Behaviour change in generalised HIV epidemics: impact of reducing cross-generational sex and delaying age at sexual debut

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Background: Sexual behavioural change is essential to prevent HIV infections in Africa and statistical analysis of risk factors at the individual-level may be used to design interventions. The importance of reducing cross-generational sex (young women having sex with older men) and delaying age at first sex on the spread of HIV at the population-level has been presumed but not scientifically investigated and quantified.
Methods: A mathematical model of heterosexual spread of HIV was developed to predict the population-level impact of reducing cross-generational sex and delaying sexual debut.
Results: The impact of behaviour change on the spread of HIV is sensitive to the structure and reaction of the sexual network. Reducing cross-generational sex could have little impact on the risk of infection unless it is accompanied by a reduction in the number of risky sexual contacts. Even peer-to-peer sexual mixing can support high endemic levels of HIV. The benefit of delaying sexual debut is comparatively small and is reduced if males continue to prefer young partners or if young women spend more time unmarried. In Manicaland, Zimbabwe, if older men were to use condoms as frequently as young men, the reduction in risk of infection could exceed that generated by a two-year delay in first sex.
Conclusions: At the individual-level avoiding sex with older partners and delaying sexual debut can decrease the risk of infection but at the population-level these interventions may do little to limit the spread of HIV without wider-ranging behavioural changes throughout the sexual network.

The HIV pandemic continues to spread devastation globally.[1] In the generalised epidemics in sub-Saharan Africa, most of the risk is associated with heterosexual sex,[2–5] and behaviour change is essential to reduce the number of new infections. Funding has been made available for interventions to promote behaviour change,[6 7] but care must be taken to target resources at changing those aspects of sexual behaviour that are most important in the spread of HIV.

Observational studies show that usually HIV prevalence among young women far exceeds that among young men.[8] This has prompted some to emphasise the importance of protecting young women from infection in particular.[2 8–11] Statistical analyses of individual behaviour data show that the risk of HIV infection is lower among women who avoid older sexual partners[12 13] and begin sexual activity later.[12 14 15] For this reason, it has been suggested that behaviour interventions should focus on reducing cross-generational sex (young women forming sexual partnerships with older men) and delaying sexual debut.[8 16 17] The importance of these changes at the population level has been presumed but not scientifically investigated and quantified.[8 11 13 16–20]

Mathematical models allow an assessment of the potential effects of proposed behaviour interventions and can provide a guide to the factors most critical to their success.[21] Increasingly, the insights gained from mathematical models are well understood and applied,[22–24] and consulting mathematical models before implementing epidemiological interventions has become standard practice for emerging epidemiological problems.[25–27] It can be argued that the same approach should be used to assess the effects of proposed behavioural change interventions on generalised HIV epidemics.

In the present study we considered two questions about proposed behavioural change interventions:

- What population-level effect could discouraging cross-generational sex and promoting delayed age at first sex have on the HIV epidemic?
- What properties of the sexual network determine the size of this impact?

To answer these questions we designed a deterministic mathematical model of the heterosexual transmission of HIV with a detailed yearly age structure of young adults so that changes in age at sexual debut, ages of sexual partners and rates of partner change in those recently entering the sexually active population could be investigated. We have parameterised the model using data collected in a cross-sectional survey in rural Zimbabwe[12] to provide a detailed and well-informed example to illustrate the qualitative results rather than provide an exhaustive description of the various generalised HIV epidemics in Africa.

METHODS

Data sources

A stratified population-based survey was carried out in the Manicaland province of eastern Zimbabwe between July 1998 and January 2000.[12] A follow-up survey was completed after three years.[28] A structured face-to-face interview was conducted with almost 10 000 men and women in 12 distinct communities: two forestry plantations, two tea and coffee estates, two small towns, two roadside trading centres and four subsistence farming areas. In three-quarters of interviews with literate respondents, the answers to sensitive questions about sexual behaviour were recorded using a confidential voting method, the use of which has been associated with reporting of greater sexual activity.[29] Condoms were used in all reported sex acts in the last sexual partnership by 17% of males and 8% of females who reported a sexual partnership in the past month. Sex acts were self-defined in the questionnaire, but here we assume that all sex acts are insertive penile–vaginal. The distribution of age difference between sexual partners (male's age minus female's age) takes a similar form for women of all ages and can be modelled by a log-logistic function (figs S1 and S2 in the supplementary material, see http://sti.bmj.com/supplemental). The mean age difference is 7 years, and in approximately 25% of partnerships the age difference is 10 years or more.

Mathematical simulation model

We developed a deterministic mathematical model of the heterosexual transmission of HIV in a sex, age and activity-stratified population. The model is defined by a set of partial differential equations with respect to time and age that are solved numerically with a four-stage Runge–Kutta algorithm (time-step = 0.02 years). Full details of the model can be found in the online supplementary material (see http://sti.bmj.com/supplemental) but the key assumptions in the model are described here.

HIV is assumed to be transmitted through heterosexual partnerships or at the time of birth from an infected mother to her child. To represent the long and variable incubation period and stage-dependent HIV transmission probability, those infected progress through three stages of asymptomatic infection prior to AIDS: the first stage lasts three months and is associated with a high transmission probability; the second stage lasts for several years (up to a mean of 10 years, depending on age) and is associated with a low transmission probability; and the third stage lasts six months and is associated with a high transmission probability.

The population is divided into several sexual activity groups with different numbers of sexual partnerships formed in a year. To permit study of the effect of varying age at first sex and the pattern of partnership formation with respect to age, a detailed yearly age structure was incorporated. On sexual debut most individuals enter the group with the lowest sexual activity, but a few enter groups with much higher sexual activity. An individual of a particular sex, age and sexual activity forms a set number of sexual partnerships each year that are directed preferentially towards those in a similar sexual activity class and between older men and younger women. The fraction of women's partnerships that are formed with men a given number of years older is determined by the log-logistic function. This distribution allows the age difference to be moderate in most sexual partnerships but much greater in others. It can be parameterised so that the pattern of partnership formation matches that observed in Manicaland or varied to represent alternative scenarios (fig S3 in the supplementary material, see http://sti.bmj.com/supplemental). Two types of intervention to reduce cross-generational mixing are simulated:

- a change in the distributional form of the allocation of young women's partnerships among older men, preserving the total number of partnerships formed; and
- removal of a fraction of partnerships with a given age difference, so that there are less partnerships in total.

