HIV VACCINE IN A SMALL WORLD

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RESUMO

O mundo tem conhecimento da AIDS por mais de um quarto de século. Durante esse tempo a doença já se espalhou por todas as partes do mundo e nos países mais afetados ela já causou o atraso do desenvolvimento humano por décadas. Embora já se tenha feito avanços em controlar o progresso da doença, não há previsão de cura. A esperança de controlar a epidemia da AIDS está no desenvolvimento de uma vacina eficaz contra o HIV, contudo o custo da imunização será alto até mesmo para nações mais ricas. Como a maior demanda por vacina virá dos países com menor poder de compra, uma boa estratégia de vacinação será necessária. Neste trabalho, apresentamos resultados experimentais usando o model HIVacSim para avaliar opções efetivas de promover imunização contra o HIV, quando disponível, para uma população ou um grupo de pessoas.

PALAVRAS CHAVE. Redes mundo pequeno, HIV, Modelos em saúde

Área principal: Simulação

ABSTRACT

The world has known about AIDS for more than a quarter of a century. During this time the disease has spread to every corner of the world and in the worst affected countries it has set back human progress by decades. Although advances have been made in slowing down the progress of the disease, no cure is in sight. The best hope for controlling the HIV/AIDS pandemic lies in the development of an effective HIV vaccine, however the cost of immunity will be high even for the wealthiest nations. With the greatest demand for vaccine in the countries least able to pay for them, good vaccination strategies will be required. In this work we present experimental results derived by using the HIVacSim model to evaluate effective options for providing HIV vaccine immunisation when available, to a population or group of individuals.

KEYWORDS. Small world networks, HIV, Health care modelling.

Main area: Simulation

1. Introduction

Sexually transmitted diseases (STD) are known to be the source of many common health problems throughout the world and despite the growth of industrialised civilisation and sophisticated medicine they are still rampant today. HIV is having a serious impact on many societies and economies. Unlike the other big killers of the world, HIV kills people at the most productive time of their lives, mostly young adults and parents of young children. The world must once again learn crucial lessons about what works best in preventing new infections and improving the care for people living with HIV.

In the first years of the HIV epidemic, there was a great urge to look for historical models as a means of dealing with the AIDS pandemic by finding its similarities with other well known STDs. However, HIV requires sophisticated approaches, capable not only of recognising how HIV is like past epidemics, but precisely identifying the ways in which it is different. From the start of the HIV pandemic, scientists have been working round the clock to develop an effective cure for HIV. Despite the success of the Highly Active Anti-Retroviral Therapy (HAART) in slowing down the disease process, no cure is in sight. Additionally, HAART is an expensive treatment for all but the wealthiest societies, therefore the development of an effective vaccine for HIV will bring hope for millions of people at risk or already infected with HIV.

It is likely that the first HIV vaccine that proves effective will be only partially effective due to genetically distinct subtypes of the HIV virus, with the predominant subtype varying by region (HIV-B is common in North America and Europe, HIV-A is common in east Africa and HIV-C is prevalent in southern Africa and many parts of Asia). It is not clear if the HIV subtype matters for vaccine design, that is, whether it will be possible for a single product to be effective worldwide, or if subtype-specific vaccines will be needed (Esparza, 2001). This means that it may be effective just for some people or for a limited period of time. Or it may not stop HIV infection, but rather thwart progression to AIDS in immunised individuals who later are infected.

Partially effective vaccines can still have benefit because all vaccines derive their power from group immunity, as the prevalence of a transmissible disease diminishes among a population, each individual's risk of contracting the disease also lessens, regardless of whether they are directly protected (Francis et al., 2003). Any partially effective HIV vaccine must be dispensed alongside education and a wide range of effective prevention programmes. Those who receive the vaccine must understand that their risk of contracting disease is not eliminated.

With the greatest demand for a vaccine in the countries least able to pay for them, private industry has been slow to get involved. Governments have failed to take leadership for what would be an international public good of the highest order. A HIV vaccine must be practical for delivery worldwide. Ideally, a vaccine would be manufactured using technology that is inexpensive, administered orally or by other means besides injection and confer long-lasting protection in no more than a few low doses. Unfortunately, no HIV vaccine currently in human trials is specifically designed to meet all these criteria, therefore the cost of immunity will be high and good vaccination strategies will be required (Esparza, 2001).

