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Outside Sexual Partnerships and Risk of HIV Acquisition for HIV **Uninfected Partners in African HIV Serodiscordant Partnerships**

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Abstract

Background—As African countries scale up couples HIV testing, little is known about sexual behaviors and HIV risk for HIV uninfected partners in known HIV serodiscordant relationships.

Methods—We conducted a prospective study of 3,380 HIV serodiscordant partnerships from 7 African countries. Self-reported sexual behavior data were collected quarterly from HIV uninfected partners.

Results—The proportion of HIV uninfected partners reporting sex with their known primary HIV infected partner decreased during follow-up (from 93.5% in the prior month at baseline to 73.2% at 24 months, p<0.001). Simultaneously, an increasing proportion reported sex with an outside partner (from 3.1% to 13.9%, p<0.001). A small proportion (<5%, stable throughout follow-up) reported sex with the infected partner and an outside partner in the same month (concurrent). Unprotected sex was more common with outside partners than with their primary

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known HIV infected partners (risk ratio 4.6; 95% CI 4.2–5.2). HIV incidence was similar for those reporting sex only with their primary HIV infected partner compared to those who reported an outside partner (2.87 vs. 3.02 per 100 person-years, p=0.7), although those who had outside partners were more likely to acquire HIV that was virologically distinct from that of their primary partner (p<0.001).

Conclusion—For uninfected members of HIV serodiscordant couples, sex with the infected partner declined as sex with outside partners increased, likely reflecting relationship dissolution and risk shifting from a known infected partner. Risk reduction messages for HIV uninfected partners in serodiscordant partnerships should include strategies to reduce HIV acquisition from outside partners.

Keywords

HIV serodiscordant couples; sexual behavior; condom use

INTRODUCTION

Approximately half of HIV infected adults in sub-Saharan Africa have an uninfected partner. ^{1–4} Prospective studies have found high HIV incidence among HIV uninfected partners in serodiscordant relationships,^{5,6} particularly in couples unaware of their serodiscordant status. Population-based surveys and mathematical modeling studies have suggested that a substantial proportion of new HIV infections in Africa may occur within stable, HIV serodiscordant sexual partnerships.^{1,7}

Several African countries are increasingly adopting couples HIV testing through clinic and home-based initiatives as an HIV prevention strategy.^{8–10} As a result, more couples of previously unknown serostatus are becoming aware of being HIV serodiscordant. Little is known about the sexual behavior of HIV uninfected partners of serodiscordant couples and their risk of HIV acquisition after they become aware of their HIV serodiscordance.^{3,11,12} Knowledge of being in an HIV serodiscordant relationship may lead an HIV uninfected partner to initiate sexual relationships with outside partners, potentially of unknown HIV serostatus, who might be perceived as lower risk than their known primary HIV infected partners, and the relationship to risk of HIV acquisition, is important in developing HIV risk reduction messages for serodiscordant couples and designing HIV prevention interventions for uninfected partners.

We conducted a prospective study measuring self-reported sexual behaviors of HIV seronegative partners in known HIV serodiscordant partnerships, including condom use with the primary HIV infected partner versus outside partners, gender differences in sexual behavior, and risk of HIV acquisition from within or outside the primary HIV serodiscordant partnership.

METHODS

Population and procedures

Between November 2004 and April 2007, we enrolled heterosexual HIV serodiscordant couples from 7 African countries (Botswana, Kenya, Rwanda, South Africa, Tanzania, Uganda, and Zambia) into the Partners in Prevention HSV/HIV Transmission Study, a randomized, placebo-controlled clinical trial of HSV suppression given to HSV/HIV dually-infected persons for the prevention of HIV transmission to their HIV uninfected partners.^{13,14} As previously detailed,⁴ couples were recruited from a HIV voluntary

counseling and testing centers, HIV care centers, and direct community outreach. Enrolled couples, 18 years of age or older, sexually active, and intending to remain together for at least 24 months. Study inclusion criteria included that HIV infected partners be seropositive for both HIV and HSV, have a CD4 count \geq 250 cells/mm³, and not be taking antiretroviral therapy at the time of study entry. As previously reported, acyclovir failed to reduce the risk of HIV transmission within the couples.¹³

Participants were followed for up to 24 months, with all participants completing the study by October 2008. HIV uninfected partners were seen every quarter, for assessment of sexual behavior and HIV serostatus. HIV infected partners were seen monthly. All participants received HIV risk-reduction counseling (both individual and as a couple) at each visit, as well as treatment of sexually transmitted infections and free condoms throughout study follow-up. The study was approved by the University of Washington Human Subjects Review Committee and institutional review boards at each study site and at collaborating institutions. Participants provided written informed consent.

