Asymmetries in gender- and age-specific HIV prevalence in Southern Africa

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Abstract

Young adults, particularly young women, carry a disproportionate share of the burden of HIV prevalence in Southern Africa. This asymmetry of HIV prevalence in gender and age impacts HIV epidemiology, human demography, and the socioeconomic burden of HIV. We evaluate possible causes of observed patterns using a mathematical model of HIV transmission and human demography, parametrized using demographic and epidemiological data from sub-Saharan Africa. We find that a contributing factor to high prevalence in young women is disproportionate numbers of young women having sex with older men. Our results also point to possible increased susceptibility of young women to HIV infection compared with older women.

Introduction

HIV prevalence exceeds 15% in eight of the ten mainland countries in Southern Africa [1]. HIV has reversed decades of progress in public health, significantly reducing life spans, increasing infant mortality, and degrading quality of life [2,3]. HIV in Southern Africa disproportionately affects women, particularly young women. Women between 15 and 24 are more than three times as likely to be HIV positive as men of the same age [4] (Figure 2). Asymmetries in the prevalence between men and women of different ages are fundamental to HIV transmission dynamics, to public-health burden, and to demographic trends in Southern Africa. Additionally, the economic consequences of the HIV epidemic in Southern Africa are exacerbated by the disproportionate impact on young adults. The HIV epidemic is resulting in the demise of the most productive members of society and the orphaning of millions of children [5].

Many factors could contribute to the increased prevalence of HIV in young women. Epidemiological evidence from Europe and North America suggests that men are more likely to infect women during vaginal intercourse than vice versa [6–9]. However, long-term studies in sub-Saharan Africa of monogamous partnerships (in which one partner is HIV positive and the other HIV negative) show the same rate of female-to-male and male-to-female transmission [10–13]. The higher rate of male-to-female transmission compared with female-to-male transmission observed in developed countries may be at least partially explained by much higher rates of male circumcision in those countries [14–17]. Another factor that could contribute to elevated prevalence in young women is increased levels of sexual contact between young women and older men [18–20]. It also has been suggested that young women may be more susceptible to infection than older women, for example, due to cervical ectopy during puberty or due to infection with other sexually transmitted infections [21–24].

To investigate the age-specific asymmetry in HIV prevalence in Southern Africa between men and women, we constructed a mathematical model for HIV that includes gender, age, and HIV progression. We parametrized our model using demographic data from South Africa and epidemiological data from Uganda and Namibia. To parametrize contacts between women of one age with men of another, we used the ages of mothers and fathers from birth registration in South Africa [25]. Although we used demographic and contact data from South Africa, we expect our model to be applicable to much of

Southern Africa provided that demographic and social factors are not too different from those in South Africa. The birth-registration data do indeed exhibit a high level of contact between young women and older men. Despite this high level of age-skewed contacts, our model results show that this factor alone does not completely explain the current high prevalence in young adults. We used the model to explore the possibility that increased susceptibility in young women can explain this high prevalence.

Results

We constructed a gender- and age-structured differential-equation model of HIV transmission in South Africa (Methods). This model incorporates some assumptions that overestimate spread of the disease. Most importantly, the birth-registration data used to parametrize sexual contacts does not provide any information on partnerships, so we have assumed that each sexual contact is with a random member of the population. Additionally, since the data used for parameter estimation are from an era with little drug therapy, we have excluded the effect of drug therapy to treat those who are infected and to prevent transmission from mother to child. We first estimate the basic reproductive number for the model and parameters and then investigate possible mechanisms to explain asymmetries in gender- and age-specific HIV prevalence.

The basic reproductive number, R_0, is the mean number of secondary infections caused by a single infected individual in a completely susceptible population [26]. From our parametrized model, we estimated the basic reproductive number for HIV in modern-day South Africa. Using the next-generation-matrix technique [27, 28] to compute the basic reproductive number, we find $R_0 = 1.6$ for our baseline parameter values. It should be emphasized that this is in fact the basic reproductive number because the next-generation-matrix technique uses a completely susceptible population. This value of R_0 is similar to estimates for sub-Saharan Africa of 1.7 [29][1] and 2.2 [30] found in other simulation studies, but considerably lower than 6.4 ± 1.6 [31]. Our model was initialized with survey-based estimates of 2005 age- and gender-specific prevalence of HIV in South Africa, which results in a whole-population prevalence of 10.8% [32]. For the purpose of comparison, we use the asymptotic prevalence from the model as a simple measure, which is 31.8% for the baseline parameters (Figure 1).

The model age-specific asymptotic prevalences can be compared with current estimates (Figure 2). The most striking difference is that the model prevalence is much higher in older adults than current estimates due to the model not incorporating repeated sexual contacts between partners. Here we will focus on young adults: the model predicts age-specific asymptotic prevalences that are lower in young adults (age groups 15–19 and 20–24) in both females and males than the current prevalences for those age groups. For females 15–19 and 20–24, 2004 prevalences are 7.6% and 24.7%, respectively, while the asymptotic prevalences from the model are 5.1% and 21.8%. For males, 2004 prevalences are 0.5% and 9.5% while the asymptotic prevalences are 1.3% and 6.0%, for age groups 15–19 and 20–24, respectively. The fact that the asymptotic prevalence from the model is below the 2004 prevalence for women 15–24 and men 20–24, despite several factors in the model that overestimate prevalence, suggests that the model is not capturing some biological or social factor leading to higher prevalence in these adults.

One biological factor not incorporated in the baseline parameters is possible increased susceptibility in young women relative to older women [23]. Such an increase in susceptibility would lead to higher prevalence in young women, resulting in higher exposure and prevalence for young men, since young women are their preferred partners. Letting young women (15–19 and 20–24) be 70% more susceptible than older women (i.e. $\phi_{15} = \phi_{16} = 1.7$) results in an asymptotic prevalence above the 2004 prevalence in all gender and age groups. The higher susceptibility increases R_0 to 2.03, a 3% increase, and increases the asymptotic prevalence from 31.8% to 36.5%.

[1] Gray et al. [29] estimate 1.44 in a population with 14% prevalence, although this estimate is only from infection to 10 years, not the total duration of infection.

The modeling study of Rapatski, Suppe, and Yorke [33] of the HIV epidemic in homosexual men in San Francisco in the 1980s estimates that late-symptomatic-stage infectivity is 12.5 times acute-stage infectivity. Anal intercourse is more efficient at HIV transmission than vaginal intercourse [34], so we do not simply use the infectivities from this study directly, but rather we adjust the ratio of the two infectivities while keeping the average between the two constant. For our baseline parameters, the ratio of late-symptomatic-stage infectivity to acute-stage infectivity is 0.38 and, on average, more than 8 years are spent in the late-symptomatic state compared to only 2.5 months for the acute stage. As a consequence of the large difference in the durations of the acute and late-symptomatic stages, our results are quite sensitive to making the large change from 0.38 to 12.5 in the ratio of the two infectivities, with the magnitude of the epidemic increasing dramatically ($R_0 = 4.79$ and asymptotic prevalence of 49.5%). However, if we also reduce the duration of the late-symptomatic stage from 8.1 years to 2.1 years, while lengthening the symptomatic stage by the same amount, from 2.4 years to 8.4 years, similar to what Rapatski, Suppe, and Yorke assume for the duration of these stages, the results are remarkably similar to our baseline case: $R_0 = 1.85$ and asymptotic prevalence of 29.8%. In this case, the gender- and age-specific asymptotic prevalences are even lower than our baseline in young adults, again suggesting the need for increased young-female susceptibility or some other factor.

