Articles

Probability of HIV-1 transmission per coital act in monogamous, heterosexual, HIV-1-discordant couples in Rakai, Uganda

*Ronald H Gray, Maria J Wawer, Ron Brookmeyer, Nelson K Sewankambo, David Serwadda, Fred Wabwire-Mangen, Tom Lutalo, Xianbin Li, Thomas vanCott, Thomas C Quinn, and the Rakai Project Team**

Summary

Background The probability of HIV-1 transmission per coital act in representative African populations is unknown. We aimed to calculate this probability overall, and to estimate how it is affected by various factors thought to influence infectivity.

Methods 174 monogamous couples, in which one partner was HIV-1 positive, were retrospectively identified from a population cohort in Rakai, Uganda. Frequency of intercourse and reliability of reporting within couples was assessed prospectively. HIV-1 seroconversion was determined in the uninfected partners, and HIV-1 viral load was measured in the infected partners. Adjusted rate ratios of transmission per coital act were estimated by Poisson regression. Probabilities of transmission per act were estimated by log-log binomial regression for quartiles of age and HIV-1 viral load, and for symptoms or diagnoses of sexually transmitted diseases (STDs) in the HIV-1-infected partners.

Results The mean frequency of intercourse was 8·9 per month, which declined with age and HIV-1 viral load. Members of couples reported similar frequencies of intercourse. The overall unadjusted probability of HIV-1 transmission per coital act was 0·0011 (95% CI 0·0008–0·0015). Transmission probabilities increased from 0·0001 per act at viral loads of less than 1700 copies/mL to 0·0023 per act at 38 500 copies/mL or more (p=0·002), and were 0·0041 with genital ulceration versus 0·0011 without (p=0·02). Transmission probabilities per act did not differ significantly by HIV-1 subtypes A and D, sex, STDs, or symptoms of discharge or dysuria in the HIV-1-positive partner.

Interpretation Higher viral load and genital ulceration are the main determinants of HIV-1 transmission per coital act in this Ugandan population.

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*Members listed at end of paper

Departments of Population and Family Health Sciences (R H Gray MD, X-B Li PhD), **Biostatistics** (R Brookmeyer PhD), **and Medicine** (T C Quinn MD), **School of Hygiene and Public Health, Johns Hopkins University, Baltimore, MD, USA; Heilbrun Center for Population and Family Health, Columbia University, Joseph L Mailman School of Public Health, New York, NY, USA** (M J Wawer MD)**; Department of Medicine and Clinical Epidemiology Unit** (N K Sewankambo MB) **and Institute of Public Health** (D Serwadda MB, F Wabwire-Mangen PhD), **Makerere University, Kampala, Uganda; Rakai Project, Uganda Virus Research Institute, Entebbe, Uganda** (T Lutalo MSc); **Walter Reed Army Institute of Research, Rockville, MD** (T vanCott PhD)**; and National Institute of Allergy and Infectious Diseases, National Institutes of Health, Bethesda, MD** (T C Quinn)

Correspondence to: Dr Ronald H Gray, Suite 4030, Johns Hopkins University, School of Hygiene and Public Health, 615 N Wolfe Street, Baltimore, MD 21205, USA

(e-mail: rgray@jhsph.edu)

Introduction

The probability of HIV transmission per sexual act of vaginal intercourse, or infectivity (γ), has been estimated from prospective studies of HIV-discordant partners or male contacts with prostitutes.[1] Published estimates of transmission probabilities per act vary from γ=0·0001 to 0·0014 in US and European studies of discordant couples,[2–6] and to γ=0·002 in Thai couples.[7] However, higher transmission probabilities (γ=0·056–0·100 per act) have been reported among men who had contacts with prostitutes in Thailand[8] and Kenya.[9] The higher transmission probabilities associated with commercial sex might be attributable to the presence of other sexually transmitted diseases (STDs), which are thought to increase infectivity of or susceptibility to HIV,[2,8,9] or to possible errors in reported contact frequency. Other factors that increase transmission include lower CD4 counts or AIDS in the HIV-positive index partner, and anal intercourse.[2,5,8,9] Male-to-female HIV transmission is usually more efficient than female-to-male transmission in US and European populations, but the small numbers of HIV-positive female index partners limit conclusive sex-specific estimates of transmission probabilities per sex act.[2–5,10,11]

