Mathematical Formalism

by James M. Hyman and E. Ann Stanley

We will buildup the equations for our risk-baaed model of AIDS through successive modifications of the basic equation of epidemiology, the equation of mass action. Its simplest form is given by

$$\frac{dI}{dt} = \alpha I \left(1 - \frac{I}{N}\right), \tag{1}$$

where $I(t)$ is the number infected, N is the total population and a is a constant. Equation 1 describes the spread of HIV infection by random sexual contact among a sexually active population of fixed size N. As explained in the main text, if a population mixes homogeneously, this equation gives rise to an initial exponential growth in the number infected with constant relative growth rate of α.

As the number infected becomes comparable to the total population the growth rate will decrease, so we rewrite Eq. 1 to show that time dependence:

$$\frac{dI}{dt} = \lambda(t)S(t), \tag{2}$$

where $S(t) = N - I(t)$ is the number of persons susceptible to infection and $\lambda(t) = \alpha I(t)/N$. So far the only independent variable is time t and $\lambda(t)$ is the time-dependent relative growth rate of the number infected.

To describe the AIDS epidemic over long times, we must account for individuals who eventually develop AIDS and die. Thus the total population will not remain constant but will change with time. We divide the population into three sectors: the sexually active, uninfected susceptible $S(t)$; those infected with HIV who do not have AIDS $I(t)$; and people with AIDS $A(t)$. We assume the susceptible and the infected are sexually active (and therefore can infect others) but that those with AIDS are not. Thus the sexually active population N(t) is equal to $S(t) + I(t)$. Moreover, we assume that people mature, or migrate, into the sexually active susceptible population and retire from it at a constant relative rate μ, so that in the absence of AIDS the susceptible population would remain constant at the value SO, that is, $N(t) = S(t) = S.$ in the absence of HIV.

We also introduce the parameter γ, the relative rate at which people who are infected develop AIDS, and δ, the relative rate at which people die from AIDS.

Now we can write down a set of rate equations for changes in $S(t)$,$I(t)$ and $A(t)$ with time.

The rate of change in the number infected is like Eq. 2 except the right-hand side includes negative terms that account for decreases due to conversion to AIDS at a rate $\gamma I(t)$ and aging of the infected at a rate $\mu I(t)$:

$$\frac{dI(t)}{dt} = \lambda(t)S(t) - (\gamma + \mu)I(t). \tag{3}$$

The number of uninfected susceptible increases through maturation of "juveniles" at a rate μS_0. and decreases through-aging at a rate $\mu S(t)$ and through infection with HIV at a rate $\lambda(t)S(t)$:

$$\frac{dS(t)}{dt} = \mu(S_0 - S(t)) - \lambda(t)S(t). \tag{4}$$

The number of people with AIDS increases through conversion of infecteds at a rate $\gamma I(t)$ and decreases through death at a rate $\delta A(t)$:

$$\frac{dA(t)}{dt} = \gamma I(t) - \delta A(t). \tag{5}$$

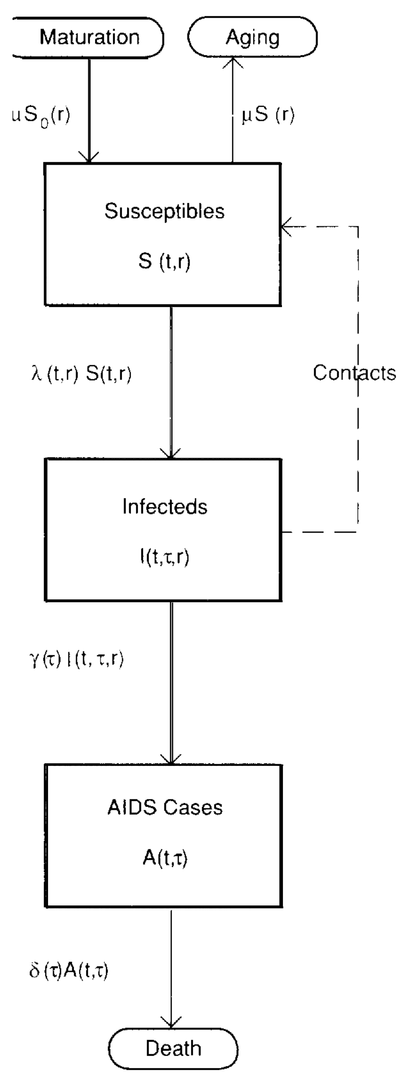
The accompanying block diagram illustrates the inputs and outputs to each of the three sectors of the population.