In this paper, we use the HIVacSim simulation model, proposed by Vieira (2005) and Vieira et al (2008), to derive experimental results and illustrate how policy-makers can evaluate the costs and benefits of delivering HIV vaccine to the general population, determine where the initial focus should be, decide what to do if the first available vaccines are only marginally effective or have significant side effects. The Brazilian HIV prevalence in 2007 (0.5% – 0.8%) as published by the Joint United Nations Programme on HIV/AIDS (UNAIDS, 2008) is used as the initial HIV prevalence in the demonstration. The small world network randomness parameter (probability of casual partnership) was set to 0.2. This parameter has a direct and nonlinear effect on HIV transmission as shown by Vieira (2005). For the reader's convenience, a short description of the HIVacSim model structure is reproduced at the end of this article in Appendix A.

2. HIV Vaccine and Intervention

The HIVacSim model allows multiple preventive vaccines to be defined, although only a single HIV vaccine intervention can take place at a time within each core group. The definition of

a preventive HIV vaccine within the model requires basic information about the effectiveness of the vaccine in stopping the HIV transmission and the duration of the protection provided by the vaccine for the vaccinated individuals. Table 1 summarizes the required information when defining a preventive HIV vaccine.

Table 1- HIV vaccine definition

Variables	**Description**
Effectiveness	The effectiveness of the vaccine in stopping HIV transmission
Protection	Does the vaccine provide a lifelong protection against HIV infection?
Length	Length of the vaccine protection (if not lifelong)

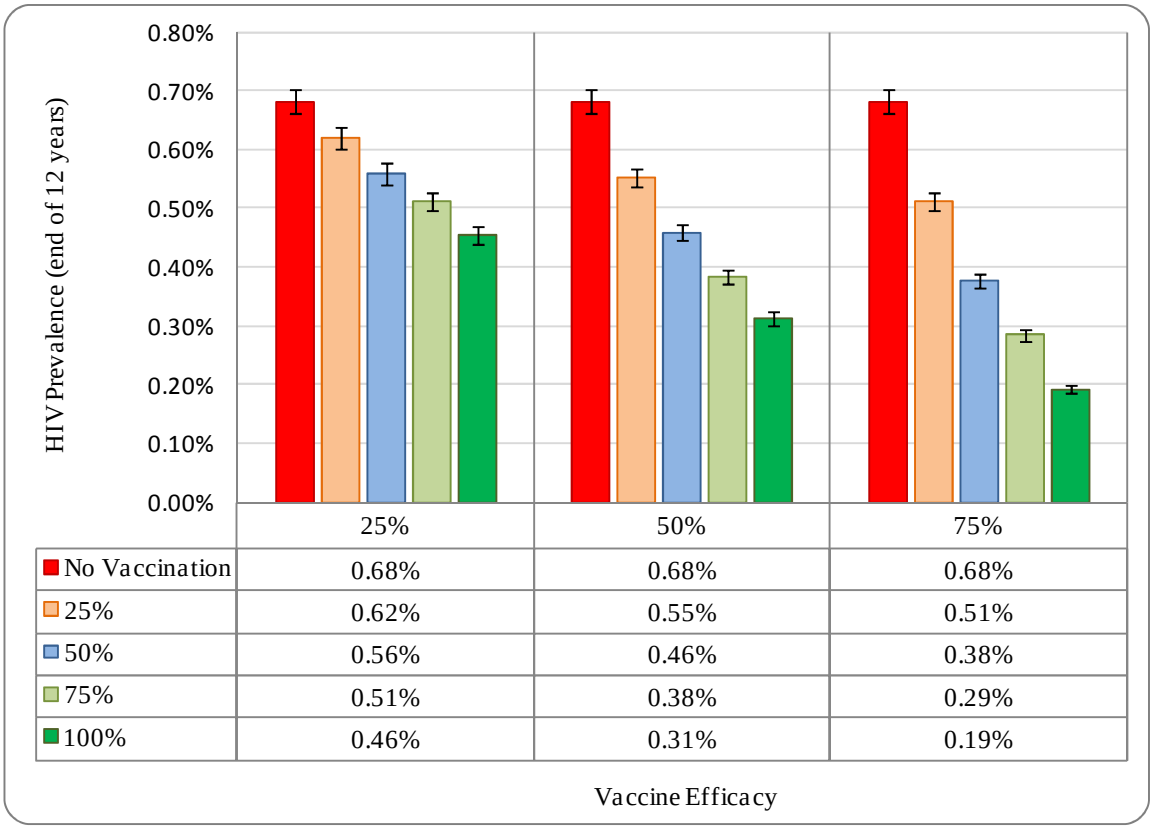
The implementation of different vaccination strategies can be defined within the model and will depend on: core groups' definitions, available HIV vaccines, number of interventions, HIV testing and testing results. Intervention strategies therefore may target specific core groups and use different types of vaccines in order to minimise the costs and maximise the effectiveness. The following options can be used when defining vaccine interventions.

