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Age-Dependent Choice of Sexual Partners and the Transmission Dynamics of HIV in Sub-Saharan Africa

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Age-dependent choice of sexual partners and the transmission dynamics of HIV in Sub-Saharan Africa

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CONTENTS

SUMMARY

A mathematical model of the transmission of HIV-1 within heterosexual populations in Sub-Saharan Africa is described and its properties analysed. The model incorporates epidemiological and demographic processes and extends previous work in this area via the inclusion of age and sex dependency in rates of sexual partner change, and sexual partner choice dependent on age. Parameter assignments are made on the basis of current data on the transmission dynamics of HIV-1 and the demography of human populations in Africa.

Both age-dependent rates of sexual activity and the sexual contact of males with females younger than themselves act to enhance the predicted demographic impact. With realistic parameter values, the model suggests AIDS is able to reverse the sign of population growth rates from positive to negative values over a timescale of a few decades. The sensitivity of this prediction is examined in relation to changes in the pattern of sexual contact between different age classes of females and males, different patterns of change in the age-dependent rate of sexual partner change, different assumptions concerning the doubling time of the epidemic in its early stages, and the relative efficiencies of viral transmission between men and women, and vice versa. The impact AIDS is predicted to have on the number of young and elderly persons as a fraction of the number of productive adults (the dependancy ratio) is examined under various assumptions concerning the weighting to be applied to mirror the burden imposed by the care of those with AIDS. The paper includes an assessment of the influence of the timing of changes in sexual behaviour, or the promotion of the use of condoms, on the predicted course of the epidemic. The paper concludes with a discussion of data needs and the model refinements required to more accurately mirror current understanding of the epidemiology of HIV-1.

1. INTRODUCTION

Serological studies of the prevalence of the human immunodeficiency virus type 1 (HIV-1) in various Sub-Saharan African countries reveal a depressing picture of continued spread in the latter part of the 1980s and the attainment of high levels of infection in many urban and, to a lesser extent, rural populations (De Cock *et al.* 1990; Killewo *et al.* 1990; Berkley *et al.* 1990). A few examples serve to illustrate this point. In figure 1 and 2, age and sex stratified seroprevalence data are recorded for various populations (blood

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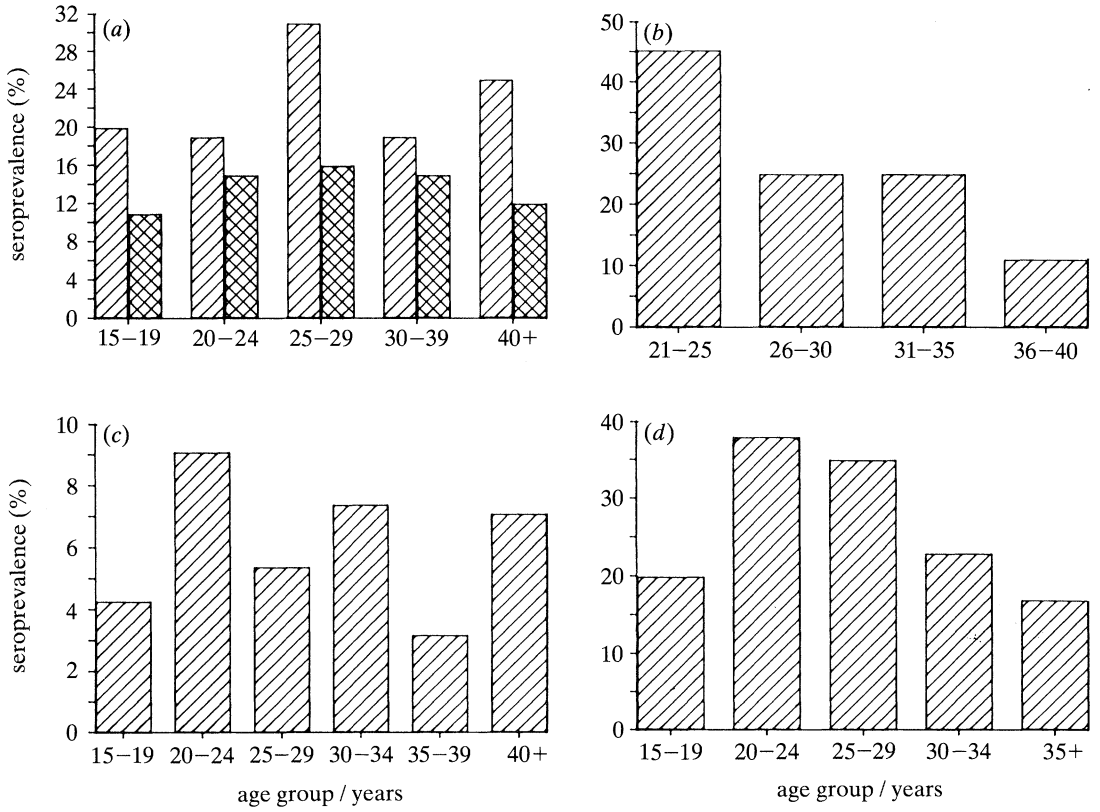

Figure 1. Age- and sex-stratified cross-sectional horizontal serological surveys for the presence of antibodies to HIV-1. (*a*) Blood donors in Kampala, Uganda, 1986 (females ▨; males ▩); (*b*) female bar workers in Dares Salaam, Tanzania, 1986; (*c*) pregnant women, Mbeya, Tanzania, 1988; (*d*) pregnant women, Kigali, Rwanda, 1989. Data sources (*a*) Carswell (1989); (*b*) Mhalu *et al.* (1987); (*c*) Hemed *et al.* (1989); (*d*) LePage *et al.* (1989).

donors, pregnant women, female bar workers, sexually transmitted disease (STD) patients and the general population) in different countries and cities (Benin, Central African Republic, Uganda, Tanzania and Rwanda). In some regions levels of infection in the general population are of the order of 20–40%, whereas in high risk populations such as female prostitutes (=bar workers) the levels are often much higher (40–80%) (U.S. Bureau 1990). As yet there is little evidence to suggest that the rate of spread of HIV-1 is slowing in Sub-Saharan Africa.

There is therefore an urgent need to assess the likely demographic and economic impact of the infection and the associated disease AIDS over the coming years. More broadly, this issue is becoming of increasing significance in other regions of the world, such as Southeast Asia and India, where evidence is accumulating of extensive spread in female prostitutes and intravenous (IV) drug using communities and of the concomitant spread into the general population.

The first analysis of the likely demographic impact of AIDS in Sub-Saharan Africa, where transmission of HIV is largely via heterosexual contact, was based on a very simple age-structured model that combined epidemiological and demographic processes (see Anderson *et al.* 1988; May *et al.* 1988*a*, *b*). The major conclusion of this study was that AIDS is capable of changing population growth rates from positive to negative values over timescales of a few decades from the introduction of HIV-1 into a defined population. This conclusion attracted some criticism at the time of publication due to the high rates of transmission assumed in our analyses and the lack of detail concerning sexual behaviour incorporated in the model. A subsequent publication by Bongarts (1989) suggested that the potential demographic impact of the disease was likely to be much less than suggested by the analyses of Anderson *et al.* (1988) and May *et al.* (1988*a*, *b*). However, the simulations of Bongarts (1989) covered a limited time span (a few decades) and were based on what now appear to be low rates of spread of the virus (see, for example, figures 1 and 2). Subsequent work, founded on more elaborate models with greater detail of sexual behaviour and more up-to-date estimates of the major epidemiological parameters, support the view that AIDS is likely to have a very major demographic impact in some African Countries (Anderson 1989; Anderson *et al.* 1989, 1990).

The present paper describes the further development of a model framework that incorporates demographic and epidemiological processes, to address the question of how age-dependent patterns of sexual activity in males and females influences earlier conclusions concerning the likely pattern of spread of HIV-1 and the potential demographic impact of AIDS. Specifically, we address the questions of how different mixing patterns between the age classes of the two sexes ('who mixes with whom', by age and sex) (figure 3), and age-dependent rates of sexual partner change

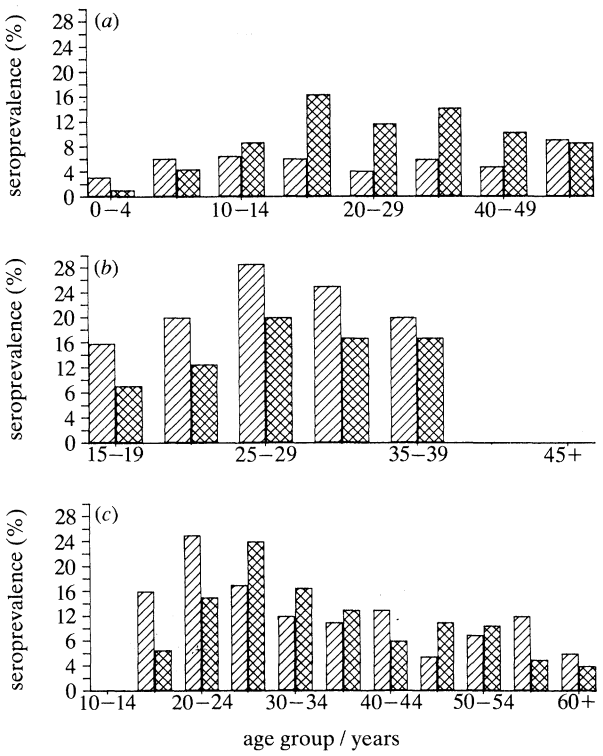

Figure 2. Horizontal sex-stratified cross-sectional surveys of HIV-1 seroprevalence in Africa. (*a*) General population in Zou, Benin, 1989; (*b*) sexually transmitted disease patients Banjui, Central Africa Republic, 1989; (*c*) general population, Uganda, 1987–1988. Data sources, (*a*) Chippaux *et al.* (1989); (*b*) Gresenquet *et al.* (1989); (*c*) Berkley *et al.* (1989). Females ▨; males ▩.

(figure 4), influence model predictions. Where possible we employ quantitative estimates of the major demographic and epidemiological parameters but we also highlight the areas in which data availability is poor at present. A particular feature of the study is an analysis of how patterns of sexual contact change as AIDS-induced mortality influences the age and sex structure of the population. We base our approach on the description of a set of qualitative behaviourial rules which govern what happens when the 'demand'

Figure 3. Mean difference in years between the age of a man minus the age of his wife, stratified by age in Bandim, Guinea-Bissau, 1989 (data from Hogsberg & Aaby (1991)).

Figure 4. Mean number of female sexual partners over the past 12 months reported by males in Guinea-Bissau (data from Hogsberg & Aaby (1991)).

by a particular sex and age group for sexual partners of the opposite sex in a defined age group exceeds the 'supply'. The qualitative rules are then translated into a set of quantitative definitions for incorporation within the framework of the model.

The central problem that necessitates the construction of such rules hinges on the issue of supply (what is available) and demand (preference) of sexual partners, and differences in the probabilities of transmission of the virus from males to females and females to males. Current data, based on the study of transmission from persons infected via blood or blood products to their spouses, suggest that the probability of transmission from males to females is a factor two to three times greater than that from females to males (Ahmed *et al.* 1989; Laga *et al.* 1989). As such AIDS is likely to induce greater mortality among women than men, other factors being equal. A further imbalance is generated by the observed preference in many societies (and particularly in certain African populations) of males for female sexual partners younger than themselves (figure 4). For examples, in figures 1 and 2 note than on average women tend to acquire higher levels of infection at a younger age than males. As AIDS induced mortality begins to alter the age and sex structure of the population, these factors generate a situation in which the demand for young female sexual partners is greater than the supply. When this occurs a set of behaviourial rules must be defined to ensure that supply matches demand. Under these circumstances, the questions that arise include (i) whether males reduce their rates of sexual partner change to match supply, (ii) whether females increase sexual activity to match demand and (iii) how such changes are distributed across the different age classes of both sexes. For example, with respect to the latter point, a number of situations may pertain including older men having preference over younger men, or vice versa.

In all these behaviourial issues, quantitative data is not available at present to guide the formulation of a set of rules. We therefore explore various assumptions and assess their different impacts on model predictions.

