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Modeling HIV transmission risk among Mozambicans prior to their initiating highly active antiretroviral therapy

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Modeling HIV transmission risk among Mozambicans prior to their initiating highly active antiretroviral therapy

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Abstract

Understanding sexual behavior and assessing transmission risk among people living with HIV-1 is crucial for effective HIV-1 prevention. We describe sexual behavior among HIV-positive persons initiating highly active antiretroviral therapy (HAART) in Beira, Mozambique. We present a Bernoulli process model (tool available online) to estimate the number of sexual partners who would acquire HIV-1 as a consequence of sexual contact with study participants within the prior three months. Baseline data were collected on 350 HAART-naive individuals 18–70 years of age from October 2004 to February 2005. In the three months prior to initiating HAART, 45% ($n = 157$) of participants had sexual relationships with 191 partners. Unprotected sex occurred in 70% of partnerships, with evidence suggesting unprotected sex was less likely with partners believed to be HIV-negative. Only 26% of the participants disclosed their serostatus to partners with a negative or unknown serostatus. Women were less likely to report concurrent relationships than were men (21 versus 66%; OR 0.13; 95%CI: 0.06, 0.26). Given baseline behaviors, the model estimated 23.2 infections/1,000 HIV-positive persons per year. The model demonstrated HAART along with syphilis and herpes simplex virus type 2 (HSV-2) treatment combined could reduce HIV-1 transmission by 87%; increasing condom use could reduce HIV-1 transmission by 67%.

Introduction

As HAART improves quality and length of life, HIV-positive individuals on HAART may be more likely to have sex more frequently and with a greater number of partners (Baggaley et al., 2005; Blower 2001; Law et al., 2001). Increases in transmission-related behavior may occur if HAART recipients perceive that treatment reduces their infectiousness or if the general population no longer fears acquisition of HIV-1 infection. However, as seen in Uganda, effective strategies can reduce the risk of HIV-1 transmission from HIV-positive individuals receiving HAART to their HIV-negative sexual partners (Bunnell et al., 2006; Malamba et al., 2005), these include providing specific 'prevention with positives' counselling and voluntary counselling and testing for sexual partners.

Understanding culturally specific sexual risk behavior patterns is crucial for the design and implementation of effective HIV-1 transmission prevention strategies. Few studies have described sexual behavior and assessed transmission risk (Chakraborty et al., 2001; Weinhardt et al., 2004) in resource-limited countries (Gray et al., 2001; 2004) particularly in HAART-naïve HIV-positive patients (Bunnell et al., 2006; Wawer et al., 2005). Studies from Africa, where HAART access is expanding rapidly, are particularly needed (Gray et al., 2001; 2004; McClelland, 2006; Wawer et al., 2005).

Researchers in sexually transmitted diseases have developed Bernoulli process models to explore and compare the impact on risk of various HIV/AIDS interventions—including increased condom use, reductions in the number of sexual partners and the careful selection of partners (Fineberg, 1988; Hearst & Hulley, 1988; Pinkerton & Abramson, 1998; Wiley & Herschkorn, 1988)—as well as to derive estimates of the per-contact probability of HIV transmission for unprotected sexual intercourse (DeGruttola et al., 1989). In this type of model, each act of sexual intercourse is treated as an independent Bernoulli trial and the probability of a 'success' (i.e. HIV transmission) in any one trial is assumed to

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equal the per-contact probability of transmission (Pinkerton & Abramson, 1998).

In this study, we interview 350 men and women initiating HAART in Beira, Mozambique where the HIV/AIDS prevalence is approximately 30% among 15–49 year olds (Mozambique Ministry of Health, 2005). We describe participants' overall sexual behavior and sexual partner risks and determine the prevalence of unprotected sex. Additionally, we use a modelling tool to estimate the number of sexual partners who would acquire HIV-1 as a consequence of sexual contact with study participants within the prior three months and conduct modelling exercises to determine how behavioral and treatment factors may affect these transmission estimates.

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Methods

Procedures and setting

The data reported in this paper are from baseline interviews of men and women before randomisation into a controlled trial of peer-supervised modified directly observed therapy (see Pearson et al., 2006). The study was conducted between October 2004 and May 2006 at the HIV care clinic in Beira Central Hospital, a public institution providing high-volume, free specialised HIV care and antiretroviral medications to all Mozambicans in Beira and the surrounding area.

The research manager, in consultation with clinic staff, assessed the following study eligibility requirements for each potential participant: at least 18 years old, initiating HAART, and physically and mentally capable of participating. Of the 433 eligible persons approached, 350 (81%) agreed to participate and gave written consent. The day the participant was initiating HAART, trained study staff administered a 30–45 minute baseline interview in Portuguese or the local languages of Ndau or Sena at the clinic. Institutional Review Boards at the University of Washington and the Comité Nacional de Bioética para a Saúde de Mozambique approved the procedures.