- **Population to be Vaccinated**
  - All groups or
  - Custom, then
    - ✓ Select specific groups
  - Time for intervention as a function of the clock *t*
  - % of population to be vaccinated [1 – 100%]
  - Vaccine to be used
- **HIV Testing**
  - ✓ Not important
  - ✓ Vaccine only tested individuals
    - **HIV Testing Results**
      - Not important
      - Only HIV negative
      - Only HIV positive

3. HIV Vaccine Intervention Results

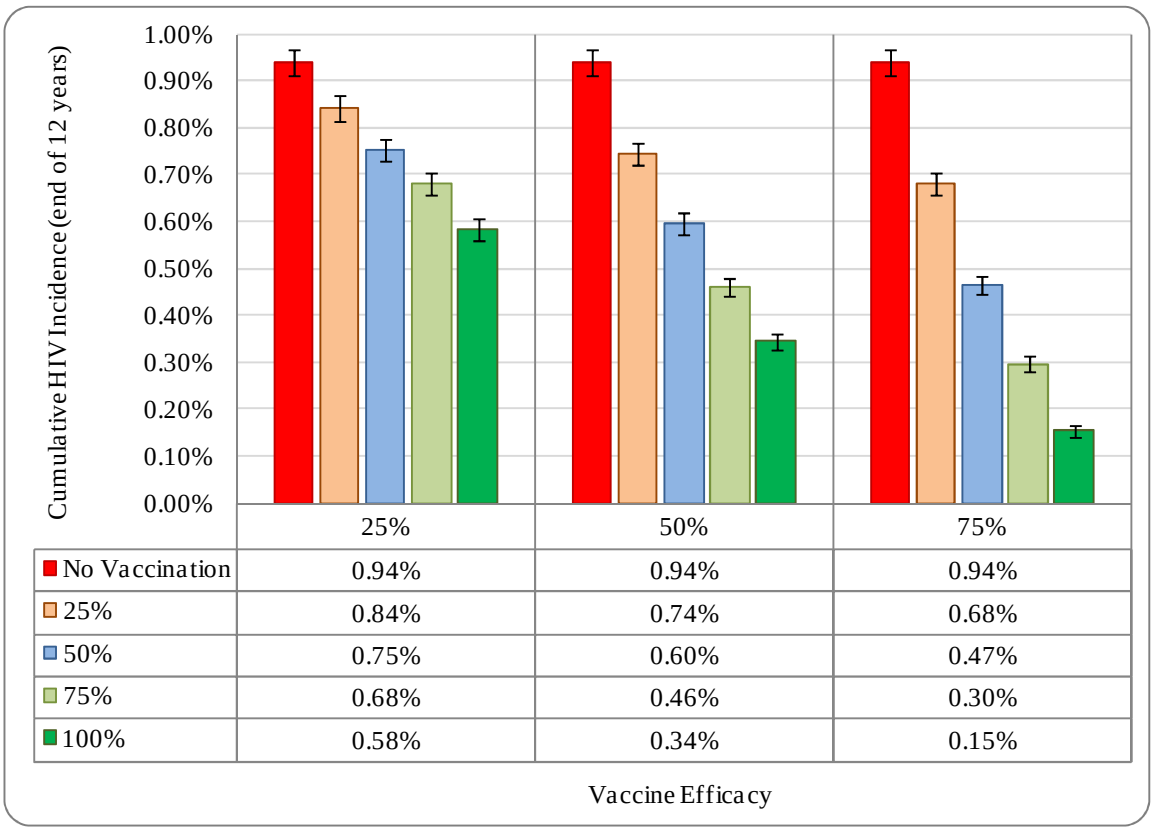
In this section we evaluate the effects of a preventive HIV vaccine on the HIV/AIDS epidemic, based on the Brazilian HIV prevalence, as mentioned previously. In this experiment, we consider lifelong immunisation interventions using preventive HIV vaccines with varying levels of efficacy (25%, 50% and 75%) and population coverage (No vaccination, 25%, 50%, 75% and 100%). Vaccination covers only HIV negative individuals and takes place at the beginning of the simulation (time = 1).

