Effect of Circumcision on Incidence of Human Immunodeficiency Virus Type 1 and Other Sexually Transmitted Diseases: A Prospective Cohort Study of Trucking Company Employees in Kenya

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To determine the effect of circumcision status on acquisition of human immunodeficiency virus (HIV) type 1 and other sexually transmitted diseases, a prospective cohort study of 746 HIV-1–seronegative trucking company employees was conducted in Mombasa, Kenya. During the course of follow-up, 43 men acquired HIV-1 antibodies, yielding an annual incidence of 3.0%. The annual incidences of genital ulcers and urethritis were 4.2% and 15.5%, respectively. In multivariate analysis, after controlling for demographic and behavioral variables, uncircumcised status was an independent risk factor for HIV-1 infection (hazard rate ratio [HRR] = 4.0; 95% confidence interval [CI], 1.9–8.3) and genital ulcer disease (HRR = 2.5; 95% CI, 1.1–5.3). Circumcision status had no effect on the acquisition of urethral infections and genital warts. In this prospective cohort of trucking company employees, uncircumcised status was associated with increased risk of HIV-1 infection and genital ulcer disease, and these effects remained after controlling for potential confounders.

The relationship between circumcision status and sexually transmitted diseases (STDs) was first described almost 150 years ago by Hutchinson [1]. He observed that the incidence of syphilis among non-Jewish male patients was much higher than among Jewish patients, and he attributed this to the difference in circumcision status in the two groups. A study of Canadian soldiers during World War II found that 90% of syphilis infections occurred among uncircumcised men [2]. Similar findings were reported from the Venereal Clinics of the US Naval Hospital in 1945 [3]. Some 40 years later, there was renewed interest in the relationship between circumcision and STDs, and a number of cross-sectional studies were done on different continents. In Perth, Australia, there was a significant association between uncircumcised status and herpes, gonorrhea, candidiasis, and syphilis [4]. In Seattle, Cook et al. [5] found a positive association between uncircumcised status and syphilis and gonorrhea and a negative association with genital warts. In an STD clinic in Nairobi, Kenya, presence of a male foreskin was significantly associated with genital ulcer disease [6]. A prospective study conducted in Nairobi found that uncircumcised men were at significantly increased risk for human immunodeficiency virus (HIV) type 1 infection [7]. This observation was followed by ecologic studies that found that areas of high HIV-1 seroprevalence in Africa corresponded geographically with areas of low circumcision prevalence [8, 9]. Despite accumulating evidence that uncircumcised status is associated with higher risk of HIV-1 and STDs, it is estimated that only ∼15% of the world's men are circumcised [10].

A prospective cohort of male trucking company employees was established as part of the PAVE/HIVNET initiative in Mombasa, Kenya, in 1993 [11–13]. One of the specific aims of this cohort study was to evaluate the effect of circumcision status on incidence of HIV-1 and other STDs. Detailed information about sexual behavior was collected prospectively to enable control for exposure variables that may serve as potential confounders of the relationship between circumcision and HIV-1 or STD acquisition.

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Informed consent was obtained from all participating subjects before enrollment in the study. The study was approved by the ethical review committees of the University of Nairobi and University of Washington.

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Methods

Study participants and procedures. HIV-1–seronegative male trucking company employees in Mombasa were enrolled in a prospective cohort study between March 1993 and June 1997 as described elsewhere [10–12]. Mobile clinics were held on a weekly basis at 5 different trucking companies. All men underwent pretest counseling and serologic testing for HIV-1 antibodies. Men who tested HIV-1–seronegative were enrolled in the prospective cohort study. All men were tested by *Treponema pallidum* hemagglutination assay (TPHA) and rapid plasma reagin (RPR); a subset had *Haemophilus ducreyi,* herpes simplex virus (HSV) type 2, and *Chlamydia trachomatis* serologic assays.