The most important assumptions in any model of AIDS are embedded in the definition of $\lambda(t)$, the rate of infection per susceptible. In the simple model just presented, all members of the population are assumed to be equal in their susceptibility and the rate of infection per susceptible is given by

$$\lambda(t) = i\ c\ p\ \frac{I(t)}{I(t)+S(t)}, \tag{6}$$

where the constant i is the probability of infection per sexual contact, the constant c is the average number of sexual contacts per partner, the constant p is the average number of partners per year, and $\frac{I(t)}{I(t)+S(t)}$ is the infected fraction of the sexually active population.

STRUCTURE OF THE RISK-BASED MODEL



Independent Variables

t: Time

τ: Time since infection

r: Number of partners per year

Dependent Variables

$S(t,r)$: Distribution of susceptibles by number of partners per year

$I(t,\tau,r)$: Distribution of infecteds by number of partners per year and time since infection

$A(t,\tau)$: Distribution of AIDS cases by time since diagnosis

Parameters

$S_0(r)$: Distribution of susceptibles in the absence of HIV

$\lambda(t,r)$: Relative rate of at which susceptibles with r partners per year get infected

μ: Relative rate at which people mature into and retire from the susceptible population

$\gamma(\tau)$: Relative rate of developing AIDS at a time τ after infection

$\delta(\tau)$: Relative rate of death at a time τ after diagnosis

Note that this simple model produces exponential growth at the start of the epidemic. All members are equally at risk (homogeneous mixing) and the probability of infection per contact i remains constant throughout the years of infection.

We will now modify the simple model defined by Eqs. 3-6 to account for two crucial aspects of the AIDS epidemic. First, since AIDS takes many years to develop and the infectivity during the period of infection may vary in time, we introduce an additional independent variable τ, the time since infection. Second, since individuals who are very active sexually and who change partners frequently have a greater risk of becoming infected, we introduce the variable r, which quantifies the level of risky behavior in the sexually active population. In this model, r is defined as the number of new partners per year.

Using the two new independent variables τ and r, we distribute $I(t)$, $S(t)$ and $A(t)$ over risk behavior and/or time since infection. (See the definitions in the block diagram.) In addition, the constant S_0 is the integral of an equilibrium distribution over risk behavior, $S_0 = \int_0^\infty S_0(r)dr$. Note that $S_0(r)$ corresponds to $N(r)$ in the main text; also the main text presents evidence that $S_0(r) \propto r^{-3}$ for large r.

We can now write down the equations of our risk-based model that correspond to Eqs. 3–5. Equation 3 for the infected population is replaced by Eqs. 7a and b. Equation 7a specifies that the rate at which people of risk r are becoming infected is $\lambda(t,r)S(t,r)$. Equation 7b says that rate at which the infecteds develop AIDS is proportional to the conditional probability $\gamma(\tau)$, which is a function of the time since infection, and the rate at which they leave the population is proportional to μ.

$$I(t,0,r) = \lambda(t,r)S(t,r). \tag{7a}$$

$$\frac{\partial I(t,\tau,r)}{\partial t} + \frac{\partial I(t,\tau,r)}{\partial \tau} = -\gamma(\tau)I(t,\tau,r) - \mu I(t,\tau,r). \tag{7b}$$

Equation 8 for the susceptible has a structure similar to that of Eq. 4 except that now the rate of infection per susceptible $\lambda(t,r)$ depends on the risk behavior r:

$$\frac{\partial S(t,r)}{\partial t} = \mu(S_0(r) - S(t,r)) - \lambda(t,r)S(t,r). \tag{8}$$

Equation 9a says that the rate at which AIDS cases are being diagnosed at time t is equal to the rate at which infecteds convert to AIDS, $\gamma(\tau)I(t,\tau,r)$, integrated over all risk behaviors r and times since infection τ. Equation 9b accounts for loss of AIDS cases due to death.

