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POSSIBLE DEMOGRAPHIC CONSEQUENCES OF AIDS

IN DEVELOPING COUNTRIES

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Simple mathematical models of the transmission dynamics of HIV that incorporate demographic and epidemiological processes to assess the potential impact of AIDS on human population growth and structure in developing countries suggest that AIDS is capable of changing population growth rates from positive to negative values over timescales of a few decades. The disease is predicted to have little if any impact on the dependency ratio of a population, defined as the number of children below age 15 years and elderly people over 64 years, divided by the number of adults between 15 to 64 years.

A LARGE number of cases of acquired immune deficiency syndrome (AIDS) are now being reported to the World Health Organization (WHO)—in October 1987, 123 countries reported at least one case[1]—and evidence is accumulating of the degree to which the aetiological agent of the disease (Fig. 1), the human immunodeficiency virus (HIV), has penetrated heterosexual communities in developing countries (particularly in Sub-Saharan Africa and South America[2-7]). This has prompted governments and international agencies to give urgent consideration to the degree to which the pandemic of AIDS will influence the demography and socio-economic development of large areas of the world in the coming decades.

Scientific assessment of this problem is complicated by our limited understanding of the epidemiology of the infection (HIV) and the disease (AIDS)[3]. Uncertainties include: the fraction of those infected who will proceed to develop AIDS and the time scale of this progression[5-9]; the likelihood of vertical transmission from infected mother to child *in utero*, during childbirth, and by breast feeding[10-14]; the pathogenicities of human retroviruses other than HIV-1 (such as HIV-2) that are currently spreading in certain countries[15]; the importance of cofactors such as genital ulcers in heterosexual transmission[16]; the degree to which the infectiousness of infected patients changes throughout incubation of the disease[17,18]; the probabilities of horizontal transmission from male to female and vice versa[19,20]; and patterns of sexual behaviour in defined communities[21-23]. The long and variable incubation period of AIDS means that epidemiological knowledge will only accumulate slowly from long-term studies of infection and disease incidence, the rise in the former preceding that in the latter by many years.[3,11]. Current estimates of the mean period between HIV infection and development of AIDS, derived from transfusion-associated cases in the United States, are 8-9 years[24], although the mean may be lower in developing countries where people are exposed more frequently, and to a larger range of infectious agents, than in the developed world[3,11,25]. A combination of social and political sensitivities, and the more practical difficulties in accurate diagnosis and reporting of infection and disease in poor countries, has hindered the study of the spread of infection[3,11,25,26] in these parts of the world.

Quantitative data on the epidemiological processes outlined above, plus data on age-specific fertility and mortality, is essential for precise predictive work on the demographic impact of AIDS. The need to assess the magnitude of the problem however, is urgent to facilitate the long-term planning of governments and international aid agencies. It therefore seems sensible to study mathematical models that combine the demography of populations having positive net growth rates with the presently known epidemiological characteristics of the heterosexual transmission of HIV-1. In this paper we develop simple models with the aim of obtaining a crude understanding of how AIDS deaths

might affect demographic patterns, of the timescales of such effects and of the influence of demographic and epidemiological parameters on population sizes. Mathematical study of these deliberately simplified models is a preliminary to future numerical exploration of much more complicated and realistic models possible once data accumulates. The qualitative understanding that simple models can provide make it easier to recognize what needs to be measured, together with the appropriate timescales and parameter ranges in subsequent and more elaborate studies[19,26,27].

Definition of a basic model

A theoretical framework for exploring how infectious diseases may affect animal population sizes has been developed over the past decade[28-31]. More recently, a number of mathematical studies have combined demographic and epidemiological considerations to examine the impact, transmission, and control by mass vaccination, of directly-transmitted childhood infections such as measles in developing countries[32,33]. A mathematical framework for the study of the transmission dynamics of HIV has begun to be developed[19,26,34-36] but as yet it does not address the question of demographic impact.

We begin by considering a total population $N(t)$ at time t, subdivided into $X(t)$ susceptibles and $Y(t)$ infecteds[37] (assumed to be infectious), all of whom develop AIDS on some characteristic long timescale (a growing body of evidence suggests that a very high fraction of those infected will eventually develop symptoms of the disease[38,39], so in this basic model the fraction, f, of infecteds who develop AIDS is assumed to be one). For simplicity, we do not consider a separate class for AIDS patients as the average incubation period $(1/(\alpha + \mu))$ appears long in relation to the life expectancy of an AIDS patient $(1/(\alpha + \mu) >$ nine years while life expectancy with AIDS is about one year). In this calculation α is the disease-related death rate and deaths from all other causes occur at a constant rate μ (type II survival, giving an exponential age distribution which is a reasonable approximation for many developing countries). These assumptions yield the following pair of differential equations for $N(t)$ and $Y(t)$:

$$dN/dt = N[(\nu - \mu) - (\alpha + (1-\varepsilon)\nu)(Y/N)] \tag{1}$$

$$dY/dt = Y[(\beta c - \mu - \alpha) - \beta c(Y/N)] \tag{2}$$

We define the net birth rate of the community B as:

$$B = \nu[N - (1-\varepsilon)Y] \tag{3}$$

Here ν is the per capita birth rate (females per female, or equivalently offspring per capita for a 1:1 sex ratio) in the absence of infection; ε is the fraction of all offspring born to infected mothers who survive and $(1-\varepsilon)$ is the fraction who acquire infection by vertical transmission and die rapidly from
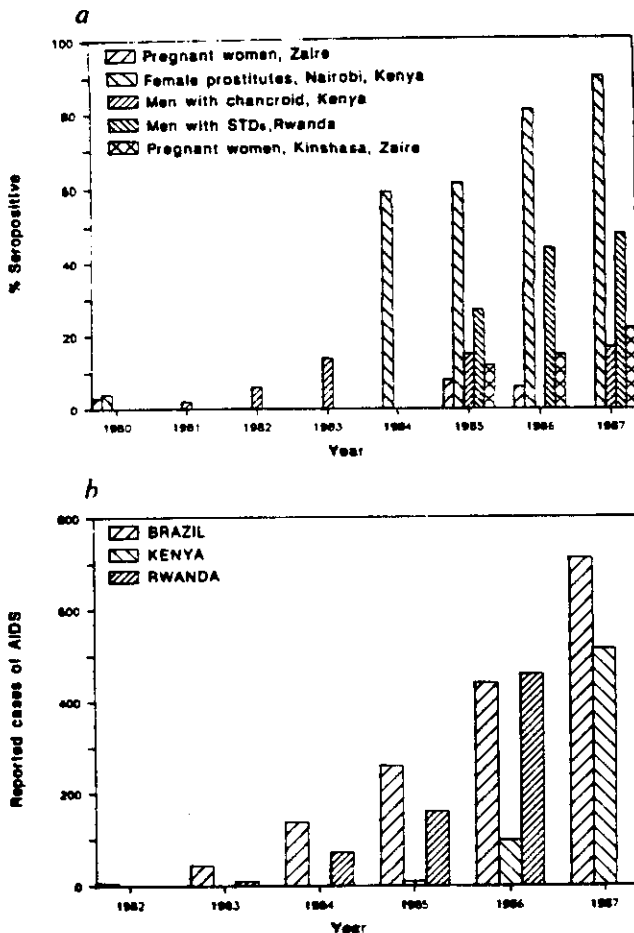
Fig. 1 a, Longitudinal changes in the proportion of people in various at-risk groups in Africa, who have antibodies to HIV-1 antigens (seropositive) (data sources refs 11, 48, 50–52). □, Pregnant women in Zaire; ▢, Female prostitutes in Nairobi, Kenya; ▉, Men with chancroid, Kenya; ▩, Men with STD infections, Rwanda; ▉, Pregnant women, Kinshasa, Zaire. b, Longitudinal trends in cases of AIDS reported to WHO in Brazil, Kenya and Rwanda.

AIDS (effectively at birth). The per capita rate at which adults acquire infection, λ, is assumed to be given by $\lambda = \beta c Y/N$ where β is the probability of acquiring infection from any one infected partner, c is the average rate of acquiring partners (c is not the mean number, but is the mean, m, plus the variance to mean ratio, σ^2/m, of the relevant distribution of partner-change rates[19,26]), and Y/N is the probability that any one partner is infected. More generally for heterosexual transmission we should deal with two distinct populations, N_1 of males and N_2 of females, with females acquiring infection from males at a rate $\beta_1 c_1$, and vice versa for female-to-male transmission at a rate $\beta_2 c_2$. However, for simplicity we assume that $\beta_1 c_1 = \beta_2 c_2 = \beta c$ such that the two-sex model collapses to equations (1) and (2). This appears to be a reasonable assumption as we have shown elsewhere[19] that in the early stages of the epidemic the ratio of the number of seropositive males to seropositive females is roughly $(\beta_1 c_1/\beta_2 c_2)^{1/2}$. Observations in a variety of African countries suggest these rates are roughly equal[5,19].

To clarify discussion we introduce the following notation: r is defined as the growth rate of the population before the initial HIV infection, A as the initial exponential growth rate of the infection within the population, and θ as the extra mortality linked to infection (arising from horizontal and vertical transmission). These rates are given by

$$r = \nu - \mu,\ A = \beta c - (\mu + \alpha),\ \theta = \alpha + \nu(1-\varepsilon) \quad (4)$$

The model defined by equations (1) and (2) has an exact solution for $N(t)$ and for the prevalence of infection $y(t)\ (= Y(t)/N(t))$ where

$$N(t) = N(0)e^{rt}[1 + (b/a)\Delta(e^{at}-1)]^{-\theta/b}\ \text{and} \quad (5)$$

$$y(t) = [\Delta\ \exp\ (at)]/[1 + (b/a)\Delta[\exp\ (at)-1]] \quad (6)$$

Here $N(0)$ and $Y(0)$ (where $\Delta = Y(0)/N(0)$) are respectively the initial total population and number of infecteds at time $t = 0$. The parameter combinations a and b are defined as

$$a = A - r\ \text{and}\ b = a + \varepsilon\nu \quad (7)$$

The model exhibits three patterns of behaviour. The basic reproductive rate of infection, R_0, defined as the number of secondary cases of infection typically generated by one primary case in a susceptible population, is given by (see refs 19, 26):

$$R_0 = \beta c/(\mu + \alpha) \quad (8)$$

Hence if $R_0 < 1$ (which implies $A < 0$, see equation (4)) the infection cannot establish and there will be no epidemic (note that equation (8) defines the control problem: sexual behaviour, c, must be changed such that $R_0 < 1$). Given the rapid spread of HIV in certain countries, of more importance are the two cases that arise when $R_0 > 1$. If $A/\beta c > r/\theta$, mortality associated with infection is so high that deaths eventually exceed births and the population begins to decline. In principle, therefore, sexually transmitted infections that also spread via vertical transmission are capable of causing the extinction of their host population.