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2. METHODS

(a) *Preference matrices*

We define the number of people of a given sex and age a at time, as $N(a,t)$. We employ a 'dash' notation to record the numbers of age a at time t, of the opposite sex, $N'(a,t)$. The rate of sexual partner change of individuals of age a at time t is defined as $c(a,t)$, where $c'(a,t)$ denotes the same rate for the opposite sex. We further define a continuous preference function $J(a,a',t)$ which denotes the probability that, at time t, an individual of age a chooses a sexual partner of the opposite sex of age a'. Similarly, $J'(a,a',t)$ defines the mixing function for the opposite sex. These continuous functions must satisfy the following three properties.

$$0 \leqslant J(a,a',t),\ J'(a,a',t) \leqslant 1,$$

$$\int_{a'} J(a,a',t)\ \mathrm{d}\ a' = 1 = \int_{a'} J'(a,a',t)\ \mathrm{d}\ a',$$

$$c(a,t)\ \ N(a,t)\ \ J(a,a',t) = c'(a',t)\ \ N'(a',t)\ \ J'(a',a,t).$$

These constraints have been discussed in detail by Jaquez *et al.* (1988), Anderson (1989), Anderson *et al.* (1989) and Gupta *et al.* (1989). To help in the clarification of what types of behaviour are encapsulated in different forms of the preference function $J(a,a',t)$, we divide the continuous age distribution of the population of each sex into a series of discrete age classes to represent different age bands, such that $N_i(t)$ defines the number in age class i at time t. We define the total population size of a given sex as $N(t) = \Sigma N_i(t)$ and the contact (or stochastic) matrix of elements that define probabilities of contacts between different age classes of the two sexes as $p(i,j)$, where i and j represent the discrete age classes. Dropping the time suffix, t, for a two-sex model (and with notation as defined previously), the constraints on p_{ij} and p'_{ij} are

$$0 \leqslant p_{ij},\ p'_{ij} \leqslant 1, \tag{1}$$

$$\Sigma_j p_{ij} = 1 = \Sigma_j p'_{ij}, \tag{2}$$

and, less trivially, the group-specific 'sum rule' that says that the number of females of age j that are partners of males of age i, is identically equal to the number of males of age i that are partners of females of age j:

$$c_i N_i p_{ij} = c'_j N'_j p'_{ji}. \tag{3}$$

The overall sum rule is a trivial consequence of equation (3), as it intuitively must be that

$$\Sigma_i c_i N_i = \Sigma_j c'_j N'_j. \tag{4}$$

If we are only interested in proving formal theorems about existence, uniqueness or the stability of the model the constraints remain formal. But if we wish to perform numerial studies to obtain an explicit understanding of dynamic behaviour, the constraints pose serious computational problems. For example, if both male and female partner number distributions, $\{c_i\}$ and $\{c'_i\}$, are specified, then the constraints (1)–(3) make construction of the preference matrices a very messy job.

We choose, instead, to specify the partner numbers, $\{c_i\}$, and the preference matrix, $\{p_{ij}\}$, for one sex, and then let the constraints (1)–(3) determine both partner numbers, $\{c'_j\}$, and preferences, $\{p'_{ji}\}$, for the other sex.

Explicitly, if we specify $\{c_i\}$ and $\{p_{ij}\}$, then $\{p'_{ji}\}$ are given from equation (3) as

$$p'_{ji} = c_i N_i p_{ij} / c'_j N'_j. \tag{5}$$

But the constraint that $\Sigma_i\ p'_{ji} = 1$ now gives us an equation or constraint that, in effect, specifies the other sexes' partner number distribution:

$$c'_j = (\Sigma_i c_i N_i p_{ij}) / N'_j. \tag{6}$$

Substituting this back into equation (5), we get the other sexes' preference matrix elements given by

$$p'_{ji} = c_i N_i p_{ij} / (\Sigma_i c_i N_i p_{ij}). \tag{7}$$

In summary, equations (6) and (7) specify $\{c'_j\}$ and $\{p'_{ji}\}$ when $\{c_i\}$ and $\{p_{ij}\}$ are defined. All constraints (1)–(3) are fulfilled in these circumstances.

(b) *Examples*

We first consider some special cases ((i)–(iv)) of preference and mixing before moving to the description of the more general approaches adopted in the simulations described in the results section of the paper.

(i) *Strictly within-group mixing*

If both sexes only choose sexual partners of the opposite sex from within their own age class then

$$p_{ij} = \delta_{ij}, \tag{8}$$

where δ_{ij} is the koronecker delta (see Anderson *et al.* 1988). Given c_j then

$$c'_j = c_j N_j / N'_j, \tag{9}$$

and

$$p'_{ji} = \delta_{ij}. \tag{10}$$

(ii) *Proportional mixing*

If males (or females) choose partners of the opposite sex of a given age in proportion to the representation of that age class in the total population of the opposite sex (N') then

$$p_{ij} = N'_j / N'. \tag{11}$$

Again given c_i then

$$c'_j = \Sigma_i c_i N_i N'_j / (N' N'_j) = \Sigma_i c_i N_i / N',$$

but

$$\Sigma_i c_i N_i = \Sigma c'_j N'_j,$$

so we can write

$$c'_j = (\Sigma_i c'_i N'_i) / N' = \text{constant}.$$

In fact

$$c'_j = \langle c' \rangle, \tag{12}$$

where $\langle c' \rangle$ is the overall average number of partners for this sex, defined in the standard way as

$$\langle c' \rangle = (\Sigma c'_i N') / (\Sigma N'_i).$$

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In summary, $c'_j = \langle c' \rangle =$ constant, for all j. This results in

$$p'_{ji} = (c_i N_i N'_j)/(N' \langle c' \rangle N'_j),$$

or

$$p'_{ji} = (c_i N_i)/(\langle c' \rangle N').$$

But, by definition, $\langle c' \rangle N' = \langle c \rangle N$ because

$$\langle c' \rangle N = (\Sigma c'_i N'_i)(\Sigma N'_i)/(\Sigma N'_i).$$

Thus we can more transparently write the preference matrix for the other sex, assuming proportional mixing for the first sex, as

$$p'_{ji} = c_i N_i / \langle c \rangle N = (c_i N_i)/(\Sigma c_i N_i). \quad (13)$$

(iii) *Within-group mixing, against a background of proportional mixing*

This example illustrates a bias for within age group mixing overlaid on a background of proportional mixing where

$$p_{ij} = (\alpha N'_j/N') + (1-\alpha)\delta_{ij}. \quad (14)$$

Note that if $\alpha \to 0$ case (i) is recovered, and when $\alpha \to 1$ case (ii) is recovered. Given c_j then

$$c'_j = ((1-\alpha)c_j N_j + \alpha(\langle c \rangle N)(N'_j/N'))/N'_j. \quad (15)$$

The preference matrix is given from equation (7), as

$$p'_{ji} = \frac{c_i N_i\,(\alpha(N'_j/N') + (1-\alpha\,\delta_{ij})}{\langle c \rangle N\,(\alpha(N'_j/N') + (1-\alpha)(c_j N_j)/(\langle c \rangle N))}. \quad (16)$$

(iv) *Sub-diagonal mixing – preference for women an age class younger than men – against a background of proportional mixing*

This describes a preference matrix where men in youngest age class have proportional mixing, whereas in all other age classes there is a fraction $(1-\Upsilon)$ mixing with the next-youngest female age group, and the remaining fraction, Υ, is mixing in a proportional manner with other age classes of females.

The preference matrix p_{ij} is defined as

$$p'_{ij} = \Upsilon(N'_j)/(N') + (1-\Upsilon)\delta_{i-1,j},$$
$$p_{ij} = N'_j/N' \quad \text{for} \quad i = 1. \quad (17)$$

Given $\{c_i\}$ then the $\{c'_j\}$ are defined by

$$c'_j N'_j = (N'_j/N')(\langle c \rangle N \Upsilon + (1-\Upsilon)c_i N_i) + (1-\Upsilon)c_{j+1} N_{j+1} \quad (18)$$

Then from equation (7)

$$p'_{ji} = (c_i N_i / c'_j N'_j) p_{ij} \quad (19)$$

(c) *More general cases*

The algebraic structures defined in cases (i)–(iv) above limit the range of behavioural mixing or preference characteristics captured within the matrices. For example, in case (iii), the choice of a value for the parameter α (between 0 and 1) only allows relatively small deviations from the background of proportional mixing. In this paper we examine more general cases by considering situations in which the number of males in a given age class differs from the number of females in the same age class ($N_i \neq N'_i$) (often as a consequence of the differential mortality induced by AIDS) and in which male and female rates of sexual partner change differ ($c_i \neq c'_i$). In particular we allow rates of sexual partner change to vary with age class in different ways for the two sexes. Our approach is to specify the partner number, $\{c_i\}$, and the preference matrix, $\{p_{ij}\}$, for one sex and use equations (5)–(7) to determine the equivalent vector, $\{c'_j\}$, and matrix, $\{p'_{ij}\}$, for the opposite sex. In this paper we concentrate on the influence of age-related changes in sexual behaviour but the approach can be generalized to consider other stratifications of the population (other than sex and age) such as the rate of sexual partner change, the geographical locality (e.g. urban and rural) or socio-economic class (e.g. professional or manual workers). For example, consider a population divided into discrete classes by age, i, sexual activity, s, and sex (the 'dash' notation). For a given sex the number of people in age class i and sexual activity class s is $N_{is}(t)$ at time t (the number of the opposite sex is $N'_{is}(t)$). The rates of sexual partner change in age class i and sex activity class s are defined as $c_{is}(t)$ at time t. The discrete class preference matrix p_{ijsv} defines the probability that a person of one sex in age class i and sexual activity class s chooses a sexual partner of the opposite sex in age class j and sexual activity class v. The constraints on the elements of the matrix (dropping the time suffix t) are as detailed in equations (1)–(3) where

$$0 \leqslant p_{ijsv},\ p'_{ijsv} \leqslant 1, \quad (20)$$

$$\Sigma_j \Sigma_v\, p_{ijsv} = 1 = \Sigma_j \Sigma_v\, p'_{ijsv} \quad (21)$$

$$c_{is} N_{is} p_{ijsv} = c'_{jv} N'_{jv} p'_{jivs}. \quad (22)$$

Given that $\{p_{ijsv}\}$ and $\{c_{is}\}$ are specified we can compute p'_{jivs} from equation (22):

$$p_{jivs} = (c_{is} N_{is} p_{ijsv})/(c'_{jv} N'_{jv}). \quad (23)$$

The constraint $\Sigma_j \Sigma_v\, p_{ijsv} = 1$ specifies the other sexes' partner number distribution

$$c'_{jv} = (\Sigma_i \Sigma_s\, c_{is} N_{is} p_{ijsv})/N'_{jv}. \quad (24)$$

Substituting back into equation (23) we get the opposite sexes' preference matrix elements;

$$p'_{jivs} = (c_{is} N_{is} p_{ijsv})/(\Sigma_i \Sigma_s\, c_{is} N_{is} p_{ijsv}) \quad (25)$$

If we further stratify the population by other criteria such as geographical location or socio-economic class the algebra becomes more complex but the procedure outlined above can be employed to determine the partner number distribution and preference matrix of one sex given information about these quantities for the other sex (plus, of course, information on the population distribution by each stratification class).

(d) *Mathematical model*

We base our numerical studies on the model defined in the papers by Anderson *et al.* (1988, 1989). The structure is briefly outlined in this present paper. The model is compartmental in structure where susceptibles of sex k, age a at time t, $X_k(a,t)$, on acquiring

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infection, pass sequentially through three infected classes, $Y_{i,k}(a,t)$. They join the first at a per capita rate $\lambda_k(a,t)$ and leave each class (to join the next) at rates $\gamma_{i,k}(a)$. In the third class it is assumed that all leave to join the class $A_k(a,t)$ which denotes the development of the disease AIDS (i.e. all those infected with HIV-1 develop AIDS). Three infected classes are defined to facilitate the representation of differing levels of infectiousness throughout the incubation period of AIDS. The average incubation period, $T_k(a)$ is defined by the sum of the average durations of stay in the three infected classes, $Y_{i,k}(a,t)$, where

$$T_k(a) = \Sigma\, 1/\gamma_{ik}(a). \tag{26}$$

The incubation period is assumed to be the same for both sexes and independent of age, excepting in infants who acquire infection via vertical transmission from their infected mothers. In the latter class different values of $\gamma_{i,k}(a)$ are employed as noted in the following section on parameter values. The background per capita death rate is defined as $\mu_k(a)$, which is age and sex dependent, and the death rate of AIDS patients is defined as $\alpha(a)$ and assumed to be independent of sex but dependent on age.