Measures

Data were collected from interviews and medical records. The interview assessed demographic and clinical characteristics and sexual partners and behaviors (including egocentric sexual network data on the last three sexual partnerships) (Morris & Kretzschmar, 1997). To ensure comprehensive content and the conceptual validity and reliability of the final instrument, most items and scales were selected from published and validated measures and all items were tested for cultural appropriateness through three rounds of translation and back translation, feedback from four focus groups, and pretests the instrument ($N = 20$) (Morris, 1997). The questionnaire (in English and Portuguese) is available online at http://sprc.washington.edu/services/modeling.shtml.

Sociodemographics

Participants indicated their age and marital status as well as their socioeconomic status based on education level, type of gainful employment and income.

Clinical and other characteristics

Study staff abstracted from medical records data on CD4 counts, sexually transmitted infections (STIs), opportunist infections and stage of disease. Participants indicated number of months since their HIV diagnosis and whether they were circumcised. Parenteral exposure information included number of injections in the prior year and approximate proportion that involved an uncleaned previously used needle. Alcohol and substance use in the past year were assessed using validated screening items (Brown et al., 1997; Brown et al., 1998).

Sexual partner characteristics

For each of their last three sexual partners, participants indicated whether the partner was a main partner (someone they had lived with or seen a lot or to whom they had a special emotional attachment); secondary partner (someone with whom they had sex with three or more times but was not main partner) or other partner (someone they had sex with one or two times only and was not a primary or secondary partner). Participants also provided for each partner basic sociodemographic data, presence of STIs, HIV status (status unknown or known to have tested positive or negative), financial contribution to the relationship (providing, receiving, equal contribution, none), the estimated number of concurrent relationships and approximate start and end dates for each sexual relationship. Additionally, participants indicated whether their male partners had ever had sex with another man.

Sexual behavior

Additional items queried sexual behaviors over the participant's lifetime as well as the last three months of their last three partnerships with specific focus on the three months prior to initiating HAART. All participants were asked about same-sex and opposite-sex partners, with questions based on gender-specific pairings.

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Participants indicated age at their first sexual encounter, whether their first sexual encounter was voluntary and the number of their lifetime partners. They also indicated whether they ever had sex with an anonymous partner or a same-sex partner and, if so, the date of the last such encounter.

Specific questions for each of the participants' last three sexual partners assessed number and type of sex acts (oral, anal, or vaginal and insertive or receptive), concurrent relationships (overlapping sexual partners), condom use at last sexual encounter as well as at each sex act, frequency of condom use and condom use errors (breakage, slippage or incorrect application). If more than three lifetime partners were reported, summary questions were used to capture number of partners, sex acts and condom use per sex act for the other partners. Items on disclosure to sexual partners examined whether the partner knew the participant's serostatus and whether the participant was the one to tell the partner.

Data analysis

We used odds ratios (ORs) as a way of comparing whether the probability of demographic or clinic characteristic or sexual behaviors (i.e. condom use with partners of different serostatus) between women and men were the same for the two groups. An OR of one implies that the event is equally likely in both groups. An OR greater than one, implies that the event is more likely among women (who were coded as being in the first group). An OR less than one implies that the event is less likely among women than among men. Group difference in ratio and interval level data was computed using *t*-test with unequal variance.

HIV-1 transmission risk model

The outcome of the transmission risk model is the estimated probability that a participant would transmit HIV-1 to a sex partner within the three months prior to their initiating HAART (i.e. the time of the baseline assessment). We based our model on the work of Pinkerton et al. (2000) and Weinhardt et al. (2004); however, we modified their model to include transmission probabilities for male circumcision (Auvert et al., 2001), syphilis and herpes simplex virus type 2 (HSV-2) infections (Celum et al., 2005; Grosskurth et al., 2000; Kurth 2003; Nusbaum et al., 2004) and stage of HIV-1 disease in the index participant. The model is summarised below, with details presented in the Appendix.

We estimated the transmission risk using the following equation:

$$Pij = (1 - \lambda_{ij})\left[1 - \left(1 - \left(\prod_{t=1}^{5} RRt\right)\beta_{si}\right)^{aij}\right]$$

P_{ij} is the probability that participant i would transmit HIV-1 to sex partner j, given behaviors and characteristics noted in the three-months prior to HAART initiation. The total number of new infections expected among the sex partners of participant i equals the sum of the transmission probabilities for each of his or her partners j: $\Sigma_j Pij$.[6,23] The total number of new infections expected from the entire study population for the three-month assessment interval is the sum of all secondary infections from each study participant $\Sigma_i(\Sigma_j Pij)$.

