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Sexual behaviors over a 3-year period among individuals with advanced HIV/AIDS receiving antiretroviral therapy in an urban HIV clinic in Kampala, Uganda

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Abstract

Background—Few studies have prospectively examined sexual behaviors of HIV-infected person on antiretroviral therapy (ART) in Sub-Saharan Africa.

Methods—From 2004 to 2005, 559 HIV-infected, ART-naïve individuals initiating ART at an HIV clinic in Kampala, Uganda were enrolled into a prospective study and followed to 2008. Clinical and sexual behavior information was assessed at enrollment and semi-annually for three years after ART initiation. Using log-binomial regression models, we estimated prevalence ratios (PRs) to determine factors associated with being sexually active and having unprotected sex over three-years after initiating ART.

Results—559 adults contributed 2,594 person-visits of follow-up. At the time of ART initiation, 323 (57.9%) were sexually active of which 176 (54.5%) had unprotected sex at last sexual intercourse. Majority (63.4%) of married individuals were unaware of their partner's HIV status. Female gender (PR=2.97; 95% CI: 1.85, 4.79), being married (PR=1.48; 95% CI: 1.06, 2.06), and reporting unprotected sex prior to ART (PR=1.68; 95% CI: 1.16, 2.42) were among factors independently associated with unprotected sex while on ART. Overall, 7.3% of visit intervals of unprotected sex, 1.0% of intervals of sexual activity, occurred when plasma viral load >1,500 copies/ml, representing periods of greater HIV transmission risk.

Conclusions—Although unprotected sex reduced over time, women reported unprotected sex more often than men. Disclosure of HIV status was low. Integration of comprehensive prevention programs into HIV care is needed, particularly ones specific for women.

Keywords

HIV/AIDS; antiretroviral therapy; sexual behavior; unprotected sex; condom use; positive prevention; Uganda

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INTRODUCTION

In both resourced and resource-limited settings, effective antiretroviral therapy (ART) for HIV infection leads to increased survival, decreased morbidity and improved quality of life in treated individuals[1–4,5–7]. ART is associated with return of sexual desire and sexual activity[8,9]. Furthermore, lowered perceived infectiousness in persons with undetectable plasma viral load may lead to increased high risk sexual behaviors such us unprotected sexual intercourse and having multiple sexual partners[10,11].

Studies of sexual behaviors while on ART are mainly from the developed countries, consisting mainly men who have sex with men and other populations whose sexual culture and practices are different from those in Sub-Saharan Africa[12,13]. Relatively fewer studies are published from Sub-Saharan Africa where HIV transmission is mainly due to heterosexual sex, women are disproportionately affected, and ART is often initiated at advanced stage of HIV disease when plasma HIV RNA concentration and, thus, infectiousness is high[14]. Therefore, we examined the prevalence of and factors associated with sexual activity, unprotected sex, and having multiple sexual partners among HIV-infected adults prior to and up to three years after initiating ART in an urban HIV clinic in Kampala, Uganda that had free condoms available.

METHODS

Study Setting and Population

As described previously, between April 2004 and April 2005, HIV-infected, ART-naïve adults aged at least 18 years were enrolled in a prospective study at the Adult Infectious Diseases Clinic in Kampala, Uganda to describe responses to ART[15]. ART was initiated based on the Uganda Ministry of Health guidelines which were adapted from the World Health Organization (WHO) guidelines for resource-limited settings[16]. In addition to co-trimoxazole prophylaxis, subjects received either a nevirapine- or efavirenz-containing regimen with a backbone of lamivudine with either stavudine or zidovudine. Counseling on nutrition, ART adherence, safer reproductive health and contraception including provision of male condoms were also provided. Clients were informed that if they were to have sex, regardless of their partners' HIV status, they needed to use a condom to prevent transmission of HIV and other sexually-transmitted infections.

Study assessments and follow-up

Study visits were conducted at enrolment and every three months for clinical evaluations. For every six months up until 3 years of ART (April 2008), laboratory evaluation, socio-demographics, sexual behaviours during the previous six months, knowledge/beliefs about ART and HIV transmission by a trained nurse-counselor, through a structured interviewer administered questionnaire in either English or Luganda (a local vocabulary). Participants were classified as being currently married if they reported being married or cohabiting and as unmarried if they were single, widowed or divorced. Participants were considered sexually active if they had had sex in the previous six months, to have engaged in unprotected sex if they did not use a condom the last time they had had sex, and to have multiple partners if they had engaged in sexual activity with two or more people in the previous twelve months.

