Interaction Effects in the Sexual Spread of HIV/AIDS

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ABSTRACT

As HIV continues to spread to previously unaffected areas of the world, improved understanding of the factors that operate to produce or suppress epidemics remains crucial. This paper employs a biobehavioral macrosimulation model to assess the interaction effect between two of the most critical behavioral determinants of the sexual spread of HIV: the rates of sexual partner change and patterns of sexual mixing between population subgroups. Results simulated under two rate of partner change scenarios and under various degrees of assortativeness in sexual mixing patterns reveal that when the rate of partner change is high, greater assortativeness tends to decrease the ultimate size of the epidemic, but the opposite relationship is revealed in simulations under relatively low rates of partner change. This interaction effect, which further depends on the underlying HIV transmission probabilities, is consequential for the size and shape of the epidemic curve and identification of high-risk population subgroups.

BACKGROUND

The Human Immunodeficiency Virus (HIV) and associated Acquired Immune Deficiency Syndrome (AIDS) continues to exact its devastating toll in populations around the globe. An estimated 40 million people are living with HIV/AIDS today, 4.9 million of whom are believed to have contracted the virus in the past year alone (UNAIDS 2005). The Joint United Nations Programme on HIV/AIDS (UNAIDS) reports that more than 25 million lives have already been lost as a direct result of HIV infection and projections suggest that the AIDS death toll will more than triple within twenty years (UNAIDS 2002).

Since its discovery more than two decades ago, HIV/AIDS has spread to every populated continent, but has not affected all regions equally. In western nations, HIV prevalence has remained relatively low in the population as a whole with the epidemic concentrated largely in the subpopulations of men who have sex with men (MSMs) and injecting drug users (IDUs). In the U.S. for example, adult (ages 15 to 49) HIV prevalence in 2004 was estimated at 0.6% and more than 80% of confirmed AIDS cases were attributed to exposure through male-to-male sexual contact and/or injecting drug use (UNAIDS 2004d). Through extensive HIV/AIDS education and prevention campaigns and the widespread availability of anti-retroviral therapies, most countries of North America, and Western and Central Europe have thus far avoided generalized HIV epidemics[1] and kept AIDS deaths comparatively low (UNAIDS 2004a). However, women make up a growing proportion of newly diagnosed cases in these countries (approximately one third at present) and evidence points to heterosexual contact as an increasingly dominant mode of transmission, placing the general population at increased risk for infection in the future (UNAIDS 2005).

In contrast to the experience of the west, generalized HIV/AIDS epidemics have become well established in the populations of several South-East Asian and sub-Saharan African populations, where estimates of adult prevalence exceed 30% in several areas (UNAIDS 2005). The South-East Asian countries of Thailand and Cambodia have witnessed HIV spread driven by a combination of injecting drug use and commercial sexual activity. In Cambodia, where recent adult HIV prevalence is estimated at 2.6%, infection is more common among female sex workers (FSWs) than any other risk group with 18% of direct FSWs in the capital city of Phonm Phem testing positive (UNAIDS 2004c). While

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[1] UNAIDS/WHO defines a generalized HIV/AIDS epidemic as one in which HIV prevalence meets or exceeds 1% in sentinel surveillance of pregnant women attending ante-natal clinics (UNAIDS 2003).

commercial sexual activity has also contributed to the spread of HIV in sub-Saharan Africa, heterosexual contact among the general population is the dominant mode of transmission, with important implications for the population at risk of acquiring HIV. For example, in Botswana, where adult HIV prevalence exceeds 40%, more than half of those infected are women (UNAIDS 2004b).

Evidence is mounting that nascent HIV epidemics have gained strength in populations previously unaffected by the disease including India, China, Russia as well as several smaller countries of Eastern Europe and Central Asia (UNAIDS 2005). Uncertainty about the prevalence of various risk behaviors has led to wide-ranging estimates of the future course of the epidemic in those countries. In China, for example, the United Nations estimates that there will be between 10 and 20 million HIV infections by the year 2010 (United Nations 2002). Believed to be still concentrated among Russia, China and India's IDUs (UNAIDS 2005), the ultimate course of their epidemics will be largely determined by the extent to which HIV is spread to and within the general population—that is, the degree to which heterosexual contact becomes a major route of HIV transmission.

As the course of the HIV pandemic evolves to include new risk groups and previously unaffected populations, improved understanding of the disease transmission dynamics remains a top priority. This paper seeks to illustrate a few select features of those dynamics with a special focus on the behavioral characteristics that come together to produce or suppress an HIV epidemic in a population where heterosexual contact is the dominant mode of transmission.

Two characteristics of behavior in a population largely determine the potential for the sexual spread of HIV. These include the rate of partner change and the prevailing patterns of sexual mixing between risk groups (Anderson and May 1991). The rate of partner change (the number of new sexual partners acquired per unit time) is often cited as the most important factor influencing the sexual transmission of HIV (Bongaarts 1989; Hyman and Stanley 1988; May and Anderson 1987; Anderson 1992; Sattenspiel et al. 1990). As the rate of partner change for an individual increases, so too does that individual's likelihood of selecting an HIV seropositive partner. Extending that association to the population level, the widely accepted conclusion is that as the average rate of partner change in a population increases, so too will the incidence of HIV transmission.

The pattern of sexual mixing between population subgroups also determines the degree to which individuals are exposed to HIV-infected partners. Numerous studies have utilized mathematical models to illustrate the importance of sexual mixing patterns for HIV spread (e.g., Gupta et al. 1989; Garnett and Anderson 1993; Boily and Masse 1997; Kault 1995; Hyman and Stanley 1988; Anderson et al. 1991; Morris 1995; Sattenspiel et al. 1990), and limited empirical evidence further supports the importance of sexual mixing patterns (Service and Blower 1995). These patterns describe the probabilities of sexual contact between individuals with varying degrees of similarity with regard to some demographic (e.g., age, race, place of residence) or social (e.g., education, rate of sexual partner change) characteristic.

Patterns of sexual mixing between population subgroups may be represented by a matrix that describes the probability that a member of one group has a sexual relationship with a member of another. Empirically informed mixing matrices are extremely difficult to construct as they require a great deal of data on the realized sexual network. To compensate for the lack of observed sexual mixing patterns, many have operationalized a theoretical mixing matrix to describe and then simulate the key features of the mixing pattern. By convention, patterns of sexual mixing between population subgroups are often expressed on a continuum ranging from perfectly "assortative" in which individuals select partners from their own group and do not have sexual contacts with partners in other groups, to "disassortative" in which individuals demonstrate a preference for partners in other groups and an aversion to partners in their own groups. Also important in research on sexual mixing are "random" (or proportionate) mixing patterns characterized by random partner selection from the population without regard to subgroup.

Much early work on sexual mixing patterns in the context of HIV focused on the effect of sexual contacts between partners of different ages. Some of the most illustrative and influential work in this area was led by Anderson and colleagues who demonstrated that when there is a tendency to select partners outside of one's own age group (disassortative), a path is created by which HIV may spread from one generation to the next. In contrast, when sexual partner selection is limited to one's own age group (assortative), HIV may spread rapidly within that age group but diffuse more slowly throughout the population as a whole (Anderson et al. 1990; Anderson et al. 1991; Anderson et al. 1992; Garnett and Anderson 1993).

Other studies produced around the same time sought to examine the effect of sexual mixing between population subgroups defined by their rates of partner change. These mixing patterns summarize one feature of the sexual network that links individuals to their own sexual partners and to their partners' partners. Thus an assortative scenario describes one in which people who, for example, acquire two new partners per year on average select partners who also acquire two new partners per year. Conversely, a disassortative scenario would be one in which people with two new sexual partners per year would select only partners who acquire either strictly greater than or less than two new partners per year. Results from simulation studies that compared the implications of strongly assortative versus disassortative and random mixing patterns between sexual activity groups for the spread of sexually transmitted infections (STIs) and HIV have fairly consistently shown higher endemic levels associated with both disassortative and random mixing (Garnett and Anderson 1993; Boily and Masse 1997; Hyman and Stanley 1988; Anderson et al. 1990; Morris 1995; Sattenspiel et al. 1990; Gupta et al. 1989). Under assortative mixing patterns, the virus tends to move gradually from one sexual activity group to the next, characterized by a multipeaked HIV incidence curve with sequential waves of infection that correspond to emerging within-group epidemics (Gupta et al. 1989; Anderson et al. 1990; Anderson 1992).