The parameter λ_{ij} is the probability the partner j is HIV-positive. If the partner is reported as having tested HIV-positive, $\lambda_{ij} = 1$; if the partner is reported as having recently tested HIV-negative, $\lambda_{ij} = 0$. If the HIV-1 status is unknown, the probability is assigned using the population-level prevalence. The multiplier parameters are risk ratios (RRs) that will either increase or decrease the probability of HIV-1 transmission. The three RRs that would decrease transmission are circumcision among male partners, condom use, and HAART adherence, and the two RRs that would increase transmission are syphilis and HSV-2. Highly active antiretroviral therapy adherence is used only in additional modelling exercises as the assessment interval was prior to participants initiating HAART.

The model's parameters include transmission probabilities for type of sex act as vaginal or anal and insertive or receptive. Stage of HIV disease is defined as early (up to three months after seroconversion) (Cohen & Pilcher, 2005), mid, or late (CD4 copies/mL less than 100 or World Health Organization HIV-1 infection stage four as indicated in the medical record) (Attia et al., 2001; Kassa et al., 1999; Morgan 2002).

The probabilities of transmission for a heterosexual vaginal sex act by stage of HIV-1 infection (β_{si}) were 0.0031 for late stage and 0.0007 for mid stage (Wawer et al., 2005). We did not separate the transmission probabilities for women or men as the literature among African populations consistently has found no differences (Gray et al., 2001; 2003; Wawer et al., 2005). Finally, a_{ij} denotes the number of sex acts between participant i and partner j.

Modelling exercises were conducted to determine how the probabilities used for the following parameters affected the estimated number of new infections: HAART adherence, male circumcision, effective condom use, changes in syphilis and HSV-2 prevalence, and partners' concurrent sexual relationships.

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The model and additional parameter notations are available for use through the University of Washington Center for AIDS Research (CFAR) web site, at http://sprc.washington.edu/services/modeling.shtml.

Results

Socio-demographic and clinical characteristics

As seen in Table I, there were a number of differences by participant sex in socio-demographic and clinical characteristics. Compared to women, men were older, had higher incomes, were more likely to be married and still living with their partners and were less likely to report ever having an STI. Other analyses (not presented in Table I) indicated there was no sex difference in stage of disease (late stage 32%; mid stage 68%) and average number of injections received in the last year (Median (MDN) = 7; Interquartile range(IQR) = 3, 15), with most (84%) injections delivered by a clinician; 14% of the participants believed at least some of the needles were re-used without being cleaned.

Sexual partner characteristics

Participants who were sexually active in the three months prior to initiating HAART described their partners as a main partner (74%), a secondary partner (20%) or another partner (6%). The age difference between partners was greater than ten years for over a third of the participants (38%), with women (94%) more likely than men (17%) to be ten years younger than their male partner, (OR: 82.2; 95%CI: 13.6, 794.4). A financial element was common in these relations: 85% of all partnerships involved general monetary exchange, with men providing (64%), women receiving (66%) and 18% reporting an equal exchange. Only 1% of the women suspected their male partners ever had sex with another man. Yet many women suspected their partners' infidelity (74% of women versus 44% of men, OR: 5.7; 95%CI: 2.9, 11.4) and reported knowing their partner was married to someone else at the time they were sexually involved (42% of women versus 22% of men, OR: 2.5; 95%CI: 1.2, 5.0).

Sexual behaviors

Men were older at their first sexual experience than women (MDN = 18 years; IQR = 17, 20 years versus MDN = 17 years; IQR = 16,18 (difference 1.8; 95%CI: 1.2, 2.4), and had three times as many partners in their lifetime (MDN = 7; IQR = 5; 15 versus MDN = 3; IQR = 2,5; difference 9.2; 95%CI: 5.8, 12.8). About a quarter (21%) of the women reported involuntary first sex, compared to only 2% of the men (OR: 10.0; 95%CI: 3.6, 40.8) and 4% of the women versus 24% of the men reported ever having sex with an anonymous partner (OR: 0.14; 95%CI: 0.05, 0.31). Almost all (99%) of sexual activity reported was insertive or receptive vaginal sex with 1% heterosexual anal sex. Only 25% of the participants reported using a condom at last sex, which did not vary by women or men.

In the three months prior to initiating HAART, 157 of the 350 participants (45%) reported sexual activity with a total of 191 partners with no difference between women (n = 90; mean (M) = 1.2; standard deviation (SD) = 0.58) and men (n = 101; M = 1.3; SD = 0.59). Almost all sexual activity was vaginal;

Table I. Demographic and clinical characteristics of 350 HIV-positive Mozambican patients on highly active antiretroviral therapy.