Behavioral assessment

HIV negative partners completed an interviewer-administered structured sexual behavior questionnaire at enrollment and each quarterly visit. The questionnaire asked about the sexual behavior in the previous month with the primary HIV infected partner (with whom they enrolled in the study) and with outside partners. Data were collected for each partner type on the number of acts with each partner type protected by condoms. Data on the HIV status (known or perceived) of outside partners and on specific questions about dissolution of the relationship with the primary HIV infected partner were not collected.

Laboratory methods

HIV serologic testing was by rapid HIV antibody tests, with positive results confirmed by ELISA and Western blot.¹³ For HIV uninfected partners who seroconverted to HIV, analysis of HIV *env* and *gag* gene sequences from viruses obtained close to seroconversion from both members of the couple was used to determine whether transmission was genetically linked within the partnership, or was unlinked and thus likely acquired from an outside partner.¹⁵

Statistical analysis

A total of 3,408 couples were enrolled in the Partners in Prevention HSV-2/HIV-1 Transmission Study; of these, 27 were found to not be eligible based on confirmatory lab testing¹³ and were excluded from the present analysis. For couples in which the initially HIV uninfected partner acquired HIV, visits after seroconversion were censored.

For the present analysis, the primary outcome measure was any sexual activity with an outside partner, as assessed at each quarterly visit (thus, a time-varying measure). We used generalized estimating equations (GEE) with logistic link to assess the trends over time as well as differences by gender in the occurrence of sex with an outside partner (as a dichotomous yes/no variable), thus adjusting standard errors for correlation within observations from the same participant. For the analysis of trends over time a linear time trend was assumed. Time trends for sex with the primary partner were examined using the same methods. We used multivariate logistic GEE to simultaneously evaluate whether key *a priori*-defined demographic, behavioral, and clinical factors were associated with having outside partnerships.

To determine if condom use differed for sexual acts with the known HIV infected partner versus outside partners, we used GEE with a log link and binomial errors. This allows

reporting of relative risks, which is preferred to odds ratios when the outcome is common, as unprotected sex was in some subgroups.

To examine relationships between outside partnerships and risk of HIV acquisition, we defined an additional time-varying covariate which indicated, for each visit, whether the participant had ever reported sex with an outside partner in the study up to that time; this cumulative measure thus reflected any reporting of outside partners. HIV incidence rates and 95% confidence intervals were estimate using the Poisson distribution, and Cox regression was used to estimated hazard ratios and p-values. Fisher's exact test was used to compare proportions of linked seroconversions among seroconversions occurring after HIV uninfected participants reported an outside partner versus not reported an outside partner. All analyses were conducted using SAS 9.2 (Cary, NC, USA).

RESULTS

Participant characteristics

Of 3,381 HIV serodiscordant couples enrolled, 2,284 (67.6%) were those in which the HIV uninfected partner was male (Table 1). The median age of these HIV uninfected partners was 33 years (interquartile range [IQR] 28–40). The majority of couples (76%) were married, the median duration of the relationship was 5.4 years (IQR 2.3–10.4), and most (90%) lived in the same household. A median of four sex acts were reported with the HIV infected study partner in the month prior to enrollment (IQR 2–8). Median follow-up for HIV uninfected women and men was 18 (IQR 15–24) and 18 months (IQR 12–24), respectively. Retention at 12 and 24 months was 96% and 92% for women and 93% and 88% for men.

Proportion reporting and correlates of outside partnerships during study follow-up

Over the 24 month follow up period, the proportion of these HIV uninfected partners reporting sex with an outside partner increased steadily, from 3.1% to 13.9% overall (p<0.001) (Table 2). This increase was seen among both men (from 4.3% to 19.1%, p<0.001) and women (from 0.5% to 4.0%, p<0.001). Overall, men were significantly more likely than women to report a sexual partner other than their HIV infected study partner (p<0.001).

