Published in final edited form as:
AIDS Behav. 2011 May ; 15(4): 687–692. doi:10.1007/s10461-010-9787-8.

Concurrent Sexual Partnerships and Primary HIV Infection: A Critical Interaction

Jeffrey W. Eaton,
Department of Infectious Disease Epidemiology, Imperial College London, St. Mary's Campus, Norfolk Place, London W2 1PG, UK, jeffrey.eaton08@imperial.ac.uk

Timothy B. Hallett, and
Department of Infectious Disease Epidemiology, Imperial College London, St. Mary's Campus, Norfolk Place, London W2 1PG, UK; Institute for Global Health, Imperial College London, London, UK

Geoffrey P. Garnett
Department of Infectious Disease Epidemiology, Imperial College London, St. Mary's Campus, Norfolk Place, London W2 1PG, UK; Institute for Global Health, Imperial College London, London, UK

Abstract

The combination of long-term concurrent sexual partnerships and high infectiousness early in HIV infection has been suggested as a key driver of the extensive spread of HIV in general populations in sub-Saharan Africa, but this has never been scientifically investigated. We use a mathematical model to simulate HIV spreading on sexual networks with different amounts of concurrency. The models show that if HIV infectiousness is constant over the duration of infection, the amount of concurrency has much less influence on HIV spread compared to when infectiousness varies over three stages of infection with high infectiousness in the first months. The proportion of transmissions during primary infection is sensitive to the amount of concurrency and, in this model, is estimated to be between 16 and 28% in spreading epidemics with increasing concurrency. The sensitivity of epidemic spread to the amount of concurrency is greater than predicted by models that do not include primary HIV infection.

Keywords

Concurrency; Primary HIV infection; Mathematical model; Sexual network; Sexual behavior

Introduction

Concurrent sexual partnerships, or partnerships that overlap in time, may be among the key drivers of the severe HIV epidemics in sub-Saharan Africa [1–3]. Concurrency can increase the number of partners exposed to infection for a given number of lifetime partners and reduces the time between when an individual is infected by one partner and exposes another partner to transmission, compared to when partnerships are 'serially monogamous', in which case the infecting partnership must end before a new partner can be exposed. This effect has

Correspondence to: Jeffrey W. Eaton.

Electronic supplementary material The online version of this article (doi:10.1007/s10461-010-9787-8) contains supplementary material, which is available to authorized users.

Europe PMC Funders Author Manuscripts

been observed in mathematical models [4–6], but not, thus far, demonstrated empirically. It has been argued that empirical evidence linking concurrency and HIV spread has remained elusive because having concurrent partners is expected to increase the risk of transmitting infection, rather than the risk of an individual acquiring infection, and because the measurement of concurrency in populations has not been contemporaneous with the rapid spread of HIV [3, 7, 8]. Existing models have been confined to studying the early growth of epidemics and used parameter values for HIV transmission that now seem unrealistically high in light of data [9, 10], which has caused some to question the generalizability of these models [11]. Nevertheless, in HIV prevention there is an increasing focus on interventions that aim to reduce concurrency [12].

It is often presumed that the impact of concurrency is increased by the short period of high infectiousness in the first few weeks of HIV infection [2, 13–16]. A brief period of high infectiousness following initial infection would make transmission more dependent on a newly-infected individual having sex with a susceptible individual shortly after his or her own infection [17–19]. It would follow that the contribution of the primary infection stage would depend on features of the sex partner network [20], including concurrency [18]. A few papers have attempted to quantify the proportion of transmissions due to primary infection [18, 21, 22], but these models have not included overlapping sexual partnerships, and hence were unable to examine the synergy between concurrency and primary infection for HIV transmission. Xiridou et al. examined the contribution of primary infection in an epidemic amongst a population of men who have sex with men using a model where individuals may have a single steady partnership and additional one-off causal contacts, finding that primary infection plays a particularly important role in transmission during one-off casual partnerships [23]. The model did not consider multiple steady partnerships at the same time, such as those suggested to be important in sub-Saharan Africa.