Three observations suggest that the effect of assortativeness in mixing patterns between sexual activity groups on the course of an HIV epidemic may be incompletely described in the existing literature. First, in a simulation of the effect of patterns of mixing between groups defined by their sexual preference (heterosexual males, females, bisexual males and homosexual males) Morris (1995) clearly illustrated that the association between assortative mixing and disease prevalence varies according to the prevailing rates of partner change. She compared scenarios in which homosexual men acquired 25 partners per year on average to those in which homosexual men acquired an average of only partners per year to demonstrate an interaction effect. Results showed that when the rate of partner change was high, disease prevalence under assortative mixing was consistently lower than that produced with random mixing over the course of a 50-year simulation period. However, the prevalence produced by the two mixing scenarios tended to converge over time. In contrast, when the rate of partner change was low, assortative mixing produced greater disease prevalence relative to random mixing in the early years of the epidemic, but the prevalence curves eventually cross to yield a lower prevalence under assortative mixing in the latter years.

Second, recent work using mathematical simulation to assess the sensitivity of HIV spread in China to variations in the biological and behavioral parameters indicated that a decrease in assortativeness is not universally associated with higher endemic levels of HIV prevalence (Merli et al. 2006). That study compared two highly assortative mixing scenarios, one marked by "perfect assortative" mixing where all sexual partnerships were formed within each sexual activity group defined by the rate of partner change and the other a "99% assortative" scenario in which 99% of partnerships were formed within the sexual activity groups and the remaining 1% were formed disassortatively across groups. Simulation results indicate that the perfect assortative scenario may be associated with higher endemic HIV prevalence relative to the 99% assortative scenario, especially when the average rate of partner change in the population is low.

Third, most existing research on the sexual behavior determinants of HIV spread and the influence of sexual mixing patterns in particular has focused on high-risk population subgroups display high rates of sexual partner change. One simulation of HIV spread among a population of MSMs empirically identified average rates of partner acquisition of 8.8 new partners per year (Anderson, Gupta and Ng 1990), while Morris' study of sexual preference mixing considered a high of 25 partners per year for MSM's and a low of two partners per year (Morris 1995). Another study that sought to simulate the role of sexual mixing patterns between sexual activity groups in producing HIV epidemics in Africa lacked empirical data to inform the rates of sexual partner change (Anderson et al. 1991). The authors instead employed an assumed average rate of 3.4 new partners per year. Assortative mixing patterns were multipeaked and produced smaller epidemics overall relative to disassortative mixing, but the authors did not consider how their assignment of the average rate of partner change impacted their conclusions surrounding mixing patterns.

More research is needed to understand the dynamics of heterosexual HIV transmission in general populations that may display rates of sexual partner change that are vastly different from those employed in previous simulation studies. Table 1 shows the average number of sexual partners per year estimated with several nationally representative surveys of sexual behavior. The Chinese Health and Family Life Survey (CHFLS) collected over the period 1999 to 2000 indicates that Chinese males ages 20 to 64 reported an average of 1.13 sexual partners over the past twelve months while females reported 0.94 partners on average. The Demographic and Health Survey (DHS) for Kenya (2003) indicates 1.06 partners in the past year for males ages 15 to 54 and 0.88 partners on average for females ages 15 to 49. The DHS for Uganda and Zambia and the 1992 National Health and Social Life Survey (NHSLS) conducted in the United States indicate average reported numbers of sexual partners in the past twelve months well under two for both males and females. While the data presented in Table 1 is not equivalent to the rate of partner change (this would require that all reported partners were *new* partners in the past twelve months) they support the notion that the rates of partner change simulated in previous research are not generalizable to the sexual behavior observed in general populations currently believed to be at risk for HIV. Because some proportion of each population most certainly retains the same partner(s) from one year to the next, the numbers in the last column of Table 1 represent high estimates of the rates of partner change. That in all cases the high estimate remains lower than the rates of partner change simulated in previous research further motivates the need for additional simulation work under comparatively lower rates of partner change.

This paper seeks to test whether the impact of sexual mixing patterns on the spread of HIV varies according to the prevailing rates of sexual partner change in a population where heterosexual contact is the dominant mode of transmission. I simulate HIV spread in two hypothetical populations, one with the relatively high rate of partner change measured among MSMs and utilized in Anderson's previous simulation studies (Anderson et al. 1990), and the other with a comparatively low rate of partner change as has been estimated recently for China's general population (Merli et al. 2006). We have already seen that existing research points to disassortative mixing patterns producing larger epidemics relative to assortative mixing under high rates of partner change. Any indication that disassortativeness is instead associated with lower population-level HIV incidence when the prevailing rates of partner change in the population are relatively low supports the notion of an interaction effect.

A possible interaction between the rate of partner change and prevailing sexual mixing patterns may influence which population subgroups are most at risk for HIV infection. To test whether this is the case, I examine the simulated HIV incidence by population subgroup and compare the contribution of each subgroup to the overall HIV incidence under both rate of partner change scenarios and with various degrees of assortativeness in sexual mixing patterns. Differences in the impact of HIV on population subgroups holds important implications for the design and success of targeted prevention and intervention campaigns.

Finally, I consider the contribution of a third important determinant of the sexual transmission of HIV, the underlying probabilities of transmission per sexual contact, in producing the interaction between rates of partner change and patterns of sexual mixing between population subgroups. The magnitude of population HIV epidemic differences have been partially attributed to disparities in the sexual transmission probabilities (Oster 2005; Auvert et al. 2001). Consideration of the interaction between the two behavioral parameters addressed here must be assessed in the context of the several factors that enhance or suppress those transmission probabilities.

The discussion and conclusions section of this paper reflects on the implications of these finding for developing priorities for data collection on sexual behavior and sexual mixing patterns, for the development of targeted intervention programs, and for assessing the predicted impact of those interventions within the context of a given sexual behavior regime.

METHODS

Macrosimulation Model

To simulate the effect of sexual mixing patterns on the spread of HIV under both high and low rate of partner change scenarios, I employ a modification of a biobehavioral macrosimulation model first developed by Palloni and Lamas (1991)[2]. As a macrosimulation model, it deals with population aggregates, partitioning the population into homogeneous subgroups based on gender, age, and the annual rate of sexual partner change. Figure 1 illustrates the partitioning of the simulated population into the relevant subgroups. First males and females are assigned based on a predetermined age and sex distribution of the population. Subsequently, the population of males and the population of females are partitioned into six sexual activity classes, each of which is homogeneous with respect to the rate of partner

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[2] A complete description of the model can be found in Palloni and Lamas (1991) and Palloni (1996). Provided here is a brief description of the major components of the model and of modifications made specific to these analyses.

change[3]. Sexual activity class 1 has the lowest rate of acquisition of new partners, while sexual activity class 6 is assigned the highest rate of partner change.

[Figure 1]

The macrosimulation model generates a cohort population projection to follow the population subgroups through three states: healthy, HIV infected but asymptomatic, and symptomatic AIDS. It models transitions between these three states and from each of these states to death. Figure 2 illustrates the state space for the simulation model.

[Figure 2]

λ_1 represents the force of HIV infection and determines the proportion of the population that will become HIV infected with each projection cycle (in this case, simulation year). λ_2 represents the force of transition from the asymptomatic HIV seropositive state to symptomatic AIDS. μ_1, μ_2, and μ_3 are the forces of mortality for those who are healthy, HIV infected but asymptomatic, and symptomatic AIDS respectively.