Discussion

For our gender- and age-dependent mathematical model and its parametrization, we estimate the basic reproductive number, R_0, of HIV in South Africa to be approximately 2. Our R_0 estimate is significantly lower than the $R_0 = 6.4$ of Williams et al. [31]. Their estimates are based on prevalence data from early in the epidemic [35], while ours is based on *current* contact data[2]. Decreasing sexual-contact rates as a response to increasing prevalence are one explanation which could account for the difference, although it is doubtful that contact rates would have decreased by 70%. While other factors, such as heterogeneity in contact rates within gender and age groups, which we discuss below, could cause us to underestimate R_0, our finding that R_0 is about 2 is consistent with other studies [29, 30].

Our age-dependent-prevalence results suggest that sexual-contact patterns contribute to the distribution of HIV prevalence among age classes and between genders, but do not completely explain high prevalences in young adults. By increasing the susceptibility of young women by 70% relative to older women, our model was able to reproduce the observed levels of prevalence in young women. Thus, heightened susceptibility might be an important factor increasing the risk of infection for young women.

For simplicity of the model formulation, we have neglected repeated contact between sexual partners. Instead, our model assumes that each sexual contact is randomly drawn from the whole population of the opposite gender. Monogamous partnerships where both partners are negative protect both partners from exposure (however there is some concern about how often partnerships are in fact monogamous [18, 36]), therefore, our model *overestimates* the magnitude of the epidemic. Moreover, our assumption that all HIV-induced death occurs in the final stage will further overestimate the epidemic. Since our conclusion is that the young-adult prevalences from our model are too low, these factors only further emphasize that point.

Glynn et al. [23] state, "It is likely that the greater susceptibility of women to HIV infection is an important factor both in explaining the male–female discrepancy in HIV prevalence and in driving the epidemic." Our results are consistent with this claim. Other sexually transmitted infections and other infectious diseases have been suggested to increase HIV susceptibility or infectivity, often due to the presence of genital lesions [37]. At high prevalence of these diseases, gender- or age-dependent effects of these infections could cause increased susceptibility in young women. For example, schistosomaiasis infection affects young women and causes genital lesions leading to increased HIV susceptibility [38, 39].

[2]Our R_0 estimate is the *basic* reproductive number, not the effective reproductive number, as it applies the current contact data to a wholly uninfected population. See Methods.

There are other factors that could explain the high prevalence in young adults. For one, the birth registration data we used to parametrize contacts between women and men of different ages has a large number of births for which the mother's or father's age is not known. If the age of one parent of these births are biased toward young adults, we would then underestimate sexual contacts and, therefore, prevalences in these age groups. Also, there could be age-dependent rates of contraceptive use or abortion that would lead to an underestimation of contacts. As an alternative to age-dependent susceptibility, which depends on the age of the *uninfected* partner, varying infectivity of *infected* partners of different ages could also contribute to underestimation of young-adult prevalence if their partners, particularly men aged 20–34, have heightened infectivity. Immunity to HIV acquired by exposure would tend to cause a person to be infected early on or not at all. Moreover, variability between individuals of the same gender and age in sexual-activity level, susceptibility, or infectivity could explain the increase in prevalence in young adults. Anderson et al. [40] and Garnett and Anderson [41], among others, have included sexual-activity-level heterogeneity explicitly in their models and Schneeberger et al. [42] fit sexual activity in Zimbabwe to scale-free network models. When the variance in numbers of sexual contacts is large, infection occurs quickly in the highly active and rarely in the least active [33], again providing a situation in which an individual tends to either become infected immediately or not at all.

In this paper, we have considered separately the biological factor of age-dependent susceptibility and the behavioral factor of age-dependent sexual-partnership preference. Partnership preference was not sufficient to explain observed patterns in prevalence without also including increased susceptibility in young women. Long-term studies of monogamous couples (e.g. [13]) may be able to confirm or reject whether differences exist in susceptibility between women of different ages, particularly differences of the large magnitude needed in our model to replicate observed prevalence. Should such differences be shown to exist, interventions that protect young women, for example by delaying sexual debut, could have an disproportionate impact on the epidemic.

Methods

We constructed a mathematical model that incorporates age, gender, and HIV progression into a system of partial differential equations. HIV transmission is modeled as standard incidence [43] with age-dependent contact preferences [44]. The model also includes births and transmission of infection from mothers to newborns.

First, we introduce the mathematical model used and then review its parametrization from a variety of data sources. We then describe the numerical solution of the model and use next-generation-matrix technique [27, 28] to calculate the basic reproductive number, R_0.

Model

Our gender- and age-structured model integrates both epidemiological and demographic dynamics. Anderson and coworkers [40,45,46] have developed a gender- and age-structured model for HIV transmission. Hadeler [47] also incorporated monogamous 'pair formation' to explicitly describe repeated contacts between individuals.

In our model, we divide the population into gender, with subscript $i = 1, 2$ for females and males, respectively, and susceptibles and infectives with N_{I} stages of infection, with subscript $j = 1, 2, \ldots, N_{\mathrm{I}}$. Let $S_i(t, a)$ be the number of susceptibles of gender i of age a at time t and, similarly, let $I_{ij}(t, a)$ be the number of infective people of gender i in infection stage k of age a at time t.

Our model is then given by the system of partial differential equations

$$\frac{\partial S_i}{\partial t} + \frac{\partial S_i}{\partial a} = -\left[\mu_i(a) + \lambda_i(t,a)\right] S_i, \tag{1a}$$

$$\frac{\partial I_{i1}}{\partial t} + \frac{\partial I_{i1}}{\partial a} = -\left[\gamma_{i1}(a) + \mu_i(a) + \nu_{i1}(a)\right] I_{i1} + \lambda_i(t,a) S_i, \qquad \text{for } j = 1 \tag{1b}$$

$$\frac{\partial I_{ij}}{\partial t} + \frac{\partial I_{ij}}{\partial a} = \gamma_{i,j-1}(a) I_{i,j-1} - \left[\gamma_{ij}(a) + \mu_i(a) + \nu_{ij}(a)\right] I_{ij}, \qquad \text{for } j = 2, 3, \ldots, N_{\mathrm{I}}, \tag{1c}$$

$$S_i(t,0) = p_i \int m(a) \left[S_1(t,a) + \sum_{j=1}^{N_{\mathrm{I}}} (1-\sigma_j) I_{1j}(t,a) \right] \mathrm{d}a, \tag{1d}$$

$$I_{i1}(t,0) = p_i \int m(a) \left[\sum_{j=1}^{N_{\mathrm{I}}} \sigma_j I_{1j}(t) \right] \mathrm{d}a, \qquad \text{for } j = 1, \tag{1e}$$

$$I_{ij}(t,0) = 0, \qquad \text{for } j = 2, 3, \ldots, N_{\mathrm{I}}, \tag{1f}$$

where $i = 1, 2$. The gender- and age-specific rate of progression from infection stage j to stage $j+1$ is $\gamma_{ij}(a)$, with $\gamma_{iN_{\mathrm{I}}}(a) = 0$ so that there is no progression from the final stage. The gender- and age-specific non-HIV-related death rates are given by $\mu_i(a)$, while the HIV-related death rates structured by gender, infection stage, and age are given by $\nu_{ij}(a)$. Boundary conditions (1d–f) represent births, where $m(a)$ is the age-specific fertility rate, which is assumed to be independent of infection status, and σ_j is the proportion of the offspring of stage-j infected mothers who are infected. The parameter p_1 is the proportion of newborns who are female, while $p_2 = 1 - p_1$ is the proportion of newborns who are male.

