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Does heterosexual transmission drive the HIV/AIDS epidemic in Sub-Saharan Africa (or elsewhere)?

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Abstract

A two-sex Basic Reproduction Number (BRN) is used to investigate the conditions under which the Human Immunodeficiency Virus (HIV) may spread through heterosexual contacts in Sub-Saharan Africa. (The BRN is the expected number of new infections generated by one infected individual; the disease spreads if the BRN is larger than 1). A simple analytical expression for the BRN is derived on the basis of recent data on survival rates, transmission probabilities, and levels of sexual activity. Baseline results show that in the population at large (characterized by equal numbers of men and women) the BRN is larger than 1 if every year each person has 82 sexual contacts with different partners. the BRN is also larger than 1 for commercial sex workers (CSWs) and their clients (two populations of different sizes) if each CSW has about 256 clients per year and each client visits one CSW every two weeks. A sensitivity analysis explores the effect on the BRN of a doubling (or a halving) of the transmission probabilities. Implications and extensions are discussed.

KEYWORDS: Basic reproduction number, transmission probability, log-log complementary model, Weibull distribution.

1 Introduction

There is a growing debate as to whether heterosexual contacts are the main mode of transmission of HIV-1 in Sub-Saharan Africa (Gisselquist, Potterat, Brody and Vachon 2003; Brewer *et al.* 2003; French, Riley and Garnett 2006; Deuchert and Brody 2007). Some question the conventional wisdom of a heterosexual epidemic on the basis that assumed transmission probabilities per coital act are inflated (Deuchert and Brody 2007). Others, on the contrary, have developed complex mathematical models to show that alternatives such as the use of unsafe medical injections were unlikely to be the main route of transmission because they rely on unfeasibly high iatrogenic transmission probabilities (French *et al.* 2006).

In this paper we will show that a complex mathematical model is not necessary in order to assess the feasibility of a heterosexual epidemic. Indeed, the question can be studied by focusing on the basic reproduction number (BRN), which is the expected number of *secondary infections* generated by one infected individual in a completely susceptible population (i.e. at the beginning of an epidemic). The disease will spread if and only if the *BRN* is > 1 , i.e. each infected individual infects more than one other person.

The calculation of the BRN hinges crucially on the evolution over the course of the infection of the transmission probability per coital act. A careful study of a population-based cohort of discordant couples (one person infected) in Rakai, Uganda, has shed light on this question (Gray *et al.* 2001; Wawer *et al.* 2005). The first high-infectivity stage of the infection is characterized by an early peak in the viral load. This pattern is paralleled by a rise in the transmission probability per coital act that reaches a peak of about 0.008 before declining sharply one year into the infection. During the long second (asymptomatic) stage, the viral load is very low. The probability of transmission remains also very low, at around 0.001 per coital act. The third and last stage of the infection is characterized by a late peak in the viral load (and in the probability of transmission).

The likelihood of a heterosexual epidemic depends on the transmission probabilities but also on the number of partners. For example, with such relatively low probabilities, the disease may not take hold in a serially monogamous population, but could spread within high activity groups characterized by rapid changes in partnerships.

For this reason it is sufficient to focus on the possible heterosexual spread between high-activity groups. Indeed, if the disease can spread between such groups, it will spill over to others even if the transmission is inefficient from high to low activity sexual partners. The example that comes to mind is that of an epidemic that may spread efficiently between commercial sex workers (CSWs) and their clients. The latter, in turn, may infect, however inefficiently, their long-term female partners and thus spread the virus significantly among low activity women.

We will first derive an analytical expression for the viral load on the basis of recently available information obtained from the Rakai study (Gray et al. 2001; Wawer et al. 2005). We will then use the log-log complementary model to obtain an expression for the probability of transmission per coital act. This probability will be a function (via the viral load) of the infective age ia (time since infection) and of the infective age at death iad (time from infection to death). We will call $ptr(ia, iad)$ this transmission probability.

Highly active groups (such as CSWs and their clients) will be characterized by annualized numbers of coital acts $NCA(ia, iad)$ (assumed to take place always with new partners). This number depends on the infective age and the infective age at death because the number of coital acts decreases as a person advances in the disease and approaches death (Wawer et al. 2005).