Recent improved estimates of HIV transmission rates during different stages of infection [19] offer an opportunity to begin to quantify the hypothesized relationship between time-varying infectiousness and concurrent sexual partnerships, which could have important implications for research in both areas. This study uses a simple mathematical model to simulate HIV spreading across sexual networks, illustrating how changing transmission probabilities over the course of an infection alters the influence of concurrency and how different types of sexual networks can affect the contribution of primary infection to HIV spread.

Methods

We replicated and then extended a mathematical model including concurrency and HIV developed by Morris and Kretzschmar [5, 24, 25]. In the model population, the total number of partnerships is held constant while more concurrency can be permitted by changing the probability that an individual already in a partnership forms a new partnership. Partner selection in the model only depends on whether an individual already has a partner, and there is no individual heterogeneity in the propensity to form sexual partnerships. Following Morris and Kretzschmar, all partnerships last for a mean of about 6.5 months (median 4.5 months) and each individual has, on average, 1.22 new sexual partners per year [5].

Eleven different levels of concurrency were simulated ranging between no concurrency (i.e. serial monogamy), and random partner acquisition (where there can be concurrency, since the probability of forming a new partnership does not depend on whether an individual already has a partner). Two measures of concurrency are reported: the first is the point prevalence of concurrency, which is the proportion of individuals that have more than one partner at a point in time [26]; the second is the κ_3 measure proposed by Morris and

Europe PMC Funders Author Manuscripts

Kretzschmar, which approximates the proportion of partnerships that are concurrent [25]. Different networks are simulated allowing for a point prevalence of concurrency ranging between 0% ($\kappa_3 = 0$) and 14% ($\kappa_3 = 0.67$). The upper end of this range is similar to estimates of concurrency point prevalence reported by men in Southern and Eastern Africa [2, 27, 28].

Three different stages of HIV infection are modeled, representing primary infection (2.9 months), asymptomatic infection (8.38 years), and symptomatic (i.e. AIDS) infection (9.0 months) [19]. Following the three stages of infection, there is a period of 10 months before death with no transmission risk due to ill health, as observed by Hollingsworth et al. [19]. Each stage and the period between infection and death allows for a different daily transmission probability, β_p, β_a, β_s, and β_0, respectively. For the "staged transmission" scenario, we set: $\beta_p = 0.0073$, $\beta_a = 0.0003$, $\beta_s = 0.0021$, and $\beta_0 = 0$ based on observed rates of transmission among sero-discordant couples in Rakai, Uganda [14, 19]. We compared this with a "constant transmission" scenario, setting: $\beta_p = \beta_a = \beta_s = \beta_0 = 0.00056$, which gives the same average transmission probability over the entire duration of infection. The total duration between infection and death is 10.2 years. Table 1 summarizes the parameter values used for the simulations.

Populations of 20,000 men and women are simulated for 250 years after the epidemic begins. The epidemic is seeded by randomly infecting 1% of the population with HIV, with each seed infection being assigned a random duration since infection. The large size of the seed avoids stochastic extinction of epidemics to ensure that outbreaks that die out indicate epidemics that would always fail to spread, rather than resulting from 'unlucky' seeding. Each scenario is simulated 100 times and the mean is reported. Software and source code for reproducing the simulations are available in the electronic material accompanying this paper.

Results

Figure 1 shows the trend in HIV prevalence over time for the staged and constant transmission scenarios at different levels of concurrency and Fig. 2 compares box plots of the final HIV prevalence in the 100 simulations of staged and constant HIV transmission risk for each level of concurrency. In each scenario, increasing concurrency increases both the growth rate of the epidemic and the endemic prevalence of HIV. However, the influence of concurrency is weaker when transmission probability is constant (Fig. 1a, 2, black boxes) than with the staged transmission (Fig. 1b, 2, red boxes). Indeed, with staged transmission, concurrency makes the difference as to whether an epidemic can spread at all—for instance, with staged transmission and up to 8% of individuals having concurrent partnerships, HIV fails to spread, but with 14% of partnerships being concurrent, HIV becomes hyper-endemic, with prevalence greater than 15%.

While the difference made by concurrency is greater in the staged transmission scenario, the endemic level of HIV prevalence is greater with constant transmission. With point prevalence of concurrency at 14%, HIV prevalence is 21% with constant transmission, but 16% with staged transmission.