λ_2, the rate of transition from HIV seropositive but asymptomatic to the symptomatic AIDS state, is entirely defined by the incubation function of HIV. Previous research has shown that both Weibull and gamma distributions are well suited to describe the HIV incubation function (Cooley et al. 1996; Anderson and May 1991). This model employs a Weibull distributed (shape parameter=5) incubation function in operationalizing $\lambda_{2,}$ corresponding to a median incubation time of nine years. The choice of the Weibull distribution imposes the assumption that all individuals with HIV who do not first die of another cause will eventually convert to AIDS as the rate of transition tends toward infinity.

λ_1 describes the rate at which individuals in the population transition from the healthy

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[3] For simplicity, the model imposes the assumption that at the outset of the simulated period, the distribution of individuals into sexual activity groups is constant with age.

state to the HIV infected but asymptomatic state. When sexual transmission is the sole means of spread, λ_1 may be defined as a function with two components: the probability that an individual has sexual contact with an infected partner and the probability that HIV is transmitted during a sexual contact. Because λ_1 is largely determined by the rate of partner change, the sexual mixing patterns, and any interaction between the two, it is the transition of greatest consequence for the analysis presented here.

To explicitly model the effect of different sexual mixing patterns, I have expanded the Palloni and Lamas model to include a sexual mixing matrix that defines the rules of contact between the sexual activity classes. I follow the method outlined by Anderson, May, Ng and Rowley (1992) which describes the network of contacts within a population through an NxN stochastic mixing matrix $\{ p(s,i,j)\}$, where $p(s,i,j)$ is a discrete probability function that specifies the proportion of partners from group j among the total partners of an individual of sex s in group i. That function has the properties:

$$0 \leq p(s,i,j) \leq 1 \qquad (1)$$

$$\Sigma_j\, p(s,i,j) = 1 \qquad (2)$$

The mixing function in the two sex model must also satisfy the requirement that the number of females in sexual activity class j that are partners of males in class i must be identically equal to the number of males in class i who are partners of females in sexual activity class j. What Anderson and colleagues have termed the class-specific “sum rule” is expressed by equation 3 below:

$$c(s,i)N(s,i)p(s,i,j) = c(s',j)N(s'j)p(s',j,i) \qquad (3)$$

Where apostrophes are used to denote the opposite sex, $c(s,i)$ is the rate of partner change for a person sex s in sexual activity class i, and $N(s,i)$ is the size of the sex- and class-specific group.

In order to maintain consistency in the heterosexual simulation model – to ensure that equation three is satisfied – the rates of partner change and the sexual mixing matrix are initially specified only for females. Sexual mixing probabilities for males are then calculated based on the distribution of females by sexual activity class and the matrix of mixing probabilities for females, subject to constraints (1) through (3).

Adding partner selection probabilities from the mixing matrix to the age preferences in the Palloni and Lamas model yields the age- and sexual activity class-specific probability of an individual entering a sexual relationship with an HIV-infected partner given by:

$$IP(s,x,i,j) = 1-[1-H(s',x,j)]^{c(s,i)*p(s,i,j)} \tag{4}$$

If s refers to females then $IP(s,x,i,j)$ is the probability that a female age x in class i has a sexual relationship with an infected male partner in group j; $H(s,x,j)$ is the weighted proportion of males in class j and within the age preferences for a female in class i that are HIV-infected; $c(s,i)$ is the rate of new partner acquisition for an individual in class i; and $p(s,i,j)$ is the probability that a female in class i selects a male partner from class j. From equation 3, it is clear that the probability that an individual has sexual contact with an infected partner is wholly determined by the HIV prevalence among potential partners, the individual's sexual behavior as defined by the number of new partners per year, and the sexual mixing matrix that describes the likelihood that an individual selects a partner from each of the sexual activity classes.

The probability that an individual will acquire HIV within a unit of time is closely related to the probability of entering a relationship with an infected partner, but is further determined by that individual's frequency of coitus and the per coitus infectivity of HIV. Because HIV is most infections in the period immediately following HIV seroconversion and in the time following the onset of symptoms of AIDS (Pilcher et al. 2004; Royce et al. 1997; Klausner and Kent 2004; Ambroziak and Levy 1999), the model imposes the assumption that HIV is trebly infectious in the year following seroconversion and after transitioning to symptomatic AIDS. *T(s,x,i,j)* is the probability that HIV is transmitted to a person sex *s* and age *x* in sexual activity class *i* through sex with a opposite-sex partner in class *j* and is given by:

$$T(s,x,i,j) = 1-\{1-H(s',x,j)*[1-(1-\beta_s)^{A(i)}]\}^{c(s,i)*p(s,i,j)} \tag{5}$$

where *A(i)* is the average number of coituses for an individual in class *i* with each sexual partner; β_s is the per coitus transmission probability of an individual of sex *s* contracting HIV from an opposite sex partner; and *H(s',x,j)*, *c(s,i)* and *p*(s,*i*,*j*) are as defined in equation 4.

Model Inputs

Rate of Partner Change

In order to define the two rate of partner change scenarios to be simulated, data have been accessed from two sources. The first represents a high rate of sexual partner change and comes from a sexual behavior survey conducted among MSMs in England and Wales during the period from February1986 through January 1987. These data were employed by Anderson and colleagues (1990) to describe the impact of sexual mixing patterns on the spread of HIV in their one-sex simulation model.

The second rate of partner change scenario comes from the Chinese Health and Family Life Survey (CHFLS) (PIs: William Parish and Edward Laumann, University of Chicago), a sexual behavior survey of 3,821 adults between the ages of 20 and 64 sampled from China's general population in 1999 and 2000. Unfortunately, because the CHFLS included only a question on the number of partners in the past 12 months and did not specifically ask about the number of *new* partners in the past 12 months (a data point that is required in order to directly measure the rate of partner change), the rate of partner change is instead estimated based upon information collected on sexual partners in the lifetime (Merli et al. 2006). The total reported lifetime partners are divided by the years from reported sexual debut up to the survey date for each individual subject. The individual-level estimates are then averaged using survey weights to obtain an estimate of the average annual rate of partner change for the population.

Table 2 provides the population mean and sexual activity class rates of partner change from the MSM data cited in Anderson et al (1990) and from the CHFLS. These population distributions by sexual activity class and the sexual activity class-specific mean rates of partner change are utilized as inputs to the macrosimulation model. The overall mean rate of partner change in the MSM data to represent a high rate of partner change is 8.81 new partners per year and is substantially greater relative to the average of only 0.29 new partners per year obtained based on the CHFLS.

The proportions of the population that fall into each sexual activity class according to the MSM data are taken directly from the data table provided by Anderson et al (1990: Table 1, p.423). According to this source, 57% of MSMs fall into sexual activity class 1 and have an average annual rate of partner change of 0.45 new partners per year. 14% of MSMs are in class 2 with an average rate of partner change of 3.2 new partners per year. Classes 3 and 4 contain 10% and 8% of the MSM population studied with average rates of partner change of 7.02 and 13.84 new partners per year respectively. The two sexual activity classes with the highest rates of partner change according to the MSM data, classes 5 and 6, contain 7% and 4% of the population respectively. The average rate of partner change for those in class 5 is 43.6 new partners for year and for class 6 is 81.23 new partners per year.

To define the sexual activity classes based on the CHFLS data, I have constrained the distribution of the simulated population by sexual activity class to be very similar to the distribution specified by Anderson et al. for the MSM data. In doing so, I ensure that any changes in the simulated spread of HIV associated with a shift in the rate of partner change scenario is wholly attributable to the rate of partner change and not to a shift in the population distribution by sexual activity class.