Clinical status was recorded using WHO clinical stage and Karnofsky performance score. $CD4^+$ T cell count was enumerated by FACS Count (Becton Dickinson, San Jose, CA, USA) for the first year and later by FACS Calibur (Becton Dickinson, San Jose, CA, USA). Plasma HIV RNA concentration was determined by the Amplicor HIV-1 Monitor PCR Test version 1.5 (Roche Diagnostics, Indianapolis, IN, USA) with a lower limit of detection of

400 copies/ml. CD4 and viral load were made available to providers to monitor response to ART and manage HIV care according to WHO guidelines at the time. The study was approved by the Institutional Review Board of Makerere University and the Uganda National Council of Science and Technology.

Statistical Methods

The proportions of subjects reporting sexual activity, unprotected sex, and having multiple partners at the time of ART initiation, the baseline visit, were estimated. Pearson's chi-square and Wilcoxon ranksum tests were used to examine categorical and non-normally distributed continuous factors associated with these sexual behaviors, respectively. Trends in high-risk sexual behavior over time were examined using Pearson's chi-square test.

Factors associated with being sexually active and the occurrence of unprotected sex among sexually active adults over three-years after ART initiation were modeled using log-binomial models with a robust variance estimator using a modified Poisson approach[17]. Log-binomial regression yields the prevalence ratio (PR) and chosen over standard logistic regression since the PR is a better estimator of the relative risk than is the odds ratio when outcomes of interest are not rare. Given that the data represented a period cross-section with multiple observations per individual, we used marginal generalized estimating equations with a log link function, an unstructured correlation structure, and robust variance estimation. Factors whose association with the dependent variable were statistically suggestive ($p<0.2$) in univariable analysis or were conceptually important were entered into a multivariable model. Variables retained in the final models were age and those that were independently associated with unprotected sex.

To highlight the potential for further sexual transmission of HIV and possible drug-resistant virus, we examined the prevalence of unprotected sex among participants with at least two consecutive visits with plasma HIV RNA concentration above 1,500 copies/ml after ART initiation. We used a cut off of 1,500 copies/ml due to the very low transmission risk below this level[18]. Statistical analyses were conducted using SAS v.9.2 (SAS Institute Inc. Cary, NC, USA).

RESULTS

Study population

A total of 559 ART-naïve, HIV-infected individuals were enrolled at the time of initiation of first line ART. The majority, 494/559 (88.4%) had advanced HIV/AIDS with WHO clinical stage III or IV disease (Table 1). The median (interquartile range; IQR) age, $CD4^+$ T cell count and $\log_{10}$ plasma HIV RNA were 38 (33–44) years, 98 (21–166) cells/mm^3 and 5.4 (5.1–5.8), respectively. Three hundred eight-five (68.9%) were women and 261 (46.7%) were married or cohabiting. Among married/cohabitating persons, one-third (n=78) had a confirmed HIV-infected partner while 16 (6.1%) had an HIV-uninfected partner. The majority, 163 (63.4%) were unaware of their partner's HIV status.

Pre-ART sexual behaviors

A total of 323 (57.8%) individuals reported sexual intercourse within the 6 months preceding ART initiation (Table 1). Among those who were sexually active, 54.5% (176/323) reported unprotected sex at their last sexual encounter. Overall, 70 (12.6%) reported having more than two sexual partners in the previous twelve months. Ninety-two (28.5%) reported that their last sexual encounter was with a non-regular partner.

Being sexually active and having more than two sexual partners in the previous year were reported by higher proportions of men, the employed, and those with greater monthly household income. Among sexually-active adults, unprotected sex was reported more often by women, unmarried individuals, and those with lower income although the latter was the only one that achieved statistical significance. Although clinical factors (WHO HIV clinical stage, baseline $CD4^+$ T cell count, Karnofsky score, and duration of HIV positivity) were not associated with being sexual active, unprotected sex among sexually active adults was more often reported by those with advanced HIV disease and lower Karnofsky performance score.

