Changes in sexual behavior and risk of HIV transmission after antiretroviral therapy and prevention interventions in rural Uganda

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Background: The impact of antiretroviral therapy (ART) on sexual risk behavior and HIV transmission among HIV-infected persons in Africa is unknown.

Objective: To assess changes in risky sexual behavior and estimated HIV transmission from HIV-infected adults after 6 months of ART.

Design and methods: A prospective cohort study was performed in rural Uganda. Between May 2003 and December 2004 a total of 926 HIV-infected adults were enrolled and followed in a home-based ART program that included prevention counselling, voluntary counseling and testing (VCT) for cohabitating partners and condom provision. At baseline and follow-up, participants' HIV plasma viral load and partner-specific sexual behaviors were assessed. Risky sex was defined as inconsistent or no condom use with partners of HIV-negative or unknown serostatus in the previous 3 months. The rates of risky sex were compared using a Poisson regression model and transmission risk per partner was estimated, based on established viral load-specific transmission rates.

Results: Six months after initiating ART, risky sexual behavior reduced by 70% [adjusted risk ratio, 0.3; 95% confidence interval (CI), 0.2–0.7; $P = 0.0017$]. Over 85% of risky sexual acts occurred within married couples. At baseline, median viral load among those reporting risky sex was 122 500 copies/ml, and at follow-up, < 50 copies/ml. Estimated risk of HIV transmission from cohort members declined by 98%, from 45.7 to 0.9 per 1000 person years.

Conclusions: Providing ART, prevention counseling, and partner VCT was associated with reduced sexual risk behavior and estimated risk of HIV transmission among HIV-infected Ugandan adults during the first 6 months of therapy. Integrated ART and prevention programs may reduce HIV transmission in Africa.

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Introduction

Access to antiretroviral therapy (ART) is increasing globally [1]; however the impact of ART on sexual risk behavior and transmission of HIV in Africa is unknown. Although ART may prevent HIV transmission through reduced infectivity [2], this could be offset by increases in risky sexual behaviour [3]. In addition, cell-associated genital HIV shedding may occur in people with low plasma HIV viral load [4,5] allowing for the potential transmission of drug-resistant strains of HIV [6]. Models developed for South Africa and Uganda have suggested that increases in risky sexual behavior by those initiating ART could reduce expected declines in HIV incidence [7,8]. HIV transmission from people on ART will depend on the effectiveness of ART in reducing viral load and of ART programs in reducing sexual risk behavior.

The association between taking ART and sexual behavior in industrialized countries is unclear. Some studies of men who have sex with men, heterosexual, and injecting drug user populations in the United States have demonstrated that risky sexual behaviors [9–11] and STI incidence [12] are higher among HIV-infected persons on ART than among those not on treatment. In contrast, other studies, including several from Europe, have shown significantly lower rates of risky sex among those on ART [13–16]. Aggregated data from 16 studies from industrialized countries showed that prevalence of unprotected sex was no higher among those receiving ART than those not on ART [17].

While ART has been shown to reduce viral load [18,19] and mortality[18,20] in Africa, its effect on risky sexual behavior has not been assessed in a prospective cohort [21]. We assessed sexual behavior before and 6 months after initiation of ART in a cohort of 926 HIV-infected adults in rural Uganda, including: (1) factors associated with sexual activity; (2) changes in desire and frequency of sexual behavior after 6 months of ART; and (3) changes in estimated risk of HIV transmission based on viral load, risky sex, and established condom failure rates.

Methods

Enrollment

Between May 2003 and November 2004, we enrolled and followed persons with HIV-1 infection who were clients of the Tororo branch of The AIDS Support Organization (TASO), a non-governmental organization that has provided HIV/AIDS care and support since 1987. Registration at TASO is free. Forty-six percent of the general population in the Tororo area lives below the Ugandan poverty line, defined as a household's ability to meet minimum caloric requirements [22]. Clients with a CD4 cell count ≤ 250 cells/μl or symptomatic AIDS (defined as CDC category B or C conditions) living within a 100 km^2 catchment area were eligible for enrollment. We translated consent forms and questionnaires into six local languages. All participants and their household members provided written informed consent. We offered home-based HIV voluntary counseling and testing (VCT) to all participants' household members at enrollment and after 1 year [23] and provided free ART for those clinically eligible.

