Sexual networks, partnership mixing patterns and the sex ratio of HIV infections in generalized epidemics

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Abstract

Empirical estimates of the female-to-male sex ratio of infections in generalized HIV epidemics in sub-Saharan Africa range from 1.31 in Zambia to 2.21 in Ivory Coast. Gender inequalities in the sex ratio of infections can arise because of differences in exposure (to HIV positive partners), susceptibility (given exposure), and survival (once infected). Differences in susceptibility have to date received most attention, but neither the relatively high sex ratio of infections nor the heterogeneity in the empirical estimates in generalized epidemics is fully understood. In this contribution we focus on partnership network attributes and sexual mixing patterns that could lead to gender differences in the exposure to HIV positive partners. Using agent-based simulations, we show that gender asymmetric partnership concurrency, rapid partnership turnover, elevated partnership dissolution in female positive serodiscordant couples and lower partnership re-entry rates among HIV positive women can produce (substantial) differences in the sex ratio of infections. Coital dilution and serosorting have modest moderating effects.

Introduction

About 60% of adults living with HIV in sub-Saharan Africa are women, and that corresponds to a female-to-male sex ratio of infections of 1.48 (UNAIDS 2010). [1] Empirical estimates of the sex ratio of infections in African populations with an HIV prevalence level above 1%, range from 1.31 in Zambia to 2.21 in Ivory Coast (Figure 1). The highest sex ratios are found in a string of African countries along or just above the equator. Interestingly, the sex ratio does not exceed 1.60 in the southeastern African countries that are most severely affected by the AIDS epidemic. Our understanding of this variation in the sex ratio of infections in generalized epidemics is rather weak and that is partly because two sex serosurveys have only been conducted on a regular basis since the availability of rapid HIV testing technologies (i.e., since the early 2000s). Caution is, however, necessary when interpreting empirical estimates of the sex ratio of infections because they may be affected by relatively high male non response bias (Reniers and Eaton 2009; Barnighausen et al. 2011).[2] Distortions in empirical estimates of the sex ratio can also arise from the restricted age range to which these apply (often 15-49) because the female-to-male sex ratio of prevalent infections is generally lower (in some cases reversed) at older ages.[3]

Figure 1 about here

Aside from the data artifacts listed above, three categories of explanations exist for the relatively high female-to-male ratio of HIV infections in generalized epidemics: (1) women's exposure to infected men is greater than men's contact with HIV positive women, (2) women's susceptibility or acquisition probability per coital act with an HIV infected partner is higher than that of men, and (3) HIV positive women survive longer than HIV positive men. In this contribution, we study the mechanisms that contribute to the first of these explanations, namely differences in exposure to HIV positive partners. Our evidence comes from agent-based simulations wherein we model (gender symmetric and gender asymmetric) partnership concurrency, partnership turnover, coital dilution, HIV status-dependent partnership formation

and dissolution, and serosorting as causal factors of interest. Before introducing the model, we briefly review what is known about sex differences in exposure, susceptibility and survival.

Gender differences in the survival of HIV positives arise because men tend to be infected at older ages (see below), and an advanced age at infection is negatively correlated with survival post infection (Todd et al. 2007; Gregson and Garnett 2000). Gender differences in survival may also result from differences in the uptake or adherence to antiretroviral therapy (ART). [4]

Women's greater susceptibility is attributed to a number of biological mechanisms, including differences in genital immunology that are well described in the literature (Higgins et al. 2010; Yi et al. 2013; Chersich and Rees 2008). A variety of co-factors may alter one's susceptibility to HIV infection, including the presence of both viral and bacterial sexually transmitted infections (STI) (Cohen 2004; UNAIDS/WHO 2000; Glynn et al. 2001; Hertog 2008),[5] and male circumcision (Hertog 2008; Auvert et al. 2005). The contributions of pregnancy (Gray et al. 2005; Morrison et al. 2007), and hormonal contraceptives to women's disproportionally high infection rates are less certain (WHO 2012). Other factors with repercussions for HIV transmission pertain to the sex acts themselves, including vaginal versus anal sex, the use of vaginal drying agents, and forced sex (Chersich and Rees 2008). Finally, gender differences in ART uptake might alter the sex ratio of infections because onward transmission is reduced due to viral suppression.

Several studies of serodiscordant couples in high income countries confirmed the gender difference in susceptibility (Nicolosi et al. 1994; Mastro and de Vincenzi 1996), and it is now often assumed that women's acquisition risk per coital act is at least twice as high as that of men. However, estimates of the sex ratio of transmission probabilities per coital act for low income countries are much more diverse and not consistently above unity. The sources for that heterogeneity are not well understood (Boily et al. 2009; Powers et al. 2008).

Of the class of explanations that revolve around gender differences in exposure, age-mixing is probably best researched. Because men are usually older than their female partners, the exposure to HIV in these partnerships tends to be higher for women than for men and age-mixing has thus been proposed as an explanation for the relatively high prevalence rates in young women in particular (sex differences in HIV prevalence are more modest or even reversed in late adulthood) (Gregson et al. 2002; Kelly et al. 2003; Clark 2004; Leclerc-Madlala 2008).[6]

Studies addressing gender differences in other exposure factors are fairly limited. Worth noting, however, is the proposition that the sex ratio of infections is related to epidemic maturity: during the early phase of an epidemic, HIV infection is thought to be concentrated in female sex workers and their partners so that male prevalence exceeds that of women. With time, new HIV infections shift to the long-term partners of those sex worker clients and the female-to-male sex ratio of infections may increase as a result of that (Gregson and Garnett 2000; Carpenter et al. 1999). Even though couched in different language, it is essentially a hypothesis about partnership concurrency and its implications for the sex ratio of infections as the epidemic establishes itself in a population. [7] We take this as our point of departure, and compare the sex ratio of infections in monogamous sexual networks and sexual networks with different levels of gender symmetric and gender asymmetric concurrency. We introduce the distinction between gender symmetric – assumed in the early modeling by Morris and Kretzschmar (1997)– and gender asymmetric concurrency because the latter is the characteristic for populations that practice polygynous marriage. Empirical estimates of partnership concurrency, both formal (marriage) and informal, are also much higher for men than for women (Sawers 2013).[8] We also assess the compensating effect of a reduction in the per partner number of sex acts during episodes of concurrency (hereafter named *coital dilution*).[9]

We extend the analysis of concurrency effects to other attributes of sexual networks, including the rate of partnership turnover and HIV-status based partnership mixing. The importance of fast partnership turnover for epidemic propagation has been known for quite a while (May and Anderson 1987), but its implications for the sex ratio of infections has not been described to date. Simple math predicts that rapid partnership turnover will maximize the gender differences in HIV prevalence provided that the susceptibility of men and women is indeed different. As partnerships last longer, the virus is more likely to spread to seronegative partners of HIV positive individuals irrespective of the transmission probability, and the sex ratio of infections will come to depend more on other attributes of the network structure such as partnership concurrency.

