

APPENDIX

Contribution of high risk groups' unmet needs may be underestimated in epidemic models without risk turnover: a mechanistic modelling analysis [☆]

Jesse Knight^a, Stefan D. Baral^b, Sheree Schwartz^b, Linwei Wang^a, Huiting Ma^a, Katherine Young^c,
Harry Hausler^c, Sharmistha Mishra^{a,d,e,f,*}

^aMAP Centre for Urban Health Solutions, Unity Health Toronto

^bDepartment of Epidemiology, Johns Hopkins Bloomberg School of Public Health

^cTB HIV Care, South Africa

^dDivision of Infectious Disease, Department of Medicine, University of Toronto

^eInstitute of Health Policy, Management and Evaluation, Dalla Lana School of Public Health, University of Toronto

^fInstitute of Medical Sciences, University of Toronto

A Turnover Framework	1
A.1 Notation	1
A.2 Parameterization	1
A.3 Previous Approaches	7
B Supplemental Equations	9
B.1 Model Equations	9
B.2 Complete Example Turnover System	10
B.3 Redundancy in specifying all elements of \hat{e}	10
B.4 Factors of Incidence	10
C Supplemental Results	12
C.1 Equilibrium health states and rates of transition	12
C.2 Equilibrium Prevalence Ratios	14
C.3 Equilibrium Incidence	15
C.4 Equilibrium prevalence and number of partners before and after model fitting	16
C.5 Influence of turnover on tPAF of the high risk group before and after model fitting	17
C.6 Effect of treatment rate on the influence of turnover on equilibrium prevalence	18

[☆] On behalf of the Siyaphambili study team

* Corresponding author (sharmistha.mishra@utoronto.ca)

A Turnover Framework

We introduce a system of parameters and constraints to describe risk group turnover in deterministic epidemic models with heterogeneity in risk.¹ We then describe how the system can be used in practical terms, based on different assumptions and data available for parameterizing turnover in risk. We conclude by framing previous approaches to this task using the proposed system.

A.1 Notation

Consider a population divided into G risk groups. We denote the number of individuals in risk group $i \in [1, \dots, G]$ as x_i and the set of all risk groups as $\mathbf{x} = \{x_1, \dots, x_G\}$. The total population size is $N = \sum_i x_i$, and the relative population size of each group is denoted as $\hat{x}_i = x_i/N$. Individuals enter the population at a rate ν per year, and exit at a rate μ per year. We model the distribution of risk groups among individuals entering into the population as $\hat{\mathbf{e}}$, which may be different from individuals already in the population $\hat{\mathbf{x}}$.² Thus, the total number of individuals entering into population \mathbf{x} per year is given by νN , and the number of individuals entering into group i specifically is given by $\hat{e}_i \nu N$.

Turnover transitions may then occur between any two groups, in either direction. Therefore we denote the turnover rates as a $G \times G$ matrix ϕ . The element ϕ_{ij} corresponds to the proportion of individuals in group i who move from group i to group j each year. An example matrix is given in Eq. (A.1), where we write the diagonal elements as $*$ since they represent transitions from a group to itself.

$$\phi = \begin{bmatrix} * & x_1 \rightarrow x_2 & \cdots & x_1 \rightarrow x_G \\ x_2 \rightarrow x_1 & * & \cdots & x_2 \rightarrow x_G \\ \vdots & \vdots & \ddots & \vdots \\ x_G \rightarrow x_1 & x_G \rightarrow x_2 & \cdots & * \end{bmatrix} \quad (\text{A.1})$$

Risk groups, transitions, and the associated rates are also shown for $G = 3$ in Figure A.1.

A.2 Parameterization

Next, we present methods to illustrate how epidemiologic data can be used to parametrize turnover in epidemic models. We construct a system like the one above which reflects the risk group dynamics observed in a specific context. We assume that the relative sizes of the risk groups in the model ($\hat{\mathbf{x}}$) are already known, and should remain constant over time. Thus, what remains is to estimate the values of the parameters: ν , μ , $\hat{\mathbf{e}}$, and ϕ , using commonly available sources of data.

¹ A preliminary version of this framework was used by Knight et al. (2019).

² We could equivalently stratify the rate of entry ν by risk group; however, we find that the mathematics in subsequent sections are more straightforward using $\hat{\mathbf{e}}$.

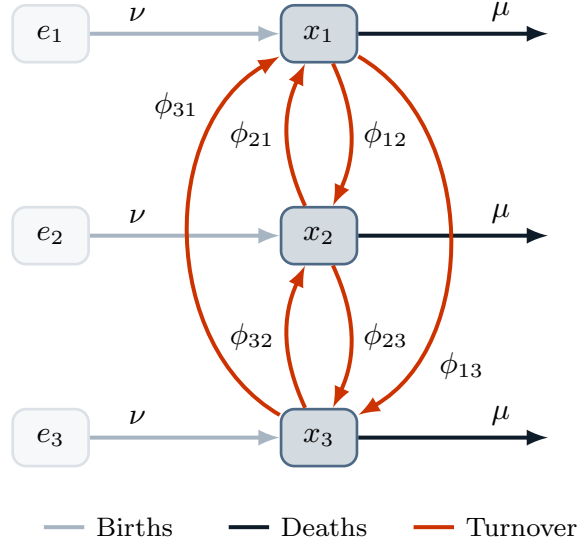


Figure A.1: System of $G = 3$ risk groups and turnover between them.

x_i : number of individuals in risk group i ; e_i : number of individuals available to enter risk group i ; ν : rate of population entry; μ : rate of population exit; ϕ_{ij} : rate of turnover from group i to group j .

A.2.1 Total Population Size

The total population size $N(t)$ is a function of the rates of population entry $\nu(t)$ and exit $\mu(t)$, given an initial size N_0 . We allow the proportion entering the system to vary by risk group via \hat{e} , while the exit rate has the same value for each group. We assume that there is no disease-attributable death. Because the values of ν and μ are the same for each risk group, they can be estimated independent of \hat{x} , \hat{e} , and $\hat{\phi}$.

The difference between entry and exit rates defines the rate of population growth:

$$\mathcal{G}(t) = \nu(t) - \mu(t) \tag{A.2}$$

The total population may then be defined using an initial population size N_0 as:

$$N(t) = N_0 \exp\left(\int_0^t \log(1 + \mathcal{G}(\tau)) d\tau\right) \tag{A.3}$$

which, for constant growth, simplifies to the familiar expression (Malthus, 1798):

$$N(t) = N_0(1 + \mathcal{G})^t \tag{A.4}$$

Census data, such as (DataBank, 2019), can be used to source the total population size in a given geographic setting over time $N(t)$, thus allowing Eqs. (A.3) and (A.4) to be used to estimate $\mathcal{G}(t)$.

If the population size is assumed to be constant, then $\mathcal{G}(t) = 0$ and $\nu(t) = \mu(t)$. If population growth occurs at a stable rate, then \mathcal{G} is fixed at a constant value which can be estimated via Eq. (A.4) using any

two values of $N(t)$, separated by a time interval τ :

$$\mathcal{G}_\tau = \frac{N(t + \tau)^{\frac{1}{\tau}}}{N(t)} - 1 \quad (\text{A.5})$$

If the rate of population growth \mathcal{G} varies over time, then Eq. (A.5) can be reused for consecutive time intervals, and the complete function $\mathcal{G}(t)$ approximated piecewise by constant values. The piecewise approximation can be more feasible than exact solutions using Eq. (A.3), and can reproduce $N(t)$ accurately for small enough intervals τ , such as one year.

Now, given a value of $\mathcal{G}(t)$, either $\nu(t)$ must be chosen and $\mu(t)$ calculated using Eq. (A.2), or $\mu(t)$ must be chosen, and $\nu(t)$ calculated. Most modelled systems assume a constant duration of time that individuals spend in the model $\delta(t)$ (Anderson and May, 1991) which is related to the rate of exit μ by:

$$\delta(t) = \mu^{-1}(t) \quad (\text{A.6})$$

In the context of sexually transmitted infections, the duration of time usually reflects the average sexual life-course of individuals from age 15 to 50 years, such that $\delta = 35$ years. The duration δ may also vary with time to reflect changes in life expectancy. The exit rate $\mu(t)$ can then be defined as $\delta^{-t}(t)$ following Eq. (A.6), and the entry rate $\nu(t)$ defined as $\mathcal{G}(t) - \mu(t)$ following Eq. (A.2).

A.2.2 Turnover

Next, we present methods for resolving the distribution of individuals entering the risk model $\hat{\mathbf{e}}(t)$ and the rates of turnover $\phi(t)$, assuming that entry and exit rates $\nu(t)$ and $\mu(t)$ are known. Similar to above, we first formulate the problem as a system of equations. Then, we explore the data and assumptions required to solve for the values of parameters in the system. The (t) notation is omitted throughout this section for clarity, though time-varying parameters can be estimated by repeating the necessary calculations for each t .