At study enrollment, all men were interviewed, by use of a standardized form, regarding their demographic and sexual behavior characteristics and medical history. All had physical examinations that included genital examination to evaluate circumcision status and presence of genital ulceration and urethral discharge. Study participants were asked to return for follow-up visits at 3-month intervals. At each subsequent visit, a behavioral questionnaire was administered, a physical examination was done, and 10 mL of blood was drawn for HIV-1 antibody testing. Syphilis testing was repeated at annual intervals. If urethral discharge was present, swabs were taken for Gram's stain and detection of *Neisseria gonorrhoeae* and *C. trachomatis.* In the case of a genital ulcer, the base was scraped and cultured for *H. ducreyi,* and blood was obtained for syphilis testing. Men with urethral discharge or genital ulcer received free standardized treatment. At each visit, men received health education counseling on STD and HIV prevention by the project health educator and a supply of free condoms.

Laboratory procedures. HIV-1 serologic testing was done by ELISA (Detect-HIV; Biochem ImmunoSystem, Montreal). A second confirmatory ELISA (Recombigen; Cambridge Biotech, Worcester, MA) was performed if a sample tested positive on the screening ELISA. All HIV-1 seroconversions during follow-up were confirmed by HIV-1 Western blot (Cambridge Biotech).

Syphilis serologic testing was done by RPR test (Becton Dickinson, Cockeysville, MD) and TPHA (Biotech Laboratories, Lightwater, UK). Incident syphilis infections were defined by a $\geqslant$4-fold increase in RPR titer with a positive TPHA. Prevalent and past syphilis infections were defined by a positive TPHA.

Urethral swabs were cultured for *N. gonorrhoeae* on modified Thayer-Martin medium and tested for *C. trachomatis* antigen by EIA (MicroTrak II; Syva, San Jose, CA). The mean number of polymorphonuclear (PMNL) cells in 3 oil immersion fields of a Gram's-stained slide was determined: urethral inflammation was defined by the presence of $\geqslant$5 PMNL cells. Genital ulcers were cultured on activated charcoal media for detection of *H. ducreyi.*

Antibodies to *H. ducreyi* were detected by lipo-oligosaccharide ELISA [14, 15]. HSV-2 antibody testing was by Western blot, and the distinction between HSV-2 and HSV-1 antibodies was made with densitometric analyses [16]. *C. trachomatis* antibodies were detected by a microimmunofluorescence test [17].

STD definitions. Urethritis was defined by the presence of urethral discharge on physical examination and/or urethral inflammation on a Gram's-stained slide of urethral secretions in the case of missing clinical data. A history of urethral discharge since the last visit was considered an interim case of urethritis and was analyzed separately from cases that were confirmed by use of objective criteria in the clinic. Gonorrhea was diagnosed if a culture of a urethral swab was positive. Because of the few positive samples for *C. trachomatis* antigen, they were grouped with urethral infections. Genital ulcer disease was defined by the presence of a genital ulcer on physical examination or by a culture for *H. ducreyi* in the case of missing clinical data. A history of a genital ulcer since the last visit was considered an interim case. Genital warts were clinically diagnosed. Only the first appearance of genital warts in an individual was included in analysis, since no treatment was provided for this condition and persistence versus recurrence of warts could not be differentiated.

Data management and analysis. Data were double entered by use of SPSS software (SPSS, Chicago) and verified by comparison of line listings and the clinic files. For data analysis, we used SPSS statistical software and S-PLUS (MathSoft, Seattle). For purposes of analysis, men were censored from the time of last documented HIV-1–seronegative visit for analysis of circumcision and incident STDs and from the time of documented HIV-1 seroconversion for analyses of circumcision and incident HIV-1. Enrollment and follow-up information on demographic, behavioral, and clinical characteristics of circumcised and uncircumcised men were compared by use of Pearson's χ^2 test and Fisher's exact test for categorical variables and the Mann-Whitney U test for continuous variables. The effects of potential risk factors for HIV and STDs were evaluated via the hazard rate ratio (HRR), by use of Cox proportional hazards models with the Anderson-Gill adjustment for recurrent STDs (i.e., urethritis, gonorrhea, and genital ulcers). Multivariate analyses controlling for potential confounding factors were performed by use of Cox proportional hazards models. The proportional hazards assumption underlying the models was assessed by Harrell's z test [18].