There are no data on per-contact probability of transmission from representative heterosexual couples in sub-Saharan Africa, and there is little information on the efficiency of transmission associated with HIV-1 viral subtypes.[2] The eastern and southern African HIV epidemic is predominantly caused by HIV-1 subtypes A, C, and D, and the rapid progression of the epidemic in these parts of Africa might, in part, be associated with greater infectivity of these HIV-1 subtypes.[12] We assessed this possibility by examining transmission probabilities for subtypes A and D in Uganda. Conversely, some have postulated that the slower evolution of the HIV epidemic in western Africa might be due to the higher proportion of less transmissable recombinant HIV-1 subtypes in that region.[13] To address these issues, we estimated the per-contact probability of HIV-1 transmission among monogamous, heterosexual HIV-1-discordant couples in rural Rakai District, Uganda, in which the HIV-1 epidemic is due to viral subtypes A and D. Estimates of HIV transmission probabilities rely on the accuracy of reports of the frequency of sexual intercourse,[1] and previous studies have not assessed the reliability of such data. Therefore, we also assessed the intracouple reliability of reports of sexual frequency and examined factors such as age, sex, and viral load, which might be associated with frequency of intercourse.

Participants and methods

Participants

Data were collected between November, 1994, and October, 1998, in a community-randomised trial of STD control for AIDS prevention in the rural district of Rakai.[14] The original trial enrolled 15 127 individuals aged 15–59 years, who were followed up in their homes every 10 months.

Among the 15 127 participants, 8898 were married or in a consensual union, and information was requested on the identity of their partners. However, to maintain confidentiality, linkage of members of couples was not done during the course of the study. After completion of the trial in 1998, we linked members of couples and identified 415 couples who, at enrolment, were HIV-1-discordant (ie, one member of the couple was HIV-1-positive whereas the other was HIV-1-negative).[15] Both members of 174 such couples reported that they were monogamous and that the HIV-1-negative partner reported no extramarital partners during the period of observation. Data from these 174 monogamous couples were used to estimate the probabilities of HIV-1 transmission per coital act, since it was assumed that the only source of infection in the HIV-1-negative partner would be the linked HIV-1-positive partner. The information on usual frequency of intercourse had been collected from both members of the couples, but for these analyses we used the sexual frequency information reported by the HIV-1-positive partner.

Participants were enrolled as individuals, gave written informed consent at the time of enrolment, and were asked to give consent again at each follow-up visit. The consent form guaranteed complete confidentiality of the information provided. Voluntary HIV counselling and testing was offered, and condoms were promoted and provided free of charge by the project. In keeping with Ugandan governmental policy,[16] receipt of HIV results was encouraged but not mandatory. Individual HIV results were kept strictly confidential, but recipients were encouraged to share their results with their sexual partners. Involuntary disclosure of results is not permitted under Ugandan governmental policy. The trial was reviewed and approved by institutional review boards at the Uganda Virus Research Institute, the AIDS Research Subcommittee of the Uganda National Council for Science and Technology, Columbia and Johns Hopkins University human subjects review boards, and the National Institutes of Health Office for Protection from Research Risk. Safety during the trial was assessed by an independent data safety and monitoring board.

Methods

At each 10-month contact, biological samples were collected, and interview information obtained on sociodemographic characteristics and sexual behaviours, including the number of partners and use of condoms. Additionally, participants were asked about the usual frequency of intercourse with each partner. The specific question was: "When you have/had relationships with this partner, how frequently did you usually have intercourse, per day, per week and per month?". This information was used to estimate the number of coital acts per follow-up period. Information was also obtained on symptoms suggestive of STDs such as genital ulcers, discharge, or dysuria during the preceding period of risk.