The gender- and age-specific forces of infection are of standard incidence form [43]:

$$\lambda_i(t,a) = \frac{\phi_i(a)}{\tilde{N}(t)} \int_{\mathcal{A}_i} \rho_i(a,\hat{a}) \left[\sum_{\hat{\jmath}=1}^{N_{\mathrm{I}}} \beta_{\hat{\imath}\hat{\jmath}}(\hat{a}) I_{\hat{\imath}\hat{\jmath}}(t,\hat{a}) \right] \mathrm{d}\hat{a}, \tag{2}$$

where $\hat{\imath}$ denotes the opposite gender, i.e. if $i = 1, \hat{\imath} = 2$ and if $i = 2, \hat{\imath} = 1$. Force of infection (2) is derived from the contact rates between people of gender i and age a and people of the opposite gender, $\hat{\imath}$, (i.e. all sexual contacts are heterosexual) and age $\hat{a}$ given by

$$C_i(t,a,\hat{a}) = \rho_i(a,\hat{a}) \frac{N_i(t,a) N_{\hat{\imath}}(t,\hat{a})}{\tilde{N}(t)}, \tag{3}$$

where $\tilde{N}(t)$ is the total size of the sexually active population at time t,

$$\tilde{N}(t) = \sum_{i=1}^{2} \int_{\mathcal{A}_i} N_i(t,a) \, \mathrm{d}a, \tag{4}$$

$\mathcal{A}_i$ are the sexually active ages for gender i, and

$$N_i(t,a) = S_i(t,a) + \sum_{j=1}^{N_{\mathrm{I}}} I_{ij}(t,a). \tag{5}$$

This contact rate is known as a marriage function in mathematical demography and there are many alternative choices for its form [48]. The form chosen here is similar to the one used by others [44,47,49]. The contact parameters $\rho_i(a,\hat{a})$ describe, for $i = 1$ ($i = 2$), women (men) of age a having sex with men

(women) of age $\hat{a}$. The rate at which people of gender i and age a have contact with the opposite gender, $\hat{\imath}$, and age $\hat{a}$ is given by

$$\rho_i(a,\hat{a})\frac{N_{\hat{\imath}}(t,\hat{a})}{\tilde{N}(t)}. \tag{6}$$

Therefore ρ incorporates both the rate of contact and the preference for partners of different ages. (Note that ρ is taken to be constant in time, so that the contact rate and the partner age preference are constant in time.) Since HIV is sexually transmitted, the total number of contacts per unit time between women of age a and men of age $\hat{a}$ must be the same as the total number of contacts per unit time between men of age $\hat{a}$ and women of age a: $C_1(t,a,\hat{a}) = C_2(t,\hat{a},a)$. This constraint on the total number of contacts imposes the symmetry in the contact parameters $\rho_1(a,\hat{a}) = \rho_2(\hat{a},a) = \rho(a,\hat{a})$. (See [44] for a detailed derivation of a similar contact function.)

Given the contacts, the probability of infection per contact of a susceptible person of gender i and age a with a stage-$\hat{\jmath}$ infective of age $\hat{a}$ is given by $\phi_i(a)\beta_{\hat{\imath}\hat{\jmath}}(\hat{a})$, where $\phi_i(a)$ is the susceptibility of gender i and age a and $\beta_{\hat{\imath}\hat{\jmath}}(\hat{a})$ is the infectivity of gender $\hat{\imath}$, infection stage $\hat{\jmath}$, and age a. New infections all begin in the first infection stage, $j = 1$.

For our model equations (1), although we have not rigorously shown it to be the case, we believe, and all our numerical simulations suggest, that since our model is homogeneous of degree 1 [50,51], there exist stable proportions of each gender, age, and infection class, while the total population size grows or decays exponentially in time. The disease-free state is the solution to a linear eigenvalue problem, which guarantees this behavior in the absence of disease. For the baseline parameter values and all others with $R_0 > 1$, numerical simulations reveal a single endemic state, which can also be found as the solution to a nonlinear eigenvalue problem, although we have not systematically tried to rule out the presence of a second, unstable endemic equilibrium [52, 53]. (See [50, 51, 54] for a more thorough discussion of homogeneous systems.)

Parameters

We initialize our model at the beginning of the year 2005 ($t = 0$), although we will use demographic data from 2001, the date of last census.

We parametrize our model with demographic data from South Africa because of the availability of excellent demographic statistics from Statistics South Africa, the national statistics board. The initial age distribution is from 2001 (Table 1), the last available census [55], and is used as the initial condition for our model.

The model uses a continuous age variable, while data is necessarily for discrete age groups. We use piecewise-constant functions to translate from discrete-age data to continuous-age functions.

For stages of infection, we use an acute stage ($j = 1$), followed by the World Health Organization (WHO) Staging System for HIV Infection and Disease in Adults and Adolescents, which uses four stages (stage I: asymptomatic, $j = 2$; stage II: symptomatic, $j = 3$; stage III: late symptomatic, $j = 4$; stage IV: AIDS, $j = 5$) (see, for example, Annex 1 of [56]). We are unaware of data to parametrize the initial prevalence by stage and age. Instead, we use the model results of Dorrington et al. [57] for the end of 2004 to estimate the number in the disease stages. Dorrington et al. give gender- and age-structured prevalences and the number of HIV cases in each stage separately (Figure 2 and Table 2). From these separate percentages, we estimate the combined gender-, age- and stage-structured numbers by simply taking the product of the prevalence by gender and age, the proportion in each stage, and the total number of each gender and age. For example, there are 2 195 230 20–24-year-old females, 24.7% of whom are HIV positive and 23.0% of those are in stage II, for a total of about 124 600 20–24-year-old women in stage II.

The fertility rates, $m(a)$ for 2001 (Table 3) [58]. For the birth ratio, birth registrations from 2002 [25] give the proportion of female newborns as $p_1 = 0.4967$ and the male proportion as $p_2 = 0.5033$. The

proportion of infected offspring of infected mothers is taken to be independent of the mother's infection stage, $\sigma_j = \sigma = 0.35$, that is, 35% of offspring of HIV-infected mothers are HIV infected [59]. This is without drug therapy to prevent the infection of the child; this treatment is cheap and becoming much more accessible throughout the world (see, for example, [60]).

Long-term partner studies in sub-Saharan Africa suggest that female-to-male and male-to-female per-coital-act infection probabilities are similar [10–13]. Thus, we take the infectivities to be the same for men and women and independent of age, $\beta_{ij}(a) = \beta_j$. After Wawer et al. [13] (in parentheses are references to their Table 1), we use for acute infection, $\beta_1 = 0.0082$ (0–5 months after seroconversion); in the asymptomatic phase, stage I, $\beta_2 = 0.00125$ (mean of 6–15 and 16–35 months after seroconversion); for the symptomatic stage, stage II, $\beta_3 = 0.0007$ (all prevalent combined); and for the late-symptomatic stage, stage III, $\beta_4 = 0.0031$ (all late-stage combined)[3] (Figure 4). (See also [61] for a reanalysis of the same data.) We assume individuals with AIDS ($j = 5$) are sexually inactive, so, although their infectivities are likely high, we set $\beta_5 = 0$. We are unaware of any data on susceptibility varying with age, so we take $\phi_i(a) = 1$ for $i = 1, 2$ and all a.