Follow-up experience

Of the 559 subjects enrolled, 472 (84.4%) returned for at least one follow-up visit contributing 2,594 person-visits. A total of 399 (71.4%) returned for all the 6 follow up visits (Figure 1). Of the 160 subjects followed for less than three years, 99 (62%) had died with 78/99 (78.8%) deaths due to AIDS-associated opportunistic infections mainly with in the first 3 months of ART [19]. Thirty-three (5.9%) individuals were lost to follow up, while 26 withdrew from the study because they transferred their HIV care to outside the clinic catchment area[19]. There were no statistically significant differences in losses to follow-up by age, gender, marital status, baseline plasma HIV RNA concentration, and baseline sexual behavior condom use.

Sexual behaviors after ART initiation

Sexual behavior data were available for 92.4% of person-visits (2,327/2,594). Sexual intercourse was reported at 1,189 (51.1%) person-visits and unprotected sex at the last intercourse was reported at 14.6% (174/1,189) of person-visits. The proportion of subjects reporting sexual intercourse decreased in the first six months after ART initiation from 58% to 50% but remained steady over the subsequent two years at an average of 51% (p=0.911; Figure 1). Among sexually-active subjects, unprotected sex decreased over the first 12 months on ART from 53% to 15% and stabilized thereafter around 11.5% over the next two years of the study (p=0.348). The proportion of subjects reporting two or more sexual partners declined from baseline level of 18.3% to an average of 9.2% at the first follow-up visit and remained constant at an average proportion of 9.0% over the next 2.5 years (p=0.829). Thirty-eight (9.8%) women became pregnant during the study period.

In multivariable analysis, factors independently associated with being sexually active while on ART were being married and reporting sexual activity at the time of ART initiation (Table 2). Female gender, lower household income, and believing that HIV-infected persons should abstain from sexual intercourse were independently associated with not being sexually active while on ART.

Being a woman, being unmarried, having lower household income, reporting unprotected sex at the time of ART initiation, having no children, and believing that ART reduced the risk of HIV transmission were independently associated with higher prevalence of unprotected sex in the adjusted analysis. Although women receiving ART were less sexually active than men, those who engaged in sexual intercourse were three times more likely than men to report unprotected sex in multivariable analysis. There was a statistically significant interaction between gender and time on ART. As compared to sexually active men, the relative proportion of women reporting unprotected sex increased over time: PR=1.72, 2.14, 5.12, 7.09, and 6.20 for 0.5, 1.0, 1.5, 2.0, and 3.0 years on ART, respectively. At study visit 5 (2.5 years after ART), none of the men interviewed reported unprotected sex. The interaction term was not retained in the final multivariable model since it did not confound other variables.

Unprotected sex and detectable plasma HIV RNA concentration

Plasma HIV RNA concentration was recorded at 96.8% (2,512/2,594) of visit pairs after ART initiation and sexual behavior data during the interval enclosed by these visit pairs were available at 89.8% (2,257/2512) of visit pairs. Sexual activity was reported during 1,152 (51.0%) of these intervals and unprotected sex occurred during 14.2% (164/1,152) of these intervals of sexual activity. Overall, 7.3% (12/164) of intervals of unprotected sex, 1.0% (12/1,152) of intervals of sexual activity occurred during a period when plasma viral load was greater than 1,500 copies/ml, representing periods of higher risk for HIV transmission; most (10/12; 83.3%) of these occurred within the first year after ART initiation.

The median (IQR) viral load at the visit preceding the unprotected sexual event was 5.19 (4.69, 5.43) $\log_{10}$ copies/ml while that recorded at the evaluation visit was 5.21 (4.46, 5.34) $\log_{10}$ copies/ml. Sexually-active individuals with a plasma viral load >1,500 copies/ml despite being on ART for at least 6 months (i.e., evidence of possibly failing treatment) were not more likely to have reported high-risk sex (unprotected sex or having multiple sex partners; PR=1.12; 95% CI: 0.66, 1.91).

DISCUSSION

Despite the advanced HIV disease and very low baseline $CD4^+$ T cell counts, 58% of subjects were sexually active, over half of whom had unprotected sex, at ART initiation. Over three years of ART, we observed no increase in sexual activity and a significant decrease in reported unprotected sex and multiple sex partners.