During the trial, participants were asked to provide a blood sample which was tested for HIV-1 by two different ELISAs (Vironostika HIV-1, Organon Teknika, Charlotte, NC, USA; and Cambridge Biotech, Worcester, MA, USA) with confirmation of discordant ELISAs by western blotting (HIV-1 Western Blot, Bio-Merieux-Vitek, St Louis, MO, USA). Serology was done for syphilis (Toluidine Red Unheated Serum Test [TRUST], New Horizons, Columbia, MD, USA), and TRUST-positive samples were confirmed by treponemal-specific tests (*Treponema pallidum* haemagglutination assay [Sera-Tek, Rujibero, Tokyo, Japan], or fluorescent treponemal antibody absorption test [IFA Test System, Zeus Scientific, Raritan, NJ, USA]). Herpes simplex virus type 2 (HSV-2) infection was detected by an enzyme-linked immunodot assay.[17] *Neisseria gonorrhoeae* and *Chlamydia trachomatis* were detected by ligase chain reaction on urine samples (LCx Probe System, Abbott Laboratories, Abbott Park, IL, USA). In women, self-collected vaginal swabs were used for culture of *Trichomonas vaginalis* (InPouch TV culture, BioMed Diagnostics, San Jose, CA, USA), and bacterial vaginosis was detected by quantitative morphology of gram-stained slides.

The HIV-1 viral load for HIV-1-positive partners in discordant relationships was quantified by reverse-transcriptase PCR by use of an Amplicor HIV-1 Monitor 1.5 Assay (Roche Molecular Systems, Branchburg, NJ, USA), which reliably quantifies the predominant Ugandan HIV-1 subtypes A and D. HIV-1 subtypes were determined by peptide competition serotyping assay for V3-loop peptides of HIV-1 subtypes A–F and O.[18] The sample for the viral load assay was the one taken from the index HIV-1-positive individual at the 10-month visit before detection of the seroconversion in the partner.[15] This sample approximates to the HIV-1 viral load about 5 months before infection of the HIV-1-negative partner, assuming infection occurred uniformly throughout the interval of risk. Couples in whom no seroconversion occurred were matched to the seroconverting couples by age (to within 5 years), and sex of the HIV-1-positive and HIV-1-negative partners. The viral load assay in the HIV-1-positive partners of persistent discordant couples was determined for the sample obtained closest in time to that of the matched seroconverting partners. Thus, the viral loads of the HIV-1-positive transmitting partners were matched for age, sex, and time to the viral loads of the HIV-1-positive non-transmitting index partners. Repeat measurements of viral load were available for 43 non-transmitting, HIV-1-positive partners, so we used the mean of two or more viral loads to obtain a better measure of the mean exposure of the uninfected partner during the period of risk.

Antiretroviral drugs were not available in Uganda at the time of the study. The efficacy of trimethoprim-sulphamethoxazole prophylaxis for symptom-free HIV-1-infected individuals was not yet established, and because of concerns about resistance, the Ugandan Ministry of Health did not approve routine prophylaxis. Isoniazid prophylaxis for tuberculosis could not be provided because we were unable to exclude patients with active tuberculosis in this rural setting, and use of isoniazid in cases of active disease would rapidly select for resistant mycobacteria. The study provided STD treatment and general health care.

Statistical analysis

The statistical analysis first examined the reliability of the sexual frequency information reported by each member of a couple. We determined the within-couple differences in reported frequency of intercourse, and mean differences were assessed by paired *t* tests. We also estimated mean frequency of intercourse by sex, age, and viral load of the HIV-1-positive partner. The number of sex acts over the follow-up period was estimated from the intercourse frequency per month reported by the HIV-1-positive partner, multiplied by the number of months of follow-up for each couple, and then summed over all couples. In the Poisson regression,[19] adjusted rate ratios of transmission per act were estimated, incorporating covariates for sex of the HIV-1-positive partner, quartiles of age (15–24, 25–29, 30–34, and ⩾35 years), quartiles of viral load (<1700, 1700–12 499, 12 500–38 500, and >38 500 copies/mL), and STD symptoms and diagnoses in the HIV-1-positive partner.

