Agent-based model of HIV transmission in the population of Dutch MSM

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1 Introduction

HIV transmission in the population of men who have sex with men (MSM) occurs predominantly via anal sexual intercourse [1]. This interaction occurs within the context of sexual partnerships. Thus, to accurately model the transmission dynamics of HIV in the population of MSM, the model should capture the dynamic nature of the sexual network and its dependence on the demographic makeup of this group.

The model we describe in this document incorporates the demographic process of inflow and outflow of individuals in the population, as well as formation and dissolution of sexual partnerships. This model was based on an agent-based model used by Kretzchmar et al [2] to evaluate effects of screening and partner notification on Chlamydia positivity in the United States.

2 The model

The model is a stochastic agent-based model, viewing the population as a set of distinct individuals, who enter and leave the population. While being a part of the population, as time of the simulation goes by, individuals age and subsequently some of their demographic properties (e.g., background death rate) and sexual mixing properties (e.g., propensity to form new partnerships) change. Two different type of partnerships can appear between individuals and subsequently dissolve: steady (a long-term partnership) and non-steady (a much briefer partnership). Below we provide the summary of our approach to modeling demographic and sexual networking processes.

2.1 Demographic processes

The demographic processes involve entrance of individuals to the population, their exit from the population and ageing. The simulation starts with a non-empty population of MSM. Each individual has an age. Here, we consider only the individuals who are sexually active, thus we consider the individuals between ages of 15 and 75 years. As time in the simulation passes by, individuals age. We model ageing where all individuals in the population age by 1 year every 365 days, starting from the start of the simulation run. At the age of 75 years, individuals are removed from the population without replacement. In addition to leaving the population after cessation of sexual activity, individuals can leave the population at any other moment as a result of background age-dependent mortality. We assign the mortality rates as follows. We divide the age interval of 15-75 into 6 sub-intervals of length 10: 15-25, 25-35, ... , 65-75. To each sub-interval we assign a mortality rate [3]. Thus, each individual is characterized by a mortality rate corresponding to the age bracket to which they belong. As individuals age and move from one bracket to the other, their mortality rate changes respectively. To model appearance (or "birth") of new individuals in the population we assume that birth of new individuals is a Poisson process with mean of λ individuals per year. We also refer to λ as a mean birth rate. All new individuals are assigned the age of 15 years, their mortality rate is set respectively and they are assigned empty sexual history.

The demographic component of the model requires the following parameters and distributions:

1. **Initial population size.** It can be shown that in analogous deterministic model with similar mechanisms of birth, death and ageing, the population size remains in a quasi-stationary state. We expect a similar outcome in our stochastic agent-based model. While the size of the population of MSM in the Netherlands is estimated to be between 200,000 and 300,000 individuals [4], simulations with this population size would not be computationally tractable. We use the size of the population equal to 20,000 individuals which is both computationally tractable and large enough to provide representative results that can be extended to the national level.

2. **Distribution of mortality rates for each age bracket.** We will use WHO life tables for the Netherlands [3] to directly calculate the background mortality rate corresponding to each bracket.

3. **Mean birth rate.** As mentioned above, the population size resides in the state of pseudo-equilibrium which we set to be 20,000 individuals. Using this value and known distribution of mortality rates, we will calculate mean birth rate using the analogous deterministic model.

4. **Initial age distribution of the population.** We will use the publicly available data for the general male population of the Netherlands [5].

2.2 Sexual network formation models

In the course of their lifetime individuals in the population can participate in two types of partnerships: steady and non-steady. Respectively, we refer to partners in these partnerships as steady and non-steady partners. We use the definition of steady partnerships given in EMIS 2010 [6] and EMIS 2017 [7]: individuals currently participating in a relationship such that they do not consider themselves to be single. Non-steady partners are partners in all other partnerships where sex is taking place. According to the classification used in Amsterdam Cohort Study survey, these partnerships can be further classified by their duration into three sub-types: 1. one time contacts; 2. ongoing sexual partnership arrangements ("sex-buddy") and 3. the partnerships which involve more than one contact but which are not sustained for a long time. The current version of the model is based on the data collected during EMIS 2010 survey [6]. This survey, while highly detailed in many respects, does not enquire into duration of partnerships for either steady or non-steady partnerships (except for currently ongoing steady partnerships). Therefore, to estimate the average duration of both types of partnership we will use ACS data. In the current version of the model, the three types of non-steady partnerships are not distinguished and are treated as one type of partnership that lasts on average for a few days. In the version to follow, we will introduce the sub-classification of non-steady partnerships, each with respective average duration.