Alternatively if $0 < A/\beta c < r/\theta$ the population will eventually settle to exponential growth, the infection being maintained within it, provided $R_0 > 1$. The critical combination of parameter values that divide the two cases is when

$$\varepsilon\nu = (\mu + \alpha)(A - r)/A \quad (9)$$

When the right-hand side exceeds the left-hand side, extinction occurs; in the opposite case, sustained growth occurs. Note that extinction cannot occur unless $A > r$; that is, the exponential rate at which the infection initially spreads must exceed the overall population growth rate, otherwise a decreasing fraction will experience infection, even though the absolute number of infected individuals is growing. When the population continues to grow with the infection being maintained, the prevalence of infection approaches a constant value, y^*, (as $t \to \infty$) where

$$y^* = (A - r)/[(A - r) + \varepsilon\nu] \quad (10)$$

The asymptotic exponential rate at which $N(t)$ and $Y(t)$ grow, ρ (provided the fraction infected who develop AIDS, f, is equal to 1), is

$$\rho = -(\mu + \alpha) + [\varepsilon\nu(A + \mu + \alpha)]/[A - r + \varepsilon\nu] \quad (11)$$

In the case where $\rho < 0$ and population growth is eventually halted by AIDS, the period of time before the population ceases its previously exponential growth, t_c, is given by:

$$t_c = \left(\frac{1}{A-r}\right) \ln\left(\frac{r[1 - \Delta(b/a)]}{\Delta[\theta - r(b/a)]}\right) \quad (12)$$

where Δ is the fraction infected at $t = 0$.

Time-delayed recruitment

The basic model dealt with the total population. In reality, however, HIV spreads predominantly among sexually active adults, and births occur only from sexually mature females, so that it is more realistic to interpret $N(t)$ as the population of sexually active adults (subdivided into $X(t)$ and $Y(t)$). If τ is the average time taken to attain sexual maturity (say 15 years), the relationship between the average birth rate (ω) expressed per adult, and the average birth rate per member of the total population (ν) is:

$$\nu = \omega e^{-(\mu+r)\tau} \quad (13)$$

Table 1 AIDS cases reported to WHO as of September 1987 and demographic parameters for a selection of countries

	Kenya	Zaire	Uganda	United Kingdom
Total number of AIDS cases	625	335	1,138	935
Rate per 1,000 population	0.028	0.010	0.071	0.017
Time period to which demographic data apply	1984–85	1984–85	1984–85	1984–85
Crude population size 1987 (millions)	22.397	31.796	16.018	55.678
Crude live birth rate per 1,000 population yr^{-1}	55.1	44.8	50.3	12.9
Crude per capita birth rate yr^{-1}, ν	0.0540	0.0442	0.0495	0.0129
Life expectancy at birth (yrs)	52.9	52.0	51.0	73.7
Crude per capita death rate yr^{-1}, μ	0.0189	0.0192	0.0196	0.0136
Population growth rate per 1,000 yr^{-1}	41.1	30.3	33.5	1.5
Crude per capita growth rate yr^{-1}, r	0.0403	0.0299	0.033	0.0015
Urban population (% of total)	15.5	36.6	9.5	87.7
Dependency ratio (ages < 15, > 64)/(ages 15–64)	1.190	0.928	1.023	0.529
Child dependency age < 15/(ages 15–64)	1.150	0.871	0.973	0.298
Population density, km^{-2}	38.0	13.6	68.0	230.0

From World Bank and United Nations data series.

Here $e^{-\mu\tau}$ defines the proportion of new births that survive to sexual maturity at age τ with mortality rate μ; the factor $e^{-\tau\tau}$ measures the sexually mature fraction of the population (assuming type II survival). The demography and epidemiology of HIV in the adult population is now described by equations (1), (2) and (13) but with the original ν replaced by the ν defined in equation (13). The time delays make these equations significantly more complicated and no exact solution is possible. However, we get the earlier results for ρ (equation 11) and for y^*, the asymptotic fraction infected (equation 10) with ν now being replaced by:

$$\nu \to \omega e^{-\mu\tau-\rho\tau} \qquad (14)$$

The replacement is also made in $r = \nu - \mu$. This again leads to equation (9) being the critical condition dividing population growth ($\rho > 0$) from population decline ($\rho < 0$), with the proviso that ν in equation (9) is interpreted as $\omega e^{-\mu\tau}$ and r is interpreted as $(\omega e^{-\mu\tau} - \mu)$.