The study includes a randomized ART efficacy monitoring trial evaluating clinical monitoring, clinical monitoring with quarterly CD4 cell count measurements, and clinical monitoring with quarterly CD4 cell counts and HIV viral load. Participants received weekly home-based ART delivery and monitoring by lay field officers and referral as needed for free medical and psychosocial care at the study clinic. The first line ART regimen was stavudine, lamivudine, and nevirapine or efavirenz. Results of this trial will be presented elsewhere.

The Uganda National Council of Science and Technology and the Institutional Review Boards of the Uganda Virus Research Institute, the University of California, San Francisco, and the Centers for Disease Control and Prevention (CDC) approved the study. Funding was provided by the US Department of Health and Human Services/CDC through the Emergency Plan for AIDS Relief.

Study design and procedures

At enrollment and every 3 months thereafter, study counselors conducted private home-based structured interviews with participants. Counselors were trained in rapport-building techniques and eliciting information from participants on sensitive topics in a non-judgmental manner. They asked participants about their sexual desire, opportunities to meet new partners, expectations for future sexual activity, and frequency of sex and condom use with each partner for the previous three months.

We obtained frequency of condom use for the prior 2 weeks as act-specific use of a condom and for the previous 3 months as 'always', 'sometimes', or 'never'. The number of unprotected sexual acts in last 3 months was estimated from the frequency of sex and condom use for each partner. For those reporting 'always' using a condom with a particular partner, the number was estimated as zero unprotected sex acts. For those reporting 'never' using a condom with a partner, the frequency of sex with that partner was used for the estimate of unprotected sex acts. For those reporting 'sometimes' using a condom with a partner, the number of sex acts with and without a condom were estimated by multiplying the average 2-week condom coverage rate of all persons reporting sometimes using a condom and the

frequency of sex with a specific sexual partner over the previous 3 months. Participants provided each sexual partner's HIV serostatus (tested positive, tested negative, unknown) and partner type (spouse, steady or casual partner). We defined abstinence as having no sexual intercourse during the prior 3 months and risky sex as participant-reported inconsistent condom use with a HIV-negative or unknown serostatus partner.

All participants received a behavioral intervention that included group education on ART at enrollment and testing of cohabitating partners through home-based family VCT. In individual sessions, participants developed personal sexual behavior plans in which they assessed their motivation for avoiding transmission and their current risk situation and made risk reduction plans that included how they might cope with increased sexual desires. Risk reduction options discussed by counselors included abstinence, condom use, reduced frequency of sex, and alternative forms of sexual expression. Counselling emphasized risk reduction with HIV-negative or unknown status partners and free condoms were provided to clients who requested them. Although participants had received some prevention counseling previously as TASO clients, partner VCT was not provided and emphasis was on avoiding re-infection.

We measured HIV plasma viral loads using Cobas Amplicor HIV-1 Monitor version 1.5 (Roche, Branchburg, New Jersey, USA) and enumerated CD4 cells using TriTEST reagents following an in-house dual platform protocol and MultiSET and Attractors software using a FACScan flow cytometer (Becton-Dickenson, Franklin Lakes, New Jersey, USA). We tested dried blood spots of household-members for HIV using a parallel enzyme immunoassay (EIA) screening algorithm [Genetic Systems rLAV EIA; Bio-Rad, Redmond, Washington, USA and Vironostika HIV-1 EIA; BioMerieux, Durham, North Carolina, USA or Vironostika HIV Uni-Form II plus O; BioMerieux, Boxtel, The Netherlands].

Data management and statistical analysis

We double-entered questionnaire data using Epi-Info 2002 (CDC, Atlanta, Georgia, USA) and conducted analysis using SAS version 9.1 (SAS Institute, Cary, North Carolina, USA). We included only adults who had their baseline data collected within 2 weeks of initiating ART. We excluded data from clients who were ARV-experienced at enrollment or who initially enrolled as household members because their ART exposure periods were different from index participants. We analyzed follow-up data collected between 150 and 210 days after initiating ART.