Results

Population characteristics. Between March 1993 and June 1997, 992 HIV-1–seronegative men were enrolled in the prospective cohort study. We excluded from analysis 236 men who had no follow-up after the enrollment visit. Also excluded were 6 men who were partially circumcised, 1 man with unknown circumcision status, and 3 men who had no HIV serologic test after enrollment. Thus, 746 men who were HIV-1–seronegative at enrollment and returned for $\geqslant$1 follow-up visit were included in the analysis. These men contributed 4713 clinic visits. Men who did not return to the clinic after enrollment were similar with respect to age, marital status, religion, occupational travel, history of sex with prostitutes, history of condom use, and circumcision status.

The median duration of follow-up was 20 months for the whole group and 21 and 20 months for uncircumcised and circumcised men, respectively ($P = .8$). The median number of follow-up visits, 4 (range, 1–18), was the same for uncircumcised and circumcised subjects. The median time between 2 consecutive visits was 4 months (range, 0.6–42). Compliance with follow-up was 69% at 1 year, 52% at 2 years, and 38% at 3 years. There was no significant difference in rates of follow-up by circumcision status. Drivers and assistants showed a significantly greater loss to follow-up than mechanics and ancillary workers.

Enrollment characteristics by circumcision status. Ninety-five (13%) of the 746 men were uncircumcised. For only 1 man were there discordant results between self-reported circumcision status and results of the physical examination. In Kenya, circumcision is often performed shortly before puberty, and the median age at circumcision was 10 years (range, ⩽1–35). Only 14% of the men were circumcised within 1 year of birth. The median age at first sexual intercourse was 15 years, and, among circumcised men, 81% were circumcised before first sexual intercourse.

Uncircumcised men were younger than circumcised men (26 vs. 29 years, $P = .01$) and therefore had fewer years of sexual activity at the time of enrollment (12 vs. 13 years, $P = .06$) (table 1). There were significantly fewer drivers and drivers' assistants among the uncircumcised men, and they spent significantly fewer days per month on the road than circumcised men. Sexual relations with prostitutes during the year prior to study enrollment occurred less often in the uncircumcised group, but there was no significant difference between the two groups in the number of men with a lifetime history of sex with a prostitute. Fewer uncircumcised men reported a history of condom use. Smoking of cigarettes was less common in the uncircumcised group, but the use of alcohol, miraa (an amphetamine-based substance that is chewed), and marijuana was similar in both groups.

Prevalence of STDs at enrollment. At enrollment, 8% of the study population had specific antibodies against *T. pallidum.* A subgroup of the cohort had a number of other tests: 25% were seropositive for *H. ducreyi,* 46% for HSV-2, and 40% for *C. trachomatis.* There were no significant differences between uncircumcised and circumcised men for seropositivity to these STD pathogens.

Sexual behavior characteristics during follow-up and incidence of STDs and HIV-1. In table 2, aggregated follow-up data are shown for sexual behavior during the 3 months prior to each clinic visit. Almost 70% of men reported extramarital sex during the prior 3 months, including 17% who reported unprotected sex with a prostitute. The frequency of extramarital sex acts was low (median, 1 per 3-month period), and unprotected sex contacts were most likely for a married couple. There was no significant difference between uncircumcised and circumcised men for any of the sexual behavior variables.

Forty-three men became infected with HIV-1 during the study period. The annual incidence of HIV-1 infection in this cohort was 3.0%. The annual incidence of observed genital ulcer disease was 4.2%, and the incidence of genital warts was 1.4%. Ninety-two percent of the observed ulcers and 100% of the

Table 1. Demographic, behavioral, and serologic characteristics at enrollment, stratified by circumcision status.