The transmission rate for an individual who has been infected ia years and will die at iad years is now $NCA(ia, iad)ptr(ia, iad)$. If $s(x)$ is the density function of the infective age at death, the basic reproduction number R_0 is the expected value of the number of secondary infections generated by one individual during his/her infective life course (with

maximum duration ω):

$$R_0 \stackrel{def.}{=} \int_{y=0}^{\omega} s(y) \int_{x=0}^y NCA(x, y) ptr(x, y) dx dy. \quad (1)$$

This is the BRN of a single sex model in which transmission is the same between all individuals. In particular the transmission rate and density of survival time are assumed to be the same for both sexes. However, survival differs slightly between men and women (UNAIDS 2002). There can also be large differences in the number of coital acts when dealing with groups of different sizes such as CSWs and male clients. Transmission rates may be different for the two sexes. For example there is a growing consensus that male circumcision reduces significantly female-to-male transmission (Nagelkerke, Moses, de Vlas, Bailey 2007).

For these reasons we must consider two sex-specific basic reproduction numbers: the number R_{fm} of secondary males infected by one infected woman ("the female to male BRN"), as well as R_{mf} , the male to female BRN. The product $R_{fm}R_{mf}$ is therefore the number of same-sex *tertiary infections* generated by one infected person. The expressions for R_{mf} and R_{fm} will be those of Eq. (1) with the three functions $s(y)$, $NCA(x, y)$ and $ptr(x, y)$ indexed by m for R_{mf} and by f for R_{fm} .

Although one could have defined the two-sex BRN as the product $R_{fm}R_{mf}$, it is generally defined as the harmonic mean

$$R_0 \stackrel{def.}{=} \sqrt{R_{fm}R_{mf}} \quad (2)$$

of the two sex-specific BRNs. This definition reflects the fact that transmission takes place over two generations (Heesterbeek and Roberts 2007). It is also consistent with the definition of the BRN as the dominant eigenvalue of the next-generation matrix $\begin{pmatrix} 0 & R_{mf} \\ R_{fm} & 0 \end{pmatrix}$.

The threshold condition for an epidemic flare-up is now $R_0 > 1$, i.e. $R_{fm}R_{mf} > 1$: the number of same-sex tertiary infections generated by one infected individual must be larger than 1 for the epidemic to take hold.

We will show that with a set of realistic baseline parameter values, then in the population at large (characterized by equal numbers of men and women), the basic reproduction number R_0 is larger than 1 if each year every person has 82 sexual contacts with different partners. Within the CSW-client populations (where men outnumber women) the infection can spread if each CSW has about 256 clients per year and each client visits one CSW every two weeks.

The paper is organized as follows. In Section 2 below we derive expressions for the viral load, the transmission probability per coital act, the annualized number of coital acts, and the density function of survival times. In Section 3 we give an expression for the two-sex basic reproduction number and formulate the threshold condition in terms of the Index of Sexual Activity. Results are then illustrated with realistic parameter values pertaining to Sub-Saharan Africa. The sensitivity of the results are discussed for different values of the probability of transmission function. In Section 4 we discuss our findings, their implications and possible extensions.

2 The four components of the basic reproduction number

The construction of the basic reproduction number is the same for both sexes. For ease of exposition we will therefore drop the indexes f and m from the functions (and parameters) used to define R_{fm} and R_{mf} .

2.1 Viral load

In the absence of treatment, the logarithm base 10 (\log_{10}) of the viral load (measured in copies/mL) follows a well-established pattern as a function of the infective age ia and of the infective age at death (iad) (Rapatski, Suppe, Yorke 2005). During the first year of infection the logarithm increases to approximately 5 and decreases rapidly thereafter (first stage). It then remains around 3 during the long asymptomatic second stage. About a year before death there is a second peak in the viral load.

We now describe a function noted $LVI(ia, iad)$, that captures this "twin peaks" pattern in the \log_{10} of the viral load during the course of the infection. The parameters that define the function are given in Table 1, together with baseline numerical values which reflect empirical results obtained from the Rakai study (Gray et al. 2001; Wawer et al. 2005). We take the same parameter values for both sexes.

<i>Parameter</i>	<i>Baseline value</i>
ia_1 : Infect. age at first peak	0.4 year
M_1 : Value of $LVI(ia_1, iad)$ at 1st peak	5
m : Low value of $LVI(ia, iad)$ during second stage	3
τ_1 : Time preceding death at 2nd peak	1 year
M_2 : Value of $LVI(ia_1, iad)$ at 2nd peak	4.8
α_1, α_2 : Parameters that determine the variance in the 1st peak	1.3; 0.2
α_3 : Parameter that determines the variance in the 2nd peak	0.7

We first define the function

$$h_1(x, \alpha_1, M_1, ia_1) \stackrel{def.}{=} \frac{M_1 x^{\alpha_1 - 1} \exp\left[\frac{x(1 - \alpha_1)}{ia_1}\right]}{ia_1^{\alpha_1 - 1} \times \exp(1 - \alpha_1)} \quad (3)$$

which reaches a maximum of M_1 for $x = ia_1$. We then need the largest root x^* of the equation $h_1(x, \alpha_1, M_1, ia_1) = m$ in the unknown x ; $x^* = 1.647$ and will be used to obtain the low value m during the long asymptomatic second stage.

