Sexual behavior of HIV discordant couples after HIV counseling and testing

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Background and objectives: Sexual behavior following voluntary HIV counseling and testing (VCT) is described in 963 cohabiting heterosexual couples with one HIV positive and one HIV negative partner ('discordant couples'). Biological markers were used to assess the validity of self-report.

Methods: Couples were recruited from a same-day VCT center in Lusaka, Zambia. Sexual exposures with and without condoms were recorded at 3-monthly intervals. Sperm detected on vaginal smears, pregnancy, and sexually transmitted diseases (STD) including HIV, gonorrhea, syphilis, and *Trichomonas vaginalis* were assessed.

Results: Less than 3% of couples reported current condom use prior to VCT. In the year after VCT, > 80% of reported acts of intercourse in discordant couples included condom use. Reporting 100% condom use was associated with 39–70% reductions in biological markers; however most intervals with reported unprotected sex were negative for all biological markers. Under-reporting was common: 50% of sperm and 32% of pregnancies and HIV transmissions were detected when couples had reported always using condoms. Positive laboratory tests for STD and reported extramarital sex were relatively infrequent. DNA sequencing confirmed that 87% of new HIV infections were acquired from the spouse.

Conclusions: Joint VCT prompted sustained but imperfect condom use in HIV discordant couples. Biological markers were insensitive but provided evidence for a significant under-reporting of unprotected sex. Strategies that encourage truthful reporting of sexual behavior and sensitive biological markers of exposure are urgently needed. The impact of prevention programs should be assessed with both behavioral and biological measures.   © 2003 Lippincott Williams & Wilkins

Introduction

Over 80% of adults living with HIV reside in sub–Saharan Africa, where the epidemic continues to spread and resources are limited [1]. In Zambia, a southern African country with a population of 9 million, 45% of

childbearing women live in cities where one in four adults have HIV infection [2−4]. By the age of 25 years, over 90% of women have had a child and more than 85% of pregnant women are married [4,5]. In the capital city of Lusaka, approximately one in five cohabiting couples have one HIV positive and one HIV negative partner ('discordant couples') [6]. Although all couples may benefit from voluntary HIV counseling and testing (VCT) [7,8], studies have reported the greatest impact in discordant couples [9−12].

Couples in Africa face many obstacles to condom use and it is not clear how accurate self-report measures are or how long behavior change is maintained. Validation studies in individuals have yielded mixed results [13], with some finding good correlation between reported exposures and sexually transmitted disease (STD) [14] and others not [15]. Several studies have assessed reliability of self-report in couples [16−19], but none have attempted to validate these measures with biological markers.

Estimates of HIV transmission rates in African discordant couples who do not know their HIV results range from 20 to 25% per year [12,20]; this fits well with a per heterosexual exposure transmission risk of 1/500 to 1/1000 multiplied by a frequency of sex of two or three times per week [21,22]. In comparison, reported seroconversion rates in counseled discordant couples range from 3 to 8% per year [12,23−26]. Discordant couples should be highly motivated to use condoms, but the desire to have children [27−29] and the lack of alternative barrier methods may diminish the impact of VCT.

Ethics preclude clinical trials that randomize discordant couples to a group that is not informed of their serostatus. Quantification of the impact of VCT on risk reduction must therefore be based on before−after comparisons with validation of self-report measures. This study presents long-term follow-up of the largest single-site study of heterosexual discordant couples. Condom use before and after VCT is described, patterns and correlates of self-reported condom use after VCT are assessed, and validity of self-report is determined with several biological markers.

Methods

Screening through a VCT center
Study participants were discordant cohabiting couples (one spouse is HIV seropositive while the other is seronegative) and a comparison group of concordant HIV-negative couples who were identified during confidential HIV VCT at the Zambia-UAB HIV Research Project (ZUHRP). The same-day couples' VCT services has been described previously [6] and included free treatment for syphilis, condom skills training, and free condoms.