In multivariate analysis (Table 3, simultaneously evaluating key population characteristics), those who had no children were more likely to report outside partnerships, and this was true for both women and men. Men who were from East Africa, who were younger, who lived apart from their study partner, and who reported multiple spouses at the time of study enrollment were also more likely to have partners other than their HIV infected study partner. For both women and men during follow-up, those who reported sex with their HIV infected study partner during the prior month were substantially less likely to report sex with an outside partner in the same month (adjusted odds ratio 0.1, p<0.001 for women and 0.2, p<0.001 for men).

Sexual behavior with HIV infected partners and concurrent outside partners during followup

The proportion of HIV uninfected partners who reported sex with their HIV infected partner declined steadily during follow-up: from 93.5% during the month prior to enrollment to 73.2% at 24 months (p<0.001). This decline was seen in both women (from 92.1% to 74.0%, p<0.001) and men (from 94.2% to 73.0%, p<0.001) (Table 4). Sex with the known HIV infected partner and an outside partner in the same month (i.e., concurrent sexual partnerships) was uncommon: 3-5% of persons at each quarterly visit overall (0.3–0.8% in

women and 4–7% in men) and this proportion was stable throughout follow-up. However, of the 569 (25%) men and 83 (9%) women who ever reported an outside partner, the proportion reporting sex with their primary partner a subsequent visit were 67% and 44%, respectively. There was a steady increase throughout follow up for both women and men of the proportions reporting no sexual activity, and reporting sexual activity only with outside partners (indicators of possible sexual relationship dissolution with the primary study partner).

Sex that was unprotected by condoms was reported by HIV uninfected partners significantly more frequently with outside partners than with their known HIV infected primary partners (54.1% of visits versus 11.6% of visits, risk ratio [RR] 4.6, 95% confidence interval [CI] 4.2–5.2, p<0.001), with a similar pattern for both men and women. Among participants who ever reported an outside partner, this finding was similar: 54.1% versus 12.9% of visits, RR 4.2, 95% CI 3.5–5.1, p<0.001). Finally, when restricted to those study visits at which HIV uninfected partners reported sex with the study partner as well as sex with an outside partner, the findings were similar (RR 6.3, p<0.001 for women and RR 3.7, p<0.001 for men).

HIV incidence and relationship to outside partnerships

The rate of HIV acquisition among those reporting sex with outside partners was similar to that among those who did not report outside partners for both women (4.61 vs. 3.62 per 100 person-years, p=0.4) and men (2.64 vs. 2.28 per 100 person-years, p=0.6) (Table 5). Notably, based on HIV viral sequencing, 18 of 21 (86%) of those who reported outside partners acquired HIV that was virologically distinct from that of their primary partner based on sequencing, compared to 23 of 106 (22%) who reported no outside partners (OR 21.7, p<0.001). Thus, although there was no difference in overall HIV incidence, the rate of HIV infection that was unlinked to the study partner was significantly higher among those reporting outside partnerships than those who did not report outside partnerships.

DISCUSSION

In this prospective study of almost 3,400 HIV uninfected partners from 7 African countries who were in HIV serodiscordant relationships and aware of their HIV discordant serostatus, we observed substantial changes in sexual risk behaviors during 24 months of follow-up. The proportion of HIV uninfected partners having sex with their HIV infected partner declined significantly over time, while the proportion reporting sex with an outside partner increased steadily. The HIV uninfected participants who only reported sex with their HIV infected study partner during follow-up were no more likely to acquire HIV than those who ever reported sex with outside partners.

The observation that those who reported outside partners were less likely to use condoms with their outside partner(s) and, if they became HIV infected, were more likely to have acquired HIV from an outside partner, highlights potential differences in HIV risk perception within versus outside of known serodiscordant partnerships. It also emphasizes that knowledge of partner's serostatus does not necessarily reduce HIV risk if it is accompanied by risk shifting away from a known HIV infected partner to outside partnerships of potentially unknown HIV serostatus. Our results provide new insights into counseling needs related to changing HIV risk over time for HIV uninfected members of HIV serodiscordant couples. Importantly, these results come from a study setting with frequent individual and couples risk reduction counseling.