	Median (range) or no. (%)		
	Uncircumcised (n = 95)	Circumcised (n = 651)	P
Age	26 (17–58)	29 (16–62)	.01
Currently married	53 (56)	413 (63)	.2
Religion			<.001
Christian	91 (96)	454 (70)	
Muslim	1 (1)	159 (24)	
Other	3 (3)	38 (6)	
Years of education	9 (0–13)	9 (0–16)	1.0
Years of employment in company	3 (0–24)	4 (0–38)	.3
Occupation			<.001
Drivers and assistants	12 (13)	217 (33)	
Mechanics and ancillary workers	83 (87)	434 (67)	
Days on road/month			.009
0	65 (68)	362 (56)	
1–14	21 (22)	140 (22)	
>14	9 (10)	149 (23)	
Age at first sexual intercourse	15 (10–28)	15 (9–30)	.3
Years of active sex	12 (1–38)	13 (0–45)	.06
History of sex with prostitutes	49 (52)	372 (57)	.3
History of condom use	41 (43)	362 (56)	.02
Extramarital sex in past year	60 (63)	450 (69)	.2
Unprotected extramarital sex in past year	55 (58)	366 (56)	.8
Sex with prostitute in past year	21 (22)	214 (33)	.03
Unprotected sex with prostitute in past year	18 (19)	127 (20)	.9
No. of sex partners in past year	2 (0–50)	2 (0–99)	.5
Use of cigarettes	21 (22)	276 (42)	<.001
Use of alcohol	47 (50)	299 (46)	.5
Use of miraa[a]	11 (12)	94 (14)	.5
Treponema pallidum hemagglutination assay–positive	11 (12)	48 (8)	.1
Haemophilus ducreyi antibodies (n = 408)	10 (18)	91 (26)	.2
HSV-1 antibodies (n = 113)	48 (100)	64 (99)	1.0
HSV-2 antibodies (n = 113)	20 (42)	32 (49)	.4
Chlamydia trachomatis antibodies (n = 116)	15 (31)	31 (46)	.1

NOTE. HSV, herpes simplex virus.

[a] Plant containing amphetamine-based substance.

Table 2. Sexual behavior characteristics during follow-up.

	Median (range) or no. (%)		
	Uncircumcised (n = 95)	Circumcised (n = 651)	P
No. of sex partners[a]	1 (0–30)	1 (0–10)	.7
Frequency of sex acts	13 (0–59)	12 (0–126)	.8
Frequency of sex acts with wife	8 (0–58)	9 (0–75)	.8
Frequency of unprotected sex acts with wife	8 (0–58)	9 (0–75)	.8
Frequency of unprotected sex acts	12 (0–59)	12 (0–75)	.8
Frequency of extramarital sex acts	2 (0–30)	1 (0–90)	.6
Frequency of unprotected extramarital sex acts	0.5 (0–30)	0.3 (0–50)	.4
Any sex with prostitute	26 (27)	156 (24)	.5
Any extramarital sex	66 (70)	444 (68)	.8
Any unprotected sex	87 (92)	607 (93)	.5
Any unprotected sex with prostitute	22 (23)	107 (16)	.1
Any unprotected extramarital sex	58 (61)	375 (58)	.5

[a] Per 3-month period for all variables.

genital warts were penile. Forty-one men reported 48 episodes of genital ulcer disease occurring between clinic visits, yielding an annual incidence of self-reported genital ulcers of 3.4%. There were 220 episodes of observed urethritis (annual incidence, 15.5%) and 124 episodes of self-reported urethritis (annual incidence, 9.1%). For 198 observed episodes, a culture was obtained, and 102 (51.5%) were positive for *N. gonorrhoeae* (annual incidence, 7.2%).

In univariate analysis, uncircumcised status was associated with significantly increased risk of HIV-1 infection (HRR = 2.3, P = .02) (table 3). Uncircumcised status was also significantly associated with observed genital ulcers (HRR = 1.9, P = .04), self-reported genital ulcers (HRR = 2.8, P = .008), and all genital ulcers (HRR = 2.3, P = .001). There was no significant relationship between male circumcision and observed urethritis (including gonorrhea), reported urethritis, or warts.

Cox proportional hazards models were used to explore the effect of potential confounders on the influence of circumcision status on the acquisition of HIV-1, genital ulcer disease, and urethritis. These models included observed episodes of genital ulcer disease and urethritis and not self-reported episodes. Enrollment demographic and occupational variables that were associated with circumcision status with $P \leqslant .1$ (age, religion, occupation, days on the road, and smoking) and sexual behavior variables during follow-up (any unprotected sex with a prostitute, any unprotected sex with a girlfriend or casual partner, any extramarital sex, and any condom use) were considered for inclusion in the multivariate models. Those variables that were significantly associated with the outcome variable of interest were retained in the final models.

