PHILOSOPHICAL TRANSACTIONS OF THE ROYAL SOCIETY B BIOLOGICAL SCIENCES

Factors Controlling the Spread of HIV in Heterosexual Communities in Developing Countries: Patterns of Mixing between Different Age and Sexual Activity Classes

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Factors controlling the spread of HIV in heterosexual communities in developing countries: patterns of mixing between different age and sexual activity classes

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CONTENTS

SUMMARY

The paper describes the development and analysis of a mathematical model of the spread and demographic impact of HIV in heterosexual communities in developing countries. The model extends previous work in this area by the representation of patterns of mixing between and within different age and sexual activity classes in a two sex structure. Summary parameters are derived to represent different mixing patterns, ranging from assortative via random to disassortative, as are methods to ensure that particular mixing patterns between different age and sexual classes (stratified on the basis of rates of sexual partner change) meet constraints that balance the supply and demand for sexual partners as AIDS induced mortality influences the demographic structure of a population. Analyses of model behaviour rely on numerical methods due to the complexity of the mathematical framework, and sensitivity analyses are conducted to assess the significance of different assumptions and different parameter assignments. Simulated patterns of HIV spread across the two sexes and various age classes are compared with observed patterns in Uganda. The principle conclusion of the study is that the pattern of mixing between age and sexual activity classes, combined with the assumptions made to balance supply and demand between the sexes have a very major influence on the predicted pattern of HIV spread and the demographic impact of AIDS. The paper ends with a discussion of future needs in model development and data acquisition.

1. INTRODUCTION

(*a*) *The HIV pandemic*

The pattern and rate of spread of the human immunodeficiency viruses (HIV-1 and HIV-2) varies greatly both within and between different countries (Piot *et al.* 1991; Quinn *et al.* 1990; Anderson *et al.* 1991; WHO Collaborating Centre on AIDS, March 1992) (figure 1). The World Health Organisation's Global Programme

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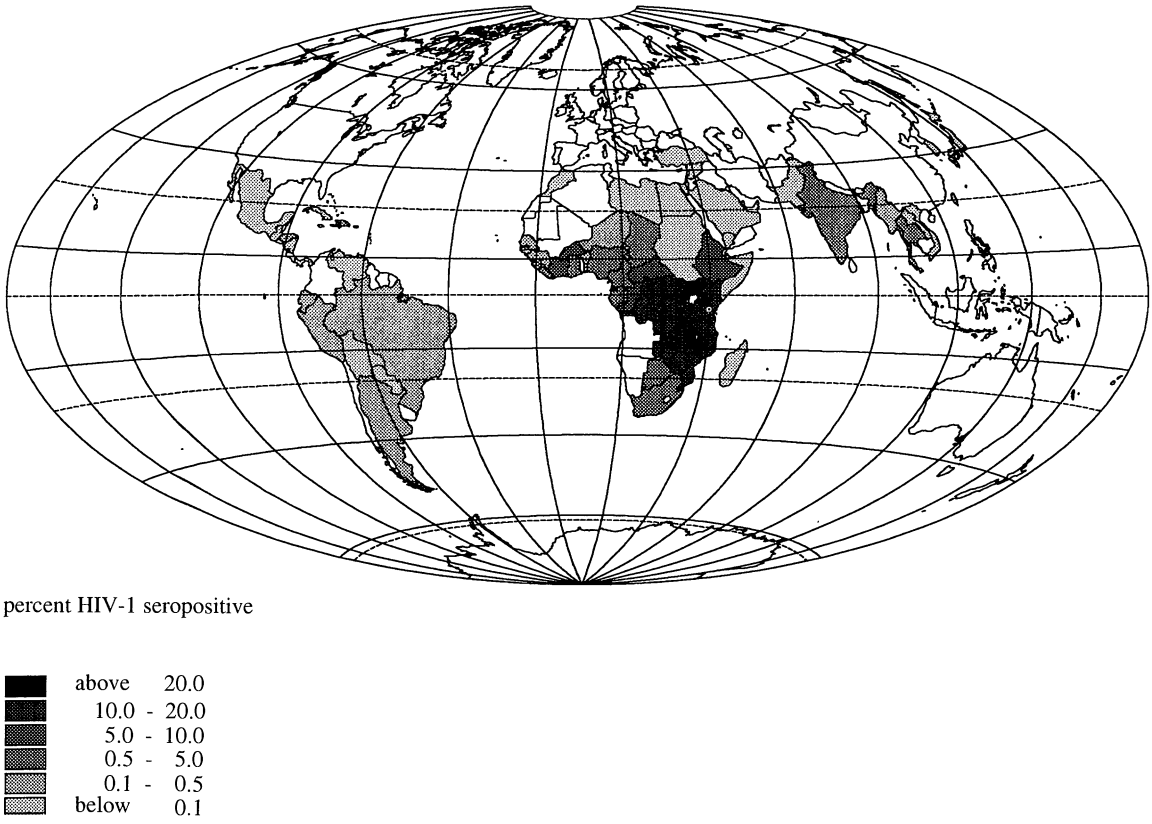

Figure 1. Prevalence of HIV-1 in low risk men and women in urban settings, in different developing regions of the world, 1989–1992. The overall prevalence for a particular country is the most recent serological survey from among childbearing women (or blood donors if data from childbearing women is unavailable) from surveys within the U.S. Bureau of Census, HIV data base.

on AIDS initially categorized the HIV epidemic in different countries according to the estimated time at which the virus entered the country and the particular risk groups (male homosexuals, intravenous drug users (IVDUs) and heterosexuals) first affected (i.e. Patterns I, II and III) (WHO Global Programme on AIDS, April 1991). However, the initial patterns have altered over time and much heterogeneity in spread is apparent even within countries initially designated to a particular pattern. For example in pattern I countries (infection focused in male homosexuals and IVDUs) the virus has begun to spread in the heterosexual population but to varying degrees with rapid spread in some poor urban areas in the United States and very limited spread as yet in many Western European countries (e.g. Sweden and the United Kingdom). Within pattern II countries (infection focused in heterosexuals) the prevalence of infection continues to rise in most regions (e.g. Uganda, Kenya, Tanzania) but in some areas such as Kinshasa, Zaire, infection levels are reported to have attained a low endemic state at around 6%–8% of the sexually active population (figure 1). There is much uncertainty surrounding these supposedly 'endemic' patterns due to the paucity of carefully designed longitudinal cohort studies of HIV spread, particularly in Africa, but also in India, Southeast Asia and South America.

The notion that the epidemic has attained an endemic equilibrium in some communities has led some researchers to describe the epidemic as consisting of three major phases representing an early silent phase of slow spread, a rapid epidemic phase and an endemic plateau in seroprevalence (Garcia-Calleja *et al.* 1992). This is far too simplistic a view as in reality the epidemic is formed from a series of waves of infection representing transmission within and between different risk groups (e.g. perhaps defined on the basis of rates of sexual partner change). A number of studies have indicated that the overall epidemic may even be multi-peaked if mixing between the different groups is limited (Jacquez *et al.* 1989; Boily & Anderson 1991; Gupta *et al.* 1989). A wide range of factors determine the overall shape of the epidemic curve. These include the presence of other sexually transmitted diseases (STDs) that act as co-factors in the transmission (Plummer *et al.* 1991), poverty promoting commercial sexual activity (Prual *et al.* 1991), the supply and acceptability of barrier contraceptives (Lamptey & Goodridge 1991), social disruption created by armed conflict (Smallman-Raynor & Cliff 1991), patterns of mixing between sexual activity classes and different geographical locations (Anderson *et al.* 1991) and the manner sexual activity changes with age in the two sexes and patterns of sexual contact between age classes (Anderson *et al.* 1992). The relative importance of each of these and other factors in promoting HIV transmission varies widely in different societies. Such heterogeneity makes pre-

diction of the pattern of the epidemic in the coming decades extremely difficult. However, mathematical models can be used to generate insights into how these different factors combine to shape the epidemic in a manner akin to the protocol adopted by an experimental scientist. One or a few factors can be allowed to vary in the model structure while the rest remain constant in order to pinpoint the influence of each factor on the shape of the epidemic. More generally, they can be used to determine what needs to be measured to improve understanding, to gain a qualitative impression of the potential demographic impact of AIDS in defined localities and, most importantly to generate insights into the potential effectiveness of different intervention strategies, either used in isolation or in combination (Rowley *et al.* 1990). At present they cannot be used to produce precise quantitative predictions of the future trends as there are many gaps in our knowledge, particularly concerning patterns of sexual behaviour and how these may change in response to the emerging epidemic.

This paper extends previous work to consider in detail the influence of mixing patterns between sexual activity and age classes of the two sexes on the shape and demographic impact of the epidemic. We begin with a brief review of published work on modelling the AIDS epidemic in developed and developing countries before detailing the structure of our model and the key assumptions embedded in it. Parameter assignments are then discussed before turning to patterns predicted by the model under various assumptions concerning the degree of assortative (like-with-like) or disassortative (like-with-unlike) mixing between age and sexual activity classes (defined on the basis of rates of sexual partner acquisition). The final section compares model predictions with observed trends in sub-Saharan Africa and considers future research needs and further refinements to the structure of the model. Throughout our aim is to improve understanding of how different factors influence the pattern and impact of the epidemic.

(*b*) *Different approaches to predicting the spread of HIV*

The numerous factors that determine the spread of HIV and the paucity of our knowledge of many of these (i.e. patterns of sexual behaviour) argues that model development should be an iterative process with complexity added in a stepwise manner as knowledge accumulates so that the role of each factor in determining spread is fully understood. Unfortunately many involved in debates concerning the likely spread of HIV in the coming decades fail to appreciate the different roles of various models. Short-term prediction over one to a few years, based on extrapolation using a suitable mathematical function that describes past trends, is often helpful. However, this approach is unlikely to be reliable in the longer term because past trends may be described equally well by a variety of different mathematical functions (e.g. exponential, logistic, etc.; Anderson *et al.* 1987), each of which generates different projections for the future. Models of the transmission dynamics of HIV are necessarily more complex in structure and require detailed information on a variety of epidemiological and behavioural variables about which we know little at present. They may be able to make qualitative projections about the likely shape of the epidemic in coming decades but they cannot be used to make quantitative predictions. Their main use is to broaden understanding of what factors are important in determining observed pattern. This is not always well understood by public health specialists as illustrated by a recent paper by Chin & Lewanga (1991) on AIDS case projections in which they describe transmission models as 'explanatory' but then proceed to criticize their power to make 'reliable' projections.

Projections by the World Health Organization and other international or national agencies are often based on so called 'tactical' models which use simple mathematical functions to project into the future given information on past trends. Unfortunately, most reports containing projection of future trends based on these simple models rarely detailed the precise assumptions on which they are based or the sensitivity of outcome to changes in these assumptions.

A good example of this problem is provided by the 'epi-model' developed by the WHO Global Programme on AIDS (Chin & Lwanga 1991; Garcia-Calleja *et al.* 1992; Soro *et al.* 1992), projections from which have received wide publicity in the press. The model is essentially a gamma function for the prevalence of infection with time given by $t^{p-1}\,e^{-t}/(p-1)!$ where p is set at 5 (the assumed shape of the epidemic) and to make projections three pieces of empirical information are required. These are an estimate of the point HIV prevalence in a particular country or region, an assessment of the time to when extensive spread of HIV commenced and information on the rate of progression from infection to AIDS (the incubation period distribution). The simplicity of the model is appealing; but are the assumptions upon which the model is based correct? For instance, is the shape of the epidemic gamma in form? Many factors will influence the precise nonlinear pattern of the epidemic and it seems highly unlikely that the gamma function will suffice as a description. Further problems arise in the assignment of parameter values and the method employed to fit the gamma distribution. Little is understood of the incubation period of AIDS in heterosexual adults in developing countries and even in developed countries only one half of the full distribution has yet been observed. A sensible fit of the gamma distribution is not possible on the basis of a guess on when HIV commenced and a single estimate of the prevalence of HIV at one instance in time. The point highlighted by this example is the fragility of the assumptions and parameter estimates contained within simple as well as complex models. Simplicity and ease of comprehension and use by the non-specialist should not be confused with accuracy of prediction.

At the other end of the complexity spectrum are the sophisticated simulation models of Auvert (AIDSTECH Family Health International 1991) called SIMULAIDS and the Inter-agency Working Group

(IWG) model (AIDSTECH Family Health International 1991), which are being used by the WHO to help identify AIDS control programme targets (Culotta 1991). SIMULAIDS is a hybrid stochastic-deterministic model where chance events in transmission and demographic changes are simulated by monte-carlo methods. The model describes events in a population of 200 000 individuals, stratified by their age, sex and the types of sexual relationship they participate in, and mimics complexities such as variable infectiousness over the incubation period, the influence of cofactor STDs on the likelihood of HIV transmission probabilities defined per type of sexual act and the definition of casual, commercial and regular sexual partnerships. The IWG model includes similar detail within a deterministic compartmental framework. Both models require large arrays of data inputs to specify the values or range of values for the large number of parameters they contain. When the outputs of those models are discussed in in-house reports (or when released to the press) no detail is provided of the precise mathematical structures of the models or the sensitivities of output to assumptions and parameter variation. Of particular significance in this context is the failure to discuss what assumptions are made concerning patterns of mixing (=sexual contact) between different strata of the population such as age, sex, sexual activity class and geographical location. A body of research on this specific area has emerged over the past 5 years and it is now understood that mixing patterns are major determinants of observed pattern (Jacquez *et al.* 1989; Gupta *et al.* 1989; Anderson *et al.* 1992).

