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REVIEW

Heterosexual transmission of HIV in Africa: an empiric estimate

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Summary: For more than a decade, most experts have assumed that more than 90% of HIV in African adults results from heterosexual transmission. In this exercise, we show how data from studies of risk factors for HIV can be used to estimate the proportion from sexual transmission, and we present our estimates.

Calculating two ways from available data, our two point estimates — we do not estimate confidence intervals — are that 25–29% of HIV incidence in African women and 30–35% in men is attributable to sexual transmission; these estimates assume 10% annual epidemic growth. These findings call for reconceptualization of research to more accurately assess routes of HIV transmission.

Keywords: HIV, sub-Saharan Africa, heterosexual transmission, epidemiology, risk factors

Background

In 1988, prominent organizations and experts circulated estimates attributing about 90% of HIV infections in African adults to heterosexual contact[1–3]. Estimates have inched upwards since. According to the World Health Organization's 2002 *World Health Report*, 'current estimates suggest that more than 99% of HIV infections prevalent in Africa in 2001 are attributable to unsafe sex' (quoted from page 9[4]). A recent special series in the *Lancet* on Africa's HIV/AIDS epidemic averred that most infections are from heterosexual intercourse, while 'blood transfusions, injections with infected needles, and scarification are thought to represent only a few infections.'[5] We have been unable to locate any document — from the 1980s or later — that describes a process to estimate a 90% sexual contribution to Africa's HIV epidemic from empirical studies of risk factors for HIV. Computer simulations of sexual transmission constructed to mimic aspects of Africa's HIV/AIDS epidemic have only been loosely and opportunistically linked to selected empiric data[6].

From the late 1980s, researchers accepting the 90% hypothesis as fact have typically studied risk factors for HIV in African adults without collecting or reporting information essential to test this estimate; for example, many studies of HIV incidence in African adults have not tested stable partners for evidence of HIV infection[7–8]. Instead, researchers have assumed sexual transmission and focused on factors influencing its efficiency. For example, the three largest studies of HIV incidence initiated during the 1990s — in Mwanza, Tanzania, and in Rakai and Masaka, Uganda — studied the impact of changes in sexually transmitted disease (STD) treatment (and behaviour change interventions in Masaka) on HIV incidence[9]. Although neither of the two studies that have reported detailed results thus far — in Mwanza and Rakai — gives a complete account of HIV incidence associated with sexual behaviour, some estimates are possible.

The Mwanza study recorded 130 incident cases in 8549 persons HIV-negative at baseline and followed for two years. Across both study arms, baseline HIV prevalence of 4.1% and incidence of 0.77 per 100 person-years (PYs) suggests annual epidemic expansion of about 9% (assuming 10% annual mortality for HIV-infected adults)[10]. Of all HIV-negative adults followed for two years, 5999 were married, and the baseline HIV status of spouses was known for 3446 (from Table 3 of reference 11). Only nine incident infections occurred in persons with known HIV-positive spouses (assuming that seroconversion was sequential in three couples that were concordant negative at baseline and concordant positive two years later). Assuming that all married persons were equally likely to have discordant partners and to seroconvert at the same rate, we estimate 16 (=9×5999/3446) incident cases — 12% of the 130 cases in all adults — due to sexual transmission from an HIV-infected spouse[12]. The Mwanza team has not yet reported other information, such as numbers of sexual partners, that could be used to

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estimate sexual transmission from non-marital partners.

The Rakai trial observed 190 incident cases in 9376 adults followed for a total of 12,667 PYs[13]. Incidence of 1.5 per 100 PYs was approximately 10% of the 15.9% baseline prevalence, suggesting a stable epidemic. Most incidence — 121 (64%) of 190 cases — occurred in adults married or in consensual union, among which the HIV status of both partners was known for 74 cases; of these, 33 (45%) occurred in couples serodiscordant at baseline. Assuming that incidence in all couples followed the same pattern, we can estimate that 29% of total incidence (45% of 64%) occurred in serodiscordant couples. Other information from Rakai permits an estimate of sexual transmission from most non-marital partners: 23% of adults reported >1 sexual partner during the period in which they seroconverted, and the rate ratio for HIV incidence associated with >1 partner was 2.3; thus the crude population attributable fraction (PAF) of HIV incidence associated with having >1 partner is 11%. Taken together, incidence associated with having a seropositive spouse (29%) and >1 partner (11%) accounts for 40% of observed incidence. The only sexual transmission not covered in this calculation is transmission from first or only sexual partners during follow-up intervals for unmarried adults.

From these two studies, estimated transmission between serodiscordant partners is less than a third of what would be necessary to sustain the epidemic (29% of incidence in a static epidemic in Rakai; and 12% of incidence that is about double what would be required to maintain a stable epidemic in Mwanza). Even adding the 11% of incidence in Rakai that can be associated with having >1 sexual partner, incidence that can be related — based on published evidence — to sexual exposures in both studies falls far short of what is required for an expanding epidemic. In addition, it is notable that sexual transmission among serodiscordant partners is relatively more important as a component of total incidence in Rakai — with a stable epidemic — than in Mwanza; in other words, transmission due to unidentified and possibly non-sexual risk is more important in the community with the expanding epidemic.

Although these and many other studies of risk factors for HIV in Africa taken alone provide a frustratingly incomplete report of the evidence required to associate HIV infections with sexual exposures, it is nevertheless possible to assemble a composite picture by collating information from accumulated studies across Africa over the last 17 years. In this communication, we: (a) show how available epidemiologic data can be used to estimate the proportion of HIV-1 attributable to sexual behaviour; (b) identify and estimate parameters that describe various categories of sexual transmission; and (c) present estimates of the proportion of HIV-1 in adults in sub-Saharan Africa from sexual transmission.