The only variables that were significantly associated ($P <$ .05) with HIV-1 seroconversion were circumcision status, occupation, religion, and extramarital sex during follow-up (table 4). Uncircumcised men had a 4-fold increased hazard for acquiring HIV-1 (HRR = 4.0, 95% confidence interval [CI], 1.9–8.3), compared with circumcised men, after adjusting for potential confounders. The fact that the HRR increased from 2.3 to 4.0 between the univariate and the multivariate models may be explained by the higher risk profile of the uncircumcised men. When we considered a multivariate model for HIV-1 acquisition that included genital ulcer disease, the estimated HRR for circumcision decreased slightly (from 4.0 to 3.7, data not shown). The effect of genital ulcer disease was not significant.

Next, we explored the association between circumcision status and genital ulcer disease. The variables significantly associated with genital ulcer disease in a multivariate model were circumcision status, occupation, and unprotected extramarital

Table 3. Incidence of sexually transmitted diseases stratified by circumcision status.

	Incidence/100 person-years (no.)[a]			Hazard rate ratio	95% CI	P
	All men	Uncircumcised	Circumcised			
Human immunodeficiency virus type 1	3.0 (43)	5.9 (11)	2.5 (32)	2.3	1.1–4.4	.02
Observed genital ulcer	4.2 (59)	7.3 (13)	3.7 (46)	1.9	1.0–3.6	.04
Self-reported genital ulcer	3.4 (48)	7.9 (14)	2.8 (34)	2.8	1.3–6.1	.008
All genital ulcers (observed + self-reported)	7.6 (107)	15.2 (27)	6.5 (80)	2.3	1.4–3.9	.001
Observed urethritis	15.5 (220)	17.5 (31)	15.3 (189)	1.1	0.7–1.8	.6
Gonococcal	7.2 (102)	7.9 (14)	7.1 (88)	1.1	0.6–2.1	.8
Nongonococcal	6.8 (96)	8.5 (15)	6.6 (81)	1.3	0.7–2.4	.4
Self-reported urethritis	9.1 (124)	9.2 (16)	9.1 (108)	1.0	0.5–2.0	.9
All urethritis (observed + self-reported)	24.3 (344)	26.4 (47)	24.0 (297)	1.1	0.7–1.7	.6
Genital warts	1.4 (19)	1.7 (3)	1.3 (16)	1.3	0.4–4.4	.7

NOTE. CI, confidence interval.
[a] No. of episodes of each condition. For warts, only first episode was included.

Table 4. Multivariate analysis of covariates for HIV-1 seroconversion and acquisition of other STDs.

Risk factor[a]	Hazard rate ratio	95% confidence interval	*P*
HIV-1			
Uncircumcised	4.0	1.9–8.3	<.001
Driver/assistant	4.9	2.5–9.5	<.001
Non-Christian/non-Muslim	3.5	1.3–9.2	.009
Extramarital sex	3.7	1.3–10.6	.01
Genital ulcer disease			
Uncircumcised	2.5	1.1–5.3	.02
Driver/assistant	2.2	1.2–4.1	.02
Unprotected extramarital sex	3.6	1.9–6.7	<.001
Urethritis			
Uncircumcised	1.1	0.7–1.8	.7
Driver/assistant	1.3	4.9–10.7	<.001
Unprotected extramarital sex	7.2	0.9–1.9	.2

[a] The reference category for each variable is converse of that variable.

sex during follow-up. Uncircumcised men were at significantly higher risk for acquiring genital ulcers, with an adjusted HRR of 2.5 (95% CI, 1.1–5.3). In a similar multivariate model with circumcision status, occupation, and unprotected extramarital sex as covariates, there was no significant association between urethritis and circumcision status.

For all three models, when additional potentially confounding variables, other than those shown in table 4, were included, the conclusions as to the effect of circumcision on the outcome (acquisition of HIV-1, genital ulcer disease, or urethritis) were essentially unchanged.

