Risk Group Dynamics in Simulated STI Epidemics

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Contents

Key Contributions

1. Formalize a mathematical framework for risk group dynamics
2. Describe methods for deriving risk group dynamics parameters from common data sources
3. Illustrate differences in modelled projections for different implementations of risk group dynamics, using an example sexually transmitted infection

1 Background

** R O U G H **

- key factors in risk of HIV acquisition
- intro HIV modelling, prior work showing importance of heterogeneity
- prior work on turnover, comment on need for "equilibration"

Some papers to include in Table 1: [1, 2, 3, 4, 5, 6, 7, 8, 9, 10]

What do we mean by "risk group dynamics"?

1. inclusion of risk groups at all (yes / no)
2. inclusion of turnover among these groups (yes / no, how?)
3. consideration of how groups are re-balanced given differential attributable death

From Eaton and Hallett (2014) [3]: *Two behavioral parameters – the rate of transition from higher- to lower-risk groups and* [...] *– were particularly important for simulating the observed prevalence trend in many different ways, as well as determining the intervention impact.*

2 The System

This section introduces a system of compartments, flows, and equations which describe a reasonably complete formulation of risk group dynamics.

We denote the variable representing the size of risk group $i \in [1, \dots, \mathrm{G}]$ as x_i and the vector of all x_i as $\boldsymbol{x}$. The total population size is denoted $\mathrm{N} = \sum_i x_i$, and the proportions represented by each group by $\hat{x}_i = x_i \mathrm{N}^{-1}$. The rate of population entry for all groups is denoted by ν, and the rate of exit by μ; this is separated from the rate of disease-attributable death, which varies by group and is denoted ϕ_i. All rates have units *per year* (yr^{-1}). The proportion of the entering population who are in group i, which may not be equal to the proportion of the current population in group i, is denoted $\hat{e}_i$. Since the rate of entry ν is typically expressed as a proportion of the total population size N, we model the theoretical entering population $\boldsymbol{e}$ as also having size N, so that $e_i = \hat{e}_i \mathrm{N}$.

Turnover transitions can occur between any two groups, in either direction; therefore we denote the turnover rates as a $\mathrm{G} \times \mathrm{G}$ matrix ζ, where ζ_{ij} corresponds to the transition $x_i \to x_j$. An explicit definition is given in Eq. (2.1), where the diagonal elements are denoted $*$ since they represent transitions from a group to itself, which is inconsequential.

$$\zeta = \begin{bmatrix} * & x_1 \to x_2 & \cdots & x_1 \to x_{\mathrm{G}} \\ x_2 \to x_1 & * & \cdots & x_2 \to x_{\mathrm{G}} \\ \vdots & \vdots & \ddots & \vdots \\ x_{\mathrm{G}} \to x_1 & x_{\mathrm{G}} \to x_2 & \cdots & * \end{bmatrix} \tag{2.1}$$

These transition flows and the associated rates are summarized for $\mathrm{G} = 3$ in Figure 1.

2.1 Parameterization

This section outlines methods for defining the values of parameters in the system described above, directly from some commonly available sources of data. In particular, we are interested in estimating ν, μ, $\hat{\boldsymbol{x}}$, $\hat{\boldsymbol{e}}$, and ζ, since ϕ is essentially a biological parameter whose value will not depend on the epidemic context.

In most cases, there will not be sufficient data to directly estimate all parameters, especially ζ. The next section outlines additional methods to solve for these values.

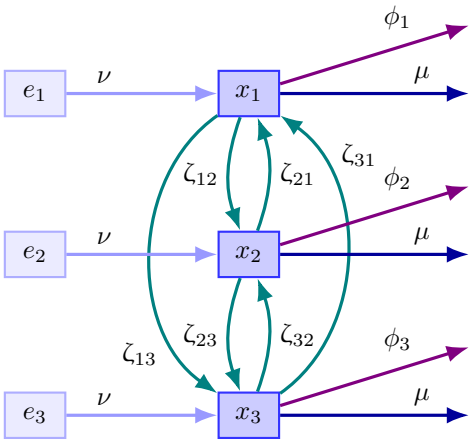

Figure 1: System of compartments and flows between them for $\text{G} = 3$

* (discuss latent assumptions with each of these approaches)

If we know the population size over time $\text{N}(t)$, then ...