Figures 1 and 2 show the effects of the different preventive HIV vaccination strategies in the HIV prevalence and incidence respectively according to vaccine efficacy and intervention coverage, error bars represent 95% confidence interval.



	25%	50%	75%
No Vaccination	0.68%	0.68%	0.68%
25%	0.62%	0.55%	0.51%
50%	0.56%	0.46%	0.38%
75%	0.51%	0.38%	0.29%
100%	0.46%	0.31%	0.19%

Figure 1 - Preventive vaccine effects on HIV prevalence



	25%	50%	75%
No Vaccination	0.94%	0.94%	0.94%
25%	0.84%	0.74%	0.68%
50%	0.75%	0.60%	0.47%
75%	0.68%	0.46%	0.30%
100%	0.58%	0.34%	0.15%

Figure 2 - Preventive vaccine effects on HIV incidence

The results obtained through the model compare well with those reported by Gray et al. (2003) (50% efficacy vaccine with 75% coverage could reduce the HIV prevalence by 80% over 20 years). It shows that even a low efficacy vaccine (e.g. 25%) can reduce HIV transmission if coverage is high (e.g. 100%). However the epidemics would not be under control as the HIV incidence would remain relatively high. On the other hand, with higher vaccine efficacy the HIV pandemic could be markedly reduced. Even a moderately protective HIV vaccine of 50% efficacy with broad population coverage of 75% could reduce the HIV prevalence and incidence by as much as 44% and 50% (this value, 44%, is 1-0.38/0.68 for example) respectively over 12 years; while a vaccine with 75% efficacy could achieve 57% and 68% reduction respectively within the same time scale for a similar coverage.

4. Conclusions

The dynamics of HIV transmission is a highly complex process and varies enormously. Not only is the HIV epidemic dynamic in terms of treatment options, prevention strategies and disease progression, but also in terms of sexual behaviour, which is widely diverse and deeply embedded in individual desires, cultural relationships, environment, economic status and the enormous social network where everyone lives.

The interventions to stem the spread of HIV throughout the world are as varied as the contexts in which we find them. However the development of a preventive HIV vaccine is the best hope of controlling the HIV pandemic in the long-term. Even a low 25% efficacy vaccine can reduce HIV transmission if coverage is high, while a 75% efficacy vaccine could markedly reduce the HIV pandemic with relatively low coverage. In any case, vaccine intervention must go alongside education and a wide range of effective prevention programmes. Those who receive the vaccine must understand that their risk of contracting HIV infection has lessened but has not vanished.

The HIVacSim model defines a network of spontaneous order, where neighbours are defined by geography and social rules. Its connectivity gives rise to rich forms of self-organisation, people live in a small world and diseases or information is always dynamically transmitted over the network. The structure and flexibility of the model should contribute towards a better understanding and quantitative evaluation of the costs and benefits of delivering an effective HIV immunisation program to a population or group of individuals.

References

Dietz, K. and Hadeler, K. P. (1988), Epidemiological models for sexually transmitted diseases, *Mathematical Biology*, **26**, 1–25.

Esparza, J. (2001), An HIV vaccine: how and when, *Bulletin of the World Health Organisation*, Special Theme HIV/AIDS, **79**(12), 1133-1137.

Francis D.P., Heyward W.L., Popovic V., Orozco-Cronin P., Orelind K., Gee C., Hirsch A., Ippolito T., Luck A., Longhi M., Gulati V., Winslow N., Gurwith M., Sinangil F. and Berman P.W. (2003), Candidate HIV/AIDS vaccines: lessons learned from the world's first phase III efficacy trials. *AIDS*, **17**:147–156.