We compared baseline demographic and behavioral characteristics between men and women using chi-squared tests. To assess factors associated with being sexually active and changes in sexual activity over time we conducted participant-level analyses (unit of analysis was a participant initiating ART). We developed multivariate logistic regression models to assess predictors of being sexually active at baseline and to compare sexual activity at baseline with follow-up.

We also conducted sexual partner-level analyses (unit of analysis was a sexual partner of a participant initiating ART) incorporating into a model partner HIV-status, number of sexual contacts, condom use, and the cohort member's HIV viral load. Multiple partners of the same participant were included as separate units of analysis. The number of sexual acts and unprotected sexual acts per year were analyzed using Poisson regression models. In both the logistic and Poisson regression models, we used generalized estimating equation methods with an exchangeable correlation structure to adjust for repeated observations for the same cohort member.

HIV transmission risk

We calculated partner-specific transmission risks and summed these to assess overall transmission risk for the population. Expected sero-conversions in the last 3 months were calculated using number of partners, partner-specific condom use, partner HIV status, frequency of sexual behavior, and viral load. We conservatively calculated and used in our model a mean log viral load from the 3-month and 6-month viral loads of the participants. Probabilities of transmission per coital act based on viral load and age were derived from sero-conversion studies of HIV-discordant couples in Uganda [24,25]. For protected sexual acts, we conservatively applied a 20% condom failure rate.[26,27] We also estimated HIV transmission rates at baseline and follow-up using partner HIV-status based on baseline laboratory results, rather than participant report of their partner's HIV status. These analyses were restricted to cohabiting partners of participants for whom laboratory HIV results were available.

Results

Participant characteristics and follow-up

A total of 926 ART-naive adults, from 905 households, were included in the baseline analysis. Of these, 40 (4%) died prior to follow-up and four (0.4%) did not complete a follow-up interview. For 882 persons who had follow-up interviews, the mean time interval from ART initiation to follow-up data collection was 185 days; 815 (93%) fell between 150 to 210 days and were included for follow-up analysis.

The median age at enrollment was 41 years for men and 37 years for women. The population had advanced HIV infection at baseline, with a mean CD4 cell count of 124 cells/μl and a median serum HIV-1 RNA level of

Table 1. Baseline characteristics of men and women initiating antiretroviral therapy in rural Uganda.

	Men		Women		All		
	%	(No./total)	%	(No./total)	%	(No./total)	*P* value
Demographics							
Age (years)							
18–25	1	(2/235)	3	(18/691)	2	(20/926)	0.0000
26–35	26	(60/235)	40	(278/691)	37	(338/926)	
36–45	45	(106/235)	43	(295/691)	43	(401/926)	
46–55	23	(53/235)	11	(79/691)	14	(132/926)	
56+	6	(14/235)	3	(21/691)	4	(35/926)	
Highest level of education completed							
None	10	(22/228)	28	(191/680)	23	(213/908)	0.0000
Primary	56	(128/228)	53	(358/680)	54	(486/908)	
Post primary	26	(59/228)	15	(101/680)	18	(160/908)	
Tertiary	8	(19/228)	4	(30/680)	5	(49/908)	
Current marital status							
Single	4	(8/228)	4	(30/680)	4	(38/908)	0.0000
Married/co-habiting	68	(156/228)	24	(165/680)	35	(321/908)	
Separated/divorced	13	(30/228)	12	(80/680)	12	(110/908)	
Widowed	15	(34/228)	60	(405/680)	48	(439/908)	
Main source of income							
Farming	39	(89/228)	31	(212/680)	33	(301/908)	0.0055
Wages & salaries	19	(44/228)	13	(89/680)	15	(133/908)	
Remittances	20	(45/228)	24	(166/680)	23	(211/908)	
Trade	21	(48/228)	30	(207/680)	28	(255/908)	
Religion							
Traditional Christian	78	(174/224)	79	(533/676)	79	(707/900)	0.2057
Moslem	6	(14/224)	4	(24/676)	4	(38/900)	
Christian Fundamentalist	16	(36/224)	18	(119/676)	17	(155/900)	
Drinks alcohol	29	(69/235)	10	(70/690)	15	(139/925)	0.0000
Number of children alive Mean (SD)		4.9(3.2)		3.7(2.1)			0.0000
Desires more children	9	(20/234)	3	(18/675)	4	(38/909)	0.0001
Number of lifetime sexual partners							
1–2	5	(11/233)	36	(246/686)	28	(257/919)	0.0000
3–4	15	(35/233)	37	(257/686)	32	(292/919)	
5–6	15	(36/233)	13	(92/686)	14	(128/919)	
7+	64	(150/233)	13	(91/686)	26	(241/919)	
Clinical status							
Baseline CD4 cell count (cells/μl)							
< 100	45	(105/235)	39	(268/691)	40	(373/926)	0.0176
100–199	41	(97/235)	39	(267/691)	39	(364/926)	
≥ 200	14	(33/235)	23	(156/691)	20	(189/926)	
Baseline viral load							
< 1700	0	(1/235)	1	(9/691)	1	(10/926)	0.0038
1700–12499	2	(4/235)	5	(33/691)	4	(37/926)	
12500–38500	4	(9/235)	9	(63/691)	8	(72/926)	
> 38500	94	(221/235)	85	(586/691)	87	(807/926)	

