JAIDS Journal of Acquired Immune Deficiency Syndromes
27:202–208 © 2001 Lippincott Williams & Wilkins, Inc., Philadelphia

HIV-1 Incidence Among Male Workers at a Sugar Estate in Rural Malawi

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Objectives: To determine incidence of HIV and associated risk factors in two cohorts of men working at a sugar estate in rural Malawi.

Design: Prospective studies.

Methods: After counseling and obtaining informed consent, male workers were tested for HIV-1 and syphilis. Baseline HIV-seronegative men were enrolled in two follow-up studies in 1994 and 1998, and were retested for HIV and syphilis at 6-month follow-up visits. Demographic, behavioral, and medical history was collected at baseline. Cumulative HIV incidence based on Kaplan-Meier methods was estimated. HIV incidence was also estimated per 100 person-years (p-y). Crude and adjusted rate ratios for the association of risk factors with incident HIV infection were obtained using Cox proportional hazards models.

Results: HIV prevalence was 24.3% among 1692 men screened in 1994 and 21.0% among 1349 men screened in 1998 ($p < .03$). HIV incidence was extremely high during 1994 to 1995 (17.1% for that 1-year period). Incidence dramatically declined in 1996, averaging about 3.5% per year from 1996 through 1999. Among men enrolled in the 1998 cohort, HIV incidence during 1998 to 1999 was 3.8%. After controlling for potential confounders reactive syphilis was associated with a twofold risk of HIV acquisition in each cohort.

Conclusions: Urgent preventive measures are needed to control the spread of HIV in this economically important occupational cohort. In addition to conventional educational messages to reduce risky sexual behavior, treatment of other sexually transmitted diseases should be considered. **Key Words:** HIV incidence—Malawi—Occupational cohort.

The World Health Organization (WHO) estimates that 24.5 million adults and children are currently living with HIV/AIDS in sub-Saharan Africa, accounting for over 70% of the world's burden of infection (1). Malawi, a land-locked country of 12 million inhabitants bounded by Mozambique, Tanzania, and Zambia, has experienced an HIV epidemic similar to that of its neighbors, with approximately 16% of its adult population infected. Prevalence rates increased from 2% among women attending antenatal clinics in Blantyre (the main commercial center) in 1985 to 30% in 1993; since then have remained stable (2). Overall HIV incidence among pregnant and postpartum women was 4.2 per 100 person-years, but higher among young women (6.0 per 100 person-years) (2). Among men, estimates of rates of acquisition of HIV-1 in Malawi are limited.

In southern and eastern Africa, several studies on occupationally distinct populations have been conducted to

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Manuscript received November 9, 2000; accepted March 21, 2001.

determine rates of HIV seroconversion and to identify associated risk factors. For example, among male factory workers in Harare, Zimbabwe during 1993 to 1995, incidence of HIV was 2.9 per 100 person-years, and factors that included reported genital ulcers, multiple sexual partners, and being married but separated from their spouses were each significantly associated with seroconversion (3). In a military cohort in Uganda, HIV incidence was 3.6 per 100 person-years in 1993 (4). In Dar es Salaam, Tanzania, incidence of HIV during 1994 to 1998 was about 2.0 per 100 person-years (5) in a cohort of police officers. Studies on HIV incidence and its determinants, especially among economically productive groups, are needed to guide planning of possible interventions. In this study, we examine the incidence of HIV-1 infection among two cohorts of male workers recruited in 1994 and 1998 from a large sugar plantation in rural Malawi.

METHODS AND MATERIALS

Setting

The Sugar Corporation of Malawi (SUCOMA) is located at Nchalo in southern Malawi. The sugar estate employs 7,000 permanent workers, mostly men. These men work and reside in designated communities spread throughout the estate. More than 80% of men live with their wives and dependents. Between March and December, an additional 2,000 men are employed to harvest the sugar cane. There is a trading center close to the factory where postal, banking, wholesale, and retail commercial services are available. There are several night clubs, bars, and rest-houses around the trading center that represent the main social gathering places for the local population, factory workers, and truck drivers.