Enrollment of couples in prospective follow-up
Eligibility criteria for inclusion in the analysis of couples included: (i) cohabitation in a sexual relationship for at least 6 months and residence in Lusaka, Zambia at the time of enrollment; (ii) age ≤ 48 years for women and ≤ 65 years for men; and (iii) at least one follow-up appointment beyond the enrollment visit. HIV status was established with two rapid antibody tests and ELISA confirmation [6]. Both partners signed a joint informed consent and were assigned a study number to ensure confidentiality. Each couple was provided with a sexual diary and shown how to record sexual intercourse with and without condoms.

Data collection
At enrollment, demographic information, prior sexual history, and frequency of alcohol use was documented. Questionnaires were administered separately to men and women by same-sex interviewers who maintained a neutral attitude to minimize under-reporting.

At 3-monthly intervals thereafter, the number of encounters with and without a condom, both with the spouse and with other partners, was recorded. Sexual exposures within the couple were quantified using the sexual diary. Each member of the couple was interviewed separately to allow reporting of outside contacts (which were not recorded in the diary), and to indicate privately whether there had been problems with condom use with the spouse. Discrepancies between husbands' and wives' reports (noted at < 15% of visits) were resolved with a repeat interview of both partners, separately and then together, to achieve consensus. Additional counseling was provided on request and when unprotected contacts were reported.

Sperm and *T. vaginalis* were identified by microscopic examination of a vaginal swab wet preparation. Gonorrhea was detected by Gram stain and culture of an endocervical swab. The Rapid Plasma Reagin (RPR) test, with confirmation by *Treponema pallidum* hemagglutination (TPHA), was used to detect syphilis. All STD screening tests except the gonorrhea culture were carried out while the couple was on the premises, and free treatment was provided to both partners. Women with positive gonorrhea cultures were contacted and advised to come for treatment with their spouse.

Follow-up samples from the HIV negative partner were tested with a rapid HIV antibody test and seroconversion was confirmed with a second rapid test and two ELISA tests. When an initially HIV seronegative person became seropositive, DNA was processed from both

partners in the couple and epidemiologic linkage was confirmed by HIV sequencing [30]. There were 107 seroconversions during the study period, 94 had adequate available DNA for sequencing. 82 out of 94 (87%) of those were linked and the remaining 12 had acquired HIV outside the marriage. Given the high proportion of linkage, the 13 couples with missing sequence data were considered linked for the purposes of analysis.

Data analysis

Our objectives were to: (i) describe self-reported sexual behavior in cohabiting discordant couples before and after VCT; (ii) assess the validity of self-reported sexual behavior through comparison with biological markers; and (iii) compare discordant couples (at high risk of HIV transmission) and concordant HIV negative couples (low risk) with respect to unprotected sexual intercourse.

Discordant couples who attended study appointments at 3, 6, 9, and 12 months ('regular attenders'), those who missed one or more appointments between enrollment and the 12-month visit ('irregular attenders'), and those who dropped out before the 12-month visit were compared to assess potential retention biases. Regular attenders were analyzed with respect to the number of intervals in which intercourse with and without a condom were reported and the number of vaginal smears in which sperm was detected. Reported sexual contacts outside the marriage in the year after enrollment were also evaluated in this group.

Validation analyses compared self-report and biological measures, using follow-up intervals from all enrolled couples. Sperm on vaginal smear, pregnancy, and linked HIV transmission were used to validate reported unprotected sex within the couple.

Gonorrhea, syphilis, and *T. vaginalis* were used to validate self-report of extra-marital sexual contact by either partner. For ethical reasons, participants with positive RPR with undiluted serum (low titer) were treated. However, only newly positive RPR titers of $\geq 1:2$ in a previously RPR negative individual, confirmed by the TPHA test, were considered incident syphilis in the analysis. Early treatment may have preempted the definition of some incident syphilis cases that did not reach a titer of $\geq 1:2$.

In the validation analyses, pre-existing pregnancy, syphilis, or HIV were removed from the respective 'at risk' couple-interval denominators. Three-month intervals were used for sperm, pregnancy, and *T. vaginalis*. Six-month intervals were used for incident HIV, gonorrhea, and syphilis to allow for incubation periods between exposure and detectable disease.

Data entry, management and analysis were performed with the SAS statistical package (version 8; Statistical Analysis Software, North Carolina, USA). Chi-square tests of significance were used for comparison of proportions, t tests for comparison of means, and non-parametric tests for comparison of medians as indicated.