	Women $n = 188$ (54%) Mdn (IQR)	Men $n = 162$ (46%) Mdn (IQR)	Mean Difference (95%CI)
Age in years	31.5 (27–37)	39 (32–45)	6.6 (4.8, 8.4)
Monthly income US$	0 (0–42)	63 (42–111)	56 (39, 73)
CD4 count	130 (60–190)	116 (67–163)	−5.8 (−23.1, 11)
Time since HIV-positive diagnosis (months.)	5 (4–9)	6 (3–12)	1.2 (−1.1, 3.5)
	n (%)	*n* (%)	OR_{ua} (95%CI)
Ever had a sexually transmitted disease	51 (27.1)	18 (11.2)	2.9 (1.5, 5.6)
Education 8+ years	68 (36.2)	74 (45.7)	0.68 (0.42, 1.1)
Marital status			
Never married and not living with partner	30 (16)	17 (10.5)	1.6 (.82, 3.2)
Unmarried and living together	40 (21.3)	32 (19.8)	1.1 (.63, 1.9)
Married and living together	31 (16.5)	69 (42.6)	0.26 (.15, 0.44)
Married and not living together	30 (16)	8 (4.9)	3.6 (1.6, 9.5)
Divorced/widowed	57 (30.3)	36 (22.2)	1.5 (.91, 2.6)

Note: Mdn (IQR) = Median and Interquartile range, CI = confidence intervals, OR_{ua} = unadjusted odd ratio.

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only six participants reported any anal sex. During this 3-month assessment period, 21% of the women and 66% of the men (OR: 0.13; 95%CI: 0.61, 0.30) reported concurrent relationships.

As seen in Table II, there was no difference between women and men with respect to unprotected sex and partners' perceived serostatus. However, there was evidence to suggest a difference in unprotected sex across serostatus. Overall unprotected sex was less likely if the partner was perceived to be HIV-negative (OR: 3.3; 95%CI: 1.4, 7.6).

Across men and women, condoms were used on any occasion in only 46% (88/191) of partnerships; within these partnerships, 28.4% (25/88) condom use error occurred. Overall unprotected sex occurred in 70% (133/191) of all relationships with unprotected sex or condom error occurring in 71% (24/34) of sero-discordant relationships and 82% (42/51) of the relationships in which serostatus was unknown.

Among the 1,223 total sex acts in the three months prior to initiating HAART, 798 (65%) were unprotected (432 for women and 366 for men). The majority of unprotected sex acts ($n = 619$) took place with main partners, of which 29% (177/619) of the sex acts were with HIV-negative partners or partners of unknown serostatus. Among secondary partners, unprotected sex took in place in 138 acts, of which 54% (75/138) of the sex acts were with HIV-negative partners or partners of unknown serostatus. For partners described as other, unprotected sex took in place 41 acts, of which 90% (37/41) of the sex acts were with HIV-negative partners or partners of unknown serostatus.

Across sex acts, overall correct and consistent use of condoms was poor (see Table III). Although 100% condom use was reported in 30% (58/191) of the partnerships, in 19 of these partnerships there was condom use error, yielding a 0.27 mean correct and consistent condom use score (range 0–1, see appendix for equation). More specifically, with HIV-negative partners, 51% (95/188) of the sexual acts were unprotected or involved condom use error and where partners' serostatus was unknown, 88% (216/246) of the sexual acts were unprotected or

Table II. Partnerships involving unprotected sex and condom use by partner serostatus among HIV-positive sexually active women and men in Mozambique in the three months prior to initiating highly active antiretroviral therapy.

	Women $n=78$ n (%)	Men $n=79$ n (%)	OR_{ua} (95%CI)
Serostatus of partner(s)	90	101	
HIV-positive	52 (58)	54 (53)	1.19 (0.64, 2.2)
HIV-negative	15 (17)	19 (19)	0.86 (0.38, 1.9)
HIV-unknown serostatus	23 (25)	28 (28)	0.89 (0.45, 1.8)
Unprotected sex and condom use by partner serostatus			
HIV-positive partners			
Any unprotected sex	40 (77)	37 (69)	1.5 (0.59, 4.0)
Any condom use	23 (44)	26 (48)	0.85 (0.37, 2.0)
Reported condom error among condom users	8 (35)	7 (27)	
HIV-negative partners			
Any unprotected sex	7 (47)	9 (47)	0.97 (0.20, 4.6)
Any condom use	8 (53)	13 (68)	0.53 (0.10, 2.7)
Reported condom error among condom users	3 (38)	5 (39)	
HIV-unknown partners			
Any unprotected sex	17 (74)	23 (82)	0.62 (0.13, 2.9)
Any condom use	9 (39)	9 (32)	1.5 (0.41, 5.5)
Reported condom error among condom users	1 (11)	1 (11)	
Any unprotected sex with HIV-negative and HIV-unknown partners verses HIV-positive partners			
	HIV- n (OR_{ua};95% CI)		HIV-? n (OR_{ua};95% CI)
Women (unprotected sex with HIV-positive partner 40/52)	7 (3.8; 0.96, 15.0)		17 (1.18; 0.31, 4.1)
Men (unprotected sex with HIV-positive partner 37/54)	9 (2.4; 0.72, 8.1)		23 (0.47; .12, 1.6)