We also need the function

$$h_2(ia, \alpha_2, x^*) \stackrel{def.}{=} x^*[1 + \exp(-\alpha_2)] \times \left[\left(1 + \exp \left[\alpha_2 - \frac{ia(1 + \exp(\alpha_2))}{x^*} \right] \right)^{-1} - (1 + \exp(\alpha_2))^{-1} \right] \quad (4)$$

which will be used as the argument x in the function h_1 . This will produce the first peak followed by the low value during the asymptomatic stage.

The function

$$h_3(x, y, \alpha_3, \tau_1) \stackrel{def.}{=} \exp[-\alpha_3(x - y + \tau_1)^2] \quad (5)$$

will be used to obtain the late-stage peak. We combine these elements to finally define

$$LVl(ia, iad) \stackrel{def.}{=} h_1(h_2(ia, \alpha_2, x^*), \alpha_1, M_1, ia_1) + [M_2 - h_1(h_2(ia, \alpha_2, x^*), \alpha_1, M_1, ia_1)]h_3(ia, iad, \alpha_3, \tau_1). \quad (6)$$

The \log_{10} of the viral load function $LVl(ia, iad)$ corresponding to the parameter values in Table 1 is plotted in Figure 1 for an infective age at death (iad) of 7 years (together with the transmission probability function derived below). For a later infective age at death the function is similar with just a longer asymptomatic stage.

2.2 Transmission probability per coital act

Gray et al. (2001) propose the log-log complementary model for the transmission probability per coital act with (chronological) age and viral load as covariates (variables age and vl). Under this model this probability of transmission is of the form

$$ptr_0(age, vl) \stackrel{def.}{=} 1 - \exp[-\exp(\kappa_0 + \kappa_1 vl + \kappa_2 age)] \quad (7)$$

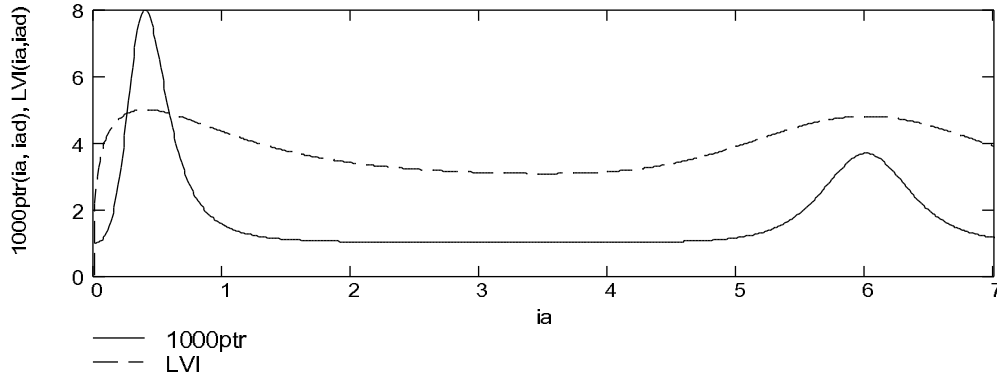


Figure 1: \log_{10} of viral load function $LVI(ia, iad)$ and 1000 times probability of transmission per coital act function ($1000ptr(ia, iad)$) for a person who dies seven years into the infection ($iad = 7$).

with parameters $\kappa_m (m = 0, 1, 2)$.