If we know the annual growth rate over time $\mathcal{G}(t)$, then ...

$$\mathcal{G} = \nu - \mu \tag{2.2}$$

If we know the duration of time spent in a particular group, then ...

$$\mathcal{D}_i = \left(\mu + \phi_i + \sum_j \zeta_{ij} \right)^{-1} \tag{2.3}$$

If we know the proportion z of group i who transition to group j in a given year, then ...

$$\zeta_{ij} = z \tag{2.4}$$

Overall, we can write the system as a mass-balance equation, so that the rate of change of group x_i is simply the sum of flows in / out of the group,

$$\frac{d}{dt} x_i = \nu \, e_i + \sum_j \zeta_{ji} \, x_j - x_i \left(\mu + \phi_i + \sum_j \zeta_{ij} \right) \tag{2.5}$$

While Eq. (2.5) is written in terms of absolute population sizes $\boldsymbol{x}$ and $\boldsymbol{e}$, it is equivalent to divide through by N, yielding a system in terms of $\hat{\boldsymbol{x}}$ and $\hat{\boldsymbol{e}}$, the latter often proving more useful, since N need not be known.

2.2 Solving the System

In order to solve the system, we first note that the desired rate of change for risk group i will be equal to the growth of the risk group, $\mathcal{G} x_i$. Substituting this quantity into Eq. (2.5), we have

$$\mathcal{G} x_i = \nu \, e_i + \sum_j \zeta_{ji} \, x_j - x_i \left(\mu + \phi_i + \sum_j \zeta_{ij} \right) \tag{2.6}$$

which, using the definition of $\mathcal{G}$ in Eq. (2.2), we can simplify to

$$\nu \, x_i = \nu \, e_i + \sum_j \zeta_{ji} \, x_j - x_i \phi_i - x_i \sum_j \zeta_{ij} \tag{2.7}$$

Table 1: Summary of prior work with respect to modelled risk group dynamics.

Ref.	Year	Author	Risk Groups G	Mortality ϕ	Dynamic Rebalance RB	Turnover ζ
[6]	2008	Hallett et al.	3	Yes	None	None
[1]	2012	Barnighausen et al.	1	Yes	None	N/A
[4]	2012	Estill et al.	1	Yes	None	N/A
[2]	2013	Cremin et al.	3	Yes	None	None
[3]	2014	Eaton and Hallett	3	Yes	None	Constant
		...				

2.2.1 Solving for ζ

To solve for We rearrange Eq. (2.7) to obtain [1]

$$\nu\,(x_i - e_i) + \phi_i\,x_i = \sum_j \zeta_{ji}\,x_j - \sum_j \zeta_{ij}\,x_i \tag{2.8}$$

which, considering all i, can be refactored to yield a system of the form:

$$\boldsymbol{b} = A\boldsymbol{z} \tag{2.9}$$

where $\boldsymbol{b} = \nu(\boldsymbol{x} - \boldsymbol{e}) + \boldsymbol{\phi}\,\boldsymbol{x}$ is a G-length vector, A is a $\mathrm{G} \times \mathrm{G}^2$ matrix of coefficients, and $\boldsymbol{z} = \mathrm{vec}(\zeta)$ is the G^2-length vectorization of ζ.

2.2.2 Solving for e

To solve for $\boldsymbol{e}$, we rearrange Eq. (2.7) to obtain

$$e_i = x_i - \left[\sum_j \zeta_{ji}\,x_j - \sum_j \zeta_{ij}\,x_i - \phi_i\,x_i\right]\nu^{-1} \tag{2.10}$$

2.2.3 Numerical Solutions

* (from `/docs/idea/turnover.pdf`, § 2.2)

2.3 Prior Work

In this section, we will examine previous approaches to modelling risk groups in simulated HIV epidemics, and the assumptions inherent to these methods. Box 1 summarizes the most common assumptions regarding the dynamics of these risk groups, while Table 1 summarizes previous works with respect to these assumptions.

Many of the previously proposed models of HIV transmission follow Assumption 1.1. and do not consider heterogeneity in risk of acquisition within major demographic groups, such as heterosexual men / women, and MSM. This is a significant assumption, and may lead to large discrepancies with models which do consider risk heterogeneity, as explored in Section 3. Moreover, this assumption precludes any consideration of turnover, since there is only one risk group, $\mathrm{G} = 1$.

* (discussion of each assumption in turn)

3 Experiment

In this section, we explore differences in projected model outputs under different implementations of risk groups dynamics, using a simple model of heterosexual HIV transmission.

[1] Using matrix notation, we *could* rewrite the RHS of Eq. (2.8) as: $(\boldsymbol{x}^\mathsf{T}\zeta)^\mathsf{T} - \zeta\,\boldsymbol{x}$, but this doesn't actually help us too much here.