(*c*) *Mathematical models as epidemiological research tools*

Much of the mathematical research on the epidemiology of HIV and AIDS is not orientated towards the prediction of future events in specific populations. It is aimed more generally at improving understanding of observed pattern. This body of work is published in the reviewed scientific literature (as opposed to in-house reports) and hence assumptions on which the models are based and parameter assignments are open for scrutiny and comment (Anderson *et al.* 1986, 1992; Jacquez *et al.* 1988; Dietz & Hadeler 1988; Busenberg & Castillo-Chevez, 1991; Hethcote & Van Ark 1992). Its foundation can be traced back to the work of Yorke and colleagues on the epidemiology and control of gonorrhoea in which a deterministic compartmental framework was developed to describe the transmission dynamics of STDs (Yorke *et al.* 1978; Hethcote & Yorke 1984). A particular feature of this research was the recognition of heterogeneity in sexual activity by the division of the population into two groups, namely a small fraction who changed sexual partners frequently (the so called 'core' group) and a majority who change partners infrequently, if at all. In the context of HIV this work was first extended by Anderson and colleagues (1986) for a single sex population (male homosexuals), to consider random or proportional mixing in a population finely stratified according to sexual activity (rate of sexual partner change). Various developments rapidly followed including the representation of transmission events per sexual act (Kaplan 1990), the representation of sexual activity by rate of partner formation and dissolution (Dietz & Hadeler 1988), the relaxation of the assumption of proportionate mixing to mirror disassortative and assortative patterns (Jacquez *et al.* 1988; Gupta *et al.* 1989; Busenberg & Castillo-Chevez 1991), the explicit treatment of heterosexual transmission (May & Anderson 1987; Hethcote & Van Ark 1992), the role of cofactor STDs in the transmission of HIV (Anderson & May 1988), the melding of epidemiological and demographic processes in a single mathematical framework (Anderson *et al.* 1988; May *et al.* 1988*a*,*b*) and the gradual introduction of more complex patterns of mixing to mirror contacts within and between sexual activity classes, age classes and geographical locations (Anderson *et al.* 1992; Anderson *et al.* 1991).

A particular area of interest has been the development of models to assess the potential demographic impact of AIDS in defined populations (Anderson *et al.* 1988, 1991, 1992; Bongaarts 1989; John 1991; Garnett & Anderson 1993*b*). Varied conclusions have been drawn from such analyses and some controversy has surrounded early predictions that AIDS has the potential to induce population decline some decades after the commencement of HIV spread even in communities with high net growth rates prior to the introduction of the disease (Anderson *et al.* 1988; Bongaarts 1989). However, as more complexity has been added to these models, and as more is understood about the factors that determine the spread of the virus, the consensus of opinion is moving towards the view that AIDS has the potential to cause population decline in badly affected areas but the severity within countries in Africa, South Africa, India and Southeast Asia will be very variable due to much heterogeneity in sexual customs and mixing patterns (Anderson and May 1992; Garnett & Anderson 1993*b*).

2. METHODS

We extend previous work in this area to take explicit account of mixing or contact patterns between and within heterosexual populations. The mathematical framework is an extension of published work (see Anderson *et al.* 1989, 1991, 1992), it is deterministic and compartmental in structure and it describes epidemiological and demographic events in an age-structured population of males and females. To ease understanding of the methods section Table 1 provides a glossary of the symbols used to describe variables and parameters, plus estimates of the parameters employed. The following subsection (§ 2*b*) provides a very brief review of the data sources on which these estimates are based.

The model consists of a system of partial differential equations to describe changes in the numbers of susceptibles (X), of infecteds (Y) and of individuals

with AIDS (A) of both sexes with respect to time t and age a. It has the following structure:

$$\frac{\partial X_{kl}(a,t)}{\partial a} + \frac{\partial X_{kl}(a,t)}{\partial t} = -[\lambda_{kl}(a,t) + \mu_k(a)]X_{kl}(a,t), \quad (1)$$

$$\frac{\partial Y_{1kl}(a,t)}{\partial a} + \frac{\partial Y_{1kl}(a,t)}{\partial t} = \lambda_{kl}(a,t)X_{kl}(a,t) - [\gamma_1(a) + \mu_k(a)]Y_{1kl}(a,t), \quad (2)$$

$$\frac{\partial Y_{skl}(a,t)}{\partial a} + \frac{\partial Y_{skl}(a,t)}{\partial t} = \gamma_{(s-1)}(a)Y_{(s-1)kl}(a,t) - [\gamma_s(a) + \mu_k(a)]Y_{skl}(a,t), \quad (3)$$

$$\frac{\partial A_{kl}(a,t)}{\partial a} + \frac{\partial A_{kl}(a,t)}{\partial t} = \gamma_3(a)Y_{3kl}(a,t) - [\mu_k(a) + \alpha(a)]A_{kl}(a,t). \quad (4)$$

Here $X_{kl}(a,t)$ denotes the number of susceptible individuals of sex k, sexual activity group l, age a at time t. Sexual activity groups are defined on the basis of rates of sexual partner change per unit of time (n in total). Once infected individuals pass via three states ($s = 1$, 2 and 3) to denote disease progression prior to developing AIDS. This division of the infected but non-AIDS variable Y into three categories is made to mirror variable infectiousness over the incubation period of AIDS (Blythe & Anderson 1988), with patients moving from a state of high infectiousness via a state of low infectiousness back to a state of high infectiousness just prior to the development of AIDS. The other subscript labels on $Y_{skl}(a,t)$ are as defined for $X_{kl}(a,t)$ and they also apply for the AIDS compartment, $A_{kl}(a,t)$. The total population at time t, $N(t)$ is given by

$$N(t) = \sum_{k=1}^{2}\sum_{l=1}^{n}\left[\int_0^{\infty}\left(X_{kl}(a,t) + \sum_{s=1}^{3}Y_{skl}(a,t) + A_{kl}(a,t)\right)\mathrm{d}a\right]. \quad (5)$$

Note that the flow of individuals from Y to A is based on the assumption that all who acquire infection eventually develop AIDS. It is possible that some small fraction of infecteds may not progress to AIDS within their natural lifespan but as yet the magnitude of this proportion is unknown.

Susceptibles acquire HIV infection at a sex, sexual activity group, age and time dependent rate $\lambda_{kl}(a,t)$ and enter the first stage of infection $Y_{skl}(a,t)$ where $s = 1$. They pass through the three stages of infection at a stage and age dependent rate $\gamma_s(a)$. Individuals are removed from the population at an age- and sex-dependent *per capita* mortality rate $\mu_k(a)(\mathrm{year}^{-1})$ and those who have AIDS also have an additional age dependent mortality rate $\alpha(a)$ (year^{-1}).

The *per capita* force of infection ($\lambda_{kl}(a,t)$ susceptible^{-1} year^{-1}) determines the rate of spread of the virus and is defined as follows:

$$\lambda_{kl}(a,t) = \int_{\tau}^{\psi}\sum_{m=1}^{n}\left[c_{klm}(a,a',t)\rho_{klm}(a,a')\frac{\sum_{s=1}^{3}(\beta_{sk}Y_{sk'm}(a',t))}{N_{k'm}(a',t) - A_{k'm}(a',t)}\right]\mathrm{d}a', \quad (6)$$

where $c_{klm}(a,a',t)$ is the rate per year at which someone of sex k, sexual activity group l and age a acquires new sexual partners of the opposite sex in the activity group m, of age a' at time t. The dependency on time is necessary to take account of differential mortality due to AIDS in the different sexual activity classes and consequent adjustments in behaviour to balance supply and demand for sexual partnerships (Anderson *et al.* 1992). The term $\rho_{klm}(a,a')$ is the probability that someone of sex k, sexual activity class l and age a will have a sexual partner of the opposite sex in the activity class m of age a'. The proportion of those partners that are at a particular stage of HIV infection is given in equation (6) by $Y_{sk'm}(a',t)/(N_{k'm}(a',t) - A_{k'm}(a',t))$ where $Y_{sk'm}(a',t)$ is the number of individuals of sex k', activity group m and age a' in infection stage s at time t, and $N_{k'm}(a',t)$ is the total number of people of sex k', activity group m, age a' at time t. It is assumed for simplicity that those with AIDS are not sexually active. In some communities, however, it may be that those with AIDS are still involved in sexual partnerships due to economic and social pressures. This could easily be included in the model by changing equation 6 to:

$$\lambda_{kl}(a,t) = \int_{\tau}^{\psi}\sum_{m=1}^{n}\left[c_{klm}(a,a',t)\rho_{klm}(a,a')\frac{\left[\sum_{s=1}^{3}(\beta_{sk}Y_{sk'm}(a't)) + \beta_{Ak}A_{k'm}(a',t)\right]}{N_{k'm}(a',t)}\right]\mathrm{d}a'. \quad (7)$$

The transmission probability defined per partnership from an infected of sex k' in stage s to someone of sex k is given by the constant β_{sk}. The integral over age and over sexual partnership classes is from τ, the age of commencement of sexual activity, to ψ, the age of cessation of sexual activity.

Within the model defined by equations (1)–(5) each individuals age is specified as a continuous variable. However, to ease numerical analyses, those who are sexually active are divided into seven 5-year age classes with $\tau = 15$ years and $\psi = 50$ years. Hence, for computational purposes the force of infection is defined as:

$$\lambda_{kl}(a,t) = \sum_{i=1}^{7}\sum_{m=1}^{n}\left[c_{klmij}(t)\rho_{klmij}\frac{\sum_{s=1}^{3}(\beta_{sk}Y_{sk'mj}(t))}{N_{k'mj}(t) - A_{k'm}(t)}\right]. \quad (8)$$

The initial numbers in each sexually active class at time $t = 0$ are:

$$X_{kli}(0) = N_{kli}(0) - 1, \quad (9)$$

$$Y_{skli}(0) = 1, \quad (10)$$

$$A_{kli}(0) = 0. \quad (11)$$

Those initially infected provide a seed for the epidemic

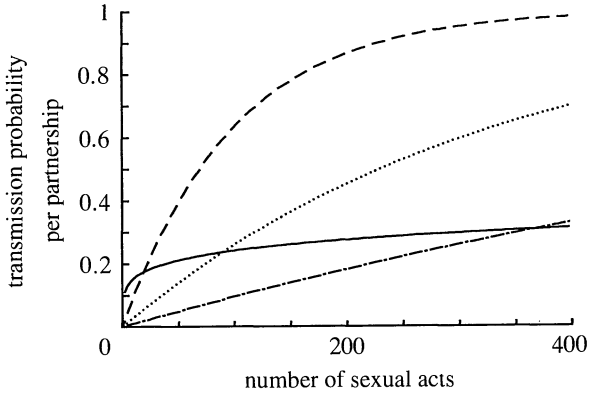

Figure 2. Predicted relationship between the transmission probability defined per partnership and the number of sexual acts per unit of time as defined by the model of Jewell & Shiboski 1990 (solid line) (transmission probability $= 1 - \exp[-\exp(-2.3 + 0.22 \ln(\text{acts}))]$) and a model that assumes a constant probability of transmission per sexual act, δ, with the overall probability per partnership based on the compounding of a series of independent acts (see May & Anderson 1988) (δ set equal to 0.1 (dashed line), 0.003 (dotted line) and 0.001 (dot–dashed line)).

and are evenly distributed throughout the population. N_{kli} the initial size of each subpopulation is defined by:

$$N_{kli}(0) = \int_{a_{i-1}}^{a_i} N_{kl}(a',0)\mathrm{d}a', \tag{12}$$

where:

$$N_{kl}(a',0) = N_{kl}(0,0)(1 - \mathrm{e}^{\mu k(a) + \varpi}). \tag{13}$$

Here ϖ is the *per capita* growth rate prior to the introduction of HIV. $N_{kl}(0,0)$ is the size of the current birth cohort, which throughout simulations is the sum of the boundary conditions for all the state variables at age $a = 0$. These are:

$$X_{kl}(0,t) = \zeta_k \eta_l \sum_{i=1}^{7} (\theta_i X_{2li}(t)) + \sum_{s=1}^{3} ((1 - \vartheta_s) Y_{s2li}(t))), \tag{14}$$

$$Y_{1kl}(0,t) = \zeta_k \eta_{kl} \sum_{i=1}^{7} \left(\theta_i \sum_{s=1}^{3} (\vartheta_s Y_{s2li}) \right), \tag{15}$$

and

$$A_{kl}(0,t) = 0, \tag{16}$$

where $k = 2$ implies women, ζ_k is the sex ratio of individuals at birth, θ_i is the *per capita* yearly fertility rate of women in age group i and ϑ_s is the probability of perinatal transmission when a mother is in the stage s of infection. The proportion η_{kl} divides infants into the sexual activity classes they will eventually move into if they survive to sexual maturity. These classes only become operational above the age τ and below the age ψ. It is assumed that those women with AIDS do not produce children. This assumption can quite easily be relaxed.