2.3 Formation of steady partnership network

Analysis of EMIS 2010 data has shown that while a large proportion of men who have sex with men were either single (approximately 49%) or in a steady partnership with one man only (44%), there is a significant proportion of them (7%) who at the time of the survey were in a steady partnership with more than one man. Since this proportion is non-negligible and the concurrency is a very important factor in driving spread of sexually transmitted diseases [8], our model assumed that at any moment in time an individual can be single or in a partnership with one or two men.

At each point in time, in our model, a number of individuals can form new partnerships and a number of existing partnerships can dissolve. The number of new pairs depends on the number of available individuals (i.e. individuals with less than two steady partners) and the rate of steady partnership formation. The number of dissolved partnerships depends on the average duration of a steady partnership. Since the proportion of individuals in two concurrent steady partnerships is significantly smaller than proportion of people who participate in one steady partnership only, we model that individuals with one existing partnership have lower probability of participating in a second steady partnership than single individuals. We assume that each individual when single has the same rate of entering a steady partnership and that the duration of each partnership is on average is the same for each pair.

Finally, in the current version of the model, steady partnership formation does not incorporate age mixing. This assumption will be relaxed in the model version to follow.

The formation process of non-steady partnership networks requires the following parameters and distributions:

1. **Average duration of steady partnership:** This value can be calculated directly form ACS data.

2. **Formation rate of steady partnerships:** While this value is hard to calculate directly, it is possible to obtain by calibrating models outputs to the available data. We will use the following two distributions: current number of steady partners and the number of steady partners within the last 12 months. Our model indicates that after a transient period both of these distributions settle in a quasi-stationary state.

3. **Reduction in probability of entering a new steady partnership when already participating in one:** We will estimate this parameter by calibrating the model output to the distribution of the current number of steady partners.

2.4 Formation of non-steady partnership network

In addition to steady partnerships, individuals can form non-steady partnerships. The data indicates that propensity to form such partnerships is heterogeneous with some individuals reporting very few (0-2, [6]) over 12 month period, while others reporting much higher numbers (> 12) over the same period of time. Available data from ACS indicates that most non-steady partnerships are brief, lasting just a few days. Therefore, the approach we took with modeling steady partnership formation is not a suitable fit for non-steady partnership formation, as due to their brevity, the non-steady partnerships for most individuals rarely overlap. It is more organic to instead consider the possibility that each individual has a characteristic rate (propensity) of forming non-steady partnerships. Individuals with higher propensity have a higher chance of being recruited to form such partnerships than individuals with lower.

Similar to steady partnerships modeling paradigm, at each point in time individuals can form a new non-steady partnerships and existing non-steady partnerships can dissolve.

The number of new pairs formed at each point in time depends on the number of individuals in the population and the formation rate of non-steady partnerships. If the simulation determines that a pair is to be formed, it recruits two potential partners from population such that individuals with higher propensity to form this type of the partnership are picked with higher probability. The number of partnerships that dissolve depend on the average duration of a non-steady partnership.

The formation process of non-steady partnership networks requires the following parameters and distributions:

1. **Average duration of a partnership:** This value can be calculated directly using data from Network Study among MSM in Amsterdam.

2. **Distribution of propensities to form a non-steady partnership:** It is not tenable to measure this distribution directly due to the challenges of quantifying it. However, ultimately we seek to match the available data [6, 7] about the number of non-steady partners individuals report per year. Therefore, we use this reported distribution as a proxy to the propensity of forming new partnerships. Its scale is non-consequential as we re-scale the sum of propensities of all individuals in the population to 1.