226 000 copies/ml. Women were less educated, less likely to drink alcohol, less likely to want more children and more likely to be widowed than men. Only 23% of participants had education beyond primary school (Table 1).

Sexual activity at baseline

At baseline, 53% of men and 79% of women reported abstinence in the previous 3 months. Of these, 34% had chosen to abstain, and 66% reported temporal reasons for abstinence including poor health, no partner, and no interest. Of the 318 living in stable relationships for whom sexual behavior information was available, 100 (65%) men and 96 (59%) women reported that they had had sexual intercourse in the past 3 months. Of the 605 not living with a regular partner, 13% of men and 9% of women reported sexual intercourse in the previous 3 months. Overall, 234 (92%) of those sexually active had had only one partner and 191 (75%) had had sex only with a spouse in the previous 3 months. There were 193 participants who had sex with spouses, 37 with steady partners, and 25 with casual partners. Among the sexually active, 44% of women and 45% of men reported unprotected sex with at least one partner.

In multivariate analysis, factors independently associated with sexual activity at baseline included age, marital status, main source of income, viral load and number of lifetime sexual partners. Sexual activity decreased with each increasing year of age [odds ratio (OR), 0.96; 95% confidence interval (CI), 0.93–0.98; $P = 0.0005$]. Those

Table 2. Sexual behavior at baseline and after 6 months of antiretroviral therapy.