In the above comparison we maintained the same average transmission probability over the duration of infection. In an alternative analysis, we kept the same endemic HIV prevalence for the serial monogamy case across simulations with constant and staged transmission. In this case, there was a similar increased importance of concurrency with staged transmissibility: with staged transmission, as concurrency increases, the endemic prevalence

ranges from 16% (serial monogamy) to 37% (with concurrency), compared to 16 and 21%, respectively, with constant transmission probabilities (see supplementary material B.1).

For the levels of concurrency where the epidemic spreads, Fig. 3 shows the proportion of transmissions that occur during each HIV infection stage once the epidemic has reached a steady state. The amount of concurrency has a strong influence on the proportion of HIV infections attributed to primary infection. For the lowest level of concurrency where the epidemic spreads (point prevalence 8%, $\kappa_3 = 0.3$), the primary, asymptomatic and symptomatic stages account for 16, 53, and 31% of transmissions, respectively. At the highest levels of concurrency (point prevalence 14%, $\kappa_3 = 0.67$), the three stages are responsible for 28, 46 and 26% of transmissions.

To assess the sensitivity of the results to the specific partnering parameters taken from Morris and Kretzschmar's simulations, we replicated the simulations using partnership parameters based on baseline data from the Manicaland HIV/STI Prevention Project in northeastern Zimbabwe [29] (see Supplementary material B.2). In baseline data adults age 15–49 reported an average of 0.78 current partnerships per person, and reported 0.59 new partners in the past year. Using these data to calculate model parameters yields an average partnership duration of 1.31 years. With these parameters, the model creates sexual networks with amounts of concurrency ranging between serial monogamy and 19% of individuals having concurrent partnerships, or κ_3 between 0 and 0.80.

The results of the simulations with these parameters are similar to when using Morris and Kretzschmar's parameters. When transmission probabilities are constant over the duration of infection, endemic HIV prevalence ranges from 15 to 26% as concurrency increases. With staged transmission probabilities infection does not spread when there is no concurrency. The lowest level of concurrency at which the epidemic spreads is when 9% of individuals have concurrent partnerships ($\kappa_3 = 0.27$). Endemic prevalence increases to 23% at the highest level of concurrency. The proportion of transmissions attributable to primary infection ranges between 15% when 9% of individuals have concurrent partnerships to 29% when 19% of individuals have concurrent partnerships. Further details are available in the supplementary material.

Discussion

This study systematically compares a constant transmissibilty model of HIV transmission to one where the transmission probability depends on the time since infection to understand how the presence of primary HIV infection affects the importance of concurrency and vice versa. The model shows that primary infection substantially amplifies the importance of concurrent sexual partnerships, and that the sensitivity of epidemic spread to the degree of concurrency is much greater than suggested by earlier models without primary infection. The reason for this powerful interaction is that the potential for transmission in primary infection is "wasted" under serial monogamy, since the newly infected individual is held in a sero-concordant partnership [30]. With concurrency, the potential for transmission in the primary stage is better realized, since the newly infected individual can also be in another partnership with an uninfected individual. With constant infectiousness, the overall spread of the virus is less dependent on onward transmission within the first few months of infection, so the delay for a new partner under serial monogamy has less effect. As illustrated through this model, exposing susceptible individuals to transmission during primary HIV infection is likely to be an important factor in creating large HIV epidemics such as those experienced in sub-Saharan Africa and elsewhere; concurrency is one efficient means of generating such exposures.

Another finding is that, at all levels of concurrency, the endemic prevalence of HIV was lower when the transmission probability varied over the course of infection compared to when it was constant. This is because, when there is a variable number of contacts per sexual partnership, adding variability in the transmission probability over the course of infection reduces the average infection probability per discordant partnership (irrespective of patterns of concurrency) [31]. The reduction in endemic prevalence associated with variable infectivity is not manifested in models that do not model partnership durations because they assume that sexual partnerships consist of a single instantaneous contact. This finding may have important implications for making predictions based on models that assume fixed infection probability per partnership.