The system of equations describing the changes in the numbers of individual of age a at time t, in each of the five classes is defined as follows

$$\partial X_k(a,t)/\partial t + \partial X_k(a,t)/\partial a = -(\lambda_k(a,t) + \mu_k(a))X_k(a,t), \tag{27}$$

$$\partial Y_{1,k}(a,t)/\partial t + \partial Y_{1,k}(a,t)/\partial a = \lambda_k(a,t)X_k(a,t) - (\gamma_{1,k}(a) + \mu_k(a))Y_{1,k}(a,t), \tag{28}$$

$$\partial Y_{i,k}(a,t)/\partial t + \partial Y_{i,k}(a,t)/\partial a = \gamma_{i-1,k}(a)Y_{i-1,k}(a,t) - (\gamma_{i,k}(a) + \mu_k(a))Y_{i,k}(a,t) \quad \text{for} \quad i = 2,3, \tag{29}$$

$$\partial A_k(a,t)/\partial t + \partial A_k(a,t)/\partial a = \gamma_{3,k}(a,t)Y_{3,k}(a,t) - (\mu_k(a) + \alpha_k(a))A_k(a,t). \tag{30}$$

The force or per capita rate of infection (via horizontal, or sexual contact, transmission), $\lambda_k(a,t)$, is defined as

$$\lambda_k(a,t) = \left\{ \int_{a1}^{a2} c_k(a,a',t)J_k(a,a',t) \sum_{i=1}^{3} \beta_{ik} \frac{Y_{ik}'(a',t)}{N_k'(a,t)} \mathrm{d}a' \right\}. \tag{31}$$

Here k denotes one sex and k' the opposite sex. $J_k(a,a',t)$ defines the probability that a person of sex k and age a at time t has sexual contact with a partner of age a' of the opposite sex (preference matrix). The limits a_1 and a_2 define, respectively, the lower and upper age bounds of sexual activity. The term $\beta_{i,k}$ is the probability of transmission for sex k (per partnership contact) arising from contacts between susceptibles and infecteds in infectious class $i (i = 1,2,3)$ (assumed independent of age). As defined earlier, $c_k(a,a',t)$ defines the mean rate of sexual partner change of sex k and age a with individuals of the opposite sex of age a' at time t.

In the numerical solution of equations (27)–(30) discrete age classes are employed, where the subscript i denotes the age class, and the equivalent version of equation (31) is as follows:

$$\lambda_k(i,t) = \left\{ \sum_{i=m}^{n} \left[c_k p(i,j,t)\, p(i,j,t) \sum_{s=1}^{3} \left[\beta_{sk} \frac{Y_{sk}'(i,t)}{N_k'(i,t)} \right] \right] \right\},$$

where n and m define the upper and lower age classes that bound the sexually active age groups.

The methods employed in the numerical solution of this sytem of equations ((12)–(15)) were as described in Anderson *et al.* (1989). For the hyperbolic system of equations to be well posed we require initial conditions that define the age distributions in each infection class (i.e. $X_k(a,0)$, $Y_{i,k}(a,0)$, $A_k(a,0)$). We employ a set of age-specific death rates (see the following section), $\mu_k(a)$ for each sex to define the initial age distribution of susceptibles at the point of introduction of HIV-1 at time $t = 0$. To trigger the epidemic we introduce a few infecteds into class $Y_{i,k}(a,0)$ at time $t = 0$, and assume that all other classes are zero at the start of the simulation. We also require boundary or renewal equations, given the assumption that $(1 - \varepsilon)$ of children born to women in the three $Y_{i,k}(a,t)$ classes, between the fertility lower and upper age bounds of b_1 and b_2, respectively, acquire HIV-1 infection from their mothers via vertical transmission. Because of their short life expectancy and poor health we assume that AIDS patients are unable to produce viable off spring (those children that are born to such mothers die rapidly and hence are ignored in our analyses). The renewal equations are as follows (where $k = 1$ denotes the female sex):

$$X_k(0,t) = 1/2 \int_{b1}^{b2} m(a)X_1(a,t)\mathrm{d}a + 1/2 \int_{b1}^{b2} \varepsilon m(a)(\Sigma Y_{i,1}(a,t))\mathrm{d}a, \tag{33}$$

$$Y_{1,k}(0,t) = 1/2 \int_{b1}^{b2} (1 - \varepsilon)m(a)(\Sigma Y_{i,1}(a,t))\mathrm{d}a, \tag{34}$$

$$Y_{i,k}(0,t) = 0 \quad \text{for} \quad i = 2,3. \tag{35}$$

The factor 1/2 denotes an assumed 1:1 sex ratio of males and females at birth. We further assume that the age-specific fertility rate, $m(a)$, is the same for the susceptibles and all three infected classes.

(e) *Parameter values*

(i) *Demography*

The age-specific mortality ($\mu(a)$) and fertility ($m(a)$) rates employed in the numerical studies of model properties were chosen to represent profiles typical of Sub-Saharan African countries at present. The age specific rates are portrayed in figure 5 and table 1. The rates employed generate a slightly longer life expectancy at birth for women, by comparison with men (52.1 years for men and 54.7 years for females). The initial population size at time $t = 0$ was set at 16.6 million people (1:1 sex ratio) with a disease-free annual population growth rate of 4%. The fertility class age bounds were set at $b_1 = 15$ years and $b_2 = 50$ years. The sexual activity age class bounds were similarly set at $a_1 = 15$ years and $a_2 = 50$ years.

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Table 1. *Age specific mortality ($\mu(a)$) and birth ($m(a)$) rates, defined per year*

mortality rates			birth rates	
age class	males	females	age class	females
1	0.117	0.100	15–19	0.175
1–4	0.019	0.019	20–24	0.313
5–9	0.007	0.006	25–29	0.324
10–14	0.004	0.004	30–34	0.271
15–19	0.004	0.004	35–39	0.201
20–24	0.006	0.005	40–44	0.125
25–29	0.007	0.006	45–49	0.053
30–34	0.007	0.006		
35–39	0.008	0.007		
40–44	0.010	0.008		
45–49	0.012	0.009		
50–54	0.016	0.012		
55–59	0.021	0.016		
60–64	0.030	0.024		
65–69	0.044	0.038		
70–74	0.068	0.060		
75–79	0.105	0.094		
80+	0.189	0.174		

(ii) *Epidemiology*

The probability of vertical transmission from infected mother to new born infant, $(1-\varepsilon)$, was set at 0.5 (i.e. 50% chance of transmission). This value is at the upper end of the range of observed values (20%–50%, see Anderson & Medley 1988) but it is the figure close to that suggested by a recent study of HIV-1 transmission in Zambia (Hira *et al.* 1989). In this study, of 109 babies born to seropositive mothers, 42 were infected (39%) and of these, 44% had died by 2 years of age. In accord with this, and other studies (see Lallemant *et al.* 1989), we assume that infected children have a life expectancy of approximately 3.0 years from birth (for infants $\gamma_1=\gamma_2=\gamma_3=1.5$ per year) with an average incubation period, T_k, of 2 years and a life expectancy with AIDS $(1/\alpha)$ of 1 year (Auger *et al.* 1988).

In the case of sexually active adults we assumed the average incubation period, T_k to be 8 years (see Bacchetti & Moss 1989) with $\gamma_1=2.0$ per year, $\gamma_2=0.1818$ per year and $\gamma_3=0.5$ per year. Given the limited data at present on infectiousness during the incubation period we assume that $\beta_{1,k}=\beta_{2,k}=\beta_{3,k}$. On the basis of data from studies of transmission between heterosexual couples, where one partner acquired infection from contaminated blood or blood products, we assume that $\beta_{i,1}$ (male to female) $=3\beta_{i,2}$ (female to male) (see Ahmed *et al.* 1989; Laga *et al.* 1989). We estimate the numerical values of the $\beta_{i,k}$ s′ on the basis of various assumptions concerning the doubling time of the epidemic in its early stages (for details see Anderson *et al.* 1986, 1989; May and Anderson 1987). For an early doubling time (doubling in the numbers infected, or AIDS cases) of 1.5 years, $\beta_{i,1}$ (male to female) $=0.3$ (per partnership), $\beta_{i,2}=0.1$; for a doubling time of 2.5 years, $\beta_{i,1}=0.2013$, $\beta_{i,2}=0.0671$; for a doubling time of 3.5 years, $\beta_{i,1}=0.1591$, $\beta_{i,2}=0.053$ and for a doubling time of 4.5 years, $\beta_{i,1}=0.1345$, $\beta_{i,2}=0.0452$. The average life expectancy of an adult AIDS patient $(1/\alpha)$ was assumed to be 1 year (see Anderson & Medley 1988; Reeves 1989).

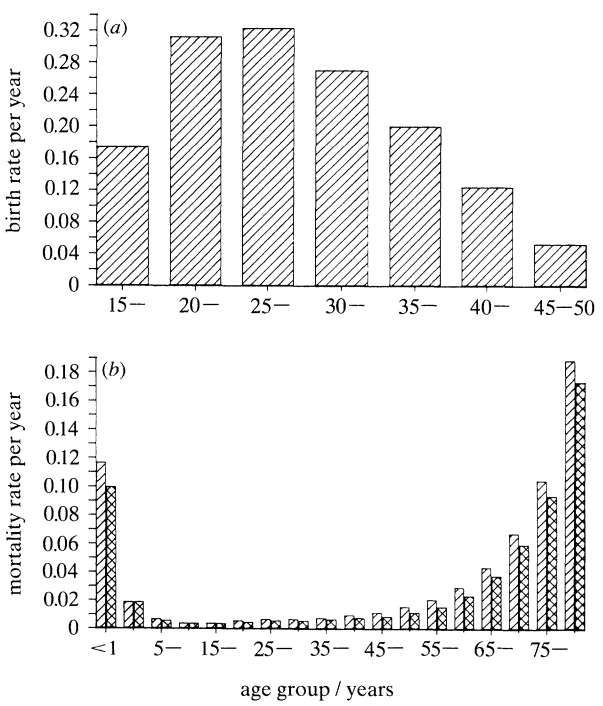

Figure 5. (*a*) The age specific fertility and (*b*) mortality rates employed in the numerical studies of the behaviour of the model. In (*b*): males ▨; females ▩.

(iii) *Mixing and sexual activity*

As indicated in the opening subsection of the methods, the precise values of the elements of the mixing matrices (p_{ij} or p'_{ij}) based on partner choice by age classes, of the two sexes (the prime denoting the opposite sex) depend on the assumptions made concerning the behavioural rules that govern partner formation, and the details of how mean rates of partner acquisition vary with age and sex (figure 2). We examine a variety of cases as detailed below.

Model (A). Restricted mixing within age classes. For restricted mixing individuals in a given age class are assumed to have a preference for sexual partners of the opposite sex in the same age class as themselves (see case (i) in § 2*b*). The mixing probabilities p_{ij} at the start of the epidemic were the same for both sexes as defined in Table 2. We consider three cases where the overall mean rate of partner change (over all age classes) was set at 3.4 partners per year for males and females at the start of the epidemic. In each case we assume that age-dependent changes are identical for men and women. In case A1 we assume that the mean is 3.4 per year for all male and female age classes (i.e. independent of age). In case A2 we assume that sexual activity increase with age with the pattern defined in table 2. In case A3 we assume that sexual activity (the rate of partner acquisition) decreased with age as defined in table 2.