For disease progression, we assume that the progression rates are independent of gender, $\gamma_{ij}(a) = \gamma_j(a)$. Following Wawer et al. [13], we assume that the mean duration of the acute phase ($j = 1$) is 2.5 months, so that $\gamma_1(a) = 4.8\,\mathrm{yr}^{-1}$ for all a. We assume seroconversion (i.e. the development of HIV antibodies) occurs at the end of the acute stage. Based on the work of Morgan and coworkers [62–64] in Uganda, the median time for adults (ages 15 and up) from seroconversion to stage II is 25.4 months, from seroconversion to stage III is 45.5 months, and from seroconversion to AIDS is 9.4 years. Assuming the time spent in each stage is exponentially distributed, as in the model differential equations (1), gives the adult progression rates $\gamma_2(a) = 0.3275\,\mathrm{yr}^{-1}$, $\gamma_3(a) = 0.6371\,\mathrm{yr}^{-1}$, and $\gamma_4(a) = 0.1551\,\mathrm{yr}^{-1}$ for $a \geq 15$ (Figure 4). (See also Hethcote and Van Ark [65] for somewhat different stages and durations from US data.) Data is lacking for children ($a < 15$) so we assume a mean of 1 year in stage I, 1 year in stage II, and 2 years in stage III. The disease progression rates for children are then $\gamma_2(a) = \gamma_3(a) = 1\,\mathrm{yr}^{-1}$ and $\gamma_4(a) = 0.5\,\mathrm{yr}^{-1}$ for $a < 15$. The age-specific prevalence (Figures 2 and 3) shows that HIV-positive children do not survive to adulthood and, therefore, are not responsible for further infections.

For natural mortality, we use mortality rates from the 2001 census [66]. To distinguish between HIV-induced mortality and natural mortality, Dorrington et al. [57] estimate the proportion of deaths due to HIV: 42% for children under 15, 70% for adults 15–49, and 45% for adults 15 and older. The age categories for these proportions overlap, so using the total numbers of deaths for 2001 [66], we estimate the proportion of deaths due to HIV in non-overlapping age groups, 0–14, 15–49, and 50 and older. Using these HIV death proportions, $h(a)$, and the total death rates, $d_i(a)$, gives the natural mortality rates

$$\mu_i(a) = [1 - h(a)]d_i(a). \tag{7}$$

(See Table 3 for the values of μ.)

For HIV-induced mortality, we assume all mortality is in the AIDS stage and that mortality is independent of gender and age, i.e. $\nu_{ij}(a) = \nu_j$ and $\nu_j = 0$ for $j = 1, 2, 3, 4$. Morgan et al. [63] give the median time from onset of AIDS to death of 9.2 months, which, assuming an exponential distribution, gives $\nu_5 = 0.9041\,\mathrm{yr}^{-1}$. Note that combining our disease-stage progression rates and AIDS-induced death rate gives a median time from seroconverion to death of 10.5 years, about 7% longer than the median time of 9.8 years that Morgan et al. [63] give in addition to median time from AIDS to death (9.2 months) and median time from seroconversion to AIDS (9.4 years), both of which our parametrization fits exactly.

[3]Note that because the study only surveyed participants for 40 months, the late-symptomatic stage used in [13] is 6–35 months prior to death, while we use a substantially longer mean duration of the late-symptomatic stage; see below. We test the model for sensitivity to this stage length in Results.

Contacts

For parametrizing contacts between men and women of different age groups, we use data on mother's age and father's age of recorded live births in South Africa for 2002 [25]. We only use births for which the ages of both the mother and father are known, which are only about 37% of the recorded live births. These data are reported for mothers ages 15–55 and fathers ages 15–65, so we use these age ranges to define the sexually active ages ($\mathcal{A}_1 = \{15 \le a < 55\}$ and $\mathcal{A}_2 = \{15 \le a < 65\}$).

From the registered birth data, we work backwards to estimate the age-dependent contact parameters. First, fecundity, the biological ability for women to have children [67], decreases with age [68]. Similarly the ability of men to father children (which we also refer to as fecundity) varies with age [68] (Table 4). The relative number of contacts between women in age group a and men in age group $\hat{a}$ is given by

$$\tilde{C}_1(a,\hat{a}) = \frac{B(a,\hat{a})}{f_1(a)f_2(\hat{a})}, \tag{8}$$

where $B(a,\hat{a})$ is the number of registered births to a mother of age a and father of age $\hat{a}$ and $f_i(a)$ is the relative fecundity of women ($i = 1$) or men ($i = 2$) of age a, i.e.

$$f_i(a) = \frac{\tilde{f}_i(a)}{\max_a \tilde{f}_i(a)}, \tag{9}$$

where $\tilde{f}_i(a)$ are the absolute fecundity values (Table 4).

We use the resulting relative number of contacts to estimate the scaling factor $c_{\max}$ so that

$$C_1(a,\hat{a}) = c_{\max}\,\tilde{C}_1(a,\hat{a}) = c_{\max}\frac{B(a,\hat{a})}{f_1(a)f_2(\hat{a})} \tag{10}$$

gives the absolute number of contacts between age classes. The mean number of contacts for women of different age classes is

$$c_1(a) = \frac{c_{\max}}{N_1(a)}\int_{15}^{65}\frac{B(a,\hat{a})}{f_1(a)f_2(\hat{a})}\mathrm{d}\hat{a}, \tag{11}$$

and likewise for men,

$$c_2(\hat{a}) = \frac{c_{\max}}{N_2(\hat{a})}\int_{15}^{55}\frac{B(a,\hat{a})}{f_1(a)f_2(\hat{a})}\mathrm{d}a. \tag{12}$$

We choose $c_{\max}$ so that the maximum per person rate at which any gender and age class has sexual contacts is 120 per year (10 per month) [11, 13] (Figure 5). Then, using contact equations (10) and (3) at $t = 0$ gives $\rho(a,\hat{a})$ (Table 5). We find 55% of contacts have the male 5–10 years older than the female and in 68% of contacts, the male is 5 or more years older than the female (Figure 6), consistent with survey results from Zimbabwe [18] and Carletonville, South Africa [19].

Numerical Simulations

Partial differential equation model (1) has age as a continuous variable, which the parameters depend on (e.g. $\mu_i(a)$). In contrast, the parameter data are for discrete ages (e.g. Table 3). The discrete parameter data were converted to continuous data by using piecewise constant functions, e.g.

$$\mu_1(a) = \begin{cases} 0.0280 & \text{for } 0 \le a < 1, \\ 0.0100 & \text{for } 1 \le a < 5, \\ 0.0005 & \text{for } 5 \le a < 10, \\ \quad\vdots & \end{cases} \tag{13}$$

The numerical solution of partial differential equation model (1) was computed using the method of lines, that is discretizing in age (using an age step of $\Delta a = 0.1$) to approximate the system of partial differential equations with a large system of ordinary differential equations. Derivatives with respect to age were approximated by the 1st-order backward difference and integrals were approximated by the composite trapezoid rule. The resulting system of ordinary differential equations was solved numerically with the 4–5th-order Runge–Kutta–Fehlberg method.

Calculating R_0

Here we use the next-generation-matrix technique [27, 28] to calculate the basic reproductive number, R_0. This technique uses a population consisting entirely of susceptible individuals, as required by the definition of R_0 [26].