(*a*) *Parameter assignments*

The complexity of the model gives rise to a large number of parameters for which numerical assignments are required in order to explore the properties of the structure by numerical methods. Because the focus of this paper is on patterns of sexual contact between different age and sexual activity classes the parameters that determine them will be varied in the numerical analyses. The remaining epidemiological parameters are assigned values which are largely based on empirical studies in developed countries due to the paucity of information from regions of the developing world in which the virus is spreading rapidly.

(i) *Probability of transmission through sexual contact*

The horizontal probability of transmission via penetrative sexual intercourse between men and women (β_{sk}) is a key parameter in the determination of the magnitude of the force of infection, $\lambda_{kl}(a,t)$. The model defines the parameter per partnership and as a function of sex (k) and of the stage of infection (s) (equation 7). Perhaps the most controversial aspect of this definition is that of a fixed probability per partnership as opposed to the more logical definition of transmission likelihood per sexual act. The reasons for our choice are in part due to the nature of available data, in part due to desire to keep the model as simple as possible and in part on theoretical grounds. In early studies of the transmission within partnerships (where one partner acquired infection via infected blood or blood products), no clear relationship was reported between the likelihood of transmission and the number of penetrative sexual acts within the partnership (Peterman *et al.* 1988; May & Anderson 1988). In most studies the duration of sexual contact is ill defined but in the paper of Peterman *et al.* (1988) very few partnerships reported less than 20 sexual acts over period of the study. In a more recent analysis of transmission in 159 partnerships where 24 partnerships reported fewer than 10 sexual acts, the transmission probability per partnership was found to increase as the number of sexual acts increased but to plateau rapidly to a constant value after a relatively few sexual acts (Jewell & Shiboski 1990). This is not what would be predicted by treating the number of acts per partnership per unit of time as a Poisson process with a constant probability of transmission per act (May & Anderson 1988) as depicted in figure 2. Other variables such as stage of infection (i.e. time since acquisition of HIV) confound the interpretation of these studies, as does heterogeneity in the number of acts per unit of time. Hence, observations indicate that more complex models are required to mimic the rapid saturation of the probability to a constant value as the number of sexual acts rises (Jewell & Shiboski 1990; Kaplan 1990).

Most studies of discordant partnerships (one partner initially infected) record the probability of the other partner being infected without reference to either the number of acts, the duration of the period

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Table 1. *Glossary of variables and parameters plus numerical values of the parameters used in the numerical analysis*

symbol	meaning	units	values
subscripts			
i,j	age groups		
l,m	sexual activity groups		
k	sex		
s	stage of infection		
state variables			
$X_{kl}(a,t)$	susceptibles	number	
$Y_{skl}(a,t)$	infected	number	
$A_{kl}(a,t)$	AIDS cases	number	
$N_{kl}(a,t)$	total population	number	
biological parameters			
$\lambda_{kl}(a,t)$	force of infection	rate *per capita* per year	varies
$\gamma_s(a)$	rate of transition between infection stages	*per capita* per year	
	for $a<\tau$ years $s=1$, 2 and 3		1.5
	for $a>\tau$ years $s=1$		2.0
	for $a>\tau$ years $s=2$		0.154
	for $a>\tau$ years $s=3$		1.0
$\alpha(a)$	AIDS associated death rate $a<\tau$ and $a>\tau$	*per capita* per year	1.0
β_{sk}	transmission probability	per partnership	
	from men to women		0.2
	from women to men		0.1
ϑ_s	perinatal transmission probability	per birth	0.35
demographic parameters			
$\mu_k(a)$	death rate	*per capita* per year	table 2
θ_i	birth rate	per woman per year	table 2
η_k	sex ratio at birth		1
behavioural parameters			
$c_{klm}(a,a',t)$	mean rate of sexual partner change	per year	varied
$\rho_{klm}(a,a')$	probability of mixing		varied
ζ_l	proportion of adults in sexual activity class		varied
τ	age at start of sexual activity	years	15
ψ	age at end of sexual activity	years	50

of sexual contact post acquisition of infection by the index case nor measures of viraemia (related to infectiousness) in the index patient. The available data is therefore largely in the form of estimates of the transmission probability per partnership. A good example of this type of study is provided by a recent paper from the European Study Group on Heterosexual Transmission of HIV (1992), which reported on transmission between 159 couples in which women were the index case and 404 couples in which the man was the index case. In these partnerships 12% of men became infected and 20% of women, figures in good agreement with the weighted mean values calculated in a review of published studies (Anderson *et al.* 1991). The European study also provided further evidence that the stage of infection influences the likelihood of transmission. This particular aspect has been a focus in a number of theoretical studies (Anderson 1988; Blythe & Anderson 1988; May & Anderson 1990) and variations in the value of β_{ks} over the incubation period of AIDS is a feature of some of the more complex simulation models described earlier. In the absence of good data on how the value β_{ks} varies over the incubation period, we make use of the available data and assume that the value is constant over the period but higher for transmission from men to women (0.2) than from women to men (0.1) (see table 1).

A growing body of evidence suggests that other STDs may enhance the likelihood of HIV transmission, particularly in developing countries where infections such as chancroid and gonorrhoea are much more prevalent than is typically the case in developed countries (due to the dearth of diagnostic and treatment facilities in poor countries) (Cameron & Padian 1990; Laga *et al.* 1991). As such our estimates of β_k (0.2 for $k=1$ (male to female) and 0.1 for $k=2$ (female to male)) based on data from developed countries in partnerships where other STDs were not prevalent, are likely to be underestimates of the true values in many communities in the developing world. Conversely, our definition of a fixed transmission probability per partnership is likely to overestimate the likelihood of transmission to and from those with high rates of partner change who have few acts with each partner unless there is a strong positive association between acts per unit of time and partners per unit of time. Recent large scale surveys of sexual behaviour in developed countries suggests such an association exists (May & Anderson, 1988) but data is limited at present.

Table 2. *Median period from HIV infection to AIDS calculated in different studies*

reference	study population	number in cohort	median incubation period (years)
Hendrik *et al.* (1992)	homo-/bisexual men in Amsterdam	348	7.3 to 9.2
Farewell *et al.* (1992)	homo-/bisexual men in Canada	159	7.66
Taylor *et al.* (1990)	homosexual men in a multi-centre study	1907	9.5
Bachetti (1990)	from prevalence and diagnosis patterns		9.8
Longini *et al.* (1989)	varied risk factors in San Francisco	603	8.3
Lui *et al.* (1988)	homo-/bisexual men in San Francisco	84	7.8
Anzala *et al.* (1991)	female prostitutes in Nairobi, Kenya		3.5

(ii) *Vertical transmission*

The probability of transmission from an infected mother to the foetus, the neo-nate or the young infant is again difficult to quantify. A key problem is the diagnosis of HIV infection in infants. It is made complicated by the presence of maternally derived antibodies and the resultant need to establish whether or not the virus is present in the infant using polymerase chain reaction (PCR) techniques (Ryder & Hassig 1988; European Collaborative Study 1992). Furthermore, as in the case of horizontal transmission the likelihood of the virus passing from mother to infant appears to depend on the stage of infection in the mother, with transmission more likely if the mother shows symptoms of immunodeficiency. A recent review of studies in sub-Saharan Africa by Ryder & Temmerman (1991) based on births to 1175 mothers from Zambia, Rwanda, Burkino Faso, Kenya and Zaire gave a range of 0.3 to 0.39 with a mean (weighted according to sample size) vertical transmission probability of 0.37. In all model simulations we employ a value of 0.35.

Interestingly, the reported values from studies in African populations are much higher than those reported in developing countries. For example, the extensive European Collaborative Study (1992) of 721 children born to HIV infected mothers gave a probability of 0.14 infections per live birth. The difference in magnitude could be a consequence of the fact that most mothers in the European Study were in the relatively early stages of the incubation period or it could be a consequence of differences in patterns of breast feeding or birth practices. Recent work has suggested that the virus may be transmitted via breast feeding (Dunn *et al.* 1992).

Aside from the likelihood of passing infection from mother to child, other factors of relevance to assessments of likely demographic impact of AIDS include the likelihood of a live-birth in HIV infected women by comparison with uninfected women, and the quality of care to a new born infant provided by infected women in the late stages of the incubation period of AIDS (Ryder *et al.* 1989).

(iii) *The incubation period of AIDS*

The period between initial infection and the development of AIDS is long and variable. There are two key problems in accurately assessing the average duration of the incubation period. First, it is often difficult to establish precisely when those infected with HIV actually acquired infection. Second, the epidemic is quite recent, which means that the full probability distribution for progression to AIDS has not yet been observed in any single cohort of infected persons. It is still not yet clear what proportion of those infected will eventually progress to AIDS (Hendriks *et al.* 1993; Farewell *et al.* 1992). Estimates of mean incubation periods may be obtained in cohort studies of those infected by blood or blood products, or by prospective studies of high risk individuals who are uninfected and by observation of if and when infection is acquired. In many studies of the distribution, summary statistics are derived on the basis of fitting specific probability distributions such as the Weibull or gamma to observed data which records part of the distribution (the largest study of gay men in San Francisco now provides 13 years of observations but the pattern of progression to AIDS has changed over time due to improvements in the management of HIV infection and changes in the definition of the disease AIDS). Which particular probability distribution is the best mirror of the true distribution will emerge as the data accumulates (Hendriks *et al.* 1993).

Table 2 provides a summary of the information recorded in some of the better studies of the incubation period distribution for which a median period has been derived. Other studies of the hazard function for progress to AIDS are present in the literature for gay men (Hessol *et al.* 1989) and for haemophiliacs (Brookmeyer & Goedert 1989; DeGruttola & Lagakos, 1989; Lee *et al.* 1991) and much debate surrounds the interpretation and representativeness of such data (Bacchetti *et al.* 1992). Here we take a crude figure for the average incubation period of 8 years, which seems a reasonable estimate for different risk groups in developed countries. A more detailed analysis appears unwarranted given the paucity of data from Africa. Only one study has been reported from Africa and this is of a small sample of female prostitutes in Nairobi in which the median period from infection to AIDS was 44.6 months (Anzala *et al.* 1991). Many researchers now believe that the mean incubation period of AIDS in poor communities in developing countries is much shorter than that reported in developed countries due to malnutrition and the continual insult of a wide range of infectious agents (Webster *et al.* 1989; Smallman-Raynor & Cliff 1992). We opt for an optimistic value of 8 years for the mean period and this, in conjunction with the assumption of three stages of infection with exponential distribution of waiting

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times in each (average periods of 6 months, 6.5 years and 1 year) gives rise to the incubation period distribution depicted in figure 3*a* (distribution) and 3*b* (hazard function). Once AIDS has been diagnosed, life expectancy is thought to be about one year or less in Africa. The period is lengthening in many developed countries due to better treatment and management of opportunistic infection plus the use of zidovudine (Reeves 1989). However, these advances in patient management will not have much effect in developing countries. A mean rate of progression to death of one year is used in the model, which is probably an optimistic estimate.

(iv) *Incubation periods and mortality rates in infected infants*

Recorded rates at which infants progress to AIDS and then on to mortality are variable. The probability of survival of an infected infant appears to be strongly dependent upon initial symptoms of HIV infection, and possibly, on the stage of foetal development when the HIV virus was transmitted from the mother. Among 94 infected French infants the probability of survival to 3 years was 0.48 in the third of patients who had early onset of opportunistic infections or severe encephalopathy, but increased to 0.97 in those with either no symptoms, bacterial infections or lymphoid interstitial pneumonitis (LIP) (Blanche *et al.* 1990). These results are similar to those reported from an earlier study of 172 children in a Florida hospital, where the 17% initially diagnosed with LIP (median age at diagnosis 14 months) had a mean survival time from diagnosis of 72 months, whereas, the 9% initially diagnosed with *Pneumocystis carinii* (median age at diagnosis 5 months) had a mean survival time of only one month (Scott *et al.* 1989). Similarly, among 215 infected infants in New York 20% progressed to AIDS in the first year of life followed by 8% for each year thereafter (Auger *et al.* 1988). In a more recent study of 529 Italian children the mortality rate was 8.9% in the first year but 3.5% per year thereafter, until the age of 8 years when it again increased (Tovo *et al.* 1992).