Under the low rate of partner change scenario defined using the CHFLS, class 1 has an average rate of partner change of 0.07 new partners per year, class 2 has 0.16, class 3 has 0.26, and class 4 has 0.41 new partners per year on average. The two sexual activity classes with the highest rates of partner change under the CHFLS scenario, classes 5 and 6, have respectively 0.96 and 2.51 new partners per year on average.

Sexual Mixing Patterns

Empirical data on sexual mixing patterns are not widely available, but the value of data on this key determinant of the sexual spread of HIV is increasingly recognized and several surveys that aim to measure sexual mixing patterns have been recently fielded or are in the planning stages. In the absence of empirical data, I have chosen to represent sexual mixing patterns between sexual activity classes along the continuum of assortativeness ranging from nearly perfectly assortative, with 99% of partnerships formed within each sexual activity class, to nearly perfectly disassortative with only 1% of partnerships formed within each sexual activity class. Once empirical data on sexual mixing patterns do become available, they can be compared to results produced along this continuum in order to gain preliminary insights into their implication for the sexual spread of HIV.

In order to represent the range of sexual mixing patterns used in these analyses, I have adopted the concept of "restricted assortative" mixing. In these types of scenarios a given proportion of each sexual activity class is assumed to mix assortatively with partners in that class. The remaining partners are selected from the other five activity classes. The "restricted assortative" mixing pattern is represented by a matrix in which the probability of selecting a partner within one's own sexual activity class is constant across classes ($p(s,i,j) = \gamma$ for all $i=j$). The remaining 1- γ proportion of each class' partnerships is distributed across the remaining sexual activity classes with those classes that are closer to the reference class in terms of rate of partner change preferred to those classes that are more distant (Merli et al. 2006).

Infectivity

To test the sensitivity of the effects of sexual partner change rates and mixing patterns on HIV spread to changes in the biological parameters that impact HIV transmission, simulations are obtained while varying the per coitus heterosexual transmission probabilities. Consistent with estimates obtained from longitudinal studies of HIV serdiscordant couples, the baseline per coitus infection probabilities are set to .0009 per contact for female to male transmission and .0015 per contact for male to female transmission (Mastro and deVincenzi 1996). The presence of STI comorbidities enhance the per coitus transmission probabilities by reducing immune function, increasing viral shedding in the HIV-infected partner, and providing an efficient path for the virus to enter the body in the susceptible partner (Flemming and Wasserheit 1999). Simulations are run for a population in which 4% of adults are assumed to be currently infected with an STI, corresponding to the proportion of adults testing positive for gonorrhea, chlamydia, or trichomoniasis based on the urinalysis that accompanied the CHFLS. Those STIs are modeled with an average per coitus infectivity enhancement factor of four, consistent with the results of population-based studies of the effects of STI comorbidities on the sexual transmission of HIV (Røttingen et al. 2001). To test the impact of changes in the average HIV transmission probabilities experienced in a population, the simulation results obtained with 4% prevalence of comorbid STIs are compared to those obtained assuming an arbitrary increase in the prevalence of STIs to 20%.

Other Inputs

A hypothetical population of 200,000 persons at the outset is simulated as they move through the three HIV-related states over a period of 50 years according to the annual transition rates determined by the biological and behavioral input parameters. The initial population is defined using the age and sex distributions from China's 1990 census. HIV is introduced in simulation year zero by assigning minimal HIV prevalence (0.001%) to the sexual activity class with the highest rate of partner change (class 6). The other five sexual activity classes are assigned zero prevalence at the outset and are thus exposed to HIV only through their sexual partnerships formed during the simulation period. Partners are selected according to the age preferences of partners determined based on existing partnerships reported in the CHFLS. Age-specific mortality from causes other than HIV corresponds to mortality rates from China's 1990 census and HIV/AIDS related mortality is determined by the incubation function built into the model.

RESULTS

Overall HIV Incidence

Panel 1 presents the annual adult HIV incidence in the simulated population under the two rate of partner change scenarios (high and low) and the 11 sexual mixing scenarios (ranging from 99% to 1% assortative). In the high rate of change scenarios displayed in Chart A, the simulation results confirm the pattern described in previous literature on the effect of sexual mixing patterns. The 99% assortative scenario is characterized by a multi-peaked HIV incidence curve, a maximum annual HIV incidence just under 6,000 new infections, and an incidence curve that flattens out to just under 2,000 new infections per year after approximately 37 simulation years. As expected, decreasing the proportion of sexual partnerships formed assortatively from 99% to 90%, results in a change in the shape of the HIV incidence curve as well as a larger epidemic overall. The 90% assortative curve is marked by fewer peaks, a maximum annual incidence of about 9,000 new HIV infections per year and an eventual flattening out of the curve at around 3,000 new HIV cases per year. Further decreases in the proportion of partnerships that are formed assortatively continues to yield higher peak and endemic incidence, although the relative increase with each additional simulation becomes smaller as mixing becomes more disassortative. The final simulation characterized by only 1% of partnerships formed within sexual activity classes, reveals a somewhat slower acceleration relative to the more assortative patterns but higher peak prevalence at greater than 18,000 new HIV infections in simulation year six and an endemic annual incidence at around 4,000.

[Panel 1]

Chart B displays the results of simulations that are identical to those presented in Chart A, with the sole exception that the class-specific rates of partner change are decreased to be consistent with those estimated from the CHFLS. The y-axis on Chart B is reduced by a factor of ten relative to Chart A so that the effect of changes in the sexual mixing pattern may be clearly detected even with the substantial decrease in annual incidence. The 99% assortative scenario shows a peak HIV incidence of approximately 950 new infections in simulation year eight, dropping down to close to 200 new infections in simulation year 15 and then leveling to an annual incidence around 400. Decreasing the proportion of partnerships that are formed assortatively with respect to sexual activity class to 90% reveals a deviation in the relationship noted in Chart A under high rates of sexual partner change. Similar to Chart A, the 90% assortative mixing scenario in Chart B continues to show multiple peaks and a higher endemic annual adult HIV incidence relative to the 99% scenario. However, contrary to the association in Chart A, the 90% assortative scenario in Chart B is characterized by a slightly lower peak annual incidence relative to the 99% assortative mixing scenario. As the percentage of partnerships formed assortatively in the low rate of partner change scenario continues to decrease to 80%, 70%, 60% and then 50%, this pattern continues. Decreasing assortativeness is associated with lower peak annual incidence but eventually flattens out to higher endemic incidence during the simulation period. When the percent mixing assortatively is decreased further to 40% however, the pattern further deviates from what was observed under high rates of partner change. Under low rates of partner change, the 40% assortative mixing scenario reveals both a lower peak annual incidence and a lower endemic incidence relative to the 50% assortative scenario. This latter pattern continues as the percent of partnerships formed assortatively declines from 40% through to 1%. While the 1% assortative scenario was associated with the highest peak and endemic incidence levels in Chart A, in Chart B it produces by far the smallest epidemic producing no more than ten new HIV infections during any single simulation year.

Panels 2 and 3 illustrate the sexual activity class composition of incident HIV cases simulated in year 30. Panel 2 displays the number of incident HIV cases contributed by each of the six sexual activity classes to the overall adult HIV incidence simulated for year 30. Under the high rate of partner change scenario shown in Chart C, overall incidence ranges from about 1,800 new HIV cases in the 99% assortative mixing scenario to just over 3,700 new HIV cases in the 1% assortative mixing scenario. Chart C clearly demonstrates that increases in the number of new infections to individuals in sexual activity class 1, the class with the lowest rate of new partner acquisition, accounts for the majority of the increase in incidence associated with decreasing assortativeness in the mixing pattern. Chart E in Panel 3 confirms that association. It shows the proportional contribution of each of the six sexual activity classes to the overall adult HIV incidence in simulation year 30. As mixing becomes less assortative, new HIV cases in sexual activity class 1 make up a growing proportion of all incident cases, from 5% in the 99% assortative scenario to greater than 50% with 1% assortative mixing. The proportional contribution of each of the remaining five sexual activity classes decreases as mixing becomes less assortative.