Both of these interventions generate the same reduction in the fraction of young women's sexual partnerships that are ''cross-generational'' but the former replaces those cross-generational partnerships with partnerships among peers whereas the latter does not. For consistency, the derived pattern of partnership formation for one sex must match that of the other, and the extent to which males' demand for sexual partnerships is accommodated by the female population (or vice versa) has to be specified.

Mortality and fertility rates were chosen to represent an African population in the pre-AIDS era and the model was run for 100 years to establish a stable population structure. The infection was introduced to 0.01% of males aged 25–29 years in the highest sexual activity group.

RESULTS

Running the model with the different mixing patterns showed that with more cross-generational mixing, endemic prevalence (among those aged 15–49 years) was slightly higher (fig 1A (bars)). Female-to-male prevalence ratios for 15–24-year-olds at least equal to those observed can be created in the model without assuming any difference in susceptibility to HIV infection between men or women or over age (fig 1A (line)).

If all sexual partnerships are formed between peers the epidemic cannot become established (fig 1B). If 1% of sexual partnerships are formed with partners one year older or younger, HIV can become endemic. Simulating an intervention that reduced cross-generational mixing but preserved the total number of sexual partnership formed, showed that such a behavioural change could substantially reduce HIV prevalence among young women but prevalence among young men might rise (fig 1C (solid lines)). With this intervention, the lifetime risk of infection (the expected chance at birth that an individual will have been infected with HIV by their fifty-fifth birthday) is reduced by 10% for females and 5% for males. In contrast, if the same reduction in cross-generational mixing is simulated but without any compensatory increase in the number of partnerships among peers (dashed lines), prevalence among males can decrease and prevalence among females can decrease further. With this intervention, the lifetime risk of infection is reduced much more: by 25% for females and 22% for males.

This pattern of sexual mixing (young women forming partnerships with older men) means that the impact of young women delaying sexual debut is sensitive to the behavioural response of older men—that is, if males' would-be young sexual partners become abstinent, they may seek to replace those last partnerships with the youngest sexually active females available. Females' risk of infection in the first years of sexual activity is therefore linked to whether or not males seek to replace lost partnerships and the extent to which males control the structure of the sexual network (fig 2A). If males do seek to replace the lost partnerships, incidence is increased among women for the first years of sexual activity and this effect is greater if males are able to control the structure sexual network. The reduction in lifetime risk of infection for women is greater if males do not seek to replace lost partnerships (fig 2B). The benefit of delaying sexual debut is even greater if women become less susceptible to infection as they get older. However, in all scenarios the reduction in lifetime risk of infection associated with delaying sexual debut is relatively small.

Another issue is the relative timing of sexual debut and marriage.[30] The risk of infection when sexually active but not married (2% per person-year at risk during the first three years of follow-up in this population) is greater than when married (1% per person-year). This means that the benefit of delaying first sex depends on the time spent unmarried. For example, increasing the age at first sex from 18 to 21 could lead to lifetime risk of infection being reduced by 9% (if women are unmarried for 12 months less), reduced by 6% (no change in relative timing of marriage) or remain almost unchanged (if women are unmarried for an extra three years).