The number of risk groups G dictates the number of unknown elements in $\hat{\mathbf{e}}$ and ϕ : G and $G(G - 1)$, respectively. We collect these unknowns in the vector $\boldsymbol{\theta} = [\hat{\mathbf{e}}, \boldsymbol{\phi}]$, where $\boldsymbol{\phi} = \text{vec}_{i \neq j}(\phi)$. For example, for $G = 3$, the vector $\boldsymbol{\theta}$ is defined as:

$$\boldsymbol{\theta} = \left[\hat{e}_1 \quad \hat{e}_2 \quad \hat{e}_3 \quad \phi_{12} \quad \phi_{13} \quad \phi_{21} \quad \phi_{23} \quad \phi_{31} \quad \phi_{32} \right] \quad (\text{A.7})$$

We then define a linear system of equations which uniquely determine the elements of $\boldsymbol{\theta}$:

$$\mathbf{b} = A\boldsymbol{\theta} \quad (\text{A.8})$$

where A is a $M \times G^2$ matrix and \mathbf{b} is a M -length vector. Specifically, each row in A and \mathbf{b} defines a constraint: an assumed mathematical relationship involving one or more elements of $\hat{\mathbf{e}}$ and ϕ . For example, a simple constraint could be to assume the value $\hat{e}_2 = 0.20$. Each of the following four sections introduces a type of constraint, including: assuming a constant group size, specifying elements of $\boldsymbol{\theta}$ directly, assuming an average

duration in a group, and specifying a relationship between two individual rates of turnover. Constraints may be selected and combined together based on availability of data and plausibility of assumptions. However, a total of $M = G^2$ constraints must be defined in order to obtain a “unique solution”: exactly one value of θ which satisfies all constraints. The values of $\hat{\epsilon}$ and ϕ can then be calculated algebraically by solving Eq. (A.8) with $\theta = A^{-1}\mathbf{b}$, for which many algorithms exist (LAPACK, 1992).

1. *Constant group size.* One epidemiologic feature that epidemic models consider is whether or not the relative sizes of risk groups are constant over time (Henry and Koopman, 2015; Boily et al., 2015). Assuming constant group size implies a stable level of heterogeneity over time. To enforce this assumption, we define the “conservation of mass” equation for group i , wherein the rate of change of the group is defined as the sum of flows in/out of the group:

$$\frac{d}{dt}x_i = \nu N \hat{\epsilon}_i + \sum_j \phi_{ji} x_j - \mu x_i - \sum_j \phi_{ij} x_i \quad (\text{A.9})$$

Eq. (A.9) is written in terms of absolute population sizes \mathbf{x} , but can be written as proportions $\hat{\mathbf{x}}$ by dividing all terms by N . If we assume that the proportion of each group \hat{x}_i is constant over time, then the desired rate of change for risk group i will be equal to the rate of population growth of the risk group, $\mathcal{G}x_i$. Substituting $\frac{d}{dt}x_i = \mathcal{G}x_i$ into Eq. (A.9), and simplifying yields:

$$\nu x_i = \nu N \hat{\epsilon}_i + \sum_j \phi_{ji} x_j - \sum_j \phi_{ij} x_i \quad (\text{A.10})$$

Factoring the left and right hand sides in terms of $\hat{\epsilon}$ and ϕ , we obtain G unique constraints. For $G = 3$, this yields the following 3 rows as the basis of \mathbf{b} and A :

$$\mathbf{b} = \begin{bmatrix} \nu x_1 \\ \nu x_2 \\ \nu x_3 \end{bmatrix}; \quad A = \begin{bmatrix} \nu & \cdot & \cdot & -x_1 & -x_1 & x_2 & \cdot & x_3 & \cdot \\ \cdot & \nu & \cdot & x_1 & \cdot & -x_2 & -x_2 & \cdot & x_3 \\ \cdot & \cdot & \nu & \cdot & x_1 & \cdot & x_2 & -x_3 & -x_3 \end{bmatrix} \quad (\text{A.11})$$

These G constraints ensure risk groups do not change size over time. However, a unique solution requires an additional $G(G - 1)$ constraints. For $G = 3$, this corresponds to 6 additional constraints.

2. *Specified elements.* The simplest type of additional constraint is to directly specify the values of individual elements in $\hat{\epsilon}$ or ϕ . Such constraints may be appended to \mathbf{b} and A as an additional row k using indicator notation.³ That is, with b_k as the specified value v , and A_k as the indicator vector, with 1 in the same position as the desired element in θ :

$$b_k = v; \quad A_k = [0, \dots, 1, \dots, 0] \quad (\text{A.12})$$

³ Indicator notation, also known as “one-hot notation” is used to select one element from another vector, based on its position. An indicator vector is 1 in the same location as the element of interest, and 0 everywhere else.

For example, for $G = 3$, if it is known that 20% of individuals enter directly into risk group 2 upon entry into the model ($\hat{e}_2 = 0.20$), then \mathbf{b} and A can be augmented with:

$$b_k = \begin{bmatrix} 0.20 \end{bmatrix}; \quad A_k = \begin{bmatrix} \cdot & 1 & \cdot & \cdot & \cdot & \cdot & \cdot & \cdot & \cdot \end{bmatrix} \quad (\text{A.13})$$

since \hat{e}_2 is the second element in $\boldsymbol{\theta}$. If the data suggest zero turnover from group i to group j , then Eq. (A.13) can also be used to set $\phi_{ij} = 0$.

The elements of $\hat{\mathbf{e}}$ must sum to one. Therefore, specifying all elements in $\hat{\mathbf{e}}$ will only provide $G - 1$ constraints, as the last element will be either redundant or violate the sum-to-one rule. As shown in Appendix B.3, the sum-to-one rule is actually implicit in Eq. (A.11), so it is not necessary to supply a constraint like $1 = \sum_i \hat{e}_i$.

3. Group duration. Type 1 constraints assume that the relative population size of each group remains constant. Another epidemiologic feature that epidemic models considered is whether or not the duration of time spent within a given risk group remains constant. For example, in STI transmission models that include formal sex work, it can be assumed that the duration in formal sex work work remains stable over time, such as in (Mishra et al., 2014; Boily et al., 2015). The duration δ_i is defined as the inverse of all rates of exit from the group:

$$\delta_i = \left(\mu + \sum_j \phi_{ij} \right)^{-1} \quad (\text{A.14})$$

Estimates of the duration in a given group can be sourced from cross-sectional survey data where participants are asked about how long they have engaged in a particular practice – such as sex in exchange for money (Watts et al., 2010). Data on duration may also be sourced from longitudinal data, where repeated measures of self-reported sexual behaviour, or proxy measures of sexual risk data, are collected (The DHS Program, 2019; ICAP, 2019). Data on duration in each risk group can then be used to define ϕ by rearranging Eq. (A.14) to yield: $\delta_i^{-1} - \mu = \sum_j \phi_{ij}$. For example, if for $G = 3$, the average duration in group 1 is known to be $\delta_1 = 5$ years, then \mathbf{b} and A can be augmented with another row k :

$$b_k = \begin{bmatrix} 5^{-1} - \mu \end{bmatrix}; \quad A_k = \begin{bmatrix} \cdot & \cdot & \cdot & 1 & 1 & \cdot & \cdot & \cdot & \cdot \end{bmatrix} \quad (\text{A.15})$$

Similar to specifying all elements of $\hat{\mathbf{e}}$, specifying δ_i may result in conflicts or redundancies with other constraints. A conflict means it will not be possible to resolve values of ϕ which simultaneously satisfy all constraints, while a redundancy means that adding one constraint does not help resolve a unique set of values $\boldsymbol{\theta}$. For example, for $G = 3$, if Type 2 constraints are used to specify $\phi_{12} = 0.1$ and $\phi_{13} = 0.1$, and $\mu = 0.05$, then by Eq. (A.14), we must have $\delta_1 = 4$. Specifying any other value for δ_1 will result in a conflict, while specifying $\delta_1 = 4$ is redundant, since it is already implied. There are innumerable situations in which this may occur, so we do not attempt to describe them all. Section A.2.2 describes how to identify conflicts and redundancies when they are not obvious.