[Panel 2]

[Panel 3]

The sexual activity class composition of the adult HIV incidence pattern simulated for year 30 is vastly different when the rate of partner change is low. Chart D shows that the annual HIV incidence begins at just under 400 new HIV cases under the 99% assortative mixing scenario, increasing to near 750 incident cases in the 60% assortative scenario, and declining thereafter to only 7 new adult HIV cases in simulation year 30 in the 1% assortative mixing scenario. Chart D seems to indicate that through all of the assortative mixing scenarios, the bulk of simulated new HIV cases occur in sexual activity classes five and six, the two classes with the highest rates of partner change. Chart F in Panel 3 confirms that observation. Classes five and six account for more than half of new infections in all assortative mixing scenarios ranging from 98% of incident cases in those two classes under 99% assortative mixing to 54% of new HIV cases in classes five and six with only 1% of partnerships formed assortatively. As was the case in the high rate of partner change scenario presented in Chart E, Chart F shows that the proportional contribution of the class with the lowest rate of partner change, class 1, to the overall HIV incidence increases as mixing becomes less assortative. Class 1 contributes less than 1% of incident cases in the most assortative scenario and more than 15% of incident cases in the least assortative scenario.

An interesting pattern emerges in the proportional contribution of sexual activity classes to the overall adult HIV incidence displayed in Chart F. The proportion of new infections attributable to the two highest sexual activity classes, five and six, declines as we move along the sexual mixing continuum from 99% assortative to 60% assortative mixing. After that point, the proportion of incident cases that are from class six increases until mixing is 20% assortative. The proportion of new HIV cases from sexual activity class six then declines again in the 10% and 1% assortative scenarios, although caution must be taken in interpreting this result as the overall population incidence associated with these scenarios is extremely small (see Chart D). The inverted U-shape produced by the proportion of incident cases from class six over the first nine sexual mixing scenarios with the inflection point between 60% and 50% assortative mixing corresponds closely to the point at which the strong evidence of the interaction effect was identified in Panel A. Thus while in the high rate of partner change scenarios, the increasing incidence associated with decreasing assortativeness in mixing patterns was largely due to incidence in the *lowest* sexual activity class, changes in the shape of the epidemic curve are driven by the rate of infections in the *highest* sexual activity class when the rate of partner change is low.

To assess the impact of changes in the underlying heterosexual transmission probabilities, the proportion of the population assumed to be infected with STI comorbidities is increased from 4% to 20%, resulting in enhancement of infectivity rates. Chart G in Panel 4 again shows the baseline simulations under the low rates of partner change determined from the CHFLS and assumed 4% prevalence of STI comorbidities, identical to the simulation results displayed in Chart B. Chart H presents the results of simulations conducted under low rates of partner change and an assumed STI prevalence of 20%. As expected, the resulting enhancement to the sexual transmission probabilities produces higher annual adult HIV incidence relative to Chart G. The 99% assortative scenario shows multiple pronounced peaks with a maximum incidence of nearly 1,400 new HIV infections in simulation year six and a leveling off around 700 new cases annually after simulation year 30.

Close examination of the relationship between assortativeness in sexual mixing patterns and the adult HIV incidence curve in Chart H reveals a notable change in the interaction effect identified in Panel 1 that is the direct result of enhancing the sexual transmission probabilities. When the proportion of partnerships formed assortatively declines to 90% in Chart H, the pattern becomes more similar to that observed in Chart A under the high rates of sexual partner change. The peak annual HIV incidence is now higher (nearly 1,600 new cases in simulation year 14) compared to that simulated with 99% assortative mixing and the leveling off occurs higher at around 1,100 incident cases per year. This relationship between assortativeness in sexual mixing patterns and HIV incidence, very similar to that observed with high rates of partner change, continues to be observed as the percent mixing assortatively declines through 30%. But as the scenarios further decline in assortativeness, the relationship between mixing patterns and annual HIV incidence again shifts to more closely resemble the less assortative scenarios observed under low rates of partner change in Chart B. The 20% assortative scenario shown in Chart H has a lower peak incidencre relative to the 30% scenario as well as a lower endemic incidence. As the percent mixing assortatively continues to decline through 20%, 10% and finally 1%, the size of the epidemic decreases precipitously such that the 1% assortative scenario shows a peak annual incidence of only 1,100 new infections around simulation year 28.

DISCUSSION AND CONCLUSIONS

An HIV epidemic is the product of the many biological and behavioral factors that determine the rate of disease transmission in a population. A great deal of existing research on the behavioral parameters that influence HIV spread has focused on each of those determinants individually, omitting discussion of any interaction effect that may substantially alter the associations described. The analyses presented in this paper systematically assess the interaction between two of the most important behavioral determinants of HIV spread, the rates of sexual partner change in the population and the prevailing patterns of sexual mixing between population subgroups defined by the rates of partner change. This interaction effect is powerful and has important implications for the population adult HIV prevalence—both the magnitude and the shape of the epidemic curve and the degree to which sexual activity classes (risk groups) are exposed to HIV infection.

Previous research has shown that larger epidemics are associated with disassortative mixing patterns and have done so by simulating the spread of HIV in high-risk populations characterized by high rates of sexual partner change. In assortative mixing scenarios, sexual contacts between groups are infrequent and infection remains concentrated in the highest sexual activity classes. As mixing becomes less assortative, partners in other sexual activity classes are exposed, accelerating the spread of disease in the population. The results presented above confirm this association in populations with high rates of partner change, but indicate that the direction of the association is not constant across all rate of partner change scenarios. When the rate of partner change is relatively low, as is estimated based on data obtained in the CHFLS, patterns of disassortative mixing yield smaller epidemics. For an epidemic to be sustained in a population, the reproductive rate of infection (the average number of secondary cases produced from a given infection) must necessarily be greater than one (May and Anderson 1987). When the rate of partner change is sufficiently low and those with multiple partners do not mix among themselves (mixing is disassortative) the average individual's probability of contact with an infected partner is low such that the epidemic fails to reproduce at a rate large enough to sustain itself.

The explanation for the interaction becomes clearer when HIV spread is evaluated in the simulated population subgroups. With high rates of change, the resulting HIV incidence in the highest sexual activity class is large and steady regardless of the sexual mixing pattern selected. The increase in population HIV incidence observed with decreasing assortativeness is clearly due to an increase in incidence among the lower sexual activity classes who are less shielded from infected partners when mixing becomes disassortative. But with low rates of partner change, decreasing assortativeness eventually yields a failure to sustain HIV incidence among all sexual activity classes, including the one with the highest rate of new partner acquisition. Indeed, it is the rate of new infections in the most sexually active class that drives the overall population incidence curve across the continuum of sexual mixing scenarios.

These findings underscore the necessity of understanding both the rates of partner change in a population and the prevailing sexual mixing patterns in order to more precisely identify the groups most at risk for acquiring HIV. In the high rate of partner change example above, highly assortative mixing means that those with more rapid rates of partner change are most at risk of acquiring HIV infection. But diassortativeness in the sexual mixing pattern under precisely the same rates of partner change leads those with the lowest rates of partner change to constitute a major at-risk group. In contrast, under low average rates of partner change in a population, the epidemic is driven and sustained by the sexual partnerships of those with the highest rates of partner change, regardless of the sexual mixing pattern. By assessing the potential for HIV spread in the context of both the rates of sexual partner change and the sexual mixing patterns between population subgroups, interventions may be developed and implemented that are expressly targeted to the epidemic dynamics at hand. In addition, one must consider the potential for changes in epidemic dynamics that may accompany any targeted intervention. Anderson et al. (1991) imagine that a program initially aimed at reducing the average rates of sexual partner change, may actually influence changes in the sexual mixing patterns as the supply and demand for partnerships shift in the population, with unintended consequences for rates of new infection.