Study Population

In February 1994 and March 1998, male workers in SUCOMA were invited to enroll in studies of epidemiologic and biologic determinants of HIV infection. Workers were contacted through local clinics, posters, and health education talks. Selection of study participants was based mainly on attendance of workers at designated recruitment posts located in their communities on specific days of the week. These recruitment procedures were similar for the 1994 and 1998 cohorts, and likewise, the same communities were targeted for recruitment of participants into these cohorts. All categories of workers (e.g., those involved in cane cutting, irrigation, machinery) were invited to participate, and we did not discriminate between casual and permanent workers.

Recruitment and Follow-Up

Participants 18 years or older who agreed to enroll were provided pretest and posttest HIV counseling. Informed consent for initial screening and subsequent follow-up was obtained after proper counseling. Participants who had HIV-seronegative results were requested to enroll in a longitudinal HIV study. A few HIV-positive participants were also requested to enrol in the study to maintain confidentiality of study participants. The only direct incentives in this study were HIV counseling and education, and treatment for sexually transmitted diseases (STDs) and condoms were provided at no cost at each visit. At enrollment, each participant had blood (about 5 ml) drawn to test for HIV and syphilis. All serologic results were kept confidential. Results and posttest counseling were made available to participants only through trained study personnel. Individual test results and information on risk factors were not accessible to employers. Participants were followed up at approximately 6-month intervals. No active tracing was attempted for men who were late or those not returning for their scheduled visits. Men enrolled in 1994 were observed until approximately the end of 1999; the 1998 cohort was also observed to that endpoint. Individuals who were HIV seronegative at enrollment and had at least one follow-up HIV test result were included in the present analysis.

Collection of Data

Trained interviewers used structured questionnaires to collect data. Sociodemographic information collected at enrollment included age, marital status, and education. HIV risk-related questions included STD history, condom use, number of sexual partners, and type of sexual partners (e.g., prostitute, casual, friend, or mistress). A sexual partner was defined as a woman involved with the respondent in a nonmarital relationship. Reported circumcision was also recorded. At each follow-up visit, participants were asked the same risk-related questions referring only to events occurring between visits. HIV and syphilis testing was performed at each visit.

HIV-1 and Syphilis Testing

The HIV status of participants was determined by two independent enzyme-linked immunosorbent assays (ELISA) and Western blot tests. In 1994, initial HIV screening was carried-out using Behring Diagnostika (Behringwerke AG, Frankfurt, Germany), and all reactive samples were retested with a second ELISA test, Wellcozyme (Wellcome Diagnostics, Dartford, U.K.). In 1998, the first and second HIV tests were performed using Genetic Systems LAV enzyme immunoassay (EIA) (Redmond, WA, U.S.A.) and Wellcozyme HIV Recombinant EIA (Murex Diagnostics, Dartford, Kent, UK), respectively. All HIV seroconversions were confirmed using Western blot test (Biorad, Richmond, CA, U.S.A.). These tests were conducted at the Johns Hopkins Research Project laboratory in Blantyre, Malawi. Syphilis testing was performed using Rapid Plasma Reagin (RPR) test (Macro-Vue, Becton Dickinson, Cockeysville, MD, U.S.A.) for screening. Syphilis confirmatory tests were performed on follow-up samples using *Treponema pallidum* hemagglutination assay (TPHA; Sera-Tek, Miles Inc, Elkhart, IN, USA). No laboratory assays were conducted for other STDs. No confirmatory syphilis tests were performed on enrollment sera. Individuals with reactive syphilis test results were provided appropriate treatment at the closest health center (a network of five health centers and a main referral clinic are available within the estate). Other STDs were treated syndromically, based on Malawi Ministry of Health guidelines. No contact tracing was performed; participants were counseled to refer their partners to the nearest health center for treatment.