Note: OR_{ua} = unadjusted odd ratio, CI = confidence intervals.
Condom use errors comprise breakage, slippage and placing the condom on incorrectly.
Condom correctness & consistency score range from 0–1 and is calculated as the number of sex acts with a condom with partner j minus the total number of errors divided by the number of all sex acts. If a condom was not used or was used and an error occurred at every use then this score would be zero.

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involved condom use error. As indicated in Table III, although there was no difference in sexual activity or condom use per sex act within serostatus for either male or female participants, across partner's serostatus, women were more likely to practice unprotected sex with HIV-positive partners or with partners of unknown serostatus than with their HIV-negative partners.

Sexually active persons in the study sample reported knowing their HIV-positive status median 150 days (IQR: 120, 365). Overall, disclosure of HIV-1 status did not differ between men and women; however, there was a difference according to the serostatus of sexual partners. Specifically, 90% (87/97) of participants disclosed to their HIV-positive partners (with a total of 85% [90/106] of all HIV-positive partners informed); however, 27% (18/67) of participants disclosed to their HIV-negative/unknown partners (with a total of 26% [22/85] of all HIV-negative/unknown partners informed). Discloser and non-disclosers did not differ in the length of time since the participant had been diagnosed (mean difference 80 days; 95%CI: 23, 185).

Outcomes from the HIV-1 transmission model

Overall, the study participants reported sexual relationships in the prior three months with a total of 85 partners with HIV-negative or unknown serostatus. Based on our model parameters, 0.91 infection per 157 persons (0.57 as a result of sex with men and 0.34 as a result of sex with women) would be expected to become infected with HIV-1 as a result of their sexual relationships with the study participants during the 3-month assessment interval (or approximately 23.2 incident infections per year given 1,000 similar HIV-positive individuals. However, most (56%) of the samples partners were HIV-positive; if we assumed that only a quarter of the partners were HIV-negative during the study period (similar to the general Beira prevalence rate), the estimated number of persons infected would more than double to 2.12 (54.1 infections/1,000 HIV-positive persons per year). Estimates are sensitive to the per-act transmission probabilities based on stage of disease, STI prevalence, proportion of partners who are already HIV-positive and risk ratio values.

Table IV demonstrates how various treatment and prevention strategies can reduce transmission risk. For example, modelling exercises demonstrated that increasing condom use and pharmacologic treatment for HIV and other STIs could decrease HIV-1 transmission risk by 86%. Male circumcision, while promising as one HIV-1 risk-reduction strategy (Cohen, 2005), had a lesser risk reduction impact (11%, if circumcision were increased by 140% from current levels in the Beira area to cover 75% of the male population).

Additionally, we considered the effects of concurrent sexual relationships, which are known to significantly affect the speed and distribution of HIV spread (Morris, 1997) (data not shown in Table IV). Although data were not collected on the precise overlap of study participant partners' other sexual relationships (i.e. our data were egocentric not sociometric), the model demonstrates how the outcome might change if partners' concurrency were considered. For example, concurrency among study participants' partners might lead to as many as half of the 51 with unknown serostatus actually being infected with HIV-1, thereby decreasing the study

Table III. Sex acts involving unprotected sex by partner serostatus among HIV-positive sexually active women and men in Mozambique in the three months prior to initiating highly active antiretroviral therapy.

Total number of sex acts	Women $n=624$	Men $n=599$	OR_{ua} (95%CI)
HIV-positive partners, number of sex acts (median, IQR)	412(5, 2–9)	377 (5.5, 3–9)	
Unprotected sex acts (n(%))	293(71.1)	216(57.3)	1.8(1.5, 2.5)
HIV-negative partners, number of sex acts (median, IQR)	84(4, 2–8)	104(4, 3–5)	
Unprotected sex acts (n(%))	31(36.9)	50(48.1)	0.63(0.34, 1.2)
HIV-unknown partners, number of sex acts (median, IQR)	128(3, 2–6)	118(3, 2–6)	
Unprotected sex acts (n(%))	108(81.5)	100(84.7)	0.97(0.46, 2.1)
Overall condom correctness & consistency score (mean and standard deviation)			mean difference (95%CI)
HIV-positive partner	0.25(0.39)	0.34(0.43)	−0.09(−0.25, 0.7)
HIV-negative partner	0.51(0.48)	0.37(0.43)	0.14(−0.17,0.46)
HIV status unknown partner	0.24(0.39)	0.24(0.40)	0(−0.22, 0.22)