The conclusions drawn here are limited in that they focus primarily on a single interaction between only two behavioral determinants of HIV spread. Other characteristics of a population are also important in the development of an HIV epidemic and must also be considered when evaluating the respective roles of the rate of sexual partner acquisition and patterns of mixing between population subgroups. The analyses presented above reveal that the identified interaction effect is further sensitive to changes in the underlying sexual transmission probabilities of HIV. The situation is considered where sexual transmission probabilities are enhanced by an increase in the prevalence of STI comorbidities. However, other factors not explicitly considered here also impact the sexual transmission probabilities experienced in a population. For example, male circumcision is believed to have a protective effect against female-to-male HIV transmission (Buve et al. 2001, Auvert et al. 2005) and use of antiretroviral drug therapy lowers transmission probabilities by decreasing the viral load in the HIV-infected partner (Porco 2004).

Other behavioral patterns within a population may further alter the interaction effect observed between the rates of sexual partner change and patterns of sexual mixing in the spread of HIV. Concurrency in sexual relationships, for example, has been shown to accelerate HIV spread by increasing sexual contacts within the initial highly-infectious stage of acute HIV-infection (Morris 1997; Morris and Kretzschmar 2000). Assessments of the potential for the spread of HIV in specific contexts must also consider the prevalence of concurrent sexual relationships in that population.

Despite continued calls for advanced data collection (e.g., Morris 1997), few surveys are designed to amass the data necessary to empirically estimate the sexual behavior determinants of HIV epidemics, including the rates of new partner acquisition and sexual mixing patterns. Representative population-based surveys are needed to assess not simply the total number of sexual partners of respondents per unit time, but also the number that were *newly* acquired during that time so that the rate of new partner acquisition may be estimated. This can be accomplished by assessing the beginning and ending dates for each sexual partnership, which will additionally facilitate identification of concurrent relationships. Surveys are also needed to collect data on the sexual network that defines the formation of sexual partnerships. The most resource intensive in this genre involves graphing the complete sexual network in a closed population. However, in spite of the risk of gathering some misinformation, valuable gains may be had from assessing the local network by simply asking respondents to report on the demographic, social, and sexual behavior characteristics of their partners. Such efforts will go a long way toward expanding our understanding of HIV epidemic dynamics in populations newly at risk for HIV infection and informing the design of interventions targeting those most at risk for fueling the epidemic into the future.

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Figure 1: Macrosimulation population sub-groups

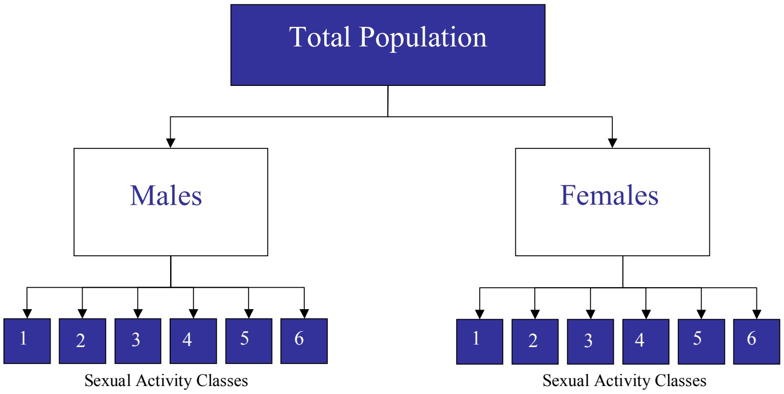


Figure 2: States and flows in the Palloni and Lamas (1991) macrosimulation model

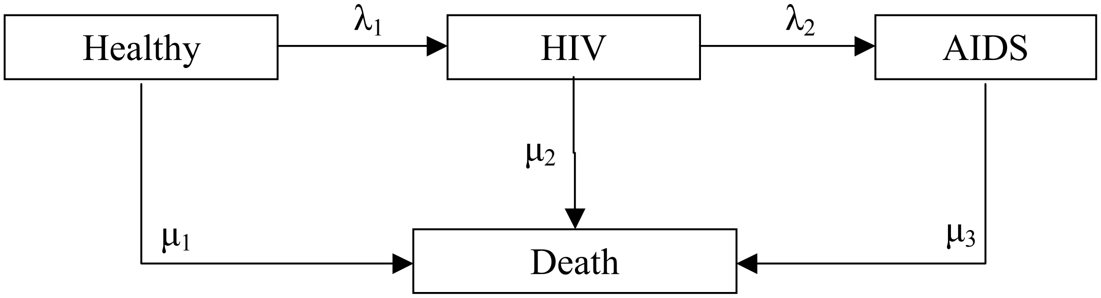


Table 1: Average total number of sexual partners in the past twelve months for males and females from selected national sexual behavior surveys.

	Population	Data source	Age range	N obs	Sexual partners past 12 months[a]
Males	China	CHFLS (1999-2000)	20-64	1540	1.13
	Kenya	DHS (2003)	15-54	2999	1.06
	Uganda	DHS (2000)	15-54	1638	1.18
	United States	NHSLS (1992) [b]	18-60	1505	1.68
	Zambia	DHS (2001-2002)	15-59	1927	1.26
Females	China	CHFLS (1999-2000)	20-64	1578	0.94
	Kenya	DHS (2003)	15-49	6770	0.88
	Uganda	DHS (2000)	15-49	6335	0.90
	United States	NHSLS (1992) [b]	18-60	1919	1.15
	Zambia	DHS (2001-2002)	15-49	6775	0.87

[a] Mean total number of sexual partners reported in the previous year weighted according to sampling probabilities.

[b] In the NHSLS, the variable for sexual partners in the past 12 months for respondents reporting greater than four partners was recorded categorically. The midpoint for each category was used in the mean reported above. Thus respondents reporting between 5 and 10 partners in the past twelve months were assigned 7.5 partners, those reporting 11 to 20 were assigned 15.5 partners, 21 to 100 were assigned 60.5 partners, and those reporting 100+ partners (the highest category) were assigned exactly 100 partners.

Table 2: Model Inputs – Sexual activity classes and rates of partner change

Sexual Activity Class	**1**	**2**	**3**	**4**	**5**	**6**
High rate of partner change scenario: MSMs (mean = 8.81 new partners/yr)						
Prop of population in class	.57	.14	.10	.08	.07	.04
Annual rate of partner change	0.45	3.2	7.02	13.84	43.6	81.23
Low rate of partner change scenario: CHFLS (mean = 0.29 new partners/yr)						
Prop of population in class	.57	.16	.08	.09	.06	.04
Annual rate of partner change	0.07	0.16	0.26	0.41	0.96	2.51

Sources: Anderson et al. (1990: Table1, p.423) and Chinese Health and Family Life Survey (2000)

Panel 1: 50-year simulated annual adult HIV incidence under high and low rates of partner change and various sexual mixing scenarios