A final set of sexual mixing patterns under consideration relate to HIV status-based partnership formation and dissolution, namely (1) elevated dissolution rates in serodiscordant couples,[10] (2) lower partnership formation rates of HIV positives, and (3) serosorting or homogamy on HIV status. HIV status-based partnership choices will become an increasingly

important factor in the epidemiology of HIV as the uptake of HIV testing and counseling (HTC) increases, but from previous research we also know that individuals often act on imperfect information about one's own or someone else's HIV status (Watkins 2004). There are at least five studies that have suggested that partnership dissolution rates (through widowhood and divorce or separation) are significantly higher in serodiscordant couples, and particularly so in female positive serodiscordant couples (Porter et al. 2004; Grinstead et al. 2001; Carpenter et al. 1999; Mackelprang et al. 2013; Floyd et al. 2008). We will retain this gender imbalance in our simulations. Similarly, we will develop scenarios with lower partnership formation rates among HIV positive women. Such a pattern may arise from HIV related morbidity, but also because those who are known or suspected to be HIV positive are less desirable partners or withdraw from the partnerships market on their own initiative. Two studies from rural Malawi have identified these HIV status-based partner recruitment strategies (Reniers 2008; Anglewicz and Reniers under review). In combination with elevated dissolution rates in serodiscordant couples, the disproportionate recruitment of HIV negative women into new partnerships causes the *drift of HIV positives* from the core to the periphery of sexual networks. [11] The drift of HIV positive women also explains the relatively high HIV prevalence rates in divorced and widowed compared to (re)married women in cross-sectional studies (de Walque and Kline 2012). Serosorting, in turn, has been well described among men who have sex with men in concentrated epidemics (Suarez and Miller 2001; Parsons et al. 2005), but received little attention as a mediating factor in populations with generalized epidemics (Reniers and Helleringer 2011).

Methods

We demonstrate the effect of the sexual network structure and mixing patterns described above with a discrete-time agent-based model with one-month time steps built in NetLogo (Wilensky 1999). The simulation tracks the characteristics of adult men and women and models their partnerships. We only account for heterosexual relationships and do not distinguish between formal and informal sexual partnerships. Each relationship has a constant hazard rate of dissolving, and each individual may have up to three relationships simultaneously. The rates for forming new partnerships are automatically selected so that the desired steady-state distribution of the number of partners for men and women in a user-defined scenario is attained. Before the

start of the simulation of HIV transmission, the relationship part is run for 10 years to ensure that the initial partnerships distribution is in a steady-state. Entry and exit rates from partnerships can be made dependent on HIV status as is also the case for the choice of future partners.

HIV transmission is a key part of the model. The simulation tracks the HIV status of each individual as well as the stage of infection: acute, chronic, or AIDS. The acute stage and the final AIDS stage are 8 times and 4 times as infectious as the chronic stage, respectively. A woman in the chronic stage will infect any HIV negative partner with a probability of 0.019 each month. The monthly transmission probability from an untreated man in the chronic stage to his partner is 0.038. In accordance with (some) empirical findings, we thus assume a greater susceptibility of women compared to men. These transmission parameter settings do not match one particular study, but fall in the range of values that have been reported in the literature (Boily et al. 2009; Wawer et al. 2005). Note also that these are monthly transmission probabilities and not the probabilities per coital act.

In scenarios with coital dilution, the probabilities are multiplied by a factor that represents the per partner reduction in coital frequency in partnerships with concurrency. More precisely, we multiply the monthly transmission probability by 0.8 if the index persons has two partners, and by 0.6 if he or she has three partners. Note that these assumptions imply that more concurrency is associated with a larger number of coital acts in the simulated population. These assumptions differ from another coital dilution modeling study that rests on the stronger assumption that higher levels of concurrency leads to a reduction in the population-level number of coital acts (Sawers et al. 2011).

The model is initialized by randomly allocating HIV infection to 5% of the subjects. We have chosen 5%, because we are primarily interested in the dynamics of generalized epidemics and not so much in the conditions that explain or characterize the early expansion of the epidemic. The time of infection for these seed cases is set to match the historical estimates of incidence in Williams et al. (2006). An infected individual is in the acute stage for the first three months after seroconversion. The length of their remaining life is chosen from a Weibull distribution with mean 9.7 years and shape factor of 2.25 and these simulations assume that treatment is not available. The last 10% of the remaining lifespan is considered to be in the in the final AIDS stage.

Our model focuses on adults aged 15-50. We assume that the number of males and females are equal, and that the age distribution for each sex is similar to that of Zambia. We do not model specific patterns of age-mixing in partnership formation, however. Individuals may die from AIDS or from causes unrelated to AIDS at a rate of 0.006/12 per month. One further constraint is that the simulated population is held constant: each person who dies or turns 50 re-enters the population as an uninfected 15-year old individual of the same sex without existing relationships.

The global model settings and key scenario assumptions are summarized in Table 1. We distinguish three types of sexual networks: populations with monogamous partnerships only, populations with gender asymmetric partnership concurrency (only men have concurrent partners), and populations with gender symmetric concurrency. In each of these networks we vary the quantum of partnerships, and in the concurrency networks we also vary the level of concurrency. The quantity of partnerships is indexed by the mean number of partnerships per individual at any point in time (m), and the concurrency level is measured by the percentage of partnerships in the population that are concurrent (k) as defined by Morris and Kretzschmar (1997). A scenario with gender asymmetric concurrency of level k=40 (and m=0.9), represents a population wherein 24% of the adult men have more than one partner at any point in time. In Togo, one of the countries with the highest polygyny rates sub-Saharan Africa, 25% of the men aged 15-59 have more than one spouse (Anipah et al. 1999). In the symmetric case, k=40 implies a sexual network where about 12% of both men and women have multiple partnerships. Note that the scenarios with low and high levels of concurrency also differ in terms of the mean number of partnerships per person. The latter has implications for the interpretation of the results that we highlight later.

Table 1 about here

Populations with a low rate of partner change are those where the monthly partnership dissolution rate through separation or divorce is d=0.0167. We contrast those with networks wherein the monthly dissolution rate is d= 0.0556. These separation rates translate into average partnership durations (in the absence of death) of 5 and 1.5 years, respectively. These levels are

not necessarily chosen to match empirically observed patterns for entire populations, but could represent the partnership turnover rates in sub-populations.