Epidemiological parameters

The models reveal that whether or not AIDS will change positive population growth rates to negative ones, and the timescale of such changes, depends critically on the magnitudes of various key demographic and epidemiological parameters. The demographic parameters (birth, death and population growth rates, ν, μ, and r respectively) for a series of countries in which HIV is spreading rapidly (Kenya, Zaire and Uganda) are recorded in Table 1. For comparison, data from the United Kingdom are also presented. Note the very high population growth rates in the developing countries (4% per annum in Kenya). As mentioned earlier, epidemiological data are extremely limited and in certain areas we can only guess at parameter ranges. The fraction of those infected who will eventually develop AIDS, f, appears likely to be very high as long-term studies of infected homosexual men in developed countries reveal no decrease in the rate (2–7% per annum) of conversion from HIV infection to AIDS[38-41]. Disease progression in African heterosexuals appears to occur at similar rates[11,42]. Roughly 30–40% of infected male homosexuals appear to develop AIDS on an 8–9 year timescale[5,39,41], and it seems likely that most of the rest will convert to disease over a longer period (perhaps 15–20 years). Limited studies from North America and Europe have recorded HIV infection in 30–65% of babies of HIV seropositive mothers[12-14,43-45] and similar studies in Nairobi, Kenya and Kinshasa, Zaire, suggest figures of 46–51%[11]. In utero infection appears to be the dominant mode of vertical transmission and death rates among infected babies are very high—nearly 20 times that of children born to uninfected mothers in one study[2,11]. Data on the transmission probability, β (either from men to women or vice versa), in heterosexuals and the effective
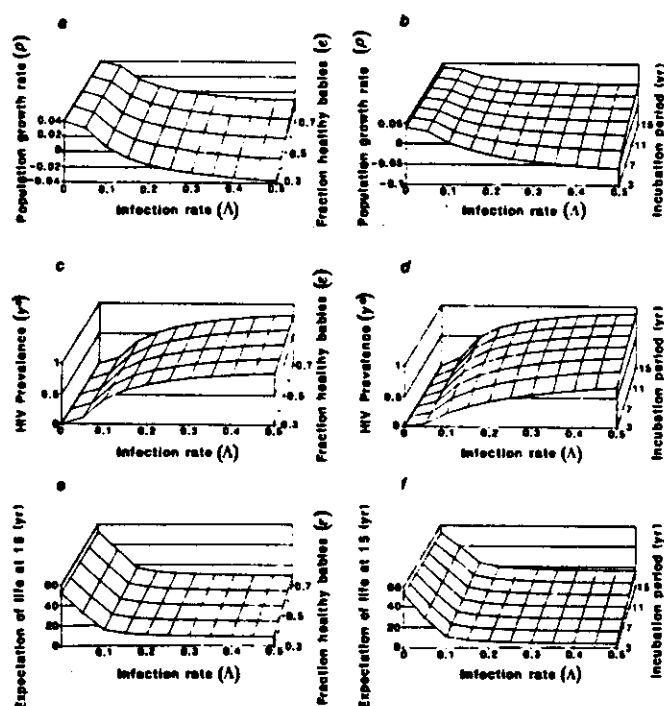

Fig. 2 *a* and *b*, The asymptotic population growth rate per head, (ρ) *c* and *d*, the asymptotic prevalence, that is the fraction of the population infected (y^*); *e* and *f*, the expectation of life at age 15 years. Each graph refers to a human population infected with HIV-1 with varying values for the epidemiological parameters A (rate of infection per capita per year), ε (fraction of babies born to infected mothers who do not acquire infection via vertical transmission) and $1/(\alpha+\mu)$ (average incubation (= infectious) period). Predictions are based on the simple delayed-recruitment model described in the main text. In graphs *a*, *c* and *e* the duration of the incubation (= infectious) period was set at eight years. In graphs *b*, *d* and *f* the fraction of healthy babies born to infected mothers was set at 0.5.

rate of partner change, c, are very limited at present for developing countries. One study suggests a value of β in the range 0.05–0.1 per partner for female to male transmission, provided cofactors (genital ulcers) are present[46]. A rough guide to the parameter combination βc can be obtained indirectly from a knowledge of the rate of increase of the infected population[18,26] (or from the doubling time of the epidemic). The limited data on trends in the rise in seropositivity in specific African countries are summarized in Table 2. The rate of spread is highest in urban areas in Africa[2,3,11], and is particularly fast in people with