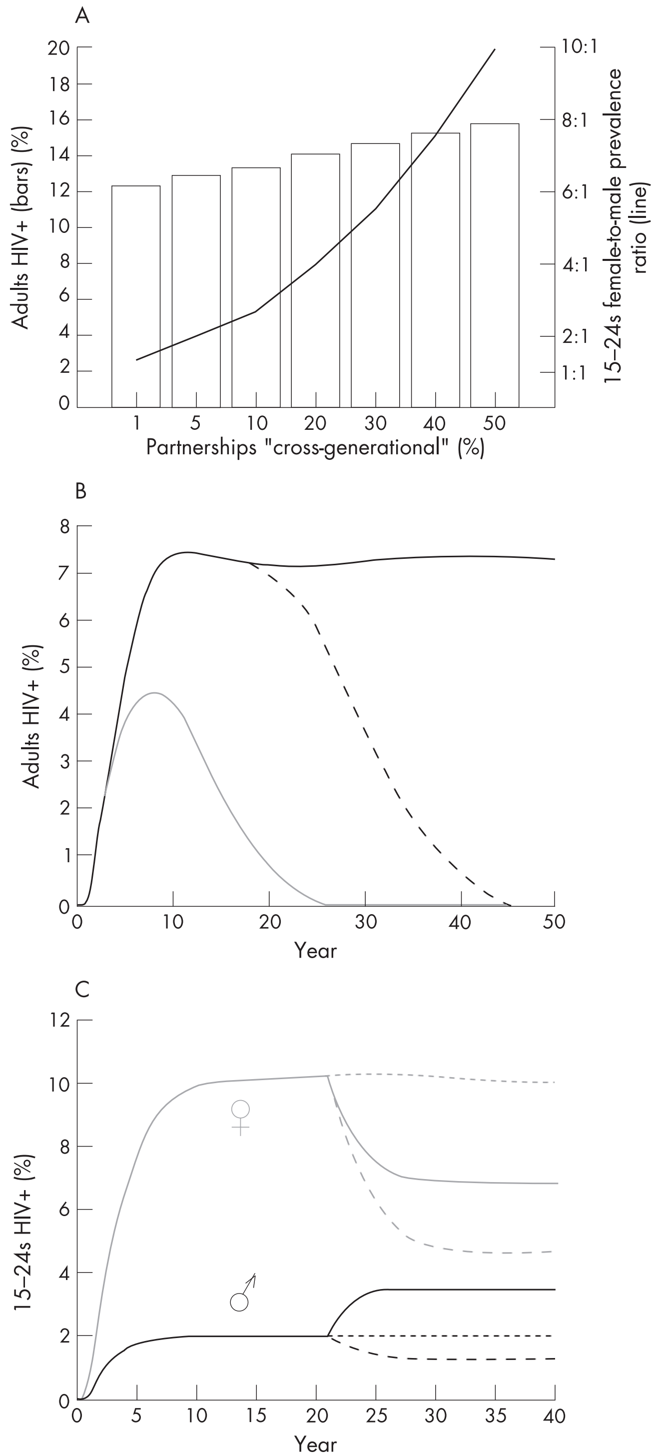

Figure 1 The impact of reducing cross-generational sex on the heterosexual spread of HIV. (A) HIV prevalence among 15–49-year-olds (bars) and female-to-male prevalence among 15–24-year-olds (line) with different levels of cross-generational mixing (percent of females' partnerships formed with males 10 or more years older), 20 years after infection introduced. (B) HIV prevalence over time if all partnerships are formed between individuals the same age (grey line) or if 1% of partnerships are formed between individuals one year older or younger (black line), or if an intervention eliminates any non-peer-to-peer partnerships at year 20 (dashed line). (C) HIV prevalence over time for 15–24-year-old males (black) and females (grey) if the proportion of cross-generational partnerships is reduced from 20% to 5% at year 20 and if there is replacement with peer-to-peer partnerships (solid lines) or if there is no replacement (dashed lines); dotted lines show ''no change'' scenario.

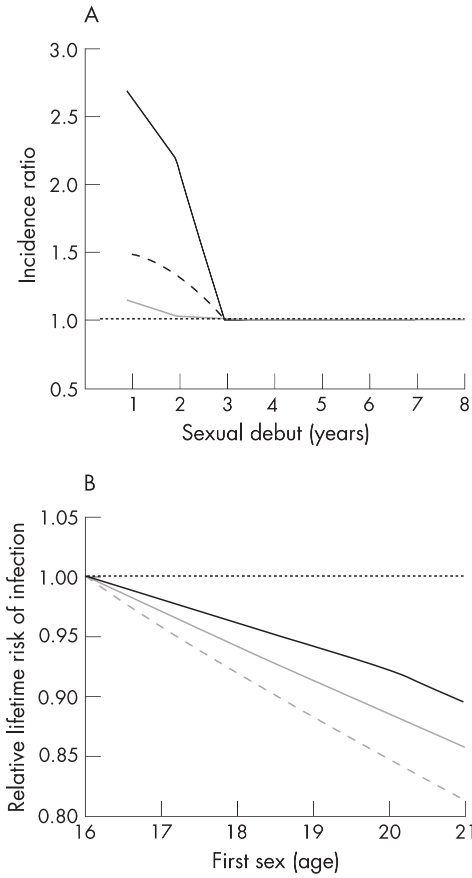

Figure 2 The impact of delaying age at first sex on the heterosexual spread of HIV. (A) HIV incidence ratio for women when age at first sex is delayed by two years for both sexes if males seek to maintain their current level of sexual activity and if mixing is determined by males (black line), females (grey line) or is an equal compromise (dashed line). (B) Relative lifetime risk of infection when age at first sex is increased from 16 years if males seek to maintain their number of sexual partnerships (black line) or if partnerships are not replaced (grey line) or if partnerships are not replaced and susceptibility to infection decreases with age (dashed line).

In rural Zimbabwe, the probability of reporting having used a condom consistently with their most recent sexual partner is particularly low for older men (25 years or older) but is higher if either the man or his partner has had many sexual partners (fig 3A). If condom use by older men is increased to the level currently reported by younger men, the lifetime risk of infection could be reduced by ~20% for both males and females. This exceeds the impact of doubling condom use in the whole population or males and females delaying sexual debut by two years under the most optimistic assumptions (fig 3B).

DISCUSSION

Sexual behaviour change is crucial to prevent HIV infections in sub-Saharan Africa.[2] Cross-sectional surveys of individuals' self-reported sexual behaviour show that young women who have had sex with an older man or begun sexual activity when young are more likely to have been infected with HIV.[12–15] On this basis, interventions aiming to change behaviour have been proposed that focus on discouraging cross-generational sex and delaying sexual debut.[8 16 17] Although it is clear that these changes will somewhat reduce the risk of infection to the individual it was not known what impact they could have on the spread of HIV through the population. Despite this uncertainty the importance of cross-generational sex in supporting high HIV prevalence has been presumed,[17] and an increase in abstinence among young people has been partially

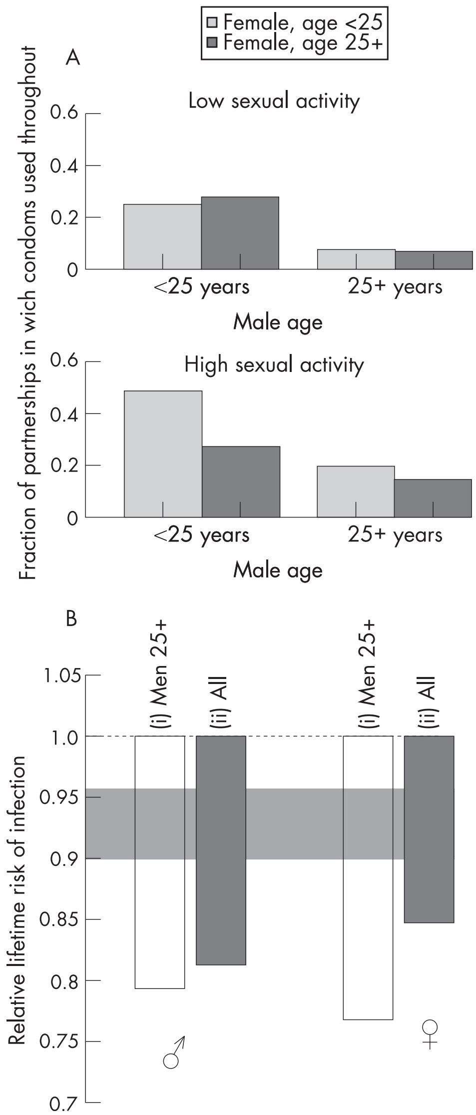

Figure 3 The impact of increasing condom use on the heterosexual spread of HIV. (A) The proportion of reported partnerships in which condoms were used in all sex acts, by the age of each partner and whether either one of the partners reported having had six or more previous sexual partners (highly sexually active). (B) Relative lifetime risk of infection for males and females if (1) condom use among males older than 25 increases to the level reported by males under 25 (open bars), (2) condom use overall is doubled (grey bars). The horizontal grey shading gives the comparable range of effects that could be expected if age at first sex for males and females is increased by two years.

credited with the decline in HIV prevalence rates in Uganda.[31 32] In this study we used a mathematical model to quantify the reduction in the average lifetime risk of HIV infection that reducing cross-generational sex and delaying first sex could bring. The model was carefully parameterised using detailed data from a rural district in eastern Zimbabwe[12] and we expect that the qualitative insights will be generalisable to other African settings with epidemics.