The proportional contributions of each stage of infection in our model was calculated without a statistical fit to empirical HIV prevalence and sexual behavior data, so should not be interpreted as literal estimates of these quantities. These findings are also not directly comparable with other model estimates that do not include concurrency but do include heterogeneities in risk behavior and different patterns of partnership formation [22]. Rather, we illustrate the potential for this interaction, and how concurrency can dramatically change the importance of primary infection in a particular population where individuals have a relatively large number of short duration partnerships over their lifetime. The model also does not include possible reductions is risk behavior associated with ageing or illness, which would likely increase the relative importance of primary infection. In our simulations, and those of the Morris and Kretzschmar [5], the method of increasing concurrency also increases the variance in numbers of sexual partnerships, which could to contribute to the observed impact of concurrency on epidemic spread [13].

Concurrency is sometimes considered as an alternative mechanism to high partner change rates in high-risk subpopulations for generating a large generalized epidemic. However, this model produces HIV epidemics that grow more slowly than those observed in southern Africa, suggesting that factors not included here—in particular, small groups with greater number of sexual partners and cofactors that increase HIV transmission—also contribute to accelerating the spread of HIV [32, 33].

These results reinforce the conclusion that concurrent sexual partnerships could be an important determinant of large generalized HIV epidemics, such as those experienced in Southern and Eastern Africa. In the model with stages of HIV infection, a threshold level of concurrency was required to even create an epidemic. Small changes in the proportion of individuals having concurrent partnerships effected large differences in endemic HIV prevalence, suggesting that slight differences between sex partner networks in different settings could underlie disparate HIV epidemic levels. For example increasing from 10 to 11% of individuals having concurrent partnerships increased the mean endemic HIV prevalence from 3 to 7%. Further increasing concurrency to 12% pushed HIV prevalence to 11%. This presents challenges for empirical work seeking to link concurrency and HIV transmission in surveillance data; random statistical variation or small temporal changes in the amount of concurrency could mask associations. On the other hand, this sensitivity to the amount of concurrency could have positive implications for HIV prevention efforts. These model results suggest that intervention programs that are *effective* at reducing concurrency may play a crucial role in stemming the incidence of new HIV infections.

Future work needs to focus on combining empirical data with sexual network models to robustly estimate the contribution of concurrency and stages of transmission in different HIV epidemics and predict the possible outcomes of intervention programs that aim to reduce concurrency. Accurate modeling of concurrency and primary infection is also likely to be important for assessing the efficacy of interventions that target prevention of onward

transmission by HIV positive individuals, in particular universal HIV testing and immediate treatment [34], and interventions that target those currently in primary infection [35]. Our results show that the roles of concurrent sexual partnerships and primary HIV infection can only be understood in combination, and that primary infection in the context of concurrent sexual partnerships may be the factor that has enabled HIV to spread through general populations to such high levels.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

