MATHEMATICAL BIOSCIENCES
AND ENGINEERING
Volume **6**, Number **1**, January **2009**

doi:10.3934/mbe.2009.6.135

pp. **135–143**

MODELING HIV OUTBREAKS: THE MALE TO FEMALE PREVALENCE RATIO IN THE CORE POPULATION

Brandy Rapatski

Department of Mathematics
Richard Stockton College of New Jersey, Pomona, NJ 08240, USA

James Yorke

Departments of Mathematics & Physics
University of Maryland, College Park, MD 20742, USA

(Communicated by Abba Gumel)

Abstract. What affects the ratio of infected men to infected women in the core population in a heterosexual HIV epidemic? Hethcote & Yorke [5] introduced the term "core" initially to loosely describe the collection of individuals having the most unprotected sex partners. We study the early epidemic during the exponential growth phase and focus on the core group because most infected people were infected by people in the core. We argue that in the early outbreak phase of an epidemic, there is an identity, which we call the "outbreak equation." It relates three ratios that describe the core men versus the core women, namely, the ratio E of numbers of all core men to all core women, the ratio C of numbers of infected core men to core women, and the ratio M of the infectiousness of a typical core man to that of a typical core woman. Then the relationship between the ratios is $E = MC^2$ in the early outbreak phase. We investigate two very different scenarios, one in which there are two times as many core men as core women ($E = 2$) and the other in which core men equal core women ($E = 1$). In the first case, the HIV epidemic grows at a much faster rate. We conclude that if the female core group was larger, that is, if more women in the total population were promiscuous (or if fewer men were promiscuous) then the HIV epidemic would grow more slowly.

1. **Introduction.** Until recently, many populations have had more men infected with HIV than women [14, 1]. In Senegal, as in other African countries, the ratio of the reported number of women infected to the number of men infected has changed rapidly: in 1986 the reported ratio was 1 infected woman for every 6 infected men; in 1990, 1 to 3; in 1997, one to two; and in 1999, between 1.2 and 1.3 to 1 [11].

Women are reported to be significantly less infectious than men [12]. In studies of married couples where one spouse contracted HIV via blood transfusion, infected husbands are observed to be much more likely to infect their wives than the reverse [13]. Logically, greater infectiousness of men seems to suggest that men are infecting women faster than women are infecting men, and that at any moment

2000 *Mathematics Subject Classification.* Primary: 92D30.

Key words and phrases. human immunodeficiency virus, infectiousness, core population, infectiousness multiplier, effective contact rate.

The authors are supported by Richard Stockton College of New Jersey Research Professional Development Grant, NSF grant DMS 0616585 and NIH grant 1R01HG0294501.

in the heterosexual epidemic outbreak, more women would be infected than men. Our result explains the apparent contradiction. It has long been recognized that female sex workers can play a key role in transmission and our results make this connection precise. We discuss the question of relative infectiousness extensively in [16], comparing the above references with [17].

In this paper we focus exclusively on outbreaks of sexually transmitted diseases (and specifically HIV) that are driven by heterosexual transmission. We define the "male core group" to be men engaging in unprotected sex with the most partners and the "female core group" to be the women engaging in unprotected sex with the most unprotected sex partners. The "core" is the male core group plus the female core group.

2. **Methods.**

2.1. **Definitions for the "outbreak" or "exponential growth" phase of the epidemic.**

We study the dynamical balance between the female core group and the male core group in a heterosexual HIV outbreak. Let $X(t)$ and $Y(t)$ denote the cumulative total number of core women and men infected at time t. These numbers include those who are no longer alive. The following result oversimplifies a real growing epidemic and only investigates the factors that drive the epidemic's growth. As the core population becomes saturated with infected people and depleted of its susceptibles, the behavioral profile will change. We assume we are investigating the epidemic up to some time T, which is before this change in dynamics. We refer to this period as the "exponential growth phase" of the epidemic.