Our model simulations suggest that HIV prevalence is only slightly higher with much more cross-generational mixing. Furthermore, even if 99% of sexual partnerships are formed between peers, HIV can still reach a high endemic level. This is contrary to the suggestion that without cross-generational mixing HIV could not persist endemically.[17] Cross-generational sex helps increase prevalence because few of the partnerships of infected older males are with older females who are already infected too and more will probably be with uninfected younger females. However, the link is not strong because the infection will reach all age groups eventually under almost any mixing scenario, and then young women will be exposed instead to the high rates of sexual activity of their male peers. Sex with older men is more risky than sex with younger men partly because of the greater possibility of the former to be infected with HIV, having been exposed to the risk of infection for longer. However, the observed gradient in HIV prevalence among males by age is partly a *result* of the cross-generational mixing; prevalence among young men is suppressed by cross-generational mixing because they have only limited access to their peers and instead have sex with even younger uninfected women or not at all. A switch to peer-to-peer mixing will increase prevalence among young men making, from a female perspective, formerly ‘‘low-risk’’ contacts increasingly ‘‘high risk’’. In this way, the benefit of peer-to-peer over cross-generational mixing to the young women is negatively frequency dependent; one young woman will put herself at less risk by choosing partners her own age over older men but as more women come to do the same the benefit of this behaviour change is reduced as HIV prevalence among young men increases.

The real impact of cross-generational sex on the population-level spread of HIV is the power imbalance in those partnerships and the implications this has for the chance that condoms will be used.[12 19] Our results show that behaviour change interventions should aim to minimise unprotected sexual contact by young women with anyone and should not target the age difference between sexual partners per se. Nonetheless, this pattern of partnership formation between older men and younger women does seem to underlie the high female-to-male HIV prevalence ratio among young people; the model generates ratios at least as extreme as those observed without assuming any difference in susceptibility to infection by sex or age. Cross-generational mixing must be considered when examining other types of behavioural intervention; the demand for their sexual partnerships could undermine the benefit young women get from remaining abstinent for longer and the importance of transmission from older men makes the frequency with which they use condoms especially important.

Abstinence (through delaying the onset of sexual activity) removes the risk of infection for only a few years—a small fraction of one’s lifetime exposure. This period may be important because the first years of a woman’s sexual activity may carry the greatest risk of transmission for a number of biological[33–35] and behavioural[12 18] reasons. However, even assuming that susceptibility declines strongly with age, the lifetime benefit of delaying sex for two years is expected to be, at most, only 8%. The benefit is smaller (3%) if the ‘‘demand’’ for their sexual partnerships is not reduced. Although

Key messages

- The impact of behaviour change on HIV spread is sensitive to the structure and reaction of the sexual network.
- Reducing cross-generational sex may have little effect on the risk of infection unless it is accompanied by a reduction in the number of risky sexual contacts.
- The benefit of delaying age at sexual debut is comparatively small and is reduced if males continue to prefer young partners or if young women spend more time unmarried.

abstinence undeniably reduces the risk of infection, its impact on the spread of HIV and the average chance of infection over a lifetime is small. It is probable, therefore, that the dramatic prevalence decline in Uganda[31] was primarily mediated through increased condom use and fidelity rather than the two-year delay in first sex that was also reported.[32]

In the coming years, ongoing and proposed behaviour interventions will be assessed and their potential effect estimated. This modelling work has highlighted the sensitivity of the efficacy of some behaviour changes to unknown properties of the sexual network (eg the response of males to female behaviour change) and projections should incorporate this uncertainty.

From an individual-level perspective it is possible to identify those elements of sexual behaviour that are associated with the highest risk of infection. However, without a dynamic description of HIV transmission it is not clear how these changes will limit the spread of HIV at the population level. The chance of infection is only partly determined by one's own sexual behaviour and interventions should not be narrowly targeted at particular at-risk groups (for example, young women) but instead should tackle risky behaviour throughout the sexual network.

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AUTHOR CONTRIBUTIONS
All authors conceived the study, assisted with model design and analysis, and drafted the manuscript.

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Behaviour change in generalised HIV epidemics: The impact of reducing cross-generational sex and delaying age of sexual debut

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SUPPLEMENTARY MATERIAL

Full Description of the Mathematical Model

The model is defined by a set of partial differential equations with respect to time and age that are solved numerically with a four-stage Runge-Kutta algorithm (time-step = 0.02 years). The population is stratified by gender (k=1 for males, k=2 for females) and sexual activity (m=0 (lowest) to 4 (highest)). The model treats HIV infection status as either HIV negative (X), HIV acute infection (Y^1), latent infection (Y^2), pre-AIDS (Y^3) or full blown AIDS (Z). The model is run for 100 years to establish a stable population structure before the introduction of infection with 0.01% of males aged 25-29 years in the highest sexual activity group moving from X to Y^1.