Model (B). Mixing with own and next younger age class (2 off diagonal). In this example males in a given age

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Table 2. *Restricted mixing within age classes*

mixing probabilities, p_{ij} (males and females)

		age class a'/years						
		15–19	20–24	25–29	30–34	35–39	40–44	45–49
	15–19	1	0	0	0	0	0	0
	20–24	0	1	0	0	0	0	0
age	25–29	0	0	1	0	0	0	0
class	30–34	0	0	0	1	0	0	0
a/years	35–39	0	0	0	0	1	0	0
	40–44	0	0	0	0	0	1	0
	45–49	0	0	0	0	0	0	1

mean rates of partner change per year

	age class/years						
case	15–19	20–24	25–29	30–34	35–39	40–44	45–49
A1 $c=c'$	3.4	3.4	3.4	3.4	3.4	3.4	3.4
A2 $c=c'$	1.8	2.0	3.0	4.0	5.0	6.0	8.0
A3 $c=c'$	5.7	4.0	3.0	2.5	2.0	1.0	0.5

class were assumed to have a preference for females of the same age and the age class immediately below their own. Similarly, if female preference sets the values of the elements of the matrices this would imply female preference for males in the same age class and the age class immediately above their own. At the start of the epidemic the preference matrices were as defined in table 3.

To meet the constraints defined in the first part of the methods section, it was assumed that male sexual activity increased with age and female activity remained fairly constant with age. The age-class-

Table 3. *Mixing with own and next younger age class (two off diagonal)*

mixing probabilities, p_{ij}

		age class a'/years						
		15–19	20–24	25–29	30–34	35–39	40–44	45–49
					males			
	15–19	1	0	0	0	0	0	0
	20–24	0.75	0.25	0	0	0	0	0
age	25–29	0	0.75	0.25	0	0	0	0
class	30–34	0	0	0.75	0.25	0	0	0
a/years	35–39	0	0	0	0.75	0.25	0.25	0
	40–44	0	0	0	0	0.75	0.75	0
	45–49	0	0	0	0	0	0	0.25
					females			
	15–19	0.6	0.4	0	0	0	0	0
	20–24	0	0.22	0.78	0	0	0	0
age	25–29	0	0	0.24	0.76	0	0	0
class	30–34	0	0	0	0.25	0.75	0	0
a/years	35–39	0	0	0	0	0.26	0.74	0
	40–44	0	0	0	0	0	0.24	0.76
	45–49	0	0	0	0	0	0	1.0

mean rates of partner change per year

	age class/years						
	15–19	20–24	25–29	30–34	35–39	40–44	45–49
				males			
c per year	1.8	2.0	3.0	4.0	5.0	6.0	8.0
				females			
c' per year	3.0	2.3	3.1	4.0	4.8	6.2	2.0

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Table 4. *Mixing with own and three next younger age class (four off diagonal)*

mixing probabilities, p_{ij}

		age class a'/years						
		15–19	20–24	25–29	30–34	35–39	40–44	45–49
		males						
	15–19	1.0	0	0	0	0	0	0
	20–24	0.5	0.5	0	0	0	0	0
age	25–29	0.4	0.35	0.25	0	0	0	0
classes	30–34	0.4	0.3	0.2	0.1	0	0	0
a/years	35–39	0	0.4	0.3	0.2	0.1	0	0
	40–44	0	0	0.4	0.3	0.2	0.1	0
	45–49	0	0	0	0.4	0.3	0.2	0.1
		females						
	15–20	0.428	0.182	0.184	0.195	0	0	0
	20–24	0	0.277	0.232	0.211	0.280	0	0
age	25–29	0	0	0.211	0.180	0.268	0.341	0
classes	30–34	0	0	0	0.102	0.203	0.290	0.406
a/years	35–39	0	0	0	0	0.169	0.322	0.509
	40–44	0	0	0	0	0	0.322	0.678
	45–49	0	0	0	0	0	0	1.0

mean rates of partner change per year

	age class/years						
	15–19	20–24	25–29	30–34	35–39	40–44	45–49
				males			
c per year	1.8	2.0	3.0	4.0	5.0	6.0	8.0
				females			
c' per year	4.2	3.6	3.5	3.9	3.0	1.9	0.8

specific mean rates of sexual partner change (overall mean 3.4 partners per year) are as defined in table 3.

Model (C). Mixing with own and three next younger age classes (four off diagonal). In this case males in a given age class were assumed to have a preference for females in their own age class and the next three younger age classes, and vice versa for females. At the start of the epidemic the preference matrices were defined as listed in table 4. The age and sex-specific mean rates of partner change (with an overall mean at the start of the epidemic of 3.4 per year) were set as defined in table 4. The patterns represent a rise in activity with age for males and a decline with age for females.

Model (D). Mixing with own and all younger age classes (lower triangle). In the fourth example males in a given age class are assumed to form sexual partnerships with females in all younger age classes and vice versa for females. At the start of the epidemic the mixing matrices were set as defined in table 5.

The age- and sex-specific mean rates of partner change (with an overall mean at the start of the epidemic of 3.4 partners per year) were set as defined in table 5. The patterns represent a rise in activity with age for males and a decrease with age for females.

Model (E). Mixing with all age classes but a bias towards older men forming partnerships with younger women. In the final example males in a given age class mix with females in all other age classes, but with a bias in the elements of the matrix to represent partnership formation with younger women. The reverse situation is represented for females. The mixing matrices are as defined in table 6. In this particular case the mean rate of partner change was assumed to be independent of age and was set at 3.4 partners per year for both females and males at the start of the epidemic.

In all the examples, and associated numerical simulations, the preference matrices were calculated as defined in the methods section by equations (5)–(7). The values of the elements of the matrices remained constant and independent of time.

Balancing supply and demand for sexual partners. As noted above we assumed that the structures of the male and female mixing matrices remain unaltered as the epidemic of AIDS progressed. However, because the rate of sexual activity is age dependent and the transmission probability from males to females is greater than that from females to males, a higher rate of AIDS-induced mortality among females by comparison with males (due to greater efficiency in transmission and concomitently higher levels of infection among women by comparison with men) results in the demand by men for female sexual partners exceeding the supply if the prefered rates of sexual partner change defined at the start of the epidemic remain unchanged. A number of options exist for

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Table 5. *Mixing with own and all younger age classes (lower triangle)* mixing probabilities, p_{ij}

		age class a'/years						
		15–19	20–24	25–29	30–34	35–39	40–44	45–49
					males			
	15–19	1	0	0	0	0	0	0
	20–24	0.75	0.25	0	0	0	0	0
age	25–29	0.5	0.25	0.25	0	0	0	0
class	30–34	0.4	0.3	0.2	0.1	0	0	0
a/years	35–39	0.35	0.25	0.2	0.15	0.05	0	0
	40–44	0.3	0.20	0.2	0.15	0.1	0.05	0
	45–49	0.3	0.2	0.2	0.15	0.1	0.025	0.025
					females			
	15–19	0.268	0.181	0.144	0.122	0.107	0.087	0.092
	20–24	0	0.144	0.172	0.219	0.182	0.138	0.146
age	25–29	0	0	0.230	0.195	0.194	0.195	0.195
class	30–34	0	0	0	0.185	0.276	0.263	0.277
a/years	35–39	0	0	0	0	0.204	0.388	0.408
	40–44	0	0	0	0	0	0.655	0.345
	45–49	0	0	0	0	0	[illegible]	1.0

mean rates of sexual partner change per year

	age class/years						
	15–19	20–24	25–29	30–34	35–39	40–44	45–49
				males			
c per year	1.8	2.0	3.0	4.0	5.0	6.0	8.0
				females			
c' per year	6.6	3.5	3.3	2.2	1.2	0.5	0.2

Table 6. *Mixing probabilities p_{ij}, for mixing with all age classes but a bias towards older men forming partnerships with younger women*

		age class a'/years						
		15–19	20–24	25–29	30–34	35–39	40–44	45–49
					males			
	15–19	0.2548	0.2039	0.1624	0.1294	0.1031	0.0819	0.0646
	20–24	0.4178	0.1713	0.1298	0.0968	0.0704	0.0493	0.0646
age	25–29	0.2138	0.4087	0.1215	0.0884	0.0621	0.0409	0.0646
class	30–34	0.2034	0.1525	0.4195	0.0780	0.0516	0.0305	0.0646
a/years	35–39	0.1902	0.1394	0.0979	0.4521	0.0385	0.0173	0.0646
	40–44	0.1735	0.1227	0.0812	0.0481	0.5092	0.0006	0.0648
	45–49	0.1511	0.1009	0.0594	0.0264	0.0000	0.5970	0.0646
					females			
	15–19	0.2548	0.3345	0.1363	0.1033	0.0769	0.0558	0.0385
	20–24	0.2548	0.1713	0.3255	0.0968	0.0704	0.0493	0.0319
age	25–29	0.2548	0.1630	0.1215	0.3341	0.0621	0.0409	0.0236
class	30–34	0.2548	0.1525	0.1110	0.1780	0.3601	0.0305	0.0132
a/years	35–39	0.2548	0.1394	0.0979	0.0648	0.0385	0.4046	0.0000
	40–44	0.2548	0.1227	0.0812	0.0481	0.0218	0.0006	0.4708
	45–49	0.2546	0.2039	0.1624	0.1294	0.1031	0.0819	0.0646

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balancing supply and demand, ranging from the extremes of female sexual activity rising to match the increased demand created by a growing proportion of males in the population, to male sexual activity decreasing to match the partnerships available from a decreasing proportion of women. Data are not available to guide the choice of a suitable assumption under these circumstances. We therefore adopt a procedure in which the mean rates of sexual partner change in a defined age group of either sex, alter in a manner related to the proportional availability of the opposite sex in each of the different age classes. More formally we make the following assumption. We define the mean rate of sexual partner formation of individuals of sex k in age class a with individuals of the opposite sex of age a' at time t, $c_k(a,a',t)$, as

$$c_k(a,a',t) = d_k(a,a')\,N_k(a',t)/(N_1(t)+N_2(t)), \qquad (36)$$

where $N_k(a',t)$ is the number of sexually active individuals of sex k and age a' at time t and $N_k'(t)$ ($k=1$, males and $k=2$, females) is the total number of sexually active individuals of sex k at time t over all age classes. Note that the sexually active classes includes susceptible individuals (X) and all infecteds ($Y_1+Y_2+Y_3$), but excludes people with AIDS who are assumed to be sexually inactive due to their illness. The term $d_k(a,a')$ is set as an initial condition (its value is constant and independent of time) at the start of the epidemic such that

$$d_k(a,a') = c_k(a,a',0)(N_1(0)+N_2(0))/N_k'(a,0). \qquad (37)$$

Here the term $c_k(a,a',0)$ defines the initial age and sex-dependent mean rates of sexual partner change. Having fixed these initial rates of partner change, and the structures of the mixing matrices for both sexes, it can be shown that the conditions defined by equations (1)–(3) are satisfied for all values of t provided the $c_k(a,a',t)s'$ are calculated as defined in equation (36). This method ensures that the total number of sexual partnerships formed by males equals that formed by females at all times during the course of the epidemic as female mortality due to AIDS exceeds male mortality.

3. RESULTS

We first consider the influence of age-related changes in sexual activity under the assumption of restricted within age class mixing (Model A).

(a) *Age-related changes in sexual activity*

As defined in the previous section we examine the predictions of the model under three sets of assumptions concerning how sexual activity (mean rates of sexual partner change within an age class) changes with age, namely, cases A1 (mean constant and independent of age), A2 (mean increases with age) and A3 (mean decreases with age). In each example the overall mean rate of sexual partner acquisition was fixed at 3.4 partners per year at the start of the epidemic. Note that in cases A2 and A3, where the rate of sexual partner acquisition alters with age,

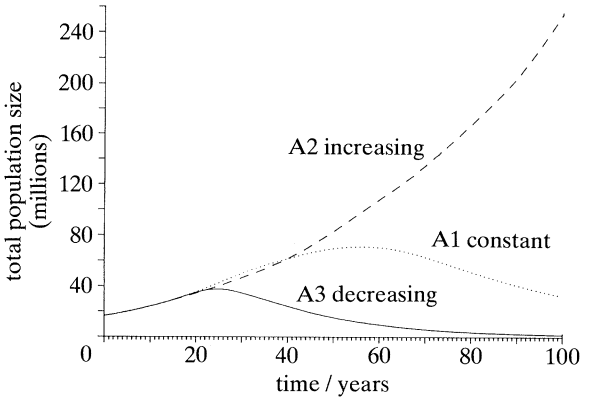

Figure 6. Model A. Predicted temporal changes in total population size following the introduction of HIV-1 at time $t=0$. Cases A1 to A3 denote the mean rate of sexual partner change with A1 constant with age, A2 increasing with age and A3 decreasing with age, respectively (see main text). Sexual partners are chosen within and not between age classes (restricted mixing).

the overall mean of 3.4 per year in the total population has a variance attached to it, which at the start of the epidemic was 3.3 for case A2 and 2.8 for case A3 (calculated on the basis of the age-specific rates and the proportions in each age class).