The probability of HIV-1 transmission per sex act was estimated as follows: the probability of transmission in the "i"th couple (P_i), depends on the number of acts during the follow up period (n_i), and is $1-(1-\gamma)^{n_i}$, where the infectivity (γ), is the probability of transmission per act.[1,20] Overall infectivity and 95% CI were estimated without adjustment for covariates. Allowing the infectivity to depend on covariates (eg, quartiles of age and viral load) through a complementary log-log link leads to the regression model $[\log-\log(1-P)]=\log n_i + b_0 + b_1X_1$, where b_1 and X_1 are vectors of regression coefficients and covariates, respectively. This model was fitted by use of statistical methods for generalised linear models, specifically binomial regression with a complementary log-log link and offset term log n_i (SAS Institute, Cary, NC, USA).[20] Various regression models were fitted with several covariates, including quartiles of age and HIV-1 viral load, sex, STD symptoms (genital ulcer disease, or discharge or dysuria), and STD diagnoses of the HIV-1-infected partner. Sex-specific models were also fitted for HIV-1-positive male circumcision status, and for HIV-1-positive female diagnoses of bacterial vaginosis and trichomonas. Covariates significant at $p<0·1$ were included in final models. These include single covariate models (separately for quartiles of age or viral load), and combined covariate models with both age and HIV-1 viral load, as well as combined models for genital ulcer disease and viral load. Goodness of fit was assessed by χ^2 test relative to a saturated model.

Results

Among the 174 HIV-discordant monogamous couples, the HIV-1-positive partners had a median age of 29·0 years (mean 30·2), and a median viral load of 12 476 copies/mL. In 97 couples, the male partner was HIV-1-positive, 17 of whom transmitted the virus to their wives (17·5%). In 77 couples, the woman was the HIV-1-positive partner, 21 of whom transmitted HIV-1 to their husbands (27·3%). HIV-1-infected men were significantly older than infected women (mean ages 34·0 years and 27·1, respectively; $p<0·0001$).

The mean reported frequency of intercourse was 8·9 (median 8·0) acts per month in the whole population. Among the 97 couples in which the man tested HIV-1 positive first, the infected men reported a mean of 8·3 (SE 0·70) acts of intercourse per month, and their HIV-1-negative female partners reported 8·8 (0·62) acts per month ($p=0·49$). In the 77 couples in which the woman tested HIV-1 positive first, the infected women reported 9·7 (0·76) acts per month, and their HIV-1-negative male partners reported 9·8 (0·62) acts per month ($p=0·67$). Thus, there was relatively good agreement in the sexual frequency independently reported by both members of couples. There were no significant differences in the frequency of intercourse reported by infected men versus infected women ($p>0·20$). As shown in table 1, the frequency of intercourse declined with older age, although the overall trend was not significant ($p=0·2$). Coital frequency was 10·0 per month for ages 15–24, compared with 7·4 per month for individuals older than 35 years ($p=0·06$). Among HIV-1-infected individuals, coital frequencies declined with higher viral loads: the mean frequency of intercourse was 10·4 acts per month in individuals with viral loads of less than 1700 copies/mL, whereas the frequency was 7·9 among those with viral loads greater than 38 500 copies/mL ($p=0·10$).

	Transmissions per couple	Average sex per month	Mean follow-up (months)	Adjusted rate ratio (95% CI)*
Sex				
Either	38/174	8·92	22·6	
Woman HIV+	21/77	9·74	22·1	1·00
Man HIV+	17/97	8·27	23·1	0·78 (0·62–2·68)
Age (years)				
15–24	12/45	10·02	22·5	2·15 (0·80–6·43)
25–29	15/46	8·98	22·4	2·06 (0·83–5·86)
30–34	5/43	9·11	21·7	0·62 (0·18–2·08)
35–59	6/40	7·44	24·4	1·00
HIV-1 viral load (copies/mL)				
<1700	1/43	10·40	26·0	1·00
1700–12 499	11/45	9·38	22·0	16·1 (3·11–295·71)
12 500–38 499	11/42	7·98	23·0	17·91 (3·44–328·65)
>38 500	15/44	7·91	18·8	27·7 (5·42–506·79)
Genital ulcer disease				
Yes	4/19	7·16	19·0	2·58 (1·03–5·69)
No	34/155	9·14	155·0	1·00