Our results suggest that HIV uninfected members in known serodiscordant partnerships adopt HIV risk reduction behaviors within the partnership, including increased condom use

and abstinence. However, the significant decline in the occurrence of sex with the primary HIV infected partner was paralleled by an increase in the proportion of participants reporting sex with outside partners. A prior study of HIV serodiscordant couples found a modest prevalence (16%) of concurrent partnerships, with low rates of condom use with outside partners.¹⁶ The change in sexual behaviors with different partner types observed in our study did not include high rates of concurrent sexual activity, suggesting relationship dissolution (or at least cessation of sexual activity) with the known HIV infected partner in conjunction with establishment of new partnerships. Condom use was substantially less common within outside partnerships, indicating that risk reduction strategies used within the known HIV serodiscordant partnership did not necessarily carry over into new relationships. This finding has implications in terms of HIV prevention interventions for HIV uninfected partners in serodiscordant relationships, given that the majority of HIV infected persons in sub-Saharan Africa have not been tested and thus are unaware of their HIV status.¹⁷

One of the limitations of the study is that study subjects were participants in a biomedical HIV prevention clinical trial and thus there is potential for selection for couples who may have been more likely to remain in their partnership. In addition, couples received ongoing risk reduction counseling, which likely reinforced lower risk behaviors. We did not specifically ask whether sex with outside partner was with the same partner throughout the period of follow up, the HIV status of outside partners, or if there was change in the status of the primary study serodiscordant partnership. Lastly, data were gathered only on the last month prior to the scheduled study visit, yet participants were seen on a quarterly basis; thus, our data may underestimate the proportion of HIV uninfected partners who ever had an outside partnership.

Couples HIV counseling and testing is being promoted in Africa in order to identify couples who are unaware of their HIV serodiscordant status and to prioritize them for HIV prevention interventions, potentially including earlier antiretroviral therapy for the HIV infected partner.¹⁸ Risk-reduction messaging for HIV uninfected partners in serodiscordant couples has received relatively attention as a topic of research or public health practice, and uninfected partners often has infrequent contact with health care systems after receiving an initial seronegative HIV test. An important component of counseling HIV serodiscordant couples about risk reduction is addressing risk perception and anticipating behavior change by the HIV uninfected partner, including the potential to increase condom use with their known HIV-infected partner but not using condoms with new partners of unknown HIV serostatus. This potential shift in risk to having outside partners of unknown HIV serostatus with whom condom use may be lower is part of the rationale for biomedical prevention strategies, such as antiretroviral pre-exposure prophylaxis (PrEP) for HIV-uninfected partners in HIV serodiscordant couples. As HIV prevention efforts increasingly target HIV testing in couples and identify HIV serodiscordant couples, risk reduction messages will need to focus on both the infectiousness of the HIV infected partner as well as the potential susceptibility of the HIV uninfected partner from outside sexual partnerships.

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REFERENCES

- Dunkle KL, Stephenson R, Karita E, et al. New heterosexually transmitted HIV infections in married or cohabitating couples in urban Zambia and Rwanda: an analysis of survey and clinical data. Lancet. 2008; 371:2183–2191. [PubMed: 18586173]
- Eyawo O, de Walque D, Ford N, Gakii G, Lester RT, Mills EJ. HIV status in discordant couples in sub-Saharan Africa: a systematic review and meta-analysis. Lancet Infect Dis. 2010; 10:770–777. [PubMed: 20926347]
- Guthrie BL, de Bruyn G, Farquhar C. HIV-1-discordant couples in sub-Saharan Africa: explanations and implications for high rates of discordancy. Curr HIV Res. 2007; 5:416–429. [PubMed: 17627505]
- Lingappa JR, Lambdin B, Bukusi EA, et al. Regional differences in prevalence of HIV-1 discordance in Africa and enrollment of HIV-1 discordant couples into an HIV-1 prevention trial. PLoS ONE. 2008; 3:e1411. [PubMed: 18183292]
- Gray RH, Wawer MJ, Brookmeyer R, et al. Probability of HIV-1 transmission per coital act in monogamous, heterosexual, HIV-1-discordant couples in Rakai, Uganda. Lancet. 2001; 357:1149– 1153. [PubMed: 11323041]
- Carpenter LM, Kamali A, Ruberantwari A, Malamba SS, Whitworth JA. Rates of HIV-1 transmission within marriage in rural Uganda in relation to the HIV sero-status of the partners. AIDS. 1999; 13:1083–1089. [PubMed: 10397539]
- Robinson NJ, Mulder D, Auvert B, Whitworth J, Hayes R. Type of partnership and heterosexual spread of HIV infection in rural Uganda: results from simulation modelling. Int J STD AIDS. 1999; 10:718–725. [PubMed: 10563557]
- Tumwesigye E, Wana G, Kasasa S, Muganzi E, Nuwaha F. High uptake of home-based, districtwide, HIV counseling and testing in Uganda. AIDS Patient Care ST. 2010; 24:735–741.
- Were WA, Mermin JH, Wamai N, et al. Undiagnosed HIV infection and couple HIV discordance among household members of HIV-infected people receiving antiretroviral therapy in Uganda. JAIDS. 2006; 43:91–95. [PubMed: 16885775]
- Lugada E, Levin J, Abang B, et al. Comparison of home and clinic-based HIV testing among household members of persons taking antiretroviral therapy in Uganda: results from a randomized trial. JAIDS. 2010; 55:245–252. [PubMed: 20714273]