References

1. Hudson CP. Concurrent partnerships could cause AIDS epidemics. Int J STD AIDS. 1993; 4:249–53. [PubMed: 8218510]
2. Halperin DT, Epstein H. Concurrent sexual partnerships help to explain Africa's high HIV prevalence: implications for prevention. Lancet. 2004; 364:4–6. [PubMed: 15234834]
3. Mah TL, Halperin DT. Concurrent sexual partnerships and the HIV epidemics in Africa: evidence to move forward. AIDS Behav. 2010; 14:11–6. [PubMed: 18648926]
4. Watts CH, May RM. The influence of concurrent partnerships on the dynamics of HIV/AIDS. Math Biosci. 1992; 108:89–104. [PubMed: 1551000]
5. Morris M, Kretzschmar M. Concurrent partnerships and the spread of HIV. AIDS. 1997; 11:641–8. [PubMed: 9108946]
6. Morris M, Kretzschmar M. A microsimulation study of the effect of concurrent partnerships on the spread of HIV in Uganda. Math Popul Stud. 2000; 8:109–33.
7. Morris M. Concurrent partnerships and syphilis persistence: new thoughts on an old puzzle. Sex Transm Dis. 2001; 28:504–7. [PubMed: 11518866]
8. Morris M. Barking up the wrong evidence tree. Comment on Lurie & Rosenthal, Concurrent partnerships as a driver of the HIV epidemic in sub-Saharan Africa? The evidence is limited. AIDS Behav. 2010; 14:31–3. [PubMed: 19997971]
9. Powers KA, Poole C, Pettifor AE, Cohen MS. Rethinking the heterosexual infectivity of HIV-1: a systematic review and meta-analysis. Lancet Infect Dis. 2008; 8:553–63. [PubMed: 18684670]
10. Boily MC, Baggaley RF, Wang L, et al. Heterosexual risk of HIV-1 infection per sexual act: systematic review and meta-analysis of observational studies. Lancet Infect Dis. 2009; 9:118–29. [PubMed: 19179227]
11. Lurie MN, Rosenthal S. Concurrent partnerships as a driver of the HIV epidemic in Sub-Saharan Africa? The evidence is limited. AIDS Behav. 2009; 14:17–24. [PubMed: 19488848]
12. Shelton JD. Why multiple sexual partners? Lancet. 2009; 374:367–9. [PubMed: 19647597]
13. Garnett GP, Johnson AM. Coining a new term in epidemiology: concurrency and HIV. AIDS. 1997; 11:681–3. [PubMed: 9108951]
14. Wawer MJ, Gray RH, Sewankambo NK, et al. Rates of HIV-1 transmission per coital act, by stage of HIV-1 infection, in Rakai, Uganda. J Infect Dis. 2005; 191:1403–9. [PubMed: 15809897]
15. Shelton JD. A tale of two-component generalised HIV epidemics. Lancet. 2010; 375:964–6. [PubMed: 20304227]
16. Epstein H. The mathematics of concurrent partnerships and HIV: a commentary on Lurie and Rosenthal, 2009. AIDS Behav. 2010; 14:17–24. [PubMed: 19488848]
17. Pilcher CD, Tien HC, Eron JJ, et al. Brief but efficient: acute HIV infection and the sexual transmission of HIV. J Infect Dis. 2004; 189:1785–92. [PubMed: 15122514]
18. Pinkerton SD. Probability of HIV transmission during acute infection in Rakai, Uganda. AIDS Behav. 2008; 12:677–84. [PubMed: 18064559]
19. Hollingsworth TD, Anderson RM, Fraser C. HIV-1 transmission, by stage of infection. J Infect Dis. 2008; 198:687–93. [PubMed: 18662132]

