Reconciling Estimates of Per-act Infectivity of HIV: Couples vs. Commercial Relationship

Abstract

Estimates from past studies on the per-act infectivity of HIV during unprotected sex vary by study type and region. Although differences between frequent (regular) and casual sexual contacts, and cofactors like STD infection are recognized as contributing to the variation, no study has tested the comparability of estimates after adjusting for these factors. To address this, we tested two scenarios using probability models on data from a Thai study among military conscripts who frequented FSWs (Nelson 1993). The overall unadjusted per-act infectivity was 0.0406 (scenario A) and 0.0761 (scenario B). Adjusted infectivity was 3.7 times less than unadjusted values. Adjusted infectivity decreased with increased number of sexual contacts, following power functions. After adjusting for STD infection and stage of HIV infection, and considering differences in number of sexual contacts, estimates were comparable to those found in studies among discordant couples. These results have important implications on HIV epidemic modeling.

Introduction

Estimations of the probability of HIV transmission per sexual contact from an infected partner to a susceptible partner are important in HIV modeling and understanding the spread of the epidemic. Despite the uncertainty of time at infection, a number of studies have managed to estimate the per-act infectivity. However, published estimates vary greatly by study type and region. In Europe and North America, studies of discordant couples typically revealed a per-act infectivity of 0.001 (range: 0.0001 - 0.0015) (De Vincenzi, 1994; Downs & De Vincenzi, 1996; Leynaert et al., 1998; Peterman et al., 1988; Royce et al., 1997; Wiley et al., 1989). One prospective study among monogamous couples in Rakai, Uganda, also estimated that the average per-act infectivity was 0.0011 (Gray et al., 2001; Wawer et al., 2005). In contrast, estimates of per-act infectivity from studies among clients of female sex workers (FSWs) in Thailand and Kenya were more than 50 times higher than those found in the aforementioned studies among couples (Cameron et al., 1989; Mastro et al., 1994).

Several explanations for such large differences in estimates have been suggested. The first is the higher prevalence of sexually transmitted diseases (STDs) among the study populations in Thailand and Kenya than among couples in the other countries. Many studies have demonstrated that the presence of an STD can increase the likelihood of HIV transmission (Gray et al., 2001; Rottingen et al., 2001; Vernazza et al., 1999). The second explanation is that many FSWs in the Thai and Kenyan studies may have been newly infected. HIV infectiousness is much higher in the acute infection stage, which occurs during the first few months after infection, than during the asymptomatic stage (Pilcher et al., 2004; Royce et al., 1997; Wawer et al., 2005). The third explanation is that the low per-act infectivity found in the studies among couples may be due to selection bias and/or accumulated immunity of the susceptible partner. Uninfected partners were believed to

acquire partial immunity, which can be reinforced by having sex with an infected partner repeatedly. The dynamics of HIV transmission may vary by situation whereby estimates from discordant couples may not reflect the probability of infection from casual contacts with a randomly selected, high-risk partner, such as a FSW (De Vincenzi, 1994).

Although such cofactors as STD infection and stage of HIV infection are believed to influence the per-act infectivity, few efforts have been made to compare estimates after adjusting for these effects. To date, no study has explored the probability of HIV infection when contacts with randomly selected high-risk partners occurred frequently. To address this issue, we fit a probabilistic model to data from a Thailand study in which HIV infection status and sexual behaviors were investigated among military conscripts who had sexual contact with FSWs. We anticipated that adjusting for the effects of STD infection and stage of HIV infection would reduce the gap in estimates and that the adjusted per-act infectivity would decrease when the total number of sexual contacts increased.

Methods

Data and Population

Data were obtained from a published paper by Nelson et al (1993), in which cross-sectional surveys were conducted among male military conscripts aged 19 to 23 in Northern Thailand in May and November 1991. The paper reported HIV serostatus of male conscripts by level of frequency of sexual contact with FSWs during the past year. Having sex with FSWs was evidenced to be the major risk for infection (Nelson et al., 1993). Other potential risks or transmission cofactors were collected through face-to-face interviews, including lifetime and recent (i.e., in the last year) sexual contact with females and males, frequency of sexual contact with girlfriends or spouses, condom use, STD history, use of illicit drugs by injection or other administration, and the receipt of blood transfusions or donation of blood.