The effect of age does not appear to be very strong (Gray et al. 2001; Wawer et al. 2005) and would complicate the expression for the basic reproduction number. As a simplification we therefore drop age as a covariate. Bearing in mind that $10^{LVI(ia, iad)}$ is the viral load, we re-express an average (across ages) probability of transmission per coital act as the function

$$ptr(ia, iad) \stackrel{def.}{=} 1 - \exp[-\exp(\kappa_0 + \kappa_1 10^{LVI(ia, iad)})]. \quad (8)$$

We parameterize this function by specifying the values ptr_{hi} and ptr_{lo} of $ptr(ia, iad)$ at the values M_1 and m of $LVI(ia, iad)$ corresponding to the first peak in viral load and to the low plateau. For given values of ptr_{hi} and ptr_{lo} , the parameters κ_0 and κ_1 are then the roots of the system

$$ptr_{hi} = 1 - \exp[-\exp(\kappa_0 + \kappa_1 10^{M_1})], \quad ptr_{lo} = 1 - \exp[-\exp(\kappa_0 + \kappa_1 10^m)] \quad (9)$$

from which

$$\kappa_0 = \frac{\ln \left[\frac{\ln(1 - ptr_{lo})}{\ln(1 - ptr_{hi})} \right]}{10^{M_1 - m} - 1} + \ln [\ln(1 - ptr_{lo})^{-1}], \quad \kappa_1 = \frac{\ln \left[\frac{\ln(1 - ptr_{lo})}{\ln(1 - ptr_{hi})} \right]}{10^m - 10^{M_1}}. \quad (10)$$

With the numerical values $ptr_{lo} = 0.001$ and $ptr_{hi} = 0.008$, the resulting function $ptr(ia, iad)$ (multiplied by 1000 in Figure 1) provides a good stylized approximation of recent empirical estimates based on the Rakai study (Wawer et al. 2005). We take the same parameter values for both sexes.

2.3 Annualized number of coital acts with different partners

We next construct a functional form for the annualized number of coital acts $NCA(ia, iad)$. This function will reflect a decreasing level of sexual activity as an infected person approaches death (Wawer et al. 2005). The parameter Δ will be the value of NCA at the time of infection ($NCA(0, iad) = \Delta$), i.e. the annual number in the absence of HIV infection.

The parameter ϕ will be the fractional number of coital acts remaining when an individual reaches the infective age $iad - \tau_1$ at which the viral load reaches its second (pre-death) peak ($NCA(iad - \tau_1, iad) = \Delta\phi$). Finally NCA will be 0 at the time of death ($NCA(iad, iad) = 0$).

We now define for $ia \leq iad$ the function $G(ia, iad)$ equal to the fractional number of (annualized) coital acts remaining for an individual infected ia years ago and who will die iad years into the disease:

$$G(ia, iad) \stackrel{def.}{=} \begin{cases} \frac{1 - ia/iad}{1 + \frac{ia(\tau_1 - \phi \cdot iad)}{iad \cdot \phi(iad - \tau_1)}} & \text{if } iad > \tau_1; \\ 0 & \text{if } iad \leq \tau_1. \end{cases} \quad (11)$$

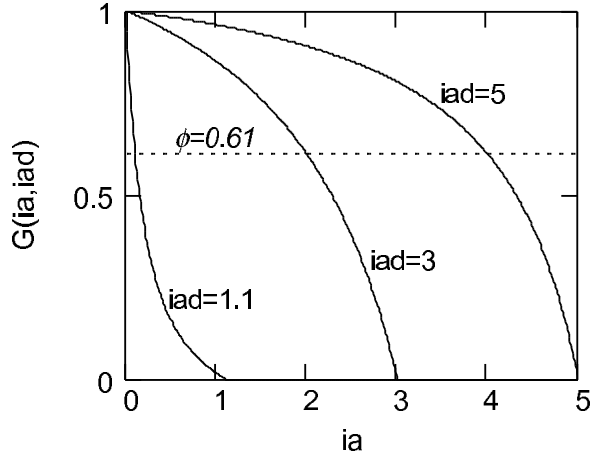


Figure 2: Fractional number $G(ia, iad)$ of (annualized) coital acts remaining ia years into the infection for an individual who will die $iad=1.1, 3$ or 5 years into the infection (with $\tau_1 = 1$ and $\phi = 0.61$, the function satisfies $G(0.1, 1.1) = G(2, 3) = G(4, 5) = \phi = 0.61$).

This function is equal to 1 for $ia = 0$, to ϕ for $ia = iad - \tau_1$ and to 0 for $ia = iad$. A function $NCA(ia, iad)$ that has the required properties is obtained by multiplying $G(ia, iad)$ by Δ :

$$NCA(ia, iad) \stackrel{def.}{=} \Delta \cdot G(ia, iad). \quad (12)$$

A baseline value of ϕ was taken equal to 0.61 on the basis of a mean reported number of coital acts per week of 10.2 at the beginning of the infection and of a mean number during a 6-15 month period prior to death of 6.2 ((Wawer et al. 2005), $10.2/6.2 = 0.61$). We take the same parameter values for both sexes.