Let $k = i + 2(j-1)$ and $\hat{k} = \hat{\imath} + 2(\hat{\jmath} - 1)$ for $i, \hat{\imath} = 1, 2$ and $j, \hat{\jmath} = 1, \ldots, N_{\mathrm{I}}$; $\delta_{i\hat{\imath}}$ be the Kronecker delta

$$\delta_{i\hat{\imath}} = \begin{cases} 1 & \text{for } i = \hat{\imath}, \\ 0 & \text{otherwise;} \end{cases} \tag{14}$$

and $\delta(a)$ be the Dirac delta

$$\delta(a) = 0 \text{ for } a \neq 0 \qquad \text{and} \qquad \int_{-\epsilon}^{\epsilon} \delta(a)\,\mathrm{d}a = 1 \text{ for all } \epsilon > 0. \tag{15}$$

The linear operator $\mathbf{F}$ gives the number of new infections of each gender, infection stage, and age caused by existing infections of each gender, infection stage, and age. Its elements are

$$F_{k\hat{k}}(a, \hat{a}) = \begin{cases} \delta_{1\hat{\imath}}\delta(a)p_i m(\hat{a})\sigma_{\hat{\jmath}} + (1 - \delta_{i\hat{\imath}})\,\phi_i(a)\rho_i(a, \hat{a})\beta_{i\hat{\jmath}}(\hat{a})S_i(a)/\tilde{N} & \text{for } j = 1, \\ 0 & \text{otherwise.} \end{cases} \tag{16}$$

The term

$$\delta_{1\hat{\imath}}\delta(a)p_i m(\hat{a})\sigma_{\hat{\jmath}} \tag{17}$$

is new infections to newborns ($a = 0$) due to mother-to-child transmission, while the term

$$(1 - \delta_{i\hat{\imath}})\,\phi_i(a)\rho_i(a, \hat{a})\beta_{i\hat{\jmath}}(\hat{a})S_i(a)/\tilde{N} \tag{18}$$

is new infections due to sexual transmission. These new infections all begin in the first infection stage ($j = 1$) and there are no new infections that begin in the other infection stages. The linear operator $\mathbf{V}$ gives the transition rates between each gender, infection stage, and age. Its elements are

$$V_{k\hat{k}}(a, \hat{a}) = \begin{cases} \delta(a - \hat{a})\left[\frac{\partial}{\partial a} + \gamma_{\hat{\imath}\hat{\jmath}}(\hat{a}) + \mu_{\hat{\imath}}(\hat{a}) + \nu_{\hat{\imath}\hat{\jmath}}(\hat{a})\right] & \text{for } \hat{\imath} = i,\ \hat{\jmath} = j; \\ -\delta(a - \hat{a})\gamma_{\hat{\imath}\hat{\jmath}}(a) & \text{for } \hat{\imath} = i,\ \hat{\jmath} = j - 1; \\ 0 & \text{otherwise.} \end{cases} \tag{19}$$

For $\hat{\imath} = i$, $\hat{\jmath} = j$ and $\hat{a} = a$, the term $\frac{\partial}{\partial a}$ is aging, $\gamma_{ij}(a)$ is progression to the next infection stage, $\mu_i(a)$ is natural mortality, and $\nu_{ij}(a)$ is HIV-related mortality. Likewise, in $V_{k\hat{k}}(a, \hat{a})$ for $\hat{\imath} = i$, $\hat{\jmath} = j - 1$ and $\hat{a} = a$, $\gamma_{ij}(a)$ is due to progression from the previous infection stage.

The values of $S_i(a)/\tilde{N}$ are the stable age distribution of the disease-free system, which is linear. Thus, the stable age distribution can be calculated explicitly as the positive eigenfunction corresponding to the largest real eigenvalue of

$$\mathbf{M} = \begin{bmatrix} M_{11}(a, \hat{a}) & 0 \\ M_{21}(a, \hat{a}) & M_{22}(a, \hat{a}) \end{bmatrix}, \tag{20}$$

where the elements are

$$M_{11}(a,\hat{a}) = \delta(a)p_1 m(\hat{a}) - \delta(a-\hat{a})\left[\frac{\partial}{\partial a} + \mu_1(a)\right], \tag{21}$$

$$M_{21}(a,\hat{a}) = \delta(a)p_2 m(\hat{a}), \tag{22}$$

and

$$M_{22}(a,\hat{a}) = -\delta(a-\hat{a})\left[\frac{\partial}{\partial a} + \mu_2(a)\right]. \tag{23}$$

The basic reproductive number, R_0, is then the largest real eigenvalue of $\mathbf{FV}^{-1}$. To numerically compute R_0, the age discretization (with $\Delta a = 0.1$) was again used, resulting in standard linear algebra computations to find R_0.

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Figure Legends

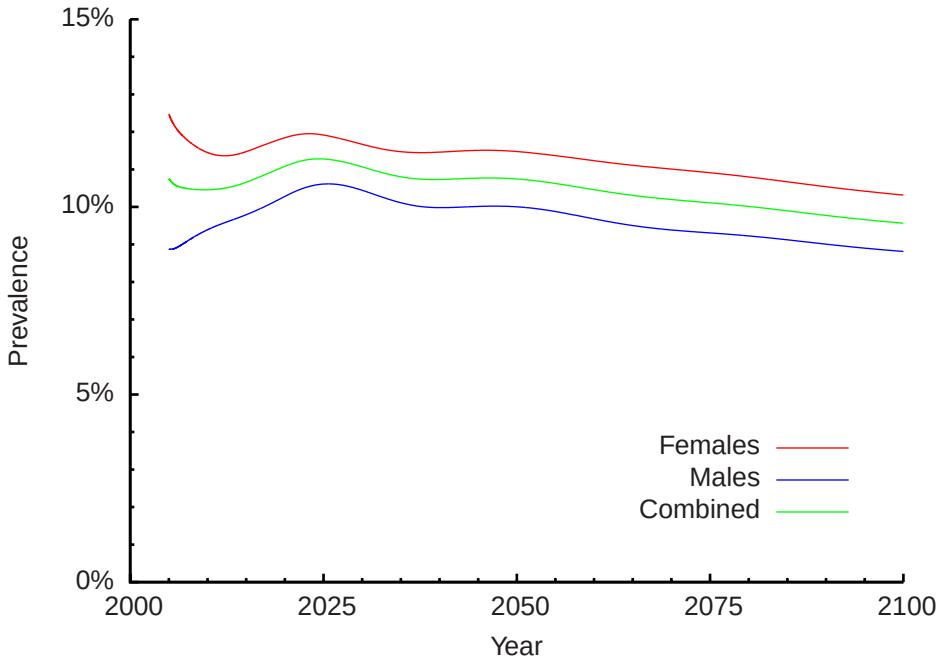

Figure 1. HIV prevalence projected from 2005 to 2100. Shown are the prevalences for females of all ages, males of all ages, and the two combined.