HIV and syphilis seroprevalence was 12% (280/2417) and 4% (96/2417), respectively. History of having sex with another male (3%), injection of illicit drugs (4 conscripts), and having a tattoo (8.8%) were found to be independent of HIV infection in the study population. Of the 2,417 conscripts in the study, 1,961 reported ever having sex with FSWs. Their infection rates are shown in Table 1 by frequency of sexual contact with FSWs during the preceding year (see columns 1 & 4; 65 conscripts who were uncertain about their frequency of FSW contacts were not reported). Rates of condom use at last sex with FSW partners was high (61.5%), but it was not associated with HIV infection.

Analytical Methods

The number of sexual contacts with FSWs in the past year was estimated by multiplying the number of FSW contacts reported by conscripts by the number of time units (e.g., months, weeks) where appropriate. HIV infection attributable to last year's visits to FSWs was calculated by subtracting the HIV infection rate of conscripts who had no sex

with FSWs in the last year from that of conscripts who visited FSWs at different frequencies (see column 5 in Table 1).

The unadjusted per-act infectivity was estimated through two Bernoulli probability models (Gray et al., 2001; Mastro et al., 1994; Satten et al., 1994). For each individual, the probability of being infected was modeled as $P = 1-(1-\beta \times \lambda)^m$, where β was the probability of each conscript meeting an HIV-positive FSW and *m* represented number of commercial partners in the past year. λ, the probability of HIV transmission within a discordant partnership, was equal to $1-(1-\gamma)^n$, where γ referred to per-act infectivity and *n* represented the number of sexual contacts with each commercial partner. Substituting the latter into the former resulted in a full equation, $P = 1-(1-\beta \times (1-(1-\gamma)^n)^m$. We assumed that the probability of HIV transmission at both partner and sexual contact level were independent, and that the probability of each conscript meeting an HIV-infected FSW was equal to the prevalence of HIV among FSWs in 1991, when the study was conducted.

Two model scenarios were tested to obtain estimates of the unadjusted per-act infectivity from the full equation. In scenario A, we assumed there were no repeat visits to the same FSW by a conscript since FSWs are highly mobile. In scenario B, to better reflect actual sexual activity and the bivariate relationship between the number of sexual contacts and the number of partners, we employed the approximation that $1-(1-\alpha)^n \cong \alpha \times n$ when α is small and *n* is not too large.

{Insert Figure 1 about here}

Adjusted per-act infectivity was estimated by considering the effects of cofactors. Figure 1 illustrates the probabilistic combinations of cofactors that an HIV negative conscript may encounter while having sex with HIV-infected FSWs. The effects of male circumcision and condom use were not included since detailed data about these factors were not available in the Nelson publication. However, data from other sources suggest that most males in Thailand are not circumcised (Mastro et al., 1994; Violante & Potts, 2004) and that rates of consistent condom use with FSWs among Thai men were approximately 30% in the early 1990s (UNAIDS 1998). Excluding the effects of condom use from the model may result in smaller estimates of adjusted infectivity. The final function for adjusted per-act infectivity was written as:

$$\gamma_{adj} = \frac{\gamma_{crude}}{P_{STD}E_{STD}E_{acute}I_{HIV}\,\mathrm{Pr} + P_{STD}E_{STD}(1-I_{HIV}\,\mathrm{Pr}) + (1-P_{STD})E_{acute}I_{HIV}\,\mathrm{Pr} + (1-P_{STD})(1-I_{HIV}\,\mathrm{Pr})}$$

where, P_{STD} represented STD prevalence among FSWs, E_{STD} effect of STD infection on per-act infectivity, E_{acute} effect of acute HIV infection on per-act infectivity, I_{HIV} HIV incidence among FSWs, and Pr the proportion of recent HIV-infected (i.e., in the past year) FSWs in the acute stage of infection.

HIV incidence among FSWs was derived from well documented data on HIV prevalence among the population in late 1980s and early 1990s in Thailand. HIV prevalence increased from 3.5% in mid-1989, to 10% in 1990, and to 21.5% in 1991, which yielded an average incidence of 6% during the period between 1989 and 1991 (UNAIDS, 1998). The effect of STD infection on a single sexual contact was set at 5 according to findings from Rottingen et al. (2001) and Satten et al. (1994). Existing studies suggest that a susceptible partner is 8-12 times as likely to be infected from a single sexual contact with an infected partner in the acute stage of infection than with a partner who is asymptomatic (Pilcher et al., 2004; Wawer et al., 2005). The per-act effect of being in the acute stage of infection was therefore set at 10. The acute period was assumed to last two months on average (Pilcher et al., 2004; Wawer et al., 2005). This means that 16.7% (i.e., 2/12) of the recent infected FSWs (i.e., in the last year) in the Thai study were in the acute stage of HIV infection. STD prevalence among FSWs in early 1990s in Thailand was assumed to be 60%.