20. Hayes RJ, White RG. Amplified HIV transmission during earlystage infection. J Infect Dis. 2006; 193:604–5. [PubMed: 16425144]
21. Koopman JS, Jacquez JA, Welch GW, et al. The role of early HIV infection in the spread of HIV through populations. J Acquir Immune Defic Syndr Hum Retrovirol. 1997; 14:249–58. [PubMed: 9117458]
22. Abu-Raddad LJ, Longini IM. No HIV stage is dominant in driving the HIV epidemic in sub-Saharan Africa. AIDS. 2008; 22:1055–61. [PubMed: 18520349]
23. Xiridou M, Geskus R, de Wit J, Coutinho R, Kretzschmar M. Primary HIV infection as source of HIV transmission within steady and casual partnerships among homosexual men. AIDS. 2004; 18:1311–20. [PubMed: 15362664]
24. Morris M, Kretzschmar M. Concurrent partnerships and transmission dynamics in networks. Social Netw. 1995; 17:299–318.
25. Kretzschmar M, Morris M. Measures of concurrency in networks and the spread of infectious disease. Math Biosci. 1996; 133:165–95. [PubMed: 8718707]
26. UNAIDS Reference Group On Estimates Modelling And Projections: Working Group On Measuring Concurrent Sexual Partnerships. HIV: consensus indicators are needed for concurrency. Lancet. 2010; 375:621–2. [PubMed: 19954832]
27. Gregson S, Garnett GP, Nyamukapa CA, et al. HIV decline associated with behavior change in eastern Zimbabwe. Science. 2006; 311:664–6. [PubMed: 16456081]
28. Gourvenec, D.; Taruberekera, N.; Mochaka, O.; Kasper, T. [Accessed 09 Feb 2010] Multiple concurrent partnerships among men and women aged 15–34 in Botswana: Baseline Study. Dec. 2007 PSI Botswana 2007.http://www.gov.bw/Global/NACAMinistry/PSIBotswana.pdf
29. Gregson S, Nyamukapa C, Garnett GP, et al. Sexual mixing patterns and sex-differentials in teenage exposure to HIV infection in rural Zimbabwe. Lancet. 2002; 359:1896–1903. [PubMed: 12057552]
30. Kretzschmar M, Dietz K. The effect of pair formation and variable infectivity on the spread of an infection without recovery. Math Biosci. 1998; 148:83–113. [PubMed: 9597826]
31. Dietz K, Heesterbeek JA, Tudor DW. The basic reproduction ratio for sexually transmitted diseases. Part 2. Effects of variable HIV infectivity. Math Biosci. 1993; 117:35–47. [PubMed: 8400583]
32. Garnett GP, Anderson RM. Factors controlling the spread of HIV in heterosexual communities in developing countries: patterns of mixing between different age and sexual activity classes. Philos Trans R Soc Lond B Biol Sci. 1993; 342:137–59. [PubMed: 7904355]
33. Robinson N, Mulder D, Auvert B, Hayes R. Proportion of HIV infections attributable to other sexually transmitted diseases in a rural Ugandan population: simulation model estimates. Int J Epidemiol. 1997; 26:180–189. [PubMed: 9126519]
34. Granich RM, Gilks CF, Dye C, De Cock KM, Williams BG. Universal voluntary HIV testing with immediate antiretroviral therapy as a strategy for elimination of HIV transmission: a mathematical model. Lancet. 2009; 373:48–57. [PubMed: 19038438]
35. Fiscus SA, Pilcher CD, Miller WC, et al. Rapid, real-time detection of acute HIV infection in patients in Africa. J Infect Dis. 2007; 195:416–24. [PubMed: 17205481]

Europe PMC Funders Author Manuscripts

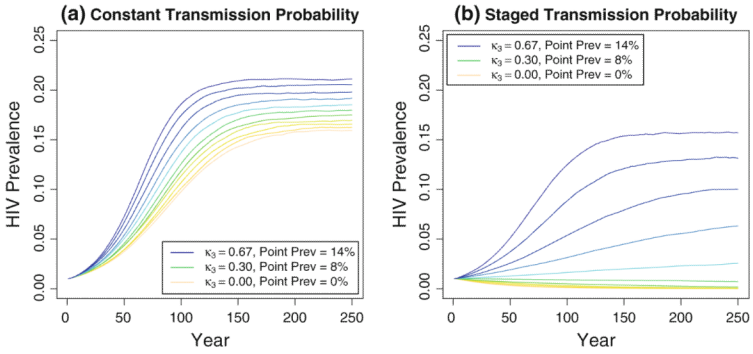

Fig. 1.

HIV prevalence over time for constant transmission scenario (**a**) and staged transmission scenario (**b**). Darker colors indicate more concurrency. Mean of 100 simulations

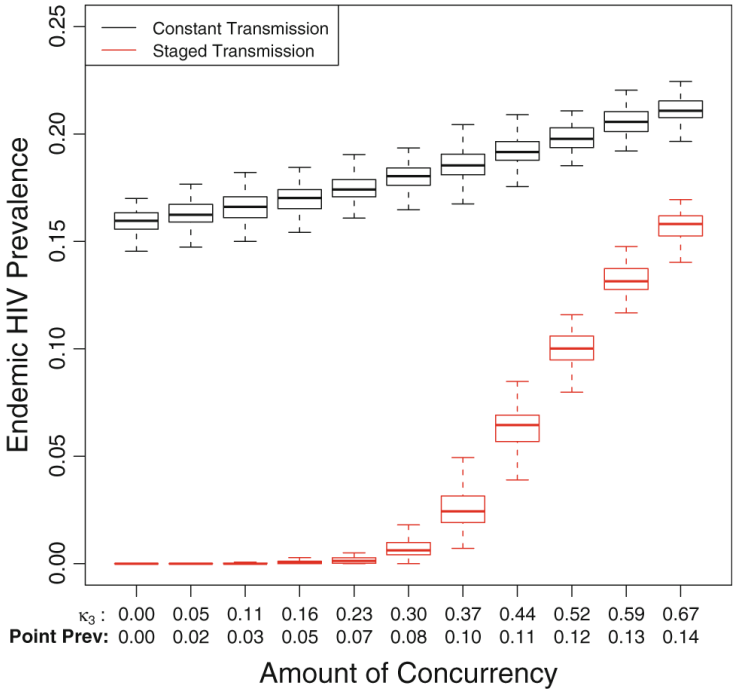

Fig. 2.