Usually disease transmission equations involve the fraction or number infected and the fraction susceptible. For the phase of the epidemic that interests us the equations are simpler because the vast majority is susceptible. We assume the number of people infected in week n is a linear function of the people infected up to N weeks earlier where N is on the order of 1000. Hence there are constants $f_j > 0$ and $g_j > 0$ for $j = 1, ..., N$. These numbers are averages and are a combination of how infectious individuals are and how many contacts they have per week, both of which depend on how many weeks, j, they have been infected. These numbers implicitly include as a factor the probability that the infected individual is still alive. That probability gets small by time 1000, so f_j and g_j are small when j is large. Notice that men infect only women and vice versa in our dynamics. Write $x(n)$ and $y(n)$ for the (expected) numbers of men and women infected in week n:

$$x(n) = \sum_{j=1}^{N} f_j * y(n-j) \tag{1}$$

$$y(n) = \sum_{j=1}^{N} g_j * x(n-j).$$

Let

$$u(n) = (x(n), x(n-1), ..., x(n+1-N))$$
$$v(n) = (y(n), y(n-1), ..., y(n+1-N)).$$

Then $w(n) = (u(n), v(n)) \in R^{2N}$. The right-hand side of system 1 is a linear function A from R^{2N} to R^{2N} and we write

$$w(n) = A(w(n-1)). \tag{2}$$

Let $||w||$ denote the L^1 norm. Let Q denote the set of vectors in R^{2N} for which all coordinates are non-negative and P the subset where they are all positive. Note that $A : Q \to Q$. If w is in Q and has at least one positive coordinate, then $A^m w \in P$ for all $m > N$. By the Frobenius-Perron Theorem, there is a unique eigenvector w_e with norm 1 in Q and in fact it is in P. Furthermore if we denote its eigenvalue by $\lambda > 0$ and if μ is any other eigenvalue, then $\lambda > |\mu|$. If $w(n-1)$ is an eigenvector in P, then $w(n) = \lambda w(n-1)$. Hence,

$$u(n+1) = (x(n+1), x(n), ...) = \lambda u(n) = \lambda(x(n), x(n-1), ...).$$

So, $x(n+1) = \lambda x(n)$ for all n and $x(n-j) = \lambda^{-j} x(n)$ for all n and j. Similarly, $y(n-j) = \lambda^{-j} y(n)$. Writing (u_e, v_e) for w_e, there are constants C_u and $C_v > 0$ for which

$$u_e = C_u(1, \lambda^{-1}, ..., \lambda^{-N+1})$$
$$v_e = C_v(1, \lambda^{-1}, ..., \lambda^{-N+1}).$$

For a positive eigen solution of 1, $y(n)/x(n) = C_u/C_v$ for all n. Notice that since λ is a simple eigenvalue, its eigenvectors differ only by a multiplicative constant. Hence C_u/C_v is independent of the choice of λ's eigenvector. If we write a non-zero real vector w_0 in Q as a sum of constants times eigenvectors (allowing complex constants), then the coefficient of w_e is non-zero. That component will grow faster than the others. We can assume λ is the dominant eigenvector,

$$A^m w_0 / ||A^m w_0|| \to w_e, \text{as } m \to \infty.$$

For any solution of 1 with positive coordinates for $n >= 0$,

$$y(n)/x(n) \to C_u/C_v, \text{as } n \to \infty.$$

Since

$$X(n) = \sum_{j=1}^{\infty} x(n-j) \tag{3}$$
$$Y(n) = \sum_{j=1}^{\infty} y(n-j)$$

and since for each j

$$y(n-j)/x(n-j) \to C_u/C_v, \text{as } n \to \infty.$$

the corresponding result for the cumulative numbers of infected also holds,

$$Y(n)/X(n) \to C_u/C_v, \text{as } n \to \infty.$$

2.2. **Definitions.** Let E denote the ratio of active core men to core women including both susceptible and infected individuals. Hence, E describes the "environment" in which most of the cases occur. When female sex workers play the predominant role in transmission, E, the ratio of the number of clients to sex workers, is large.