The mortality rates in these studies are all low in comparison to those observed in studies of infected infants in African communities (table 3), but mortality rates in these studies still appear to depend upon symptoms of infection. Studies in Africa are on the whole smaller in scale and less focused on infection in infants. For example, in a study in Zaire the mortality of infants of HIV infected mothers, rather than HIV infected infants, was compared with mortality in infants of uninfected mothers (Ryder *et al.* 1989). The probability of survival after 1 year was 20% less in those with HIV infected mothers. If we assume that 35% of infants are infected with HIV this implies that over half die of AIDS after only one year. However, the study showed that the increased risk of mortality in infants with infected mothers was due to the influence of morbidity in the mother on infant care irrespective of whether the infant was infected or not, as well as mortality associated with HIV infection in the child. In Africa, rates of mortality are likely to be high and to mirror this we set the average incubation period of AIDS in infants at 1 year and life expectancy from the development of AIDS as 1 year.

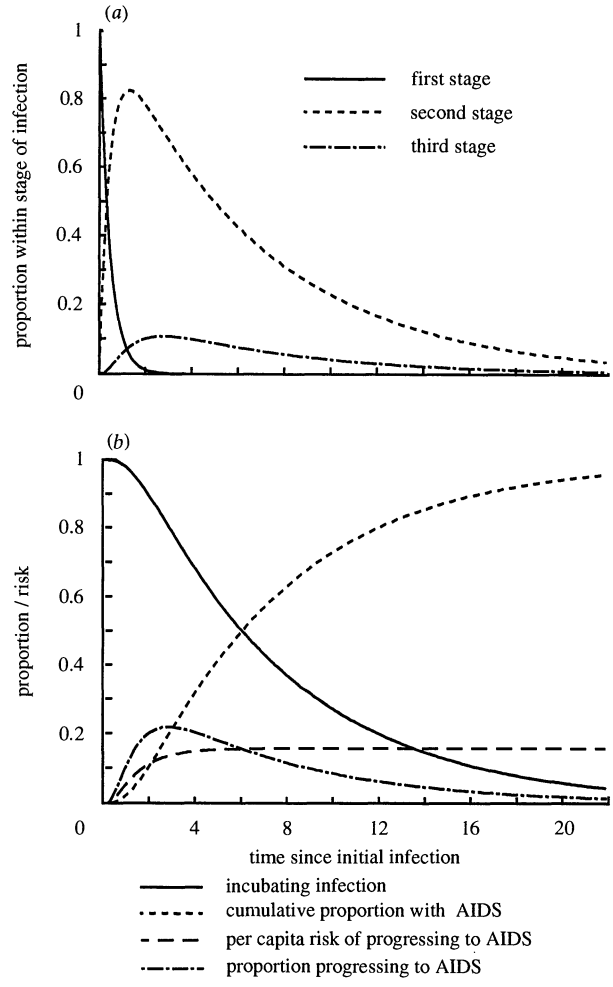

Figure 3. A three stage model of the incubation period of AIDS, with constant rates of moving from one stage to the next. Graph (*a*) records the proportion within each stage while graph (*b*) displays the cumulative proportion with AIDS as a function of time since infection and the *per capita* risk of progressing to AIDS (the hazard function). The average duration of stay in the first, second and third stage are 0.5, 6.5 and 1 year respectively.

(v) *Sexual behaviour*

Data is beginning to accumulate on patterns of sexual behaviour in different societies in both developed (Johnson *et al.* 1992; Analyse des Comportements Sexuels en France Investigators 1992; Giesecke *et al.* 1992) and developing countries (Hogsborg & Aaby 1992; Carael *et al.* 1991). Some have argued that rates of sexual partner change in many poor communities in developing countries are higher than equivalent values in the developed world (Piot & Carael, 1988; Hrdy 1987) and that this in part explains the observed differences in the rates of HIV transmission within heterosexual communities in the different regions. Recent reviews of the available data in part support this conjecture but because of the paucity of the data and heterogeneity in study design, care must be exercised in making generalizations. Inspection of

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Table 3. *A summary of studies on HIV infected infant health and survival*

Geographical location of study	number in cohort	progression to AIDS	mortality	reference
France	117	after 18 months 59% with severe disease	at 18 months 21% mortality	Blanche *et al.* (1989)
France	94	after 1 year one-third had profound immunodeficiency	at 5 years 35% mortality	Blanche *et al.* (1990)
New York, U.S.A.	215		after 1 year 20% mortality 8% each year thereafter	Auger *et al.* (1988)
Miami, U.S.A.	172		median survival 38 months post diagnosis	Scott *et al.* (1989)
Italy	529	median age of HIV symptoms 5 months	median survival 96.2 months	Tovo *et al.* (1992)
Brazzaville, Congo	64		39% survival to 12.5 months compared with 97% in controls	Lallemont *et al.* (1989)
Zambia	42		44% died of AIDS by 2 years	Hira *et al.* (1989)
Zaire			after 1 year infants with HIV + mother 26% of 448 died infants with HIV − mother 6% of 587 died	Ryder *et al.* (1989)

the data for sub-Saharan Africa suggests average yearly rates of sexual partner acquisition of between 1 and 4, but with men typically reporting many more partners than women. We examine model behaviour for various mean rates of partner change in the range 1–3 per year. In the model the population is stratified into four sexual activity classes and the proportion in each class is set to mirror observed patterns (Konings *et al.* 1988) as defined in table 4. Individuals are assigned to a particular group when they join the sexually active age classes. This is a crude assumption because in practise an individuals behaviour will often change as he or she ages. We attempt to capture observed changes with age by altering the mean rate of sexual partner acquisition in each age group with the overall pattern documented in table 4. The trend recorded in table 4 mirrors that observed in studies in Guinea-Bissau and Cote d'Ivoire (Hogsborg & Aaby 1992; Anderson *et al.* 1991; Carael *et al.* 1991) (figure 4*a*,*b*). The Guinea-Bissau study (Hogsborg & Aaby 1992) also provides information of the pattern of sexual partner choice between different age classes of the male and female segments of the study community (figure 4*b*). The observed bias for men to form sexual partnerships with women younger than themselves is mirrored in the structure of the mixing by age component of the model.

The age at which individuals start sexual activity is assumed to be the same for both sexes and is set equal to the mean age at which women have first menarche, namely, 15 years (Wyshak & Frisch 1982). Sexual activity for men and women is assumed to cease at the fixed age of 50 years.

A few attempts have been made to analyse networks of sexual contact (Granath *et al.* 1991; Haraldsdottir *et al.* 1992; Garnett & Anderson 1993*a*) but these have

Table 4. *Sexual partner acquisition rates (year^{-1}) for different activity and age groups relative (i.e. a ratio) to the minimum rate*

	proportion of population		
activity group	males	females	relative partner acquisition rate[a]
1	0.1	0.05	100
2	0.3	0.25	20
3	0.4	0.5	5
4	0.2	0.2	1

age group	15–19	20–24	25–29	30–34	35–39	40–44	45–49
relative partner acquisition rate	2	4	6	8	5	3	1

[a] The relative partner acquisition rate is the partner change rate of the group relative to the lowest group. Actual partner change rates are calculated such that the mean rate weighted according to group size for the sexually active population is three new partners per year.

Table 5. *Age-specific mortality and fertility rates*

age group (years)	mortality rate (per capita per year)		fertility rate (per woman per year)
	males	females	
1	0.1168	0.1000	
1–4	0.0193	0.0187	
5–9	0.0065	0.0063	
10–14	0.0035	0.0035	
15–19	0.0044	0.0040	0.175
20–24	0.0063	0.0048	0.313
25–29	0.0067	0.0055	0.324
30–34	0.0071	0.0063	0.271
35–39	0.0080	0.0073	0.201
40–44	0.0097	0.0084	0.125
45–49	0.0118	0.0094	0.053
50–54	0.0157	0.0121	
55–59	0.0205	0.0163	
60–64	0.0295	0.0244	
65–69	0.0440	0.0380	
70–74	0.0681	0.0602	
75–79	0.1053	0.0935	
80–84	0.1893	0.1743	

been restricted to small communities in developed countries. No data is available for communities in Africa.

The age-specific *per capita* fertility and mortality rates for the population defined in the model are listed in table 5. These figures correspond to a 3.6% per annum growth rate in the absence of AIDS, a crude death rate of 15 per 1000, a life expectancy at birth of 52 years for males and 55 years for females and a total fertility rate of 7.3. Such values are close to those estimated by the World Bank (1991) for the majority of sub-Saharan African populations.

(*b*) *Patterns of sexual contact between and within age and activity classes: mixing matrices*

As noted earlier, once the population is stratified by sex, age and sexual activity class it is necessary to define how sexual partnerships are formed within and between the different strata of the population. This is the area of human sexual behaviour about which we know the least, but a number of theoretical studies suggest that it is of great importance in determining observed pattern (Gupta *et al.* 1989; Jacquez *et al.* 1989; Castillo-Chavez & Blyth 1989). To represent different patterns of sexual contact between strata we need to define a mixing matrix (or two in the case of a heterosexual population, one for males and one for females) whose elements are the probability that an individual from one group forms a sexual relationship with an individual of the opposite sex in another group. In the absence of data our only option is to examine the influence of a range of patterns that are likely to encompass what is taking place in practice.

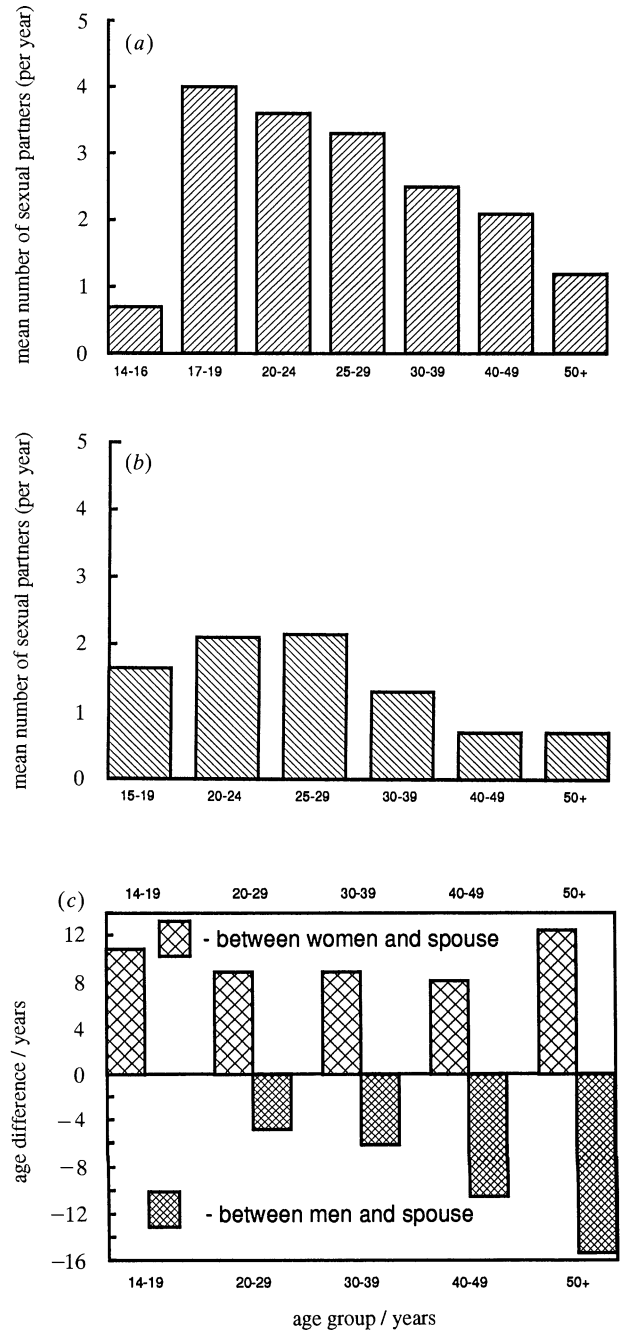

Figure 4. Sexual behaviour. Age specific rates of sexual partner change for samples of (*a*) men from Guinea Bissau (from Hogsberg & Aaby 1992), and (*b*) women from Cote d'Ivoire (Carael *et al.* 1991). (*c*) The difference in age between partners of the opposite sex in community in Guinea-Bissau (Hogsborg & Aaby 1992).

Mixing may range from fully assortative where those of one sex only form relationships with those of the opposite sex in the same age and sexual activity classes, to fully disassortative where those of one sex never form relationships with those of the opposite sex in the same age and activity classes (Gupta *et al.* 1989). Between these two extremes, many options are possible including random mixing where the probabilities in the matrix are equal to the proportions of the

total supply of sexual partnerships provided by each group

$$\left[N_j m_j / \left(\sum_{u=1}^{n} N_u m_u\right)\right].$$

Figure 5 provides a schematic representation of a mixing spectrum for the simple case of a population divided into two groups. In reality the problem is much more complex because patterns of mixing between sexual activity classes change with age and over time. The latter point is of particular relevance in the case of HIV as the disease it induces will alter the structure of the population via mortality which will be most severe in the most sexually active groups.