Methods

To estimate the contribution of sexual transmission to HIV-1 incidence we initially calculate the average rate of sexual transmission required to account for all incidence and then estimate from empirical studies the proportion of observed incidence accounted for by sexual transmission.

Sexual transmission required to account for all incidence

Average sexual transmission rates from women to men ($S_{W\to M}$) and from men to women ($S_{M\to M}$) that would be necessary to explain all observed incidence depend on the sex-specific mortality and sex ratio for persons with HIV. We assume annual death rates for women (d_W) and men (d_M) with HIV of 0.07 and 0.10, respectively, which are conservative, ie, lower than reported from many general population cohorts[14,15]. From several studies and a UNAIDS estimate[15–19] we use a female-to-male ratio of HIV infections of 1.33:1, so that $N_W = (1.33)(N_M)$ and $N_M = (0.75)(N_W)$, where N_W and N_M are the numbers of infected women and men.

If G is the proportional increase in prevalent HIV infections during one year and N_t is the number of infections at the beginning of year t, then $N_{t+1} = (N_t)(1+G) = N_t + I_t - D_t$, where I is incident infections and D represents deaths. These equations hold equally for men, women, and adults. D_t may be estimated as the death rate, d, times the average number alive with HIV during year t. $D_t = (d)(N_t + N_{t+1})/2 = (d)(N_t)(1+G/2)$. Similarly, I_{Mt}, incident cases in men in year t, may be estimated as the average rate of transmission from women to men ($S_{W\to M}$) times the average number of infected (transmitting) women in year t, $I_{Mt} = (S_{W\to M})(N_{Wt})(1+G/2) = (S_{W\to M})(1.33)(N_{Mt})$ $(1+G/2)$, and a similar equation describes incidence in women.

By substituting the above formulations for I and D in the equation $(G)(N_t) = I_t - D_t$, the rate of sexual transmission, S, required to account for all incidence can be expressed as a function of epidemic growth, death rate, and the sex ratio:

$$S_{M\to W} = \frac{G + (d_W)\left(1+\frac{G}{2}\right)}{(0.75)\left(1+\frac{G}{2}\right)},$$

$$\text{and } S_{W\to M} = \frac{G + (d_M)\left(1+\frac{G}{2}\right)}{(1.33)\left(1+\frac{G}{2}\right)}.$$

Table 1. Average annual rate of sexual transmission required to account for all incidence according to annual epidemic growth G*

G	0%	10%	26%	41%	100%
Years to double†	∞	7	3	2	1
$S_{W \to M}$	0.093	0.147	0.25	0.33	0.58
$S_{M \to W}$	0.075	0.220	0.40	0.55	0.98

*Figures in the table assume annual death rates of 0.10 (0.07) for men (women) with HIV and a sex ratio of 1.33 women to men with HIV
†Years for the number of HIV infections to double

Required sexual transmission to account for all HIV incidence increases with G, as shown in Table 1. During 1988–2002, estimated total HIV infections in Africa increased at a compound rate of 19% per year, from 2.5 to over 29 million, but rates of expansion varied widely from declines in Uganda to over 100% per year in some countries for several years[1,20]. In our subsequent calculations, we conservatively assume $G = 10\%$, which is lower than epidemic growth rates in most of Africa during the last several decades, so that calculations will tend to overestimate the proportion of HIV from heterosexual transmission.

Empirical data to estimate heterosexual transmission

With AIDSLINE and other bibliographic resources, we identified studies associating HIV with sexual exposures. We include all identified studies with information as follows:

- HIV incidence in men and women in serodiscordant and concordant negative couples from the general population, workers, voluntary counselling and testing, inpatients, and outpatients (Table 2).
- Numbers of couples concordant positive and discordant with HIV-positive men and women from populations described in the previous bullet (Table 2).
- The proportion of HIV in adults that is in married adults from general population samples and cohorts (Table 3).
- The distribution of HIV infections according to numbers of sexual partners in the last year from general population and comparable samples and cohorts such as blood donors and antenatal women (but not groups selected for high risk behaviour or high probability of HIV infection such as truck drivers and STD patients). We include all studies with at least 200 adults in a cohort or sample, except for one smaller sample of men from the general population (included because of the limited number of such studies available). For our calculations, we use information from general population samples and cohorts only.
- Data to calculate the PAF of incident HIV in men, women, or adults associated with having >1 sexual partner during the observation interval, including all studies of general population and comparable samples and cohorts as described in the previous bullet (Table 4).
- Data to calculate the PAF of HIV infections in men associated with contact with female prostitutes during the observation interval (for studies of HIV incidence) or during the last five years to lifetime (for studies of HIV prevalence), including all studies of general population and comparable samples and cohorts as described in a previous bullet (Table 5).

We also use findings from a series of surveys during 1989–93 on numbers of non-regular partners for African men and women.[21]

Many studies provide data on HIV prevalence and incidence in stable partners (hereafter referred to as married, though some may be in consensual union) that can be used to estimate HIV transmission between discordant partners. To estimate sexual transmission between non-marital partners, we take two approaches. In the first, we base our calculations primarily on PAFs for HIV incidence associated with having >1 sexual partner in the observation interval. In the second, we base our calculations primarily on reported numbers of sexual partners for men and women with HIV and estimated rates of sexual transmission per partnership. With both approaches, we add estimates of sexual transmission to marital and non-marital partners to get total sexual transmission (Table 6).