Let C denote the "core infection ratio," the ratio of the number of infected core men to infected core women; it follows that $Y(t)/X(t) \to C_u/C_v$. In the early stages of the epidemic, as the number of infected people increases, we will assume their ratio remains constant, $(C = C_u/C_v)$. That also means the rates $y(n)$ and $x(n)$ at

which core women and core men are becoming infected has the same constant ratio C for each n. We expect $C > 1$, more men infected than women.

A person's "infectiousness" is the probability he or she will transmit the infection to a susceptible partner on contact. Here we are discussing individuals who have multiple occasional, or one-time, partners. Transmission rates between regular partners may be significantly lower.

From here on we assume that men and women have the same "profile of infectiousness"; that is, there is some β such that for all j

$$g_j/f_j = \beta. \tag{4}$$

That is, women who have been infected for time j infect more people by a factor β than men who have been infected by time j (where β could be less than 1). The infectiousness of men and women will vary with time, and the rate at which that person contacts others will vary with time, but we are assuming that g_j and f_j vary in the same way.

Let M denote the "infectiousness multiplier," the ratio of the infectiousness of men to that of women. The rate at which an average infected core member infects susceptibles is the product of the infectiousness per contact with number of contacts with susceptibles per unit time. Since each sexual contact involves one man and one woman and there are E times as many men as women, the average woman has E times as many contacts per unit time as the average man. Since she is less infectious by a factor of M, we get $\beta = \frac{E}{M}$.

2.3. **Core only.** Since we expect that early in the epidemic, core members will cause the great majority of infections, and since we are investigating what drives the epidemic, we ignore all non-core members in our population study. Of course some core members will have monogamous partners as well as random contacts, and these partners may become infected and may constitute a large fraction of people infected. However, they typically will not infect others. The same holds for children, so monogamous partners and infected children are excluded from the study of how the infections in the core grow over time.

2.3.1. *A quadratic phenomenon.* In our study of the male gay population in San Francisco, the core members (the most active 10%) were more active than the men in the next most active 25% by a factor of about four [6]. Despite this small factor, the core caused 83% of all the infections. This is the result of a quadratic phenomenon: a man who is four times as active as another is four times as likely to become infected at an early stage of the epidemic, and if both were infected, the more active one will infect four times as many women. Hence on the average the four-times-more-active man will infect sixteen times as many men or women (depending on whether it is a homosexual or heterosexual epidemic) in the early stage of the epidemic. The corresponding result for women also holds. Female sex workers have many times more contacts than other women. Hence, where female sex workers are numerous, we expect that they will account for the great majority of male infections.

3. Results.

THEOREM 3.1. *Assume the following:*

1. *There is an average infectiousness and an average rate of encounters with susceptibles for men and women and that the ratios defined above, E, M, and C are constants > 0, and the epidemic is growing exponentially;*
2. *Core individuals are infected only by core individuals and all transmission is heterosexual;*
3. *Men and women have the same profile of infectiousness.*

Then

$$E = MC^2. \tag{5}$$

The letters E, M, and C have been chosen to make our result more memorable. The form of the equation is the only connection to Einstein's famous result. In our proof we do not assume $E > 1$ nor that $M > 1$ nor that $C > 1$.

It may seem strange to speak of asymptomatic results early in the epidemic. However in heterosexual populations the growth rate is modest. The earliest known infection occurred in 1953, and yet in South Africa, the epidemic took until 1990 to infect 1% of the population, having already increased by a factor of about 10^6 with still another factor of 20 or 30 yet to come [8, 10, 9, 2]. We believe $x(n)/y(n)$ would be very close to C from 1970 through 1990, though at sometime in the 1990's, saturation would cause $x(n)/y(n)$ to begin to deviate from C.