(i) *Patterns of mixing between age and sexual activity classes*

Two different ways of estimating the degree to which any given mixing matrix reflects assortative (like with like) patterns have been proposed. The first method is based on measures derived from the diagonal elements of the matrix. Three different measures have been proposed.

1. The simplest measure is the sum of the probabilities on the diagonal which is referred to as the trace of the matrix. When mixing is fully assortative, the sum is equal to the number of classes represented by probabilities within the matrix. When mixing is fully disassortative the trace is equal to zero and when mixing is random the trace is equal to unity in value where:

$$\sum_{j=1}^{n} \frac{N_j m_j}{\sum_{u=1}^{n} N_u m_u} = 1. \tag{17}$$

The magnitude of the trace is also equal to unity when mixing is proportional (= in proportion to group size) (see Anderson *et al.* 1992):

$$\sum_{j=1}^{n} \frac{N_j}{\sum_{u=1}^{n} N_u} = 1. \tag{18}$$

2. A more complicated approach suggested by Gupta *et al.* (1989) depends on a measure of Q which is a function of the sum of the eigen values of the matrix (w_i) (namely the trace) and the number of classes, n, represented in the matrix:

$$Q = \frac{\left(\sum_{i=1}^{n} w_i\right) - 1}{n - 1}. \tag{19}$$

When mixing is fully assortative $Q = 1$, when mixing is proportionate $Q = 0$ and $Q = -1/(n-1)$ when mixing is fully disassortative.

3. A third and even more complex way of assessing mixing has been suggested by Blower & McLean (1991) based on a weighting system that reflects the preference of members of one class for someone of the opposite sex in the same sexual activity (or age) class, relative to someone of the opposite sex in a different sexual activity (or age) class. These process or preference weights depend on the structure of the mixing matrix of the opposite sex since partnerships between the sexes must balance. The preference weight for someone of sex k and activity group j, for someone of the opposite sex, k', in sexual activity group i is given by $\rho_{k'ji}/\rho_{k'ii}$. This makes clear the degree to which they depend on the structure of the mixing matrix of the opposite sex. In the assortative extreme they can sum to n the number of classes, in the proportionate case the sum is $n \times n$ and as the dissortative extreme is approached their sum tends to infinity.

A schematic representation of these three different measures is presented in figure 5.

The second approach to specifying measures of assortativeness relies on the individual elements of the matrix, as opposed to those on the diagonal. A simple example is provided by a background of proportionate mixing on which is grafted a tendency for within class mixing. A specific case is provided by the definition

$$\rho_{ij} = (1 - \varepsilon)\delta_{ij} + \varepsilon\left(\frac{N_j c_j}{\sum_{u=1}^{n} N_u c_u}\right), \tag{20}$$

where δ_{ij} denotes the Kronecker delta and the parameter ε denotes the degree of assortative mixing (Anderson *et al.* 1992). When $\varepsilon = 0$, mixing is entirely assortative and when $\varepsilon = 1$ mixing is proportionate. This is a more complex approach than those described

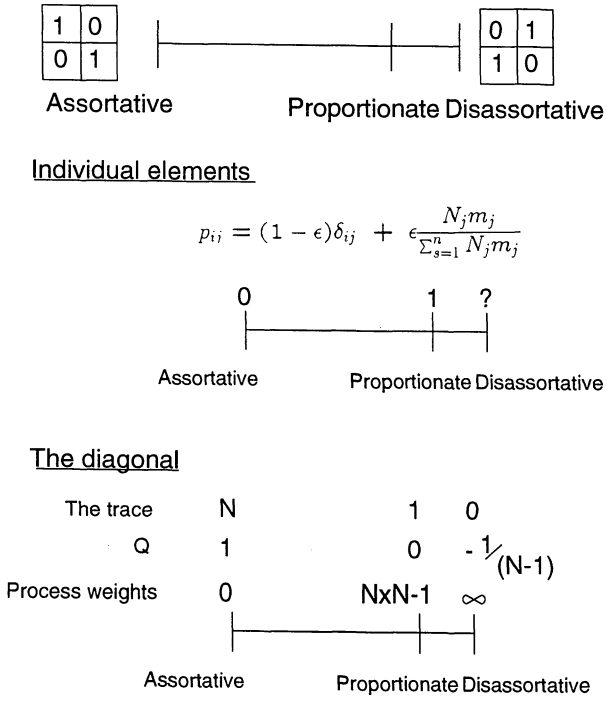

Figure 5. A diagrammatic representation of mixing patterns and different measures of the degree of assortative mixing based on a simple 2×2 matrix. The top diagram illustrates a spectrum of patterns from assortative (like with like) via proportionate (= random) to disassortative (like with unlike). The next diagram down displays a measure of assortativeness based on the individual elements of the mixing matrix (see text) while the bottom diagram illustrates measures of assortativeness based on the diagonal elements (see text) (i.e. the tract and the quantity Q).

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that are based on the magnitudes of the elements on the diagonal of the matrix. A problem with this approach is that the scale between proportionate and disassortative mixing is unclear. In the numerical simulation reported in this paper we use a combination of the first approach, based on the magnitude of the sum of the diagonal elements (the trace), and the second approach in which we only consider the spectrum of possible mixing patterns between the assortative extreme and proportionate mixing. The reason for this latter choice is a belief that in practice most mixing patterns lie within this region of the spectrum (Garnett & Anderson 1993*a*).

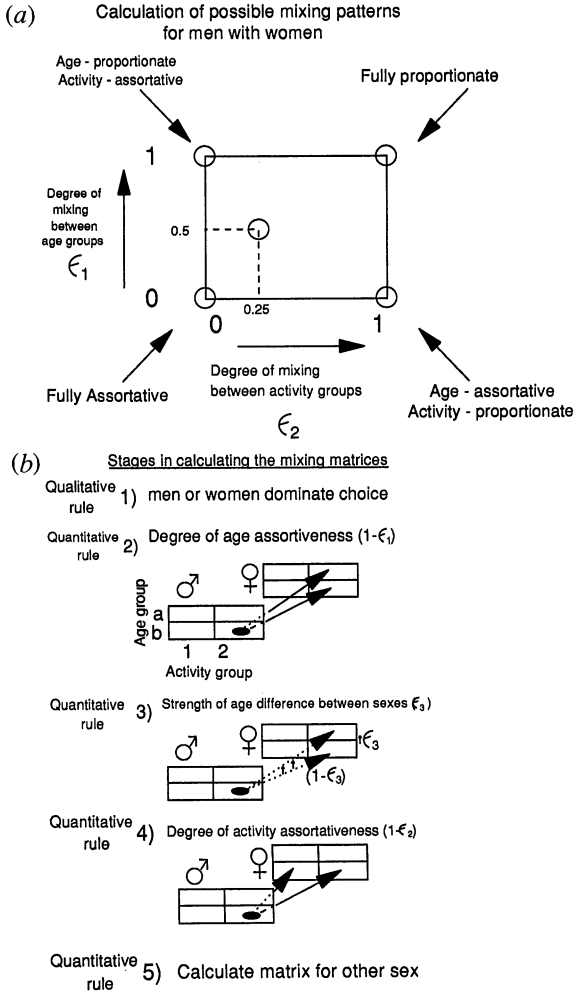

Figure 6. A diagrammatic representation of sexual mixing or contact in a population stratified by sex (i.e. heterosexual contact), age and sexual activity class. (*a*) The term ε_1 denotes the degree of assortative mixing between age classes, while ε_2 measures the degree of assortative mixing between sexual activity classes. (*b*) Pictorial representation of the stages involved in calculating the mixing matrices of the two sexes defined in terms of qualitative and quantitative rules.

(ii) *Generation of the mixing matrix*

Within a population stratified by sex, age and sexual activity class the size and the dimensions of the mixing matrix are clearly large. We depict the degree of assortative mixing between age classes as ε_1 (equation 20) and the degree of assortative mixing between sexual activity classes as ε_2. These parameters crudely describe the range of mixing patterns depicted diagrammatically in figure 6. For simplicity, our proportionate mixing specification is based on the number of people in a class as opposed to the number of sexual partnerships formed by a particular class (Anderson *et al.* 1992).

We include one further complication, namely, the specification of a parameter ε_3 to denote the degree to which men form sexual relationships with women younger than themselves. This trend is particularly strong in many societies in Africa as recorded, for example, by Hogsberg & Aaby (1992). The significance of this age mismatch to the potential demographic impact of AIDS has been described in a previous publication (Anderson *et al.* 1989). The parameter ε_3 defines the proportion of men in a particular age group who form sexual partnerships with women ten years younger than themselves.

In all manipulations of the elements of the mixing matrix the balance rule must apply in which the number of partnerships formed by males in age class i and sexual activity class l with females in age class j and sexual activity class m must equal those formed by women in age class j and sexual activity class m with men in age class i and sexual activity class l. In other words

$$c_{kli}\rho_{klmij}N_{kli} = c_{k'mj}\rho_{k'mlji}N_{k'mj}. \tag{21}$$

Where k' denotes the opposite sex from k. Furthermore the elements of the mixing matrix are probabilities hence the values of p_{klmij} summed over m and j must equal unity. These constraints imply that once the mean rates of sexual partner change and the mixing matrix are specified for one sex, the similar quantities for the opposite sex are also specified as a consequence of the initial choice. More formally:

$$c_{k'mj} = \sum_{i=1}^{7}\sum_{l=1}^{n}(c_{kli}\rho_{klmij}N_{lki})/N_{k'mj}, \tag{22}$$

and

$$\rho_{k'mlji} = c_{kli}\rho_{klmij}N_{kli}/c_{k'mj}N_{k'mj}. \tag{23}$$

This could be interpreted as an assumption in which one sex determines the rates of sexual partner change and mixing pattern of the other sex. We explore this implication by varying the sex of the controlling group. In reality it is unlikely in many societies that one sex has the dominant say in patterns of sexual behaviour. The more complex situation where both sexes play or equal or unequal roles in the determination of behaviour will be considered in a future publication.

Our numerical analyses were performed on the basis of specifying the rates of sexual partner change in different age and sexual activity classes for one sex, and specifying the structure of that sexes mixing matrix and then calculating the concomitant parameters for the opposite sex. More formally the parameters ε_1, ε_2 and ε_3 are specified in the algebraic manipulation as follows

$$\rho_{klmij} = \left(\varepsilon_1 \frac{\sum_{u=1}^{n} N_{k'uj}}{\sum_{u=1}^{n}\sum_{v=1}^{7} N_{k'uv}} + (1-\varepsilon_1)\delta_{ij}\right)\left(\varepsilon_2 \frac{N_{k'mj}}{\sum_{u=1}^{n} N_{k'uj}} + (1-\varepsilon_2)\delta_{lm}\right) \quad \text{for} \quad i \neq j,\ i \neq j+2,$$

$$\rho_{klmij} = \left[\left(\varepsilon_1 \frac{\sum_{u=1}^{n} N_{k'uj}}{\sum_{u=1}^{n}\sum_{v=1}^{7} N_{k'uv}} + (1-\varepsilon_1)\delta_{ij}\right) + \varepsilon_3\left(\varepsilon_1 \frac{\sum_{u=1}^{n} N_{k'uj+2}}{\sum_{u=1}^{n}\sum_{v=1}^{7} N_{k'uv}} + (1-\varepsilon_1)\delta_{ij+2}\right)\right] \times \left(\varepsilon_2 \frac{N_{k'mj}}{\sum_{u=1}^{n} N_{k'uj}} + (1-\varepsilon_2)\delta_{lm}\right) \quad \text{for} \quad i = j+2,$$

$$\rho_{klmij} = \left[(1-\varepsilon_3)\left(\varepsilon_1 \frac{\sum_{u=1}^{n} N_{k'uj}}{\sum_{u=1}^{n}\sum_{v=1}^{7} N_{k'uv}} + (1-\varepsilon_1)\delta_{ij}\right)\right]\left(\varepsilon_2 \frac{N_{k'mj}}{\sum_{u=1}^{n} N_{k'uj}} + (1-\varepsilon_2)\delta_{lm}\right) \quad \text{for} \quad i = j.$$

At the beginning of each simulation of the numerical properties of the model values for ε_1, ε_2 and ε_3 were specified to reflect varying degrees of assortative mixing between age (ε_1) and sexual activity (ε_2) classes, and differing degrees of mismatch between the ages of sexual partners (ε_3).

(*c*) *Balancing supply and demand for sexual partnerships in the face of variable mortality across sex, age and sexual activity classes*

The balance equation (equation 21) needs the further subscript of time t, as mortality due to AIDS will influence the different strata of the population in different ways as the epidemic develops. For example, those age and sexual activity classes with high rates of sexual partner change will be most severely affected by AIDS induced mortality. This will act to create an imbalance between the demand for and the supply of sexual partnerships and, as discussed in a previous publication (Anderson *et al.* 1992), a set of behavioural rules must be specified to correct this imbalance at every time point in the development of the epidemic. At present there is little if any empirical observation to guide us in the specification of these rules. Furthermore, these so called rules may vary widely between different societies and cultures. It is an obvious area of priority for future behavioural research in communities experiencing high rates of HIV infection and AIDS induced mortality.