Depending on available data, for most categories of sexual transmission we estimate four parameters: H, the proportion of HIV in a specified group of transmitters; s, the average annual transmission rate to specified recipients (e.g., wives to husbands); P, the prevalence of HIV among recipients; and c, the average number of partnerships per year between specified groups of transmitters and recipients. For each category of transmission, the product of $(s)(1-P)(c)$ shows average annual transmission from each person in a specified group of transmitters to all persons in a specified group of recipients. We weight this by H to calculate T, average annual sexual transmission (for a category of transmitter) averaged over all men or women with HIV (Table 6). The sum of all T's is estimated total sexual transmission, which we compare to observed incidence to see what proportion is explained by sexual transmission.

For all parameters and for our overall results, we calculate point estimates only, without confidence intervals. In general, we use unweighted averages to combine statistics from different studies; since epidemiologic processes differ across countries and over time, confidence intervals around unweighted averages — or indeed any composite statistic — would be controversial. Furthermore, information

Table 2. HIV serodiscordance and incidence in African couples

Country, year	Population studied	Couples with at least one partner HIV+(number)* M+W+	M+W−	M−W+	M+/F− as % of couples with M+†	M−/F+ as % of couples with F+†	Incidence with HIV+ partners (per 100 PYs) W	M	Incidence with HIV− partners (per 100 PYs) W	M
CAR, no date[22]	Healthy M+ and wives	20	33	—						
Côte d'Ivoire, no date[23]	In-patient M+ and wives	261‡	218‡	—						
DRC, Kinshasa, 1984–85[24]	AIDS patients, controls, spouses	11	8	0						
DRC, Kinshasa, 1987–88[25]	M workers and wives	35	114	90	23	28				
DRC, Kinshasa, 1988–89[26]	M workers and wives	NA	[80]	[69]			[2.0]	[4.4]		
DRC, Kinsbasa, 1988–90[27]	See: DRC 1988–89	NA	92	86			3.7	6.8		
Kenya, Nairobi, 1988–89[28]	M+ with STDs, partners	40	30	—						
Malawi, Karonga, 1981–89[29]	GP surveys	22	36	20	38	52				
Rwanda, Kigali, 1986[30]	Symptomatic W, husbands, others	124	4	10						
Rwanda, Kigali, 1988–90[31]	ANC and PC W, partners	103	32	25	76	80	9.5	3.8	0.6	
Rwanda, Kigali, 1991–92[32]	Couples answering ads	70	28	24	71	74				
Rwanda, Kigali, 1991–92[33]	See: Rwanda 1988–90, more M	67§	26§	11§	72§	86§	4.6‖	0	0.6‖	0.4‖
Tanzania, rural Mwanza, 1991–95[11]	GP cohort	17	22	21	44	42	10.0¶‖	5.0¶‖	0.17‖	0.45‖
Tanzania, urban Mwanza, 1991–96[34]	M workers and wives	27	45	48	38	36	8.3¶	5.0¶	0.87	0.64
Uganda, 1986?[35]	AIDS patients, partners	10	4	0						
Uganda, Rakai, 1989–90[36]	GP cohort						7.3¶††			
Uganda, Rakai, 1990–91[37]	GP cohort	88	48	35	65	72	9.2¶	8.7¶	0.82	0.94
Uganda, Masaka, 1989–97[38]	GP cohort	48	35	34	58	59	10.5¶	5.2¶	0.15	0.36
Uganda, Rakai, 1994–98[39]	GP cohort	NA	228	187			12.0¶	11.6¶		1.0††
Uganda, Rakai, 1994–98[40]	Monogamous couples from Uganda 1994–98	NA	[97]	[77]			[9.1¶]	[15¶]		
Zambia, 1985–87[41]	Most AIDS/ARC, partners	149	58	21			29	8.0		
Zambia, 1987–88[42]	W− in 1st year postpartum						10.5			
Zambia, 1988–92?[43]	M+ with STDs, partners	NA	80	30			5	19.1		
Zambia, 1995–96[44]	Couples coming for VCT	~805	~350	~350	70	70				
Zambia, 1994–00[45]	Couples from VCT centre		535	487			8.3**	7.1**		
Zimbabwe, 1986–88?[46]	Symptomatic M+, partners	45	30							
(a) Averages					54	60	10.1	7.3	0.5	0.6
(number of studies averaged)					(10)	(10)	(12)	(10)	(6)	(5)
(b) Averages from studies in which few knew their HIV status and/or practiced safe sex							10.0	7.1		
(numbers of studies averaged)							(5)	(4)		

CAR=Central AFrican Republic; DRC=Democratic Republic of the Congo; GP=general population; ANC=antenatal clinic; PC=paediatric clinic; VCT=voluntary counselling and testing. M+, W+, M−, W−: men and women with and without HIV infections. [brackets]: Numbers in brackets are included in other studies in the table. *Situation at baseline (except Uganda 1989/90–97); in polygamous marriages, each couple is counted once. †These columns show data only for studies that selected couples without regard for the HIV status or symptoms of the first partner surveyed. ‡HIV-1 with or without HIV-2. §Excluding couples with men who had previously been tested for HIV. ‖In Rwanda, both partners in one couple, and in Tanzania, both partners in three couples seroconverted in an interval; rates of incidence in the table (as reported) assume all seroconversions occurred in W−M− couples. ¶Most partners did not know their own or partner's HIV status and/or take care to prevent transmission. In Tanzania 1991–96, no serodiscordant couple used condoms; in 10 of 78 couples, the HIV+ partner used the counselling service, but both partners did so in only one case. In Tanzania 1991–95, only 5% of men reported ever using condoms at follow-up, and few asked for HIV tests. In Uganda 1990–91, 17% (2%) of men (women) in discordant couples reported condom use, and 13% (7%) of men (women) asked for both counselling and results of HIV tests. In Uganda 1989–97, no one in a discordant couple reported condom use; less than 10% of adults used available counselling to know their HIV status. In Uganda 1994–98, only 11% of HIV-partners in serodiscordant couples reported ever using condoms during follow-up. **Incidence of new infections genetically linked and presumed linked. ††Incidence for men and women