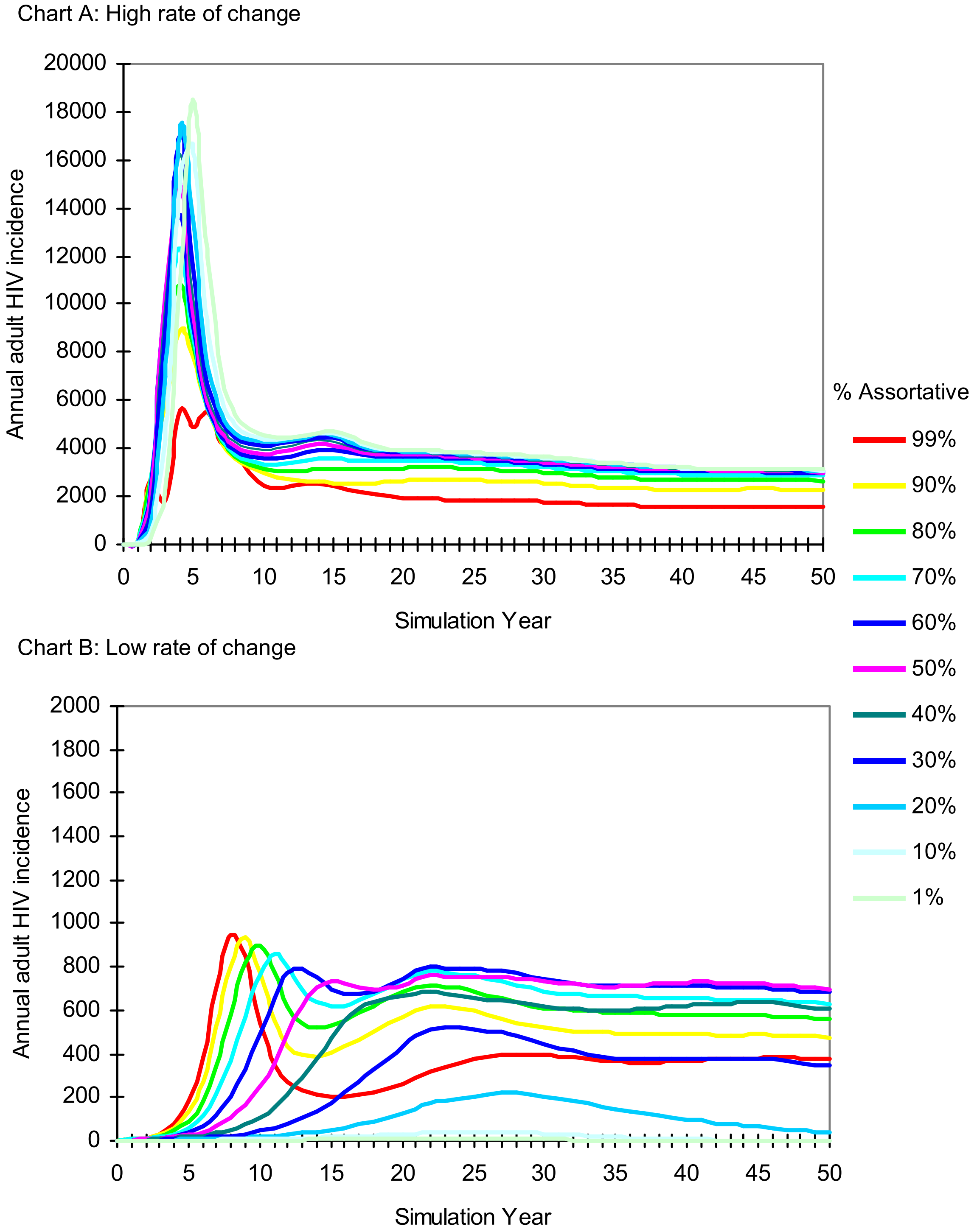


Chart A: High rate of change

Chart B: Low rate of change

Panel 2: Adult HIV incidence simulated in year 30 under high and low rate of partner change and various sexual mixing scenarios

Chart C: High rate of change

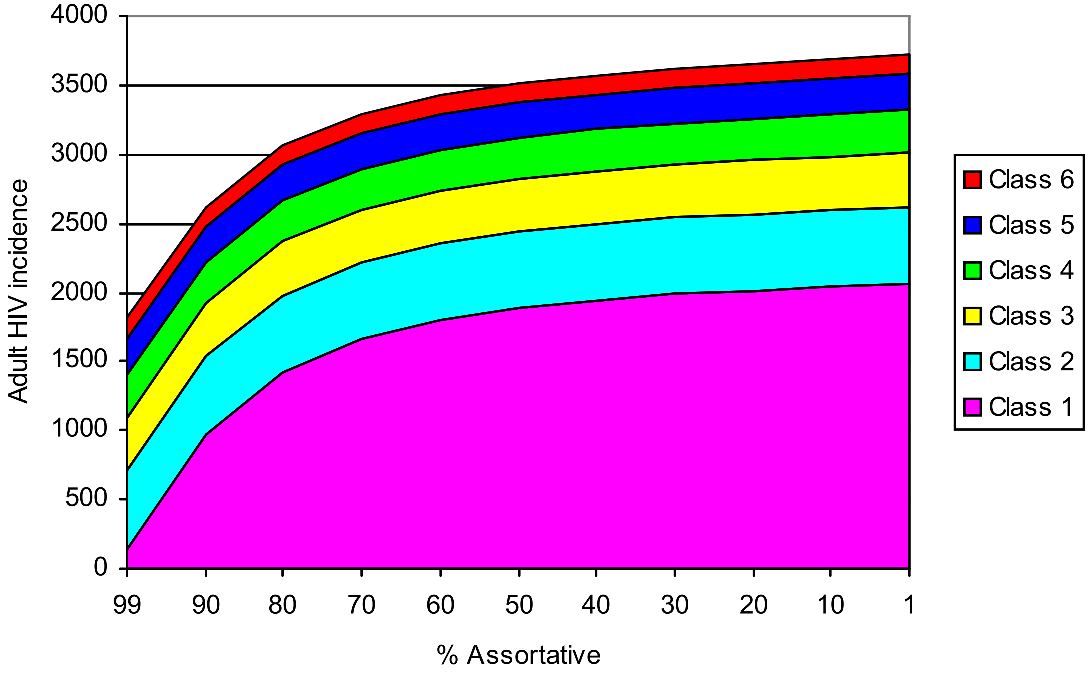
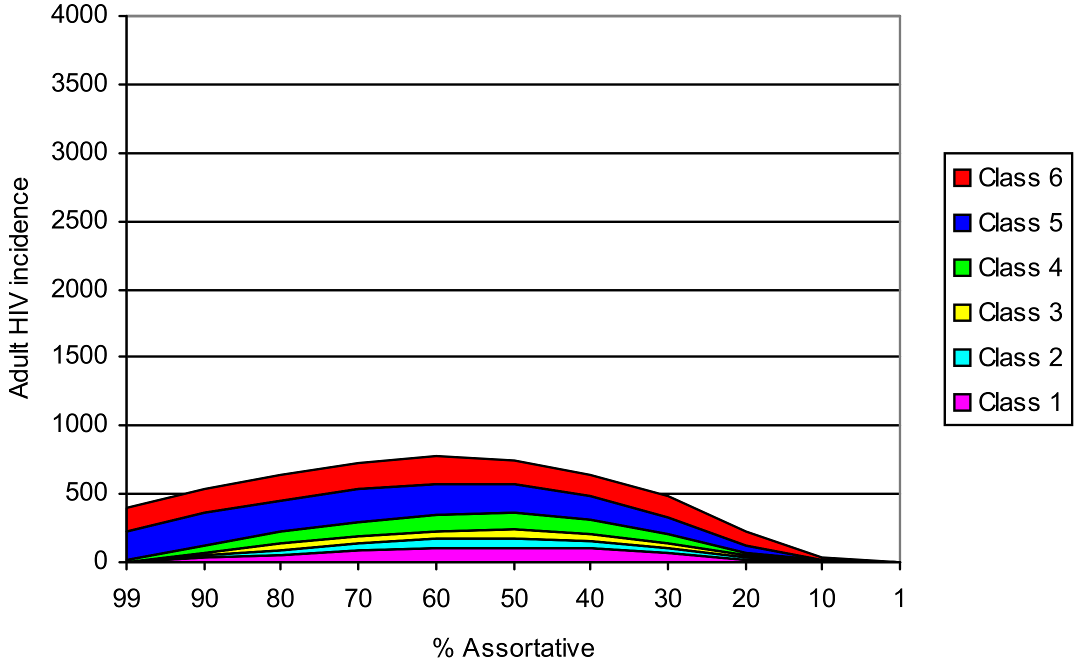


Chart D: Low rate of change



Panel 3: Proportional sexual activity class contribution to overall incidence in simulation year 30 under high and low rates of partner change and various sexual mixing scenarios