Our study conducted in a clinic in Kampala, Uganda are similar to those from North America and Western Europe, which also demonstrated that receiving ART is not associated with increased sexual risk behaviors[12]. Similarly, a study of HIV-infected injection drug users in Vancouver, Canada did not find an increase in sexual risk behaviors following initiation of treatment[20]. An earlier paper from Uganda showed that the population had misconceptions that wider ART access could result in increased risky sexual behaviors hence further HIV transmission[21]. However, in four studies, one from Cote-d'Ivoire and three from Uganda, receiving ART was neither associated with increased sexual activity nor unprotected sex [22–24], even among HIV-uninfected household members of subjects receiving ART [25]. However, these studies were cross-sectional in design or had short follow-up. A strength of this study is the long follow-up period, which allowed us to ascertain whether sexual behaviors adopted soon after initiating ART were maintained or whether patients experienced a "prevention fatigue"[10,26]. A similar study from South Africa encompassing rural and urban clinics demonstrated that sexual risk behavior significantly decreased following ART initiation among HIV-infected South African men and women in primary care program.[27].

The low levels of awareness of partner HIV status among married individuals are a cause for concern, but not an unusual finding in East Africa. Sarna and colleagues also reported that more than 40% of HIV-infected individuals in Mombasa, Kenya were unaware of the HIV status of their regular partner[32]. Fear of partner's reaction and poor communication skills between partners have been cited as some of the reasons for low disclosure rates[33,34]. Counselors need the means to assist patients to increase their self-efficacy to disclose and highlight positive outcomes HIV status disclosure[35]. However, the encouragement of patients to share their HIV status with their partners has to be balanced with the risk of violence following disclosure, particularly among women.

Although detectable plasma HIV RNA concentration in the context of ART is associated with the presence of genotypic resistance mutations[15,31], hence, a risk of transmission of drug-resistant HIV, we observed few visits where undetectable plasma viral load was associated with unprotected sex. We attribute this to pre- and post-ART adherence counseling provided at the clinic and the continuous availability of free condoms. Nevertheless, we did find that sexual behaviors prior to ART initiation were strongly associated with sexual behaviors after ART initiation.

This study has several limitations. First, sexual behaviors were based on self-report and clinic counselors also served as data collectors, which may have resulted in biased responses due to social desirability[36]. In our study, women reported having unprotected sex more often than did men with the relative reporting of his high-risk behavior increasing over the three years after ART initiation. This could have been due to a social desirability bias that increased over time in men as a reaction to an accumulation of risk-reduction messages received through ongoing counseling at the clinic. Some of the difference in reporting may also be due to the fact that men and women served by the HIV clinic represents heterogeneous populations with inherently different propensity to use protection during sexual intercourse. Also, only male condoms were made available at the clinic; thus, male partner consent and effective negotiation skills among women would be needed if they were to be used properly[28,29,30].

A second limitation is that the non-probability sampling of study enrollees may reduce the generalizability of our findings; however, this is unlikely because subjects were enrolled at all clinic times over a 14-month period. Moreover, socio-demographic characteristics of participants were comparable to those of larger clinic population and generally reflected individuals accessing ART in Uganda[15]. Third, condom use at last (most recent) sexual intercourse may not represent one's sexual behavior over the 6 months period and provides no information on persistent risk sexual behavior, but is less prone to recall bias thence increase the internal validity of our results[37]. Finally, a significant proportion of individuals did not return for any follow-up due to mortality due to AIDS. This does not necessarily invalidate our analysis of high-risk sexual behavior since those who died may not have been sexually active. There was no evidence of differential loss to follow-up or non-randomness in missing data. We obtained comparable results in analyses of individuals who completed all six visits and in those who completed fewer visits.

We attribute reductions in unprotected sex and multiple sexual partners to interventional effects of HIV care with ongoing counseling throughout the follow up period[38]. Findings from this study may be used as a resource in designing effective "prevention for positives" programs, maintenance of safer sexual behavior[39] and informing estimation of trends in the HIV incidence and potential spread of drug-resistant HIV[40,41]. Integration of comprehensive prevention programs into HIV care is needed, particularly ones specific for women. They should include counseling clients and effective skills building to safely disclose HIV status to spouses and sexual partners and making available male and female condoms and teaching women skills in negotiating safer sex[42,43–47]. These interventions need not to wait until ART is initiated and would be most effective in the prevention of ongoing HIV transmission if introduced at the time of HIV diagnosis or even HIV testing.

