Risk Group Dynamics in Simulated STI Epidemics

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November 1, 2018

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
- comments on applicability of these concepts to non-HIV transmissible diseases (other STI, non-S TI)
- prior work on turnover, comment on need for "equilibration" / "burn-in" period

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 – subject of future work

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.*

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

2 The System

This section introduces a system of compartments, flows, and equations which can be used to describe 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. We do not consider disease-attributable death, which may vary by group, though this will be the subject of future work. 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

Next, we explore methods for estimating the values of parameters in the system described above (ν, μ, $\hat{\boldsymbol{x}}$, $\hat{\boldsymbol{e}}$, and ζ) directly from some commonly available sources of data.

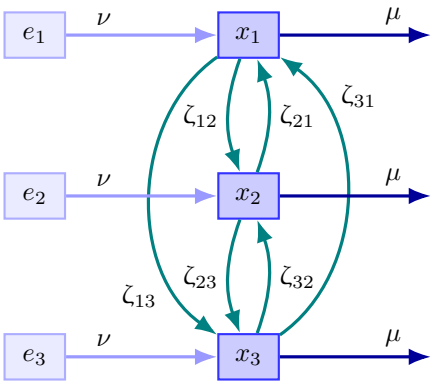

Figure 1: System of compartments and flows between them for $\mathrm{G} = 3$

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.

* (discuss latent assumptions with each of these approaches)

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

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

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,

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

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

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

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

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

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

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

2.2.1 Solving for ζ

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

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

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

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

where $\boldsymbol{b} = \nu(\boldsymbol{x} - \boldsymbol{e})$ 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

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

2.2.3 Numerical Solutions

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

* This is only applicable to 2.2.1, should rearrange ...

2.3 Previous Approaches

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)

[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. **Turnover:** Individuals may move between risk groups.
   - 2.1. **No:** $\zeta = 0$; Individuals do not move between risk groups.
   - 2.2. **Constant:** $\zeta = C$; Individuals move between risk groups at a constant rate.
   - 2.3. **Dynamic:** $\zeta = f$; Individuals move between risk groups in dynamically.
3. **Population Growth:** Increase in the total N over time.
   - 3.1. **No:** $\nu = \mu$; Population size N is constant.
   - 3.2. **Yes:** $\nu > \mu$; Population size N increases, at some constant or data-driven rate.

Table 2: Model parameters – e.g. table

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

Figure 2: Modelled health states

3 Experiment

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

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 Model Variants

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 ...

* Describe the scenario

This epidemic was simulated using each of the model variants described in § 3.2. In each case, we compared the model predictions across the variants regarding three outputs:

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

...

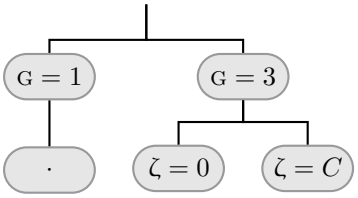

Figure 3: Summary of 3 model variants with respect to models of population turnover. G: number of risk groups, ζ: rates of population turnover, $(\cdot)$: not applicable, C: a constant

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.

Since the results of these comparisons are significantly affected by several model parameters, we performed a comprehensive sensitivity analysis. The parameter ranges specified in Table 2 were used, and ...

* (construct a GLM or something to describe the impacts?)

4 Results

5 Discussion

6 Conclusions

7 References

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