Box 1: Common assumptions regarding the dynamics of risk groups

1. **Risk Groups:** Major demographic groups are stratified by risk of HIV acquisition.
   - 1.1. **No:** $\mathrm{G} = 1$; Major demographic groups are homogeneous in risk of HIV acquisition.
   - 1.2. **Yes:** $\mathrm{G} > 1$; Heterogeneity in risk of HIV acquisition within major demographic groups is considered.
2. **Attributable Death:** Deaths attributable to HIV affect the group sizes $\boldsymbol{x}$.
   - 2.1. **No:** $\boldsymbol{\phi} = 0$; Death attributable to HIV is not considered.
   - 2.2. **Yes:** $\boldsymbol{\phi} > 0$; Attributable death is considered.
3. **Risk Group Re-Balancing:** Dynamic rate parameters attempt to re-balance the groups. (due to changes from attributable death)
   - 3.1. **No:** $\hat{\boldsymbol{x}} = f(t)$; Group proportions $\hat{\boldsymbol{x}}$ are not re-balanced.
   - 3.2. **Yes via $\hat{\boldsymbol{e}}$:** $\hat{\boldsymbol{e}} = f(\hat{\boldsymbol{x}})$; Group proportions $\hat{\boldsymbol{x}}$ are re-balanced using a dynamic distribution of the entering population $\hat{\boldsymbol{e}}$.
   - 3.3. **Yes via ζ:** $\zeta = f(\hat{\boldsymbol{x}})$; Group proportions $\hat{\boldsymbol{x}}$ are re-balanced using dynamic rates of turnover among risk groups ζ.
4. **Turnover:** Individuals may move between risk groups.
   - 4.1. **No:** $\zeta = 0$; Individuals do not move between risk groups.
   - 4.2. **Constant:** $\zeta = C$; Individuals move between risk groups at a constant rate.
   - 4.3. **Dynamic:** $\zeta = f(\hat{\boldsymbol{x}})$; Individuals move between risk groups in response to the current model state.
5. **Population Growth:** Increase in the total N over time.
   - 5.1. **No:** $\nu = \mu$; Population size N is constant.
   - 5.2. **Yes:** $\nu > \mu$; Population size N increases, at some constant or data-driven rate.

Table 2: Model parameters – e.g. table

Symbol	Description	Value
β	Probability of transmission per partnership	e.g.
	...	

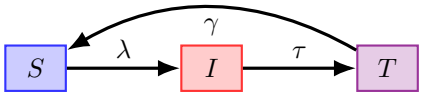

Figure 2: Modelled health states

3.1 Model Overview

Our model of HIV transmission includes 3 health states (Figure 2), and 3 levels of sexual activity (risk groups, $\text{G} = 3$). ...

3.2 Risk Group Implementations

Drawing on the most common assumptions outlined in Box 1, we define a series of model variants for investigation; these variants are summarized in Figure 3.

3.3 Simulations

The simulated epidemic is initialized in 1975 with ...

* (The outcomes in which differences will be quantified):

1. Projected prevalence for $t = 1975 - 2050$
2. Population attributable fraction of highest risk group (variants with $\text{G} = 3$ only)
3. Estimated impact of {intervention x – ART?} at reducing cumulative new infections between 2020 and 2050

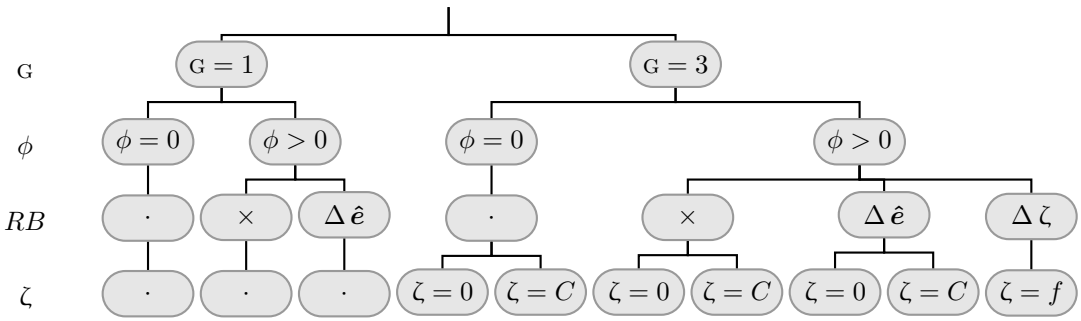

Figure 3: Summary of 10 model variants with respect to risk group dynamics. G: number of risk groups, ϕ: rate of HIV-attributable death, RB: re-balancing method, ζ: rates of population turnover, $(\cdot)$: not applicable, $(\times)$: "no", $\Delta\hat{\boldsymbol{e}}$: dynamic distribution of entering population, $\Delta\zeta$: dynamic rates of turnover, C: a constant, f: a function.

Figure 4: Projected prevalence under each of the 10 model variants.

Figure 5: Estimated impact of {intervention x} on cumulative new infections between 2020 and 2050.

4 Results

5 Discussion

6 Conclusions

7 References

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