- Hugonnet S, Mosha F, Todd J, et al. Incidence of HIV infection in stable sexual partnerships: a retrospective cohort study of 1802 couples in Mwanza region, Tanzania. JAIDS. 2002; 30:73–80. [PubMed: 12048366]
- Bunnell RE, Nassozi J, Marum E, et al. Living with discordance: knowledge, challenges, and prevention strategies of HIV-discordant couples in Uganda. AIDS Care. 2005; 17:999–1012. [PubMed: 16176896]
- 13. Celum C, Wald A, Lingappa JR, et al. Acyclovir and transmission of HIV-1 from persons infected with HIV-1 and HSV-2. N Engl J Med. 2010; 362:427–439. [PubMed: 20089951]
- Lingappa JR, Kahle E, Mugo Ne, et al. Characteristics of HIV-1 discordant couples enrolled in a trial of HSV-2 suppression to reduce HIV-1 transmission: the Partners Study. PLoS ONE. 2009; 4:e5272. [PubMed: 19404392]
- Campbell MS, Mullins JI, Hughes JP, et al. Viral linkage in HIV-1 seroconverters and their partners in an HIV-1 prevention clinical trial. PLoS ONE. 2011; 6:e16986. [PubMed: 21399681]
- Eaton A, van Der Straten A. Concurrent sexual partnerships among individuals in HIV serodiscordant heterosexual couples. Int J STD AIDS. 2009; 20:679–682. [PubMed: 19815911]
- Anand A, Shiraishi RW, Bunnell RE, et al. Knowledge of HIV status, sexual risk behaviors and contraceptive need among people living with HIV in Kenya and Malawi. AIDS. 2009; 23:1565– 1573. [PubMed: 19542867]
- Cohen MS, Chen YQ, McCauley M, et al. Prevention of HIV-1 infection with early antiretroviral therapy. N Engl J Med. 2011; 365:493–505. [PubMed: 21767103]

Table 1

Characteristics at enrollment of 3381 HIV uninfected members of African HIV serodiscordant partnerships*

	Median (IQ	R) or n (%)
	Men (N=2284)	Women (N=1097)
Demographic characteristics		
Age, years	35 (29–42)	30 (25–37)
Education, years	9 (7–12)	8 (6–10)
Any monthly income	1367 (59.9%)	285 (26.0%)
Multiple spouses (men only)	114 (5.0%)	
Couple characteristics		
East Africa (vs. southern Africa)	1476 (64.6%)	754 (68.7%)
Married	1677 (73.4%)	883 (80.5%)
Living together	2035 (89.1%)	1021 (93.1%)
Duration of partnership, years	4.9 (2.1–9.4)	6.7 (2.9–13.8)
Number of children together	2 (1-4)	2 (1-4)
Number of sex acts, prior month	4 (2–8)	4 (2–8)
Any unprotected sex acts, prior month	699 (30.6%)	293 (26.7%)
CD4 count of their HIV infected partner, cells/mm ³	483 (355–664)	424 (334–571)

* Self-reported variables (i.e., other than region and CD4 count) were as reported by the HIV uninfected partner.