Fig. 3 *a,* Population trajectories through time (recorded as $\ln(N(t)/N(0))$ where $N(0)$ is the population size at time $t=0$ when the infection was introduced) as predicted by the delayed-recruitment model defined in the main text for various values of the fraction of babies born to infected mothers who do not acquire HIV-1 infection via vertical transmission (ε). The top line denotes 4% growth in an uninfected population. The remaining trajectories, from bottom to top, denote predictions with ε set at 0.3, 0.5 and 0.7 respectively. The death rate of uninfecteds was set at $\mu = 0.019$ per capita per yr (life expectancy of 52 yrs), incubation period of the disease was set at 8 yrs ($= 1/(\alpha + \mu)$), and the time period to recruitment to the reproductively mature age-class (τ) was fixed at 15 years. The rate of infection A was set at 0.233 per capita per yr. *b,* Population trajectories through time, as in (*a*) but varying the fraction of those adults infected, *f,* who proceed to develop AIDS and die. The top line denotes 4% population growth in an uninfected population. The remaining trajectories, from top to bottom, denote predictions with *f* set at 0.25, 0.5, 0.75, 0.9, 0.95 and 1 respectively. The inclusion of the fraction *f* into the delayed-recruitment model defined in the main text is as described in refs 26, 37. Parameter values as in (*a*), with ε fixed at 0.5, assuming that an equal fraction of children born to seropositive-recovered women die effectively at birth. *c,* Growth rate *r* in the uninfected population which can asymptotically be brought to zero (stationary population) for a specified value of *f.* The other epidemiological and demographic parameters are: $A = 0.4$ per capita per year; $1/(\alpha + \mu) = 10$ yrs; $\mu = 0.02\ \text{yr}^{-1}$; $\tau = 15$ yrs. The top line is for $\varepsilon = 0$ and the bottom for $\varepsilon = 0.5$. *d,* The period of time, t_c, predicted before an infected population ceases its previous pattern of exponential growth and begins to decline after invasion by HIV-1 (equation 15) as a function of the rate of spread of infection A and the population growth, *r.*
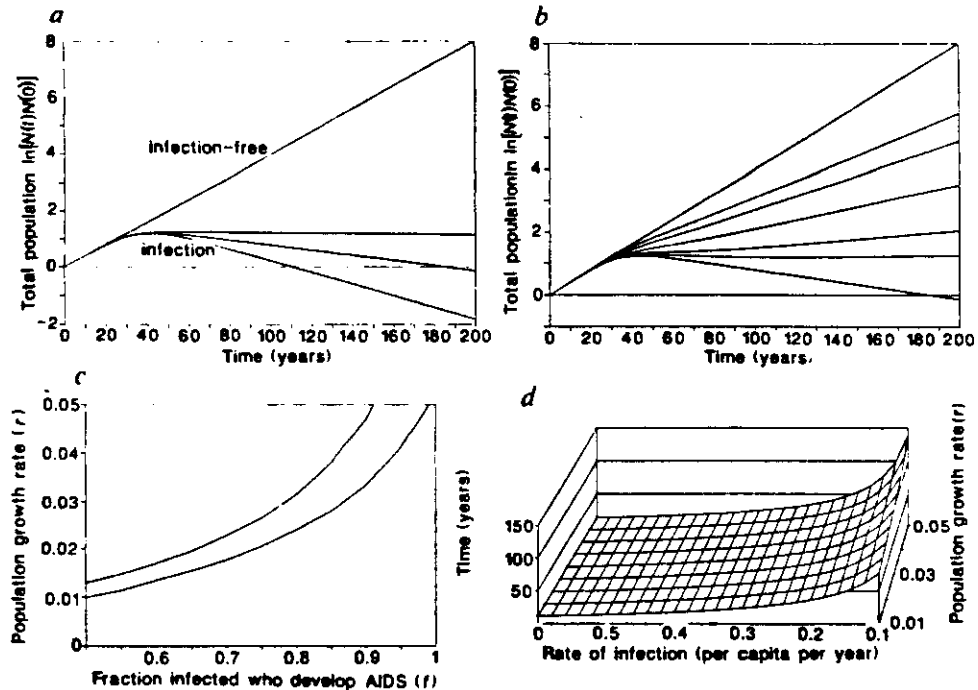
Table 2 Estimates of the rate of spread of HIV infection in various populations in developing countries (see text for details)

Location	Years	Population surveyed	Doubling time t_d (yrs)	Rate of spread of infection, A (yr^{-1})	Parameter combination $\beta c(1/(\alpha + \mu))$ $= 15$ yrs)	Basic reproductive rate, R_0 $(1/(\alpha + \mu) = 15$ yrs)	Data source (reference)
Kenya, Nairobi	1981–85	Prostitutes	1.00	0.681	0.748	11.2	53
Kenya, Nairobi	1982–85	Men with chancroid	1.00	0.677	0.744	11.1	53
Kenya, Nairobi	1981–85	Men with STDs*	1.67	0.414	0.480	7.2	53
Kenya, Nairobi	1981–82	Women with STDs	1.00	0.686	0.753	11.3	53
Kenya, Nairobi	1970–86	Pregnant women	2.87	0.241	0.308	4.6	11
Zaire, Kinshasa	1970–86	Mothers	3.50	0.198	0.265	4.0	54
Uganda, Kampala	1985–87	Women—antenatal	1.12	0.619	0.686	10.3	55

* STD, sexually transmitted disease.