Ethics

Study procedures were approved by the University of Alabama at Birmingham Institutional Review Board, the University of Zambia (UNZA) Research Ethics Committee in Lusaka, and the Office of Protection from Research Risks of the National Institutes of Health, USA. Couples signed joint written informed consent at the time of HIV counseling and testing and again at the time of enrollment into the prospective studies. Free condoms and outpatient care at the study clinic were offered throughout. An insurance policy was also purchased for study members, which covered hospitalization and evaluation at specialty clinics at UTH. Neither UTH nor the study clinic pharmacy provided antiretroviral therapy.

Results

Demographic and risk factor profiles

Between August 1994 and November 1998, 963 HIV discordant couples were enrolled with a median 12 months of follow-up (range, 3–42 months; mean, 14 months). Of these, 818 entered the study at least 1 year before the end of the follow-up period. To evaluate possible biases in retention and missing data, 'regular attenders', 'irregular attenders', and the couples who were lost to follow-up before the 12-month visit are compared in Table 1.

There were no substantial differences between discordant couples who were regular attenders, irregular attenders, and those lost to follow-up with respect to number of years cohabiting (range, 5.0–7.2 years), number of children (range, 1.7–2.1), and proportion of common law or traditional unions (range, 90–93%; the remainder was legal marriages). Men were on average 7 years older than women and reported a later age at first intercourse and more lifetime and last-year partners than women (Table 1). The average income for men was four to six times higher than the corresponding average for women. Gender-matched comparisons showed no differences between the three groups for any of these measures. Women in couples who attended regularly had higher literacy than women in the other two groups. Men in couples who attended regularly reported more frequent alcohol use than their counterparts with irregular attendance and couples who were lost to follow-up (Table 1).

Table 1. Characteristics of 818 Zambian heterosexual discordant couples enrolled ⩾ 12 months before the end of follow-up.

Demographic information and HIV risk factors	Enrolled ⩾ 12 months				Enrolled < 12months	
	Regular attenders 332 couples		Irregular attenders 252 couples		Lost to follow-up[a] 234 couples	
	Men	Women	Men	Women	Men	Women
Means						
Age (years)	35	29	35	29	33	27
Age at first sex (years)	18	17	19	16	18	16
Sex partners last year	1.9	1.1	1.9	1.1	1.8	1.2
Lifetime sex partners	10.7	3.1	10.0	2.9	10.0	3.4
Income (kwacha/month)[b]	49 321	10 375	59 221	11 482	50 521	12 436
Proportions						
Self-report of STD in last 5 years	41%	20%	39%	17%	37%	21%
Alcohol use more than once per month	57%	5%	50%	11%	47%	7%
High literacy	67%	35%	64%	28%	64%	28%
Pregnancy	–	17%	–	17%	–	13%
Breastfeeding	–	35%	–	31%	–	31%

[a]Of those lost to follow-up, 59 (7% of the 818) relocated, 42 (5%) separated, 37 (5%) suffered the death of a partner, and 96 (12%) withdrew. Reasons given for withdrawing were generally related to lack of time and logistical obstacles. [b]The value of the kwacha ranged from 700–2500/$ during this study.

Concordant HIV negative couples were similar to discordant couples with respect to age, marital status, income, and literacy. They had a longer average duration of union (10 years) and more children (mean, 3) than discordant couples. The men reported fewer sexual partners in the last year (mean, 1.4) and were less likely to report a history of STD in the last 5 years (27%) compared with men in discordant couples.

Self-report of sexual intercourse with the spouse

Prior to receiving their HIV test results, < 3% of discordant couples reported current condom use with each other. The frequency of sex with the spouse did not change after VCT, but the proportion of reported contacts with a condom increased to > 80% and remained stable through ⩾ 12 months of follow-up. In contrast, among 66 concordant negative couples followed for a median of 12 months, condom use was reported in only 28% of sexual exposures.