Within the model we have a variety of options available to us to balance supply and demand. For example rates of sexual partner change in the different groups could be altered over time, or mixing patterns could be changed, or indeed both could be allowed to vary. We chose the simple option of restricting change to the rate of sexual partner acquisition in the different strata of the population. Other options will be considered in future research.

We modify the mean rate of sexual partner acquisition of sex k, age group i and activity class l in relation to the number of people in the other group $N_{k'jm}$, relative to the number of people in these same groups at time $t = 0$, $N_{k'jm}(0)$. A relative reduction in the size of the group is assumed to result in a proportional reduction in the rate of partner change of the various groups of the opposite sex with it. Conversely, if relative group size increases (relative to the state at time 0), then the rate of partner change of groups of the opposite sex with it increases. More precisely this set of rules is specified as

$$c_{klmij} = c_{klmij}(0)\frac{\sum_{u=1}^{n}\sum_{v=1}^{7}((N_{kuv}(0)-1)+(N_{k'uv}(0)-1))}{N_{k'mj}(0)-1} \times \frac{N_{k'mj}-A_{k'mj}}{\sum_{u=1}^{n}\sum_{v=1}^{7}((N_{kuv}-A_{kuv})+(N_{k'uv}-A_{k'uv}))}.$$

Here it is assumed that those with AIDS do not take part in the formation of sexual relationships. To relax this assumption the terms in A should be removed from equation (24).

(*d*) *Sensitivity analysis*

Because of the complex stratification of the population into sex, age and sexual activity classes, the model contains a large number of parameters, particularly in the context of specifying sexual behaviour and mixing patterns. At first sight this poses a major computational problem for any formal assessment of the sensitivity of model output to parameter value variation. One such approach is to select parameter values by random sampling within defined ranges (a uniform distribution) or from defined probability distributions of likely values (e.g. the Weibull or gamma distribution (Blower *et al.* 1991). A large number of simulations can be performed using different parameter sets. The method is very time consuming and not necessarily the most efficient way of assessing sensitivity. By inspection of the structure of the equations of the model, for example, it is apparent that the major non-linear term is that defining the *per capita* rate of transmission of the virus (equation (6)). As such, parameters associated with this term are likely to have a major influence on the pattern and magnitude of the epidemic. In this paper our interest is largely focused on the influence of patterns of sexual contact between

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and within age and sexual activity classes of the two sexes. Our focus is therefore on the parameters ε_1, ε_2 and ε_3 plus the associated rates of sexual partner change of the different strata of the population. All these parameters are embedded in the transmission rate (equation (6)). For the other parameters in the model we rely on fixed values (table 1) derived from published studies (Anderson *et al.* 1991, 1992).

Numerical solutions were generated using various time step lengths for the discrete approximations of the partial differential equations. A step length of one fiftieth of a year was found to provide good numerical accuracy. Simulations were carried out over time periods of 40 to 100 years post the establishment of the virus within the population.

3. RESULTS

(*a*) *Heterogeneity in sexual partner acquisition rates*

We first consider the effects of heterogeneity in sexual activity by fixing the degree of mixing between age ($\varepsilon_1 = 0.5$, the mid point between the assortative extreme and proportionate mixing) and sexual activity ($\varepsilon_2 = 0.5$) classes for two overall mean rates (over all age and sexual activity classes) of sexual partner change (cases (a) and (b), 1 year^{-1}; cases (c), (d) and (e), 3 year^{-1}) for a population homogeneous with respect to sexual activity (all individuals have the same rate of sexual partner change as the overall mean, cases (a) and (c)) and one that is heterogeneous as represented by four sexual activity classes with activity ratios between the mean rate in each class of 100:20:5:1 (cases (b) and (d)). We also consider the case of highly assortative mixing between age and activity classes ($\varepsilon_1 = \varepsilon_2 = 0.05$) for an overall mean rate of partner acquisition of 3 year^{-1} case (e). Simulations were performed over a 100 year period and the pattern of the epidemic recorded by reference to the prevalences of infection in sexually active men and women and the per capita growth rate of the total population. The results are plotted in figure 7. Consider the cases in which the mean rate of sexual partner change is set at a low rate (1 year^{-1}, case (a)). When behaviour is homogeneous, this level of activity is insufficient to generate an epidemic (overall $R_0 < 1$). Once heterogeneity is introduced the virus is able to persist in the high activity classes who continually seed the remaining activity classes to generate an epidemic and the long term persistence of the virus. Hence, heterogeneity enhances the likelihood of an epidemic occurring. However, paradoxically once its occurrence is assured, the greater the degree of heterogeneity the smaller the size of the epidemic and the less its demographic impact on the population. This point is illustrated in figure 7 in the simulations in which the overall mean rate of sexual partner change was set at 3 year^{-1}. In the homogeneous case, the epidemic takes a long time to develop but once it takes off it affects a significant fraction of both the male and the female population. In the heterogeneous case, the epidemic

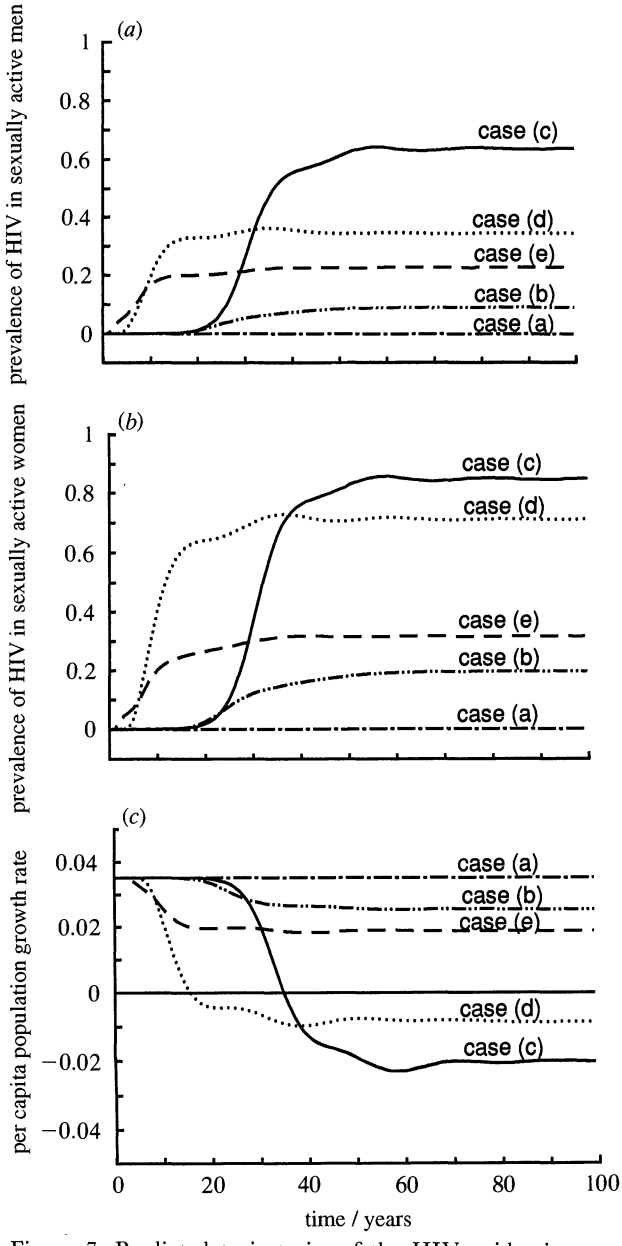

Figure 7. Predicted trajectories of the HIV epidemic over time for varying assumptions about sexual behaviour. Graph (*a*) records changes over time in the prevalence (= proportion) in sexually active men, graph (*b*) similar changes in sexually active women and graph (*c*) records temporal changes in the *per capita* population growth rate. In each case five trajectories are recorded, three for an overall mean rate of sexual partner change (at time $t = 0$) of 3 year^{-1} with homogeneous behaviour and heterogeneous behaviour for two different degrees of assortative mixing between activity classes, and two for a mean rate of 1 year^{-1} for heterogeneous and homogeneous sexual behaviour (see text). The value of ε_3 was set at 0.0. In all cases the value of ε_1 equalled ε_2. Case (a), homogeneous behaviour, $\varepsilon_1 = \varepsilon_2 = 0.5$, $\bar{c} = 1$ year^{-1}; case (b), heterogeneous behaviour, $\varepsilon_1 = \varepsilon_2 = 0.5$, $\bar{c} = 1$ year^{-1}; case (c), homogeneous behaviour, $\varepsilon_1 = \varepsilon_2 = 0.5$, $\bar{c} = 3$ year^{-1}; case (d), heterogeneous behaviour, $\varepsilon_1 = \varepsilon_2 = 0.5$, $\bar{c} = 3$ year^{-1}; case (e), heterogeneous behaviour, $\varepsilon_1 = \varepsilon_2 = 0.05$, $\bar{c} = 3$ year^{-1}.

takes off quickly due to the activities of the small fraction of the sexually active population with high rates of sexual partner change, but it affects a smaller overall fraction of the population as a result of the

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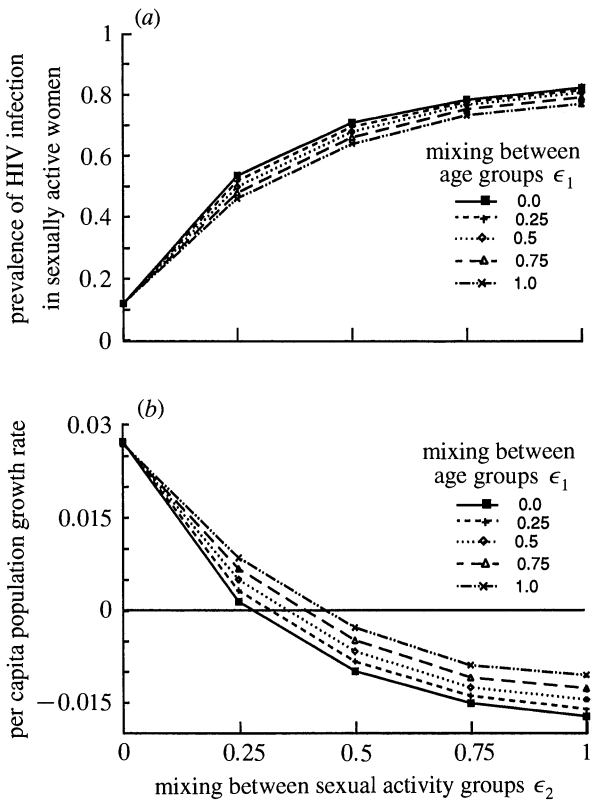

Figure 8. (*a*) Predicted relationship between the prevalence of infection in sexually active women at $t=40$ years and the degree of assortative mixing between sexual activity classes ($\varepsilon_2=0$, for fully assortative mixing), for various values of the degree of assortative mixing between age classes (ε_1). (*b*) Similar to (*a*) but recording the relationship between the *per capita* population growth rate at time $t=40$ years and ε_2. The value of ε_3 was set at 0.75. The overall mean rate of sexual partner change at $t=0$ was 3 year^{-1}, and other parameters were defined in tables 1, 4 and 5.

heterogeneity in sexual behaviour. These influences of heterogeneity are made more explicit in simple models of the HIV epidemic that do not consider host demography (Anderson *et al.* 1986; Anderson & May 1991). In all the simulations recorded in figure 7 the parameter defining the age mismatch in partnerships between the sexes, ε_3, was set at 0.75.

The influence of the other two mixing parameters, ε_1 and ε_2, is also hinted at in figure 7 in the simulation where $\varepsilon_1=\varepsilon_2=0.05$. These parameter choices reflect a highly assortative pattern of mixing which results in a smaller epidemic of limited demographic impact, when compared with an identical simulation but with a less assortative pattern of mixing ($\varepsilon_1=\varepsilon_2=0.5$). In all cases men were assumed to determine the sexual behaviour patterns of women, when balancing demand for partnerships with supply (see § 2*d*). This assumption results in higher levels of infection in women by comparison with men, than would be the case if women determined the behaviour of men. Because levels of infection in women have a much greater impact on population growth than those in men, due to the role of vertical transmission as well as the production of offspring, the assumption that the needs of men determine the behaviour of women tends to accentuate the potential demographic impact of AIDS.

(*b*) *Mixing patterns*

The previous subsection hinted at the influence of mixing patterns but in this subsection we examine this issue in more detail. To do so we set the mean rate of sexual partner change at 3 year^{-1} and assess the influence of varying the magnitude of ε_1 (age groups) and ε_2 (sexual activity groups) on the prevalence of infection in sexually active women and the *per capita* population growth rate after 40 years of viral spread (at time $t=0$ the population growth rate was 4% *per capita* per annum) (the value of ε_3 was, as before, set at 0.75). This is depicted in figure 8 and the patterns clearly reveal that the degree of mixing between sexual activity classes (ε_2) is of much greater significance to the size and impact of the epidemic than the degree of mixing between the age classes (ε_1). Note that when mixing between activity classes tends to the assortative extreme the epidemic has limited impact on population growth, while as it moves towards a proportionate value the epidemic can turn a 4% growth rate negative over the time span of 40 years. Similarly, with all other parameters fixed altering the mixing parameter (ε_2) from assortative to proportionate changes the prevalence of HIV in sexual active women from 12% to 80%.