The partial differential equations are:

$$\frac{\partial X_{k,m}}{\partial t}+\frac{\partial X_{k,m}}{\partial a}=-X_{k,m}\left(\mu_k(a).+\lambda_{k,m}(a,t)\right)$$

$$\frac{\partial Y^1_{k,m}}{\partial t}+\frac{\partial Y^1_{k,m}}{\partial a}=\lambda_{k,m}(a,t).X_{k,m}-Y^1_{k,m}\left(\mu_k(a)+\upsilon_1\right)$$

$$\frac{\partial Y^2_{k,m}}{\partial t}+\frac{\partial Y^2_{k,m}}{\partial a}=\upsilon_1(a).Y^1_{k,m}-Y^2_{k,m}\left(\mu_k(a)+\upsilon_2(a)\right)$$

$$\frac{\partial Y^3_{k,m}}{\partial t}+\frac{\partial Y^3_{k,m}}{\partial a}=\upsilon_2(a).Y^2_{k,m}-Y^3_{k,m}\left(\mu_k(a)+\upsilon_3\right)$$

$$\frac{\partial Z_{k,m}}{\partial t}+\frac{\partial Z_{k,m}}{\partial a}=\upsilon_3 Y^3_{k,m}-Z_{k,m}\left(\mu_k(a)+\alpha\right)$$

$\mu_k(a)$ is the gender and age-specific per-capita death rate; $\lambda_{k,m}(a,t)$ is the force of infection to individuals of that gender, age and activity-group at time t; $\frac{1}{\upsilon_1},\frac{1}{\upsilon_2(a)}$ and $\frac{1}{\upsilon_3}$ are the mean number of years spent with acute infection, latent infection and pre-AIDS, respectively; $\alpha(a)$ is the AIDS-associated mortality rate.

At each moment, the number of new-borns introduced into each gender and sexual activity-group in the population is:

$$X_{k,m}(0,t) = \varpi_k \gamma_m \int \varphi(a) \sum_m X_{2,m}(a,t)da + (1-\sigma) \int \varphi(a) \sum_m \left[Y^1_{2,m}(a,t) + Y^2_{2,m}(a,t) + Y^3_{2,m}(a,t) \right] da$$

$$Y^1{}_{k,m}(0,t) = \varpi_k \gamma_m \sigma \int \varphi(a) \sum_m \left[Y^1_{2,m}(a,t) + Y^2_{2,m}(a,t) + Y^3_{2,m}(a,t) \right] da$$

where $\varphi(a)$ is the age-specific fertility (assumed to be the same for uninfected and infected females), σ is the probability of mother to child transmission, ϖ_k is the fraction of babies born that gender and γ_m is the fraction of babies born into that sexual activity-group.

The risk of a susceptible individual becoming infected is a function of the yearly age-group rather than a continuous function of age such that: $\lambda_{k,m}(i - 0.5 \le i < i + 0.5, t) = F_{k,i,m}(t)$. We define the pattern of contact within the population through a matrix determining the age and activity group-specific rates of partnership formation with the age and activity groups of the opposite gender. Here one's own age and activity category is denoted *i* and *m*, respectively, and those of members of the opposite gender are distinguished with a prime (*i'* and *m'*).

$$F_{k,i,m}(t) = \sum_{m'} \sum_{i'} \left(c_{k,i,m,i',m'}(t) . P_{k',i',m'}(t) . \left(1 - \psi_{i,i',m,m'}\right)\right)$$

where $c_{k,i,m,i',m'}$ is the number of partnerships formed with individuals of the opposite gender by age and activity group, $P_{k',i',m'}$ is the risk of acquiring infection when forming partnerships with individuals of the opposite gender by age and sexual activity, and $\psi_{i,m,i',m'}$ is the chance that condoms are used consistently in partnerships formed between such individuals. The definition of each of these terms follows.

The distribution of partnerships $c_{k,i,m,i',m'}$ is calculated by sharing the total number of partnerships that are allocated to individuals in each gender, age and activity group, $C_{k,i,m}$,amongst the age and activity groups of the opposite gender.

$$c_{k,i,m,i',m'} = C_{k,i,m} \left[(1-\varepsilon)\delta_{m,m'} + \varepsilon \left\{ \frac{N_{k',i',m'} C_{k',i',m'}}{\sum_{m'} N_{k',i',m'} C_{k',i',m'}} \right\} \right] \Delta_{k,i,i'}$$

$$N_{k,i,m} = \int_{i-0.5}^{i+0.5} X_{k,m}(a,t) + Y^1_{k,m}(a,t) + Y^2_{k,m}(a,t) + Y^3_{k,m}(a,t) da$$

where and $\delta_{m,m'}$ is the identity matrix. Thus the pattern of mixing with respect to activity ranges from assortative (like-with-like, ε=0) to random (ε=1) and the pattern of mixing with respect to age is determined by the distribution $\Delta_{k,i,i'}$ - the fraction of an *i*-aged individual's partnerships that are formed with individuals of age *i*'. Data from rural Zimbabwe (1) indicates the distribution of age-difference between partners does not depend on the age of female (Figure S1). Here we assume that $\Delta_{k,i,i'}$ depends only on the age difference between partners: which for females is:

$$\Delta_{2,i,i'} = \frac{\kappa\rho^{\kappa}(i'-i+r)^{\kappa-1}}{1+((i'-i+r)^{\kappa})^{2}} \quad \text{if } i' > \mathrm{i}$$

$$\Delta_{2,i,i'} = 0 \qquad\qquad \text{otherwise}$$

And for males is:

$$\Delta_{1,i,i'} = \sum_{i'} \Delta_{2,i',i}$$

$\Delta_{k,i,i'}$ is scaled so that $\sum_{A_2'}^{B_2'} \Delta_{k,i,i'} = 1$ where A_k and B_k are the ages at which sexual activity begins and ends for that gender, respectively. Here κ, ρ and r are the shape parameters for the log-logistic distribution. This distribution allows most partnerships to be formed between women and men a few years older but a few partnerships to involve women and men many more years their senior. The distribution was parameterised by fitting to cross-sectional survey data collected in rural Zimbabwe (Figure S2).

The rate of partnership formation in the sexual activity groups is defined as:

$$C_{k,i,m} = \frac{M_{k,i}}{\tau^{\sum m\gamma_m}} \tau^{m}$$

Here $M_{k,i}$ is the gender- and age-specific geometric mean of partnership formation rate and τ independently determines the common ratio of partner change rate between the sexual-activity categories.