4. *Turnover rate ratios.* In many cases, it may be difficult to obtain estimates of a given turnover rate ϕ_{ij} for use in Type 2 constraints. However, it may be possible to estimate relative relationships between rates of turnover, such as:

$$r \phi_{ij} = \phi_{i'j'} \quad (\text{A.16})$$

where r is a ratio relating the values of ϕ_{ij} and $\phi_{i'j'}$. For example, for $G = 3$, let T_1 be the total number of individuals entering group 1 due to turnover. If we know that 70% of T_1 originates from group 2, while 30% of T_1 originates from group 3, then $0.7T_1 = \phi_{23} x_2$ and $0.3T_1 = \phi_{13} x_1$, and thus: $\phi_{23} \left(\frac{0.3 x_2}{0.7 x_1} \right) = \phi_{13}$. This constraint can then be appended as another row k in \mathbf{b} and A like:

$$b_k = \begin{bmatrix} 0 \end{bmatrix}; \quad A_k = \begin{bmatrix} \cdot & \cdot & \cdot & \cdot & \left(\frac{0.3 x_2}{0.7 x_1} \right) & \cdot & 1 & \cdot & \cdot \end{bmatrix} \quad (\text{A.17})$$

The example in Eq. (A.17) is based on what proportions of individuals entering a risk group j came from which former risk group i , but similar constraints may be defined based on what proportions of individuals exiting a risk group i enter into which new risk group j . It can also be assumed that the absolute number of individuals moving between two risk groups is equal, in which case the relationship is: $\phi_{ij} \left(\frac{x_i}{x_j} \right) = \phi_{ji}$. All constraints of this type will have $b_k = 0$.

Solving the System. Table A.1 summarizes the four types of constraints described above. Given a set of sufficient constraints on $\boldsymbol{\theta}$ to ensure exactly one solution, the system of equations Eq. (A.8) can be solved using $\boldsymbol{\theta} = A^{-1}\mathbf{b}$. The resulting values of $\hat{\epsilon}$ and ϕ can then be used in the epidemic model.

However, we may find that we have an insufficient number of constraints, implying that there are multiple values of the vector $\boldsymbol{\theta}$ which satisfy the constraints. An insufficient number of constraints may be identified by a ‘‘rank deficiency’’ warning in numerical solvers of Eq. (A.8) (LAPACK, 1992). Even if A has G^2 rows, the system may have an insufficient number of constraints because some constraints are redundant. In this situation, we can pose the problem as a minimization problem, namely:

$$\boldsymbol{\theta}^* = \arg \min f(\boldsymbol{\theta}), \quad \text{subject to: } \mathbf{b} = A\boldsymbol{\theta}; \quad \boldsymbol{\theta} \geq 0 \quad (\text{A.18})$$

where f is a function which penalizes certain values of $\boldsymbol{\theta}$. For example, $f = \|\cdot\|_2$ penalizes large values in $\boldsymbol{\theta}$, so that the smallest values of $\hat{\epsilon}$ and ϕ which satisfy the constraints will be resolved.⁴

Similarly, we may find that no solution exists for the given constraints, since two or more constraints are in conflict. Conflicting constraints may be identified by a non-zero error in the solution to Eq. (A.8) (LAPACK, 1992). In this case, the conflict should be resolved by changing or removing one of the conflicting constraints.

⁴ Numerical solutions to such problems are widely available, such as the Non-Negative Least Squares solver (Lawson and Hanson, 1995), available in Python: <https://docs.scipy.org/doc/scipy/reference/generated/scipy.optimize.nnls.html>.

Table A.1: Summary of constraint types for defining risk group turnover

Name	Eq.	E.g.	Data requirements
1. Constant group size	(A.10)	(A.11)	all values of \hat{x}_i and ν
2. Specified elements	(A.12)	(A.13)	any value of \hat{e}_i or ϕ_{ij}
3. Group duration	(A.14)	(A.15)	any value of δ_i
4. Turnover rate ratios	(A.16)	(A.17)	any relationship between two turnover rates ϕ_{ij} and $\phi_{i'j'}$

ν : rate of population entry; ϕ_{ij} : rate of turnover from group i to group j ; \hat{x}_i : proportion of individuals in risk group i ; \hat{e}_i : proportion of individuals entering into risk group i ; δ_i : average duration spent in risk group i .

A.3 Previous Approaches

Few epidemic models of sexually transmitted infections with heterogeneity in risk have simulated turnover among risk groups, and those models which have simulated turnover have done so in various ways. In this section, we review three prior implementations of turnover and their assumptions. We then highlight how the approach proposed in Section A.2 could be used to achieve the same objectives.

Stigum et al. (1994) simulated turnover among $G = 2$ risk groups in a population with no exogenous entry or exit ($\nu = \mu = 0$ and hence \hat{e} is not applicable). Turnover between the groups was balanced in order to maintain constant risk group sizes (Type 1 constraint),⁵ while the rate of turnover from high to low was specified as κ (Type 2 constraint). Thus, the turnover system used by Stigum et al. (1994) can be written in the proposed framework as:

$$\begin{bmatrix} 0 \\ \kappa \end{bmatrix} = \begin{bmatrix} \hat{x}_1 & -\hat{x}_2 \\ 1 & \cdot \end{bmatrix} \begin{bmatrix} \phi_{12} \\ \phi_{21} \end{bmatrix}, \quad \hat{e}_1 = \hat{e}_2 = 0 \quad (\text{A.19})$$

Henry and Koopman (2015) also simulated turnover among $G = 2$ risk groups, but considered exogenous entry and exit, both at a rate μ . The authors used the notation f_i for our \hat{x}_i , and assumed that the population of individuals entering into the modelled population had the same distribution of risk groups as the modelled population itself: $\hat{e}_i = f_i$ (Type 2 constraint). The authors further maintained constant risk group sizes (Type 1 constraint) by analytically balancing turnover between the two groups using: $\phi_{12} = \omega \hat{x}_2$; $\phi_{21} = \omega \hat{x}_1$, where ω is a constant. However, it can be shown that this analytical approach is also the solution to the following combination of Type 1 and Type 2 constraints:

$$\begin{bmatrix} 0 \\ \omega f_2 \end{bmatrix} = \begin{bmatrix} f_1 & -f_2 \\ 1 & \cdot \end{bmatrix} \begin{bmatrix} \phi_{12} \\ \phi_{21} \end{bmatrix}, \quad \hat{e}_i = f_i \quad (\text{A.20})$$

⁵ Due to its simplicity, this constraint is actually an example of both Type 1 and Type 4 constraints.

Eaton and Hallett (2014) simulated turnover among $G = 3$ risk groups, considering a distribution of risk among individuals entering into the modelled population \hat{e} which was different from \hat{x} . Turnover was considered from high-to-medium, high-to-low, and medium-to-low risk, all with an equal rate ψ ; the reverse transition rates were set to zero (six total Type 2 constraints). Given the unidirectional turnover, risk group sizes were maintained using the values of \hat{e}_i , computed using Type 1 constraints as follows:

$$\begin{bmatrix} \nu x_1 + 2x_1\psi \\ \nu x_2 - x_1\psi + x_2\psi \\ \nu x_3 - x_1\psi - x_2\psi \end{bmatrix} = \begin{bmatrix} \nu & \cdot & \cdot \\ \cdot & \nu & \cdot \\ \cdot & \cdot & \nu \end{bmatrix} \begin{bmatrix} e_1 \\ e_2 \\ e_3 \end{bmatrix}, \quad \begin{aligned} \phi_{12} &= \phi_{13} = \phi_{23} = \psi \\ \phi_{21} &= \phi_{31} = \phi_{32} = 0 \end{aligned} \quad (\text{A.21})$$

In sum, the framework for modelling turnover presented in this section aims to generalize all previous implementations. In so doing, we hope to clarify the requisite assumptions, dependencies on epidemiologic data, and relationships between previous approaches.

B Supplemental Equations

Table B.1: Notation

Symbol	Definition
i	risk group index
j	risk group index for “other” group in turnover
k	risk group index for “other” group in incidence
t	time
\mathcal{S}_i	number of susceptible individuals in risk group i
\mathcal{I}_i	number of infectious individuals in risk group i
\mathcal{T}_i	number of treated individuals in risk group i
N	total population size
ν	rate of population entry
μ	rate of population exit
ϕ_{ij}	rate of turnover from group i to group j
λ_i	force of infection among susceptibles in risk group i
τ	rate of treatment initiation among infected
\hat{x}_i	proportion of individuals in risk group i
\hat{e}_i	proportion of individuals entering into risk group i
δ_i	average duration spent in risk group i
C_i	number of partners per year among individuals in risk group i
β	probability of transmission per partnership
ρ_{ik}	probability of partnership formation between risk groups i and k