A scatter plot was graphed to explore the relationship between adjusted per-act infectivity and number of sexual contacts (see Figure 2). Since only the shape – and not the estimated absolute values – of the relationship curve was relevant, predicted values of per-act infectivity were constrained to be positive and less than 1. Several functions were investigated and goodness-of-fit chi-square tests were performed to determine the best fitted function by examining the differences between the observed and estimated values. Power functions were detected to fit the data well for both scenarios. Extrapolation estimates of per-act infectivity were made based on the power functions by setting the number of sexual contacts at 104 (2 per week), 156 (3 per week), and 208 (4 per week).

{insert Figure 2 about here}

Results

Among the 1,318 conscripts who reported having sex with FSWs during the past year, HIV infection was 16.6%. The average number of contacts during the past year with FSWs was 9.5 times. According to scenarios A and B, the unadjusted per-act transmission probability was 0.0406 and 0.0761, respectively.

Estimates of the unadjusted per-act infectivity by level of frequency of sexual contact with FSWs are presented in columns 6 (scenario A) and 9 (scenario B) in Table 1. Generally, the estimates decreased with an increase in the number of sexual contacts. With the exception of the sub-group who reported having only one sexual contact with FSWs in the past year, the estimates from scenario A (ranging from 0.1081 to 0.0226) were slightly higher than those from scenario B (ranging from 0.1061 to 0.0198).

{insert Table 1 about here}

Estimates for the adjusted per-act infectivity are presented in columns 7 (scenario A) and 10 (scenario B) in Table 1. The adjusted infectivity for each sub-group was

approximately 3.7 times less than the unadjusted estimate in both scenarios. For example, in scenario A, for those who had sexual contact with FSWs two to three times in the preceding year, the unadjusted infectivity was estimated to be 0.1081, whereas the adjusted infectivity was 0.0292, a factor of 3.7 times less. When the number of sexual contacts was greater than 10, the adjusted per-act infectivity was even less (in the thousandths).

The estimated per-act infectivity based on the power functions are reported in columns 8 and 11 in Table 1. When the number of sexual contacts with FSWs increased to 104 (2 per week), 156 (3 per week), and 208 (4 per week), the estimated per-act infectivity for scenario A was 0.00380, 0.00310, and 0.00269, respectively. For scenario B, it was 0.00332, 0.00268, and 0.00231, respectively.

Discussion

Our estimates of the overall unadjusted per-act transmission probability were much higher than those reported from studies among couples in Europe, North America and Uganda (De Vincenzi, 1994; Downs et al., 1996; Gray et al., 2001; Wiley et al., 1989), but quite comparable to the findings from other client studies in Thailand and Kenya (Cameron et al., 1989; Mastro et al., 1994). Adjusting for cofactors such as the rate of STDs among FSWs and the stage of infection among HIV-positive FSWs decreased the unadjusted estimates by a factor of 3.7. Although the adjusted estimates were closer to those reported in the aforementioned couple studies, they were still of a higher magnitude.

One possible explanation for the remaining gap in estimates is that other cofactors were not adjusted for, such as penile-anal sex and the presence of STDs among male conscripts. Both epidemiological and biological studies have demonstrated that the risk of infection is higher during anal contact than during vaginal penetration. The per-act infectivity of unprotected anal sex is believed to range from 0.005 to 0.03 among men who have sex with men (The World Bank Group, 1999). Among heterosexual partners, the infectivity of penile-anal sex was estimated to be 0.014 when HIV-infected partners were in the asymptomatic stage (Leynaert et al., 1998). No data on anal sex were available in the Nelson study, which limited our ability to estimate the magnitude of the potential influence of such behavior. A history of STDs was common among male conscripts (reported by 43%) in the Nelson study. Although no published studies have measured the effect of STD infection on HIV transmission when both partners are STD-positive, it is assumed that the per-act infectivity should be higher than when only one partner is infected. Failing to consider the prevalence of STDs among male conscripts would lead to higher estimates of the adjusted per-act infectivity.