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multiple sexual partners, in those who have a high rate of infection with other sexually transmitted diseases (STDs) such as chancroid[16], and in prostitutes[2,3,47,48]. For example, the doubling time (t_d) of the epidemic among prostitutes in Nairobi[2,48] from 1981 to 1985 was approximately 1.0 years. In the general urban populations in Kenya, Uganda and Zaire (as indicated by the proportion of pregnant women attending health clinics, found to be infected[2,3,11]) the rate of spread is slower, but still alarming, doubling times ranging from 1 to 3.5 years (Table 2). Assuming equality of transmission from female to male and vice versa, given the observed 1 : 1 sex ratio in seropositivity[2,3,11] and an average incubation period (= average infectious period) of roughly 15 years ($1/(\alpha + \mu)$) these doubling times in the general population yield estimates of R_0 (the number of people infected by a single seropositive individual) and βc (the rate of transmission) in the respective ranges of 4–12 and 0.2–0.8 (refs 17,26,37). The associated estimates of the rate of increase (A) in the infected population ($Y(t)$), in the early stages of the

epidemic in different countries/populations are recorded in Table 2 (range $0.2{-}0.8\ \text{yr}^{-1}$).

On the basis of these estimates we choose the following parameter ranges to explore the properties of the recruitment-delay version of the model: $\varepsilon = 0.3{-}0.7$; $1/(\alpha + \mu) = 8{-}20$ yr; $\mu = 0.019\ \text{yr}^{-1}$; $A = 0.2{-}0.5\ \text{yr}^{-1}$ (for the general urban population); $\tau = 15$ yrs; $\nu = 0.02{-}0.06\ \text{yr}^{-1}$ (where ν is the birth rate per member of the population, before AIDS). Note that from Tables 1 and 2 it appears that A always exceeds r in value; hence the infection is predicted to have a severe effect on population growth.

Population growth rates

A wide range of parameter values, all within the bounds suggested by current empirical studies, predicted asymptotically negative population growth rates even when recruitment delays are taken into account. The relationship between the asymptotic growth rate, a range of values for the rate of infection, A, and

Fig. 4 The predictions presented in graphs a to c are derived from a fully age-structured model with the following partial differential equations for the numbers susceptible $(X(a, t))$, numbers infected $(Y(a, t))$ and the total population $(N(a, t))$ of age a at time t: $\delta[X(a, t)] = -[\lambda(a, t) + \mu(a)]X$; $\delta[Y(a, t)] = \lambda(a, t)X - [a(a) + \mu(a)]Y$; $\delta[N(a, t)] = -\mu(a)N - a(a)Y$ where the operator $\delta[F]$ is short-hand for $\delta[F] = \partial F/\partial t + \partial F/\partial a$. One boundary condition is the requirement $X(0, t) = {}_0\!\int^{\infty} m(a)[N(a, t) - (1 - \varepsilon) \times Y(a, t)]da$, and $Y(0, t) = {}_0\!\int^{\infty} m(a)(1 - \varepsilon)Y(a, t)da$ with $m(a)$ defining the age-specific fertility rate. The other boundary condition is given by specifying $X(a, 0)$, $Y(a, 0)$ and $N(a, 0)$ at $t = 0$. The force of infection $\lambda(a, t)$ is given by $\lambda(a, t) = \beta c_r\!\int^T j(a, a')Y(a', t)da'/_s\!\int^T j(a, a')N(a', t)da'$ where β and c are the transmission probability and the mean rate of acquiring new sexual partners and $j(a, a')$ defines the probability that a susceptible of age a will choose a partner of age a'. For illustration we make the simplifying assumption that the death rate $\mu(a) = \mu$ (reasonable for developing countries), the birth rate $m(a) = \omega$ for $T > a > \tau$, $m(a) = 0$ otherwise (where τ defines the lower limit for reproduction and T the upper limit, set at 15 and 50 years respectively) and $j(a, a')$ has a constant value (that is, sexually active adults choose partners independent of age). We assume that the fraction of children born to infected mothers that develop AIDS $(1 - \varepsilon)$ survive for an average of two years from birth. In these circumstances we obtain equation (11) in the main text with ν defined as $\omega \exp[-(\mu + \rho)\tau]$, where ω is the birth rate per adult, for the asymptotic growth rate ρ of the population. The asymptotic prevalence $Y/N = (A - \rho)/\beta c$ where A is the initial growth rate of the seroprevalence of HIV. The fraction of infecteds who develop AIDS, f, was assumed to be 1. The model allows us to calculate time-dependent changes, and asymptotic results for the age profile of infected and uninfected populations. a, Asymptotic age distributions (fraction in each age class) of an uninfected (right-hand side) and an infected (left-hand side) population. The growth rate (r) is 4% and life expectancy $(1/\mu)$ is 52 years in the absence of HIV. The incubation period was set at 15 years $(1/(a + \mu))$ with the fraction of healthy babies born to infected mothers (ε) set at 0.3. The rate of infection in the early stages, A, was set at 0.233 yr^{-1}. b, Temporal changes in the age distribution of a population as the growth rate of the population changes from positive to negative as HIV spreads (parameter values as for left-hand side of a). c, Temporal changes in the dependency ratio ((ages <15 and >64)/ages 15–64) as HIV spreads. Four different numerical simulations of age-structured models are recorded. In all, $\tau = 15$ yr, $\mu = 0.019$ per capita per yr, $1/(a + \mu) = 15$ years; parameters (r) and (ε) are varied as follows: ($\square$) $r = 0.04$ per capita per yr, $\varepsilon = 0.7$; ($+$) $r = 0.04$ per capita per yr, $\varepsilon = 0.3$; ($\lozenge$) $r = 0.02$ per capita per yr, $\varepsilon = 0.7$; ($\triangle$) $r = 0.02$ per capita per yr, $\varepsilon = 0.3$.
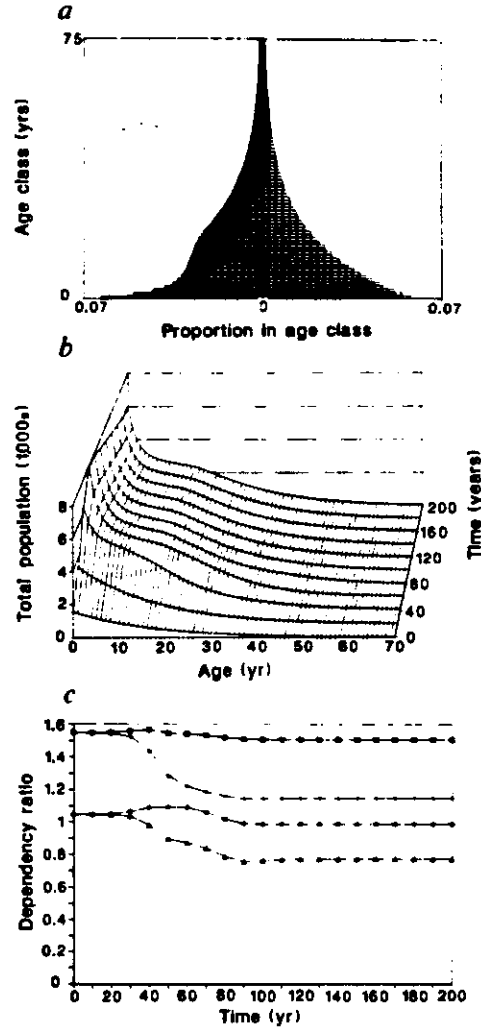
the fraction of babies born to infected mothers who do not acquire HIV via vertical transmission, ε, is recorded in Fig. 2 for various values of the incubation period. In these examples the growth rate per head of population before HIV infection, r, was assumed to be 0.04 yr^{-1} (4% growth per annum) with life expectancy 52 years. As ε decreases and A increases the asymptotic growth rate is predicted to become negative. Concomitantly, as $\varepsilon \to 0$ and A rises, the asymptotic prevalence of HIV infection is predicted to rise in the adult population (>15 yrs) to high levels (Fig. 2). For plausible ranges of parameter values, HIV infection resulting in AIDS is predicted to induce the severe changes in the population size shown in Fig. 3a and b. The growth rate in population before any HIV infection, r, which can asymptotically be brought exactly to zero (stationary population) for a specified value of the fraction infected who develop AIDS, f, is shown in Fig. 3c.