Variable	Baseline %	Baseline (*n*/*N*)	Follow-up %	Follow-up (*n*/*N*)	Adjusted odds ratios[a]	*P*-value
Men						
Sex in last 3 months	47	(110/233)	53	(109/205)	1.3 [0.9–1.9]	0.2243
Sex with a spouse	44	(104/235)	45	(94/207)	1.0 [0.7–1.5]	0.9997
Any unprotected sex	21	(49/235)	11	(23/207)	0.5 [0.3–0.8]	0.0037
Any unprotected sex with negative/unknown partner	9	(21/235)	4	(8/207)	0.4 [0.2–0.9]	0.0210
Increased sexual desire in past 3 months	2	(4/232)	38	(61/161)	69.8 [16.5–295.9]	0.0000
Expects sexual activity to increase in future	32	(72/225)	49	(99/203)	2.1 [1.5–2.9]	0.0000
Opportunities to meet potential sexual partners increased in last 3 months	3	(7/234)	30	(62/205)	15.6 [6.6–36.6]	0.0000
Women						
Sex in last 3 months	21	(145/689)	24	(143/608)	1.2 [0.9–1.5]	0.1772
Sex with a spouse	13	(93/691)	15	(93/609)	1.1 [0.9–1.3]	0.5874
Any unprotected sex	9	(65/691)	6	(37/609)	0.6 [0.4–0.9]	0.0101
Any unprotected sex with negative/unknown partner	5	(35/691)	2	(12/609)	0.4 [0.2–0.7]	0.0018
Increased sexual desire in past 3 months	1	(9/684)	14	(70/512)	12.8 [6.3–25.9]	0.0000
Expects sexual activity to increase in future	19	(128/662)	27	(166/606)	1.6 [1.3–2.0]	0.0001
Opportunities to meet potential sexual partners increased in last 3 months	4	(29/689)	25	(154/606)	8.9 [6.0–13.2]	0.0000
All						
Sex in last 3 months	28	(255/922)	31	(252/812)	1.2 [1.0–1.5]	0.0743
Sex with a spouse	21	(197/926)	23	(187/815)	1.1 [0.8–1.3]	0.6641
Any unprotected sex	12	(114/926)	7	(60/815)	0.5 [0.3–0.8]	0.0035
Any unprotected sex with negative/unknown partner	6	(56/926)	2	(20/815)	0.4 [0.2–0.6]	0.0001
Increased sexual desire in past 3 months	1	(13/916)	19	(131/672)	22.4 [11.7–42.6]	0.0000
Expects sexual activity to increase in future	23	(200/887)	33	(264/808)	1.7 [1.4–2.1]	0.0000
Opportunities to meet potential sexual partners increased in last 3 months	4	(36/923)	27	(215/810)	9.8 [6.8–14.0]	0.0000

[a]Adjusted for sex, age, marital status, and intra-client clustering.

who were married or cohabiting were more likely to be sexually active compared with those who were widowed (OR, 23.4; 95% CI, 14.6–37.6; $P < 0.0001$). Participants whose main source of income was trade were more likely to be sexually active than farmers (OR, 2.4; 95% CI, 1.4–4.0; $P = 0.0007$). Participants with viral loads $\leq 38\,500$ copies/ml were more likely to be sexually active in comparison with those with viral load $> 38\,500$ copies/ml (OR, 1.9; 95% CI, 1.1–3.4; $P = 0.0242$). Sexual activity was more common among persons with ≥ 5 lifetime partners (OR, 2.9; 95% CI, 1.7–5.1; $P = 0.0002$), or three or four lifetime sexual partners (OR, 2.0; 95% CI, 1.2–3.5; $P = 0.0134$) compared with those with < 3 lifetime sexual partners.

Sexual activity after 6 months on ART

The proportion of participants who had had sexual intercourse within the prior 3 months did not change between baseline and follow-up for either women (21 versus 24%, $P = 0.1772$) or men (47 versus 53%, $P = 0.2243$), but both reported changes in sexual feelings and experiences (Table 2). Consistent condom use increased and unprotected sex with partners of negative or unknown status decreased (Table 2).

Changes in risky sex within partnerships

At baseline 255 sexually active people had 280 partners; at follow-up 252 people had 268 partners. Partner-based analyses showed increases in consistent condom use from

Table 3. Sexual behavior within partnerships of persons at baseline and after 6 months of antiretroviral therapy.

Variable	Baseline %	Baseline (*n*/*N*)	After 6 months %	After 6 months (*n*/*N*)	Adjusted odds ratios/risk ratios[a]	*P*-value[a]
HIV negative or unknown partnerships						
Always use a condom in last 3 months	59	(82/140)	82	(85/104)	3.1 [1.7–5.8]	0.0003
Used a condom the last time	63	(90/143)	85	(89/105)	3.3 [1.7–6.4]	0.0003
Number of sex contacts in last 3 months, mean (SD)		13.7 (14.5)		13.5 (14.3)	1.0 [0.7–1.3]	0.7664
Number of unprotected sex contacts in last 3 months, mean (SD)		4.2 (9.9)		1.4 (4.3)	0.3 [0.2–0.7]	0.0017
HIV positive partnerships						
Always use a condom in last 3 months	58	(79/137)	74	(118/159)	2.2 [1.4–3.7]	0.0016
Used a condom the last time	70	(96/138)	82	(131/159)	2.2 [1.3–3.8]	0.0047
Number of sex contacts in last 3 months, mean (SD)		13.7 (12.3)		15.4 (17.0)	1.1 [0.9–1.3]	0.5407
Number of unprotected sex contacts in last 3 months, mean (SD)		3.6 (9.0)		2.3 (5.5)	0.6 [0.3–1.1]	0.0726