Table 3. Proportion of HIV infections in African adults according to recent sexual behaviour (studies listed according to prevalence)

Country, years, population studied	Sex and number	Prevalence (%)	Time period	0 sex partners		0–1 sex partners		0–2 sex partners		Married‡	
				% of people	% of HIV	% of people	% of HIV	% of people	% of HIV	% of people	% of HIV
DRC, 1987–88; workers and wives[25]	M: 7068	3.3	1 yr			72*	61*				
	W: 4548	3.8	1 yr			99	97				
Congo, 1987–88; ANC[47]	W: 1766	3.9	1 yr			89	82				
Tanzania, Mwanza, 1993; GP, M 20–54 yrs,	M: 149/394	3.7	1 yr	4	9	46	48	68	68	84	75
W 15–54 yrs[17†]	W: 189/574										
		4.4	1 yr	10	10	90	82	98	94	82	72
Kenya, 1989–90; FP[48]	W: 4404	4.9	1 yr			93	84	98	93		
Tanzania, Kisesa, 1994–95; GP 15–44 yrs[49]	M: 2271	5.9	1 yr					68	56	55	65
	W: 2752	7.5	1 yr			89	79			76	67
Burkina Faso, 1994–95; ANC[50]	W: 1294	8.0	1 yr			88	87				
Tanzania, Arusha, no date; GP W 15–54 yrs[51]	W: 567	8.5	6 mos			95	88			65	54
Cameroon, 1997–98; GP W 15–40 yrs[52]	W: 827	8.6	NA							46	45
Kenya, 1989–91; ANC[53†]	W: 325/302	8.8	2 yrs			76	69				
Uganda, Masaka, 1989–90; GP $\geqslant$13 yrs[54]	M: 1788	7.7	NA							48	60
	W: 1914	8.9	NA							48	55
Uganda, near Kampala, 1987; GP $\geqslant$15 yrs[55]	M: 1799	8.8	6 mos	18	13	59	54				
	W: 2091	13	6 mos	22	13	87	80				
Tanzania, Dar es Salaam, 1995; FP[56]	W: 897	17	3 mos			89	86				
Zimbabwe, 1993–95; workers[57]	M: 2691	19	1 yr			57	38				
Uganda, Rakai, 1990; GP $\geqslant$13 yrs[58]	M: 1397	16	1 yr	24	15	73	62			69	73
	W: 1705	22	1 yr	29	16	93	84			67	60
Uganda, Rakai, 1994–95; GP 15–59 yrs[59]	W: 4718	23	1 yr	23	20	96	95				
Malawi, 1989–90; ANC[60]	W: 6506	23	3 yrs			71	61				
Zimbabwe, 1996; GP, 15–44 yrs[61]	M: 280	15	NA							49	74
	W: 385	29	NA							55	55
Kenya, 1997–98; GP W 15–40 yrs[52]	W: 739	33	NA							69	64
Zambia, 1997–98; GP W 15–40 yrs[52]	W: 730	37	NA							64	60
Uganda, Masaka, 1991; GP $\geqslant$13 yrs[19]	M: 160	36	1 yr	21	5	61	47	81	74	62	77
	W: 229	44	1 yr	21	16	87	85	98	98	47	44
(a) Averages for men, GP studies only				17	11	60	53	72	68	61	71
(number of studies/countries)				(4/2)	(4/2)	(4/2)	(4/2)	(3/2)	(3/2)	(6/2)	(6/3)
(b) Averages for women, GP studies only				21	15	87	85	98	96	62	58
(number of studies/countries)				(5/2)	(5/2)	(7/2)	(7/2)	(2/2)	(2/2)	(10/6)	(10/6)

GP=general population adults; M, W=men, women; ANC=women at antenatal clinics; FP=women at family planning clinics; DRC=Demo-ratio Republic of the Congo; yr=years; mos=months; NA=not applicable

*The study reports distribution of HIV according to number of extramarital partners, some of the 10% of unmarried men may have had 1 extramarital partner only; if so, the per cents of men and HIV in men with 0–1 partners may be slightly higher than reported

†Case–control study, for which the table shows numbers of cases/controls, and the % of people (HIV) in a behaviour category is from controls (cases)

‡Reported for general population studies only

Table 4. Crude PAF of incident HIV associated with having >1 sex partner during follow-up (for sexually active adults)