3. **Rate of formation of non-steady partnership:** We will estimate this parameter by matching the output of our model (distribution of the number of non-steady partners in the last 12 months) to the available data. In our model, this distribution converges to a quasi-stationary state and this is the measurement that we will use to estimate this parameter.

Available data (EMIS 2010 and 2017) indicates that the individual propensity to form non-steady partnerships is age-dependent. Using the same age brackets as were defined for the demographic process, the distribution of propensities can be calculated. Thus, individuals are assigned propensity to form non-steady partnerships based on their age. As individuals age from one age bracket to the other, this propensity is re-assigned.

2.5 General simulation process

Since the model is stochastic, to obtain comprehensive description of its dynamics, for each scenario that we will consider, we will run an ensemble of simulations. Each simulation will run in the identical way in terms of processing events. Below we give the description of the simulation of demographics and sexual network formation processes. The algorithm performs operations as following:

1. At the start of the simulation, read specifications of the simulation from a user-provided file. These specifications include: total time of the simulation T (number of days), the initial size of the population, age distribution, background non-HIV related mortality rates, incoming rate of individuals to the population, rates of formation and dissolution of steady and non-steady partnerships, probability reduction parameter for forming a steady partnership when already participating in one and the distribution of the number of non-steady partners in 12 months (distributed by age).

2. Initialize the system by setting time counter t equal to 0, allocating space for the population registry containing the following information: identifier number, age (years), propensity to

form non-steady partnerships, identifying numbers of currently ongoing steady and non-steady partners and time when partnerships commenced (both current and past).

3. Increasing time counter t one day at a time perform the following operations until t exceeds T.

   (a) For each individual in the population determine whether they die at this time step. Additionally, find individuals whose age exceeds 75 years, they will also leave the population. For these individuals who are removed from the population, erase their respective records from their personal registry, as well as dissolve their currently ongoing partnerships and update their partners, steady and non-steady.

   (b) If counter t has crossed a new year mark (i.e. it is a multiple of 365), run the ageing procedure. Ageing procedure increases age of each by 1 year. For each individual who have crossed in this time unit from one age bracket to the other, adjust their mortality and propensity to form non-steady partnerships.

   (c) Determine the number of possible new steady partnerships by identifying all individuals who can form them and removing duplicates by checking whether individuals in the "available" pool are already in a steady or non-steady partnership. Select a subset of these partnerships as the ones that formed. The size of the subset is determined by the steady partnership formation rate. For each partnership that is formed select its members. Individuals with no existing steady partners are picked with higher probability.

   (d) For each existing steady pair, excluding the pairs formed in this time step, determine whether it dissolves. The dissolution rate is determined by the average duration of steady partnerships.

   (e) Determine the number of possible new non-steady partnerships by removing duplicates by checking whether individuals in the "available" pool are already in a steady or non-steady partnership. Note that the size of the "available" pool is constant and is equal to $N(t)(N(t)-1)/2$ where $N(t)$ is the size of the population at time t. Select a subset of these partnership as the ones that formed. The size of the subset is determined by the non-steady partnership formation rate. For each partnership that is formed select its members. Individuals with higher propensity to form non-steady partnerships are picked with higher probability.

   (f) For each existing non-steady pair, excluding the pairs formed in this time step, determine whether it dissolves. The dissolution rate is determined by the average duration of non-steady partnerships.

   (g) Determine the number of new individuals entering the population. Generate unique identification numbers for the incoming individuals and set their age equal to 15 years. Determine their propensity to form non-steady partnerships and initialize new records in partnership registries.

   (h) Increment time counter by 1 day.

4. Collect and record outputs.

Figure 1 contains the pictorial summary of the above described process.

Once the simulation has finished its run, the outcomes of the simulation will be quantified and recorded in .csv format for the subsequent data analysis.