We examine the predictions of the model, under the different sets of assumptions concerning sexual activity, by reference to temporal changes in total population size ($N(t)$), the number of people with AIDS ($A(t)$) and the proportion of the population infected with HIV-1 ($y(t)$). These changes are presented in Figures 6–8, for cases A1, A2 and A3 respectively. In these simulations the doubling time of the epidemic in its early stages was set at 1.5 years (a pessimistic assumption) giving a value of the basic reproductive rate, R_0, of 4.7 (for $\beta_1=3\beta_2$).

Note that in each simulation the overall mean rate of sexual partner change for men and women at the start of the epidemic was held constant at 3.4 partners per year. Whether or not the age-dependent rate rises, falls or remains constant with age has a very significant impact on the predicted course of the epidemic. When sexual partner change is higher in the younger age classes, the greatest demographic impact of AIDS is recorded, with the population growth rate becoming negative at around year 23 after the introduction of the infection. For a constant age-independent partner change rate, the growth rate becomes negative around year 58 of the simulation. When the rate increases with age, the impact of the disease is insufficient to reverse the sign of the population growth rate (figure 6). These patterns are a direct consequence of the differing impacts of the disease on the younger female age classes who contribute most to the net fertility of the population. If they acquire infection early, due to high rates of sexual partner change (c_i decreasing with age) the disease has its greatest impact. As recorded in figure 7 when the population continues to increase despite the spread of the virus (c_i increasing with age) the total number of AIDS cases continues to rise over the 100 year

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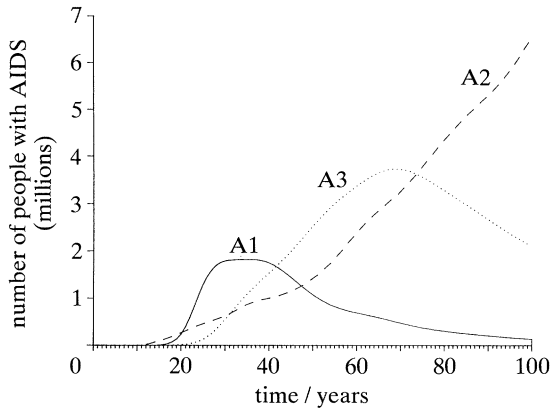

Figure 7. Model A. Similar to figure 6 but recording temporal changes in the number of people with AIDS.

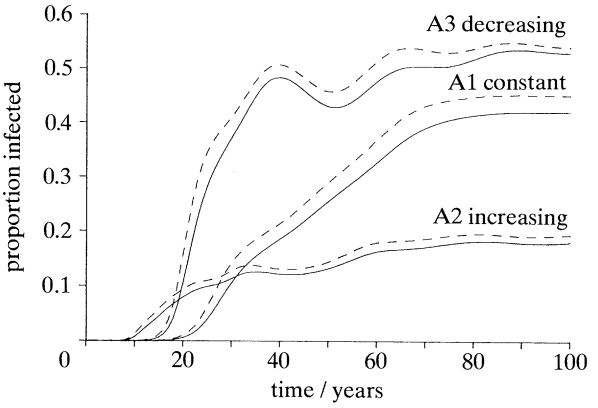

Figure 9. Model A. Similar to figure 8, but recording temporal changes in the proportion infected with HIV-1 for males (solid lines) and females (dotted lines) separately.

duration of the simulation. With respect to the proportion of the population infected with HIV, the predicted patterns are displayed in figure 8. When the mean rates of partner change decrease with age, seroprevalence of HIV-1 attains a plateau of around 45%, whereas when c_i increases with age the plateau, in the growing population, is around 15%. When the predictions are stratified by sex, as depicted in figure 9, seroprevalence in males is slightly less than that for females, although not by a significant amount. This result is of interest as the efficiency of transmission of the virus was set at a level three times higher from males to females than that in the reverse direction. The reason why the predicted seroprevalence in females is not three times greater than that in males is in part linked to the assumptions made in the model concerning the balancing of 'supply' and 'demand' in sexual partners as AIDS induced mortality alters the sex ratio of the population. As noted in the methods section, we assumed that as imbalances occur due to high initial rates of mortality in women as the epidemic develops (see figure 10), the mean rates of partner change of men alter (i.e. decrease) in a manner related to the proportional availability of women in each of the different age classes. As such, the sex ratio of AIDS cases and numbers seropositive remains close to unity in value. More generally, earlier work on simpler models of the spread of HIV in heterosexual populations, with unequal transmission probabilities from men to women (β_1) and women to men (β_2) suggests that the sex ratio of AIDS cases (men to women) in the early stages of the epidemic is given approximately by $[(\beta_2 c_2)/(\beta_1 c_1)]^{\frac{1}{2}}$ (Anderson *et al.* 1988). With values of $\beta_1 = 0.3$, $\beta_2 = 0.1$ and $c_1 = c_2 = 3.4$ per year (a doubling time of 1.5 years) the ratio predicted by this approximation is roughly 0.7–0.8. This prediction is in precise agreement with that of the model in the early stages of the epidemic (i.e. the first 20 years). Interestingly, a recent paper by Berkley *et al.* (1990) concerning HIV-1 infection in Uganda records a male to female ratio of infection of approximately 0.6–0.9 (average value 0.72).

A more detailed picture of the pattern of the epidemic and its impact on the age structure of the population is provided by three-dimensional pictures of changes in population size and the number of people with AIDS, stratified by age and time. For cases A3 (mean partner change rate decreasing with age) and A1 (mean partner change rate constant over age classes) the predicted patterns of population change are displayed in figures 11 and 13, respec-

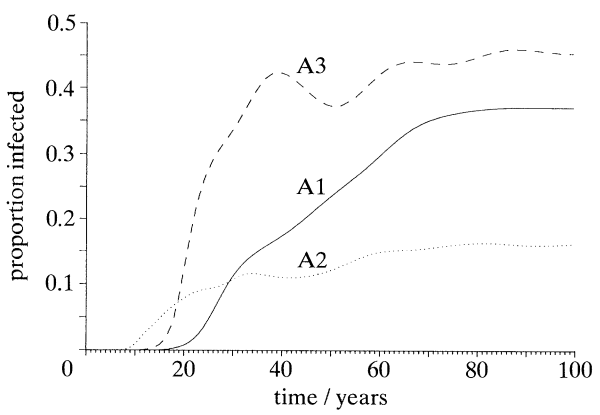

Figure 8. Model A. Similar to figure 6 but recording temporal changes in the proportion infected with HIV-1.

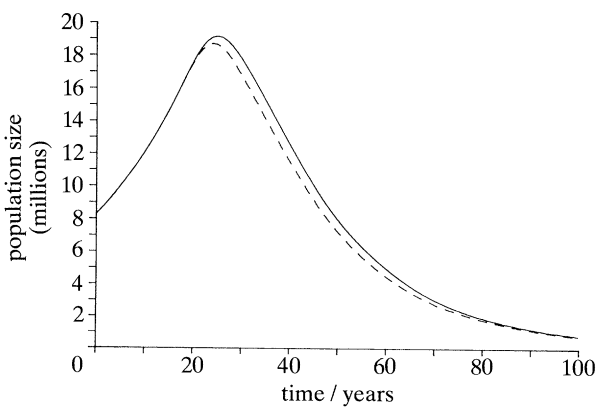

Figure 10. Model A. Mean rate of sexual partner change decreasing with age (A3). Temporal changes in the population of males (solid lines) and females (dotted lines) following the introduction of HIV-1 at time $t = 0$.

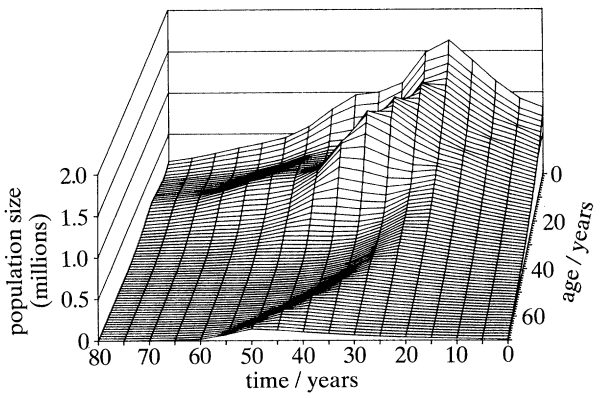

Figure 11. Model A. Predicted temporal changes in the age structure of the population after the introduction of HIV-1 at time $t=0$, for model A3 in which the mean rate of sexual partner change decreases with age.

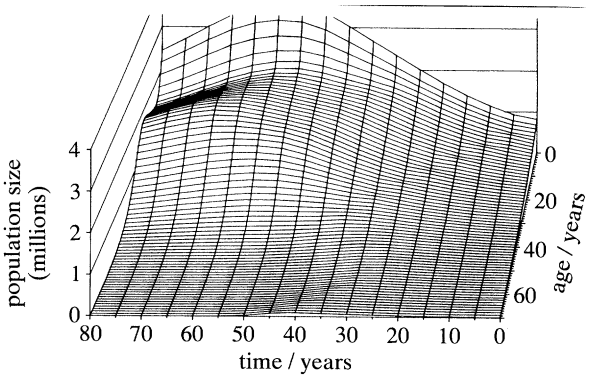

Figure 13. Model A1. Predicted temporal changes in the age structure of the population after the introduction of HIV-1 at time $t=0$, for model A1 in which the mean rate of sexual partner change is constant and independent of age.

tively. Similar plots of changes in the number with AIDS are presented in figures 12 and 14. When the rate of sexual partner change decreases with age, the epidemic induces 'ripples' in the age structure of the population as the rates of transmission of the virus from men to women and vice versa alter to accommodate changes in the supply and demand for sexual partnerships due to AIDS induced mortality which is particularly high in young women (figure 11). By contrast, when the mean rate of partner change is constant across age classes a much smoother pattern of change in age structure is recorded (figure 13). Similar trends are apparent in the age distribution of people with AIDS as depicted in figures 12 and 14. Note that the predicted age distribution of AIDS cases are broadly similar to those observed (see figures 1 and 2), excepting for the fact that a much higher number of cases in infants and young children are predicted when compared with the observed pattern. This may be due to the high rate of vertical transmission (50%) assumed in the simulations, or it may be a consequence of the difficulties of diagnosing a case of AIDS in young infants where deaths due to a variety of infectious diseases are frequent irrespective of the presence of HIV-1. We believe the latter factor is of significance in many areas of Sub-Saharan Africa at present. Careful thought should be given to the case definition of AIDS in infants in Africa and records should be kept of HIV-1 related mortality (i.e. deaths in infants infected with HIV-1, irrespective of whether or not a diagnosis of AIDS is made).

(*b*) *Who mixes with whom by age class*

In models (B) to (E) we relax the assumption of restricted mixing within age classes and progressively allow a wider range of sexual contact between the different age classes of men and women. In line with observations (see figure 3) we assume in each of the models that on average men have sexual contact with women younger than themselves. The precise patterns of mixing by age for each of the models are defined in the methods section and tables 3–6. These tables also record the age-related rates of sexual partner change, where on average the rate rises with age for men and decreases with age for women.

We first consider the impact of between age class mixing in the two models in which the mean rate of sexual partner change is held constant across age classes at the beginning of the epidemic ($c=c'=3.4$ per year), namely, models A1 and E. The

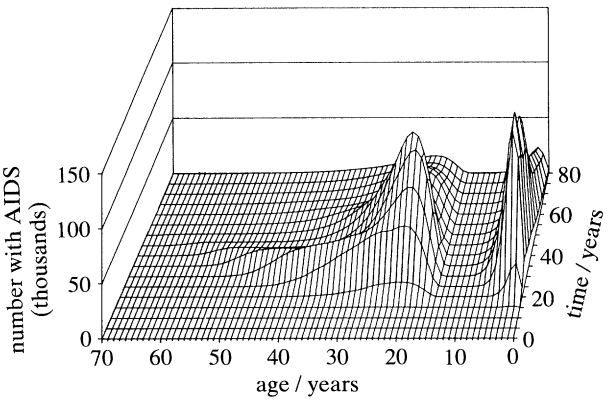

Figure 12. Model A. Similar to figure 11 but recording the age distribution of people with AIDS as the epidemic develops following the introduction of HIV-1 at time $t=0$.