[a]Adjusted for sex, age, and religion of participant, whether sex was with a spouse, steady or casual partner, and intra-index client clustering.

Table 4. HIV transmission risk within partnerships (HIV negative/unknown partner status) at baseline and 6 months after initiating antiretroviral therapy (ART).

	Baseline						After 6 months on ART					
Viral load	No. of index clients	No. of partnerships of risk	No. of sex acts with a condom	Total no. of sex acts without a condom	Total no. of unprotected sex acts of risk[a]	Expected sero-conversions in 3 months	Expected sero-conversions per 1000/ person years	No. of index clients	No. of partnerships of risk	No. of sex acts with a condom	Total no. of sex acts without a condom	Total no. of unprotected sex acts of risk[a]	Expected sero-conversions in 3 months	Expected sero-conversions per 1000/ person years
< 1700	1	1	0	3	3.0	0.000	0.5	94	100	1199	139	378.8	0.018	0.7
1700–12499	7	8	64	20	32.8	0.028	14.0	2	2	30	6	12.0	0.006	12.0
12500–38500	17	19	123	114	138.6	0.093	19.5							
> 38500	101	109	1119	438	661.8	1.445	53.0							
Overall total	126	137	1306	575	836.2	1.566	45.7	96	102	3110	145	390.8	0.024	0.9

[a]Sex acts without a condom and 20% failure rate for sex acts with a condom.

59 to 82% ($P = 0.0003$) with partners with negative or unknown HIV status. The mean number of sexual contacts in the previous 3 months did not increase significantly (Table 3). Overall, there was a 70% reduction in the number of unprotected sexual acts with a partner of known negative or unknown sero-status: among men there was a 75% reduction (5.4 sex acts versus 1.3 sex acts; $P = 0.0198$), and among women, a 58% reduction (3.5 sex acts versus 1.5 sex acts; $P = 0.0268$). Condom use increased within concordant positive partnerships although the decline in mean number of unprotected sexual contacts was not significant (Table 3). Overall 88% of risky sexual acts at baseline and 86% at follow-up occurred within married and cohabiting couples.

HIV transmission risk within partnerships

After 6 months on ART, 85% of persons engaging in sex with negative or partners with unknown status had an HIV-1 RNA level below 1700 copies/ml (Table 4), the level associated with lowest risk in previous studies. [8,25] Estimated risk of HIV transmission to partners of negative and unknown status reduced from 45.7 per 1000 person years at baseline to 0.9 per 1000 person years at follow-up, representing a 98% decrease (Table 4). When analysis was restricted to the 49 cohabiting and sexually active partners for whom HIV-negative status based on study laboratory investigations was available, results were similar (risk of HIV transmission reduced from 43.5 per 1000 person years to 0.8 per 1000 person years, representing a 98% decrease). When VCT was repeated at 1 year for these HIV-negative spouses, one male spouse of a female index participant had sero-converted. Both spouses self-reported inconsistent condom use with each other and the man reported unprotected sex with an outside steady HIV-positive partner.

Discussion

Providing ART, prevention counseling, and partner VCT reduced self-reported sexual risk behavior among HIV-infected adults in rural Uganda and also substantially reduced the risk of transmission to their uninfected partners. Overall, there was a 70% reduction in risky sex and a 98% reduction in the number of estimated sero-conversions after 6 months. Changes occurred among men and women, irrespective of age. These findings support arguments for incorporating prevention into ART programs [28] and provide initial empirical evidence that ART, when combined with prevention interventions, can help reduce HIV transmission in Africa.