Unprotected sex acts across HIV-negative and HIV-unknown partners serostatus as compared with HIV-positive partners

	HIV-negative n (OR_{ua};95% CI)	HIV-? n (OR_{ua};95%CI)
Women (unprotected sex with HIV-positive partner ($n=293$)	4.2(2.5, 7.1)	0.46(0.26, 0.78)
Men (unprotected sex with HIV-positive partner ($n=216$)	1.5(0.91, 2.3)	0.24(0.13, 0.42)

Table IV. Estimates of HIV transmission risk resulting from various treatment and prevention modeling assumptions.

Parameters/ modeling assumptions	Number of new infection in 1 year	Rate (1000/year)	Reduction in transmission (%)
Base model	2.73	23.2	–
Correct and consistent condom use (27% base model prevalence)			
50%	1.95	16.6	0.28
75%	1.08	9.1	0.61
Syphilis (16.7% base model prevalence)			
8%	1.38	11.8	0.49
5%	0.84	7	0.70
HSV-2 (90% base model prevalence)			
45%	1.35	11.7	0.50
25%	0.78	6.5	0.72
Male circumcision (31% base model prevalence)			
50%	2.58	22.1	0.05
75%	2.41	20.5	0.11
Persons on HARRT (base model is 0% adherent)			
95% adherent	1.368	12.7	0.45
80% adherent	1.152	14.5	0.38
Treatment only			
Syphilis & HSV2 (50%)	0.69	5.9	0.75
Syphilis & HSV2 (50%) & HAART (95%)	0.39	3.2	0.86

Note: The base model parameter estimates listed in parentheses above are based on data among HIV-positive sexually active women and men in Mozambique in the three months prior to initiating highly active antiretroviral therapy.
Syphilis and HSV-2 parameters are based on treatment or suppressive therapy to reduce active sexually transmitted disease prevalence.

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population transmission probability risk by 32% (to nine infections/1,000 similar HIV-positive persons per year). Additionally, concurrency on the part of participants' partners could hypothetically increase the probability of co-factor STIs (specifically syphilis since HSV-2 is already 90%). Indeed, doubling the assumed population prevalence of syphilis (from 17% to 33%) would increase the HIV transmission risk by 96% (to 45.6 infections/1,000 similar HIV-positive persons per year). Taking both concurrency factors into consideration—an increase in partners already HIV-positive and an increase in prevalent STIs—would increase the overall probability of HIV-1 transmission by 33% (to 30.9 infections/1,000 similar HIV-positive persons per year).

Discussion

This cross-sectional study among HIV-positive Mozambicans indicated that, according to their reports of sexual behavior in the three months prior to initiating HAART, sexual risk involving the possibility of HIV transmission was relatively prevalent. For example, 100% consistent and correct condom use occurred in only 20% ($n = 39$) of the relationships between the 157 sexually active study participants and their 191 partners. This finding did not vary by men or women but according to partner serostatus, as unprotected sex was less likely if the partner was known to be HIV-negative.

A Bernoulli process modelling tool using widely available clinical and behavioral surveillance data and based on the sexual behavior of the sample population was used to estimate transmission risk from HIV-positives to HIV-negatives. Findings indicated that 0.91 persons (i.e. almost one individual) would be expected to seroconvert during the 3-month assessment interval among the study population. If we extrapolate this estimate to the adult population expected to be HAART-eligible in Beira (11,250), the total expected number of secondary infections would be 23.2 infections/1,000 HIV-positive persons per year in a population eligible for HAART.

This is a conservative estimate. Many of the participant's partners (56%) were already HIV-positive and participants were initiating HAART based on CD4s <200, with most (66%) of individuals in a symptomatic phase of AIDS; therefore, they were sicker and less likely to be sexually active than HIV-positive individuals who look and feel healthy. In addition, this population had just received 11 weeks of pre-HAART clinic care, thus, it is possible that they may have been attempting to reduce their high-risk behavior as compared with those who were unaware of their serostatus or believe

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themselves and 'trust their partners' to be HIV-negative.

The findings raise a number of notable concerns from a public health perspective. First, we found a higher prevalence of unprotected sex and a lack of correct and consistent condom use than in Uganda (Kirungi et al., 2006) and Botswana (Creek et al., 2005), where condom use at last sex is reported to be as high as 89% among the general population. This difference could reflect condom availability, quality, and cost (Cohen et al., 1999). Outside of the HIV clinic, high-quality condoms in Mozambique are not easily accessible nor are they free. Moreover, even when 100% condom use was reported, condom use error occurred about 15% of the time. This high prevalence of condom use error could result from the inexperience of this population that may lack the skills to use them effectively (Aberg et al., 2004).