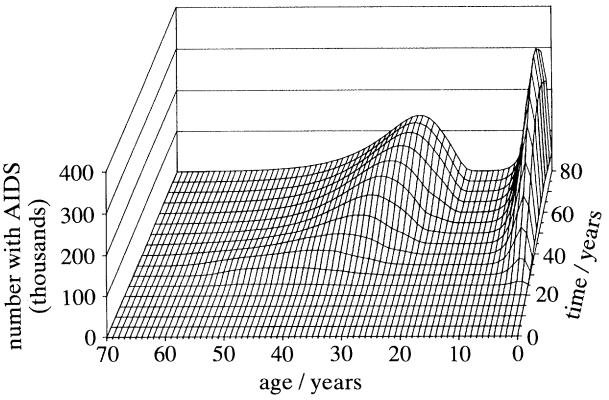

Figure 14. Model A1. Similar to figure 13 but recording the age distribution of people with AIDS as the epidemic develops following the introduction of HIV-1 at time $t=0$.

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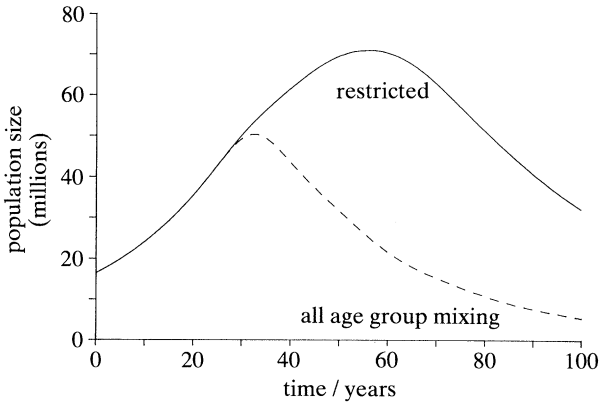

Figure 15. Models A1 and E. The predicted temporal changes in total population size after the introduction of HIV-1 at time $t=0$ for two models in which the mean rate of partner change is constant and independent of age. In model A1 sexual contact is restricted within age classes while in model E, mixing occurs across age classes but with, on average, males having sexual contact with women 5–10 years younger than themselves.

predicted temporal changes in total population size are recorded in figure 15. Note that once older men are allowed to have sexual contact with younger women, the impact of the disease is much greater and occurs more rapidly than in the case where mixing is restricted within age classes. This is a direct result of the impact of across age class mixing on the spread of HIV-1 in the younger women who contribute most to the net fertility of the population. As such the inclusion of the more realistic assumption (over that employed in earlier models; see Anderson *et al.* 1988) about mixing between the sexes acts to increase the predicted demographic impact of the disease.

More generally, the precise pattern of mixing between the age classes of the two sexes has a very

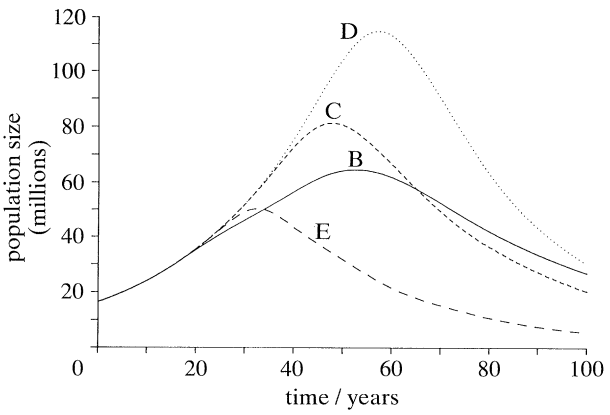

Figure 16. Models B, C, D and E. Predicted temporal changes in total population size for models with different patterns of between age class sexual contact. In all, men have contact with women younger than themselves. Model B represents mixing with own and next younger age class (5-year age classes), C represents mixing with own and three next younger age classes, D represents mixing with own and all younger age classes while E represents mixing with all age classes but with a male bias to younger female age classes.

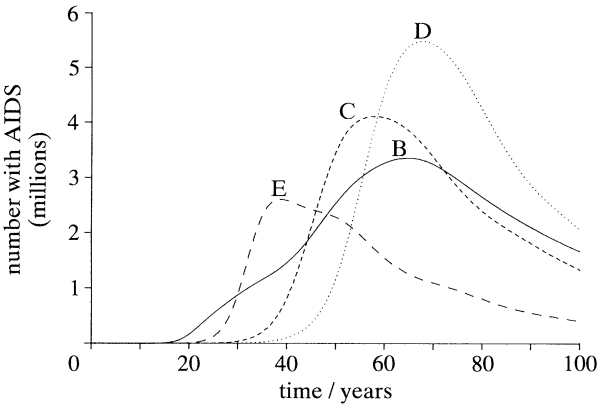

Figure 17. Models B, C, D and E. Similar to figure 16 but recording predicted temporal changes in the number with AIDS.

significant impact on the predicted course of the epidemic as portrayed in figures 16–18. In these graphs, predicted changes in population size, number of people with AIDS, and the population seropositive are recorded. The cases examined are men having sexual contact with women in their own and the next younger age classes (labelled B), with women in their own and the next three younger age classes (labelled C), with women in their own and all younger age classes (labelled D) and women in all age classes but with a bias to the younger groups (labelled E) (see tables 3–6).

The interpretation of the predicted patterns requires care since the age-dependent changes in the mean rate of sexual partner acquisition were not the same in each simulation as recorded in tables 3–6. In general the patterns are similar to those portrayed in figures 6–8, where an increasing mean rate of partner change with age in men, decreases the impact of AIDS when compared with a constant age-independent rate (model E).

However, the impact is predicted to be greatest when male sexual contact is restricted to women of the same and the next two younger age classes (B), when compared with the next three younger classes (C) or all younger classes (D). The reasons are that restricted mixing across two age classes (the same and the next

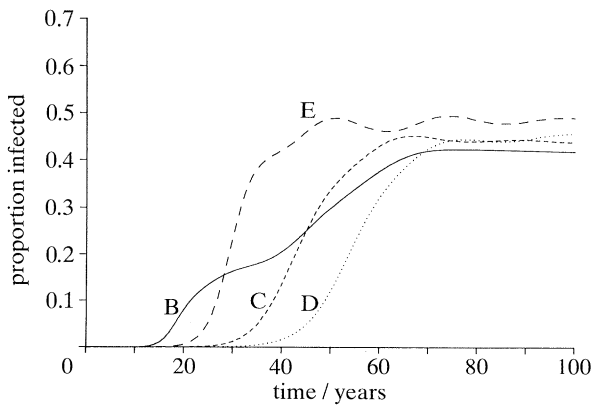

Figure 18. Models B, C, D and E. Similar to figure 17 but recording predicted temporal changes in the proportion infected with HIV-1.

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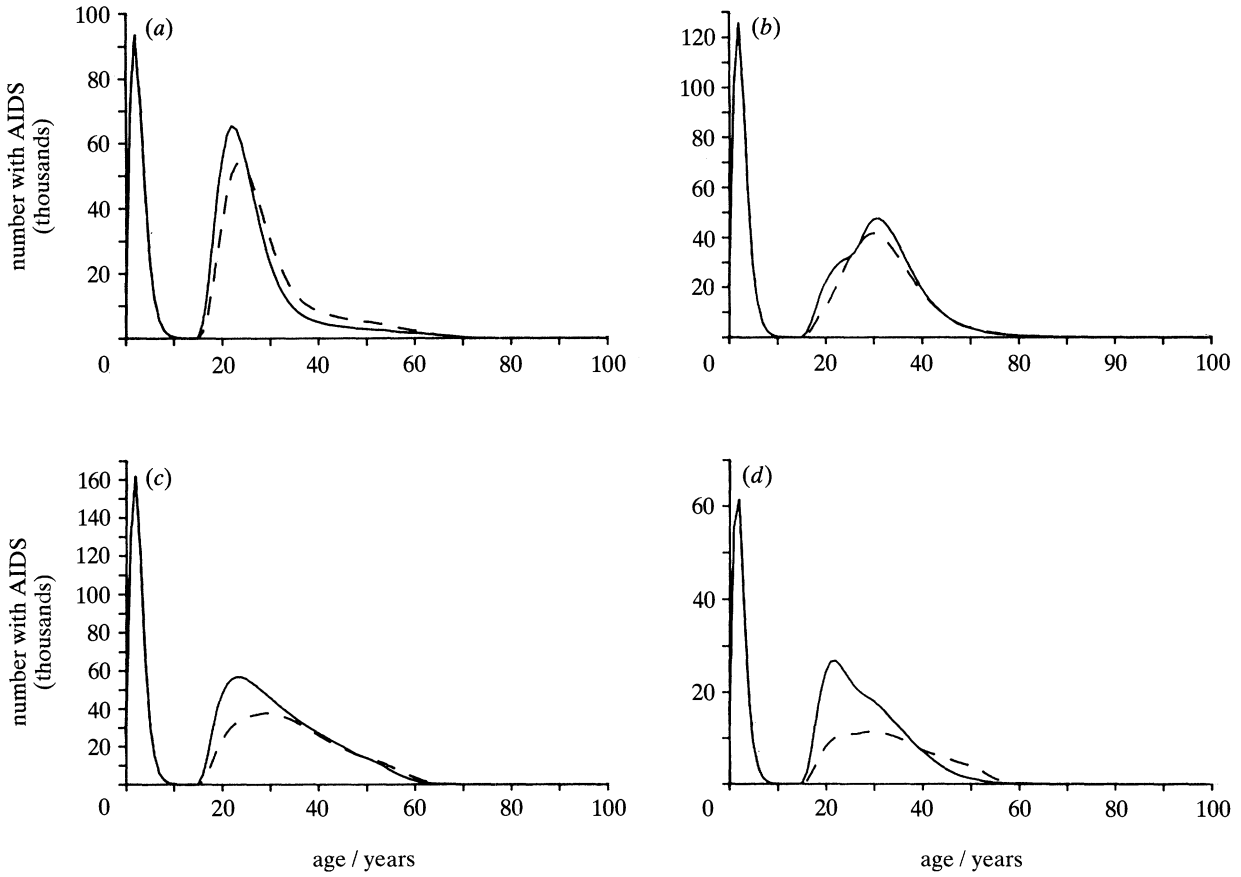

Figure 19. Models B, C, D and E. Predicted age distribution of males (dotted lines) and females (solid lines) with AIDS at year 50 of the simulations for the different sexual mixing within and between age class Models. (*a*) Model E; (*b*) model B; (*c*) model C and (*d*) model D.

younger class) acts to concentrate transmission from 30–40-year-old men to the women in the age classes of peak fertility. Men older than 30–40 years are a smaller fraction of the male population than younger men and hence are less important to the net transmission rate of the virus to women in the major childbearing age classes. Overall, however, these examples serve to illustrate the great significance of sexual mixing by age class to the predicted pattern of the epidemic.

A final point of interest relating to the predicted pattern of the epidemic, concerns the age distribution of people with AIDS stratified by sex. Here again the precise sexual contact patterns between the two sexes has a very significant influence on the age distributions. This point is illustrated in figure 19 which records the distribution for men and women in year 50 of the simulations for models E (graph (*a*)), B (graph (*b*)), C (graph (*c*)) and D (graph (*d*)). Because of the assumption that men on average have sexual contact with women younger than themselves, the predicted age distributions show a pattern in which AIDS cases peak in a younger age class in women than in men. This is what is observed in most Sub-Saharan African countries (see figures 1 and 2). However, the precise pattern varies between the simulations depending on the assumptions made concerning sexual contact between the different age classes of the two sexes. Observed patterns may therefore provide some indirect evidence of the mixing patterns pertaining in a given community.