The patterns recorded in figure 8 are somewhat deceptive due to the parameter ε_3. This describes the fraction of female partners of men (over 25 years of age) who would otherwise have been the same age group who are ten years younger than themselves. As such with $\varepsilon=0.75$, figure 8 underestimates the influence of different mixing patterns between the age classes (ε_1). This point is illustrated in figure 9 where the trace of the mixing matrix is plotted for various values of ε_1 (mixing between age groups) and ε_3 (0.75 and 0.0).

The influence of the interaction between the overall rate of sexual partner change and the pattern of

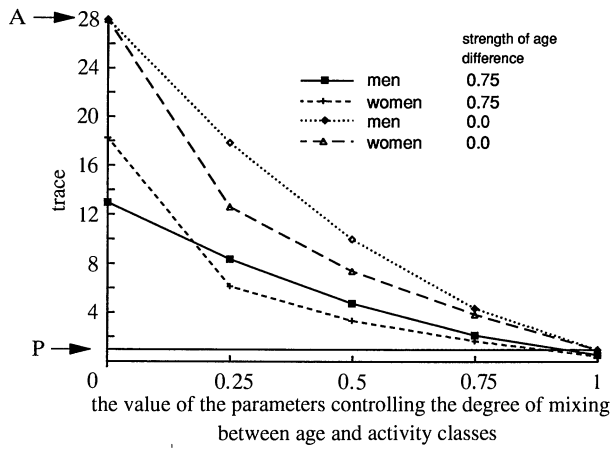

Figure 9. The relationship between the trace of the mixing matrixes for men and women, as a function of the degree of assortativeness in mixing between age groups (ε_1) and activity groups (ε_2) ($\varepsilon_1=\varepsilon_2$) for two values of ε_3 (see text). A, assortative; P, proportionate.

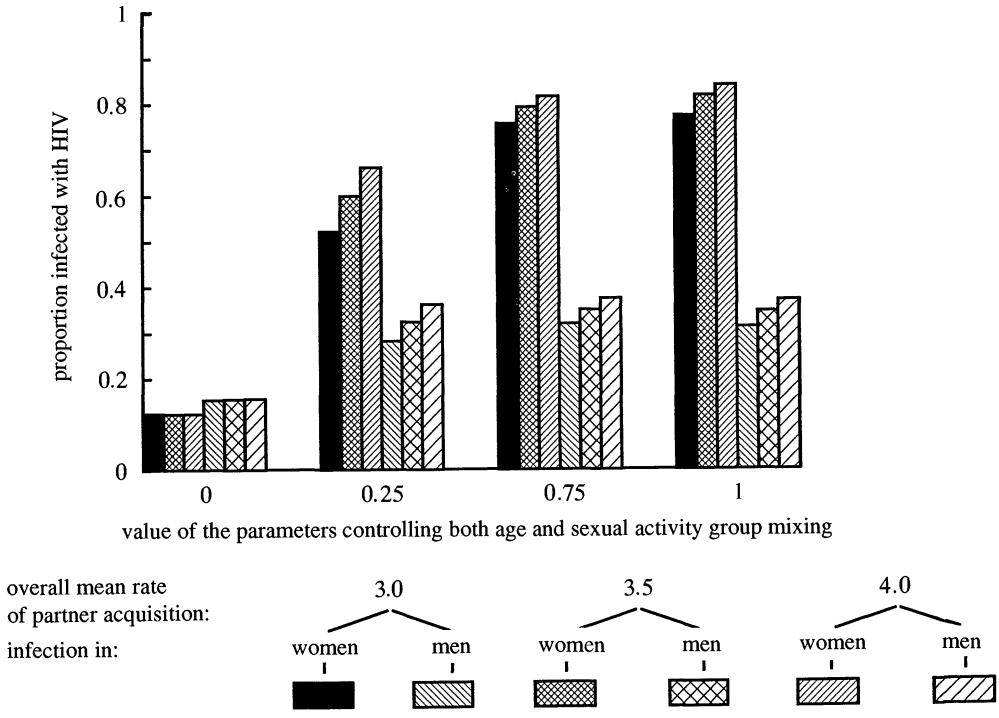

Figure 10. The predicted prevalence of infection in sexually active men and women at $t = 40$ years for various values of the parameters ε_1 and ε_2 ($\varepsilon_1 = \varepsilon_2$) and for different values of the overall mean rate of sexual partner change per annum (3.0, 3.5 and 4 year^{-1}). Other parameters as defined in tables 1, 4 and 5 and with men determining the pattern of female sexual behaviour to balance supply with demand (see text).

mixing between groups is more complex as depicted in figure 10. This graph records the proportion of men and women infected with HIV for three different average rates of sexual partner change (3.0, 3.5, 4.0, all year^{-1}) for various values of the degree of mixing between age and sexual activity classes ($\varepsilon_1 = \varepsilon_2 = 0.0$ (assortative), 0.25, 0.75, 1.0 (proportionate)). Two important points are illustrated in this graph. First, changes in the pattern of mixing can have a greater impact than changes in the average pattern of partner acquisition. Second, there is predicted to be a considerable difference between levels of infection in men (low) and women (high). The latter pattern is due to three factors: (i) the higher transmission probability from men to women than vice versa; (ii) the tendency of men to form sexual relationships with women younger than themselves; and (iii) the assumption that the pattern of male demand for sexual partners sets the pattern of female supply. The explanation of why the last factor is important rests upon the influence of high activity men. Initially if these high activity men choose to mix with low activity women (high ε_2 values in the mixing matrix of men with women) then the need to balance male demand with supply forces up the rate of partner change in this group while lowering the activity of those women in the smaller high activity classes. This introduces more homogeneous behaviour in the female population which as described in § 3*a* will lead to a larger epidemic. The need to balance the demand of men with supply also implies that the continual needs of the high activity men are met more and more from the lower activity female classes as the epidemic progresses and the fraction of higher activity women in the population declines. This trend is depicted in figure 11 by reference to the mean rates of sexual partner change of the male and female population in the different sexual activity classes (class 1 = high activity, class 4 = low activity) at the start of the epidemic and after 40 years of spread. The changes are a result of the need to balance female supply with male demand.

A further illustration of the significance of which sex sets the behavioural agenda in the supply and demand of equation is presented in figure 12. Here, the proportion of men and women infected with HIV after 40 years of spread is plotted for various values of the mixing parameters ($\varepsilon_1 = \varepsilon_2 = 0.0$, 0.25, 0.75, 1.0) under the two assumptions that (i) men set the agenda, and (ii) women set the agenda. When the latter is the case there is much less difference between the predicted levels of infection in the two sexes, despite a two fold difference in the transmission probabilities between the sexes (men to women twice that of women to men, table 1). Because observed sex ratios in the fraction of men and women infected with HIV in sub-Saharan African countries are close to 1 : 1 (WHO Global Programme on AIDS, April 1991) it may be that women have a significant influence in behavioural rules that govern matching supply and demand for sexual partnerships between the two sexes. This conclusion is very tentative, however, and the major point to note is simply that these rules will have a very significant impact on recorded levels of infection in the two sexes.

(*c*) *Predicted and observed trends*

The complexity of the model, with its detailed

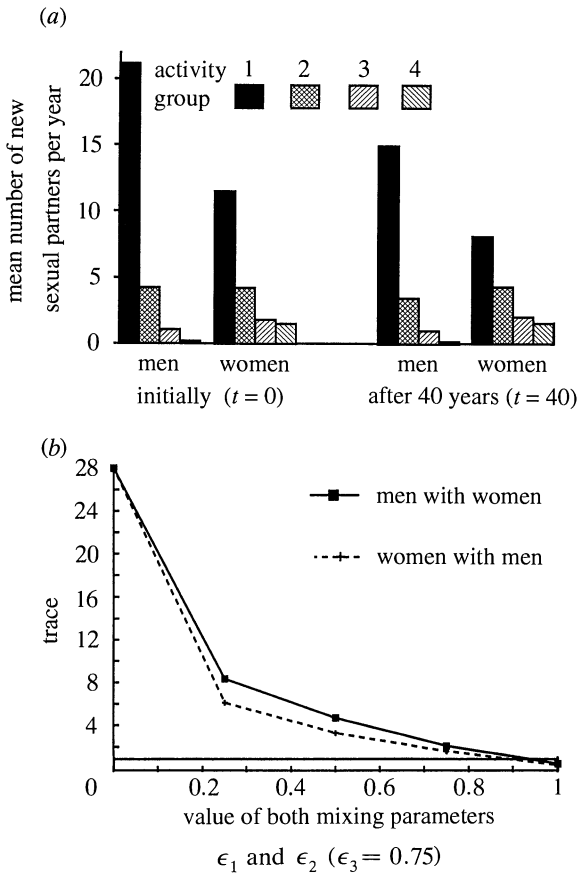

Figure 11. (*a*) The predicted rates of sexual partner acquisition (year^{-1}) in the four different sexual activity classes of men and women at $t = 40$ years and at $t = 0$ (men determining the balance between supply and demand) with the overall mean rate of sexual partner change set at 3 year^{-1}, and with $\varepsilon_2 = 0.5$. (*b*) The relationship between the trace of the mixing matrices of men and women, as a function of the magnitude of the degree of assortative mixing ($\varepsilon_1 = \varepsilon_2$, $\varepsilon_3 = 0.75$).

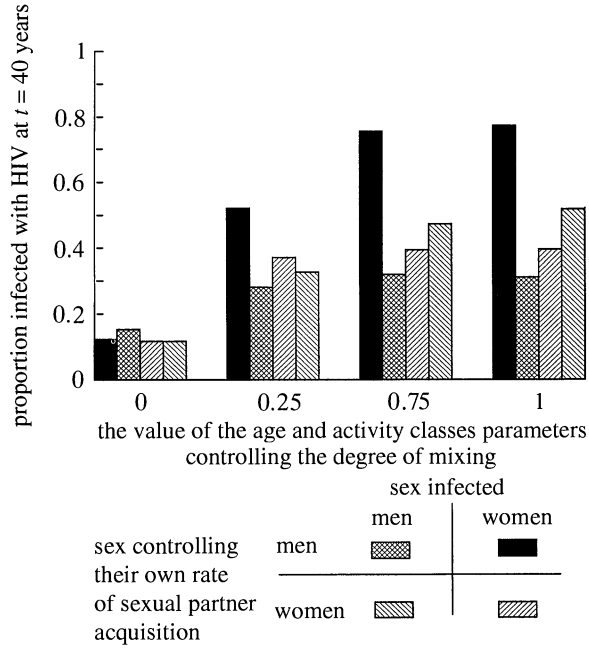

Figure 12. The predicted prevalence of HIV infection at $t = 40$ years in men and women for various values of the degree of assortative mixing ($\varepsilon_1 = \varepsilon_2$, $\varepsilon_3 = 0.75$), when men control the matching of supply and demand and when women control the matching of supply with demand.

description of mixing between and within different strata of the population, promotes confidence (perhaps falsely so!) in attempting to compare prediction with observed trends. However, great care must be exercised in such comparative research since numerical studies of model behaviour reveal that many factors determine the overall pattern and many different parameter combinations will generate a particular outcome. For example, we know that a rapidly spreading epidemic can be generated by either a high overall mean level of sexual activity, heterogeneity in sexual activity, assortative patterns of mixing or some combination of these factors. Observing rapid spread therefore does not inform about which of these factors or combination thereof, is responsible for the trend. The main purpose of comparing predictions with observation is to seek areas in which the model is not able to mimic observed pattern.