Three parameters are used for manipulating HIV status-based partnership mixing patterns. Scenarios with serosorting assume that the odds of forming a partnership with someone of the same serostatus are twice as high as the odds of forming a partnership with someone who is HIV serodiscordant. The drift of HIV positive women is controlled by two parameters: one that sets elevated dissolution rates in female positive serodiscordant couples (odds ratio=3) and one that sets lower remarriage odds in HIV positive compared to HIV negative women (odds ratio=0.5). For serosorting we do not have good empirical estimates to guide us with the parameter settings. In contrast, the settings for the drift of HIV positive women are informed by empirical estimates (Porter et al. 2004; Anglewicz and Reniers under review).

We first present long-term epidemic trajectories (25 years) for populations with different partnership network structures, and concurrency level and partnership turnover rates. This is followed by an OLS regression analysis of the sex ratio of infections after 10 years. Models where the sex ratio of infections is log transformed produced a slightly better fit, but we have given preference to presenting the model with the dependent variable in its original form because of the easier interpretation of the coefficients. This choice does not affect any of the substantive conclusions. The regressions are separately done for the three types of sexual network structures (monogamy, gender asymmetric concurrency and symmetric concurrency) to allow for all two-way interactions with other predictors.

Results

The first outputs are trends in HIV prevalence (Figure 2). Even though it is not the focus of this study, it is useful to gain an understanding of the magnitude and trajectory of the epidemics that are predicted by our simulations. In the epidemics portrayed in Figure 2, we do not assume any coital dilution or HIV status-based partnership mixing. The plots highlight the contribution of partnership concurrency as well as elevated partnership turnover rates to the magnitude of the HIV epidemic. A comparison of strict monogamy (green bars) with the two concurrency scenarios (orange and blue bars) in each panel shows that partnership concurrency increases the epidemic size, but its effect is rather small at low levels of concurrency, and

particularly in networks with low partnership turnover where the HIV epidemic never takes off. In sexual networks with k=40, the epidemic size after 25 years is almost twice that of a monogamous population with the same average number of partners per individual. The differences between symmetric and asymmetric concurrency are negligible (with the exception perhaps of networks with high concurrency and a low partner change rate), and these results corroborate the findings by Santhakumaran et al (2010).

Figure 2 about here

The differences between networks with rapid and slow partnership turnover are much more striking: irrespective of the network structure (monogamy, asymmetric or symmetric concurrency) and concurrency level, sexual networks with fast partnership turnover produce epidemics that are roughly four times as large (at 25 years) as in their variant with a low rate of partner change.

The net effect of an increase in the partnership quantum from 0.8 to 0.9 partnerships per person can be evaluated for partnership networks with monogamy (only) by comparing the epidemic trajectories of the plots on the left with those on the right (same row). Its effect is marginal in networks where partnership turnover is slow, but elevates the epidemic size after 25 years by about a third in populations where the partnership change rate is high.

Trends in the sex ratio of HIV infections are illustrated in Figure 3. In populations with strict monogamy and gender symmetric concurrency, the sex ratio of infections quickly rises from unity to about 1.20 (somewhat higher in networks with a higher partnership turnover rate). Thus even though the monthly male-to-female transmission probability is set to be twice as high as the female-to-male transmission probability, the HIV prevalence in women is only about 20% higher in women than in men. The reason is that relationships usually last longer than a few months, and the importance of sex differences in transmission probabilities per coital act declines as the lifespan of partnerships increases. Because of that networks with a higher rate of partnership turnover will maximize the gender differences in the susceptibility to HIV infection.

Figure 3 about here

Differences in the sex ratio of infections in networks with low and high rates of partnership turnover are quite small compared to those induced by gender asymmetric partnership concurrency: at high levels of partnership concurrency, the female-to-male sex ratio of infections even increases to 1.60. However, in a network with high concurrency and rapid partnership turnover (bottom right), the sex ratio decreases somewhat following a peak after 80 months. This decline is due to the disproportionally high female mortality associated with their elevated HIV prevalence, and the modeling assumption that all deaths and HIV positive exits (at age 50) are substituted by an HIV negative 15 year old of the same sex. Given that the modeled HIV prevalence in a network with high partnership turnover and high concurrency is quite high (Figure 2), this mortality effect is probably larger than we might observe in empirical populations, but it is nonetheless plausible that the sex ratio of infections declines somewhat once mortality starts taking its toll in populations where more women are infected than men.

The factors affecting the sex ratio of infections are further explored by means of an OLS regression analysis of the sex ratio after 10 years (Table 2). The regression models were fitted separately for each type of network structure (monogamy, asymmetric concurrency and symmetric concurrency), which de facto allows for all two-way interactions between the other predictors and the network structure. Other interaction effects are less important and have been suppressed. The dataset for this analysis is based on 20 simulation runs for each combination of parameter settings. Even though there is no sampling variability in simulated data and significance tests can be misleading given that we could readily inflate the sample size, we present the coefficients with their 95%-confidence interval to give readers a sense of the heterogeneity in the coefficient estimates that the simulations produce.

The explained variance (adjusted R-squared) in the female-to-male sex ratio of prevalent infections after 10 years ranges from 0.32 (asymmetric concurrency) to 0.58 (symmetric concurrency) which indicates that there is considerable random variation and that the sex ratio can be quite difficult to predict.

Table 2 about here

The value of the intercepts ranges from 1.14 for populations practicing gender symmetric partnership concurrency to 1.38 for populations with asymmetric concurrency. The relatively

large and positive coefficient for the variable identifying scenarios with high asymmetric partnership concurrency (and partnership quantum) underscores that gender asymmetry in the sexual network structure can produce substantial differences in the sex ratio of infections. The effect of gender asymmetric concurrency on the sex ratio of infections is somewhat compensated by coital dilution, but with the parameter settings that were used here, its effect is rather modest.

In a strictly monogamous population, the coefficient for an increase in the quantum of partnerships (the concurrency level is per definition zero) is negative, indicating that the importance of differences in the biological susceptibility between men and women dissipates as men and women spend a larger fraction of their reproductive lives in a union.

From Figure 2, we learned that populations with high rates of partner change tend to maximize the sex ratio of infections. In the regression analysis, this is confirmed by small but positive coefficients. Its effect seems to be the smallest for populations practicing asymmetric concurrency, and that is because these networks produce particularly large epidemics with disproportionally high AIDS mortality among women. In the simulations, these deaths are replaced by 15 year old HIV negative subjects of the same sex, and keeps the sex ratio of infections in check.