Alternatively, selection bias in studies of serodiscordant couples may contribute to the remaining gap in estimates. Such studies excluded couples in which HIV-negative partners were already infected. In addition, among the included discordant couples, HIV-negative partners may have already had sexual contact a number of times with their infected partner before the studies took place, suggesting that susceptible partners may

have already developed partial immunity to infection. It has been demonstrated that HIV is more likely to be transmitted during the first few contacts with infected partners (Downs et al., 1996; Wawer et al., 2005) than during subsequent contacts. If susceptible partners did not become infected during the first few contacts with infected partners, the per-act infectivity was assumed to decrease due to susceptible partners' accumulated immunity from having sex with infected partners repeatedly.

Our study indicated that the adjusted per-act infectivity decreased with an increase in the number of sexual contacts with FSWs. Existing studies suggest great variation in the reported number of sexual contacts in couple studies and the number of contacts reported in studies of casual relationships. In stable partner relationships, susceptible partners usually report frequent sexual contact with their infected partner. For example, nearly 70% of the couples in Padian study (1987) reported having more than 100 contacts in the study period. The average number of sexual contacts among couples was 150 in Peterman (1988) study, and 84 in during a six month follow-up in Downs (1996) study. The mean frequency of intercourse among couples was 8.9 times per month in the Uganda study. However, the average number of sexual contacts with FSWs in the last three years was 25 in another Thailand study (Satten et al., 1994). In the Kenyan study, a subsample of clients who had only one contact with FSWs during the follow-up was used for the estimate (Cameron et al., 1989). In our study, many conscripts reported having only a few sexual contacts with FSW during the preceding year. More than 40% reported 1-3 contacts and nearly three-quarters had no more than 10 contacts. When we increased the number of contacts in our study to the levels observed among couples, the estimates of per-act infectivity were nearly comparable to those reported in couple studies. The finding suggests that it is relevant to consider the number of sexual contacts while studying per-act transmission probability.

Limitations

The Nelson study was based on a cross-sectional study among young military conscripts and collected data about recent frequency of sexual contacts with FSWs retrospectively. Although the majority of HIV infections among the conscripts were demonstrated to have been acquired through sexual contacts with FSWs (Nelson et al., 1993), other risks of infection may also exist, such as injecting drug use or unprotected sexual contact with other men. In addition, even if the conscripts were infected through unprotected sex with FSWs, the infection may have occurred earlier than in the past year. To minimize the uncertainty related to infection, we subtracted the infection rate of conscripts who reported ever having sex with FSWs but not within the past year from the infection rate of those who visited FSWs during the past year. This resulted in a reasonable estimate of the infection rate attributable to last year's visits to FSWs. In addition, the four epidemic waves observed in Thailand since 1988 also suggest that the earliest possible date of HIV infection among male conscripts would have been in 1990, ample time for the study conscripts to have become infected (Weniger et al., 1991).

An additional limitation is that the number of sexual contacts used in the study may not have been the contacts during which HIV-negative conscripts became infected. However, since many conscripts reported only a few contacts with FSWs, the influence of this uncertainty may be quite small.

Summary

After adjusting for cofactors and considering differences in the number of sexual contacts, our estimates of per-act infectivity were comparable to those reported in studies among discordant couples. The findings have important implications in HIV modeling and decision-making strategies for combating the epidemic. First, cofactors such as STD infection should be collected and adjusted while studying per-act infectivity. Second, in HIV epidemic modeling or intervention effectiveness modeling, it is advisable to use a lower per-act infectivity estimate (e.g., in the thousandths) for couples (or "regular" relationships) when the number of sexual contacts is frequent. Third, a higher per-act infectivity estimate (e.g., in the hundredths) should be used for causal and commercial relationships when infrequent contacts are involved.