B.1 Model Equations

$$\frac{d}{dt}\mathcal{S}_i(t) = + \sum_j \phi_{ji}\mathcal{S}_j(t) - \sum_j \phi_{ij}\mathcal{S}_i(t) - \mu\mathcal{S}_i(t) + \nu\hat{e}_iN(t) - \lambda_i(t)\mathcal{S}_i(t) \quad (\text{B.1a})$$

$$\frac{d}{dt}\mathcal{I}_i(t) = + \sum_j \phi_{ji}\mathcal{I}_j(t) - \sum_j \phi_{ij}\mathcal{I}_i(t) - \mu\mathcal{I}_i(t) + \lambda_i(t)\mathcal{S}_i(t) - \tau\mathcal{I}_i(t) \quad (\text{B.1b})$$

$$\frac{d}{dt}\mathcal{T}_i(t) = + \sum_j \phi_{ji}\mathcal{T}_j(t) - \sum_j \phi_{ij}\mathcal{T}_i(t) - \mu\mathcal{T}_i(t) + \tau\mathcal{I}_i(t) \quad (\text{B.1c})$$

}
}
}
}
}
}

turnover into
turnover from
death
birth
incidence
treatment

We can factor the term f as:

$$\begin{aligned}
 f &= \frac{\sum_k C_k \mathcal{I}_k}{\sum_k C_k \mathcal{X}_k} \\
 &= \frac{\sum_k C_k \mathcal{I}_k}{\sum_k \mathcal{I}_k} \cdot \frac{\sum_k \mathcal{I}_k}{\sum_k \mathcal{X}_k} \cdot \frac{\sum_k \mathcal{X}_k}{\sum_k C_k \mathcal{X}_k}
 \end{aligned} \tag{B.5}$$

which we recognize as the following terms:

$$= \hat{C}_{\mathcal{I}} \cdot \hat{\mathcal{I}} \cdot \hat{C}^{-1} \tag{B.6}$$

Namely,

1. $\hat{C}_{\mathcal{I}}$ is the average number of partners among infectious individuals
2. $\hat{\mathcal{I}}$ is the proportion of the population who are infectious (overall prevalence)
3. \hat{C} is the average number of partners among all individuals (constant)

Therefore, only two non-constant factors control incidence per susceptible: 1) the average number of partners among infectious individuals $\hat{C}_{\mathcal{I}}$, and 2) overall prevalence $\hat{\mathcal{I}}$. The product of these factors $\hat{C}_{\mathcal{I}} \hat{\mathcal{I}}$, scaled by $\beta C_i / \hat{C}$, then gives λ_i . In fact, the incidence in each group individually is proportional to incidence overall, as C_i is only factor depending on i .

C Supplemental Results

C.1 Equilibrium health states and rates of transition

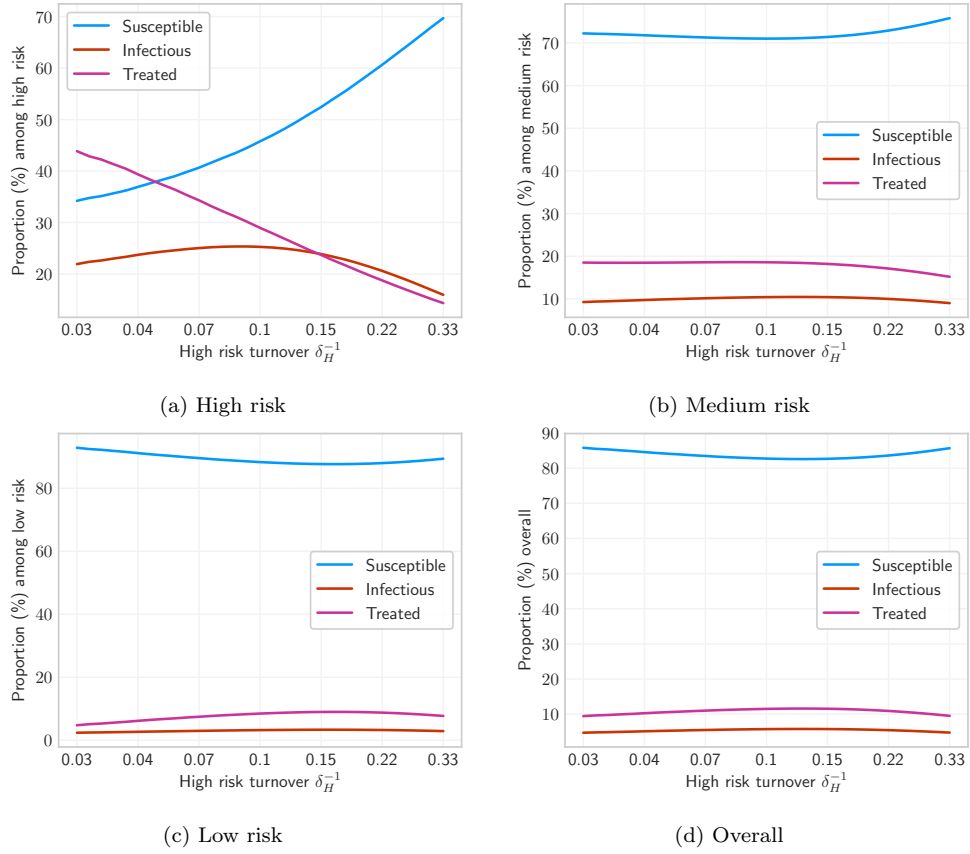


Figure C.1: Equilibrium health state proportions under different rates of turnover.

Turnover rate (log scale) is a function of the duration of time spent in the high risk group δ_H , where shorter time spent in the high risk group yields faster turnover. No turnover is indicated by $\delta_H^{-1} = 0.03$, due to population exit rate $\mu = 0.03$.

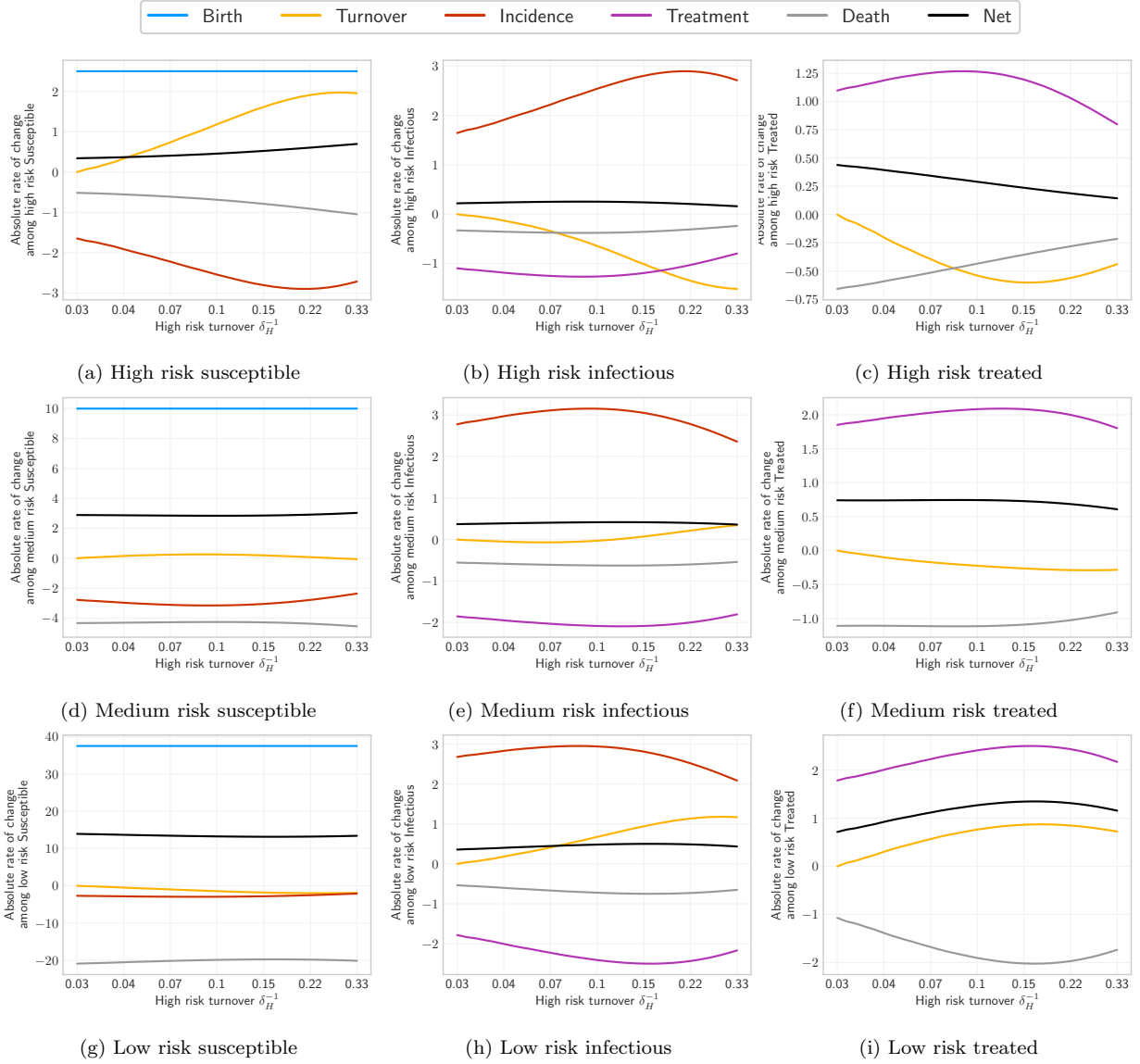


Figure C.2: Absolute rates of change at equilibrium (number of individuals gained/lost per year) among individuals in each health state and risk group, broken down by type of change: gain via births, loss/gain via incident infections, loss/gain via treatment, loss/gain via turnover, loss via death, and net change. Based on Eq. (B.1).