The key to the proof is the quantity R, which we define as

$$R = \frac{\text{the rate at which an average infected woman infects people}}{\text{rate at which an average infected man infects people}}. \tag{6}$$

Proof. The rate at which an average infected person infects a susceptible is the product of the number of contacts with susceptibles that person has and the infectiousness per contact. Since each sexual contact involves one man and one woman and there are E times as many men as women, the average woman has E times as many contacts per unit time as the average man. Since she is less infectious by a factor of M, we get

$$R = \frac{E}{M}. \tag{7}$$

Note that we are discussing the early phase of the outbreak in which the great majority of the core is susceptible and we ignore contacts in which both partners are infected. We can compute R another way. Let

$$R_1 = \frac{\text{the number of men the average infected woman has infected}}{\text{the number of woman the average infected man has infected}}. \tag{8}$$

We assume that every infected core person has been infected by a core person of the opposite sex. By definition of C, the average infected woman has infected C men and the average man has infected $\frac{1}{C}$ women. Hence the average woman has infected men C^2 times as fast as the average man has infected women, so

$$R_1 = C^2. \tag{9}$$

Since men and women have the same profile, $R = R_1$ by assumption 3. Together the two forms of R give us $\frac{E}{M} = C^2$, which is equivalent to 5.

□

It is curious to contrast the two calculations of the proof in that R concerns the instantaneous situation while R_1 concerns all the people who have been infected.

We now restate the theorem in a purely mathematical version. In the following, β corresponds to $\frac{E}{M}$ and E and M do not have a independent meaning.

THEOREM 3.2. *Assume the following:*

1. $f_j > 0$ *for* $j = 1, ..., N$;
2. *For some* $\beta > 0$, $g_j = \beta f_j$ *for all* j;
3. $(x(n), y(n))$ *is a positive eigen solution of 1 for all* n; *that is, for some* C, $y(n) = Cx(n)$ *for all* n, *and for some* $\lambda > 0$, $x(n) = x(0)\lambda^n > 0$ *for all* n.

Then

$$\beta = C^2. \tag{10}$$

Proof.

$$x(0)\lambda^n = y(0)\sum f_j\lambda^{n-j}$$
$$y(0)\lambda^n = x(0)\sum g_j\lambda^{n-j}$$
$$= x(0)\beta\sum f_j\lambda^{n-j}$$

Letting

$$Z = \sum f_j\lambda^{-j} = x(0)/y(0)$$

yields

$$1/C = Z$$
$$C = \beta Z.$$

Hence

$$1/C = C/\beta$$

so

$$\beta = C^2.$$

□

3.1. **Examples.** In the situations below we illustrate the use of equation 5.

Case 1. If twice as many men are infected as women in the core, $C = 2$, and men are nine times as infectious as women, $M = 9$, we obtain

$$E = MC^2 = 9 * 2^2 = 36. \tag{11}$$

Hence there are thirty-six times as many core men as women, and women have thirty-six times as many contacts as men. That essentially describes a population in which core women are sex workers.

Case 2. Now suppose the number of core men equals the number of core women ($E = 1$). Then they have equal numbers of contacts. With $M = 9$, we obtain

$$E = MC^2 \implies 1 = 9 * C^2 \implies C = \frac{1}{3}. \tag{12}$$

That is, there are three times as many infected women as infected men.

Case 3. Suppose that women and men have equivalent infectiousness ($M = 1$). With three times as many men infected as women in the core, $C = 3$, we obtain

$$E = MC^2 = 1 * 3^2 = 9. \tag{13}$$

Hence there are 9 times as many core men as women, and women have 9 times as many contacts as men.

3.2. **Epidemic's rate of growth.** What does the epidemic's rate of growth depend upon? The exponential growth rate of an epidemic is defined to be $\frac{Y'}{Y}$ where Y' denotes rate of change of Y, which is the total number of infected men. Since the infected female population stays in proportion to the male population, we have that $\frac{X'}{X}$ is the same as $\frac{Y'}{Y}$. These growth rates depend not only on E, M, and C but also all of the f_j and g_j's, so the exponential growth rate cannot be easily expressed. Therefore we offer a surrogate, $\frac{Q}{Y}$, where Q is the expected number of daily sexual contacts between susceptible core men and infected core women. Intuitively, the larger $\frac{Q}{Y}$ is, the bigger $\frac{Y'}{Y}$ will be, but we cannot make a direct comparison. The ratio of these two is likely to depend on the exponential growth rate of the epidemic.