(*c*) *Sexual contact between all age classes*

In this section we explore in a bit more detail the impact of various epidemiological assumptions on the predicted course of the epidemic. To do this we focus on one particular mixing pattern, namely, that defined for model E in which mixing occurs between all age classes but with a bias for men to have sexual contact with women younger than themselves (table 6). The detailed predictions of this model with respect to temporal changes in population age structure and the distribution of people with AIDS by age are recorded in figures 20 and 21, respectively. The disease is predicted to have a major impact on population size with the growth rate becomes negative at around year 35 after the introduction of the virus. The predicted age distribution of people with AIDS is broadly similar to those observed in African countries.

(i) *Doubling time of the epidemic*

If we alter the efficiency of transmission of the virus, but maintain the 3:1 ratio in efficiency between men to women and women to men, different patterns of impact are predicted. For example, if we increase by a factor of 1.67 the doubling time of the epidemic in its

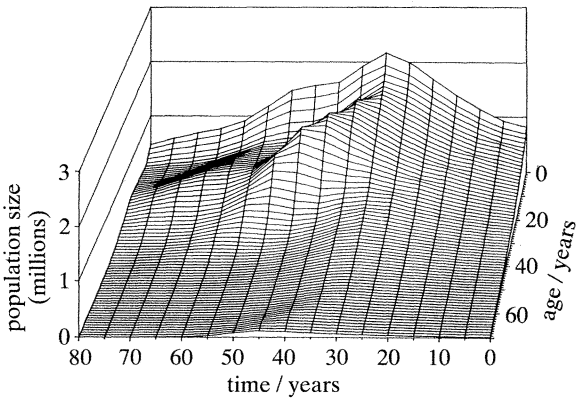

Figure 20. Model E. Mixing across all age classes but with a bias for male contact with younger women. Predicted temporal changes in the age structure of the population after the introduction of HIV-1 at time $t=0$.

early stages (i.e. to 2.5 years) the values of β_1 and β_2 are reduced from 0.3 to 0.0201 and from 0.1 to 0.067, respectively. In these circumstances the disease is still able to reverse the sign of the population growth rate but it takes longer to occur. As illustrated in figure 22*a*, if the doubling time is set at 1.5 years the change occurs at year 35 after the introduction of the virus, but if the doubling time is set at 2.5 years the change occurs at year 58 after the initiation of the epidemic. Similar changes occur in the temporal pattern of the number of people with AIDS as illustrated in figure 22b.

At present it is difficult to put precise values on the doubling time for a given country since longitudinal cohort data is required on changes in the seroprevalence of HIV-1 in the general population. However, an indirect measure comes from temporal changes in the number of reported AIDS cases. Records from many Sub-Saharan African countries suggest doubling times closer to one year than two. However, it should be noted that reporting systems are in general poor in this region of the world and, furthermore, early reports will largely reflect HIV-1 transmission in the highest at risk groups of a given population. As such, the data may exaggerate the rate of spread

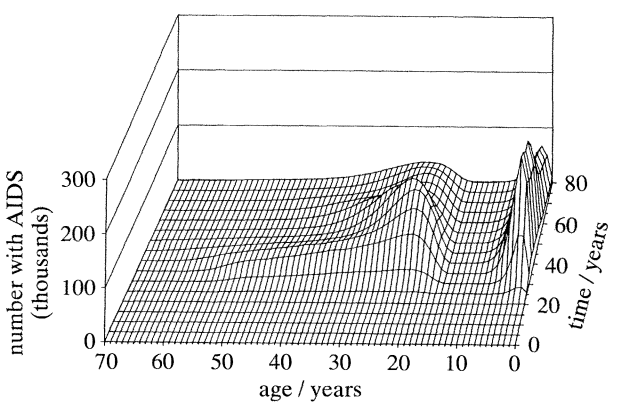

Figure 21. Model E. Similar to Figure 20 but showing the predicted age distribution of people with AIDS following the introduction of HIV-1 at time $t=0$.

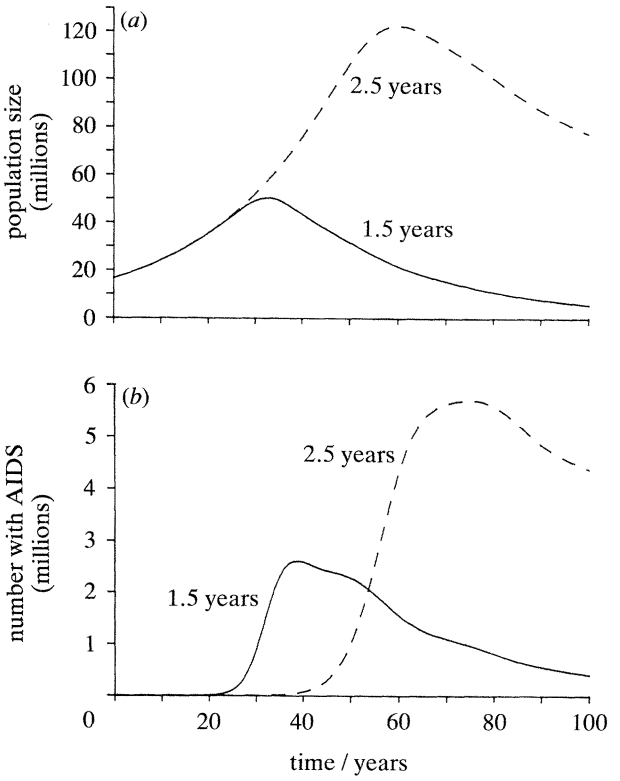

Figure 22. Model E. The influence of the force of infection (the values of β_1 and β_2) which determine the initial doubling time, t_d, of the epidemic on the predicted inpact of AIDS. Two cases are shown, are in which t_d is set at 1.5 years and the other in which it is set at 2.5 years. Changes in population size; (*b*) changes in the number of people with AIDS.

pertaining in the general population. Ideally, much better data is required based on longitudinal cohort studies, in both urban and rural settings, of representative samples of the general population.

(ii) *Efficiency of transmission from men to women and from women to men*

In the simulations described in the earlier sections the efficiency of transmission from men to women was set at a level three times that from women to men ($\beta_1=3\beta_2$). This assumption is in rough agreement with data from studies of transmission in heterosexual partnerships in developed countries, where one partner initially acquired infection from infected blood or blood products. Observed data suggests a ratio of between 2:1 or 3:1 in the efficiency of transmission between the sexes.

To assess the sensitivity of model predictions to this assumption we alter the ratio to give values of unity, 3:1, 6:1 and 9:1 in the efficiency of transmission (with the probability β_1 always being equal to or greater than β_2). The result of these simulations are recorded in figure 23 where the predicted temporal changes in the number of people with AIDS are plotted for $\beta_1=\beta_2$, $\beta_1=3\beta_2$, $\beta_1=6\beta_2$ and $\beta_1=9\beta_2$.

The patterns depicted illustrated that the predictions are fairly insensitive to the precise ratio 'defined' in any given simulation. At first sight this result

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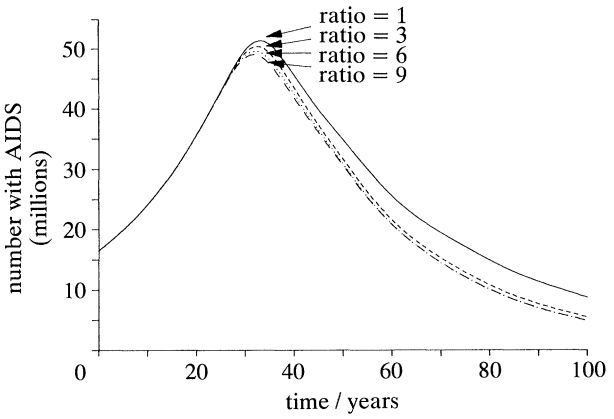

Figure 23. Model E. The influence of changes in the ratio of $\beta_1:\beta_2$ on the predicted temporal changes in the number of people with AIDS. Simulations in which the ratio was set at 1, 3, 6 and 9 are recorded (see text).

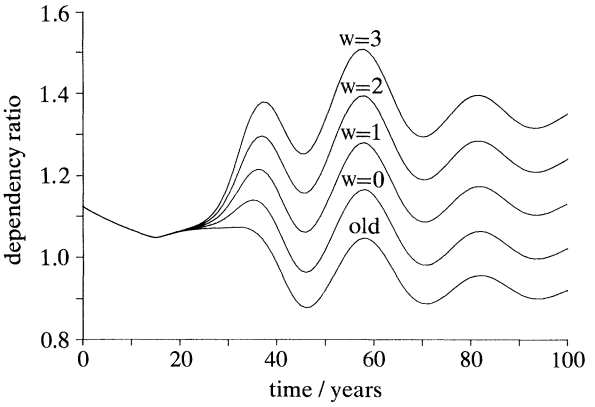

Figure 24. Model E. Temporal changes in the dependency ratio after the introduction of HIV-1 at time $t=0$. The old and new definitions are employed in different simulations (see text) and with the new definition which takes account of the care of people with AIDS, various weightings (w) are applied to the numbers with AIDS (e.g. w = 0, 1, 2 and 3).

appears counter intuitive. However, it arises as a consequence of the assumptions made in the model's structure concerning the balancing of the supply and demand for sexual partners between men and women, as AIDS-induced mortality changes the sex ratio of the population. As noted earlier, women acquire HIV infection at a younger age than men and at a faster rate, due both to the assumed contact structure between the age classes of the two sexes and the imbalance between the efficiency of transmission. As the epidemic develops higher mortality among women induces an imbalance in the supply of female partners in relation to the male demand set at the start of the epidemic. In the model we assume that this imbalance is instantaneously corrected by a reduction in male demand in proportion to the availability of female partners within the different age groups. This acts to effectively balance the net rates of transmission between men and women as illustrated in figure 23. In all the cases recorded in figure 23 the male to female ratio of people with AIDS at year 40 of the simulation was between 0.83 and 1.0. The lowest ratio arose in the case where $\beta_1 = 9\beta_2$ and the assumption induced a slightly greater demographic impact than the other assumptions.

(iii) *Dependency ratio*

In an earlier study (Anderson *et al.* 1988), a simple model of HIV transmission that incorporated epidemiological and demographic processes was employed to examine the impact of the disease AIDS on the dependency ratio of the afflicted population. This ratio was defined as population size in the age range of less than 15 years of age and greater than 64 years of age, divided by that aged 15 to 64 years (referred to as the 'old' definition). We modify this definition to take account of the burden imposed by the care of those with AIDS by including in the numerator of the ratio the number of people with AIDS in all age classes. Those with AIDS are also removed from the population represented in the denominator of the ratio. In addition, we apply a weighting of either 1, 2 or 3 to the number of people with AIDS to denote the extra burden imposed by the care of terminally ill patients.

The predicted temporal changes in the old ratio and the new ratio with weightings 1, 2 and 3, are recorded in figure 24. Note that in all cases, the ratio oscillates as the epidemic develops due to the influence of AIDS-induced mortality on the age structure of the population. Also note that the more realistic assumption that the dependency ratio should take account of the burden imposed by the care of AIDS patients acts to increase the ratio above that pertaining prior to the introduction of HIV. This is most apparent when a weighting of 3 is applied. The earlier conclusion that AIDS is unlikely to increase the dependency ratio of a population is therefore incorrect if the care of terminally ill patients is taken into account (Anderson *et al.* 1988). It should also be noted that the values recorded in figure 24 reflect the overall population ratio. On a more local scale the ratio may be considerably in excess of unity in value within specific villages or family units which are particularly badly affected by the disease. The reason why the ratio is not so greatly in excess of unity is that AIDS-induced mortality acts on infants (via vertical transmission), as well as adults in the most productive age classes of the population. population.