Over 85% of risky sexual behavior at baseline and follow-up occurred within married and cohabiting couples. HIV discordance is common within couples in Africa, ranging from 3–20% in the general population [29–31] to as high as 51% within couples in which one partner seeks

HIV care services [32,33], but knowledge of partner status and understanding of discordance is extremely low [21,34] To reduce the high risk of HIV transmission within discordant couples and to minimize primary infection with drug-resistant strains of HIV, ART programs in Africa should consider not only prevention counselling, but proactive testing of sexual partners.

Overall, sexual activity remained low in this population, with the majority still abstinent after 6 months on ART. While this may reflect our sample, which included a high proportion of older, widowed women, similar findings have been reported from Cote d'Ivoire [21]. However, both men and women experienced substantial increases in sexual desire and in opportunities to meet new partners after ART initiation, highlighting the importance of on-going prevention interventions for populations on ART.

Without a randomized efficacy trial, it is not possible to disaggregate the effects of our prevention activities, which included making a personal sexual behavior plan, partner VCT, and condom provision from the effects of providing ART alone. However, ethical considerations would probably preclude such a trial, as similar prevention interventions in the pre-ART era involving HIV-infected people in Africa, such as VCT interventions for discordant couples, also resulted in substantial increases in reported condom use – from 3 to 80% in Zambia [35] and 5 to 71% in Congo [36]. The interventions we used could be replicated by other ART programs and standards for incorporating prevention into ART programs in Africa would be beneficial. Evidence-based guidelines have already been developed elsewhere and could be rapidly adapted and disseminated in Africa [37].

Our findings are based on self-reported sexual behavior, which has been shown to be biased in some settings [38]. A further limitation of our data could be that study counselors who provided on-going risk reduction counseling also interviewed participants. This may have led to under-reporting of risky sex by participants due to social desirability. However, counselors were trained to minimize bias by using non-judgmental approaches. Moreover, within the subset of discordant spouses for whom we had laboratory confirmed HIV results at 1 year, no sero-conversions occurred among those who reported consistent condom use. The one man who sero-converted had self-reported inconsistent condom use and multiple HIV-positive partners, thereby providing evidence that self-report may be reliable in this population. Given the expense of HIV incidence studies, nearly all studies on ART and sexual risk behavior have been based on self-reported data [17]. Finally, large studies in Uganda have shown correlations between self-reported sexual behavior and HIV infection [39], suggesting that biases introduced by use of self-reported data in Uganda do not mask key associations.

We assumed conservatively that all partners of unknown status were HIV-negative and that condom failure rates were 20%; however, if some of these partners were HIV-positive or condom failure rates were lower, then we may have overestimated overall transmission risk. Our findings of equivalent transmission risk estimates among the subset with laboratory confirmed HIV status suggested that little bias was introduced because of partners of unknown HIV status. As we used established transmission rates from a population that did not contain persons with undetectable viral loads, we may have also differentially overestimated transmission risk at follow-up by assigning the same transmission risk to those with undetectable viral loads as to those with viral load < 1700 copies/ml. Finally, on-going monitoring, beyond our 6-month follow-up, will be important to assess whether the reductions in risky sex and HIV transmission risk are maintained over time. Risk behavior monitoring and prevention interventions targeting HIV-negative people as well as HIV-infected persons not on ART will also be critical as access to ART expands in Africa.

Our findings support arguments that integrated ART and prevention programs can reduce HIV incidence among uninfected sexual partners of persons on therapy in Africa. Minimizing HIV transmission by persons taking ART will also help to minimize primary infections with drug-resistant strains of HIV and help to extend the utility of less expensive first-line regimens in Africa. Randomized efficacy evaluations of simple prevention interventions that can be implemented in ART clinical settings are needed. Given the extremely high cost of ART, even for generic formulations, the added investment by ART programs for a strong prevention component would be marginal while the potential gains in reducing HIV transmission could be substantial. Our findings that an integrated ART and prevention program may reduce HIV transmission risk reinforce clinical and equity arguments for expanding ART to the millions of Africans who will soon die without it.

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