*Adjusted rate ratio of transmission per coital act. Poisson regression with quartiles of viral load, age, sex, and genital ulcer disease of HIV-positive partner.

Table 1: **Frequency of intercourse and relative risk of HIV transmission**

Table 1 shows the rate ratio of transmission per coital act estimated from Poisson regression. The rate ratio of transmission was lower for HIV-1-positive men than for HIV-1-positive women, although this difference was not significant. Compared with HIV-1-infected individuals aged 35–59, the risk of transmission risk per sex act was higher among younger people aged 15–24 and 25–29 years. Although these point estimates were not significant, a χ^2 test for trend was significant ($p=0·04$). Compared with individuals with HIV-1 viral loads of less than 1700 copies/mL, the adjusted rate ratios showed a dose response relation at higher viral loads (table 1). Genital ulcer disease in the HIV-1-positive partner was associated with an increased risk of transmission per act (table 1), but other STD symptoms or diagnoses in the HIV-1-infected partners were not associated with an increased risk of transmission (results not shown). The risk of transmission was not significantly affected by the circumcision status of HIV-1-positive male partners. All of these couples were married or in a stable consensual union; 161 (92·5%) had never used condoms, 11 (6·3%) reported occasional condom use, and only two (1·2%) reported consistent use. Thus, the effects of condom use on transmission risk could not be assessed in these monogamous couples.

The overall probability of transmission per coital act, unadjusted for covariates, was 0·0011 (95%CI 0·0008–0·0015). Table 2 shows the probabilities of HIV-1 transmission per coital act (γ), estimated from the complementary log-log binomial model for quartiles of age and HIV-1 viral load, and genital ulcer disease. The probability of transmission per act was highest for younger individuals aged 15–24 years and 25–29 years, and decreased at older ages. The transmission probability per act increased significantly with HIV viral load. At all viral loads, individuals aged 15–24 and 25–29 years had higher transmission probabilities per act than individuals older than 30 years, and in all age groups, the probability of transmission per act increased with viral load, but this association was most striking among the individuals younger than 30 years.

HIV-1 subtyping was available for 155 infected individuals. 31 were infected with subtype A (20·0%), 103 subtype D (66·4%), and the remaining 21 (13·5%) had an atypical V3 subtype, which showed complex binding patterns. The transmission probabilities per coital act were 0·0022 with subtype A, 0·0019 with subtype D, and were lower with the atypical viruses ($\gamma=0·0012$). These differences were not significant ($p=0·26$).

		Viral load (copies/mL)			
		<1700	1700 –12 499	12 500 –38 500	>38 500
Age (years)	Age†	Age and viral load§			
15–24	0·0013	0·0001	0·0020	0·0019	0·0032
25–29	0·0017	0·0001	0·0018	0·0026	0·0048
30–34	0·0006	0·00003	0·0005	0·0005	0·0014
35–59	0·0009	0·00004	0·0007	0·0008	0·0020
Viral load‡		0·0001	0·0013	0·0014	0·0023
Genital ulcer disease¶					
No	0·0041	0·0002	0·0033	0·0039	0·0049
Yes	0·0011	0·0001	0·0012	0·0014	0·0018

*Calculated from (1−exp [−exp (k)]), where $k=b_0+b_xX$ and X is the vector of regression coefficients. †Model for age alone. ‡Model for viral load alone. §Model for age and viral load. ¶Model for genital ulcer disease and viral load.