Country, years, population studied	Sex and number	Married (%)	Epidemic growth (%)‡	Risk measures		
				ρ (%)	RR [95% CI]	PAF (%)
Kenya, Nairobi, 1990–92; FP[62]*	W: 17/51	86†	24	4	0	<0
Malawi, Blantyre, 1989–93; PP[63]	W: 687	100	7–13	0	Und	0§
Malawi, Blantyre, 1990–94; ANC[64]	W: 1160	86	17–26	8	1.9 [0.6–5.5]	7
Rwanda, Kigali, 1988–90; PP[65]*	W: 16/48	94	7	6	Und	5§
Rwanda, Butare, 1989–93; ANC[66]	W: 1143	90	5	4‖	11 [5.0–24]‖	30‖
Tanzania, Mwanza, 1991–96; workers and wives[34]	M: 1427	78	0	21¶	2.1 [1.0–0.43]¶	19¶
	W: 745	100	3	10¶	1.9 [0.8–7.6]¶	8¶
Tanzania, Dar es Salaam, 1992–95; FP[67]	W: 1370	98	18	22	1.9 [1.2–3.0]	16
Uganda, Rakai, 1989–90; GP 15–39 years[36]	A: 442	70	1	13¶	3.4 [1.3–9.0]¶	23¶
Uganda, Masaka, 1990–97; GP >13 years[68]*	M: 37/93	66	−1	29	1.9 [0.8–4.4]	21
	W: 46/87	60	−2	0	Und	8§
Uganda, Rakai, 1994–98; GP 15–59 years[13]	A: 8945	62	−1	23	1.5 [1.1–2.1]	11
(a) Men (average of 2 studies)				25		20
(b) Women (average of 8 studies)				8		9
(c) Adults (average of 2 studies)				19		17

ρ=person-years (or persons) with >1 partners; RR=risk ratio; PAF=population attributable fraction; CI=confidence interval; NA=not available; M=men; W=women; A=adults; GP=general population; und=undefined; ANC=antenatal; FP=family planning; PP=postpartum

*Case–control study; the table shows cases/controls, ρ for controls, percent of controls married, OR, and PAF $= \rho(\mathrm{OR}-1)/(1+\rho[\mathrm{OR}-1])$

†Including married, widowed, and divorced; 14% were never married

‡Calculated as ([incidence/prevalence] − 0.1)[12]

§Since the OR is undefined, an estimate for the PAF is derived by supposing that the cases plus controls comprise a representative sample.

‖RR, ρ, and PAF for sex with someone other than the current child's father

¶RR, ρ, and PAF calculated from data that includes sexually inactive adults

Table 5. Crude PAF for prevalent and incident HIV in men associated with prostitute contact (studies listed by year of data collection)

Country, years, reference	Sample or cohort, number	Study design		Crude risk measures†		
		Prevalence‡ or incidence	Reporting period	ρ (%)	RR [95% CI]	PAF (%)
DRC, Nioki, 1988–90[69]	BD and HAT: 354	Prevalence	Ever	52	1.2 [0.3–5.6]	10†
Rwanda, Kigali, 1991[70]	VCT: 837	Prevalence	Ever	53	1.4 [0.9–1.8]	16
S. Africa, Carletonville, 1999[71]	GP: 530	Prevalence	Ever	2	2.7 [1.1–12]	4
Uganda, Rakai, ca 1989[18]	GP: 594	Prevalence	Ever?	6	1.9 [1.0–4.8]	5†
Uganda, Masaka, 1991[19]	GP: 126	Prevalence	Ever	26	0.8	<0
Uganda, Masaka, 1990–97[68]*	HP: 37/89	Incidence	1 year	15	1.2 [0.4–3.5]	3
Zimbabwe, Harare, 1987[72]*	BD: 69/119	Prevalence	Ever	56	1.7 [0.9–3.2]	29†
Average of 7 studies:						10

ρ=per cent of persons or person years with exposures; RR=risk ratio; NA=not available; PAF=population attributable fraction;
GP=general population; BD: blood donors; HAT=outpatients with human African trypanosomiasis (sleeping sickness); VCT=persons who volunteer for testing and counselling. DRC: Democratic Republic of the Congo; CI=confidence interval

*Case–control study, for which the table shows numbers of cases/controls, ρ for exposure among controls, odds ratio instead of RR, and PAF $= \rho(\mathrm{OR}-1)/(1+\rho[\mathrm{OR}-1])$

†When data allow, PAFs are calculated among persons sexually active in the reporting period; marked PAFs are from data including sexually inactive persons

‡For studies of risk factors for HIV prevalence, the table shows only PAFs for exposures for the last five years to lifetime

required to estimate meaningful confidence intervals is often not available; for example, PAFs for HIV associated with prostitute contact may be confounded by unreported medical injections. This is a first empiric estimate; we anticipate questions about data and procedures. We hope that future analyses will resolve these questions and will eventually be able to determine point estimates with meaningful confidence intervals.

For the sake of clarity, we report our calculations in detail. Readers not interested in these details may skip to Table 6 and the Discussion.

Results

Sexual transmission in married couples

(*a*) *Sexual transmission from wives to husbands*: From six studies of serodiscordant couples in Africa in which few if any partners knew their own or partners' HIV status and/or practised safe sex, average HIV incidence in men was 7.1 per 100 PYs (Table 2; here and later references in tables are not repeated in the text). However, not all incidence in serodiscordant couples can be attributed to sexual

Table 6. Estimated proportion of HIV incidence for 10% annual epidemic growth that is accounted for by heterosexual transmission