Statistical Analysis

Overall HIV seroincidence rates were calculated separately for each cohort as number of seroconversions divided by total person-years (p-y) under observation (per 100). Person-years were estimated as the

interval between enrollment and the most recent follow-up visit for participants who remained HIV negative. For study subjects who seroconverted, p-ys were estimated as the interval between enrolment (when an individual was seronegative) and the midpoint between the last HIV-negative and first HIV-positive test results within the above follow-up period. Confidence intervals (CIs) were calculated as exact limits assuming a Poisson distribution of seroconversions. Kaplan-Meier survival analysis was also performed to estimate HIV cumulative incidence and rates of follow-up for the 1994 and 1998 cohorts. Crude and adjusted relative hazards (and 95% CI) for the association of various risk factors with HIV seroconversion were estimated using Cox proportional hazards models. The choice of covariates in the final model was based on statistical significance ($p < .05$) in univariate analyses and on reports from the literature. The final multivariate model included both time dependent (time-varying) and time-fixed baseline variables.

RESULTS

Table 1 summarizes the number of men screened and enrolled in 1994 and 1998. There was a slight decline in HIV prevalence among men screened in 1994 (N = 1692; prevalence 24.3%) and 1998 (N = 1349; prevalence 21.0%) ($\chi^2 = 4.65$; $p = .03$). HIV-negative men who agreed to participate in the follow-up study comprised 1,280 (75.7%) in 1994 and 1,066 (79.0%) in 1998. In each of the two cohorts, a comparable proportion of men did not return for a subsequent visit after enrollment (19.6% versus 17.5%). Conversely, comparable proportions of men made at least two follow-up visits in the 1994 (74.1% [949 of 1280]) and 1998 (78.7% [830 of 1055]) cohorts. The median duration of follow-up for HIV-negative men enrolled was 16.9 months for the 1994 cohort (1735.9 p-y of follow-up), and 11.8 months for the 1998 cohort (815.8 p-y of follow-up). Overall, 190 seroconversions occurred among men enrolled in 1994 (incidence rate of 10.9 per 100 p-y during 1994–1999) and 26 seroconversions occurred among men enrolled in 1998 (incidence rate of 3.2 per 100 p-y during 1998–1999).

Baseline risk factors for HIV acquisition among men who returned for a follow-up visit in the 1994 and 1998 cohorts are shown in Table 2. Age distributions for the two cohorts were similar, with approximately 60% of each cohort <35 years of age. It should be noted that the proportion of men <25 years was slightly higher in the 1994 cohort. There were no differences between the two cohorts in proportions of men who were single, illiterate, with STDs on physical examination, or circumcised. However, the proportions of men who reported STDs or having nonmarital sexual partners during the past year (especially high-risk partners) were significantly lower among men enrolled in the more recent (1998) cohort. Proportions of men with reactive syphilis or who reported ever using condoms were higher among men enrolled in the 1998 cohort than in those enrolled in the 1994 cohort ($p < .0001$).

The same characteristics listed in Table 2 for men who returned for a subsequent visit and those who did not return (i.e., lost to follow-up) in the 1994 and 1998 cohorts were compared. More nonreturnees (N = 331) in 1994, compared with returnees (N = 949), were younger (age <25 years: 36.7% vs. 23.1% $p < .0001$), were not married (27.5% vs. 13.5%; $p < .0001$), did not report condom use (4.0% vs. 10.9%; $p < .0001$), or were not circumcised (11.5% vs. 17.5%; $p < .02$). The other risk factors in the 1994 cohort were not significantly different among returnees and nonreturnees with the exception of reported STD history, which was higher among those who returned for a follow-up visit (40.5% vs. 27.4%;

TABLE 1. *Summary of screening and enrollment of men in the 1994 and 1998 cohorts, Nchalo Sugar Estate, Malawi*

	1994 N (%)	1998 N (%)
Total screened	1692	1349
Tested HIV positive at screening	412 (24.3)	283 (21.0)
HIV negative enrolled	1280 (75.7)	1066 (79.0)
Did not return after enrollment	331 (19.6)	236 (17.5)
Made at least 2 visits	949 (56.1)	830 (61.5)

TABLE 2. *Percentage distributions of baseline demographic and risk characteristics of male workers at the Nchalo Sugar Estate in Malawi, 1994 and 1998 cohorts*