Table 2: **Probabilities of HIV-1 transmission per coital act***

The probability of transmission per act from HIV-1-positive women to their HIV-1-negative male partners was 0·0013, compared with a transmission probability of 0·0009 per act from HIV-1-positive men to HIV-1-negative women (p=0·34). The probability of transmission per act was higher if genital ulcer disease was reported by the HIV-1-positive partner than if it was not (γ=0·0041 *vs* γ=0·0011; p=0·02), and this higher transmission probability among individuals with ulceration was seen at all viral loads. The presence of genital discharge, dysuria, or laboratory STD diagnoses did not significantly affect the probability of transmission per act (results not shown).

Discussion

The overall probability of transmission per coital act of 0·0011 in the Rakai population is within the range of transmission probabilities per act (0·0001–0·0020), reported from prospective studies of European, north American, and Thai heterosexual couples.[2–7] Condom use was low in the monogamous Ugandan couples, despite the fact that condoms and counselling were offered free of charge and promoted by the project, 56% of HIV-1-positive partners in these discordant relationships had requested and received HIV counselling, and 25% stated that they had informed their partners. This finding is consistent with previous Rakai studies that showed low condom use within marriage.[21] In contrast, European, US, and Thai investigations found frequent condom use among HIV-1-discordant couples.[3–7] The European and US epidemics are predominantly caused by HIV-1 subtype B, the Thai epidemic by subtypes E and B, and the Ugandan epidemic by subtypes A and D. Therefore, since the transmission probabilities per act of sexual intercourse in these populations are similar, the generalised HIV-1 epidemic in Uganda is unlikely to be caused by a greater infectivity of subtypes A and D.

We did not see a difference in the probability of transmission per act between HIV-1 subtypes A and D. Although transmission per act seemed to be lower with atypical V3 loop viruses, this association was not significant. We do not yet have genomic sequence data on these atypical viruses, so we cannot determine whether the atypical V3 loop represents A or D, non-A/D, or possibly recombinant viruses. Nevertheless, the finding of a possibly lower transmission probability per act in individuals with atypical viruses is compatible with the hypothesis that atypical and possibly recombinant HIV-1 viruses might be less infectious than viruses with typical V3 loop sequences.[13]

Ours and other estimates of transmission probabilities per coital act among heterosexual couples are much lower than those reported for contacts with prostitutes in Thailand and Kenya.[8,9] However, the Thai estimates were based on a cross-sectional study of prevalent HIV-1 among young military conscripts, and ascertained the life-time frequency of sexual contacts with prostitutes retrospectively.[8] Recall of the frequency of commercial sexual contacts was likely to be subject to error, and under-reporting of the number of contacts could lead to overestimation of the per-contact risk. The Kenyan estimate was derived from a subgroup of men attending a STD clinic who reported a single contact with a sex worker.[9] These estimates could also be biased by under-reporting of contact frequency. Alternatively, estimates from stable heterosexual couples might not reflect the probability of infection from a single unprotected act of intercourse with a randomly selected, high-risk partner, such as a prostitute.[6] Some have suggested that coitus with prostitutes could be particularly hazardous owing to concurrent STDs or STD symptoms in the woman or her client.

We found a higher transmission probability per act among individuals who reported genital ulceration, but we did not see an increased probability of transmission per coital act among those with serological evidence of syphilis or HSV-2, and laboratory diagnoses of current gonorrhoea, chlamydia, bacterial vaginosis, or trichomonas infections, or among those reporting discharge or dysuria. With the exception of genital ulceration, the absence of an STD cofactor effect has been seen in previous analyses of HIV-1-discordant couples,[15] and the frequent HIV-1 exposure risk in such couples could possibly obscure an association between STDs and the per-contact probability of transmission. Additionally, our study had limited power to detect STD cofactor associations. Because STD diagnoses were based on samples obtained at the visit preceding the period of seroconversion risk, some infections such as gonorrhoea and chlamydia were too infrequent to assess, and symptom reporting embraced the whole period of risk. Therefore, STDs or symptoms at the exact time of seroconversion cannot be accurately determined. Also, serological tests for syphilis and HSV-2 reflect cumulative infections, so initial seroconversion (or HSV-2 recurrence) might not coincide with the timing of HIV-1 transmission.