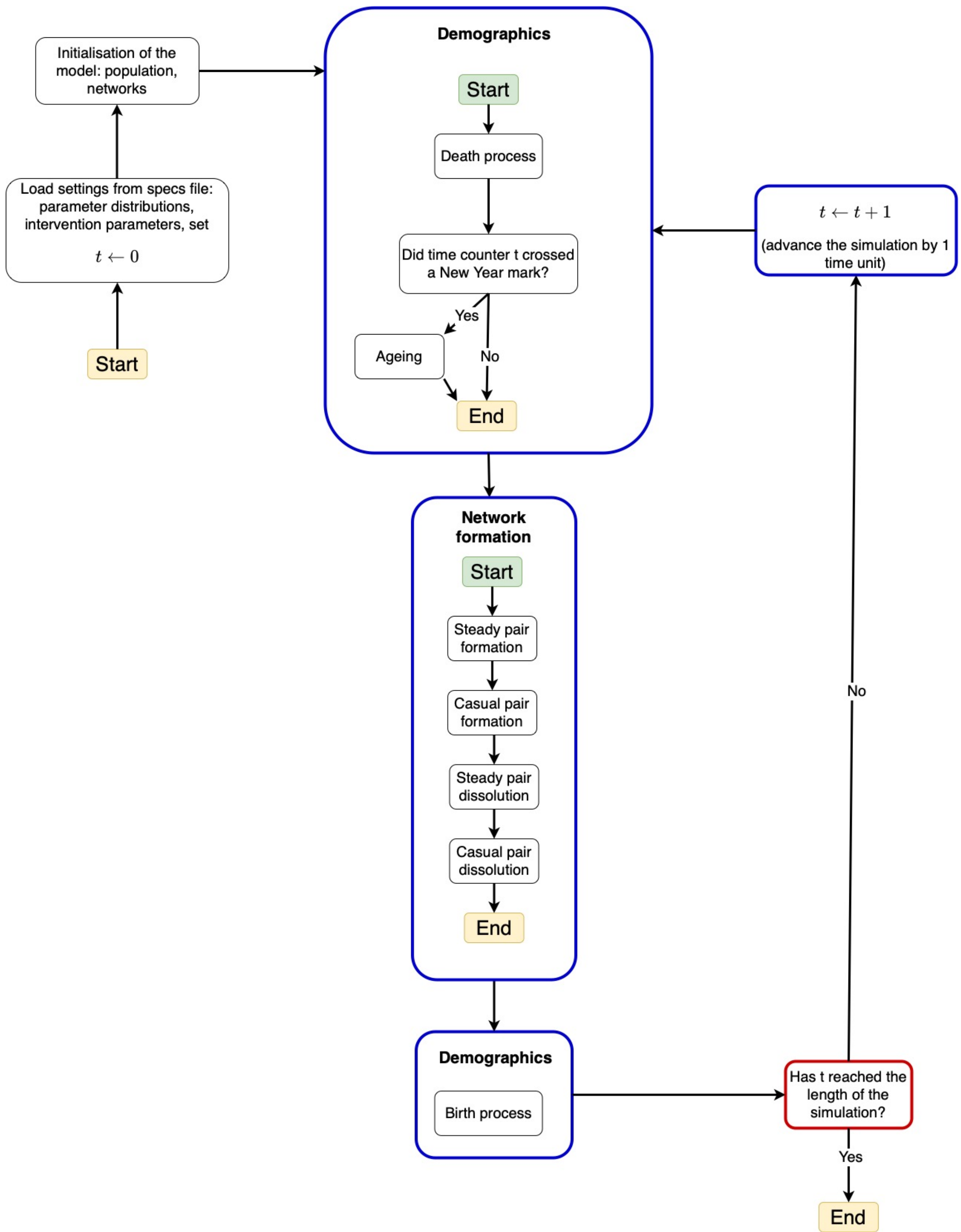

Figure 1: **Simulation flow generated by the model.** Operations contained in blue-bordered rectangles performed several times, as the simulation loops through iterations. After each iteration a stopping criterion is checked (red-bordered rectangle) and the simulation has concluded its run. Remaining operations are performed only once per simulation run.

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