Study participants' disclosure of their HIV status to sexual partners also was a concern. Although most (75%) of the study participants had known about their HIV-1 status for about one year, only 26% had disclosed their status to partners with a negative or unknown serostatus. This prevalence of low disclosure is similar to what has been reported in other African populations, where issues of stigma and safety inhibit disclosure and lack of formal risk-reduction counselling programs instituted for HIV-positive individuals are not available to provide guidance and support in disclosure (Eide et al., 2006; Nachega et al., 2005; Sethosa & Peltzer, 2005). Recent reviews of the literature, however, have failed to show a consistent association between disclosure and safer sex (Crepaz & Marks, 2003; Simoni & Pantalone, 2004). The authors argue that explicit discussions of risk reduction are more important than disclosure alone in reducing HIV-1 transmission risk.

Several study limitations should be noted. First, consistent with other sexual behavior studies, there are concerns of social desirability bias resulting in under-reporting due to the sensitivity of stigmatised sexual behaviors. For example, while no participants reported same-sex behavior, it is likely to be occurring (Gouws et al., 2006; Wade et al., 2005). Second, our data were collected via face-to-face interviews rather than with computer-assisted self-interview or ballot box procedures (Olinto et al., 2004), which may have helped better address these concerns. To minimise underreporting of sensitive items, we used a small number of trained interviewers who were the same sex as the participant, emphasised anonymity, stressed the importance and the seriousness of reporting accurate data and assured the participants the data would only be used in aggregate form and would not be used against them in any manner. Although these techniques do not completely ensure accurate reporting, the lack of reporting of sexual behaviors would err on the side of reporting fewer high-risk behaviors and thus the results from the transmission risk model would represent an overly conservative estimate. Finally, estimates presented in the paper are based on an urban population in Mozambique and may only apply to the specific situation being modeled, thus are not likely to be generalisable. However, our modelling tool is structured in such a way that users can input behaviors and characteristics relevant to their populations of interest, thus making the tool widely applicable.

Despite these limitations, our findings that half of the 350 persons initiating HAART in central Mozambique were sexually active and most were not correctly and consistently using condoms have important implications. First, they highlight how important it is for policy makers and clinicians to recognise that HIV-positive people initiating HAART are sexually active and, therefore, that it is important to incorporate prevention programs for HIV-positive individuals that can help support risk reduction practices. Periodic counselling sessions that individualise specific barriers and concerns in regard to risk reduction and that provide voluntary counselling and testing and treatment for partners would help reinforce behavior change overtime. Furthermore, given the high prevalence of STIs in the general population, implementation of STI screening and treatment for HIV-positive persons, as part of the regular health care formulary, are highly recommended. Finally, support for HAART treatment adherence is another important approach to decreasing secondary HIV-1 transmissions.

Hopefully, the HIV-1 transmission risk assessment modelling tool that we have made available will facilitate the ability of other researchers and governmental agencies to determine HIV-1 transmission risk among their population and to further develop the strategies we have recommended to help reduce this risk.

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Appendix

Computational details for parameters of the HIV sexual transmission model

If the HIV-1 status of a partner is unknown then the probability of that partner being infected is λ_{ij} and ranges between 0–1. Where as h_i is number of HIV-positive partners for study participant i, v_g is the HIV-positive prevalence rate by sex in the local area (Beira, Mozambique), u_i is the number of i's partners with unknown HIV-1 status and pt_i is the total number of partners for study participant i. Therefore, the probability the partner j being already HIV-positive is given by:

$$\lambda_{ij} = \lfloor h_i + v_g(u_i) \rfloor / pt_i$$

Multipliers either enhance or reduce the probability of HIV transmission per sex act and are all expressed in terms of a risk ratio, which sufficiently approximate ORs since the probability of HIV transmission is considered small.

Where as RR_t is various multipliers and are as follows:

The $RR_{circumcision}$ parameter for the reduction due to male circumcision is set at 0 if the study participant is male. This is because there are no studies to date that suggest that circumcision is a protective factor for women. However, since we did not have data on whether female study participants' partners were circumcised, we used the prevalence of circumcision among the male study population and applied this number as the probability that a male partner is circumcised (30.6%). Then this number is multiplied by the reduction due to circumcision: 0.60, which is based on a recent estimate among heterosexual males in South Africa (Auvert et al., 2005).

$$RR_{circumcision} = \begin{Bmatrix} 1 - .6\ (.306), & \text{if female} \\ 0, & \text{otherwise} \end{Bmatrix}$$