Key to sections in the text	Category of sexual transmission	*H*	*s*	1 − *P*	*c*	*T*	% of total incidence required for 10% epidemic growth*
Average annual transmission W to M, of which							30–35
(a)	Married W to husbands	0.58	0.065	0.40	1.0	0.015	10
(c)	Non-marital sex first estimate, of which						25
	W to M with 2nd and additional annual partners	†	†	†	†	†	<20>
	W to unmarried M with 1st annual partner	0.20	0.022	0.90	2.0	0.008	<5>
(e)	Non-marital sex second estimate, of which						20
	Non-prostitute W to non-marital partners	1.0	0.022	0.90	0.75	0.015	<10>
	Prostitutes to non-marital partners	†	†	†	†	†	<10>
Average annual transmission M to W, of which							25–29
(b)	Married M to wives	0.71	0.095	0.46	1.0	0.031	14
(d)	Non-marital sex first estimate, of which						11
	M to W with 2nd and additional annual partners	†	†	†	†	†	<9>
	M to unmarried W with 1st annual partner	0.17	0.032	0.80	1.0	0.004	<2>
(f)	Non-marital sex second estimate	1.0	0.032	0.80	1.3	0.033	15

H=proportion of prevalent HIV in men (women) in a given category of men (women). *s*: average annual sexual transmission between individuals in specified groups of transmitters and recipients; P=HIV prevalence in the recipient group; *c*=the average number of partnerships per year between individuals in specified groups of transmitters and recipients; $T = (H)(s)(1 - P)(c)$

*From Table 1, $S_{W \to M} = 0.147$ is sufficient to explain 100% of HIV incidence in men, and $W_{M \to W} = 0.220$ is sufficient to explain 100% of HIV incidence in women

†For these categories, sexual transmission as a proportion of HIV incidence is estimated from PAFs (see Tables 4, 5, and text)

transmission from the HIV-positive partner. From four of the same five studies, average incidence in men with HIV-negative wives was 0.6 per 100 PYs (Table 2). Furthermore, the one study of incidence in serodiscordant couples in Africa that sequenced HIV found that only 142 (88%) of 162 incident cases were epidemiologically linked or presumed linked to the partner's HIV[45]. Subtracting 0.6 from 7.1, we estimate *s*, average transmission from HIV-positive wives to HIV-negative husbands, at 6.5 per 100 PYs.

From 10 accounts of serodiscordant couples in Africa (that selected couples in a manner that did not bias the sample), an average of 60% of HIV-positive wives had HIV-positive husbands (Table 2), so $(1 - P) = 0.40$. Each couple in polygamous marriages has been counted separately, so $c = 1$. In 10 general population samples in six countries, an average of 62% of women were married, and these married women had on average 58% of HIV infections in women, so $H = 0.58$ (Table 3). Hence, annual sexual transmission from HIV-positive wives to husbands, averaged over all HIV in women, is $T = (H)(s)(1-P)(c) = (0.58)(0.065)(0.40)(1) = 0.015$.

In other words, for every 1000 women with HIV, 580 (58%) are married, 232 of their husbands (40% of 580) are HIV-negative, and 15 women (6.5% of 232) — or 1.5% of all women with HIV — transmit HIV to their husbands in a given year. This accounts for about 10% of the incidence in men required for a 10% annual rate of growth (Tables 1 and 6).

(*b*) *Sexual transmission from husbands to wives*: For sexual transmission from men to stable partners, calculations are similar. Average transmission to women in discordant couples may be estimated at 9.5 per 100 PYs (from average incidence of 10.0 per 100 PYs for women in five studies of serodiscordant couples that did not know their HIV status or practise safe sex, subtracting average incidence of 0.5 per 100 PYs from women in seroconcordant negative couples in four of the same studies; see Table 2). An average of 54% of married men who are infected have HIV-positive wives (Table 2), so $(1 - P) = 0.46$. From six general population samples in three countries, 61% of men with 71% of HIV infections in men are married (Table 3). Hence, $T = (0.71)(0.095)(0.46)(1) = 0.031$. In words, for every 1000 men with HIV, 710 (71%) are married, 327 have HIV-negative wives (46% of 710), and 31 (9.5% of 327) or 3.1% transmit HIV to their wives in a given year. This can account for 14% of incidence in women required for a 10% annual rate of growth (Tables 1 and 6).

Non-marital sexual transmission, first estimate using PAFs for > 1 partner

In this first estimate, we use crude PAFs for HIV incidence associated with having >1 sexual partner in the observation interval. (These PAFs may double count a small amount of sexual transmission between stable partners in polygamous and serial marriages, but that is a small matter.) With some caveats, PAFs for having >1 partner measure transmission from all nonmarital partners except first or only annual partners for unmarried adults. From general population studies we can estimate the number of unmarried sexually active adults.

(*c*) *Transmission from women to non-marital partners*: For men in two studies the average PAF for HIV incidence associated with having >1 partner in the observation interval is 20%, and for adults in two studies the average PAF is 17% (Table 4). Three of these four studies selected subjects from the general population, and the third from urban workers. In all four studies, there was virtually no annual growth in HIV infections, so that 20% of incidence in these four studies is much less than 20% of the incidence that would be required for 10% annual epidemic growth. Nevertheless, we estimate that 20% of the HIV incidence in men required for 10% epidemic growth is due to sexual transmission from women to men with their second and additional partners in a year (Table 6).