There was substantial heterogeneity in transmission probabilities in the Ugandan population: transmission probabilities per coital act were highest in younger individuals, and increased strikingly with HIV-1 viral load. Frequency of intercourse cannot explain the change in infectivity with age because this factor was controlled for in the models. Higher infectivity could possibly be due to biological factors such as cervical ectopy in younger women which might facilitate HIV-1 transmission. Partial immunity in older HIV-1-positive individuals or selective resistance to infection associated with repeated prior HIV-1 exposure in older HIV-1-negative partners might also be factors. Intercourse among younger people might be associated with more genital trauma, but we have no direct data on this issue. Anal intercourse is associated with a higher probability of transmission per sexual act,[2] but anal intercourse is not practised in this population (fewer than 1% of individuals reported anal sex, and anorectal STDs are not seen). Other investigators have reported that the probability of HIV-1 transmission per sexual contact is higher among people who are immunocompromised or who have lower CD4 counts,[2,5,9–11] and this possibility is consistent with our finding of higher transmission probabilities per coital act associated with increased HIV-1 viral loads.

Studies of discordant couples in Europe and the USA generally report higher male-to-female transmission efficiency than female-to-male, although these investigations had few female HIV-1-positive index

partners.[2-5] By contrast, we found a higher transmission probability per act from women to men than from men to women, which, although not significant, was consistent with previous incidence data from Rakai among HIV-1-discordant couples [15,22] and in the general population.[14] Similarly, higher female-to-male transmission has been reported from other less-developed countries.[23] Several African studies show that HIV-1 prevalence and incidence are higher in young women than in young men,[12] but these data suggest that the sex-specific differentials in HIV-1 prevalence are unlikely to be caused by sex differences in the efficiency of HIV-1 transmission.

The estimates of transmission probabilities per coital act rely on the accuracy of the information on sexual frequency (over-reporting of coital frequency leads to underestimation of the per-contact risk, and under-reporting of sexual frequency leads to overestimation of risk per sex act). Other studies of transmission probabilities per act have not assessed the reliability of the number of reported sex acts, and commonly use grouped data on sexual frequencies in analysis. We believe the reported frequencies of intercourse in our study are reliable since there was agreement in the number of sex acts independently reported by partners in these monogamous relationships, which suggests consistency of reporting within couples, as has been seen in other studies.[24,25] Also, reported sexual frequency declined with age, as is seen in most populations,[26] and the frequency of intercourse is compatible with that reported in other eastern African rural societies.[26,27] Thus, we have no evidence to suggest that the data on sexual frequency introduced bias into the estimates of probabilities of transmission per sex act.

The overall, unadjusted probability of HIV-1 transmission per coital act is 0·0011 in this Ugandan population, and greater infectivity of predominant HIV-1 viral subtypes is unlikely to account for the explosive HIV-1 epidemic in sub-Saharan Africa. Transmission probability per act varies greatly with the HIV-1 viral load of the HIV-1-infected partner, which suggests that interventions to reduce viral load could reduce transmission.[15,28] Younger age and genital ulceration also increased the probability of transmission per act.

Contributors

R H Gray, M J Wawer, N K Sewankambo, D Serwadda, and F Wabwire-Mangen were responsible for the design and implementation of the original trial, and contributed to the analyses of this subsample of HIV-1-discordant couples. T Lutalo was the data manager overseeing the trial and contributed to these analyses. R Brookmeyer and X Li were responsible for the statistical analysis of transmission probabilities per coital act. T vanCott provided the HIV-1 subtyping assays and T Quinn did the HIV-1 viral load assays. All investigators contributed to the preparation of the paper.

Rakai Project Team

Noah Kiwanuka, Godfrey Kigozi, Fred Nalugoda, Mohamed Kiddagavu, and Fred Makumbi (Uganda Virus Research Institute, Entebbe, Uganda).

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