The RR_{condom} parameter for the reduction due to condom use is based on a pooled analysis of studies that suggest condoms are 90–95% effective in prevention of HIV-1 transmission (Hearst & Hulley, 1988) and adjusted by an actual correct and consistent condom use score calculated for each study participant. We set mechanical (not user-related) condom effectiveness (C_E) at 0.95 to take into account product defects only. Participants were asked to report the number of times the condom broke, slipped off or was put on backwards in the prior three months. From these reports we calculated a 'correct 7 consistent condom use score' (C_C) which ranges from 0 (poor or non use) to 1 (perfect and consistent use), where N_{ij} is the total number sex acts with partner j in the last three months, n_{ij}^{c} = number of acts protected by a condom, n_{ij}^{f} =number

condom-protected acts where method or user failure occurred (Kurth, 2003). The score is given as:

$$C_C = (n_{ij}^c - n_{ij}^f)/N_{ij}$$

The risk ratio of condom effectiveness is given as:

$$\mathrm{RR}_{\mathrm{condom}} = 1 - (C_C{*}C_E)$$

As STIs have been consistently reported as a facilitator in the transmission and acquisition of HIV-1 (Celum et al., 2005; Grosskurth et al., 2000; Nusbaum et al., 2004) and HSV-2/HIV-1 dually infected individuals have reportedly higher viral loads (Celum et al., 2005, Reynolds & Quinn, 2005) we include these important parameters in our model. Beira clinic facilities lack the infrastructure to routinely test for STIs, so that syphilis and HSV-2 status is mostly unknown among study participants. We therefore use a 16.67% syphilis population-level prevalence rate (S_{ij}) and a 90% HSV-2 population-level prevalence rate (H_{ij}) among HIV-positive women based on a recent surveillance study among women attending family planning clinics and older women from the community (Menendez, email communication 12.26.2005). These data derive from the southern providence where the current HIV-1 prevalence (11.7%) is lower than in Beira.

The $\mathrm{RR}_{\mathrm{syphilis}}$ parameter represents the increase in transmission due to syphilis. Our syphilis parameter value is based on updated estimates from the Mwanza, Rakai and Masaka intervention trial that showed the impact of primary syphilis with a 7.5-fold increase (R_s) (averaged over the early phase of infection, including periods without ulcers) (Korenromp et al., 2005) with a range across studies 2.3–8.6 (Celum et al., 2005; Fleming & Wasserheit, 1999; Todd et al., 2006). A recent meta-analysis showed that HSV-2 infection increased HIV-1 acquisition risk among HIV-1 negative partners with an odds ratio (R_h) of 2.7 (95%CI: 1.93.9) (Freeman et al., 2006). The risk ratios for syphilis and HSV-2 are:

$$\mathrm{RR}_{\mathrm{syphilis}} = (S_{ij}){*}(R_s)$$
$$\mathrm{RR}_{\mathrm{HSV\text{-}2}} = (\mathrm{H}_{\mathrm{ij}}){*}(R_h)$$

Concurrent relationships (CR) would influence the prevalence data used in the model and affect secondary infections of HIV-1, syphilis, and HSV-2. Derived from an underlying stochastic process of partnership network formation and disease transmission, various levels of concurrency were found to significantly increase STI (Bauch & Rand, 2000). A partner's concurrency increases the chance that a study participant's partner is already infected with HIV, which would lower the multiplier ($1\text{-}\lambda_{ij}$); therefore the overall probability of a secondary HIV infection would decrease. However, concurrency from the participant's partner could increase the probability of co-factor STIs, which would increase the probability of HIV transmission.

HARRT has been shown to decrease HIV transmission by 0.48 (Porco et al., 2004). However, HAART is only effective if taken. Therefore in the model, we allow for the effectiveness of HAART (0.48) to be adjusted by reported adherence as a proportion of dose taken (A). This multiplier (set at a hypothesized 95% adherence data) was used in the Modelling exercises. An effect of HAART on HIV-1 transmission probability in a given sexual encounter ranges from 0.25 to 0.74 based on variations in the reported estimates (Baggaley et al., 2005; Gray et al., 2003; Porco et al., 2004; Tchetgen 2001). The probability is simply given by:

$$\mathrm{RR}_{\mathrm{HAART}} = 1 - 0.48(0.95)$$

Assumption of multiplicative association

This model assumes a multiplicative association between the different risk parameters, which is an assumption that keeps the model simple and accessible. Nonetheless, there is a minimal risk that the probability of transmission exceeds one if the model includes a large number of risk parameters with high risk ratios or if the initial probability of transmission is large.

The model user can avoid this by first predicting the log odds of transmission given a set of predictors, i.e. condom use, circumcision, etc. Then the log odds (Y) can be transformed into a probability of transmission via the equation $\frac{e^Y}{1+e^Y}$. This ensures that the probability of transmission is bounded by one.

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