Table 2

Proportion of HIV uninfected partners reporting a sexual partnership outside of their known HIV serodiscordant partnership, during 24 months of follow-up

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Months since enrollment	N N N	Reporting outside partner n (%)	WOMEN N	Reporting outside partner n (%)	MEN N	Reporting outside partner n (%)
0 (enrollment)	3380	104 (3.1%)	1097	5 (0.5%)	2283	99 (4.3%)
3	3230	164 (5.1%)	1061	9 (0.9%)	2169	155 (7.2%)
6	3121	207 (6.6%)	1029	18 (1.8%)	2092	189 (9.0%)
6	3022	254 (8.4%)	1006	27 (2.7%)	2016	227 (11.3%)
12	2835	272 (9.6%)	950	31 (3.3%)	1885	241 (12.8%)
15	2417	280 (11.6%)	809	30 (3.7%)	1608	250 (15.6%)
18	2092	260 (12.4%)	704	30 (4.3%)	1388	230 (16.6%)
21	1607	212 (13.2%)	532	18 (3.4%)	1075	194 (18.1%)
24	1250	174 (13.9%)	427	17 (4.0%)	823	157 (19.1%)

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	6518 v	WOMEN 6518 visits among 1097 women	nen	13057	MEN 13057 visits among 2248 men	u
	visits at which outside partners reported	multivariate odds ratio (95% confidence interval)	*d	visits at which outside partners reported	multivariate odds ratio (95% confidence interval)	*a
Region**						
Eastern	124 (2.6)	0.7 (0.4–1.5)	0.4	1266 (13.8)	$1.4 \left(1.1 - 1.9\right)^{***}$	0.01
Southern	56 (3.2)	1.0		377 (9.7)	1.0	
Age at enrollment						
18–24 years	57 (4.0)	1.0		136 (17.7)	1.0	
25–34 years	74 (2.6)	0.7 (0.3–1.6)		361 (14.5)	0.8 (0.5–1.1)	
35-44 years	39 (2.3)	1.1 (0.4–2.6)	0.8	370 (12.5)	0.5(0.4-0.8)	0.01
≥45 years	10 (1.8)	0.7 (0.4–2.6)		256 (9.9)	$0.6\ (0.4{-}1.0)$	
Education						
> 8 years	67 (2.8)	0.7 (0.3–1.5)	0.3	852 (12.4)	1.0 (0.8–1.3)	0.9
≤ 8 years	113 (2.8)	1.0		790 (12.8)	1.0	
Earns income						
Yes	61 (3.6)	1.8 (0.9–3.5)	0.1	954 (12.0)	1.0 (0.8–1.2)	0.7
No	119 (2.5)	1.0		689 (13.5)	1.0	
Children with HIV+ partner						
0	88 (5.7)	1.0		747 (17.6)	1.0	
I	53 (3.6)	0.3 (0.1–0.7)	0.01	433 (12.3)	0.7 (0.5–1.0)	FU U
≥2	39 (1.1)	1.3 (0.6–2.7)	10.0	463 (8.8)	1.1 (0.8–1.4)	+0.0
Lives with HIV+ partner						
Yes	154 (2.5)	0.9 (0.4–2.3)	6.0	1408 (12.0)	0.6(0.4-0.9)	0.02
No	26 (6.9)	1.0		235 (18.3)	1.0	
Duration of partnership with HIV+ partner						
Less than 2 years	33 (6.8)	1.0		271 (18.1)	1.0	

	6518 v	WOMEN 6518 visits among 1097 women	nen	13057	MEN 13057 visits among 2248 men	F
	visits at which outside partners reported	multivariate odds ratio (95% confidence interval)	*a	visits at which outside partners reported	multivariate odds ratio (95% confidence interval)	** *
2–6 years	83 (4.1)	$0.8\ (0.4{-}1.8)$		722 (14.9)	1.0 (0.7–1.3)	r 0
More than 6 years	61 (1.5)	0.6 (0.2–1.4)	4.0	641 (9.8)	0.9 (0.6–1.3)	1.0
Multiple spouses						
Yes	0 (0)	;	:	342 (48.2)	10.5 (6.9–15.9)	<0.001
No	180 (2.8)			1301 (10.5)	1.0	
Sex with HIV+ partner in past month***						
Yes	37 (0.7)	0.1 (0.0–0.1)	<0.001	779 (7.4)	0.2 (0.1–0.2)	<0.001
No	141 (12.1)	1.0		861 (33.8)	1.0	
If yes: Unprotected sex with HIV+ partner in past month***						
At least once	4 (0.8)	0.8 (0.3–2.5)	0.7	109 (8.0)	1.1 (0.8–1.5)	0.5
100% condom use	33 (0.7)	1.0		670 (7.3)	1.0	
HIV+ partner CD4 count***						
≥500 cells/μL	53 (2.5)	1.0		628 (12.0)	1.0	
350-499 cells/µL	45 (2.3)	1.3 (0.7–2.3)		396 (11.1)	1.0 (0.8–1.3)	
250–349 cells/μL	29 (1.9)	1.4 (0.7–2.3)	0.8	263 (10.8)	1.1 (0.8–1.4)	0.8
<250 cells/µL	24 (3.4)	1.1 (0.6–2.3)		151 (13.4)	1.1 (0.8–1.6)	
HIV+ partner on ART ^{***}						
Yes	7 (1.9)	0.9 (0.4–2.1)	0.7	103 (18.4)	1.0	0.2
No	136 (2.4)	1.0		1289 (11.2)	1.3 (0.9–2.0)	