Write P for the rate at which the average core man has contacts with core women. As argued above, since there are E times as many core men as women and the total rate of female contacts equals the total rate of male contacts, it follows that the average core woman has PE contacts per unit time. By the above equation 5, that equals PMC^2. Multiplying that by the number of infected women, $\frac{Y}{C}$, yields $Q = PMYC$ so

$$\frac{Q}{Y} = PMC. \tag{14}$$

If we grossly oversimplify HIV and assume that all people who have ever been infected are equally infectious and have the same effective infectiousness (the rate in which a person infects people divided by the rate at which a person had sexual contacts when he or she was healthy), then the exponential growth rate of the infection will be proportional to PMC. Different populations can have significantly different Ps and different Cs.

In the cases above, assuming P and the average infectiousness of individuals is unchanged, we find the rate of growth of the epidemic in Case 1 is six times as great as it is in Case 2.

In fact two epidemics growing at different rates will have different profiles (that is, different fractions of the infected people in different stages of infection), and the average infectiousness would be averaged over a different profile and so would be unlikely to be the same for the two populations. Nonetheless, there is a clear suggestion that an epidemic in which the core consists of sex workers will grow much more rapidly than one in which core men and women are equally promiscuous, that is, $E = 1$.

It is widely recognized that heavy use of sex workers with many contacts can drive an epidemic. Therefore, we get a curious result: if the female population was more promiscuous, or the male population was less promiscuous, then HIV would grow more slowly since C would be smaller.

4. **Discussion.** We presume men and women have the same profiles when they are infectious, but in fact we cannot demonstrate this to be true. Our theorem makes hypotheses that we believe are reasonable approximations of the truth. For example, core members will vary in their partnering rates. That is allowed by the theorem so long as the most active members are not becoming depleted of their susceptibles. We do not know the value of M, the relative infectiousness, but if we knew E and C, we could find M since $E = MC^2$, $M = E/C^2$.

The core drives the spread of a disease and then it eventually becomes saturated with infected individuals, slowing the epidemics propagation. In Rapatski et al.

[15], we studied the HIV epidemic in the San Francisco gay male population. We used the San Francisco City Clinic Cohort (SFCCC) study. The SFCCC is the only high-resolution data set documenting the onset of HIV in a promiscuous population. The data is based on blood samples from a Hepatitis B vaccine clinical trial that took place during the period in which HIV exploded through the San Francisco gay population [3, 7, 4]. The study reported that the most active 10% of the population had nearly 50% of the contacts, an average of 231 partners per year. We estimate that about 83% of the HIV infections were caused by core members as long as the epidemic remained at low levels. Hence our assumption 2, core members are infected only by other core members, is a reasonable approximation of the true situation.

We view HIV as an epidemic that repeatedly spreads from infected groups or regions to uninfected ones, and as a result, initially grows exponentially. In the early stages of the outbreak, as the total numbers of infected people grows exponentially, we expect the fractional statistics to remain fairly constant: the fraction of the infected population that is male, the fraction of the infected population consisting of female sex workers, the fraction consisting of core members, and that of non-core members. Our results describe the core population even though a significant fraction of the people are not core during the exponential growth phase.

As the epidemic progresses, the core begins to saturate, and there are few new groups for the epidemic to spread to in the overall region under investigation. In random contacts between an infected core member and another core member, it becomes more likely that both are infected, reducing the probability of new transmissions, and possibly behavior may change as people recognize the sexual nature of transmission. Male core members may become less likely to visit sex workers, and sex workers may require use of condoms.

Such changes result in stagnation of the epidemic in the population of core members, but their random contacts with non-core members can continue to spread infection to the non-core individuals. Earlier we mention the 1986 Senegal ratio of 1 infected woman per 6 infected men, which we argue is representative of a population in which female sex workers play a key role. That ration of 1:6 increased to 1.3:1 in the following thirteen years. We believe this indicates that each infected man continues to transmit infections over a period of years. We have argued [15, 16] that an infected man is likely to infect more people in his third or symptomatic stage than in the brief primary stage or the second or latent stages. We believe this is what we are seeing. If transmissions occurred mostly when the infected individual was in the primary stage, we would expect the non-core infected women to have a nearly constant ratio with core men, and that when the growth rate of the infected core men slowed, the growth rate of the infected women would slow proportionately, lagging only by the length of the primary stage, roughly two months.