Turnover rate (log scale) is a function of the duration of time spent in the high risk group δ_H , where shorter time spent in the high risk group yields faster turnover. No turnover is indicated by $\delta_H^{-1} = 0.03$, due to population exit rate $\mu = 0.03$. Rates of change do not sum to zero due to population growth.

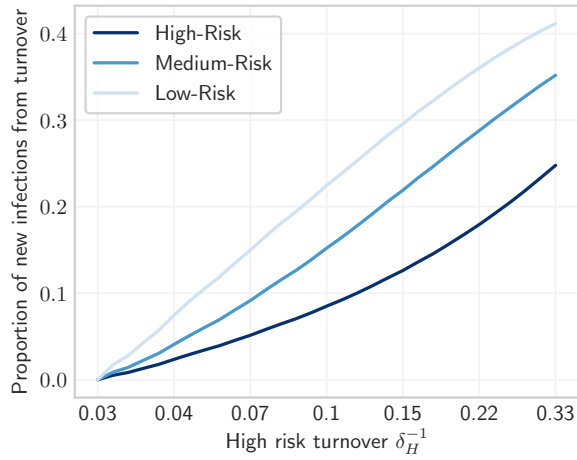
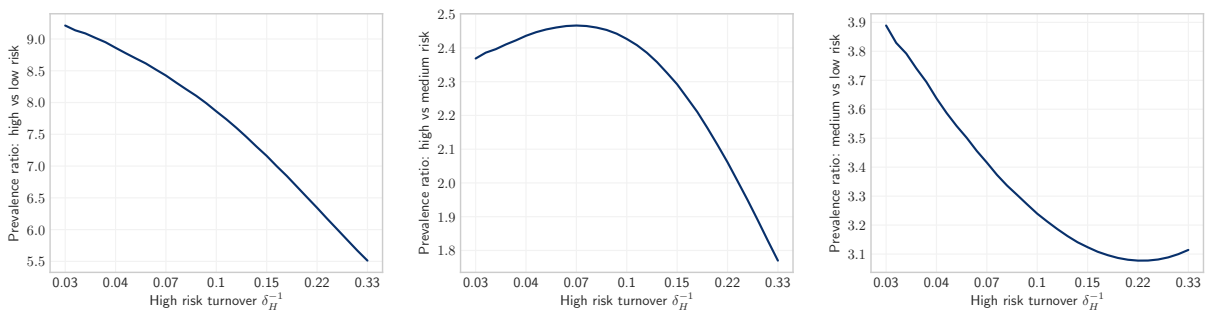


Figure C.3: Proportion of new infectious individuals in each risk group which are from turnover of infectious individuals, as opposed to incident infection of susceptible individuals in the risk group.

C.2 Equilibrium Prevalence Ratios



(a) High vs Low risk

(b) High vs Medium Risk

(c) Medium vs Low Risk

Figure C.4: Equilibrium prevalence ratios between risk groups under different rates of turnover.

Turnover rate (log scale) is a function of the duration of time spent in the high risk group δ_H , where shorter time spent in the high risk group yields faster turnover. No turnover is indicated by $\delta_H^{-1} = 0.03$, due to population exit rate $\mu = 0.03$.

C.3 Equilibrium Incidence

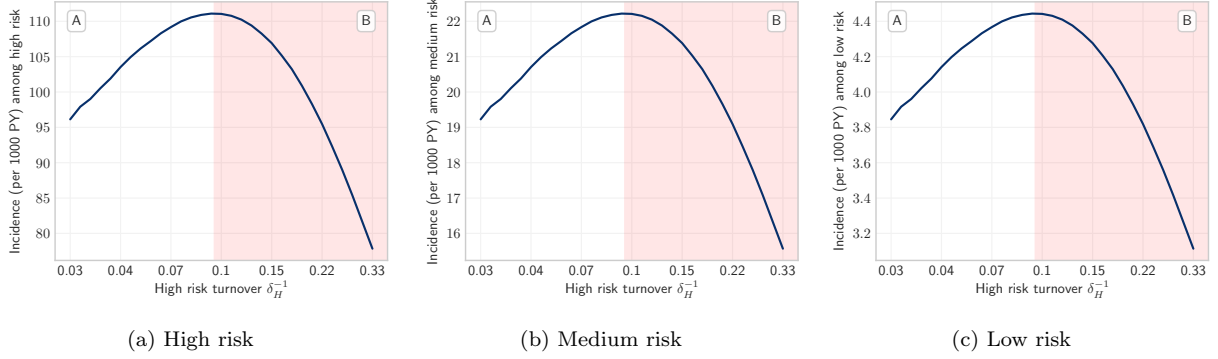


Figure C.5: Equilibrium incidence among high, medium, and low risk groups under different rates of turnover. Turnover rate (log scale) is a function of the duration of time spent in the high risk group δ_H , where shorter time spent in the high risk group yields faster turnover. No turnover is indicated by $\delta_H^{-1} = 0.03$, due to population exit rate $\mu = 0.03$. Incidence in each risk group is proportional to overall incidence with C_i as a scale factor.

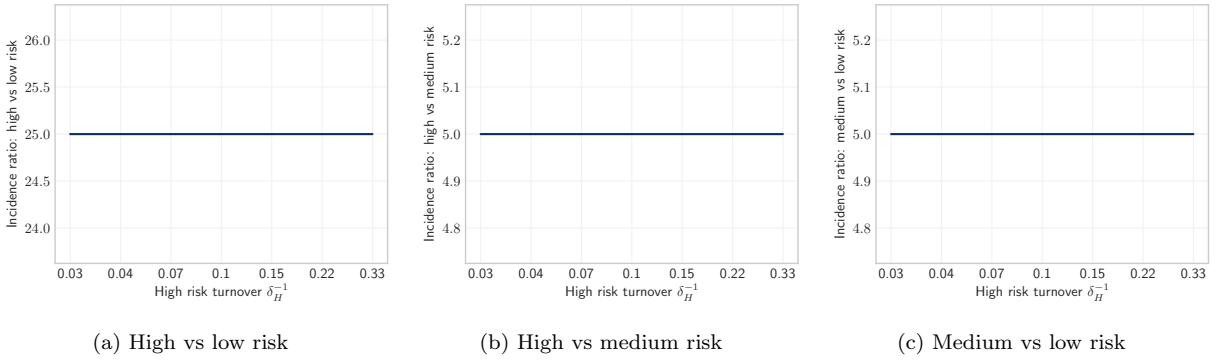


Figure C.6: Equilibrium incidence ratios between risk groups under different rates of turnover. Incidence ratios do not depend on turnover.

Turnover rate (log scale) is a function of the duration of time spent in the high risk group δ_H , where shorter time spent in the high risk group yields faster turnover. No turnover is indicated by $\delta_H^{-1} = 0.03$, due to population exit rate $\mu = 0.03$.