The function $G(ia, iad)$ is plotted in Figure 2 for three different values of iad and with $\tau_1 = 1$. As iad becomes closer to τ_1 , the function $G(ia, iad)$ of ia approaches 0 more and more rapidly as ia tends to iad . The fact that $G(ia, iad)$ is zero when the infective age at death iad drops below τ_1 means that no sexual activity is assumed for a very short infection (e.g. an infection that lasts less than one year when $\tau_1 = 1$). This drop to zero in sexual activity may not be entirely realistic, but is of little importance since there are extremely few, if any, infected individuals who will survive such a short period.

2.4 Density function of infective age at death iad

Following the World Health Organization we assume a Weibull distribution for the infective age at death (UNAIDS 2002). We parameterize this distribution with its median me and shape parameter β . If we define $\alpha \stackrel{def.}{=} me (\ln(2))^{-1/\beta}$ the density function $s(x)$ of iad is then

$$s(x) = \frac{x^{\beta-1}\beta}{\alpha^\beta} \exp \left[- \left(\frac{x}{\alpha} \right)^\beta \right]. \quad (13)$$

We use $\beta = 2.5$ for the shape parameter for both sexes and a slightly shorter median for women ($me_f = 8.6$ years) than for men ($me_m = 9.4$ years) (UNAIDS 2002).

3 Results

3.1 Threshold conditions on the basic reproduction number

In general all functions (and parameters) are indexed by f and m . The two sex-specific basic reproduction numbers are then

$$R_{fm} \stackrel{def.}{=} \Delta_f \int_{y=0}^{\omega} s_f(y) \int_{x=0}^y G_f(x, y) ptr_f(x, y) dx dy \quad (14)$$

$$R_{mf} \stackrel{def.}{=} \Delta_m \int_{y=0}^{\omega} s_m(y) \int_{x=0}^y G_m(x, y) ptr_m(x, y) dx dy. \quad (15)$$

We next define the quantity

$$I_0 \stackrel{def.}{=} \left(\int_{y=0}^{\omega} s_f(y) \int_{x=0}^y G_f(x, y) ptr_f(x, y) dx dy \times \int_{y=0}^{\omega} s_m(y) \int_{x=0}^y G_m(x, y) ptr_m(x, y) dx dy \right)^{-1/2}. \quad (16)$$

This quantity I_0 reflects at the individual level the combined effects for both sexes of variable infectivity, mortality, and sexual activity over the course of the infection. We also define the Index of Sexual Activity (ISA) as the harmonic mean of the contact rates Δ_m and Δ_f (i.e. the sex-specific annualized numbers of coital acts at the beginning of the infection):

$$ISA \stackrel{def.}{=} \sqrt{\Delta_m \Delta_f}. \quad (17)$$

The Index of Sexual Activity measures the level of sexual activity between the two groups.

With these definitions, the composite basic reproduction number

$$R_0 \stackrel{def.}{=} \sqrt{R_{fm} R_{mf}} \quad (18)$$

will be larger than 1 if and only if

$$ISA > I_0. \quad (19)$$

The (annualized) number of coital acts men have with women must be the same as the number of acts women have with men. If P_f and P_m are the sizes of the corresponding female and male populations, we must therefore have

$$P_f \times \Delta_f = P_m \times \Delta_m. \quad (20)$$

The threshold condition (19) can then be paraphrased by saying that *when both populations have the same size* then I_0 is the minimum annualized number of coital acts each person must have with different partners in order for the disease to take hold (since then Δ_f and Δ_m are equal).