At each moment, the pattern of partnership formation ($c_{i,m,i',m'}$) is constrained such that the total number of sexual partnerships formed by males of type *i,m* with females type *i',m'* must equal the total number of partnerships formed by females of type *i',m'* with males of type *i,m*. That is,:

$$N_{1,i,m} c_{1,i,m,i',m'} = N_{2,i',m'} c_{2,i',m',i,m}$$

where $N_{k,i,m}$ is the number of sexually active individuals of that gender, age and activity-group.

If this does not hold $c_{1,i,m,i,m}$ and $c_{2,i,m,i,m}$ are adjusted (denoted with *):

$$D = \frac{N_{1,i,m} c_{1,i,m,i',m'}}{N_{2,i',m'} c_{2,i',m',i,m}}$$

$$c_{1,i,m,i',m'} \to c_{1,i,m,i',m'} D^{-(1-\theta)}$$

$$c_{2,i',m',i,m} \to c_{2,i',m',i,m} D^{\theta}$$

In this way θ determines whether the demand for sexual partnerships of males ($0.5 < \theta \le 1$) or females ($0 \le \theta < 0.5$) is the strongest determinant of the pattern of partnership formation.

The other two components of $F_{k,i,m}(t)$ are the chance of infection per partnership and the probability that condom are used correctly and consistently throughout those sexual partnerships.

The probability of getting infected through sexual partnerships with individuals of the opposite gender aged *i* and in sexual activity group *m*, is $P_{k,i',m'}(t)$:

$$P_{k,i,m}(t) = \frac{\int_{i-0.5}^{i+0.5} \beta^1 Y^1_{k,i}(a,t) + \beta^2 Y^2_{k,m}(a,t) + \beta^3 Y^3_{k,m}(a,t) + \beta^4 Z_{k,m}(a,t)da}{\int_{i-0.5}^{i+0.5} X_{k,m}(a,t) + Y_{k,m}(a,t) + Y^2_{k,m}(a,t) + Y^3_{k,m}(a,t) + Z_{k,m}(a,t)da}$$

where β^1, β^2, β^3 and β^4 are the probabilities per partnership of transmission of HIV during acute infection, latent infection, pre-AIDS and AIDS respectively.

We assume that condom use is protective of infection if they are used consistently with the partnership. For simplicity we assume that the fraction of partnerships in which condoms used consistently $(\psi_{i,i',m,m'})$ depends on the age of both sexual partner and the sexual activity group of the individual in the highest (most active) sexual activity group. These values are shown in the main paper (Figure 3(a)).

Calculating Lifetime Risk

The lifetime risk of infection with HIV *R* is the expected probability at birth that an individual will have been infected with HIV by their 55th birthday. The measure is taken 10 years after the intervention is implemented (at time T).

$$R_k = 1 - \prod_{i=0}^{i=55} \left(1 - \Gamma_{k,i}(T+10)\right)$$

$$\Gamma_{k,i}(t) = \sum_m \left(\frac{N_{k,i,m}(t)}{\sum_m N_{k,i,m}(t)} \lambda_{k,i,m}(t) \right)$$

Interventions are evaluated by the relative lifetime risk of infection with an intervention ($R_{intervention}$) relative to the case when there is no intervention ($R_{baseline}$), which we call *RR*.

$$RR = \frac{R_{\text{intervention}}}{R_{baseline}}$$

Intervention Scenarios

- <u>Changes in cross-generational mixing</u>

  The parameterisation of the pattern of partnership formation with respect to age ($\Delta_{k,i,i'}$) is varied to create a range of scenarios of cross-generational mixing (Figure S3). To simulate 'peer-to-peer mixing', individuals enter the population in yearly cohorts and form partnerships exclusively within their own cohort. The intervention which reduces the proportion of partnerships that are cross-generational from 25% to 5% is simulated (i) by changing the parameterisation of the mixing distribution $\Delta_{k,i,i'}$ and (ii) by blocking transmission of HIV in all but 5% of cross-generational partnerships.

- <u>Changes in age at first sex</u>

  The parameter A_k specifies the age at which individuals of that gender begin sexual activity. When age at first sex is delay by J_k years the distribution of sexual partnership becomes:

  $$c_{1,[A_1,A_1+J_1],m,i',m'} = 0$$
  $$c_{2,[A_2,A_2+J_2],m,i',m'} = 0$$

  If males seek to maintain their current number of sexual partnerships formed per year then the following change is also made:

  $$c_{1,i,m,[A_2,A_2+H],m'} \rightarrow c_{1,i,m,[A_2,A_2+H],m'} + \frac{\sum_{i'=A_2}^{A_2+J_2} c_{1,i,m,i',m'}}{H}$$

  This allows males to seek to recoup the sexual partnerships they lost when their young would-be partners became abstinent from the sexual partnerships offered by young women in the first *H* years of sexually activity.

  Where we assume that the biological susceptibility of women decreases with older age, we multiply the probability of transmission to women in those partnerships by some factor, ω2(a) which depends on female age, a.

$\omega_2(a) = 1.5$	$a \leq 14$
$\omega_2(a) = (1.5 - (a-14)*0.0625)$	$15 \leq a \leq 22$

$\omega_2(a) = 1.0$ $a>22$

The importance of timing of marriage is addressed with an alternative model which simply calculates risk of infection as:

Risk of infection = 1- [(1-risk infection per year when single)$^{\text{years before marriage}}$.(1-risk infection per year when married)$^{\text{years after marriage}}$]

where: Years after marriage = Years sexually active – Years before marriage

The 'Years sexually active' is set at 55 and data from Zimbabwe (2) suggest that the risk of infection for sexually active unmarried women and sexually active married women are approximately 0.02 and 0.01 per person-years at risk, respectively.

- <u>Changes in condom use</u>

  The probability that condoms are used consistently in sexual partnerships $\psi_{i,i',\max(m,m')}$ is altered as follows for each of the intervention tried:

  (i) 'Increase condom use overall' $\psi_{1,i,i',\max(m,m')} \rightarrow 2\psi_{1,i,i',\max(m,m')}$

  (ii) 'Increase condom use among older men' $\psi_{1,[25,B_1],i',\max(m,m')} \rightarrow \psi_{1,24,i',\max(m,m')}$

  $\psi_{2,i,[25,B_1],\max(m,m')} \rightarrow \psi_{2,i,24,\max(m,m')}$

References

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3. Anderson RM, May RM, Ng TW, Rowley JT. Age-dependent choice of sexual partners and the transmission dynamics of HIV in Sub-Saharan Africa. Philos Trans R Soc Lond B Biol Sci. 1992 May 29;336(1277):135-55.
4. World Bank. World development report-1991. New York: Oxford University Press; 1991.