Gray, R.H., Li, X., Wawer, M.J., Gange, S.J., Serwadda, D., Sewankambo, N.K., Moore, R., Wabwire-Mangen, F., Lutalo, T., Quinn, T.C. and Rakai Project Group. (2003), Stochastic simulation of the impact of antiretroviral therapy and HIV vaccines on HIV transmission; Rakai, Uganda. *AIDS*, **17**, 1941-1951.

Joint United Nations Programme on HIV/AIDS (UNAIDS), Report on the global HIV/AIDS epidemic, Technical Report UNAIDS/08.25E / JC1510E, UNAIDS, August 2008.

Morris, M., Podhisita, C., Waver, M. J. and Handcock, M. S. (1996), Bridge populations in the spread of HIV/AIDS in Thailand, *AIDS*, **10**, 1265–1271.

Vieira, I. T. (2005), Small World Networks Models of the Dynamics of HIV Infections, PhD Thesis, School of Mathematics, University of Southampton, Southampton SO16 1BJ, UK.

Vieira, I.T., Senna, V. and Pereira, H.B.B. (2008), Safe Sex and the Spread of HIV, *XL Simpósio Brasileiro de Pesquisa Operacional*, João Pessoa, vol. 1, 153-160.

Watts, D. J. and Strogatz, S. H. (1998), Collective dynamics of 'small-world' networks, *Nature*, **393**(4), 440-442.

Watts, D. J. *Small Worlds: The dynamics of networks between order and randomness*, Princeton University Press, Princeton, 1999.

Appendix A: HIVacSim Model Definition

The small world phenomenon, also known as six degrees of separation, has been used for representing dynamic network interactions. It states that, given some random connections, the degrees of separation between any two individuals within a population can be very small compared with its size (Watts and Strogatz, 1998) and (Watts, 1999).

The original small world models are unsuitable for modelling social networks and the spread of infectious diseases. The network vertices are equally considered for rewiring or shortcuts, which are unlike the real world, as the level of interaction that an individual possesses will not be the same as for other individuals. Furthermore, the connections are equally weighted or the network is strongly connected and they do not characterise the ties/link properties of edges, essential to capture the social behaviour of an individual within the network.

The HIVacSim as proposed by Vieira (2005) and Vieira et al (2008), modifies the original small world model in order to accommodate differential selectivity (vertex properties), sexual behaviour (edge properties) and network properties such as performance and concurrency, fundamental for the modelling of human sexual contact network and the spread of HIV. Yet it is consistent with the general definition of the small world theory.

The model starts by defining the simulation clock t that moves in Δt steps (Δt = month | trimester | semester | year), which guides the definition of the population and model outcomes. Activities associated with the dynamics of population (birth and deaths), social interactions leading to the formation and dissolution of partnerships, preventive vaccination intervention, and the dynamics of sexual behaviour and transmission of HIV are evaluated for each t as shown in Figure 3. The information to be transmitted through the network over time is the HIV infection.