Characteristic	1994 cohort (N = 949)	1998 cohort (N = 830)	p value[a]
	%	%	
Age			<.0001
18–24	23.1	16.4	
25–34	36.8	43.5	
35–44	23.8	19.4	
45–54	12.3	14.6	
55+	4.1	6.1	
Not married	13.5	11.1	.15
Illiterate	16.9	14.5	.19
Ever had STD	40.5	24.6	<.0001
STD on exam	6.0	5.1	.52
Syphilis (RPR positive)	5.2	9.9	<.0001
Had nonmarital sexual partner during past year	59.9	36.6	<.0001
Sexual partner type:			<.0001
Prostitute/casual	14.3	4.7	
Friend/mistress	45.0	16.6	
Missing	0.6	15.3	
No nonmarital sexual partner	40.1	63.4	
Ever used condoms	10.9	18.1	<.0001
Circumcized[b]	17.5	18.0	.85

[a] χ^2 test.
[b] Reported circumcision.
STD, sexually transmitted disease; RPR, Rapid Plasma Reagin test.

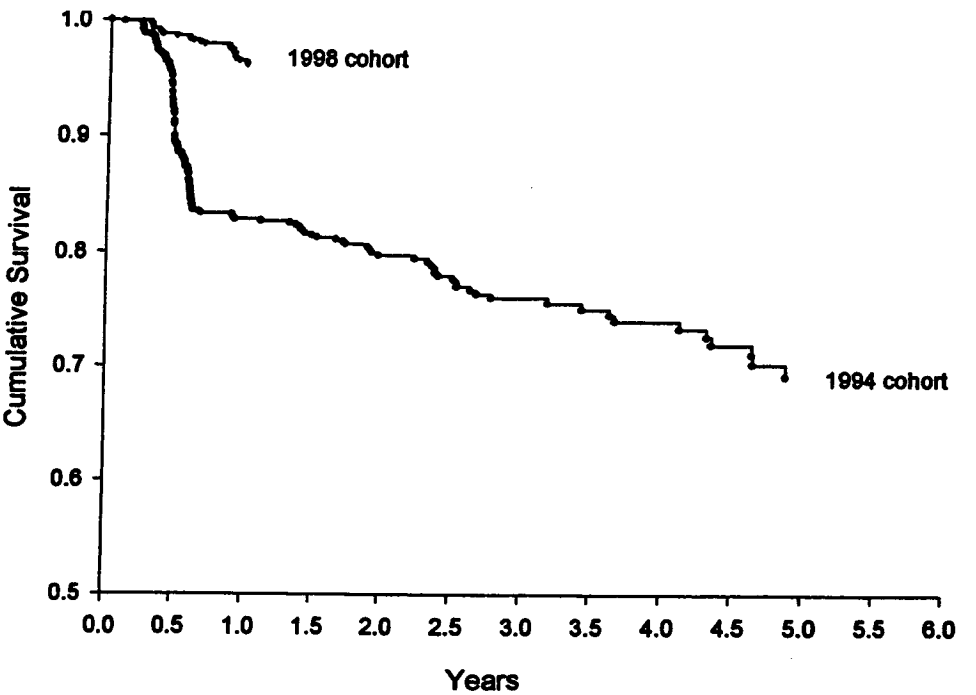
$p < .0001$). In the 1998 cohort, none of the risk factors was statistically significantly different among the returnees and nonreturnees.

Figure 1 shows Kaplan-Meier survival curves of cumulative incidence for the 1994 and 1998 cohorts. For the 1994 cohort, incidence during 1994–95 (the first year) was 17.1%; 1995 to 1996 was 3.1%; 1996 to 1997 was 4.2%; 1997 to 1998 was 2.5%; and 1998 to 1999 was 4.2%, respectively. For the 1998 cohort, incidence during 1998 to 1999 was 3.8%, comparable with the 1998 to 1999 incidence among men from the 1994 cohort.