The drift of HIV positive women from the partnerships market has a substantial effect on the sex ratio of prevalent infections Depending on the network structure, the drift elevates the sex ratio of infections by 0.23 to 0.46 points. In our simulations, the exclusion or retreat of HIV positive women from the partnerships market increases the demand for HIV negative women who are now disproportionally recruited into new partnerships and exposed to HIV infection. The effect of the drift is particularly strong in networks with symmetric partnership concurrency because HIV positive women are now less likely to act as central nodes with multiple partnerships, which further reduces the exposure for men in the population. The effect of serosorting on the sex ratio of infections is small, if not negligible.

The female-to-male sex ratios of infections predicted by our model range from 1.13 for a static network with gender symmetric concurrency, low partner turnover and without the drift of HIV positive women, to 1.75 for a population with gender asymmetric concurrency, high partnership turnover and drift.

Discussion

Sex differences in the susceptibility to HIV infection have received considerable attention and are deemed important determinants of gender differences in HIV prevalence in generalized epidemics. However, the empirical support for gender differences in the acquisition probabilities per coital act is fairly limited, particularly for low income countries. In addition, relatively large gender differences in susceptibility do not result in equally large differences in HIV prevalence and the reason is that the effect of variation in acquisition probabilities per coital act declines as partnerships last longer. In our simulation study, this is corroborated by the fact that the estimated sex ratio of infections 10 years into the epidemic is 1.25 in the baseline monogamous sexual network even though the monthly male-to-female transmission probability was set to be twice that of female-to-male transmission. The higher sex ratio of infections in populations with an elevated rate of partnership turnover lends further support to this conclusion, and confirms our proposition that networks with rapid partnership turnover will maximize gender differences in susceptibility.

Empirical estimates for the sex ratio of infections in most southeastern African populations with large HIV epidemics range between 1.40 and 1.60, and it is thus unlikely that differences in susceptibility fully account for these large sex differences in HIV prevalence. Co-factors that are known or believed to affect the transmission probabilities include male circumcision, the prevalence of STIs, and hormonal contraceptives. Women may also survive longer with HIV and that is related to their relatively young age at infection. All these factors could in theory raise empirical estimates of the sex ratio of infections observed in generalized epidemics, but were not the subject of this study.

Another class of explanations focuses on gender differences in the exposure to HIV positive partners, and it is in this realm that our simulations contribute most to the understanding of sex differences in HIV prevalence. Best described in the literature is age mixing, which explains the relatively high prevalence rates in young women. Using agent-based simulations, we further demonstrate the importance of (1) gender asymmetric partnership concurrency and (2) the drift of HIV positive women out of the partnerships market. Coital dilution (in networks with asymmetric partnership concurrency only) and serosorting have relatively modest moderating effects on the sex ratio of infections.

The scenarios with asymmetric concurrency and the drift of HIV positive women are informed by empirical studies that consistently identify higher levels of partnership concurrency

among men compared to women and the gradual exclusion or retreat of HIV positive women from partnerships. However, the results also depend on the assumption that the population-level quantity of partnerships is not correlated with the network structure or the partnership mixing patterns that are modeled. This constant partnerships assumption is common sexual network simulations studies because it allows us to isolate the net effects of the network attribute of interest (e.g., Morris and Kretzschmar 1997), but it remains largely unverified by empirical studies. We return to this issue below.

The asymmetric concurrency effect on the sex ratio operates via two mechanisms. First, asymmetric concurrency exposes seronegative concurrent partners of a man to elevated transmission probabilities associated with the high viral load during the acute phase if that man just acquired HIV from (one of) his other partner(s).[12] The second mechanism is intricately related to the modeling assumption that keeps the number of partnerships constant across the different sexual network types. Under this assumption, more male concurrency implies more isolated male nodes in the network,[13] and women will on average spend more time in partnerships than men (which increases their relative exposure to HIV). It is not clear to what extent this assumption is realistic, however. In an empirical study of the effects of polygyny for the HIV epidemic propagation, we could not find much evidence for the *monopolizing polygynists* hypothesis (i.e., the proposition that polygyny among older men leads to a deprivation of sexual partners for the younger men) (Reniers and Tfaily 2012). We do not know of other studies that have addressed this question, and it would be precipitous to entirely discard the validity of the constant partnerships assumption on the basis of one study only.

The drift of HIV positive women from the partnerships market consists of two processes that operate in parallel: (1) the relatively high partnership dissolution rates among female positive serodiscordant couples, and (2) the relatively low partnership formation rates among HIV positive women. As we have shown, this phenomenon could have considerable effects on the sex ratio of infections (particularly in networks with gender symmetric concurrency), but it also rests on the assumptions that the demand for partners in the population is unchanged. Given the constant partnerships distribution in the simulated populations, the drift leads to the substitution of HIV positive women in partnerships by HIV negative women, and that will increases HIV negative women's exposure to HIV positive men as well as decrease male exposure to HIV positive women.

Using variation in the simulated attributes of sexual networks and sexual mixing patterns, we model populations with a sex ratio of infections ranging from 1.13 to 1.75 and that suggests that these factors can indeed help explain the heterogeneity in the sex ratio of infections currently observed in empirical data. Even though the nature of our evidence comes with the disclaimer that it is entirely based on simulated data, it suggest that we need to look beyond individual behavior or gender differences in the biological susceptibility if we are to fully understand, and remedy, gender inequalities in HIV infection in generalized epidemics. Such remedies may have to target upstream or distal determinants of the inequalities between men and women that are discussed elsewhere (UNAIDS et al. 2010), but we hope that our study sheds light on the mechanisms through which they operate.

