the transmission potential from PHI is reached at both extremes.
Next, we look into the effect of fluctuation of insertive and receptive sex roles in the absence of the dual-role and no-anal-sex groups. With only the insertive-only and receptive-only risk groups, we explore the effect of varying the ratio of transmissibility between the insertive and receptive sex acts as shown in eFigure 2. For the risk group transitions based on Blower et al. [1995], the fraction of transmissions from PHI remained throughout considerably high. The standard value for the transmission of fractions for insertive and receptive sex acts is adapted from Vittinghoff et al. [1999]. In addition, the effect of directional sex ceases to exist with same transmissibility for the insertive and receptive sex acts.

With the theoretical setting for flows, we consider two cases in exploring the transmission fraction between the insertive and receptive sex versus the fluctuation rate between the insertive-only and receptive-only risk groups. eFigure 3 illustrates the case, where we have the flows in and out of all the four risk groups. In the presence of all the four risk groups, both the prevalence and the fraction of transmissions from PHI increase, although not significantly, as the transmission fraction between the insertive and receptive sex is increased. This is complemented by the increase in the fluctuation between the insertive and receptive sex, which we have explored previously in this section. We observe the effects of directional in terms of the transmission fraction as well as the switching of sex roles.

eFigure 4 refers to the case where we explore the effect of varying the ratio of transmissibility between the insertive and receptive sex acts. In this case, we consider the insertive-only and receptive-only risk groups only. With only two risk groups, i.e. the insertive-only and the receptive-only, we see considerable variation in the prevalence as the ratio of transmissibility is increased (eFigure 4; above). On the other hand, increasing fluctuation between the two risk groups also increases the prevalence even when the transmission fraction is low. The fraction of transmissions from PHI remains below 40% for the two parameters’ ranges (eFigure 4; below). We can see a similar effect in this case as the one for prevalence.
Figure 2: Prevalence and the fractions of transmission from PHI when the ratio of transmissibility is varied based on the transition rates from Blower et al. [1995].
eFigure 3: Prevalence (above) and fraction of transmission from PHI (below) when exploring the ratio of transmissibility between insertive and receptive sex acts against the fluctuation rate between insertive and receptive-only population in the presence of all four risk groups.
**Figure 4:** Exploration of transmission fraction between insertive and receptive sex acts versus the fluctuation rate between insertive and receptive-only population; in the presence of insertive-only and receptive-only risk groups only. Above: Prevalence. Below: Fraction of transmissions from PHI.
eAppendix 2: Estimating PHI to asymptomatic hazard ratios from data

To estimate the hazard ratio between primary and asymptomatic infection transmission from the Wawer et al. [2005] data, we use an approach similar to the one used by Hollingsworth et al. [2008]. One difference is that we just focus on estimating that one ratio while they estimate several parameters simultaneously. Another difference is that we assume an Erlang distribution for the distribution of times in primary infection whereas Hollingsworth et al. assume that everyone has exactly the same duration. We use only the data where there was no death due to AIDS.

Hollingsworth et al. correctly point out that Wawer et al. calculated an unrealistically large number of coital acts during the risk period for couples, where both partners converted during a 10 month period of observation. The reason is that transmission occurs relatively soon after the first partner becomes infected while Wawer et al. assumed it occurred in the midpoint of the period between when the first partner got infected and the next blood sample was drawn. By modeling transmission dynamics, ours and the Hollingsworth et al. method use a smaller and more accurate number.

We estimate a hazard ratio for use in a model with per partnership transmission probabilities and not a per act transmission probability. The dynamic process we model upon the Wawer et al. data, however, parameterizes instantaneous rate ratios which correspond to per act ratios. When transmission probabilities per act are very low, there is not much difference between per act and per partnership hazard ratios. However, as the product of the number of acts times the probabilities gets above the 0.1 range, the differences become meaningful. The per-act ratio thus overestimates the per-partnership ratio given long partnerships. With a baseline per act ratio of 0.0007 as seen in the Wawer et al. data, a per-act ratio of 90 would generate a per partnership ratio of only 70 if there were 10 acts during the primary stage of infection.