The period t_c, denoting the time taken before the population begins to decline after invasion by HIV, is given very approximately by

$$t_c \sim [\ln(1/A)]/[A - r] \qquad (15)$$

where A is the fraction infected at time $t = 0$ (ref. 37). This relationship is depicted in Fig. 3d for a range of values for the pre-HIV infection population growth rate, r (chosen to mimic developing countries—see Table 1), and the rate of HIV infection A (see Table 2). Note that for low to moderate infection rates (like those observed in the general population in Zaire, Uganda and Kenya whose $A = 0.1$–0.2 yr^{-1}) the time to the onset of population decline, t_c, is predicted to be very long, (20–70 yrs)

even in countries with low growth rates $(r = 0.02 \mathrm{yr}^{-1})$. Following onset, asymptotic rates of population decline may be dramatic (Fig. 2).

Changes in age structure

The simple model defined above can easily be extended to incorporate a variety of realistic refinements. These include: asymmetric probabilities of transmission from females to males, and males to females; asymmetries in the probability that a male or female partner will be infected, reflecting age dependency in the choice of partners of the opposite sex; only a fraction of those infected proceeding to develop AIDS; and, most importantly, a full age structure to reflect the demographic impact of AIDS on the age-distribution of infected populations[17,26,37]. The details of an age-structured model are defined in the legend to Fig. 4 in which predicted changes in the asymptotic age distribution of an infected population for a specific set of demographic and epidemiological parameters are recorded. The age profiles of the population before and after the establishment of HIV infection are represented as the relative proportions in different age classes (as opposed to absolute numbers in the declining infected population) (Fig. 4a). The effect of AIDS upon the dependency ratio—which is taken to be the population below age 15 and above age 64 years, divided by that aged 15 to 64 years—is not as great as might be expected, or has been widely suggested[2,3,11]. On the one hand, the direct effects of mortality in the sexually active adult age classes due to AIDS tends to increase the ratio. On the other hand, the general depression of overall population growth rates due to adult deaths, and to the

reduction in effective birth rates due to the deaths of infected babies, tends to decrease the ratio. The net outcome depends on the precise values of the demographic and epidemiological parameters. An important prediction is that, for some plausible ranges of values, AIDS would have little effect on, or even slightly decrease, the dependency ratio (Fig. 4c), a result in sharp contrast with the views of many informed individuals who have discussed this problem[2,3,11,49].