Chart E: High rate of change

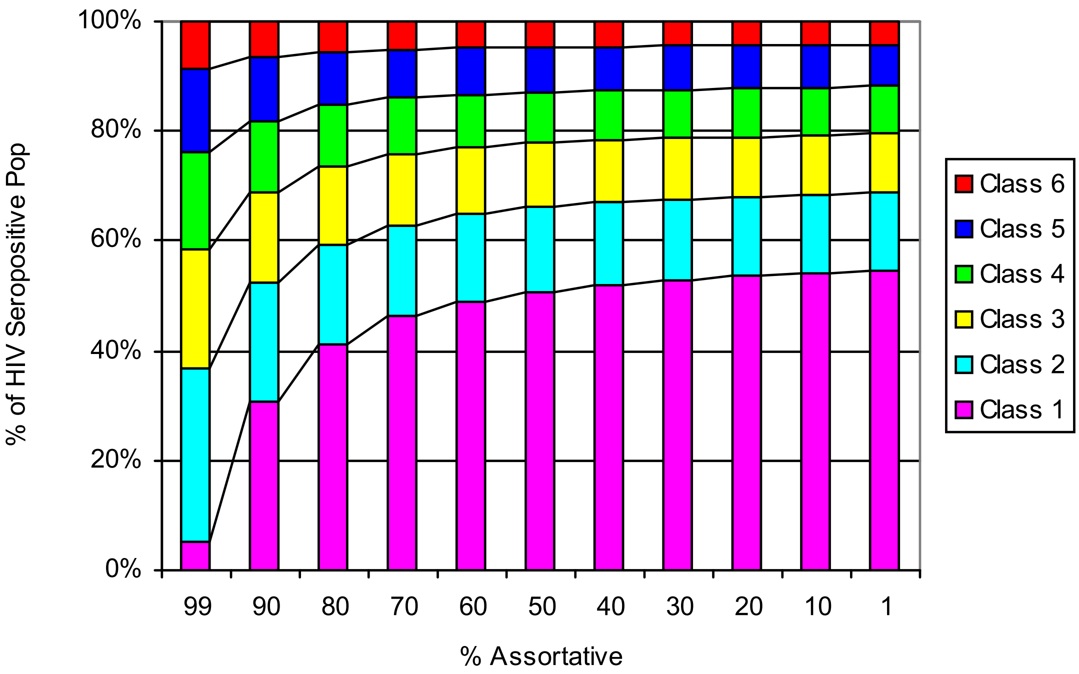
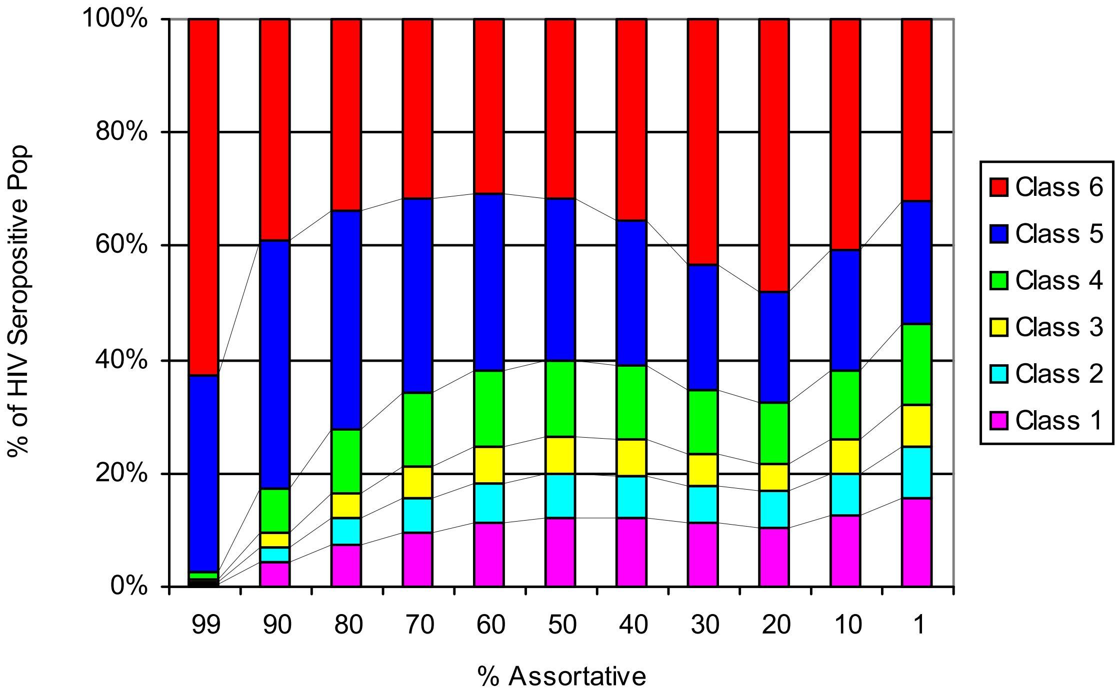


Chart F: Low rate of change



Panel 4: 50-year simulated annual adult HIV incidence under low rate of partner change, low and high prevalence of STI comorbidities, and various sexual mixing scenarios

Chart G: Low rate of change, 4% STI prevalence

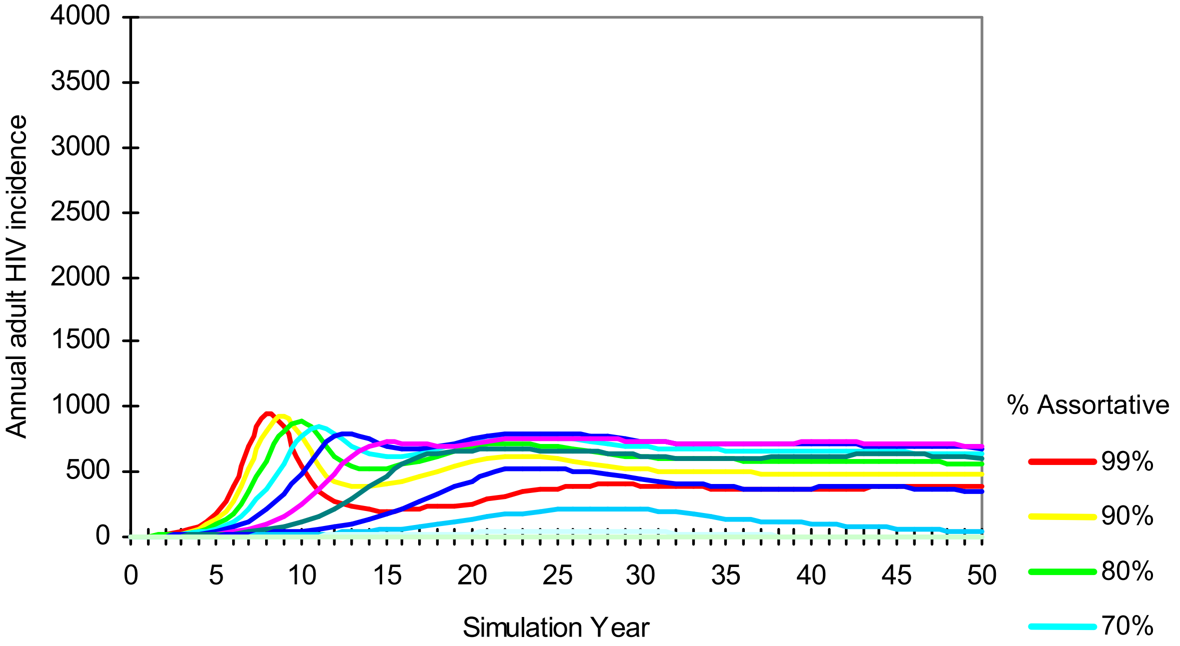


Chart H: Low rate of change, 20% STI prevalence