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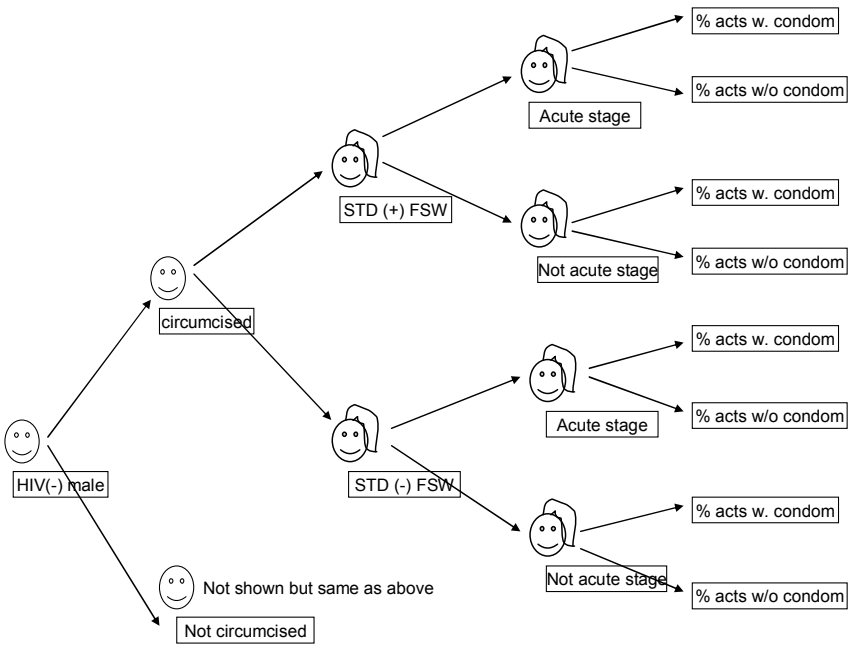

Figure 1. Probabilistic combination of HIV transmission cofactors (Male: HIV-; FSW: HIV+)

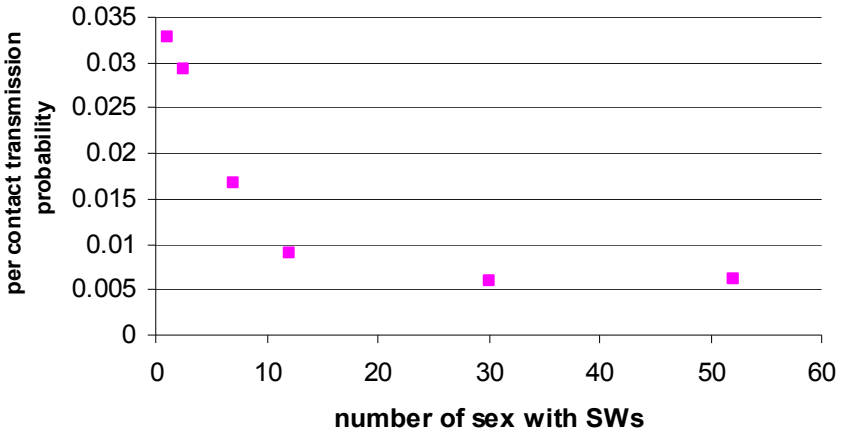

Figure 2. Relationship between frequency of sex with SWs and per contact transmission probability (adjusted)

Table 1. Per-act infectivity by frequency of sexual contacts with FSWs in the past year

Frequency of sex contacts with FSWs in last year	No. males	Mean no. sex contacts with FSWs in last year	HIV infection rate (%)	Attributable infection rate (%)	Scenario A				Scenario B		
					unadjusted	Adjusted[a]	Estimated[b]		unadjusted	Adjusted[a]	Estimated[c]
None	578	0	8.1	--							
1	192	1	10.9	2.8	0.1217	0.0328	0.0380		0.1217	0.0328	0.0380
2-3	367	2.5	14.2	6.1	0.1081	0.0292	0.0241		0.1061	0.0286	0.0235
4-10	412	7	17.7	9.6	0.0622	0.0168	0.0145		0.0596	0.0161	0.0137
1/month	159	12	17.0	8.9	0.0336	0.0091	0.0111		0.0322	0.0087	0.0103
2-3/month	144	30	22.2	14.1	0.0220	0.0059	0.0070		0.0204	0.0055	0.0064
1/week	44	52	31.8	23.7	0.0226	0.0061	0.0054		0.0198	0.0054	0.0048

Note: Sixty-five conscripts who were uncertain about their number of sexual contacts with FSWs were eliminated from the analysis;
Scenario A: assuming no repeat visit to the same FSW by each man;
Scenario B: using approximation that $1-(1-\alpha)^n \cong \alpha \times n$ when α is small and n is not too large;
a: adjusting for effects of cofactors (i.e., STD infection and acute infection stage);
b: based on $0.038 \times (No.Acts)^{-0.496}$; Goodness-of-fit: $\chi^2_{df=5} = 0.0028$, P>0.05;
c: based on $0.038 \times (No.Acts)^{-0.525}$; Goodness-of-fit: $\chi^2_{df=5} = 0.0026$, P>0.05.