There is little information available on the duration of stages in the Wawer et al. data and that can give quite different answers depending upon how one assumes that the total times spent in primary infection are distributed. Therefore, in contrast to Hollingsworth et al., we chose to use a distribution on the duration of primary infection that is consistent with observations on viral levels during primary infection. Viral levels peak early: they may not fall to the set point for quite some time. However, by a little more than a month after beginning to rise, viral levels are an order of magnitude below their peak levels. Thus we fix the average duration of primary infection at 1.18 months. Results from the individual based model, described in the next section, show that the inferences we make in our paper are unaffected by using a longer interval.

We formulate the dynamic process model seen in Equation Set 2 of the acquisition and transmission of infection in uninfected couples using the transmission probabilities for PHI and post-PHI infection. Likewise, we formulate in the latter part of Equation Set 2, a dynamic process model of the transmission of infection in couples where one of the recruited members was initially infected. These use the same two parameters, namely the transmission rates during primary and post-PHI infection (see eTable 6). We fit these parameters exactly to the two relevant data points at 10 months. The first is the number of jointly infected couples divided by the number of couples with at least one infected individual (10/23) and the second is the number.
of transmissions from an initially infected member of a couple to an initially uninfected member of a couple divided by the total number of 10 month couple observations from which those transmissions arose (36/427). Since we analyze the sensitivity of our inferences about population transmission dynamics to a broader range of parameter values than could have arisen due to chance, there is no need for confidence level estimation on these parameters. Notice that we do not use the observations in the subsequent periods to the first in the Wawer et al. data beyond the first period when both partners were initially seronegative. Our model, however, almost exactly reproduces these results when it fits the first 10 month period of observation. The ratio estimates do depend on the distribution of durations of primary infection. Using an exponential distribution the ratio for our 1.18 month duration primary infection is 93. With an Erlang distribution with a shape parameter of 22, our estimate is 60, which is the value we use for the analyses in this paper. Given the considerations above on both the distribution of observed viral levels over time and the difference between per act and per partnership ratios, we choose a ratio of 60 with extremes of 40 and 93 for sensitivity analyses.

Equation Set 2. Model for acquisition and transmission of infection in uninfected couples

\[
\frac{dSSS}{dt} = -2\lambda
\]

\[
\frac{dSSP_1}{dt} = 2\lambda - \beta_p SSP_1 - m\gamma_p SSP_1
\]

\[
\frac{dSSP_i}{dt} = m\gamma_p SSP_1 - \beta_p SSP_i - m\gamma_p SSP_i
\]

\[
\frac{dSSA}{dt} = m\gamma_p SSP_m - \beta_c SSA
\]

\[
\frac{dSI}{dt} = \sum_i \beta_p SSP_i + \beta_c SSA
\]

\[
\frac{dPS}{dt} = -\beta_p PS - \gamma_p PS
\]

\[
\frac{dAS}{dt} = \gamma_p PS - \beta_c AS
\]

\[
\frac{dll}{dt} = \beta_c AS + \beta_p PS
\]
Table 6: Model parameters, derived variables and compartmental variables for the model to estimate the hazard ratio

<table>
<thead>
<tr>
<th>Symbol</th>
<th>Description</th>
<th>Values explored</th>
<th>Std value</th>
</tr>
</thead>
<tbody>
<tr>
<td>( \lambda )</td>
<td>Force of infection outside partnership</td>
<td>0.0001-0.002 per month</td>
<td>0.001</td>
</tr>
<tr>
<td>( \gamma_p )</td>
<td>Rate of progression out of primary infection</td>
<td>0.33-0.85</td>
<td>0.85</td>
</tr>
<tr>
<td>( m )</td>
<td>Erlang shape parameter</td>
<td>1-300</td>
<td>3</td>
</tr>
<tr>
<td>( \beta_p )</td>
<td>Transmission rate of primary infection to partner</td>
<td>Fitted to Obs1 &amp; Obs2</td>
<td></td>
</tr>
<tr>
<td>( \chi_{HL} )</td>
<td>Flow rate from high to low risk phase</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Set Parameters