In the 1994 cohort, there was a linear decreasing trend in HIV incidence with increasing age, with the youngest group (18–24 years) having an incidence nearly double that of their oldest (≥55 years) counterparts ($p = .12$). In the 1998 cohort, in which men were observed on average for 1 year, and in which fewer cases of seroconversions were observed, no clear trend of declining HIV incidence with age was apparent ($p = .91$) (Table 3). The overall HIV incidence rate in the 1994 cohort was 10.9 per 100 p-y, over three times higher than the incidence of 3.1 per 100 p-y in the 1998 cohort.

Men enrolled in the 1994 cohort were recruited mainly from 11 residential communities located inside and around the sugar estate. The Nchalo trading center, as described in Methods, is an active gathering place where social activities and commercial sex exist. We used populations recruited from each community to estimate HIV incidence based on number of observed seroconversions, and stratified these community-specific incidence estimates by distance from the Nchalo trading center.

Table 4 shows that incident HIV infection was directly associated with access to Nchalo. There was a significant trend in acquisition of HIV by distance from the trading center. Among men recruited in 1994, the overall incidence (1994–1999) was highest in communities closest



Cumulative incidence

	1994-95	1995-96	1996-97	1997-98	1998-99
1994 Cohort	17.1%	3.1%	4.2%	2.5%	4.2%
1998 Cohort					3.8%

FIG. 1. HIV incidence for 1994 and 1998 cohorts.

TABLE 3. *Age-specific HIV incidence among men working at the Nchalo Sugar Estate, Malawi, 1994 and 1998 cohorts*

	1994 Cohort				1998 Cohort			
Ages	*N*	Seroconverters (no.)	Person-years	Incidence (95% CI)	*N*	Seroconverters (no.)	Person-years	Incidence (95% CI)
18–24	218	48	358.9	13.4 (9.9–17.6)	136	4	125.1	3.2 (0.9–8.2)
25–34	349	74	635.4	11.6 (9.1–14.8)	361	11	355.9	3.1 (1.5–5.5)
35–44	226	43	441.4	9.7 (7.1–13.1)	161	6	162.4	3.7 (1.4–8.1)
45–54	117	21	244.4	8.6 (5.3–13.1)	121	3	121.0	2.5 (0.5–7.3)
55+	35	4	55.8	7.2 (2.0–18.4)	38	1	41.6	2.4 (0.1–13.4)
Total	945	190	1,735.9	10.9 (9.4–12.6)	817	25	806.1	3.1 (2.1–4.5)

CI, confidence interval.

to the trading center, lowest in communities farthest from the trading center, and intermediate in communities between these two sites. Unlike HIV incidence, community-specific prevalence estimates did not show a significant trend. Syphilis prevalence at baseline also showed a similar gradient: the prevalence was 7.9% among men from communities proximal to the trading center, 5.7% in intermediate communities and 3.2% in most distal communities. We did not stratify incidence of HIV or syphilis for men recruited in 1998 by distance because the number of events were limited.

Table 5 shows crude and adjusted hazard ratios for the association of risk factors with incident HIV infection for the 1994 and 1998 cohorts. Reactive syphilis increased the hazard of HIV acquisition by about twofold among men in both the 1994 and 1998 cohorts; however, it was only statistically significant in the 1994 unadjusted and adjusted analyses. Other variables, with the exception of condom use, showed consistent associations with incident HIV in both cohorts, but none was statistically significant. Circumcision was associated with a decreased hazard of HIV infection in both cohorts; this association was of borderline significance in the 1994 cohort. In a separate analysis, circumcision was highly associated with being a Muslim in both the 1994 and 1998 cohorts (data not shown). Adjusting for religion in the final multivariate analysis did not significantly decrease the hazard of HIV infection associated with circumcision in either cohort.

DISCUSSION

Incidence of HIV among male workers in the Nchalo sugar estate was extremely high (17.1%) during 1994 to 1995, the first year of the study (Fig. 1). Following this initial high peak, HIV incidence declined dramatically over a relatively short period of time. For example, incidence of HIV during the second year of follow-up for the 1994 cohort was only 3.1%, a drop of 14% from the first year incidence of 17.1%.