C.4 Equilibrium prevalence and number of partners before and after model fitting

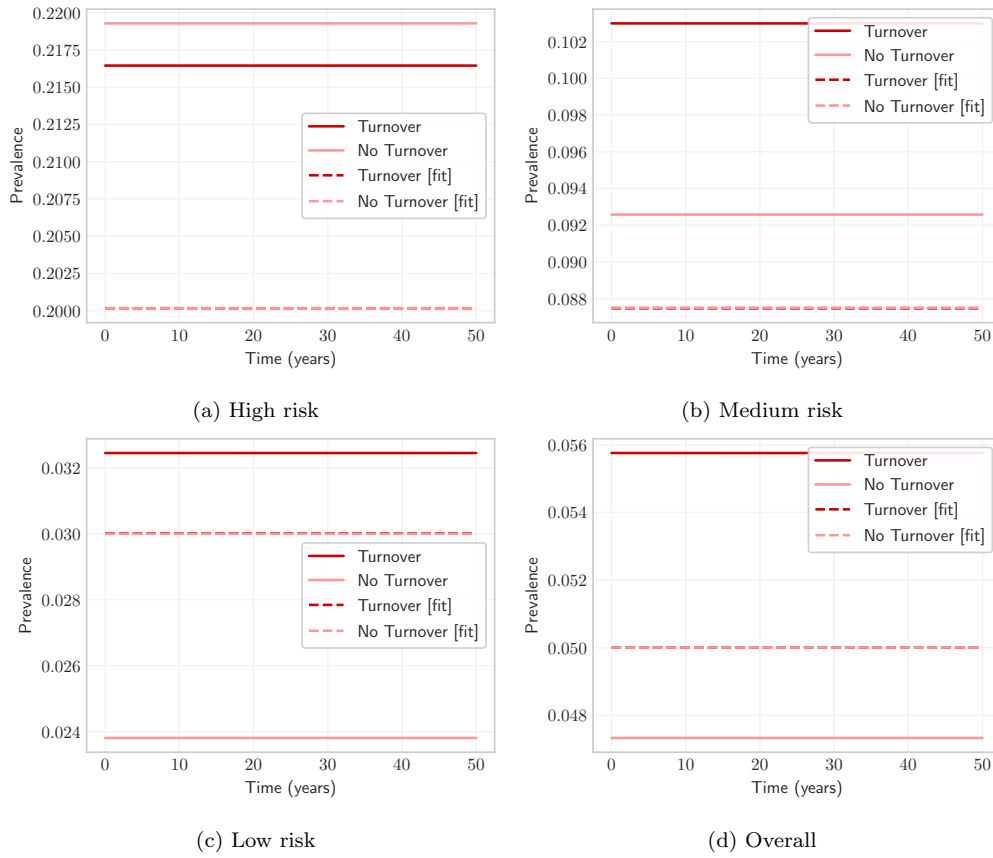


Figure C.7: Equilibrium STI prevalence among high, medium, and low risk groups as well as overall, with and without turnover, and with and without fitted C_i to group-specific prevalence.

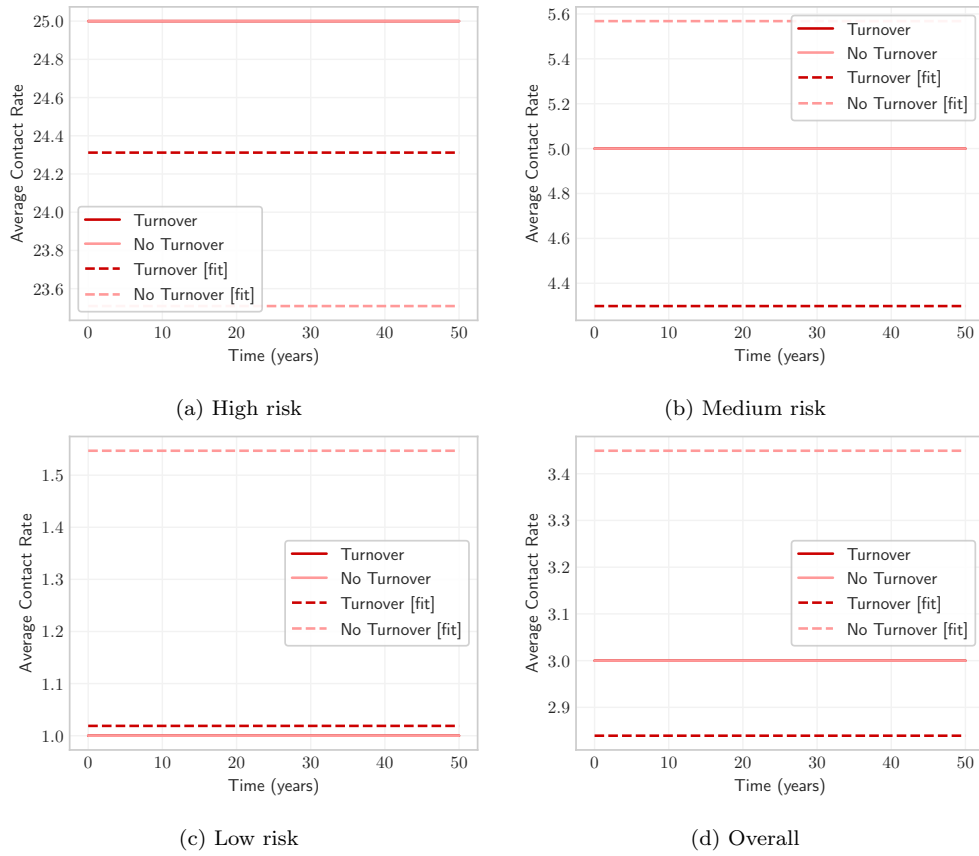


Figure C.8: Numbers of partners C_i among high, medium, and low risk groups as well as overall, with and without turnover, and with and without model fitting to group-specific prevalence.

C.5 Influence of turnover on tPAF of the high risk group before and after model fitting

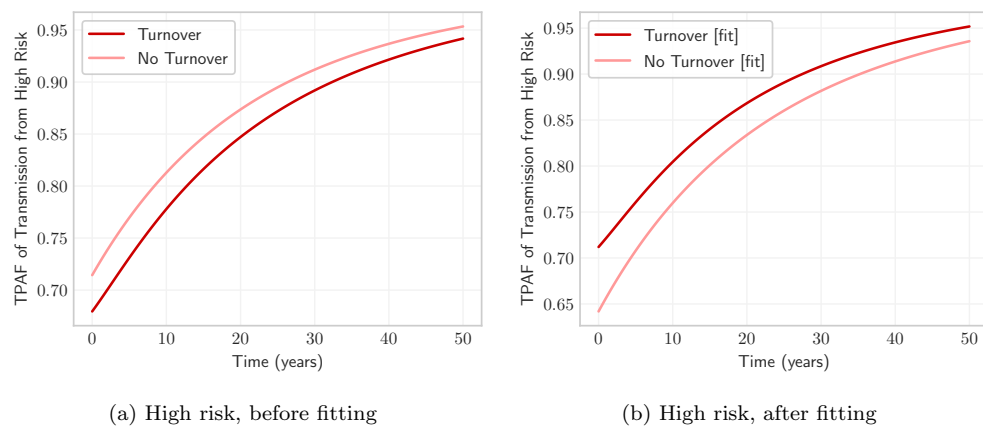


Figure C.9: Transmission population attributable fraction (tPAF) of the high risk group in models with and without turnover, before and after model fitting.

C.6 Effect of treatment rate on the influence of turnover on equilibrium prevalence

In order to examine the effect of treatment rate τ on the results of Experiment 1 – the influence of turnover on equilibrium prevalence – we recreated Figures 4 and 7 for a range of treatment rates $\tau \in [0.05, 1.0]$. The results are shown in Figure C.10.