$$A(t,0) = \int_0^\infty \int_0^\infty \gamma(\tau)I(t,\tau,r)d\tau dr. \tag{9a}$$

$$\frac{\partial A(t,\tau)}{\partial t} + \frac{\partial A(t,\tau)}{\partial \tau} = -\delta(\tau)A(t,\tau). \tag{9b}$$

The major change in this new set of equations is the form we assume for $\lambda(t,r)$, the relative rate at which susceptible with r partners per year get infected. We generalize Eq. 6 to include variation in the degree of sexual contact between individuals with different risk behaviors as well as variation in infectiousness with time since infection. The general form of $\lambda(t,r)$ is given by

$$\lambda(t,r) = r\int_0^\infty \int_0^\infty c(r,s)\rho(t,r,s)i(\tau)\frac{I(t,\tau,s)}{N(t,s)}d\tau ds, \tag{10}$$

where $c(r,s)$ is the average number of sexual contacts in a partnership between a person with risk r and one with risk s, $i(\tau)$ is the infectiousness at τ years since infection, $\frac{I(t,\tau,s)}{N(t,s)}$ is the probability that a person with risk s will be infected at time τ, and $p(t, r, s)$ is the fraction of the partners of a person with risk r who have risks. The total number of sexually active people with risk s is given by $N(t, s) = S(t, s) + \int_0^{\infty} I(t,\tau,s)d\tau$.

Equations 7-10 describe the basic structure of our risk-based model. It differs from the well-known model of Anderson and May in one major respect-the form of $\lambda(t,r)$. Anderson and May assumed homogeneous mixing among the entire population, that is, that partners are chosen purely on the basis of availability. Then $p(t, r, s)$, the fraction of the partners of a person with risk r who have risk s, is just the proportionate mixing value:

$$\rho(t,r,s) = \frac{sN(t,s)}{\int_0^{\infty} xN(t,x)dx}. \tag{11}$$

They also assumed that the average number of sexual contacts per partner and the infectiousness were constant, so that $\lambda(t,r)$ becomes

$$\lambda(t,r) = \frac{icr \int sI(t,s)ds}{\int xN(t,x)dx}. \tag{12}$$

This form for $\lambda(t,r)$ (adapted from the model of Hethcote and Yorke for the spread of gonorrhea) yields exponential growth for the early stages of the epidemic.

We suggest that the assumption of homogeneous mixing is sociologically unrealistic. Instead, we build into our model a general form for $p(t, r,s)$ that allows for biased mixing among the population. That is, $p(t, r,s)$ includes an acceptance function, $f(r, s)$, that specifies the frequency at which an individual with risk behavior r chooses a partner with risk behaviors. When the acceptance function $f(r, s)$ is 1, we return to homogeneous mixing. When $f(r, s)$ is a narrow Gaussian, for example, $f(r,s) = \exp\left(-(r-s)^2/\epsilon(r+a)^2\right)$, people choose partners who are similar to themselves. This latter assumption is presented in the main text and yields the power-law growth in AIDS cases seen in the data.

For completeness we give the general form of $p(t, r, s)$:

$$\rho(t,r,s) = \begin{cases} \left(1 - \int_0^r \rho(t,r,x)dx\right)\frac{f(r,s)sN(t,s)}{\int_r^{\infty} f(r,x)xN(t,x)dx}, & \text{for } r \le s \\ \rho(t,s,r)\frac{sN(t,s)}{rN(t,r)}, & \text{for } r > s. \end{cases} \tag{13}$$

This complicated function satisfies three necessary properties:

1. The number of partners with risk behavior s chosen by people with risk behavior r is equal to the number of partners with risk behavior r chosen by people with risk behaviors; that is,

$$rN(t,r)p(t,r,s) = sN(t,s)p(t,s,r). \tag{14}$$

2. People with risk behavior r have r partners per unit time; that is,

$$= \int_0^{\infty} \rho(t,r,s)ds. \tag{15}$$

3. The fractions $p(t,r,s)$ are positive.

In order to study the effects of different mixing patterns on the growth of the epidemic, we have chosen various forms for the acceptance function $f(r, s)$ and then solved Eqs. 7–9 numerically. The results are presented in "Numerical Results of the Risk-Based Model of AIDS." Also presented there are numerical solutions for different assumptions about infectiousness from time since infection. ■