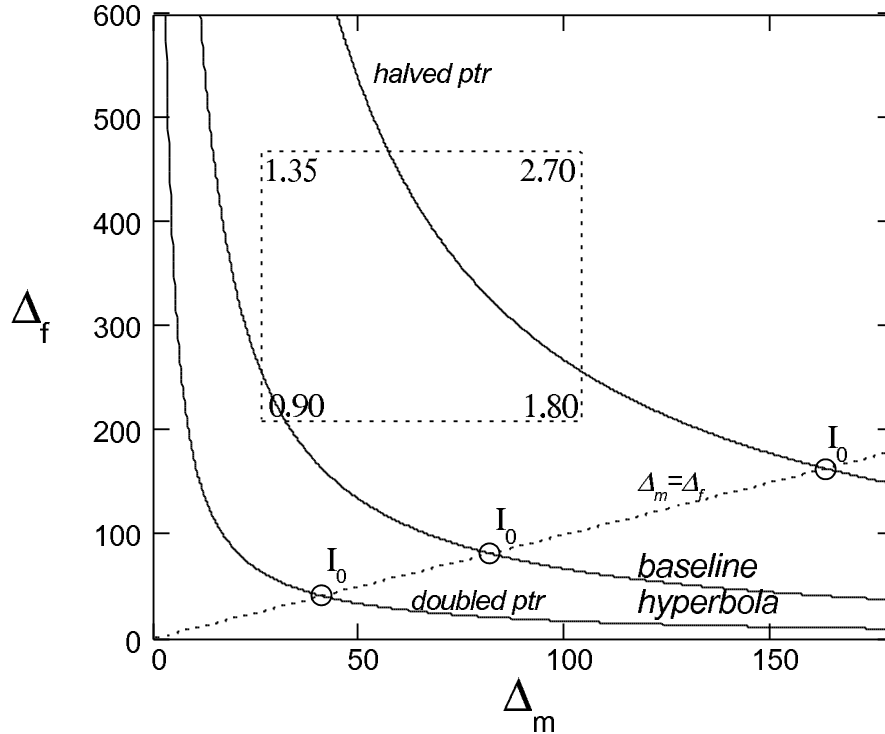


Figure 3: Phase space of annualized numbers of coital acts by women (Δ_f) and men (Δ_m) with locus $\Delta_m \Delta_f = I_0^2$ of values for which $R_0 = 1$ (baseline hyperbola obtained with parameter values of Section 2). The basic reproduction number R_0 is larger than 1 above the curve and vice-versa. The black circle on the hyperbola is the fixed point $I_0 = 81.60$, i.e. the minimum annual number of coital acts for the epidemic to spread when the male and female populations are of the same size. The "feasible rectangle" covers a range of plausible values of Δ_m and Δ_f for commercial sex workers and their clients (see text). The basic reproduction number at the four corners show that R_0 is larger than one in almost the entire feasible rectangle. The two other hyperbolae correspond to a halving and to a doubling of the probability of transmission function ptr for both sexes. The effect is linear on I_0 which is then 40.8 and 163.2. With a halving of the probabilities, R_0 is larger than one only for high levels of sexual activity (for example $\Delta_m = 100$ prostitute visits per year and $\Delta_f = 400$ customers per year for each commercial sex worker). With a doubling of the probabilities, R_0 is larger than one in the entire feasible rectangle and well below.

3.2 Numerical illustration (with baseline parameter values)

The baseline parameter values and functions are those given in Section 2. They are the same for both sexes, except

- for the crucial sex-specific contact rates Δ_m and Δ_f between the two groups that will be used for the sensitivity analysis below.
- for the slightly different median survival times $me_f = 8.6$ and $me_m = 9.4$.

The quantity I_0 is independent of Δ_m and Δ_f and its baseline value is 81.60. In the (Δ_m, Δ_f) phase space the corresponding baseline hyperbola of equation $\Delta_m \Delta_f = I_0^2$ is therefore the locus of values for which R_0 is equal to 1 (Figure 3).

With male and female populations of the same size ($\Delta_m = \Delta_f$) the fixed point $I_0 = 81.60$ (black circle) of the baseline hyperbola tells us that each newly infected person needs about 82 coital acts per year with *different* partners in order for the disease to spread. This is a small number compared to the documented 10.2 acts per week reported above. The requirement that these acts take place with different partners, on the other hand, is in stark contrast with surveys that report an average of about one partner per year in Sub-Saharan Africa (Deuchert and Brody 2007). In short, the disease can spread between groups of men and women of equal sizes for a reasonable annual number of coital acts, but with the requirement of a very high turnover of partners.

Commercial sex workers and their clients are groups of different sizes characterized by a (Δ_m, Δ_f) point that lies above the main diagonal ($\Delta_m = \Delta_f$) of the phase-space diagram in Figure 3. The number of acts per year varies considerably, however, with estimates for men in the range 0.5-2 prostitute visits per week, i.e. $26 \leq \Delta_m \leq 104$ (Nagelkerke et al. 2007). A range for annual numbers of clients is based on medians of 4 and 9 per week in rural and urban areas of Kenya (Elmore-Meegan, Conroy and Agala 2004). These medians translate into the range $208 \leq \Delta_f \leq 468$ for annualized numbers of coital acts performed