For a complete accounting of sexual transmission from women to nonmarital partners, we need to estimate HIV transmission from women to unmarried men with their first or only sexual partners in a year. As above, from six general population studies an average of 61% of men accounting for 71% of HIV in men are married; from four general population studies, 17% of men with 11% of HIV were sexually inactive in the last year, except six months in one study (Table 3); subtracting both from 100%, 22% of men with 18% of HIV infections in men are sexually active and unmarried. Some of their first or only annual partners will be young women with low HIV prevalence, but many will be from categories with relatively high HIV prevalence (eg, prostitutes or divorced women), and some of these might have several such relationships with single men. We assume that 11% of women are the first or only annual partners for two men each, accounting for the 22% of men who are sexually active and unmarried ($c = 2$), and that these women have 20% of HIV in women ($H = 0.20$, supposing that their rate of HIV prevalence is double that in other women). Since HIV prevalence in these men is about average for all men, we let $P = 10\%$, so $(1 - P) = 0.90$. (These are crude estimates, but refinements would have little impact on the overall estimate of sexual transmission.) For s, we assume an annual rate of sexual transmission per partnership of 0.022, or one-third the rate in discordant couples; this rate estimates HIV transmission through single encounters as well as longer non-marital relationships. Hence, transmission from women to unmarried men with their first annual partners, averaged across all HIV in women, accounts for an estimated $T = (H)(s)(1 - P)(c) = (0.20)(0.022)(0.9)(2) = 0.008$ transmissions per year.

Combining multiple and first non-marital partners for men, we estimate that sexual transmission from women to all non-marital partners accounts for 20% of incidence in men plus 0.008 transmission per infected woman, which taken together amounts to 25% of HIV incidence in men required for a 10% annual rate of growth (Table 6).

(*d*) *Transmission from men to non-marital partners*: From eight studies with an average epidemic growth rate of 9%, the average PAF (setting the one negative PAF to zero) for incident HIV in women associated with having >1 sexual partner in the observation interval is 9% (see Table 4). In the one study that selected women from the general population, 60% of women were married and the PAF was 8%; in the other seven studies selecting from antenatal clinics and other populations more likely to be married, 86%–100% of women were married and the average PAF was 9%.

For HIV transmission from men to women with their first or only sexual partners in a year, we estimate that 17% of women accounting for 27% of HIV infections in women are sexually active and unmarried (from above, 62% of women with 58% of HIV are married, while from five general population studies in two countries 21% of women with 15% of HIV had no sex partners in the past year, except six months in one study, see Table 3). The first (and often only) annual sex partners for these women include younger men with low HIV prevalence and older men with higher prevalence; we assume that 17% of men with 17% of HIV in men are the first or only annual partners for these women ($H = 0.17$), and that each man has one such partnership ($c = 1$). Since unmarried sexually active women have high HIV prevalence, we let $(1 - P) = 0.80$. We assume an annual rate of sexual transmission per partnership, s, of 0.032, or one-third the rate from men to women in serodiscordant couples. Hence, transmission from men to unmarried women with their first annual partners, averaged across all HIV in men, accounts for $(H)(s)(1 - P)(c) = (0.17)(0.032)(0.80)(1) = 0.004$ transmissions per year.

Combining multiple and first nonmarital partners for women, we estimate that sexual transmission from men to nonmarital partners accounts for 9% of HIV incidence in women (associated with having >1 partner) plus 0.004 transmissions per year, or 11% of HIV incidence in women required for a 10% annual rate of growth (Table 6).

Non-marital sexual transmission, second estimate using data on numbers of sexual partners per year

(*e*) *Transmission from women to non-marital partners*: We sub-divide this estimate into two components, transmission from non-prostitute women and from prostitutes. To estimate HIV transmission from non-prostitute women to non-marital partners we consider the distribution of HIV across women according to number of sexual partners (Table 3). Data averaged from five general population studies show that 21% of women who had no sex partners last year (except six months in one study) account for 15% of HIV in women. Data averaged from seven general population studies show that 87% of women who had 0–1 sex partners account for 84% of HIV in women; subtracting, 66% of women with one sex partner in the last year account for 69% of

HIV in women. Similarly, data averaged from two studies show 98% of women with 96% of HIV in women having 0–2 partners in the last year; subtracting, 11% of women with 12% of HIV in women had two sex partners in the last year. We assume that non-prostitute women with the remaining 4% of HIV had an average of four partners per year (cf: in sexual behaviour surveys in 12 African countries,[21] an average of 3.7% of women reported 2–4 non-regular partners per year, and 0.7% reported more than four). From this, we can calculate that 100 women with HIV would have on average 109(= [0][15] + [69][1] + [12][2] + [4][4]) sex partners per year, of which 58 would be husbands, leaving 51 non-marital liaisons, so that $c = 0.51$. Supposing an undercount in these figures, we make two adjustments: for non-prostitute women, we arbitrarily increase c to 0.75; and we assume that prostitutes have not been counted. For non-prostitute women, we assume an annual rate of sexual transmission to each non-marital partner of 0.022 (one-third of annual transmission from infected wives to susceptible husbands), and we assume that non-marital partners have about average HIV prevalence for men, so we set $(1 - P) = 0.90$. With these estimates, sexual transmission from non-prostitute women to non-marital partners averaged across all HIV in women is $T = (H)(s)(1 - P)(c) = (1)(0.022)(0.9)(0.75) = 0.015$.

For transmission from prostitutes to non-marital partners, we use data from studies of HIV incidence and prevalence to calculate crude PAFs for HIV associated with any prostitute contact (Table 5). Only one study of HIV incidence in men reports data sufficient to calculate a PAF of 3%. Data from six studies of risk factors for HIV prevalence for five years to lifetime contact show crude PAFs ranging from <0 to 29%. Across all seven studies, the average PAF for incident or prevalent HIV associated with prostitute contact is 10% (setting one negative PAF to zero), while the median is 5%. (Some general population studies reporting risk factors for prevalent HIV associated with prostitute contact over the last 1–3 years show much higher PAFs[3], but many others, such as the four-city study in Yaonde, Kisumu, Ndola, and Cotonou, report no association between HIV and prostitute contact[73].)