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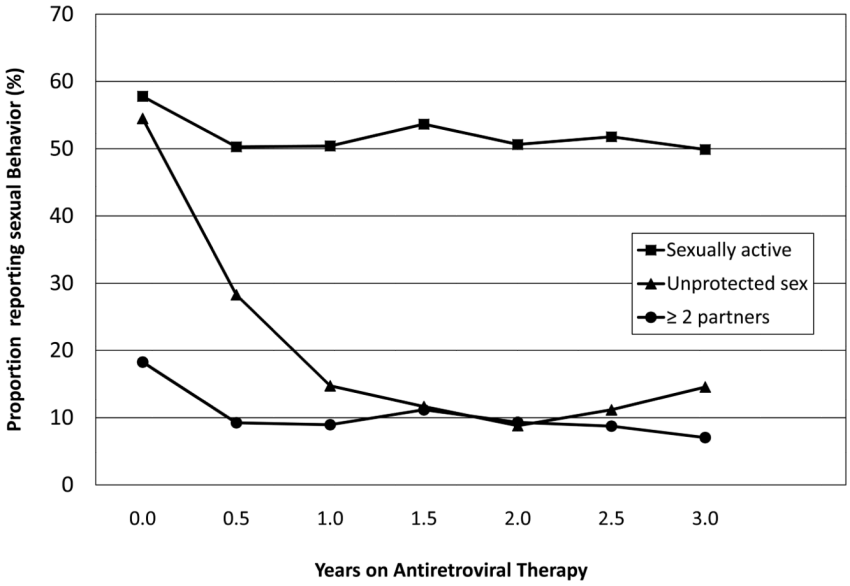

FIGURE 1.

Proportion of individuals reporting sexual activity, unprotected sex, and multiple sex partners at the time of and over three years after initiation of ART at the Infectious Disease Institute, Kampala Uganda, 2004–2008.

Table 1

Factors associated with sexual activity, unprotected sex, and multiple sex partners among 559 adults prior to initiation of antiretroviral therapy at Infectious Disease Institute, Kampala, Uganda, 2004–2005

	All subjects	Had sex in the last six months	Last sex was unprotected (within last six months)[1]	>2 sexual partners in the past 12 months[2]
Characteristic	**N**	**N (%)**	**N (%)**	**N (%)**
All subjects	559	323 (57.8)	176 (54.5)	70 (12.6)
Age (years)				
22–29	52	29 (55.8)***	20 (69.0)	7 (13.5)
30–34	142	90 (63.4)	49 (54.4)	19 (3.4)
35–39	135	99 (73.3)	50 (50.5)	17 (12.6)
40–44	103	58 (56.3)	34 (58.6)	16 (15.5)
≥45	127	47 (37.0)	23 (48.9)	11 (8.7)
Sex				
Female	386	203 (52.6)***	118 (58.1)**	30 (7.8)***
Male	173	120 (69.4)	58 (48.3)	40 (23.1)
Employed				
Yes	287	183 (63.8)**	100 (54.6)	45 (15.7)*
No	272	140 (51.5)	76 (54.3)	25 (9.2)
Highest level of education level				
No formal education	77	37 (48.1)	21 (56.8)	11 (14.3)
Primary education	180	184 (60.9)	98 (53.3)	22 (12.2)
Secondary level or higher	302	102 (56.7)	57 (55.9)	37 (12.3)
Monthly household income				
>25 USD	181	126 (69.6)***	61 (48.4)*	34 (18.8)**
Declined to answer	184	100 (54.4)	52 (52.0)	17 (9.2)
< 25USD	194	97 (50.0)	63 (65.0)	19 (9.8)
Married/cohabitating				
Yes	259	221 (85.3)***	63 (61.8)	33 (12.7)
No	300	102 (34.0)	113 (51.1)	37 (12.3)
HIV status of marital partner				
HIV negative or unknown	179	153 (85.5)	85 (55.6)	24 (13.4)
HIV positive	78	66 (84.6)	27 (40.9)	9 (11.5)
Has one or more child				
Yes	485	289 (59.6)*	153 (52.9)	63 (13.0)
No	74	34 (46.0)	23 (67.8)	7 (9.5)
Duration since known HIV positive				
<1 year	327	193 (59.0)	100 (51.8)	46 (14.1)*
1–5 years	144	78 (54.2)	42 (53.9)	12 (8.3)
>5 years	26	13 (50.0)	6 (46.2)	0 (0.0)
WHO HIV clinical stage				