Discussion

In this prospective cohort study, uncircumcised men were at 4-fold increased risk for acquiring HIV-1 infection. This is the first published prospective study with this finding in an occupationally based cohort, which may be more representative of the general population than cohorts recruited from STD clinics. In addition to HIV-1 risk, uncircumcised status was associated with a 2.5-fold increased risk of genital ulcer disease. The possibility that genital ulcer disease was in the causal pathway between circumcision and HIV-1 acquisition was assessed by comparison of multivariate models with and without genital ulcer disease. We found that the association between circumcision and HIV-1 infection was independent of genital ulcer disease. The risk of urethritis and genital warts was not affected by the presence of a foreskin.

In a literature review of circumcision and HIV-1, Moses et al. [19] identified 26 cross-sectional studies. Eleven studies found a significant difference in HIV-1 prevalence between circumcised and uncircumcised men after adjusting for potential confounders, including indices of sexual behavior, with odds ratios of 1.5–5.6. Six other studies found a significant difference, but no adjustment for possible confounders was reported. We found only 3 prospective studies published in the literature. Cameron et al. [7] studied the effect of circumcision on the risk of HIV-1 seroconversion in a group of male STD patients in Nairobi and found a risk ratio of 8.2 for uncircumcised men after adjusting for potential confounders. In studies of STD clinic patients in New York City and in Pune, India, there were trends for uncircumcised men to be at increased risk of HIV-1 acquisition, but these associations were not statistically significant [20, 21].

Several physiologic mechanisms might explain the association between an intact foreskin and increased risk of HIV-1 and genital ulcers. In uncircumcised men, the epithelium lining the glans and preputial sac is thinner and less cornified than that of circumcised men and therefore may be more susceptible to traumatic lesions during sexual intercourse and to the transfer of microorganisms between partners [22]. The environment of the preputial sac may be favorable for the survival and replication of bacteria and viruses, allowing for a longer exposure time for infections to occur. This effect may be accentuated by poor hygienic practices. Finally, the stratified squamous epithelium of the foreskin contains target cells for HIV-1 (Langerhans cells and macrophages that are coated with CD4 receptors) [22].

In an overview article, de Vincenzi and Mertens [23] summarized a number of methodologic limitations of studies evaluating the effect of circumcision status on STD and HIV infection [23]. First, differences in sexual behavior between uncircumcised and circumcised men may result in important confounding bias. In our study, men were followed prospectively, and a detailed assessment of sexual behavior was conducted at each return visit. For none of the sexual behavior variables was there a significant difference between uncircumcised and circumcised men. However, uncircumcised and circumcised men differed significantly with respect to occupation and religion, both of which were associated with HIV-1 acquisition. In a multivariate model that adjusted for confounding factors, the HRR for the association between circumcision status and HIV-1 incidence increased. Second, many studies of circumcision and HIV or STDs have been conducted in STD-clinic settings, which may limit the generalizability of results. This prospective cohort study of trucking company employees is probably more representative of a general adult male population. Third, exposure misclassification of circumcision status may occur if there is reliance on self-report. In this cohort, the self-assessment of circumcision status by men was verified during the physical examination, and there was 99% concurrence. Partially circumcised men were excluded from the analysis. Furthermore, to ensure optimal measure of the outcome variables of interest, data on STDs were collected in two ways: symptomatic STDs present at a clinic visit were assessed by physical examination and/or laboratory diagnosis, and STD syndromes occurring between clinic visits were tabulated through self-report. Observed and self-reported STDs were analyzed separately, and the circumcision associations were similar for both types of data. In the multivariate model, only observed STDs were included.