Parameter Value	Symbol (or formula)	Value
Mortality rate	$\mu(a)$	Table S2
Fertility rate	$\varphi(a)$	Table S2
Mean time with acute HIV infection	υ_{12}	3 months
Mean time with latent HIV infection	$\upsilon_{23}(a)$	Table S3
Mean time with pre-AIDS	$1/g$	6 months
Mean time in full blown AIDS before dying	$1/\alpha$	6 months
Transmission probability (acute stage, pre-AIDS and full blown AIDS)	$10\,\beta$	0.35
Transmission probability (latent stage)	β	0.035
Probability of mother-to-child transmission	σ	0.35
Fraction of partnerships formed randomly with respect to sexual activity class	ε	0.3
Age-difference between sexual partners (shape parameters for log-logistic distribution)	r κ ρ	0.11 3.04 2.85
Number of partnerships formed per year. Common ratio between sexual activity groups Age and gender-specific geometric mean	τ $M_{k,i}$	4 Table S4
Age at first sex (males and females)	$A^1_{1,2}$	16
Age at last sex (males and females)	$A^2_{1,2}$	55
Range of ages from which to recoup lost sexual partnerships if opposite gender delays first sex.	H	3

Table S1: Default parameter values

	Deaths per person-year ($\mu(a)$)		Births per female person-year ($\varphi(a)$)
Age-range	**Male**	**Female**	
<1	0.117	0.100	0
1-4	0.019	0.019	0
5-9	0.007	0.006	0
10-14	0.004	0.004	0
15-19	0.004	0.004	0.175
20-24	0.006	0.005	0.313
25-29	0.007	0.006	0.324
30-34	0.007	0.006	0.271
35-39	0.008	0.007	0.201
40-44	0.010	0.008	0.125
45-49	0.012	0.009	0.053
50-54	0.016	0.012	0
55-59	0.021	0.016	0
60-64	0.030	0.024	0
65-69	0.044	0.038	0
70-74	0.068	0.060	0
75-79	0.105	0.094	0
80+	0.189	0.174	0

Table S2: Demographic parameter values (baseline values excluding effects of AIDS) (3, 4)

Age-range	Mean years with latent infection Y^2 ($\upsilon_{23}(a)^{-1}$)
0-9	0.75
10-24	6.0
25-29	4.8
30-34	4.0
35-39	3.4
40-44	3.0
45-49	2.7
50-59	2.4
60+	2.2

Table S3: Mean years spent with latent HIV infection

	Mean number of sexual partnerships formed per year ($M_{k,i}$)	
Age-range	**Male**	**Female**
***A*-24**	2.1	1.0
24-34	1.9	1.1
35-44	1.7	0.92
45+	1.6	0.92*

Table S4: Mean partner change rates, by age (based on data from Manicaland, Zimbabwe (1))

** No data available. This value interpolated from younger age-group.*

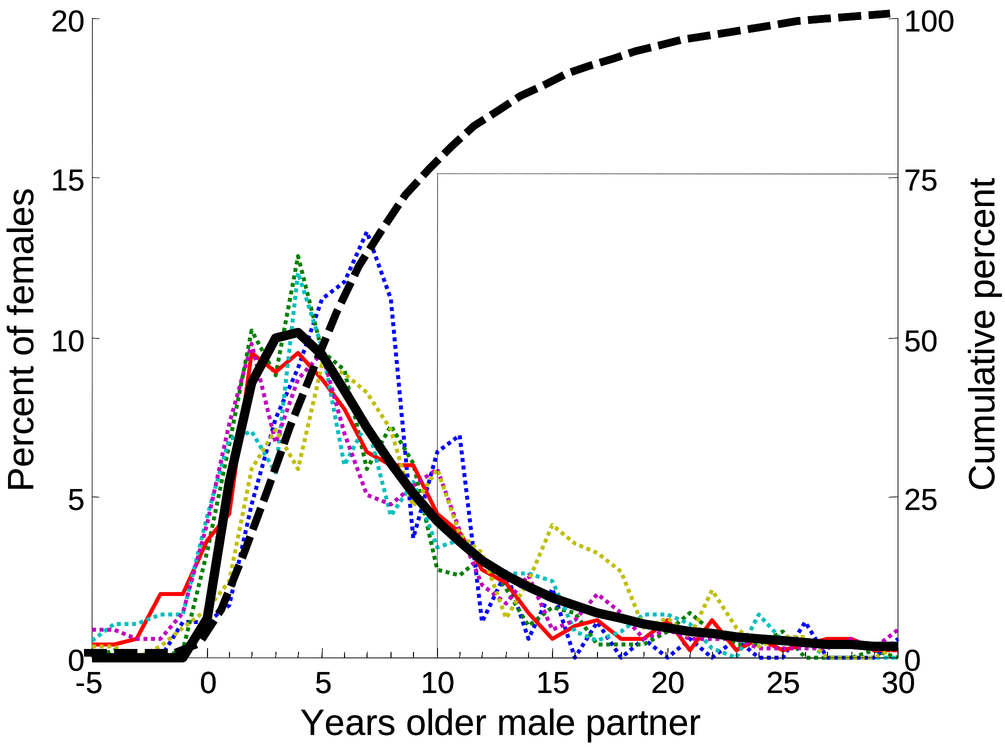

Figure S1: The percentage of females' partnerships formed with males a given number of years older (dotted line), by females aged 15-19, 20-24, 25-29, 30-34, 35-39 and 40-44 years. Solid line is log-logistic function fitted to data pooled from all ages and dashed line is corresponding cumulative distribution.