Several factors could have played a role in the incidence decline and its stability thereafter. In this closed cohort and over a short period of time, few susceptible individuals might have been left to sustain transmission at the same rapid rate of seroconversion. Rapid declines of incidence in several high-risk study populations have been observed in Africa (among prostitutes in Kenya and Zaire from 38% to 11% in 1 year and from 18% to 2.2% in 20 months, respectively) (6). Potential preventive activities which accompanied this and other studies in Nchalo that have contributed to the decline and stability of the epidemic include educational messages on HIV/AIDS, condom use, and avoidance of risky behaviors. Our own data (Table 2) show that between the two studies in 1994 and 1998, there were significant reductions in reported STDs and number and type of sexual partners. There was also a significant increase in reported condom use. As in other condom-use studies in Malawi (7), we suspect condom use was inconsistent or there were reporting errors because there was no simultaneous reduction in rates of reactive syphilis. Although we did not monitor mortality levels, it is likely that this factor too might have contributed to the rapid

TABLE 4. *HIV incidence and prevalence among male SUCOMA workers stratified by distance of communities from the Nchalo trading center, 1994 cohort*

	Men, no.[a]	1994–1999 Incidence[b]	Prevalence[c]
Closest (<5 Km)			
Five communities	1099	11.8 (133/1125.9)	24.7%
Intermediate (5–9 Km)			
Three communities	355	10.6 (39/368.6)	27.9%
Furthest (≥10 Km)			
Three communities	238	7.5 (18/241.4)	19.7%
p value (χ^2 trend test)	—	.01	.36
Total	1692	10.9 (190/1735.9)	24.4%

[a] Number of men enrolled at baseline from each community.
[b] Incidence per 100 person-years (no. seroconverters/person years of observation).
[c] Denominator: men enrolled from each community (first column).
SUCOMA, Sugar Corporation of Malawi.

change in incidence either through high rates of attrition or by changes in behavior as a consequence of witnessing the deaths of peers with the disease. Other studies in sub-Saharan Africa have confirmed high mortality levels attributable to HIV-1 among men aged 25 to 44 years; for example, more than 70% of all deaths in Uganda (8).

In addition to susceptibility among exposed individuals, the spread of HIV infection is determined by infectiousness of the host (9). Our investigation did not include partners of these male workers. Table 4, however, provides some insight into the source of infection. The rate of acquisition of HIV followed a gradient based on distance from the Nchalo trading center where most commercial sex occurs. Both HIV and syphilis rates were highest in communities closest to the trading center and lowest in communities furthest from the center. In the early years of the epidemic it appears that this core group of commercial sex workers substantially amplified transmission of the virus, especially among young men (see age-specific incidence in Table 3). The most important risk factor for HIV acquisition in both cohorts was a reactive syphilis test. Both ulcerative and nonulcerative STDs are known to increase acquisition of HIV (10,11). The lack of statistical significance in the 1998 data (Table 5) could be due to the small number of seroconversions in this cohort.

Prevalence of HIV showed a modest decline, from 24.3% in 1994 to 21.8% in 1998 ($p < .03$). The incidence estimates, however, showed a major decline from 17.1% during 1994 to 1995 to a stable rate of about 3.5% per year for the subsequent years. As reported in other studies, a high HIV incidence may be masked by a stable overall prevalence (12), or the HIV prevalence may decline whereas HIV incidence remains high or stable (13). Factors that could contribute to this equilibrium that we did not accurately assess are mortality and changes in population composition due to outmigration, death, and other changes in the labor force.