Acknowledgements

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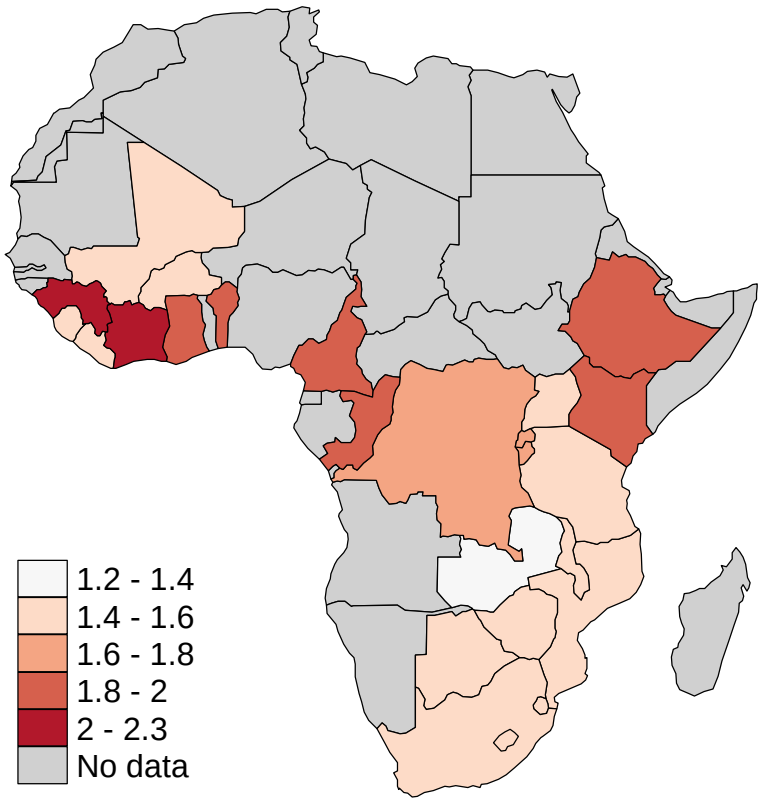
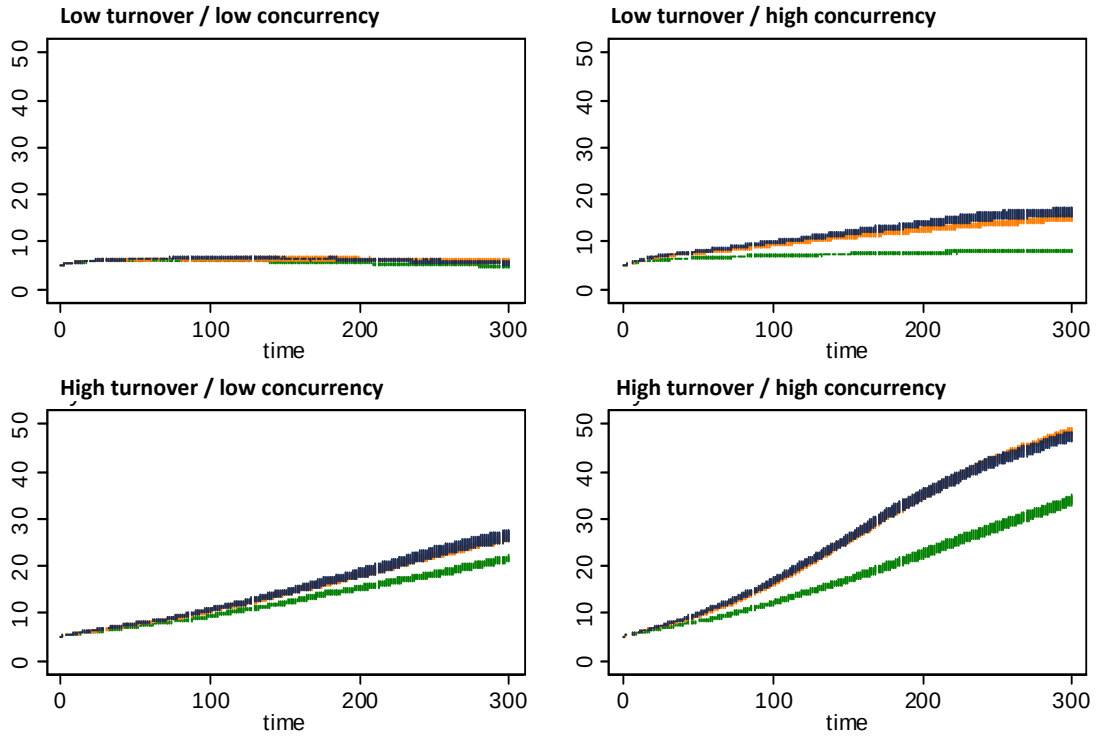
Figure 1: Female-to-male sex ratio of HIV prevalence in men and women of reproductive age (15-49, 2003-2011)



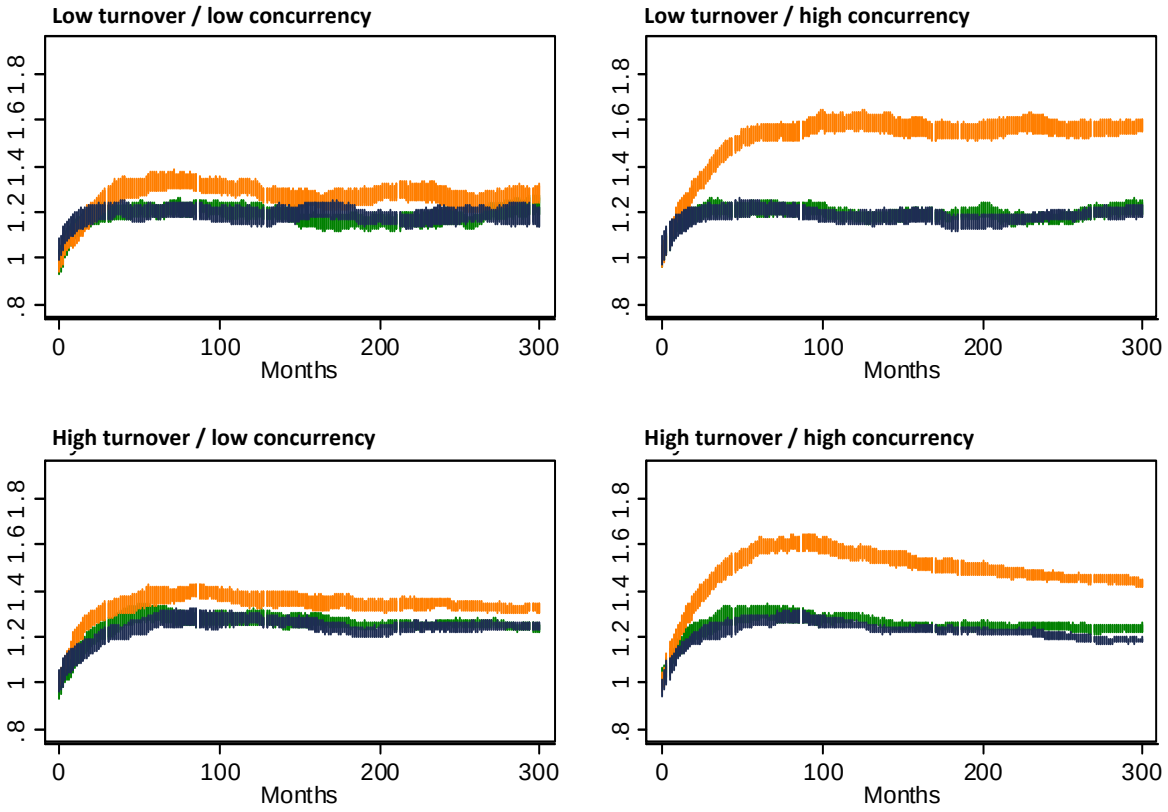
Data sources: ORC Macro (2013), Shisana (2005), and CSO [Botswana] (2009)