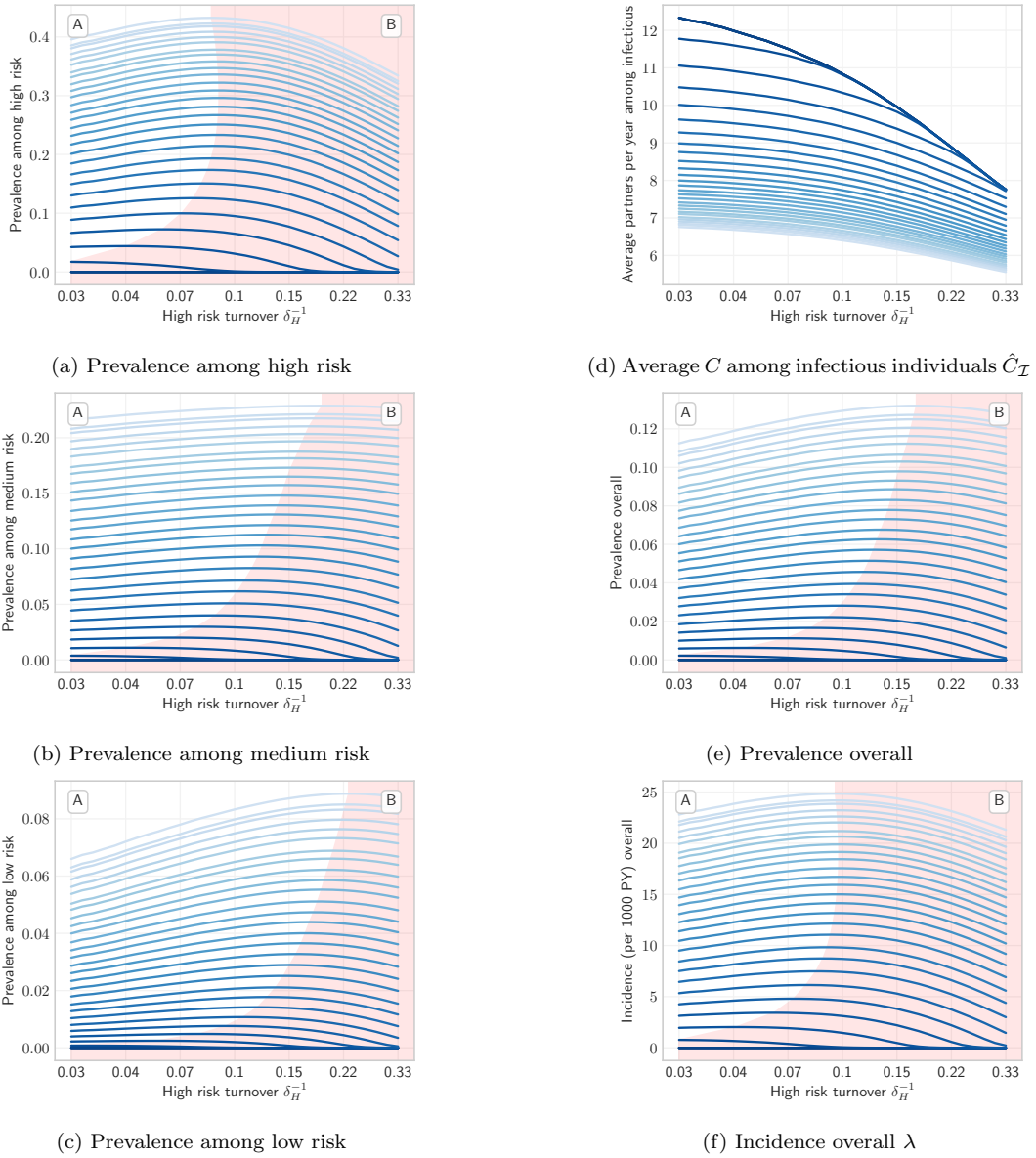


Figure C.10: Relationship between turnover rate and equilibrium STI prevalence in high, medium, and low risk groups, as well as overall STI prevalence and incidence, and average C among infectious individuals, for a range of treatment rates τ . Darker blue indicates higher treatment rate. The threshold turnover rate separating regions A and B decreases with treatment rate, meaning that increasing turnover becomes more likely to decrease equilibrium prevalence as treatment rate increases.

Turnover rate (log scale) is a function of the duration of time spent in the high risk group δ_H , where shorter time spent in the high risk group yields faster turnover. No turnover is indicated by $\delta_H^{-1} = 0.03$, due to population exit rate $\mu = 0.03$.

References

- Abdul-Quader, A.S., Baughman, A.L., Hladik, W., 2014. Estimating the size of key populations: Current status and future possibilities 9, 107–114. doi:[10.1097/COH.0000000000000041](https://doi.org/10.1097/COH.0000000000000041).
- Anderson, R.M., May, R.M., 1991. Infectious diseases of humans: dynamics and control. *Infectious diseases of humans: dynamics and control*. .
- Baral, S., Beyrer, C., Muessig, K., Poteat, T., Wirtz, A.L., Decker, M.R., Sherman, S.G., Kerrigan, D., 2012. Burden of HIV among female sex workers in low-income and middle-income countries: A systematic review and meta-analysis. *The Lancet Infectious Diseases* 12, 538–549. URL: <https://www.sciencedirect.com/science/article/pii/S147330991270066X?via=ihub>, doi:[10.1016/S1473-3099\(12\)70066-X](https://doi.org/10.1016/S1473-3099(12)70066-X).
- Baral, S., Ketende, S., Green, J.L., Chen, P.A.A., Grosso, A., Sithole, B., Ntshangase, C., Yam, E., Kerrigan, D., Kennedy, C.E., Adams, D., 2014. Reconceptualizing the HIV epidemiology and prevention needs of female sex workers (FSW) in Swaziland. *PLoS ONE* 9, e115465. doi:[10.1371/journal.pone.0115465](https://doi.org/10.1371/journal.pone.0115465).
- Baral, S., Logie, C.H., Grosso, A., Wirtz, A.L., Beyrer, C., 2013. Modified social ecological model: A tool to guide the assessment of the risks and risk contexts of HIV epidemics. *BMC Public Health* 13, 482. doi:[10.1186/1471-2458-13-482](https://doi.org/10.1186/1471-2458-13-482).
- Boily, M.C., Mâsse, B., 1997. Mathematical models of disease transmission: A precious tool for the study of sexually transmitted diseases. *Canadian Journal of Public Health* 88, 255–265. doi:[10.1007/bf03404793](https://doi.org/10.1007/bf03404793).
- Boily, M.C., Pickles, M., Alary, M., Baral, S., Blanchard, J., Moses, S., Vickerman, P., Mishra, S., 2015. What really is a concentrated HIV epidemic and what does it mean for West and Central Africa? Insights from mathematical modeling. *Journal of Acquired Immune Deficiency Syndromes* 68, S74–S82. doi:[10.1097/QAI.0000000000000437](https://doi.org/10.1097/QAI.0000000000000437).
- Case, K., Ghys, P., Gouws, E., Eaton, J., Borquez, A., Stover, J., Cuchi, P., Abu-Raddad, L., Garnett, G., Hallett, T., 2012. Understanding the modes of transmission model of new HIV infection and its use in prevention planning. *Bulletin of the World Health Organization* 90, 831–838. doi:[10.2471/blt.12.102574](https://doi.org/10.2471/blt.12.102574).
- Cori, A., Ayles, H., Beyers, N., Schaap, A., Floyd, S., Sabapathy, K., Eaton, J.W., Hauck, K., Smith, P., Griffith, S., Moore, A., Donnell, D., Vermund, S.H., Fidler, S., Hayes, R., Fraser, C., 2014. HPTN 071 (PopART): A cluster-randomized trial of the population impact of an HIV combination prevention intervention including universal testing and treatment: Mathematical model. *PLoS ONE* 9, e84511. URL: <https://dx.plos.org/10.1371/journal.pone.0084511>, doi:[10.1371/journal.pone.0084511](https://doi.org/10.1371/journal.pone.0084511).
- DataBank, 2019. Population estimates and projections. URL: <https://databank.worldbank.org/source/population-estimates-and-projections>.
- Eaton, J.W., Hallett, T.B., 2014. Why the proportion of transmission during early-stage HIV infection does not predict the long-term impact of treatment on HIV incidence. *Proceedings of the National Academy of Sciences* 111, 16202–16207. doi:[10.1073/pnas.1323007111](https://doi.org/10.1073/pnas.1323007111).
- Eaton, J.W., Johnson, L.F., Salomon, J.A., Bärnighausen, T., Bendavid, E., Bershteyn, A., Bloom, D.E., Cambiano, V., Fraser, C., Hontelez, J.A., Humair, S., Klein, D.J., Long, E.F., Phillips, A.N., Pretorius, C., Stover, J., Wenger, E.A., Williams, B.G., Hallett, T.B., 2012. HIV treatment as prevention: Systematic comparison of mathematical models of the potential impact of antiretroviral therapy on HIV incidence in South Africa. *PLoS Medicine* 9, e1001245. URL: <https://dx.plos.org/10.1371/journal.pmed.1001245>, doi:[10.1371/journal.pmed.1001245](https://doi.org/10.1371/journal.pmed.1001245).
- Fenton, K.A., Breban, R., Vardavas, R., Okano, J.T., Martin, T., Aral, S., Blower, S., 2008. Infectious syphilis in high-income settings in the 21st century. *The Lancet Infectious Diseases* 8, 244–253. doi:[10.1016/S1473-3099\(08\)70065-3](https://doi.org/10.1016/S1473-3099(08)70065-3).
- Fergus, S., Zimmerman, M.A., Caldwell, C.H., 2007. Growth trajectories of sexual risk behavior in adolescence and young adulthood. *American Journal of Public Health* 97, 1096–1101. doi:[10.2105/AJPH.2005.074609](https://doi.org/10.2105/AJPH.2005.074609).
- Ganem, D., Prince, A.M., 2004. Hepatitis B Virus Infection — Natural History and Clinical Consequences. *New England Journal of Medicine* 350, 1118–1129. doi:[10.1056/NEJMra031087](https://doi.org/10.1056/NEJMra031087).