Various patterns can be used for comparative purposes. The simplest is longitudinal trends in HIV seroprevalence in a defined risk group. One example is pregnant women and some observed trends are depicted in figure 13 (source, U.S. Bureau of the Census 1992). The data are not drawn from cohort studies, different samples of pregnant women were used to determine prevalence in different years in each of the three countries portrayed in figure 13. Child bearing women are a biased sample of the population of sexually active women, since on average they tend to fall in the younger age classes within this group. Acting in opposition to this bias is the absence of women who are infertile due to past infection with a sexually transmitted disease that induces infertility,

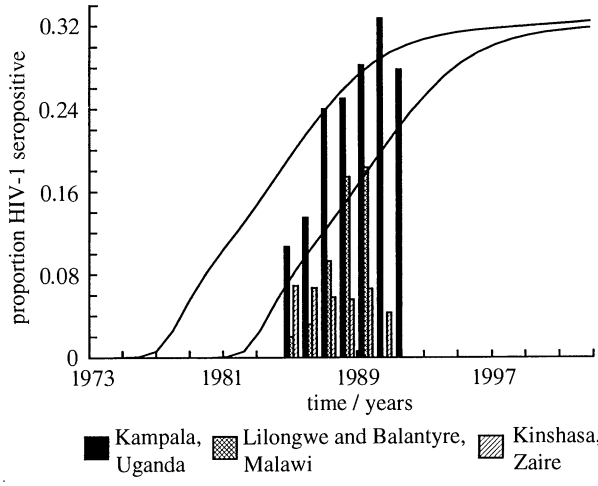

Figure 13. Longitudinal trends in HIV-1 seroprevalence in reproductively aged women in Kampala, Uganda, Lilongwe and Balantyre in Malawi and Kinshasa in Zaire (U.S. Bureau of the Census 1992). The bars denote observed values and the solid lines denote the predictions of the model with parameters as defined in tables 1, 4 and 5 and with the mean rate of partner change set at 2 year^{-1} and $\varepsilon_1 = \varepsilon_2 = 0.2$, $\varepsilon_3 = 0.75$. The two lines record two different starting points for the epidemic.

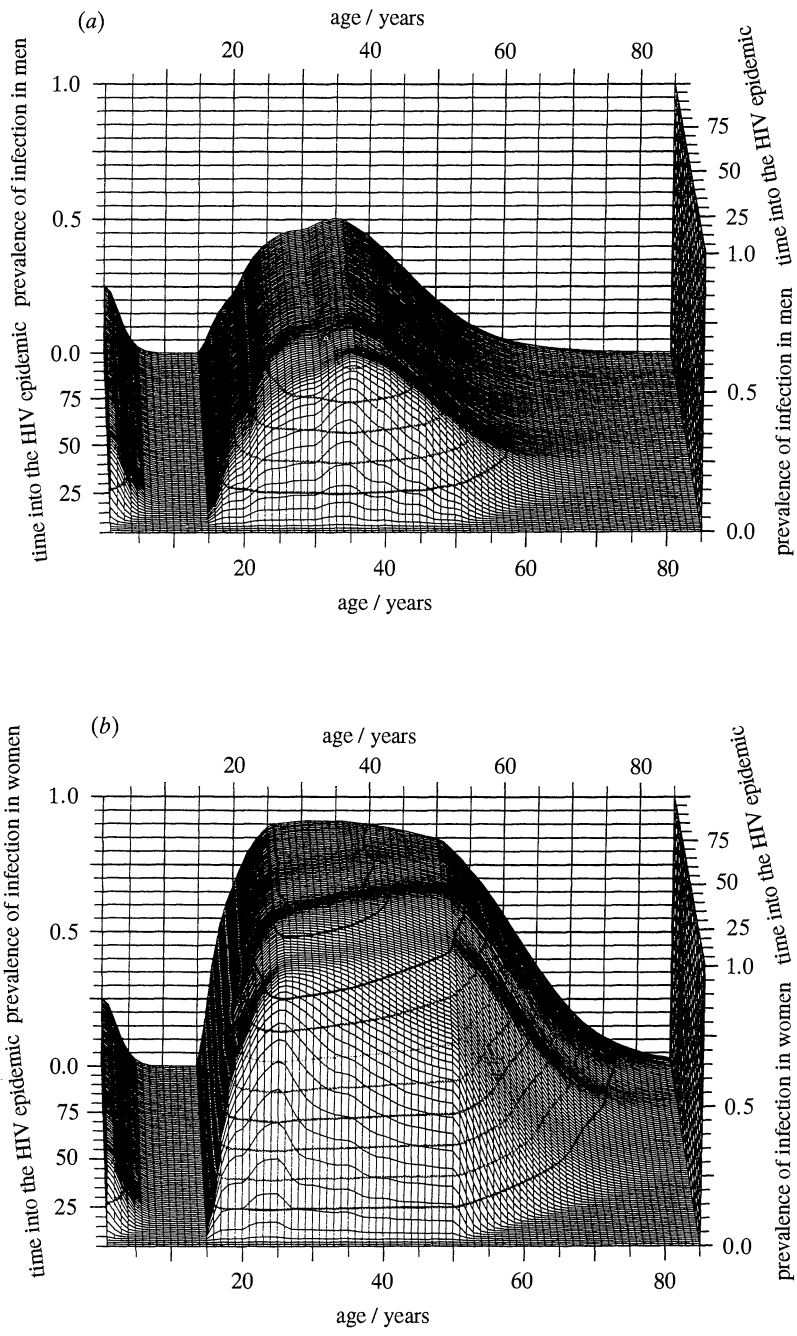

Figure 14. Predicted evolution of the epidemic (proportion of men (*a*) and women (*b*) infected) stratified by age, sex and time. The overall mean rate of sexual partner acquisition was set at 3 year^{-1}, the ratio of partner acquisition in the four sexual activity class was set at 100:20:5:1 (other parameters as defined in tables 1, 4 and 5, with $\varepsilon_1 = \varepsilon_2$, $\varepsilon_3 = 0.75$).

such as gonorrhoea. Figure 13 also records predicted patterns generated by the model. With appropriate choice of the parameters that describe mixing and sexual activity it is possible to mimic observed trends. However, a closer representation of the rapid rise in HIV prevalence among women a prevalence of around 30% which is seen in the data is more feasible if we alter the methods of balancing the supply and demand of sexual behaviour; such a representation is left for a future publication.

A further source of information with which to compare predicted trends is provided by horizontal cross-sectional studies that record HIV seroprevalence by sex and age class as illustrated in figure 14. Model predictions are recorded separately for males (figure 14*a*) and females (figure 14*b*) and the surfaces represent the growth of the epidemic over time and the pattern of its transmission across different age classes within the population. Longitudinal trends stratified by age and sex are not available from any cohort based study in Africa at present although research in progress in Uganda may produce serological surfaces akin to the model prediction recorded in figure 14. In the absence of such longitudinal data we rely for

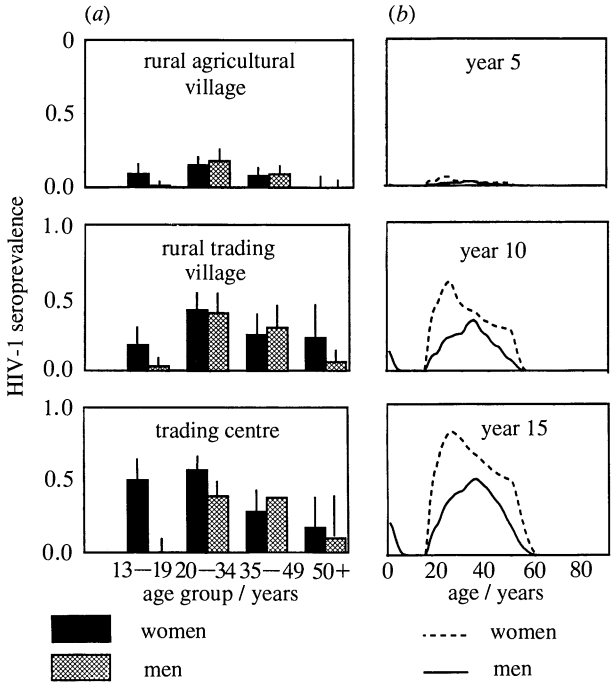

Figure 15. The observed age and sex stratified HIV-1 prevalence in (*a*) Rakai, Uganda (Wawer *et al.* 1991) in three different areas (rural village, rural trading centre and a trading centre), and (*b*) predicted patterns at year 5, 10 and 15 from the start of the epidemic. Parameter values as defined for figure 14.

comparison on research from three locations in the Rakai district of Uganda (Wawer *et al.* 1991) which records age and sex stratified seroprevalence in an area where the infection has been recently introduced (rural villages) an area where it has been present for moderate periods (rural trading village) and an area where the virus has been spreading for longer periods (trading centre). The prevalences in three areas are only a crude indirect reflection of longitudinal trends in the development of the epidemic since patterns of sexual behaviour may well differ in three spatial locations (figure 15). However, model prediction at years 5, 10 and 15 generated age- and sex-related trends in reasonable qualitative agreement with the observed patterns (figure 15). In particular, note the peak in HIV prevalence in young age classes of the female population by comparison with men and the higher overall prevalence of infection in sexually active women in both the trading centre where the infection has been spreading for some time and the model prediction at year 15. The model predicts that the sex ratio of cases will become more and more biased to women as the epidemic develops. The observed patterns appear to be in agreement with model predictions at this early stage in the development of the epidemic.

4. DISCUSSION

The major conclusion resulting from our preliminary analysis of the two sex model of HIV spread in a growing population stratified by age and sexual activity class, is the significance of mixing pattern between age and sexual activity classes of the two sexes on the overall pattern, magnitude and demographic impact of the epidemic. For example, with all other parameters constant changing the mixing pattern between sexual activity classes from assortative to proportionate can turn a small epidemic with limited demographic impact into a major epidemic capable of turning a 4% population growth rate negative over time scales of a few decades. Unfortunately, patterns of mixing between sexual activity classes or more broadly between major risk groups is the area of sexual behaviour about which we know least (Haraldsdottir *et al.* 1992; Garnett & Anderson 1993*a*). This observation plus the properties of the model argue for great caution in drawing conclusions about the future trends of the epidemic. The predictions generated by the simple models used by the World Health Organisation and others to suggest what might happen in the year 2000 are a case in point. In the absence of data on mixing patterns and how these might change as the epidemic develops much uncertainty surrounds future events.

Model formulation also raised pointers to areas for future research. Many of the major uncertainties in formulation centred on the issue of how sexual behaviour and mixing patterns are balanced within a population and how they will change as AIDS induced mortality alters the structure of the population. For example, we made the initial assumption that male demand for sexual partners dictated female behaviour, in that females in a particular age and activity group would increase their numbers of different sexual partners if demand exceeded supply. In most communities, real behaviour must reflect some sort of negotiated (explicit or implicit) compromise between the sexes relevant to cultural setting. The compromise will fall on a spectrum bounded by male domination on one end to female domination at the other. In many poor societies in the developing world it is argued that male domination is the more likely pattern of behaviour. However, little is understood in detail and more anthropological research is required.

A second area of uncertainty concerned with the rules that govern behaviour or mixing pattern change as differential mortality affects population structure is precisely who changes behaviour (i.e. which sexual activity or age classes). In this paper we assumed that individuals reduced or increased sexual activity in response to demand. Change could also take place via patterns of mixing or indeed via some combination of sexual activity and mixing. Here again, no information is available as yet to guide the choice of a sensible set of assumptions. In practise it should be possible to acquire information on this topic in badly affected communities via behavioural studies.

Future research needs in model development are many. In the absence of information in key areas, one danger is that future developments will soar free from the constraints of data, and hence reality. To combat this all efforts must be made to use the available information and to encourage the collection of better data on patterns of sexual behaviour, the incubation

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period of AIDS in Africa and the likelihoods of horizontal and vertical transmission. With this in mind, however, there are key areas for future improvements. The first of these concerns the definition of a horizontal transmission probability per partnership. In future models this should be modified to incorporate a definition per sexual act, combined with a description of the joint distribution of sexual acts and sexual partnerships per unit of time. Linked to this problem with a definition of a net transmission rate within the population, is the stratification of the population into a series of sexual activity classes. As individuals age their behaviour changes and they may move from being highly promiscuous at a young age to monogamous within a stable marriage at an older age. At present the model's structure is a very crude mimic of an individuals passage via various phases of sexual behaviour.

A final area of future study is that concerned with intervention to slow the spread of the virus. At present options are limited and include: (i) education about HIV and AIDS plus safer sex practice, given broadly or targeted at particular groups; (ii) the distribution of condoms and the encouragement of their use to reduce the risk of horizontal transmission; and (iii) the control of other sexually transmitted infections, via diagnosis and chemotherapy, that are thought to enhance the likelihood of HIV transmission (so called co-factors). Because resources are limited in most developing countries, models can play a useful role in helping to decide how best to use control options to slow spread (Rowley *et al.* 1990). One relevant question concerns the targeting of resources to high risk groups. Is this always beneficial or is targeting of greatest benefit in the early stages of the epidemic? A further question of relevance concerns the synergistic effects of two or more interventions (i.e. education plus condom use, or STD control and condoms). Is the simultaneous introduction of two types of interventions of greater or less benefit than the summed effects of the two interventions when each is implemented in the absence of the other? These and similar questions will be addressed in detail in a future publication using the model framework defined in this paper.

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ercent HIV-1 seropositive

above	20.0
10.0 -	20.0
5.0 -	10.0
0.5 -	5.0
0.1 -	0.5
below	0.1

igure 1. Prevalence of HIV-1 in low risk men and women in urban settings, in different developing regions of the orld, 1989–1992. The overall prevalence for a particular country is the most recent serological survey from among ildbearing women (or blood donors if data from childbearing women is unavailable) from surveys within the U.S. ureau of Census, HIV data base.