Couples with regular appointments through 12 months reported more frequent intercourse with condoms than couples with missing appointments or those lost to follow-up, regardless of which partner was HIV positive and whether means or medians were compared (Table 2). Regular attendance was also associated with fewer unprotected contacts, particularly in couples with HIV negative men. Discordant couples with HIV negative men had more frequent sex with their spouses than couples with HIV positive men, both with condoms (mean 17.8 versus 15.3 per interval; $P < 0.01$) and without (mean 2.9 versus 2.0 per interval; $P < 0.01$). Some comparisons were limited by the low frequency of reported unprotected exposures and the

small number of intervals available for analysis in the group that was lost to follow-up.

Among regular attenders, 23% could be characterized as 'perfect compliers' (no reported unprotected sex in any of four 3-month intervals), while 10% were 'chronic non-compliers' (unprotected sex in all four intervals). The majority of regular attenders reported regular condom use with occasional lapses: 26% reported unprotected sex in only one interval, 24% in two, and 17% in three of four intervals. Abstinence was uncommon; more than 99% of couples reported having sex with a condom at least once during the year and 56% did so during all four intervals.

Validation of self-reported sexual contacts with the cohabiting partner using sperm, pregnancy, and linked HIV transmission

Overall 19% of vaginal smears in discordant couples showed sperm, compared with 36% (115/318) of vaginal smears from 66 concordant HIV negative couples ($P = 0.001$). This represents a 47% reduction of sperm detection in discordant couples compared with concordant negative couples. Among discordant couples who were regular attenders, 60% of women had no sperm at any of the quarterly visits, 30% had sperm on one of four vaginal exams, and the remaining 10% had sperm on two or more exams. Among regular attenders who reported 100% condom use during the first 12 months, 83% had no sperm detected at any of the quarterly visits.

Biological markers detected in discordant couples in intervals with and without reported unprotected sex

Table 2. Reported sexual intercourse per 3-month interval between spouses in discordant couples after Voluntary HIV counseling and testing (VCT).

	Enrolled ≥ 12 months		Enrolled < 12months
	Regular attenders	Irregular attenders	Lost to follow-up
HIV+ men/HIV− women	171 couples; 1321 intervals	133 couples; 748 intervals	121 couples; 171 intervals
With condoms			
Mean (SD)[a]	16.8 (15.0)	13.1 (14.0)	10.1 (13.4)
Median (IQR)[b]	13 (4−26)	9 (1−21)	5 (0−15)
Without condoms			
Mean (SD)[c]	1.9 (5.0)	2.6 (7.2)	2.4 (7.0)
Median (IQR)[d]	0 (0−2)	0 (0−2)	0 (0−2)
HIV− men/HIV+ women	161 couples; 1163 intervals	119 couples; 663 intervals	113 couples; 142 intervals
With condoms			
Mean (SD)[e]	19.4 (18.4)	15.9 (18.5)	13.7 (16.5)
Median (IQR)[f]	15 (4−30)	9 (1−24)	8 (1−18)
Without condoms			
Mean (SD)[g]	2.3 (5.8)	3.6 (8.4)	3.4 (7.7)
Median (IQR)[h]	0 (0−2)	0 (0−3)	0 (0−3)

[a]t tests for significant differences in means: 16.8 versus 13.1, $P < 0.001$; 16.8 versus 10.1, $P < 0.001$; 13.1 versus 10.1, $P = 0.01$. [b]Non-parametric tests of significance in medians: 13 versus 9, $P < 0.0001$; 13 versus 5, $P < 0.0001$; 9 versus 5, $P = 0.0022$. [c]t tests for significant differences in means: 1.9 versus 2.6, $P = 0.03$; 1.9 versus 2.4, $P = 0.38$ (not significant); 2.6 versus 2.4, $P = 0.80$ (not significant). [d]Non-parametric tests of significance in medians: none of the two way comparisons are significant. [e]t tests for significant differences in means: 19.4 versus 15.9, $P < 0.001$; 19.4 versus 13.7, $P < 0.001$; 15.9 versus 13.7, $P = 0.19$ (not significant). [f]Non-parametric tests of significance in medians: 15 versus 9, $P < 0.0001$; 15 versus 8, $P < 0.0001$; 9 versus 8, $P = 0.37$ (not significant). [g]t tests for significant differences in means: 2.3 versus 3.6, $P < 0.001$; 2.3 versus 3.4, $P = 0.10$ (not significant); 3.6 versus 3.4, $P = 0.85$ (not significant). [h]Non-parametric tests of significance in medians: only the comparison of regular attenders with irregular attenders was significant $P = 0.0004$. SD, Standard deviation; IQR, interquartile range.