Box plots of HIV prevalence after 250 years at different levels of concurrency for constant transmission (*black*) and staged transmission (*red*). Box plots indicate quantiles based on 100 simulations of each scenario

Europe PMC Funders Author Manuscripts

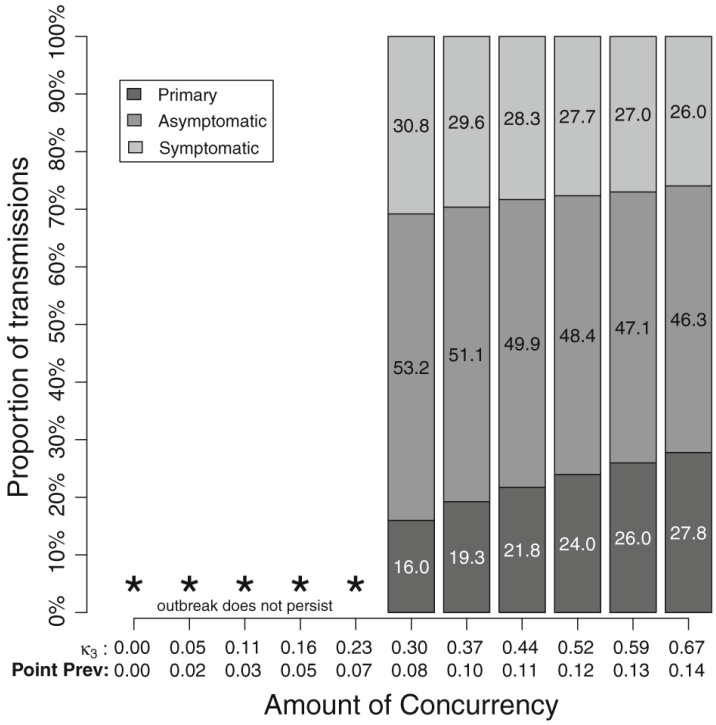

Fig. 3.

Proportion of transmissions occurring during each stage of infection once the epidemic has reached steady state for staged transmission scenarios where the epidemic spreads

Europe PMC Funders Author Manuscripts

Europe PMC Funders Author Manuscripts

AIDS Behav. Author manuscript; available in PMC 2012 December 12.

Table 1

Parameter values used in simulations

Parameter	Description	Value
N_m	Number of males in population	10,000
N_f	Number of females in population	10,000
ρ	Partnership formation rate	0.01[a]
σ	Partnership dissolution probability	0.005/day[a]
	Mean partnership duration	200 days
	Mean new partners per year	1.22
	Mean number of current partnerships	0.67
ε	Parameter controlling amount of concurrency	0–1 (see suppl. material)
β_p	Transmission probability during primary infection	0.00732/day[b]
β_a	Transmission probability during asymptomatic infection	0.00029/day[b]
β_s	Transmission probability during symptomatic infection	0.00208/day[b]
β_0	Transmission probability during severe AIDS infection	0.0/day[b]
δ_p	Duration of primary infection	88 days[b]
δ_a	Duration of asymptomatic infection	3054 days[b]
δ_s	Duration of symptomatic infection	274 days[b]
β_c	Constant transmission probability	0.00056/day
Δ	Duration between infection and death	3723 days[b]
η_m	Number of male seed infections	100 (1%)
η_f	Number of female seed infections	100 (1%)

[a]Parameter from Morris and Kretzschmar, *AIDS* (1997) [5]

[b]Parameter from Hollingsworth, Fraser, and Anderson, *J Infect Dis* (2008) [19]