With this approach, annual HIV transmission from infected women to non-marital partners averages 0.015 new infections in men for each infected woman plus 10% of all HIV infections in men (associated with prostitute contact), together accounting for 20% of HIV incidence in men required for a 10% annual rate of growth (Table 6).

(*f*) *Transmission from men to non-marital partners*: Considering men as transmitters, data from general population studies (Table 3) show that men accounting for 11% of HIV in men had no sex partners in the last year (except six months in one study), men with 42% of HIV (subtracting 11% from 53%) had one partner, and men with 13% of HIV (subtracting 53% from 66%) had two partners. We assume that 28% of men (100% less the average of 72% of men reporting 0–2 partners) with the remaining 34% of HIV in men had an average of four sex partners (cf: in sexual behaviour surveys in 12 African countries[21], an average of 12.5% of men reported 2–4 non-regular partners in the past year, and 3.7% reported more than four). From these data and estimates, we calculate that 100 men with HIV have a total of 204(= [11][0] + [42][1]+ [13][2] + [34][4]) sex partners in a year, of which 71 would be wives, leaving 133 non-marital liaisons, or an average of 1.3 per person ($c = 1.3$). For s, we assume an annual rate of sexual transmission per partnership of 0.032 (see above). We set $(1 - P) = 0.80$, assuming that many non-marital partners are prostitutes and older divorced women with high HIV prevalence. Hence, $T = (H)(s)(1 - P)(c) = (1)(0.032)(0.8)(1.3) = 0.033$.

In other words, an average of 3.3% of infected men transmit to a nonmarital partner in a year: 1000 men have 1300 partners, of which 1040 (80% of 1300) are susceptible and 33 (3.2% of 1040) contract HIV. This accounts for 15% of incidence in women required for a 10% rate of growth.

Estimated sexual transmission as a proportion of total incidence

The last column in Table 6 expresses the contribution of each category of sexual transmission and total sexual transmission as a proportion of what would be required to account for all adult incidence with 10% epidemic growth. With two estimates of non-marital sexual transmission, total sexual transmission from women to men (men to women) accounts for 30–35% (25–29%) of HIV incidence in men (women). These are point or best estimates; we do not estimate confidence intervals.

Discussion

Over the past 18 years, many studies have provided data associating HIV in African adults with sexual exposures. The consensus view that 90% of adult HIV in Africa is from sexual transmission has not — to our knowledge — been derived from or tested against this evidence. Hence, our estimate that sexual transmission accounts for 25–35% of HIV incidence in African men or women is a first empiric estimate. We recognize that many questions can be raised about the data and about our procedures, and we encourage those questions. For some of the statistics that we have used in our calculations, relevant data are so far available from only a few studies or countries. We cannot and do not intend our estimates to be the last word, but rather a step toward better evidence-based estimates of the proportions of HIV in Africa from sexual and other modes of transmission.

As currently measured, the epidemiologic substrate for sexual transmission in Africa appears to be substantially different from that required to account for the preponderance of adult HIV incidence being reported. It is conceivable that respondents to behavioural surveys give incorrect answers. However, the care with which these studies have been performed, the familiarity of investigators with local conditions, their experience in the conduct of such studies, and the consistency of response makes summary dismissal of such results untenable. Some of the discrepancy may lie in the details of sexual behaviour and unexplained variations in rates of sexual transmission. For example, prostitutes may be a hard to reach group, and may be under-represented in population surveys. In keeping with core group theory[74], a small group of persons may account for the majority of transmission both within and outside the core, particularly during times of intense propagation. While little is known about sexual networks in Africa, it is unclear whether any structure could generate rapid epidemic expansion and — at the same time — a majority of HIV infections among men and women with 0–1 sexual partners per year, as is commonly reported for African populations at all levels of HIV prevalence (Table 3) and supposed epidemic stage.

Many have speculated that sexual transmission is more efficient in Africa. One published study, for example, supposes that the probability of transmission from a casual partner may approach 1.0[71]. Anal intercourse may be under-reported[75]. Coinfection with STD and lower frequency of circumcision have both been examined in detail as factors potentiating transmission of HIV[76,77]. Large increases in HIV transmission efficiency associated with coinfection with STD are biologically plausible, but conclusions from empirical findings are at best ambiguous.

Conclusion

Our first objective has been to demonstrate that it is possible to use evidence from epidemiological studies to estimate the relative importance of a specific pathway for HIV transmission in Africa. We illustrate several ways that estimates can be calculated from data. We anticipate that others will be able to construct estimates in different ways, possibly using other categories of data.

Our second objective has been to encourage debate about the relative importance of various pathways for HIV transmission structured around parameters that can be empirically determined. We have defined and used a number of parameters. There are many considerations — focused on specific parameters — that suggest that the estimates we present are too high or too low. We hope that future discussions grounded in epidemiological research will address and resolve questions about parameters.

The third objective has been to present our estimates that roughly one-third of the spread of HIV in Africa can be associated with heterosexual transmission. This estimate is far below those that are usually invoked to explain the AIDS epidemic in Africa, and we suggest that the discrepancy should be addressed. The finding has major ramifications for current and future HIV control programmes in Africa, whose focus has been almost exclusively on sexual risk reduction and condom use.

Questioning the role of heterosexual transmission requires credible alternatives. A growing body of evidence points to unsafe injections and other medical exposures to contaminated blood[78,6] as pathways that have not yet been adequately addressed. In view of the toll that HIV continues to extract in Africa, a broadened epidemiologic agenda, including new efforts to assess the contribution of sex to transmission, and investigation of other potential sources for HIV propagation, appears warranted.

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