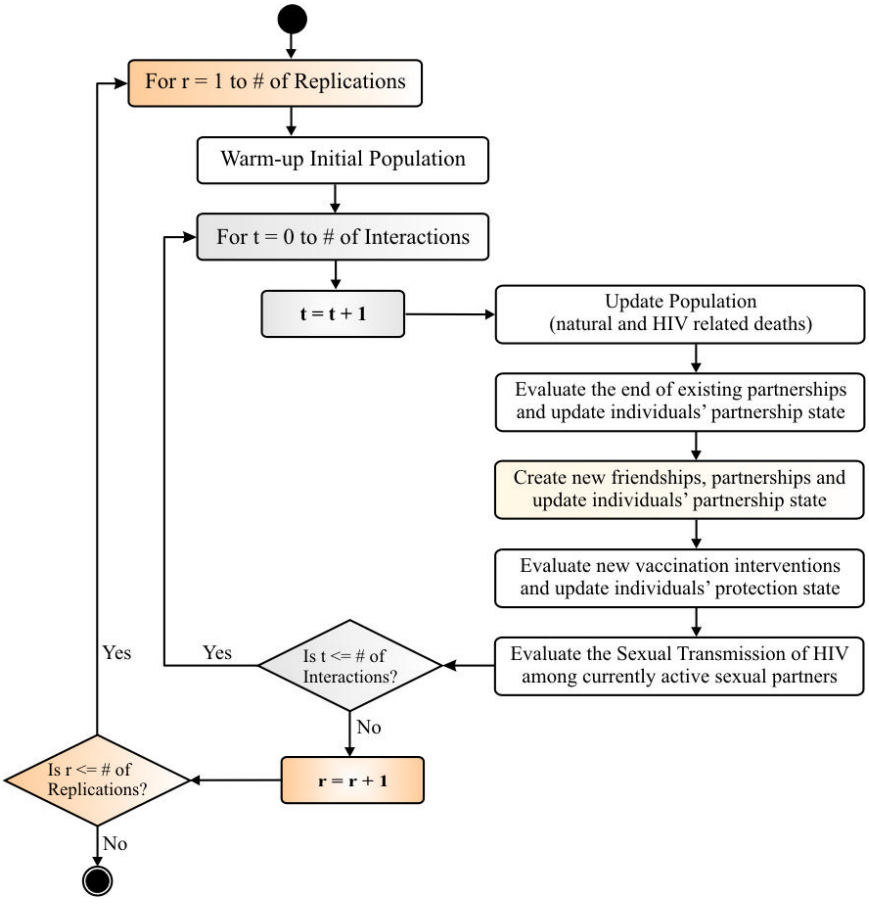


Figure 3- HIVacSim computation activity diagram.

The main activities associated with social interactions and sexual transmission of HIV are the

formation/dissolution of partnership (monogamy, concurrency and duration), rate of sexual contacts, safe sex practice and the HIV transmissibility as shown below (Figure 4).

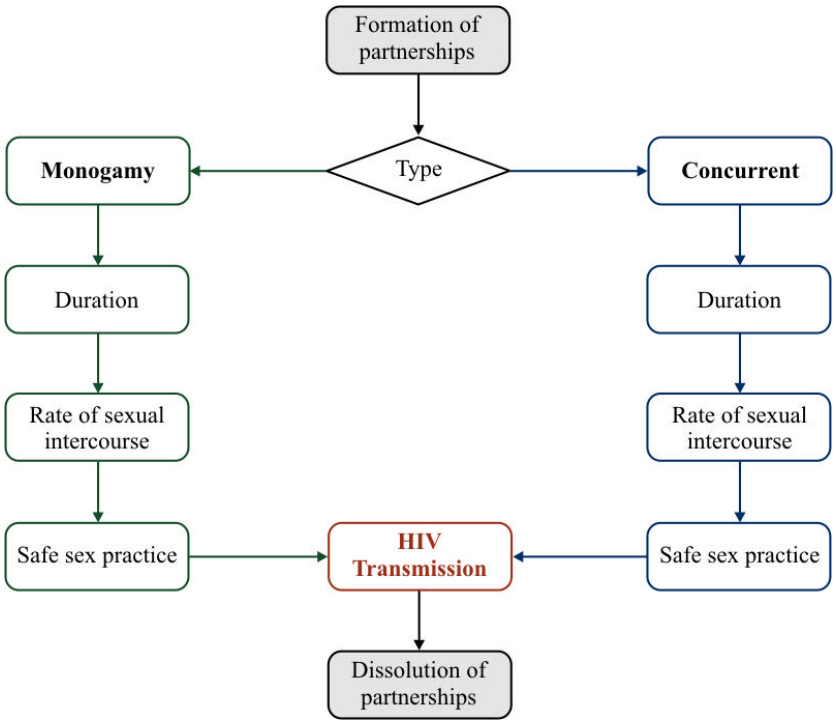


Figure 4- Sexual transmission of HIV activities.

The population characteristics are defined as a function of the simulation clock t, which can be tuned to reflect the data available. The level of detail to be included within the model will depend upon the availability of data. Table 2 shows the properties defined as a minimum requirement and Table 3 shows the parameters for the three group definitions (married, under 25 and others), as used in simulations.

Table 2- Population characteristics definition

Population structure	**Parameters and probability distributions**
Population identity	*Size n* – the size of the population in each core group.
	Age distribution – the population's age distribution used to quantify the effects of HIV infection on individuals and/or to define age based population core groups.
	Life expectancy – the distribution of life expectancy in the population without the effects of HIV infection.
	Gender – proportions of female, male and homosexuals in the population – used to define partnerships within the population.
HIV infection status	*HIV prevalence* – the currently estimated prevalence of HIV infection within the population.
	HIV lead-time distribution – the lead-time of the HIV infection among people living with HIV/AIDS, used to quantify deaths caused by HIV infection.
	HIV testing rate – the proportion of people tested for HIV infection in the population, fundamental when making decisions about treatment and preventive intervention strategies.