* P-values determined by type 3 score test from generalized estimating equations (GEE) with logistic link.

other factors had similar odds ratios as above. A multivariate model among women substituting country for region was unstable, due to the lower occurrence of reporting of outside partners, and results are (multivariate OR 0.5, 95% CI 0.3–0.9), Rwanda (multivariate OR 0.1, 95% CI 0.0–0.5), and Zambia (multivariate OR 0.2, 95% CI 0.1–0.3) and were reported at a similar proportion of visits for men from Kenya (multivariate OR 0.8, 95% CI 0.6-1.2), Tanzania (multivariate OR 1.2, 95% CI 0.8-2.0), and Uganda (multivariate OR 1.5, 95% CI 0.9-2.3). P-value for country <0.001. In that multivariate model, ** In a multivariate analysis among men substituting country instead of region, and with South Africa as the comparison country, outside partners were less commonly reported for men from Botswana not reported.

*** Time-varying covariate.

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Table 4

Sexual behavior of HIV uninfected partners in HIV serodiscordant partnerships over time, with both primary HIV infected partners and outside partners*

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WOMEN 0 7.9 3 10.9 6 13.4 9 13.8	N MEN					outside partner (concurrent partnerships)	urtner rent hips)
		WOMEN	MEN	WOMEN	MEN	MOMEN	MEN
	5.6	91.6	90.1	0.0	0.3	0.5	4.1
	7.8	88.2	85.0	0.2	1.7	0.7	5.5
	10.7	84.8	80.1	1.0	3.8	8.0	5.2
	13.2	83.5	75.6	2.0	5.7	0.7	5.6
12 15.0	14.6	81.9	72.6	2.7	9.9	0.4	6.2
15 16.2	15.3	80.1	69.2	3.5	0.6	0.3	6.5
18 19.7	14.4	76.2	69.1	3.6	10.3	9.0	6.3
21 23.1	17.5	73.5	64.6	2.8	11.0	9.0	6.9
24 22.5	14.7	73.5	66.3	3.5	12.3	5.0	6.7

 $\overset{*}{}_{\rm self-reported sexual behavior during the 1 month prior to each quarterly follow-up visit$

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Table 5

HIV incidence, and source of HIV infection, among HIV uninfected partners in HIV serodiscordant relationships

Sexual behavior with outside partners, cumulative		All HIV infections	ctions		HIV infe HIV sero by	HIV infections linked within the HIV serodiscordant partnership by viral sequencing	HIV in outside partners	HIV infections acquired from outside the HIV serodiscordant partnership by viral sequencing
	#	Incidence per 100 person-years	HR (95% CI)	d	#	Incidence per 100 person-years	#	Incidence per 100 person-years
All subjects								
Any outside partner sex	21	2.87 (1.87–4.41)	1.1 (0.7–1.8)	0.7	ю	0.41 (0.13–1.27)	18	2.46 (1.55–3.91)
No outside partner sex	130	3.02 (2.55–3.59)			105	2.44 (2.02–2.96)	25	0.58(0.39 - 0.86)
Women								
Any outside partner sex	4	4.61 (1.73–12.29)	1.5 (0.5–4.2) 0.4	0.4	1	1.15 (0.16–8.18)	3	3.46 (1.12–10.75)
No outside partner sex	57	3.62 (2.79–4.69)			49	3.11 (2.35–4.11)	8	0.51 (0.25–1.02)
Men								
Any outside partner sex	17	2.64 (2.13–3.37)	1.2 (0.7–2.0) 0.6	0.6	2	0.31 (0.08–1.24)	15	2.33 (1.40–3.86)
No outside partner sex	73	2.28 (1.64-4.24)			56	2.06 (1.58–2.67	17	0.62 (0.39–1.00)