Figure 2. HIV prevalence (95%-confidence interval) in sexual networks with low and high partnership turnover and various degrees of partnership concurrency



Legend: green= monogamy, orange= gender asymmetric concurrency, blue= gender symmetric concurrency (bars represents 95% confidence intervals)

Figure 3. The female-to-male sex ratio of infections (95%-confidence interval) in sexual networks with low and high partnership turnover and various degrees of partnership concurrency



Legend: green= monogamy, orange= gender asymmetric concurrency, blue=gender symmetric concurrency (95% confidence intervals)

Table 1: global and scenario specific model settings

Global settings

Population size	1250
% HIV positive at t_0	5%
% on ART	0%
F-to-M Monthly HIV transmission rate (chronic stage)	0.019
M-to-F Monthly HIV transmission rate (chronic stage)	0.038
Acute infectivity ratio	8
AIDS stage infectivity ratio	4
Simulation length	30 years

Scenario specific settings

(1) Mean # of partners (m) and level of concurrency (k)

		Monogamy		Asymmetric concurrency		Symmetric concurrency	
	# partners	m=0.8, k=0	m=0.9, k=0	m=0.8, k=15	m=0.9, k=40	m=0.8, k=15	m=0.9, k=40
Male	0	0.2	0.1	0.3	0.4	0.25	0.25
	1	0.8	0.9	0.62	0.36	0.71	0.63
	2	-	-	0.06	0.18	0.03	0.09
	3	-	-	0.02	0.06	0.01	0.03
Female	0	0.2	0.1	0.2	0.1	0.25	0.25
	1	0.8	0.9	0.8	0.9	0.71	0.63
	2	-	-	-	-	0.03	0.09
	3	-	-	-	-	0.01	0.03

(2) Coital dilution factor: reduction monthly probability of HIV acquisition if male has 0, 1 or 2 concurrent partners: 1, 0.8, and 0.6

(3) Partnership turnover rates: partnership dissolution (divorce/separation) rates (per month)

Static 0.01665 → mean duration: 5 years
Dynamic 0.05560 → mean duration: 1.5 years

(4) Serosorting odds ratio: 2

(5) HIV+ women's drift out of the partnerships market
F+M- divorce odds ratio (ref. F-M-): 3
F+ remarriage odds ratio (ref. F-): 0.5

Table 2: OLS regression of the sex ratio of infections after 10 years and by network structure

VARIABLES	Monogamy	Asymmetric concurrency	Symmetric concurrency
Concurrency and coital dilution			
Constant	1.25 (1.231 - 1.269)	1.38 (1.358 - 1.401)	1.14 (1.123 - 1.166)
↑ Concurrency / Quantum	-0.1 (-0.115 - -0.086)	0.11 (0.093 - 0.126)	0 (-0.014 - 0.018)
Coital dilution	-0.01 (-0.028 - 0.002)	-0.06 (-0.079 - -0.046)	0.03 (0.009 - 0.042)
Partnership turnover rate			
↑ partnership turnover	0.06 (0.042 - 0.071)	0.01 (-0.003 - 0.030)	0.11 (0.091 - 0.123)
HIV status-based mixing			
↑ Divorce (F+M-)	0.13 (0.119 - 0.148)	0.12 (0.101 - 0.134)	0.24 (0.227 - 0.259)
↓ F+ Remarriage	0.11 (0.096 - 0.126)	0.11 (0.096 - 0.129)	0.22 (0.207 - 0.239)
Serosorting	-0.02 (-0.035 - -0.005)	-0.02 (-0.036 - -0.003)	-0.02 (-0.034 - -0.002)
Observations	1,280	1,280	1,280
Adjusted R-squared	0.382	0.321	0.584

Squared semi-partial correlation coefficients in parentheses

References

Anglewicz, P., and G. Reniers. under review. "HIV status, gender, and marriage dynamics among adults in Rural Malawi."

Anipah, Kodjo, Gora Mboup, Afi Mawuéna Ouro-Gnao, Bassanté Boukpessi, Pierre Adadé Messan, and Rissy Salami-Odjo. 1999. *Enquête démographique et de santé Togo, 1998*. Calverton, Maryland USA: Direction de la Statistique et Macro International Inc.

Auvert, B., D. Taljaard, E. Lagarde, J. Sobngwi-Tambekou, R. Sitta, and A. Puren. 2005. "Randomized, controlled intervention trial of male circumcision for reduction of HIV infection risk: The ANRS 1265 Trial." *PLoS Medicine* 2 (11):e298.

Barnighausen, T., J. Bor, S. Wandira-Kazibwe, and D. Canning. 2011. "Correcting HIV prevalence estimates for survey nonparticipation using Heckman-type selection models." *Epidemiology* 22 (1):27-35.

Boily, M. C., M. Alary, and R. F. Baggaley. 2012. "Neglected issues and hypotheses regarding the impact of sexual concurrency on HIV and sexually transmitted infections." *AIDS Behav* 16 (2):304-311.

Boily, M. C., et al. 2009. "Heterosexual risk of HIV-1 infection per sexual act: systematic review and meta-analysis of observational studies." *Lancet Infectious Diseases* 9 (2):118-129.

Braitstein, P., et al. 2008. "Gender and the use of antiretroviral treatment in resource-constrained settings: findings from a multicenter collaboration." *Journal of Women's Health* 17 (1):47-55.

Carpenter, Lucy M., Anatoli Kamali, Anthony Ruberantwari, Samuel S. Malamba, and James A. G. Whitworth. 1999. "Rates of HIV-1 transmission within marriage in rural Uganda in relation to the HIV sero-status of the partners." *AIDS* 13 (9):1083-1089.

Chersich, M. F., and H. V. Rees. 2008. "Vulnerability of women in southern Africa to infection with HIV: biological determinants and priority health sector interventions." *AIDS* 22 Suppl 4:S27-40.

Chin, J. 1990. "Public health surveillance of AIDS and HIV infections." *Bull World Health Organ* 68 (5):529-536.

Clark, S. 2004. "Early Marriage and HIV Risks in Sub-Saharan Africa." *Studies in Family Planning* 35 (3):149-160.

Cohen, M. S. 2004. "HIV and sexually transmitted diseases: lethal synergy." *Top HIV Med* 12 (4):104-107.