- Garnett, G.P., Anderson, R.M., 1994. Balancing sexual partnership in an age and activity stratified model of HIV transmission in heterosexual populations. *Mathematical Medicine and Biology* 11, 161–192. doi:[10.1093/imammb/11.3.161](https://doi.org/10.1093/imammb/11.3.161).
- Hanley, J.A., 2001. A heuristic approach to the formulas for population attributable fraction. *Journal of Epidemiology and Community Health* 55, 508–514. doi:[10.1136/jech.55.7.508](https://doi.org/10.1136/jech.55.7.508).
- Henry, C.J., Koopman, J.S., 2015. Strong influence of behavioral dynamics on the ability of testing and treating HIV to stop transmission. *Scientific Reports* 5, 9467. doi:[10.1038/srep09467](https://doi.org/10.1038/srep09467).
- Hontelez, J.A.C., Lurie, M.N., Bärnighausen, T., Bakker, R., Baltussen, R., Tanser, F., Hallett, T.B., Newell, M.L., de Vlas, S.J., 2013. Elimination of HIV in South Africa through Expanded Access to Antiretroviral Therapy: A Model Comparison Study. *PLoS Medicine* 10, e1001534. URL: <http://dx.plos.org/10.1371/journal.pmed.1001534>, doi:[10.1371/journal.pmed.1001534](https://doi.org/10.1371/journal.pmed.1001534).
- ICAP, 2019. PHIA Project. URL: <https://phia.icap.columbia.edu>.
- Johnson, L.F., Geffen, N., 2016. A Comparison of two mathematical modeling frameworks for evaluating sexually transmitted infection epidemiology. *Sexually Transmitted Diseases* 43, 139–146. doi:[10.1097/OLQ.0000000000000412](https://doi.org/10.1097/OLQ.0000000000000412).
- Knight, J., Wang, L., Ma, H., Schwartz, S., Baral, S., Mishra, S., 2019. The influence of risk group turnover in STI/HIV epidemics: mechanistic insights from transmission modeling, in: *STI & HIV 2019 World Congress*, Vancouver, BC, Canada. URL: https://sti.bmj.com/content/95/Suppl_1/A83.3.
- Koopman, J.S., Jacquez, J.A., Welch, G.W., Simon, C.P., Foxman, B., Pollock, S.M., Barth-Jones, D., Adams, A.L., Lange, K., 1997. The role of early HIV infection in the spread of HIV through populations. *Journal of Acquired Immune Deficiency Syndromes* 14, 249–58. URL: <http://www.ncbi.nlm.nih.gov/pubmed/9117458>.
- Kraft, D., 1988. A software package for sequential quadratic programming. Technical Report DFVLR-FB 88-28. DLR German Aerospace Center — Institute for Flight Mechanics. Koln, Germany.
- LAPACK, 1992. LAPACK: Linear Algebra PACKage. URL: <http://www.netlib.org/lapack>.
- Lawson, C.L., Hanson, R.J., 1995. Solving least squares problems. volume 15. SIAM.
- Maartens, G., Celum, C., Lewin, S.R., 2014. HIV infection: Epidemiology, pathogenesis, treatment, and prevention. *The Lancet* 384, 258–271. doi:[10.1016/S0140-6736\(14\)60164-1](https://doi.org/10.1016/S0140-6736(14)60164-1).
- Maheu-Giroux, M., Vesga, J.F., Diabaté, S., Alary, M., Baral, S., Diouf, D., Abo, K., Boily, M.C., 2017. Changing Dynamics of HIV Transmission in Côte d’Ivoire: Modeling Who Acquired and Transmitted Infections and Estimating the Impact of Past HIV Interventions (1976-2015). *Journal of Acquired Immune Deficiency Syndromes* 75, 517–527. doi:[10.1097/QAI.0000000000001434](https://doi.org/10.1097/QAI.0000000000001434).
- Malthus, T.R., 1798. *An Essay on the Principle of Population*.
- Marston, C., King, E., 2006. Factors that shape young people’s sexual behaviour: a systematic review. *Lancet* 368, 1581–1586. doi:[10.1016/S0140-6736\(06\)69662-1](https://doi.org/10.1016/S0140-6736(06)69662-1).
- May, R.M., Anderson, R.M., 1988. The transmission dynamics of human immunodeficiency virus (HIV). doi:[10.1098/rstb.1988.0108](https://doi.org/10.1098/rstb.1988.0108).
- Mishra, S., Boily, M.C., Schwartz, S., Beyrer, C., Blanchard, J.F., Moses, S., Castor, D., Phaswana-Mafuya, N., Vickerman, P., Drame, F., Alary, M., Baral, S.D., 2016. Data and methods to characterize the role of sex work and to inform sex work programs in generalized HIV epidemics: evidence to challenge assumptions. *Annals of Epidemiology* 26, 557–569. doi:[10.1016/j.annepidem.2016.06.004](https://doi.org/10.1016/j.annepidem.2016.06.004).
- Mishra, S., Pickles, M., Blanchard, J.F., Moses, S., Boily, M.C., 2014. Distinguishing sources of HIV transmission from the distribution of newly acquired HIV infections: Why is it important for HIV prevention planning? *Sexually Transmitted Infections* 90, 19–25. doi:[10.1136/sextrans-2013-051250](https://doi.org/10.1136/sextrans-2013-051250).
- Mishra, S., Steen, R., Gerbase, A., Lo, Y.R., Boily, M.C., 2012. Impact of High-Risk Sex and Focused Interventions in Heterosexual HIV Epidemics: A Systematic Review of Mathematical Models. *PLoS ONE* 7, e50691. doi:[10.1371/journal.pone.0050691](https://doi.org/10.1371/journal.pone.0050691).

[pone.0050691](#).

- Mukandavire, C., Walker, J., Schwartz, S., Boily, M.C., Danon, L., Lyons, C., Diouf, D., Liestman, B., Diouf, N.L., Drame, F., Coly, K., Muhire, R.S.M., Thiam, S., Diallo, P.A.N., Kane, C.T., Ndour, C., Volz, E., Mishra, S., Baral, S., Vickerman, P., 2018. Estimating the contribution of key populations towards the spread of HIV in Dakar, Senegal. *Journal of the International AIDS Society* 21, e25126. doi:[10.1002/jia2.25126](#).
- Pickles, M., Boily, M.C., Vickerman, P., Lowndes, C.M., Moses, S., Blanchard, J.F., Deering, K.N., Bradley, J., Ramesh, B.M., Washington, R., Adhikary, R., Mainkar, M., Paranjape, R.S., Alary, M., 2013. Assessment of the population-level effectiveness of the Avahan HIV-prevention programme in South India: A preplanned, causal-pathway-based modelling analysis. *The Lancet Global Health* 1, e289–e299. doi:[10.1016/S2214-109X\(13\)70083-4](#).
- Pourbohloul, B., Rekart, M.L., Brunham, R.C., 2003. Impact of mass treatment on syphilis transmission: A mathematical modeling approach. *Sexually Transmitted Diseases* 30, 297–305. doi:[10.1097/00007435-200304000-00005](#).
- Prüss-Ustün, A., Wolf, J., Driscoll, T., Degenhardt, L., Neira, M., Calleja, J.M.G., 2013. HIV Due to Female Sex Work: Regional and Global Estimates. *PLoS ONE* 8, e63476. doi:[10.1371/journal.pone.0063476](#).
- Shubber, Z., Mishra, S., Vesga, J.F., Boily, M.C., 2014. The HIV modes of transmission model: A systematic review of its findings and adherence to guidelines. *Journal of the International AIDS Society* 17, 18928. doi:[10.7448/IAS.17.1.18928](#).
- Stigum, H., Falck, W., Magnus, P., 1994. The core group revisited: The effect of partner mixing and migration on the spread of gonorrhea, chlamydia, and HIV. *Mathematical Biosciences* 120, 1–23. doi:[10.1016/0025-5564\(94\)90036-1](#).
- The DHS Program, 2019. Data. URL: <https://www.dhsprogram.com>.
- Wasserheit, J.N., Aral, S.O., 1996. The Dynamic Topology Of Sexually Transmitted Disease Epidemics: Implications For Prevention Strategies. *Journal of Infectious Diseases* 174, S201–S213. URL: https://academic.oup.com/jid/article-lookup/doi/10.1093/infdis/174.Supplement_{_}2.S201, doi:[10.1109/ICPDS.2016.7756727](#).
- Watts, C., Zimmerman, C., Foss, A.M., Hossain, M., Cox, A., Vickerman, P., 2010. Remodelling core group theory: the role of sustaining populations in HIV transmission. *Sexually Transmitted Infections* 86, iii85–iii92. doi:[10.1136/sti.2010.044602](#).
- World Health Organization, 2016. Consolidated guidelines on HIV prevention, diagnosis, treatment and care for key populations. WHO Guidelines .
- Yorke, J.A., Hethcote, H.W., Nold, A., 1978. Dynamics and control of the transmission of gonorrhea. *Sexually Transmitted Diseases* 5, 51–56. doi:[10.1097/00007435-197804000-00003](#).
- Zhang, X., Zhong, L., Romero-Severson, E., Alam, S.J., Henry, C.J., Volz, E.M., Koopman, J.S., 2012. Episodic HIV Risk Behavior Can Greatly Amplify HIV Prevalence and the Fraction of Transmissions from Acute HIV Infection. *Statistical Communications in Infectious Diseases* 4. doi:[10.1515/1948-4690.1041](#).