by each CSW with her clients. The lower bound may reflect "casual" practices, while the upper one is probably conservative, with estimates of up to 15 per day ($\Delta_f = 5475$) in Ghana (Asamoah-Adu et al. 2001). The resulting "feasible rectangle" of (Δ_m, Δ_f) values is depicted in Figure 3. The values of the basic reproduction number R_0 (Eq. (18)) at the four corners are given in the rectangle. At the lower left corner each infected CSW will infect $R_{fm} = 2.47$ clients, who will each in turn infect $R_{mf} = 0.33$ CSWs. The resulting R_0 is equal to $\sqrt{R_{fm}R_{mf}} = 0.90$. This shows that despite an efficient female-to-male transmission the infection will not spread if clients visit a CSW only every other week and CSWs service only 208 clients a year. If (Δ_m, Δ_f) moves up the left side of the rectangle then R_{mf} remains unchanged and the point (Δ_m, Δ_f) enters the $R_0 > 1$ region for $\Delta_f = I_0^2/\Delta_m = 81.60^2/26 = 256.1$ (i.e. when R_{fm} reaches 3.04). For (Δ_m, Δ_f) at the upper right corner, $R_{fm} = 5.55$ and $R_{mf} = 1.32$: both BRNs are larger than 1 for an overall R_0 of 2.70.

3.3 Sensitivity analysis on transmission probabilities

There is a fair amount of uncertainty concerning the values of the peak and low transmission probabilities ptr_{hi} and ptr_{lo} whose baseline values were taken as 0.008 and 0.001. For example the 0.008 figure was an estimated probability at infective age 5 months, with a 95% confidence interval of (0.004, 0.0015) (Wawer et al. 2005).

In order to assess this sensitivity to the transmission probabilities we plotted in Figure 3 the two hyperbolae corresponding to a halving (resp. a doubling) for both sexes of both parameters ptr_{hi} and ptr_{lo} . This means a halving (resp. a doubling) of the ptr function and has a linear effect on I_0 which is doubled to 163.2 (resp. halved to 40.8). With a halving of the ptr function about two thirds of the feasible rectangle is in the $R_0 < 1$ region. Fairly high contact rates Δ_m and Δ_f are needed in order for the disease to spread. With a doubling of ptr the rectangle is entirely in the $R_0 < 1$ region and the spread will

take place with much smaller values of Δ_m and Δ_f .

4 Discussion

Our goal was to use the basic reproduction number R_0 to investigate whether HIV-1 can spread in Sub-Saharan Africa (or elsewhere) primarily through heterosexual contacts. Fraser, Riley, Anderson and Ferguson (2004) point out that published estimates of R_0 for generalized heterosexual HIV epidemics are hard to come by. This is no doubt because of complex transmission mechanisms and the heterogeneity of the populations involved.

In this paper we have introduced a data-driven analytical expression for a two-sex basic reproduction number that captures the nuances of variable infectivity and of changing levels of sexual activity over the course of the infection.

The results show that with our baseline parameter values the disease can spread between groups of men and women of equal sizes with a reasonable number of coital acts per year (82). However these contacts must take place with different partners, which implies an unusually high level of sexual activity. The infection will spread between CSWs and their clients for most plausible contact rates Δ_m and Δ_f .

By focusing on the BRN we were able to investigate conditions for a heterosexually driven HIV/AIDS epidemic on the basis of the survival, infectivity, and contact rates alone. We did not have to make the many complex assumptions needed for a full-blown dynamic model of HIV transmission (e.g. mixing patterns, partnership formation rules, etc.). Valuable insights have thus been gained with a minimum number of assumptions and parameters.

Epidemiologists, public health officials and others can now make judgements concerning the potential spread of HIV-1 by checking the simple condition $\Delta_m \Delta_f > I_0^2$ with local values of the contact rates Δ_m and Δ_f . It is wise however to take into account the

uncertainty on I_0 by considering its plausible lower and higher values of 40.8 and 163.2.

At least the overall (average) transmission probability obtained from the Rakai study is believed to be similar to that reported from "prospective studies of European, north American and Thai heterosexual couples" (Gray et al. 2001, p. 1152). The transmission function ptr may therefore be applicable to populations outside of Uganda.

Our results assume no intervention (condoms, circumcision, therapy, etc). However the survival, viral load or transmission functions can be changed to assess the effect on the basic reproduction number of longer survival and/or antiretroviral therapies. More generally, the theoretical results of Section 3.1 can be used for any sexually transmitted infection by using the appropriate function needed to calculate R_{fm} and R_{mf} .