Characteristic	All subjects N	Had sex in the last six months N (%)	Last sex was unprotected (within last six months)[1] N (%)	>2 sexual partners in the past 12 months[2] N (%)
I or II	65	39 (60.0)	17 (43.6)*	6 (9.2)
III	301	175 (58.1)	89 (50.9)	35 (11.6)
IV	193	109 (56.5)	70 (64.2)	29 (15.0)
CD4+ T-cell count (cells/mm^3)				
≥200	78	44 (56.4)	24 (54.6)	12 (15.4)
150–199	91	44 (48.4)	23 (52.3)	13 (14.3)
100–149	105	60 (57.1)	27 (45.0)	15 (14.3)
50–99	85	52 (61.2)	26 (50.0)	10 (11.8)
<50	198	123 (62.1)	76 (61.8)	20 (10.1)
Karnofsky performance score				
90–100	175	109 (62.3)	47 (43.1)**	26 (14.9)
70–80	311	174 (56.0)	99 (56.9)	37 (11.9)
≤60	73	40 (54.8)	30 (75.0)	7 (9.6)

[1] Percentages are calculated as a proportion among those sexually active

[2] Percentages are calculated as a proportion of all adults

*** <0.001,

** <0.01,

* <0.05

Table 2

Log-binomial regression of factors associated with occurrence of unprotected sex among adults over three years after initiation of antiretroviral therapy at Infectious Disease Institute, Kampala, Uganda, 2004–2008.

	Sexually active in the previous 6 months				Last sex was unprotected among sexually active adults			
	Unadjusted		Multivariable adjusted		Unadjusted		Multivariable adjusted	
Characteristic	**PR**	**(95% CI)**	**PR**	**(95% CI)**	**PR**	**(95% CI)**	**PR**	**(95% CI)**
Age (per 10 years)	0.78	(0.71, 0.86)	0.78	(0.72, 0.86)	0.85	(0.63, 1.14)	1.17	(0.92, 1.48)
Time on ART (per 6 months)	1.00	(0.98, 1.02)			0.87	(0.80, 0.95)	0.84	(0.77, 0.92)
Female gender (vs. male)	0.67	(0.59, 0.78)	0.79	(0.70, 0.89)	3.53	(2.19, 5.69)	2.97	(1.84, 4.79)
Married/cohabitating (vs. not)	2.45	(2.08, 2.89)	1.55	(1.33, 1.81)	0.57	(0.41, 0.80)	0.68	(0.49, 0.94)
Has one or more child (vs. has none)	1.38	(1.05, 1.81)			0.43	(0.30, 0.63)	0.50	(0.36, 0.70)
Monthly household income								
>25 USD	1.0		1.0		1.0		1.0	
Declined to answer	0.82	(0.70, 0.97)	0.96	(0.85, 1.09)	1.38	(0.89, 2.15)	1.13	(0.76, 1.69)
< 25USD	0.60	(0.50, 0.73)	0.79	(0.68, 0.91)	2.15	(1.42, 3.25)	1.56	(1.03, 2.36)
Reported sexual activity at enrollment (vs. did not)	3.45	(2.78, 4.28)	2.22	(1.77, 2.78)	--			
Reported unprotected sex at enrollment (vs. did not)	--				2.19	(1.51, 3.20)	1.68	(1.16, 2.42)
Believes ART reduces transmission of HIV	0.99	(0.91, 1.08)			1.34	(1.04, 1.74)	1.53	(1.12, 2.09)
Believes HIV-infected people should abstain from having sex	0.75	(0.68, 0.83)	0.77	(0.70ary, 0.83)	1.78	(1.36, 2.33)		
Last sexual partner was a casual partner (vs. spouse)	n/a				0.48	(0.26, 0.89)		
Last sexual partner was a boyfriend/girlfriend (vs. spouse)	n/a				0.91	(0.63, 1.32)		
Had ≥2 sexual partners in the past year (vs. ≤1 partners)	n/a				0.54	(0.31, 0.95)		
CD4+ cell count (per 100 cells/mm3)[1]	1.01	(0.99, 1.03)			0.89	(0.80, 0.99)		

[1] lagged one visit