Table 3. Correlation between biological markers and reported sexual intercourse between spouses.

Biological markers	Intervals with reported unprotected sex	Intervals with no reported unprotected sex	P	Reduction of biological markers in intervals with no reported unprotected sex (%)
Sperm on vaginal smear[a]				
Positive	252 (24.7%)	246 (15.1%)		39%
Negative	770 (75.3%)	1380 (84.9%)	< 0.001	
Pregnancy[b]				
Positive	117 (7.4%)	55 (2.2%)		70%
Negative	1459 (92.6%)	2492 (97.8%)	< 0.001	
Linked HIV transmission[c]				
Positive	64 (5.4%)	30 (2.6%)		52%
Negative	1128 (94.6%)	1109 (97.4%)	< 0.001	

[a]Presence or absence of sperm was noted on routine vaginal smears at 3-monthly intervals as of 1996. Vaginal exams were not performed 6 weeks antepartum to 6 weeks post-partum. [b]Intervals with pre-existing pregnancy were excluded from the denominator. [c]Serologic testing was performed for HIV negative partners at 3-month intervals; 6-month intervals were used to allow for the 'seroconversion window' between reported exposure and detectable antibodies. Intervals with pre-existing HIV were excluded from the denominator.

are presented in Table 3. Sperm was present in 24.7% of vaginal smears taken in intervals with reported unprotected sex, compared with 15.1% of smears taken when no unprotected sex had been reported. While reporting 100% condom use was thus associated with a 39% reduction in detection of sperm, the presence of sperm in 15% of 'protected' intervals with no unpro-tected sex confirmed substantial under-reporting. Con-

sistent condom use was associated with a 70% reduction in pregnancy and a 52% reduction in linked HIV transmission, but these were comparatively rare outcomes, each occurring in < 5% intervals.

Self-report of sexual contact with other partners

At baseline, 21% of HIV positive men and 15% of HIV negative men in discordant couples reported at least one sexual encounter outside the marriage in the last 3 months. These contacts represented 7% of all acts of intercourse in the 3 months preceding the study, decreasing to 3% during the first year of follow-up. Among regular attenders, 23% of men reported at least one outside contact in the year after enrollment, with 12% reporting it in only one interval and 11% in more than one.

Women reported much less contact outside the marriage than men. Only 0.3% of all acts of intercourse reported by women prior to study entry and 0.2% thereafter occurred with another partner.

Validation of reported sex with other partners using STD

Gonorrhea, syphilis, and *T. vaginalis* after enrollment were assumed to reflect sexual contact outside the couple by at least one partner. Genital ulcers noted on exams were not included because recurrent herpes simplex virus was common and unrelated to recent outside sexual partners. The incidence of gonorrhea was low but correlated well with reported outside contacts (6.1% cases of intervals with reported outside contacts were positive for gonorrhea versus 2.3% of intervals without reported outside contacts, $P < 0.001$). Similarly, syphilis was uncommon but was associated with outside partners (3.5% of intervals with reported outside contact versus 1.7% of intervals without were associated with incident syphilis; $P = 0.01$). *T. vaginalis* was the most common STD but had the poorest correlation with self-report (10.7% of intervals with outside contacts versus 7.3% of those without; $P = 0.017$). Cure for gonorrhea and syphilis required one injection and adherence was not an issue. In contrast, the treatment for *T. vaginalis* was a 7-day oral regimen of metronidazole, which is known for unpleasant side effects. Of 91 women positive for *T. vaginalis* on at least one of four consecutive vaginal exams, 20 had repeat cases. This suggests that incomplete treatment and re-infection within the couple, rather than recent outside contacts, may have been the source of many infections.

Sequencing confirmed that 13% (n = 12) of incident HIV infections were acquired from an outside partner. Only two of six men and one of six women thus infected reported outside partners in the 6 months prior to the first positive serology.