Finally we emphasize that our results are based on the assumption of instantaneous partner changes which implies a high level of sexual activity. Our results are not applicable to a population characterized by alternating periods in and out of a partnership (as in Morris and Kretzschmar 2000). Everything else being equal (survival, infectivity, etc.) expected numbers of secondary infections will be lower in such partnerships. This is because during the whole duration of a (monogamous) partnership an infected individual can transmit the virus to only one person. If that happens, there will be no more transmission until the end of the current partnership, itself often followed by a period without sexual activity. Calculating an expected number of secondary (and tertiary) infections in this case is a difficult statistical problem currently under investigation.

References

- Asamoah-Adu, C., Khonde, N., Avorkliah, M., Bekoe, V., Alary, M., Mondor, M. et al. (2001) "HIV Infection Among Sex Workers in Accra: Need to Target New Recruits Entering the Trade," *Journal of Acquired Immune Deficiency Syndromes*, 28(4): 358-366.
- Brewer DD, Brody S, Drucker E, Gisselquist D, Potterat JJ, Rothenberg RB, et al. Mount-

- ing anomalies in the epidemiology of HIV in Africa: Cry the beloved paradigm. *International Journal of STD & AIDS*, 2003;14:144-147.
- Deuchert, E., and Brody, S. (2007) Plausible and Implausible Parameters for Mathematical Modeling of Nominal Heterosexual HIV Transmission," *Annals of Epidemiology*, 17: 237-244.
- Elmore-Meegan, M., Conroy, R.M., and Agala, C.B. (2004) "Sex Workers in Kenya, Numbers of Clients and Associated Risks: An Exploratory Survey." *Reproductive Health Matters*, 12(23):50-57.
- Fraser, C., Riley, S., Anderson, R.M., and Ferguson N.M. (2004) "Factors that make an infectious disease outbreak controllable," *PNAS*, 101, 6146-6151.
- French, K., Riley, S., and Garnett, G. (2006) "Simulations of the HIV Epidemic in Sub-Saharan Africa: Sexual Transmission Versus Transmission Through Unsafe Medical Injections," *Sexually Transmitted Diseases*, 33, 3: 127-134.
- Gisselquist, D., Potterat, JJ, Brody, S., Vachon, F. (2003) "Let it be Sexual: How Health Care Transmission of AIDS in Africa Was Ignored," *International Journal of STD & AIDS*, 14(3):148-161.
- Gray, R.H., Wawer, M.J., Brookmeyer, R., Sewankambo, N.K., Serwadda, D., Wabwire-Mangen, F. et al.(2001) "Probability of HIV-1 transmission per coital act in monogamous, heterosexual, HIV-1-discordant couples in Rakai, Uganda," *Lancet*, 357 (2001):1149-1153.
- Heesterbeek, J.A.P. and Roberts, M.G. (2007) "The type-reproduction number T in Models for Infectious Disease Control," *Mathematical Biosciences*, 206, 1: 3-10.
- Morris, M. and Kretzschmar, M. (2000) "A Microsimulation Study of the Effect of Concurrent Partnerships on the Spread of HIV in Uganda," *Mathematical Population Studies*, 8(2): 109-133.
- Nagelkerke, N.J., Moses, S., de Vlas, S.J., Bailey, R.C. (2007) "Modelling the Public Health Impact of Male Circumcision for HIV Prevention in High Prevalence Areas in Africa," *BMC Infectious Diseases*, 7: 16.
- Pilcher, C.D., Tien, H.C., Eron, J.J., Vernazza, P.L., Leu, S.Y., Stewart, P.W. et al. "Brief but Efficient: Acute HIV Infection and the Sexual Transmission of HIV," *Journal of Infectious Diseases*, 2004; 189:1785-92.
- Rapatski, B.L., Suppe, F., Yorke, J.A. (2005) " HIV Epidemics Driven by Late Disease Stage Transmission," *Journal of Acquired Immune Deficiency Syndrome*, 38:241-253.
- UNAIDS (2002) "Improved Methods and Assumptions for Estimation of the HIV/AIDS Epidemic and its Impact: Recommendations of the UNAIDS Reference Group and Estimates, Modelling and Projections," *AIDS*, 16(9), W1-W14.

Wawer, M.J., Gray, R.H., Sewankambo, N.K., Serwadda, D., Li, X., Laeyendecker, O., Kiwanuka, N. (2005) "Rates of HIV-1 Transmission per Coital Act by Stage of HIV-1 Infection, in Rakai, Uganda," *Journal of Infectious Diseases*, 191, 1403-1409.