Our study had several limitations. First, retention of men in the cohort was imperfect, and loss to follow-up may have biased results. We believe that much of this loss occurred when men left employment at a given company, particularly during a period of economic recession in Kenya, while the study was ongoing. No significant correlates of loss to follow-up were identified that were likely to have influenced the results. Second, no information is available regarding HIV-1 and STD infection status of the female partners of these men. Almost one-third of the study population were truck drivers or assistants and therefore were highly mobile. Whether men acquired STD or HIV-1 infections in Mombasa or while traveling is unknown, and the relative exposure risk of female partners in different locales is also an uncertainty. Third, ideally adjustments for ethnic origin should be made, since there is a complex interaction between traditional ethnic customs (including sexual behavior), religion, and male circumcision. In Kenya, circumcision is done by most large ethnic groups, with the exception of the Luo group, a Nilotic people living near Lake Victoria [24]. The area around Lake Victoria has the highest HIV-1 seroprevalence in the general population in Kenya [25]. Because uncircumcised status and ethnicity were so closely correlated, it was not possible to independently assess the effects of circumcision and ethnic origin. If men are more likely to have sex with women of their own ethnic group, it is possible that Luo men would have a higher rate of exposure to HIV-1–infected partners. Fourth, in this cohort, only 13% of the participants were uncircumcised, resulting in low power to detect associations.

Male circumcision is practiced in different societies all over the world, for religious, cultural/secular, and medical reasons. Male circumcision as a religious tradition is practiced by Jews and Muslims, usually during the neonatal period [10]. Within sub-Saharan Africa, male circumcision is most often performed for cultural reasons and is largely determined by ethnicity. The procedure is often done shortly before or at puberty and is considered a rite of passage to adulthood. First sexual intercourse often takes place soon after the circumcision, as we found in our study [26]. In the United States, male circumcision is largely a secular decision, and its frequency has changed over time [27]. The American Academy of Pediatrics Task Force on Circumcision stated in its 1999 revision on circumcision policy that circumcision conferred potential medical benefits, which could be considered by parents but that the scientific evidence was insufficient to warrant recommending routine neonatal circumcision [28]. Currently, ~80% of men in the United States are circumcised, with higher rates for Caucasians than for African Americans and Hispanics [27]. In contrast, circumcision is less often practiced in Canada and in Europe [29], and within Asia there is considerable country-to-country variation in circumcision prevalence [30].

In the 150 years since Hutchinson [1] published his findings, a number of studies have evaluated the effect of circumcision on the acquisition of HIV-1 and STDs. The majority have found a protective effect of male circumcision on acquisition of genital ulcers and HIV-1. The results of this prospective cohort of male trucking company employees add substantial weight to these findings, since our prospective study design, detailed assessment of sexual behavior at each follow-up visit, and objective assessment of STDs avoids the major limitations that have characterized many prior studies. Despite the consensus that emerges from the literature, the implementation of circumcision promotion as a population-based intervention to reduce HIV-1 and STD incidence has not been seriously entertained. We acknowledge that attitudes toward male circumcision may be difficult to change in some settings, but we encourage behavioral scientists to conduct acceptability studies, particularly in high HIV-1–prevalence communities, to begin assessing feasibility of circumcision promotion.

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References

1. Hutchinson J. On the influence of circumcision in preventing syphilis. Med Times Gaz **1855**;2:542–3.
2. Wilson R. Circumcision and venereal disease. Can Med Assoc J **1947**;56:54–6.
3. Hand E. Circumcision and venereal disease. Arch Dermatol Syphilol **1949**;60:341–6.
4. Parker S, Stewart A, Wren M, Gollow M, Straton J. Circumcision and sexually transmitted diseases. Med J Aust **1983**;2:288–90.
5. Cook L, Koutsky L, Holmes K. Circumcision and sexually transmitted diseases. Am J Public Health **1994**;84:197–201.
6. Nasio J, Nagelkerke N, Mwatha A, Moses S, Ndinya-Achola J, Plummer F. Genital ulcer disease among STD clinic attenders in Nairobi: association with HIV-1 and circumcision status. Int J STD AIDS **1996**;7:410–4.
7. Cameron D, Simonsen J, D'Costa L, et al. Female to male transmission of human immunodeficiency virus type 1: risk factors for seroconversion in men. Lancet **1989**;2:403–7.
8. Bongaarts J, Reining P, Way P, Conant F. The relationship between male circumcision and HIV infection in African populations. AIDS **1989**;3:373–7.
9. Moses S, Bradley J, Nagelkerke N, Ronald A, Ndinya-Achola J, Plummer F. Geographical patterns of male circumcision practices in Africa: association with HIV prevalence. Int J Epidemiol **1990**;19:693–7.
10. Waszak S. The historic significance of circumcision. Obstet Gynecol **1978**;51:499–501.
11. Martin H, Jackson D, Mandaliya K, et al. Preparation for AIDS vaccine evaluation in Mombasa, Kenya: establishment of seronegative cohorts of commercial sex workers and trucking company employees. AIDS Res Hum Retroviruses **1994**;10:S235–7.
12. Jackson D, Rakwar J, Richardson B, et al. Decreased incidence of sexually transmitted diseases among trucking company workers in Kenya: results of a behavorial risk-reduction programme. AIDS **1997**;11:903–9.