Discussion

Our analyses, based on very simple models of the major demographic and epidemiological processes, yield three major conclusions. First, for plausible ranges of parameter values the disease AIDS is predicted to be capable of significantly reducing population growth rates, and even depressing them to negative values. Second, the time for these effects to become fully manifest after the initial introduction of HIV infection, is predicted to be long, of the order of many decades. Third, whether or not AIDS will decrease or increase the dependency ratio within a given population depends critically on the values of the major demographic and epidemiological parameters prevailing in the community. For plausible parameter ranges (Tables 1 and 2) our analyses suggest little change or a small, but beneficial, change. This conclusion appears fairly insensitive to variations in the fraction of those infected (f) who eventually die. Similar analyses of the impact of directly transmitted infections such as smallpox and bubonic plague, that were of great historical significance as causes of human morbidity and mortality, suggest that AIDS has greater potential to depress significantly human population growth rates[28,29]. This stems from the ability of HIV to transmit both horizontally via sexual contact and vertically from mother to unborn offspring, the high mortality associated with infection and the apparently long period over which infected persons are asymptomatic but infectious to their sexual partners.

Before proceeding to discuss these conclusions further, we emphasize that they derive from deliberately simplified models and from limited empirical data. As data accumulate, future numerical studies of more complex and realistic models must address a series of key problems. Of major importance is the assumption of homogeneous mixing made when estimating the rate of spread of infection by sexual contact. Recent theoretical and empirical studies challenge this assumption, recording marked heterogeneity, dependent on age, sex and socio-economic factors, in the frequency distributions of rates of sexual partner change[18,26,27]. Equally important is the question of promiscuity class (namely, do individuals in high sexual-partner change classes predominantly choose partners in their own activity class?), and the role of prostitutes in the spread of infection within the general population[37]. Simple cascade models in which infection is assumed to flow from a core group of highly sexually-active female prostitutes, to males (assumed all to be moderately promiscuous) and thence to the child-bearing women (assumed all to be relatively monogamous) reveal properties qualitatively similar to those outlined earlier[37]; the quantitative details depend on the actual transmission probabilities and rates of partner change among these three groups in, say, Africa, which are presently uncertain. Other problems concern infectiousness throughout incubation of the disease[17,18,24], the role of cofactors in transmission, and the assumption of equal transmissibility between the sexes. The overall average transmission rate, $\bar{\beta c}$, is the geometric mean of the average transmission rates $\beta_1 c_1$ (male to female) and $\beta_2 c_2$ (female to male), and $\bar{\beta c} = (\beta_1 c_1 \beta_2 c_2)^{1/2}$ (refs 19,37). The symmetric assumption of our simple model ($\beta_1 c_1 \approx \beta_2 c_2$) is a reasonable approximation of the more general asymmetric case ($\beta_1 c_1 \neq \beta_2 c_2$) provided $\beta c \gg (\mu + \alpha + r)$; this appears to be the case for the representative parameter values considered (Table 2, Fig. 2).

In general, heterogeneity in sexual activity, whether between urban and rural areas, or between different groups in a given community, is likely to decrease the demographic impact predicted by our simple model. For any chosen values of the early doubling rate and incubation interval, the eventual prevalence of endemic infection will be higher if all individuals are equally active sexually than if much variability exists (in which case core infection tends to be concentrated within the more active categories)[36,50]. Our parameter values, based on current data, may well lead to conclusions more representative of, say, Kinshasa and Nairobi than of Zaire and Kenya as a whole. But any assessment of the effects of such heterogeneities simply requires better data than we have at present.

Simple models, such as those described here, are useful for setting the agenda for data collection to improve the accuracy of predictions. There is a clear need for the collection of much more detailed data on all the parameters discussed above, although the social, ethical and practical problems surrounding such research are formidable. A start has been made with recent theoretical[51] and empirical[52] work that has begun to address some of the important complications induced by heterogeneity in rates of sexual partner change, and by complex networks of sexual and social interactions.

With these limitations in mind, we conclude by returning to two major predictions of the simple model. First, that the AIDS epidemic is likely to have little impact on dependency ratios, a prediction which directly contradicts current views of this problem[2,11]. From this it might be concluded that the epidemic will be less disruptive to the social organization and economic fitness of badly afflicted countries than previously feared. We do not believe this to be the case, however, as the very high predicted mortality due to a disease which requires repeated hospitalization, perhaps over periods of a few years, and which is thought to enhance morbidity due to other infections such as tuberculosis[2], will be devastating to already overloaded health-care systems in poor countries[2,11]. Small changes in the dependency ratio (whether plus or minus) are irrelevant under such circumstances.

The second prediction, that of a long time-period between the establishment of HIV-1 infection and the reversal of exponential population growth, offers hope in the sense that it provides time for educational programmes to change behaviour[11], for the development of more effective drugs and (we hope) for the discovery of an effective vaccine. It should be remembered, however, that the availability of cheap and effective vaccines (such as that against measles) is not always beneficial to people living in very poor countries where the cost of immunization is prohibitive to individuals and governments. For the foreseeable future the main hope for checking the spread of HIV lies in the development and forceful application of education programmes aimed at changing behaviour. The predictions of our simple models highlight the urgency of implementing such programmes.

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