Population structure	Parameters and probability distributions
Network and social rules governing the formation of partnerships, migration, concurrency and community structure	*Maximum number of concurrent partnerships* – network property governing the overlapping of partnerships.
	Probability of concurrent partnership – population behaviour towards multiple sexual partners or extramarital partnerships.
	Probability of a casual partnership – small world's probability p – social rule governing the network structure according to the nature of the partnerships within the population.
	Probability of looking for a sexual partner at any time – available for partnership – social rule accounting for individuals' desire to be involved in sexual partnerships.
	Probability of searching own group first for a casual partner – network rule representing the community structure of the population and the cultural behaviour of individuals when looking for casual partnerships.
Sexual behaviour of individuals in **stable partnerships**, quantifying the strength and frequency of social interactions as well as the dissolution of partnerships	*Duration of stable partnerships* – the distribution of length of long term partnerships in the population (e.g. the duration of marriage).
	Time between stable partnerships – the distribution of time between two consecutive stable partnerships. The mean time taken by individuals to find a new stable partner as described by the pair formation models (Dietz and Hadeler, 1988). However individuals can have casual partners in between stable partnerships.
	Rate of sexual intercourse for stable partnership per unit of time – the distribution of sexual contacts, the sexual behaviour of individuals when engaged in a long term partnership.
	Probability of safe sex practice during sexual intercourse for stable partnership – the behaviour of individuals engaged in stable partnerships, condom use, especially relevant to those having extramarital partnerships, the bridges for HIV (Morris et al, 1996).
Sexual behaviour of individuals in **casual partnerships**, quantifying the strength and frequency of social interactions as well as the dissolution of partnerships	*Duration of casual partnerships* – the distribution of short term partnerships in the population.
	Rate of sexual intercourse for casual partnership per unit of time – the distribution of sexual contacts between individuals when engaged in a short term sexual partnership.
	Probability of safe sex practice during sexual intercourse for casual partnership – the behaviour of individuals relating to condom use, especially among young people and those involved in multiple sexual partnerships.

Table 3. Multiple group scenario definitions.

Parameters and Probability Distributions	Group Definitions		
	Married	Under 25	Others
Population size (*n*)	1422	794	1108
Age distribution	Weibull(182.3, 336.3, 2.3)	LogNormal(144.0, 95.1, 37.0)	InvNormal(242.2, 246.9, 621.9)
Life expectancy (70 years)	840 months	840 months	840 months
Proportion of females	50%	45.8%	62.4%
Proportion of males	50%	54.3%	37.6%
Proportion of homosexual males	5%	5%	5%
HIV prevalence	0.007	0.007	0.007
HIV lead-time distribution	Weibull(64.3, 1.6)	Weibull(71.8, 1.6)	Weibull(64.3, 1.6)
HIV testing rate	16.34%	11.71%	18.29%
Maximum number of concurrent partnerships	5	5	5
Probability of concurrent partnership	0.06	0.21	0.14
Probability of casual partnership	0.06	0.40	0.27
Probability of looking for a sexual partner	1	0.78	0.64
Probability of searching own group first for casual partner	0.4	0.8	0.7
Duration of stable partnerships	Weibull(198.2, 1.6)	LogNormal(29.8, 37.2)	Weibull(89.7 1.0)
Time between stable partnerships	Gamma(20.2, 1.1)	Weibull(14.9,1.1)	Gamma(24.4, 1.0)
Rate of sexual intercourse for stable partnership per unit time	Gamma(4.7, 1.5)	Gamma(6.5, 1.1)	Gamma(5.1, 1.3)
Probability of safe sex practice during sexual intercourse for stable partnership	0.11	0.47	0.21
Duration of casual partnership	Gamma(8.8, 1.1)	Gamma(5.3, 1.0)	LogNormal(9.2, 14.6)
Rate of sexual intercourse for casual partnership per unit time	Gamma(5.0, 1.6)	Gamma(7.1, 1.1)	Gamma(5.3, 1.4)
Probability of safe sex practice during sexual intercourse for casual partnership	0.12	0.55	0.42