(iv) *Changes in sexual behaviour*

Recent experience in developed countries, particularly in male homosexual communities, suggest that behaviour changes occur as the epidemic develops either as a result of government-organized educational and publicity programmes about the manner in which HIV is transmitted, or as a result of direct or indirect contact of individuals with those with the disease. As the epidemic spreads, an individual is increasingly likely to know someone who is either infected with the virus or has the disease AIDS. This personal knowledge will, on average, act to stimulate behaviour changes via the adoption of what have been called 'safer sex' practices. These include, reduction in the

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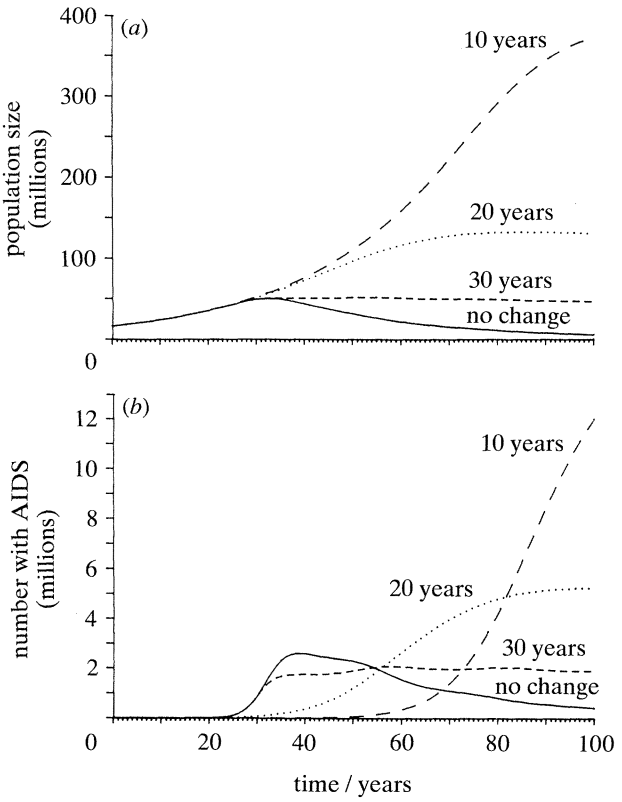

Figure 25. Model E. Predicted temporal changes in the total population size (*a*) and the number of people with AIDS (*b*) when a change in behaviour (the frequent use of condoms and/or a reduction in sexual partners) which reduces transmission efficiency by 50% is introduced at time $t = 10$, 20 and 30 years after the introduction of HIV-1 (before the change $t_d = 1.5$ years, $\beta_1 = 3\beta_2$).

number of different sexual partners, the use of condoms for penetrative penal–vaginal sex and the avoidance of certain high risk behaviours such as anal sex.

We assess the potential impact of changes in behaviour on the predicted course of the epidemic by reducing the probability of transmission ($\beta_1 = 3\beta_2$) by half (i.e. 50% of the population use condoms 100% of the time, or some variant on this theme which gives a 50% reduction in transmission). In particular, we examine the influence of the timing of this change on the spread of infection and the demographic impact of the disease. Specifically, the reduction in transmission is assumed to take place at years 10, 20 and 30 after the introduction of HIV-1 into the population. The results of these simulations are recorded in figure 25. In graph (*a*), temporal changes in total population size are recorded, whereas in (*b*) temporal changes in the number of people with AIDS are depicted. For reference, the predicted patterns under the scenario of no change in behaviour are also recorded in figure 25.

The earlier the change in transmission efficiency is introduced (assumed to reflect greater use of condoms and a reduction in sexual partners) the greater the impact on the predicted course of the epidemic. When change is introduced at year 10, the disease has a limited impact on population growth over the 100 year time span of the simulation. However, when it is introduced at years 20 or 30, AIDS is still able to reverse the sign of population growth over the time span of the simulation. Note, however, that when population growth continues unabated (where change is introduced at year 10), the total number of people with AIDS is greater than in the cases where change is introduced at years 20 or 30. This arises because of population growth. The important point to note is the proportion of the population infected in each case. For example, at year 50, 48% of the population are infected under the assumption of no change, 26% are infected when change occurs at year 30, 11% are infected when change occurs at year 20 and 7% are infected when change occurs at year 10. The message to emerge from these simulations is that the early introduction of change is very desirable even though the number of people with AIDS may be relatively small at that time. The reason is obvious. The development of the epidemic is a non-linear process and changes in behaviour introduced at an early stage in its growth have a very major impact at precisely the period when the net rate of transmission is greatest due to the high fraction of susceptible people within the population (i.e. most sexual contacts between an infected person with others in the population result in a new case of infection).

4. DISCUSSION

The numerical projections generated by the model present a depressing picture of the likely demographic impact of AIDS in Sub-Saharan Africa. The refinements added to the model all act to increase the potential impact over that predicted by the basic model, other factors being equal. These are, age dependency in the rate of sexual partner change with higher rates in younger adults than older individuals, the sexual contact of males with women younger than themselves, and unequal transmission probabilities between females and males, and vice versa, with the latter being greater than the former. The realism of these additional assumptions is supported by the available epidemiological data (figures 3 and 4).

What factors that are not at present incorporated in the model could decrease the predicted impact of AIDS. First, heterogeneity in sexual activity, not just between age classes and the two sexes but between individuals within an age class, could act to restrict the spread of HIV-1 infection within a small proportion of the sexually active population (see Anderson *et al.* (1989) for an example of this in the context of spread within male homosexual communities). Quantitative data on sexual behaviour in African communities (very limited at present) suggests that the degree of heterogeneity in the rate of sexual partner change is of similar magnitude to that recorded in developed countries (Anderson & May 1988; Anderson 1988; Konnings *et al.* 1989; Hogsberg & Aaby 1991). The recorded mean rates of partner change over a defined time period (e.g. one year) and for a fixed age class appear to be somewhat greater in Sub-Saharan African communities than in certain European populations. The significance of heterogeneity depends to a

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great extent on the pattern on mixing between the different sexual activity classes (defined on the basis of the rate of sexual partner change). If those with high rates of partner change choose their sexual partners predominantly within their own activity class (like mixing with like: assortative mixing) then heterogeneity will act to restrict the spread of HIV-1 to the small proportion of highly sexually active individuals in the population. In these circumstances, demographic impact will be less than that suggest by the predictions of the current model. However, if mixing is dissortative (like with unlike) to mirror males (perhaps migrant labourers) having frequent sexual contact with prostitutes plus contact with their monogamous steady partner (perhaps wife), then HIV-1 spread will be extensive in both high and low activity classes and the predictions of the model may underestimate demographic impact. To interpret the significance of heterogeneity it is vital to understand the network of sexual contacts prevailing in the population.

A second factor of importance again concerns heterogeneity, but is centred on the spatial linkages between different communities. If between spatial location sexual contact is low by comparison to within location contact, then the spread of the virus will be slow due to the reliance on infrequent contacts between villages or between rural and urban populations. Conversely, if movements between rural villages and urban centres (perhaps to seek work or to sell agricultural produce) are frequent such that between spatial location sexual contact is substantial, then HIV-1 spread will be rapid and extensive. Simple models of the spatial dynamics of HIV-1 transmission suggest that if between-village or town contact is low, the interval between the introduction of the virus into one location in a country, and its spread to most urban and rural centres could could be as long as 100 years or more (see May & Anderson 1990). However, the conditions prevailing in many African countries today, in particular poverty, poor economic performance and war, act to promote movements between urban and rural settings.

There are many similarities in the manner in which mathematical models can be adapted to mirror different types of heterogeneity, whether social (sexual behaviour) spatial (urban–rural) or demographic (behaviour dependent on age and sex). Some description of the heterogeneity is required to stratify the equations of the model to reflect different classes of people with different behaviours, home locations or ages and sex. But the linkages between and within these different groups of individuals are of the greatest significance to the overall spread of HIV-1. The mixing matrices described in the current paper to represent stratification by age and sex ideally require further stratification by sexual behaviour and spatial location. The probability elements of the mixing function which determine 'who has sexual contact with whom' will therefore have four dimensions, namely, age, sex, sexual activity class and spatial location. The expansion of the current model to encompass the two extra dimensions (sexual activity and spatial location) is straightforward in principle, but requires considerable computational labour to numerically evaluate model behaviour. Much more important, however, is the availability of data to define both the mixing function and the establishment of a set of behaviourial rules to guide computation when the supply of sexual partners from a particular group or location does not meet the demand as a consequence of AIDS-induced mortality. Obtaining data to guide either the derivation of the mixing function or the behaviour rules is extremely difficult in practice. For example, in the current paper it was not possible to identify a data set to guide the choice of elements for the mixing matrix stratified by sex and age, nor was it possible to define the rules to match the supply and demand of sexual partners on the basis of empirical evidence.

The difficulties that surround data acquisition, daunting as they are, should not detract from the importance of attempting to do so. Whether or not the predicted demographic impact of AIDS is less or greater than that suggested by the age- and sex-structured model depends critically on the precise details of mixing between sexual activity classes and spatial locations. Data are beginning to accumulate in certain areas, such as age and sex dependency in sexual activity and the distributional properties of partner change rates within a given class. For example, the World Health Organisation KABP (Knowledge, Attitudes, Beliefs and Practices) surveys of sexual behaviour are beginning to provide quantitative information from a number of African countries. There are many problems surrounding the interpretation of such data and in assessing veracity, but its collection represents an important beginning in the study and quantification of the activities that influence the spread of sexually transmitted infections. The step beyond the KABP surveys is that to determine mixing between classes and locations.

The final factor that could act to decrease the predicted impact of AIDS, concerns the parameter assignments for the major epidemiological processes. The range of doubling times (from 1.5 years to 2.5 years) employed may be unduly pessimistic, in the light of observations that suggest it is of the order of 1 year in high risk groups such as female prostitutes and their regular male clients in some regions of Sub-Saharan Africa (Piot *et al.* 1988). However, even when a doubling time of 2.5 years is employed, the model predicts that AIDS is able to reverse the sign of the growth rate of the population. The major difference between the predictions based on a 1.5 year or 2.5 year doubling time is simply the length of time between the introduction of the virus and the reversal of the sign of the growth rate. The mean incubation period was set at 8 years, a figure slightly less than current estimates of the average in sexually active adults in developed countries (the current estimate is approximately 10 years, Bachetti & Moss (1989)). It is probable that the mean period is somewhat less in Africa than in developed countries due to differences in both nutrition and exposure to infectious agents. To date, however, good data is unavailable for Africa. With respect to the efficiency of vertical transmission,

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an estimate of 50% was employed in the simulations. This figure is at the upper end of current estimates (Anderson & Medley 1988; Hira *et al.* 1989; Ryder *et al.* 1989; Blanche *et al.* 1989; Peckham 1990) but is perhaps unduly pessimistic.

Of the basis of the limited data that is available at present, we believe our parameter assignments are pessimistic, but not overly so. The urgent need is far better quality data, based on longitudinal cohort studies, of rates of infection, incubation periods the efficiency of vertical and horizontal (=sexual) transmission and sexual behaviour. It may be more appropriate in future work to support a few large scale multi-centre studies via international collaboration, rather than encourage each country to develop its own epidemiological research programme. The latter is required for surveillance, but the estimation of key parameters, such as the incubation period, requires well designed large scale studies which may be beyond the resource capabilities of any one country.

In conclusion we turn to the main issue, namely, the likely demographic impact of AIDS. The realistic refinements made to the model all excentuate the potential impact. We therefore believe that in certain Sub-Saharan African countries, where the spread of HIV-1 is already extensive, the disease will act to reverse the sign of population growth rates over timescales of a few decades. It is difficult to be more precise about the time scale, because of uncertainties concerning the start of HIV-1 spread in any given country. many years before the overall population growth rate begins to approach zero, the model predicts that AIDS will become the leading cause of mortality in both infants and adults. In a recent paper, DeCock *et al.* (1990) report that AIDS is already the leading cause of adult death in the West African city of Abidjan, Ivory Coast. It is to be expected that this pattern will soon be repeated, if it is not already the case, in many other urban centres in Africa in the next few years. When levels of HIV-1 infection attain 20% or more, it is probably already too late to prevent AIDS having a major demographic impact. However, in other regions with lower levels of infection in the general population, the sooner behaviour changes take place the better, as illustrated by the model simulations presented in figure 25*a*. The epidemic is a very nonlinear process and reductions in transmission early on in the course of the pattern of spread, when most of the population are susceptible, have a disproportionately greater effect on the cumulative number of cases of infection, than similar changes induced at a later stage. This message is of great importance (Rowley *et al.* 1990). International help, and the appropriate resources, must be deployed before AIDS is perceived to be a major problem if it is to have the greatest benefit. Mathematical models, that are continually refined to better mirror what is known about virus transmission and human behaviour, have an important role to play in educating public health workers, policy makers and international support agencies.

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