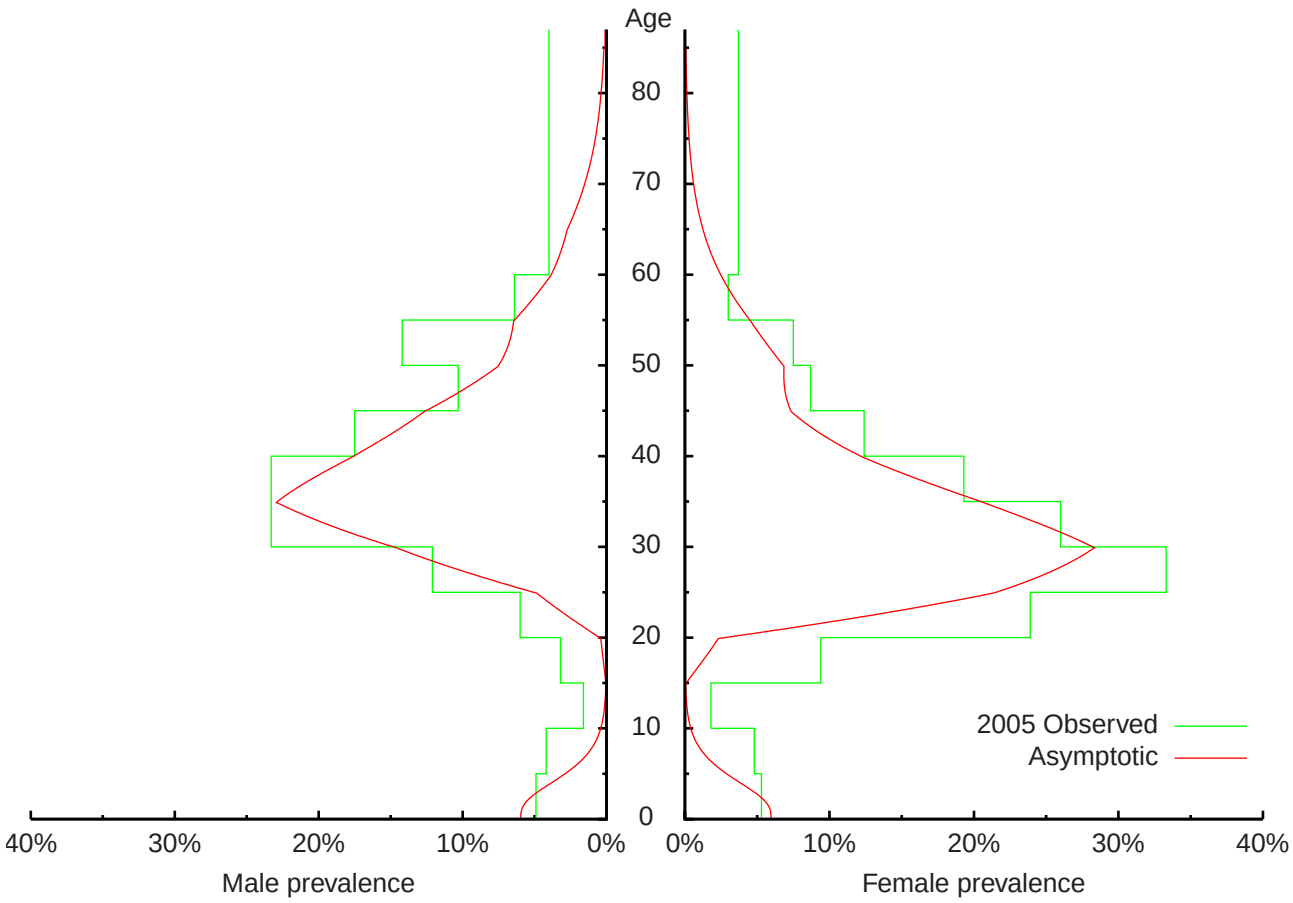

Figure 2. The prevalence by age group for 2005 prevalence and asymptotic prevalence. For women ages 15–19 and 20–24 and men ages 20–24 the asymptotic prevalence is below the current prevalence, suggesting that either the parametrization or the model itself is not capturing some biological or social factor involved in infection of these young adults.

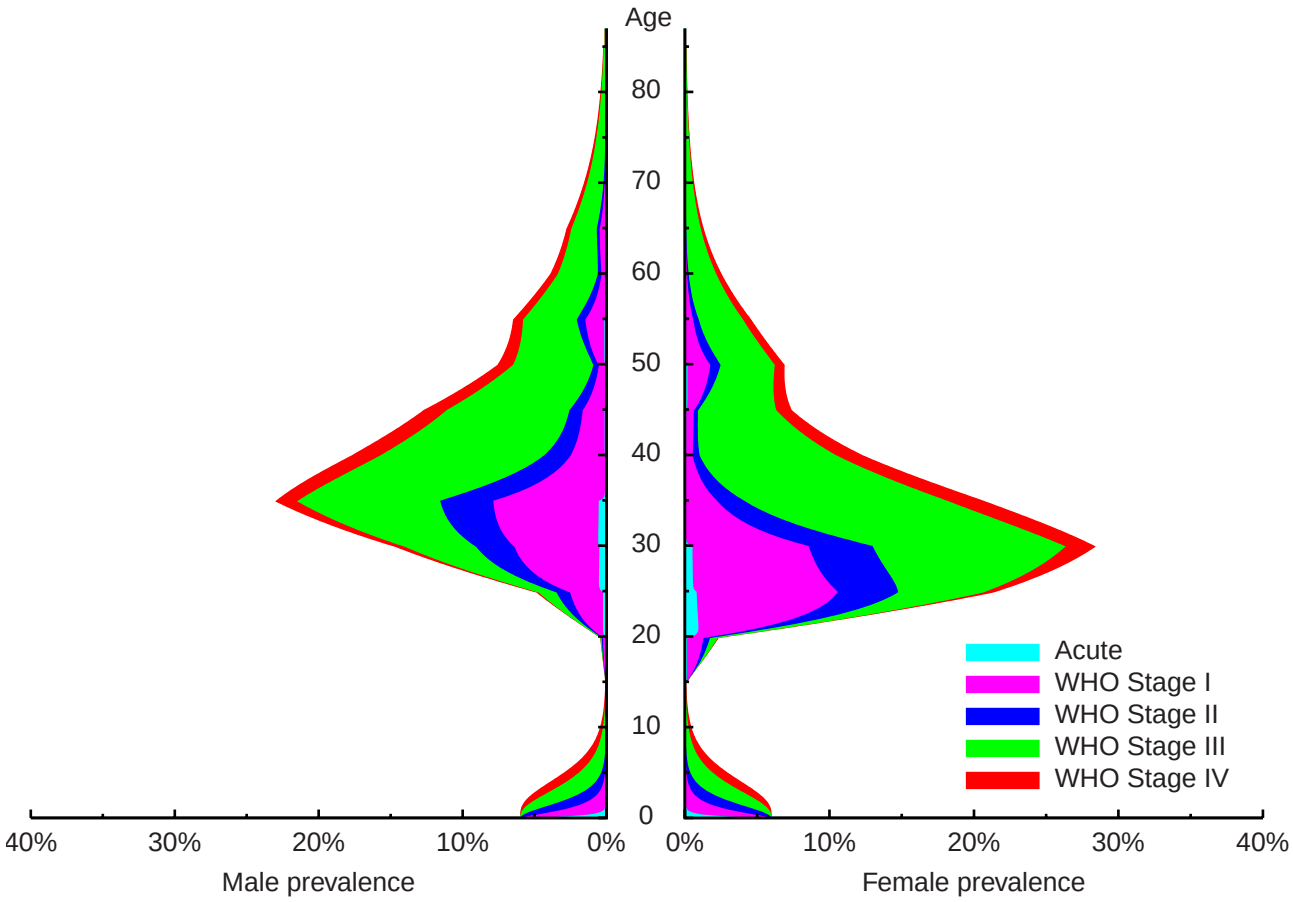

Figure 3. The asymptotic prevalence by infection stage and age.