CSO [Botswana]. 2009. "2008 Botswana AIDS impact survey III: Statistical report." In. Gaborone: Central Statistics Office

de Walque, Damien, and Rachel Kline. 2012. "The Association Between Remarriage and HIV Infection in 13 Sub-Saharan African Countries." *Studies in Family Planning* 43 (1):1-10.

Delva, W., et al. 2013. "Coital frequency and condom use in monogamous and concurrent sexual relationships in Cape Town, South Africa." *Journal of the International AIDS Society* 16:18034.

Eaton, Jeffrey W, Timothy B Hallett, and Geoffrey P Garnett. 2011. "Concurrent sexual partnerships and primary HIV infection: a critical interaction." *AIDS and Behavior* 15 (4):687-692.

Floyd, S., et al. 2008. "The long-term social and economic impact of HIV on the spouses of infected individuals in northern Malawi." *Tropical Medicine and International Health* 13 (4):520-531.

Gaydosh, L., G. Reniers, and S. Helleringer. 2013. "Partnership Concurrency and Coital Frequency." *AIDS Behav*.

Glynn, J. R., et al. 2001. "Why do young women have a much higher prevalence of HIV than young men? A study in Kisumu, Kenya and Ndola, Zambia." *AIDS* 15 Suppl 4:S51-60.

Goodreau, Steven M, Susan Cassels, Danuta Kasprzyk, Daniel E Montaño, April Greek, and Martina Morris. 2012. "Concurrent partnerships, acute infection and HIV epidemic dynamics among young adults in Zimbabwe." *AIDS and Behavior* 16 (2):312-322.

Gray, R. H., et al. 2005. "Increased risk of incident HIV during pregnancy in Rakai, Uganda: a prospective study." *Lancet* 366 (9492):1182-1188.

Gregson, S., et al. 2002. "Sexual mixing patterns and sex-differentials in teenage exposure to HIV infection in rural Zimbabwe." *Lancet* 359 (9321):1896-1903.

Gregson, Simon, and Geoff P Garnett. 2000. "Contrasting gender differentials in HIV-1 prevalence and associated mortality increase in eastern and southern Africa: artefact of data or natural course of epidemics?" *AIDS* 14 (Supplement 3):S85-S99.

Grinstead, O. A., S. E. Gregorich, K. H. Choi, and T. Coates. 2001. "Positive and negative life events after counselling and testing: the Voluntary HIV-1 Counselling and Testing Efficacy Study." *AIDS* 15 (8):1045-1052.

Helleringer, S., and H. P. Kohler. 2007. "Sexual network structure and the spread of HIV in Africa: evidence from Likoma Island, Malawi." *AIDS* 21 (17):2323-2332.

Hertog, Sara. 2008. "Sex ratios of HIV prevalence: evidence from the DHS " In *Population Association Annual Meeting*. New Orleans, LA.

Higgins, J. A., S. Hoffman, and S. L. Dworkin. 2010. "Rethinking gender, heterosexual men, and women's vulnerability to HIV/AIDS." *Am J Public Health* 100 (3):435-445.

Kelly, R. J., et al. 2003. "Age differences in sexual partners and risk of HIV-1 infection in rural Uganda." *Journal of Acquired Immune Deficiency Syndromes* 32 (4):446-451.

Leclerc-Madlala, Suzanne. 2008. "Age-disparate and intergenerational sex in southern Africa: the dynamics of hypervulnerability." *AIDS* 22:S17-S25.

Lurie, M. N., and Samantha Rosenthal. 2010. "Concurrent partnerships as the driver of the HIV epidemic in sub-Saharan Africa? The evidence is limited." *AIDS and Behavior* 14 (1):17-24.

Mackelprang, Romel D, et al. 2013. "High Rates of Relationship Dissolution Among Heterosexual HIV-Serodiscordant Couples in Kenya." *AIDS and Behavior*:1-5.

Mah, Timothy L, and Daniel T Halperin. 2010. "Concurrent sexual partnerships and the HIV epidemics in Africa: evidence to move forward." *AIDS and Behavior* 14 (1):11-16.

Mastro, T. D., and I. de Vincenzi. 1996. "Probabilities of sexual HIV-1 transmission." *AIDS* 10 Suppl A:S75-82.

May, R. M., and R. M. Anderson. 1987. "Transmission dynamics of HIV infection." *Nature* 326 (6109):137-142.

Mills, E. J., N. Ford, and P. Mugyenyi. 2009. "Expanding HIV care in Africa: making men matter." *Lancet* 374 (9686):275-276.

Morris, Martina, and Mirjam Kretzschmar. 1997. "Concurrent partnerships and the spread of HIV." *AIDS* 11 (5):641-648.

Morrison, C. S., J. Wang, B. Van Der Pol, N. Padian, R. A. Salata, and B. A. Richardson. 2007. "Pregnancy and the risk of HIV-1 acquisition among women in Uganda and Zimbabwe." *AIDS* 21 (8):1027-1034.

Nicolosi, A., M. L. Correa Leite, M. Musicco, C. Arici, G. Gavazzeni, and A. Lazzarin. 1994. "The efficiency of male-to-female and female-to-male sexual transmission of the human immunodeficiency virus: a study of 730 stable couples. Italian Study Group on HIV Heterosexual Transmission." *Epidemiology* 5 (6):570-575.

Nnko, S., J. T. Boerma, M. Urassa, G. Mwaluko, and B. Zaba. 2004. "Secretive females or swaggering males? An assessment of the quality of sexual partnership reporting in rural Tanzania." *Social Science and Medicine* 59 (2):299-310.

ORC Macro. 2013. "Demographic and Health Surveys: StatCompiler." In. Calverton, MD: Macro International Inc.

Parsons, J. T., et al. 2005. "Sexual harm reduction practices of HIV-seropositive gay and bisexual men: serosorting, strategic positioning, and withdrawal before ejaculation." *AIDS* 19 Suppl 1:S13-25.

Porter, L., et al. 2004. "HIV status and union dissolution in sub-Saharan Africa: the case of Rakai, Uganda." *Demography* 41 (3):465-482.

Powers, K. A., C. Poole, A. E. Pettifor, and M. S. Cohen. 2008. "Rethinking the heterosexual infectivity of HIV-1: a systematic review and meta-analysis." *Lancet Infectious Diseases* 8 (9):553-563.

Reniers, G., and B. Armbruster. 2012. "HIV status awareness, partnership dissolution and HIV transmission in generalized epidemics." *PLoS One* 7 (12):e50669.

Reniers, G., and J. Eaton. 2009. "Refusal bias in HIV prevalence estimates from nationally representative seroprevalence surveys." *AIDS* 23 (5):621-629.