<table>
<thead>
<tr>
<th>Derived Variables</th>
</tr>
</thead>
<tbody>
<tr>
<td>Obs1 Numerator: Dually uninfected at time 0 and dually infected at 10 months Denominator: Dually uninfected at time 0 with 1 or more infected at 10 months</td>
</tr>
<tr>
<td>Obs2 Numerator: Recruited couples with 1 infected at time 0 and 2 at 10 months Denominator: all 10 month periods with only 1 recruited infected at time 0</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Compartmental Variables</th>
</tr>
</thead>
<tbody>
<tr>
<td>SSS</td>
</tr>
<tr>
<td>SSP(_i)</td>
</tr>
<tr>
<td>SSA</td>
</tr>
<tr>
<td>SII</td>
</tr>
<tr>
<td>PS</td>
</tr>
<tr>
<td>AS</td>
</tr>
<tr>
<td>II</td>
</tr>
</tbody>
</table>

To compare this method to that of Hollingsworth et al., we set \( m=300 \) and \( \gamma_p \) to equal their estimated duration of primary infection. This method yields a ratio estimate of 29 compared to their estimate of 27. The difference is likely due to the asymptomatic rates in their method being pulled up to fit the higher transmissions in the subsequent 30 months of observation after the first 10 months period. This would not happen using an Erlang distribution for PHI duration. Nevertheless, the differences are minor.

Transmissibility during the final stage of infection will vary greatly across different conditions. For instance, in Montreal, where a high fraction of final stage cases will be under treatment, transmissibility should be low, whereas it should be higher in Rakai. Hollingsworth et al. [2008] estimated it to be 7 times the asymptomatic stage for 10 months. Therefore, we do sensitivity analyses across a broad range and do not estimate the ratio of transmissibility between the final stage of infection and the asymptomatic stage.
eAppendix 3: Implementation of the Individual-based Model (IBM)

We developed an individual based version of the deterministic compartmental model (DCM) for the Men-to-Men Sex (MSM) case. By default, we simulate 10,000 individuals and the model runs for 30,000 iterations, i.e. with fixed time steps. A time step in the IBM corresponds to one day. The model final output at equilibrium such as the prevalence and the number of secondary cases from primary HIV infection (PHI) stage is calculated as an average for the last 500 time steps. The expected output approximates to the corresponding output from the DCM.

In the IBM, rates of flows from the DCM introduced in eAppendix 1 are converted as probabilities applied on the individuals. For a given rate of flow ($\lambda$), a probability is calculated as,

$$probability = 1 - e^{-\lambda \, dt}$$

where, the value for $dt$ is determined as $\frac{1}{\text{average number of days in PHI}}$.

The simulation schedule in the individual based model consists of three main processes called at each time step. As in the DCM, initial HIV infection is introduced to 1% (default) of the total population. We assume instantaneous sex acts among the individuals.

The list of all possible events at the individual level is given as follows:

1. A receptive-only individual selects an insertive-only partner either from an insertive-only or a dual-role group for a unidirectional sex act.
2. A dual-role individual, in a receptive role, selects an insertive-only or a dual-role group for a unidirectional sex act.
3. A dual-role individual selects a partner from its group for a reciprocal sex act.
4. An insertive-only individual infects a receptive-only partner.
5. A receptive-only individual infects an insertive-only partner.
6. A receptive-only individual infects a dual-role partner.
7. A dual-role individual with an insertive role infects a receptive-only partner.
8. A dual-role individual with a receptive role infects a dual-role partner (who has an insertive role) in a unidirectional sex act.
9. An insertive-only individual infects a dual-role partner (who has a receptive role).
10. A dual-role individual with a receptive role infects an insertive-only partner in a unidirectional sex act.
11. A dual-role individual infects another dual-role individual in a reciprocal sex act.
12. An individual in the no-anal-sex group moves to the insertive-only group.
13. An individual in the no-anal-sex group moves to the receptive-only group.
14. An individual in the no-anal-sex group moves to the dual-role group.
15. An individual in the insertive-only group moves to the no-anal-sex group.
16. An individual in the insertive-only group moves to the receptive-only.
17. An individual in the insertive-only group moves to the dual-role group.
18. An individual in the receptive-only group moves to the no-anal-sex group.
19. An individual in the receptive-only group moves to the insertive-only.
20. An individual in the receptive-only group moves to the dual-role group.
21. An individual in the dual-role group moves to the no-anal-sex group.
22. An individual in the dual-role group moves to the insertive-only group.
23. An individual in the dual-role group moves to the receptive-only group.
24. An individual in the PHI infection stages progresses to the post-PHI or chronic stage.
25. An individual in the post-PHI infection stage dies of AIDS.
26. A new susceptible individual enters the system.
27. An existing individual leaves the system with an average duration of stay set as 40 years.

The probability for the above events to occur for an individual depends upon the rate in the DCM in Section eAppendix 1 and follows the simulation schedule given below:

For I = 1 to maximum-iterations
   Call Sexual-Interaction-of-Individuals
   Call Update-Individuals-Status
   Call Risk-Groups-Transitions
End

Sexual-Interaction-of-Individuals
In the IBM, the sex act rates $RRCR$ and $DRCR$ are converted into probabilities for selecting a receptive-only and a dual-role individual for a sex act respectively. This determines the sexual interaction of individuals from the insertive-only, receptive-only and dual-role risk groups.

Individuals from the receptive-only risk group chose their insertive partners either from the insertive-only or the dual-role group. The preference for an insertive-only partner over a dual-role individual is based on the same mechanism as introduced in eAppendix1. Likewise, individuals chosen from the dual-role risk group for unidirectional sex acts chose their insertive partners from the insertive-only or their own risk group. Finally, dual-role individuals select their partners for reciprocal sex based on the SCP parameter.

The parameter $SCP$ from the DCM (see eTable 2 in eAppendix 1) determines the proportion of duals that engage in unidirectional sex (insertive or receptive) and those participating in reciprocal sex.

The remainder of the agents in the dual cohort participates in reciprocal sex. The risk of transmission of infection follows the order (from highest to lowest) for the agents in sex acts with reciprocal, receptive and insertive roles respectively.

Update-Agents
At each time step, individuals leave the system with an exit rate $\mu$ ($1/$risk-duration). Also, susceptible individuals are introduced into the system, also with the entry rate ($\mu$). Infected individuals status of infection is also updated. An individual advances from the primary HIV (PHI) to post-PHI stage based on the probability calculated from the rate ($\lambda_p$). Progression from post-PHI to dying of AIDS is determined by the probability from the $\lambda_c$ (see eTable 2 in eAppendix 1).

Risk-Groups-Transitions
As in the DCM described in eAppendix 1, individuals in the IBM switch their risk groups based on the probabilities determined by the rates of transitions adapted from Blower et al. [1995] (see eTable 3 in eAppendix 1). The four risk groups are: no-anal-sex, insertive-only, receptive-only

20
and dual-role. Susceptible individuals entering in the system during the simulation are assigned risk groups depending upon the equilibrium frequency of the four risk groups at the start.

Assessing the effect of using alternative natural histories of Infection
We used the IBM to look into the robustness of our results when heterogeneity in terms of the duration of PHI and the transmission probability during PHI. We used both the Normal and the Erlang distributions so that individuals may have similar but varying natural histories of infection and transmissibility. Simulation results suggest the robustness of our results from the DCM presented in the main article.

References