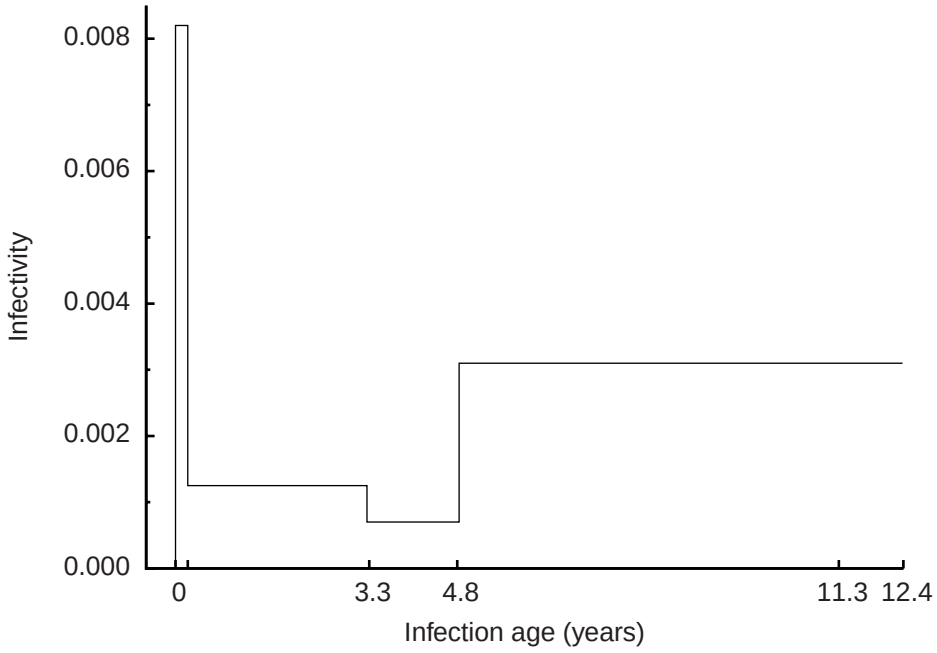

Figure 4. Per-coital-act infection probability versus infection age, which is divided into WHO stages. The initial high infectivity is during the acute phase, which is 2.5 months long; the next two phases, asymptomatic and symptomatic, have low infectivity; the late-symptomatic and AIDS phases have higher infectivity. For the model, we assume that AIDS-stage individuals do not have sex, so they effectively have no infectivity. Infectivities are from Wawer et al. [13] and stage durations are mean durations derived from Morgan et al. [63, 64].

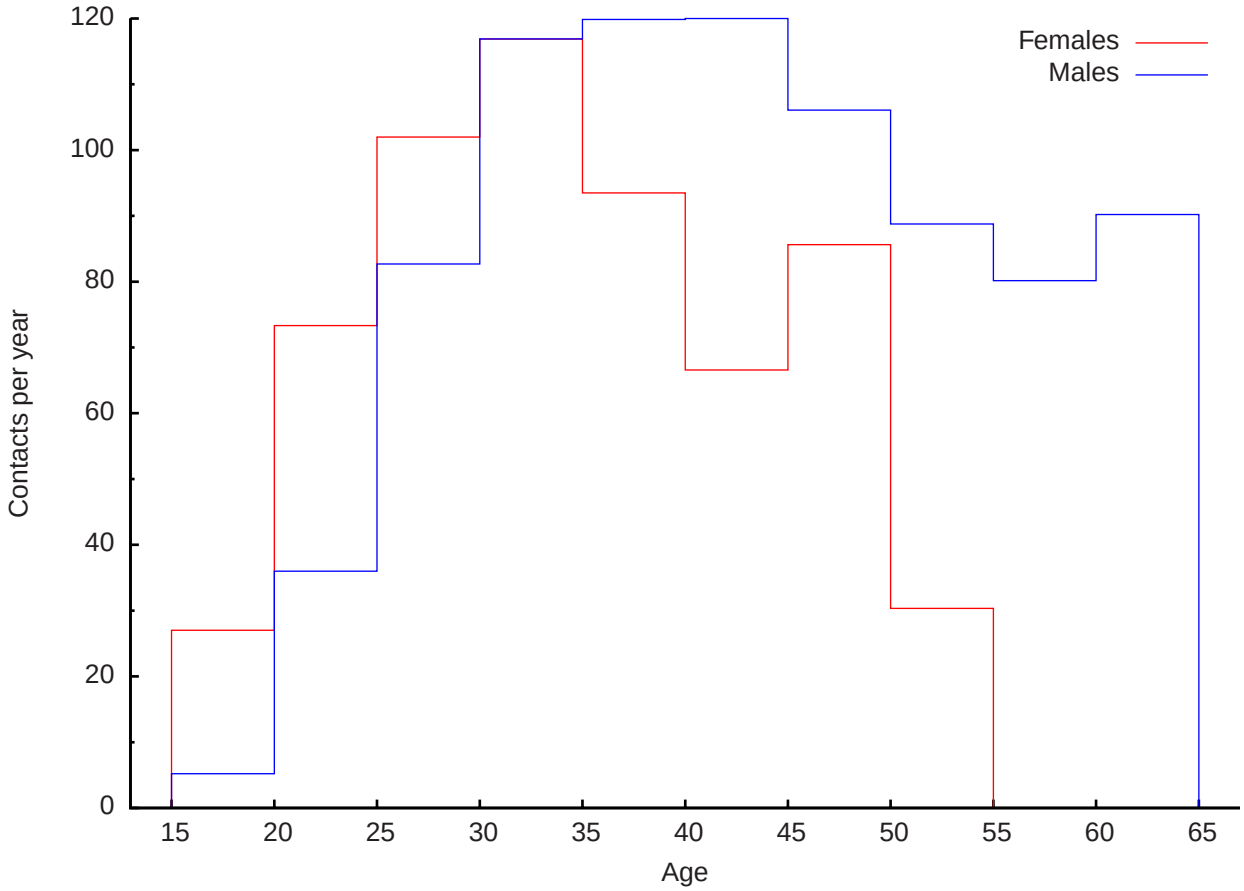

Figure 5. The number of yearly contacts for men and women of different ages at the beginning of 2005 ($t = 0$).