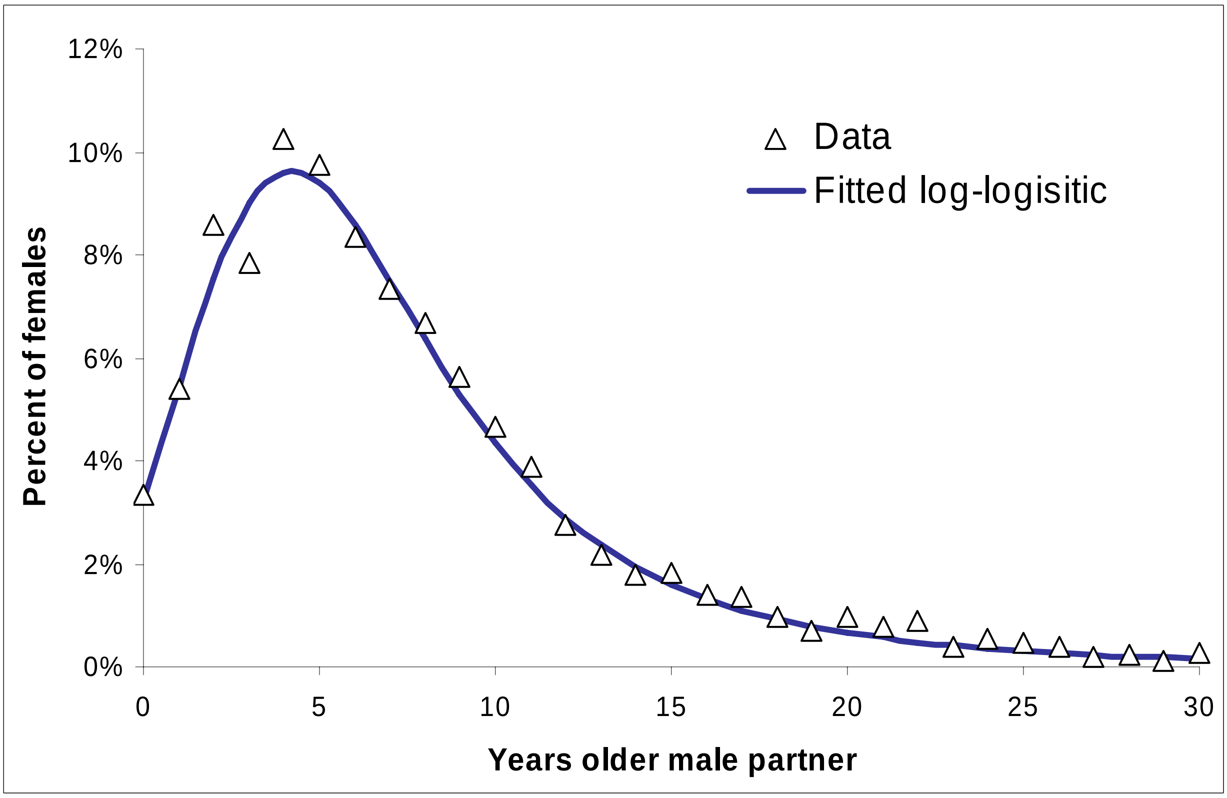

Figure S2: Age-difference (male age minus female age) for all sexual partnerships reported by females (triangles) with fitted log-logistic distribution for all non-negative age-differences (line).

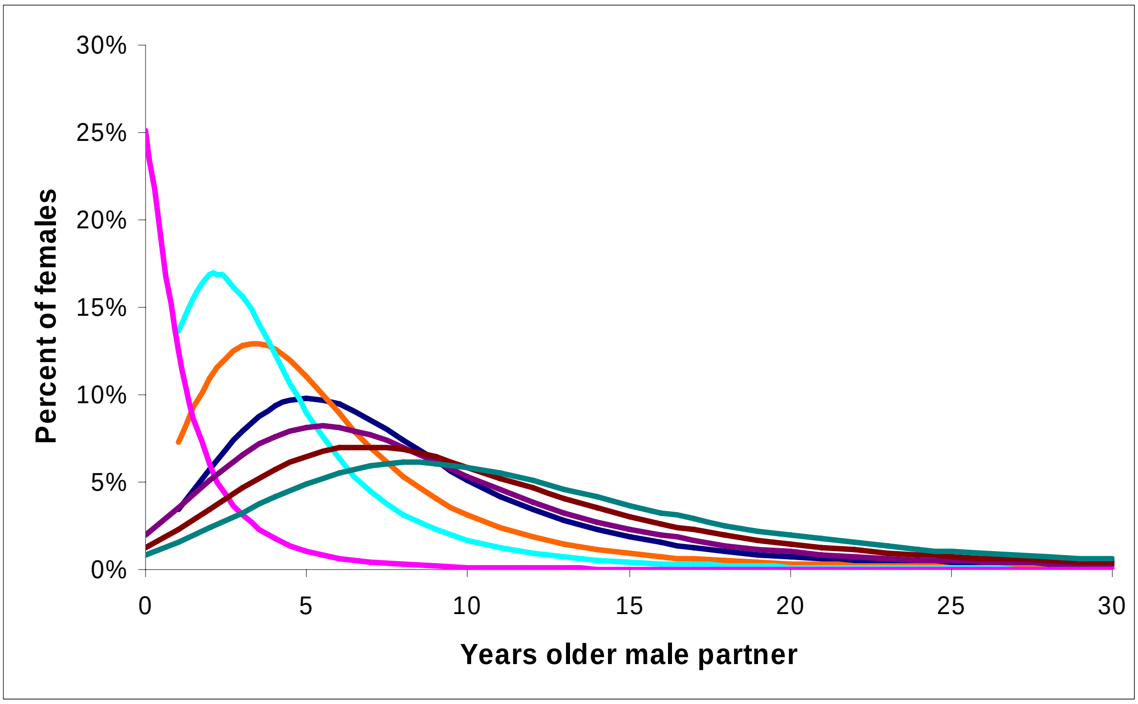

Figure S3: Age-difference distributions with different levels of cross-generational sex; 1% (pink), 5%, (light blue) 10% (orange), 20% (dark blue), 30% (purple), 40% (dark red), 50% (green). These are the distributions used to create Figure 1(b).