Reniers, G., and S. Helleringer. 2011. "Serosorting and the evaluation of HIV testing and counseling for HIV prevention in generalized epidemics." *AIDS Behav* 15 (1):1-8.

Reniers, G., and R. Tfaily. 2012. "Polygyny, partnership concurrency, and HIV transmission in Sub-Saharan Africa." *Demography* 49 (3):1075-1101.

Reniers, G., and S. Watkins. 2010. "Polygyny and the spread of HIV in sub-Saharan Africa: a case of benign concurrency." *AIDS* 24 (2):299-307.

Reniers, Georges. 2008. "Marital strategies for regulating exposure to HIV." *Demography* 45 (2): 417-438.

Sawers, L. 2013. "Measuring and modelling concurrency." *Journal of the International AIDS Society* 16:17431.

Sawers, L., A. G. Isaac, and E. Stillwaggon. 2011. "HIV and concurrent sexual partnerships: modelling the role of coital dilution." *Journal of the International AIDS Society* 14 (1):44.

Sawers, L., and E. Stillwaggon. 2010. "Concurrent sexual partnerships do not explain the HIV epidemics in Africa: a systematic review of the evidence." *Journal of the International AIDS Society* 13 (1):34.

Shisana, Olive. 2005. *South African national HIV prevalence, HIV incidence, behaviour and communication survey, 2005*: Human Sciences Research Council.

Suarez, T., and J. Miller. 2001. "Negotiating risks in context: a perspective on unprotected anal intercourse and barebacking among men who have sex with men--where do we go from here?" *Arch Sex Behav* 30 (3):287-300.

Todd, Jim, et al. 2007. "Time from HIV seroconversion to death: a collaborative analysis of eight studies in six low and middle-income countries before highly active antiretroviral therapy." *AIDS* 21:S55-S63.

UNAIDS. 2010. “UNAIDS report on the global AIDS epidemic, 2010.” Geneva.

UNAIDS, UNFPA, and UNIFEM. 2010. “Women and HIV/AIDS: Confronting the crisis.” Geneva.

UNAIDS/WHO. 2000. “Consultation on STD Interventions for Preventing HIV: What is the Evidence?” Best practice collection No. 9291731374. Geneva.

Watkins, S. C. 2004. "Navigating the AIDS epidemic in rural Malawi." *Population and Development Review* 30 (4):673-705.

Wawer, Maria J., et al. 2005. "Rates of HIV-1 transmission per coital act, by stage of HIV-1 infection, in Rakai, Uganda." *The Journal of Infectious Diseases* 191 (9):1403-1409.

WHO. 2012. “Hormonal contraception and HIV. Technical statement.” Geneva.

Wilensky, U. 1999. *NetLogo*. *http://ccl.northwestern.edu/netlogo/*. Northwestern University, Evanston, IL: Center for Connected Learning and Computer-Based Modeling.

Williams, B. G., E. L. Korenromp, E. Gouws, G. P. Schmid, B. Auvert, and C. Dye. 2006. "HIV infection, antiretroviral therapy, and CD4+ cell count distributions in African populations." *The Journal of Infectious Diseases* 194 (10):1450-1458.

Yi, T. J., B. Shannon, J. Prodger, L. McKinnon, and R. Kaul. 2013. "Genital immunology and HIV susceptibility in young women." *Am J Reprod Immunol* 69 Suppl 1:74-79.

[1] In contrast, women account for 35% of all HIV positives in Central and South America (UNAIDS 2010). This estimate correspond to a female-to-male sex ratios of infections of 0.54, and it is well understood that this large difference with generalized epidemics intimately related to the modes of transmission: the female-to-male HIV prevalence ratio is usually above unity in epidemics where heterosexual intercourse is the primary channel for new infections, and it is much lower in concentrated epidemics where sex between men or needle sharing among drug users are important epidemic drivers.

[2] It was precisely because of concerns over high refusal rates that the WHO initially chose to conduct anonymous surveillance in antenatal clinics (Chin 1990).

[3] Elaborating further on methodological issues in the measurement of gender inequity in HIV risk, it is worth noting that the sex ratio of prevalent infections, just as HIV prevalence itself, is a measure of the *stock of infections* over the whole reproductive age range. It thus includes recent as well as old infections, and it is dependent on the age structure of the population and gender differences in the survival of HIV positives (see below). Further, it is possible that higher levels of current infection in females in cross-sectional studies conceal equal or even higher cumulative HIV incidence among men (Gregson and Garnett 2000).

[4] Early reports suggest that ART use is indeed higher among infected women than among men (Braitstein et al. 2008; Mills et al. 2009).

[5] STIs can influence the sex ratio of infections because they are more prevalent in women, or, because they affect male-to-female transmission more than female-to-male rates.

[6] Young women's incidence rates are also high because the immaturity of their genital tract, which elevates susceptibility. In other words, a relatively early sexual debut and age mixing increases women's exposure to HIV as well as the transmission efficiency. In addition, a negative correlation exists between the age at infection and disease progression, and because women tend to be infected at younger ages they survive longer as HIV positives, which, in turn, elevates the sex ratio of infections in cross-sectional studies (Todd et al. 2007; Gregson and Garnett 2000).

[7] We refer to Morris and Kretzschmar (1997), Lurie and Rosenthal (2010), Mah and Halperin (2010), Sawers and Stillwaggon (2010), and Boily et al. (2012) for different points of view about the importance of partnership concurrency as an epidemic driver.

[8] A number studies have suggested that reporting bias inflates these gender differences (Nnko et al. 2004), but gender differences are likely to persist even in the absence of reporting issues.

[9] Coital dilution is a common phenomenon in polygynous marriages; the evidence for coital dilution in other studies of partnership concurrency is more mixed (Reniers and Tfaily 2012; Gaydosh et al. 2013; Delva et al. 2013).

[10] Elsewhere we have argued that elevated partnership dissolution in serodiscordant couples reduces the spread of HIV (Reniers and Armbruster 2012).

[11] We have borrowed this expression from Helleringer and Kohler, who offer it as one of the explanations for the distribution of HIV positives in their sexual network study of the Likoma Island in Lake Malawi. They found an over-representation of certain socioeconomic groups (e.g., older respondents, women, widows) in the sparser regions of the sexual network and suggest that they might have been infected when they were "closer to the dense regions of the networks but subsequently drift into smaller disjoint components" (Helleringer and Kohler 2007: 2330).

[12] See Eaton et al. (2011) and Goodreau (2012) for a comprehensive discussions of the interaction between partnership concurrency and acute infection.

[13] See Reniers and Watkins (2010) for an illustration of sexual networks with strict monogamy, gender asymmetric concurrency, and symmetric concurrency.