Loss to follow-up was large in both cohorts, because no active tracing of clients was attempted. In follow-up to the 1994 cohort, 78% of the cohort was observed for 1 year, 50% was observed for 1.8 years, and 40% of the cohort was observed for 2 years. In the 1998 cohort, 68% were observed for 1 year, but all were censored at that point. In this study, we did not discriminate between permanent and casual workers in our recruitment. Therefore, the low retention rates could possibly be due to high turnover in this occupational setting. We believe this loss may cause the incidence estimates in this study to be conservative (underestimate) because most losses could have been due to illness, death, or other factors that lead to termination of employment. Nonreturnees compared with returnees in the 1994 cohort were younger, more often single, used condoms less, and uncircumcised; these are characteristics more likely to be associated with HIV acquisition. The fact that the incidence for 1998 to 1999 of the 1994 cohort (4.2%) was comparable with the incidence in 1998 to 1999 cohort (3.8%) suggests that the effect of losses on differential acquisition of HIV in these two cohorts may be minimal. Nonetheless, loss to follow-up is a limitation of this study. Excluding casual workers with no commitment of residence in Nchalo or its immediate surrounding communities would be an appropriate approach in future studies. Other limitations to this study are our inability to perform laboratory tests for STDs other than HIV and syphilis, and lack of behavioral in-depth evaluation of the dynamics of commercial sex work in Nchalo.

Urgent interventions are needed to control the spread of HIV in this economically productive community. STDs such as syphilis and behaviors related to sexual transmission of these infections would be practical and important risk factors to target. Community-based STD interventions in Mwanza, Tanzania (14), and Rakai, Uganda (15), have produced mixed results. It is likely that a combination of these two approaches could be effective. These approaches should be accompanied by

TABLE 5. *Association of selected risk factors with incident HIV infection among male workers at the Nchalo Sugar Estate in Malawi, 1994 and 1998 cohorts*

Risk factor	1994 Cohort		1998 Cohort	
	HR_{crude} (95% CI)	$HR_{adjusted}$ (95% CI)	HR_{crude} (95% CI)	$HR_{adjusted}$ (95% CI)
Age (per 10 years)	0.90 (0.77–1.03)	0.90 (0.78–1.17)	0.90 (0.61–1.34)	0.93 (0.58–1.25)
Syphilis (RPR positive)[a]	2.16 (1.29–3.61)	1.94 (1.14–3.25)	2.38 (0.89–6.30)	2.32 (0.84–6.37)
STD history	1.30 (0.98–1.73)	1.23 (0.92–1.67)	1.23 (0.53–2.82)	1.12 (0.46–2.75)
Nonmarital sex[a]	1.10 (0.73–1.57)	1.13 (0.70–1.72)	1.15 (0.52–2.54)	1.14 (0.50–2.60)
Condom use[a]	1.60 (1.01–2.95)	1.50 (0.90–2.33)	0.62 (0.15–2.60)	0.53 (0.12–2.26)
Circumcision	0.68 (0.44–1.05)	0.70 (0.45–1.08)	0.84 (0.29–2.93)	0.93 (0.32–2.71)

[a] Time dependent variables.

HR, hazard ratio; CI, confidence interval; RPR, rapid plasma reagin test; STD, sexually transmitted disease.

continuous condom promotion and counseling on reduction of risky behaviors.

Acknowledgments: This study was partially funded by an advanced research training award to N. Kumwenda from the Fogarty International Center (grant # D43-TW00010). We are grateful for the management and staff of the Sugar Company of Malawi for their support of the study, and to all the study participants and the field staff for their excellent collaboration. We are grateful for the Health Sciences Research Committee of the Malawi Ministry of Health for their guidance throughout the study. At the Johns Hopkins University, our gratitude is for the Fogarty Research and Training Program (AITRP) for supporting this study, and our appreciation to several colleagues for their helpful comments. The 1994 survey data was part of N. Kumwenda's doctoral dissertation.

N. Kumwenda and T. Taha were the principal investigators; they designed these studies, supervised the conduct of the studies, participated in the analysis and interpretation of the results, and prepared the manuscript. D. Hoover is a biostatistician; he participated in the design, analysis, and preparation of the manuscript. D. Markakis is a data analyst; she supervised data management, performed data analyses and participated in preparation of the manuscript. G. Liomba and D. Chiphangwi are clinicians; they participated in the design, local supervision of the study conduct, and participated in interpretation of the findings and preparation of the manuscript. D. Celentano is a behavioral epidemiologist; he participated in the design, analysis, interpretation of the results, and preparation of the manuscript.

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