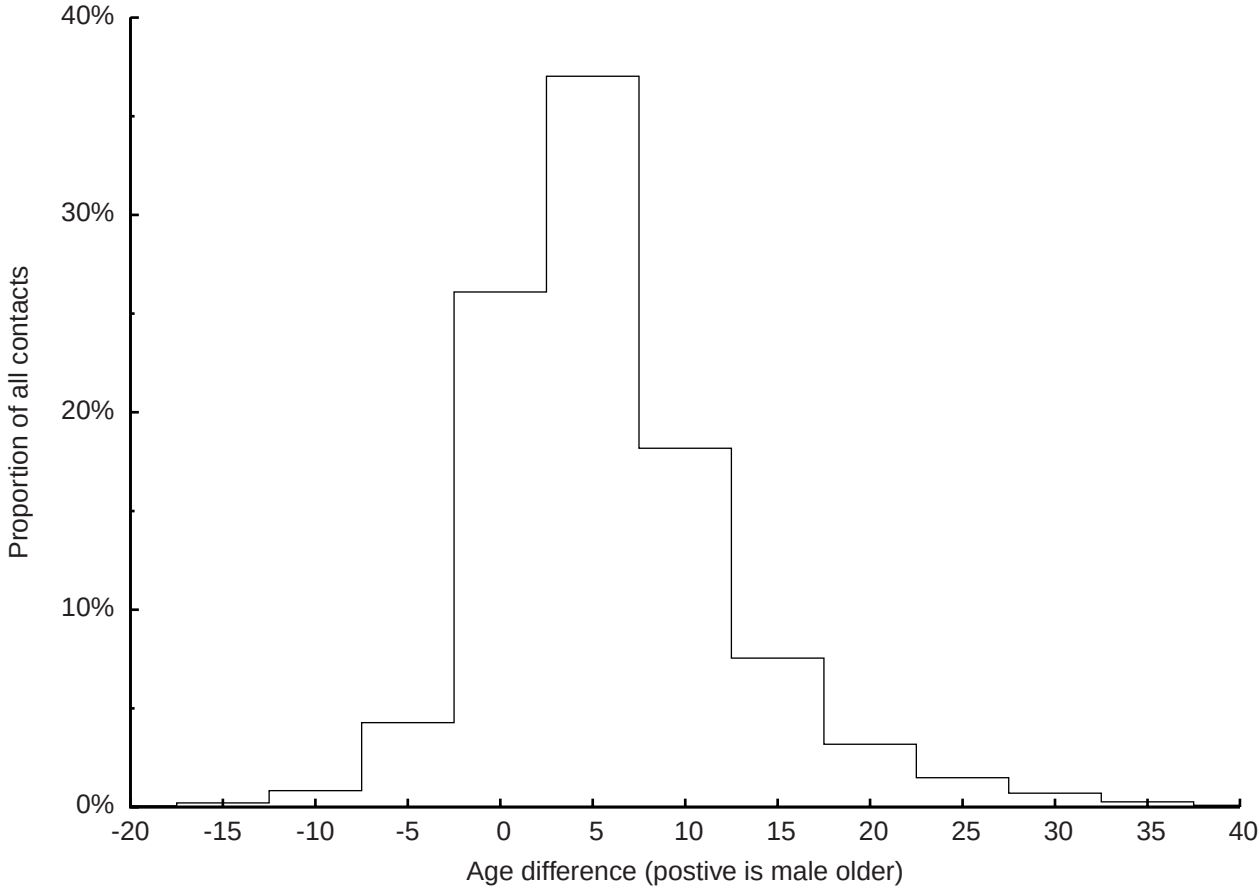

Figure 6. The age difference between partners at the beginning of 2005 ($t = 0$). Positive differences indicate the male is older than the female and negative differences denote female-older sexual contacts.

Tables

Table 1. 2001 demographics for South Africa.

Ages	**Female pop.** $N_1(0,a)$	**Male pop.** $N_2(0,a)$
0–4	2 226 085	2 223 731
5–9	2 427 751	2 425 804
10–14	2 542 961	2 518 956
15–19	2 528 642	2 453 079
20–24	2 195 230	2 099 293
25–29	2 035 814	1 899 124
30–34	1 746 412	1 594 488
35–39	1 630 264	1 441 507
40–44	1 385 832	1 233 632
45–49	1 119 776	967 604
50–54	868 521	769 499
55–59	652 943	552 323
60–64	620 784	444 510
65–69	483 164	304 763
70–74	398 922	232 547
75–79	231 101	136 436
80–84	180 111	90 835
85+	111 425	45 907
Total	23 385 737	21 434 040

Data from [55].

Table 2. End of 2004 proportion of HIV cases by WHO stage for South Africa.

HIV stage	**Child**	**Adult**
Acute	4.3%	2.0%
Stage I	20.5%	28.9%
Stage II	20.5%	23.0%
Stage III	41.1%	35.0%
Stage IV	13.5%	11.2%

Children are younger than 15 and adults are 15 and older. For adults, Dorrington et al. [57] combine the acute stage and stage I; we have split their first stage into our acute stage and stage I by simply multiplying by the mean time from our model parameters that an adult spends in each stage divided by the total mean time spent in the two stages. That is, of the mean time spent in the acute stage and stage I, an adult spends about 6.4% of his time in the acute stage and the remaining 93.6% in stage I. The stage-structured prevalence for children is given as 'Pre-AIDS' and stage IV. Like for adults, we estimate the number of children in each pre-AIDS stage simply by multiplying by the fraction of time spent in each pre-AIDS stage: 5.0% in the acute stage, 23.8% in stage I, 23.8% in stage II, and 47.5% in stage III.

Table 3. 2001 fertility rates and natural mortality rates for South Africa.

		Natural mortality	
	Fertility	**Female**	**Male**
Ages	$m(a)$	$\mu_1(a)$	$\mu_2(a)$
<1	—	0.0280	0.0313
1–4	—	0.0100	0.0111
5–9	—	0.0005	0.0006
10–14	—	0.0004	0.0006
15–19	0.065	0.0005	0.0007
20–24	0.126	0.0016	0.0016
25–29	0.143	0.0025	0.0031
30–34	0.120	0.0028	0.0043
35–39	0.075	0.0027	0.0047
40–44	0.030	0.0026	0.0052
45–49	0.075	0.0033	0.0065
50–54	0.010	0.0096	0.0196
55–59	—	0.0128	0.0247
60–64	—	0.0169	0.0380
65–69	—	0.0227	0.0393
70–74	—	0.0336	0.0553
75–79	—	0.0522	0.0812
80–84	—	0.0858	0.1215
85+	—	0.1394	0.1762

Fertility rates are in units of per year [58]. The natural mortality (i.e. non-HIV-related) rates, in units of per year, are derived from total mortality rates and total numbers of deaths for 2001 [66] and estimates of the proportions of deaths that are due to HIV in 2004 [57]. See Parameters in the text for more description.

Table 4. Fecundity.

	Fecundity	
	Female	**Male**
Ages	$\tilde{f}_1(a)$	$\tilde{f}_2(a)$
0–14	—	—
15–19	1.199	0.919
20–24	1.243	1.082
25–29	1.285	1.066
30–34	1.229	1.120
35–39	1.115	1.054
40–44	0.773	0.900
45–49	0.179	0.887
50–54	0.179	0.790
55–59	—	0.522
60–64	—	0.522
65+	—	—

Fecundity, defined as the biological ability for women and men of different ages to have children, here in units of per year, from [68]. Here we have assumed that the fecundity for women ages 50–54 is the same as for women ages 45–49 and the fecundity for men ages 60–64 is the same as for men ages 55–59. See Parameters in the text for more description.

Table 5. Per person contact rates, $\rho(a, \hat{a})$, between women and men of different ages.

		Woman's age, a							
		15–19	20–24	25–29	30–34	35–39	40–44	45–49	50–54
Man's age, $\hat{a}$	15–19	45.1	10.0	1.6	0.4	0.1	0.1	0.1	0.1
	20–24	164.7	209.9	34.7	8.2	2.2	1.2	1.7	1.5
	25–29	91.4	450.4	404.1	85.1	16.0	4.9	4.1	1.6
	30–34	33.7	248.0	658.5	564.2	93.2	19.6	13.1	3.0
	35–39	15.5	98.4	345.1	777.3	463.7	79.5	37.6	10.0
	40–44	8.6	50.2	160.4	452.4	739.2	422.6	151.3	31.3
	45–49	5.9	28.1	78.9	200.0	412.1	573.6	657.9	81.3
	50–54	3.1	17.0	47.3	118.4	216.2	350.8	861.4	279.0
	55–59	2.9	14.6	44.0	95.7	180.3	272.3	712.4	456.4
	60–64	4.6	20.0	53.9	125.8	207.8	316.2	771.4	468.8

These rates are derived from data on registered births by mother and father's ages for South Africa in 2002 [25]. The units here are per person per year.