Discussion

Most new HIV infections in Africa now occur in cohabiting couples [2,6,31,32], many of whom do not realize that only one may be HIV infected [5]. In this study, Zambian discordant couples reported a marked increase in condom use after joint VCT, and maintained this risk reduction for at least a year. The presence of sperm on vaginal smears was noted half as frequently in discordant couples compared with concordant negative couples, which corroborated differences in reported condom use. Sperm and other biological markers also indicated, however, that at least half of unprotected contacts in discordant couples were not reported. It is critical to acknowledge the problem with under-reporting in studies of sexual behavior, particularly if per-contact risks of HIV transmission are to be estimated with accuracy [22]. The HIV seroconversion rate after VCT in this cohort of discordant couples was 8/100 person–years [23], and the spouse was the index case in the majority of new infections [30]. Sex with outside partners was relatively uncommon and use of STD as a proxy for HIV risk was therefore of limited use.

As in other discordant couples studies, adoption of condom use followed receipt of HIV test results [33,34]. In this study, couples with HIV negative men had more frequent sex both with and without a condom compared to couples with HIV positive men. This may reflect a decreased libido in HIV positive men, resulting either from physical or psychological factors [35−37]. Though couples with HIV positive men had less frequent intercourse, they were more likely to report 100% condom use. This confirms that in areas where women often have difficulty negotiating condom use, many men who know they have HIV willingly use condoms to protect their uninfected spouses.

Discordant couples complied fairly well with condom use, with almost one-quarter reporting perfect compliance during 1 year of follow-up. Most couples reported occasional lapses, but only 10% reported unprotected sex at each follow-up visit. Couples who regularly attended study appointments were more likely to report 100% condom use. This does not necessarily imply a causal relationship; co-operative couples may be more likely to adhere with both scheduled appointments and condom use.

Sexual diaries can reduce recall bias and have been shown to yield different results than contemporaneous questionnaires [38,39], with discrepancies greatest in behaviors judged to be 'good' or 'bad'. As with any behavior, a longer recall period is associated with greater measurement error [40]. Weinhardt *et al.* reported good reliability using diaries to enhance recall of

sexual behavior in the preceding 3 months [41]. The combination of 3-monthly visits and joint sexual diaries was practical and acceptable to our participants. Counselors also found diaries a useful tool to prompt additional counseling.

Our results confirm that validation of sexual self-report with objective measures is critical. Examination of vaginal wet preparation for sperm provided a simple and inexpensive biological marker of unprotected intercourse. Detection of sperm correlated with self-report but confirmed that although discordant couples are having much less sex without condoms than concordant negative couples, they are still underreporting many high-risk exposures. Pregnancy and HIV transmission were also associated with self-reported exposures but were comparatively infrequent outcomes.

STD were rare in this cohort; they were detected significantly more often when outside contacts were reported, but even so, most cases occurred when both spouses denied having other partners. This under-reporting was not surprising, as sexual contact outside the marriage is not socially acceptable in Zambia. The technical aspects of STD diagnosis must also be borne in mind in future studies; positive laboratory results do not necessarily reflect recent contact with another partner. Incubation period, test sensitivity, persistent antibody responses, and relapse after incomplete treatment all complicate interpretation of test results.

Biological markers confirmed that sex without condoms was under-reported, both between spouses and with outside partners. However, even the most common objective measure, sperm, was detected in only one-quarter of intervals with reported unprotected sex, presumably because sperm can only be detected for a few days after unprotected intercourse. Self-reported behavior is thus far more sensitive than biological markers and remains a critical measure of the impact of interventions. Ideally, both self-report and biological markers should be used: self-report measures maximize sensitivity while biological markers provide an estimate of the degree of under-reporting [42,43].

HIV discordant couples have historically been considered an ideal group for research [19,39,44,45], but until recently the high proportion of new infections that could be prevented in this group was not appreciated [46−48]. Without specific educational programs, few couples understand the importance of being tested together for HIV [5]. Thus, active promotion of couples' VCT should be among the top priorities of prevention programs in high prevalence areas [49,50]. In order to measure accurately the impact of risk reduction strategies like VCT, better techniques are needed to improve both the validity of self-report and the sensitivity of biological markers.

Acknowledgements

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