13. Rakwar J, Lavreys L, Thompson ML, et al. Cofactors for acquisition of HIV-1 among heterosexual men: prospective cohort study of trucking company workers in Kenya. AIDS **1999**; 13:607–14.
14. Alfa M, Olson N, Degagne P, et al. Humoral immune response of humans to lipooligosaccharide and outer membrane proteins to *Haemophilus ducreyi.* J Infect Dis **1993**; 167:1206–10.
15. Rakwar J, Jackson D, Maclean I, et al. Antibody to *Haemophilus ducreyi* among trucking company workers in Kenya. Sex Transm Dis **1997**; 24: 267–71.
16. Ashley R, Militoni J. Use of densitometric analysis for interpreting HSV serologies based on Western blot. J Virol Methods **1987**; 18:159–68.
17. Wang S, Grayston J, Alexander E, Holmes K. Simplified microimmunofluorescence test with trachoma-lymphogranuloma venereum *(Chlamydia trachomatis)* antigens for use as a screening test for antibody. J Clin Microbiol **1975**; 1:250–5.
18. Harrell FE. The PHGLM procedure. In: SAS supplemental library user's guide, version 5. Cary, NC: SAS Institue, **1986**.
19. Moses S, Plummer F, Bradley J, Ndinya-Achola J, Nagelkerke N, Ronald A. The association between lack of male circumcision and risk for HIV infection: a review of the epidemiological data. Sex Transm Dis **1994**; 21: 201–10.
20. Telzak E, Chiasson M, Bevier P, Stoneburner R, Catro K, Jaffe H. HIV-1 seroconversion in patients with and without genital ulcer disease: a prospective study. Ann Intern Med **1993**; 119:1181–6.
21. Mehendale SM, Rodrigues JJ, Brookmeyer RS, et al. Incidence and predictors of human immunodeficiency virus type 1 seroconversion in patients attending sexually transmitted disease clinics in India. J Infect Dis **1995**; 172:1486–91.
22. Jessamine PG, Plummer FA, Ndinya-Achola JO, et al. Human immunodeficiency virus, genital ulcers and the male foreskin: synergism in HIV-1 transmission. Scand J Infect Dis Suppl **1990**; 69:181–6.
23. de Vincenzi I, Mertens T. Male circumcision: a role in HIV prevention? AIDS **1994**; 8:153–60.
24. Dodge O, Kaviti J. Male circumcision among the peoples of East Africa and the incidence of genital cancer. East Afr Med J **1965**; 42:98–105.
25. Okeyo T, Baltazar G, Stover J, Johnston A. AIDS in Kenya: background, projections, impact, intervention. Nairobi: NASCOP, **1996**.
26. Krantz I, Ahlberg B. Circumcision and HIV. Lancet **1995**; 345:730.
27. Laumann E, Masi C, Zuckerman M. Circumcision in the United States. JAMA **1997**; 277:1052–7.
28. American Academy of Pediatrics Task Force on Circumcision. Circumcision policy statement. Pediatrics **1999**; 103:686–93.
29. Schoen E. Benefits of newborn circumcision: is Europe ignoring medical evidence? Arch Dis Child **1997**; 77:258–60.
30. Weniger B, Brown T. The march of AIDS through Asia. N Engl J Med **1996**; 335:343–5.