REFERENCES

[1] S. Boseley, *HIV now a bigger threat to women than men*, The Guardian, 2004.
[2] Center for Disease Control, *HIV incidence among young men who have sex with men–seven U.S. cities 1994-2000*, MMWR, **50** (2001) 440–44.
[3] Centers for Disease Control and Prevention, *Update: acquired immunodeficiency syndrome in the San Francisco cohort study, 1978-1985*, MMWR, **34** (1985), 573–75.
[4] J. W. Curran, W. M. Morgan, A. M. Hardy, et al., *The epidemiology of AIDS: current status and future prospects*, Science, **229** (1985), 1352–57.
[5] H. W. Hethcote and J. A. Yorke, "Gonorrhea Transmission Dynamics and Control," Berlin, New York, Springer-Verlag, 1984.

[6] H. W. Hethcote and J. W. Van Ark ''Modeling HIV Transmission and AIDS in the United States," Berlin-Heidelberg, New York, Springer-Verlag, 1992.
[7] H. W. Jaffe, W. W. Darrow, D. F. Echenberg, et al., *The acquired immunodeficiency syndrome in a cohort of homosexual men: a six-year follow-up study*, Ann Intern Med, **103** (1985), 210–14.
[8] A. Kanabus and S. Allen, *The Origins of AIDS & HIV & the first cases of AIDS*, http://www.avert.org/origins.htm.
[9] Mann, J. and D. Tarantola. *Global Overview: A powerful HIV/AIDS pandemic* in "Mann, J. and D. Tarantola (eds.), AIDS in the World II: Global Dimensions, Social Roots, and Responses," The Global AIDS Policy Coalition, (New York: Oxford University Press, (1996) 5–40.
[10] A. J. Nahmias, J. Weiss, X. Yao, F. Lee. R Kodsi, M. Schanfield, T. Matthews, D. Bolognesi, D. Durack, A. Motulsky, P. Kanki and M. Essex. *Evidence for human infection with an HTLV/LAV-like virus in central Africa*, Lancet, (1986), 1279–80.
[11] S. Niang, *Reducing African women's vulnerability to HIV/AIDS*, Voices From Africa, **10** (2001).
[12] N. Padian, S. C. Shiboski, S. O. Glass and E. Vittingoff, *Heterosexual transmission of human immunodeficiency virus (HIV) in northern California: results from a ten-year study*, American Journal of Epidemiology, **146** (1997), 350–57.
[13] T. A. Peterman, R. L. Stoneburner, J. R. Allen, H. W. Jaffe and J. W. Curran, *Risk of human immunodeficiency virus transmission from heterosexual adults with transfusion-associated infections*, JAMA, **259** (1988), 55–58.
[14] K. Quirk and P. DeCarlo, "What Are Women's HIV Prevention Needs," Center for AIDS Prevention Studies UCSF AIDS Research Initiatives, From http:/www.caps.ucsf.edu/womenrev.html.
[15] B. L. Rapatski, F. Suppe and J. A. Yorke, *HIV epidemics driven by late disease-stage transmission*, J Acqr Immune Defic Syndr, **38** (2005), 241–53.
[16] B. L. Rapatski, F. Suppe and J. A. Yorke, *Reconciling different infectivity estimates for HIV-1*, J Acqr Immune Defic Syndr, **43** (2006), 253–56.
[17] M. J. Wawer, R. H. Gray, N. K. Sewankembo, et al., *Rates of HIV-1 transmission per coital act, by stage of HIV-1 infection, in Rakai, Uganda*, Journal of Infectious Diseases, **191** (2005), 1403–09.

Received October 17, 2007; Accepted September 15, 2008.

E-mail address: brandy.rapatski@stockton.edu
E-mail address: yorke@umd.edu