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Male circumcision and HIV infection in four cities in sub-Saharan Africa

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Objectives: To explore the role of male circumcision in the spread of HIV infection in four urban populations in sub-Saharan Africa.

Design and methods: A cross-sectional population based study was conducted in four cities in sub-Saharan Africa with different levels of HIV infection. HIV prevalence among adults was relatively low in Cotonou (Benin) and in Yaoundé (Cameroon), and exceeded 25% in Kisumu (Kenya) and in Ndola (Zambia). In each city, a random sample was taken of men and women aged 15–49 years from the general population. Consenting study participants were interviewed about their socio-demographic characteristics and their sexual behaviour, and were tested for HIV, herpes simplex virus type 2, syphilis, gonorrhoea and chlamydial infection. Men underwent a genital examination.

Results: In Cotonou and in Yaoundé, the two low HIV prevalence cities, 99% of men were circumcised. In Kisumu 27.5% of men were circumcised, and in Ndola this proportion was 9%. In Kisumu, the prevalence of HIV infection was 9.9% among circumcised men and 26.6% among uncircumcised men. After controlling for socio-demographic characteristics, sexual behaviour and other sexually transmitted infections, the protective effect of male circumcision remained with an adjusted odds ratio of 0.26 (95% confidence interval = 0.12–0.56). In Ndola, the prevalence of HIV infection was 25.0% in circumcised men and 26.0% in uncircumcised men. The power was insufficient to adjust for any differences in sexual behaviour.

Conclusions: The differences in epidemic spread of HIV are likely to be due to differences in the probability of transmission of HIV during sexual exposure as well as differences in sexual behaviour. Male circumcision is one of the factors influencing the transmission of HIV during sexual intercourse, and this study confirms the population level association between HIV and lack of male circumcision, as well as a strong individual level association in Kisumu, the only city with sufficient power to analyze this association.

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Introduction

The role of male circumcision in the spread of HIV in sub-Saharan Africa was first suggested more than 10 years ago [1]. Ecological studies found a correlation between the practice of male circumcision and the prevalence of HIV infection in the general population that suggested that HIV was more prevalent in areas in sub-Saharan Africa where male circumcision was not practised than in areas where men were circumcised

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[2,3]. There were several limitations to these studies. The high HIV prevalence in some areas may have been due to an earlier start of the epidemic, and no allowance was made for possible differences in sexual behaviour and in other sexually transmitted infections (STIs) between the different population groups [4].

In addition, several epidemiological studies were conducted in Africa that included male circumcision as a potential risk factor for HIV infection at the individual level. These studies allowed for differences in sexual behaviour but came up with varying strengths of the association between circumcision and HIV risk. A recent systematic review and meta-analysis of these studies showed a highly significant protective effect overall with the strongest effect in populations at high risk for HIV and STIs [5].

In the multicentre study on factors determining the differential spread of HIV in African cities, we took male circumcision into consideration as one of the possible factors that could explain the differences in rate of spread of HIV between Cotonou (Benin), Yaoundé (Cameroon), Kisumu (Kenya) and Ndola (Zambia). This paper presents the results of the analyses of the association between male circumcision and HIV.

Methods

The methods of the study are described in detail elsewhere [6]. Briefly, the study took place in four cities in sub-Saharan Africa: two with a relatively low and stable prevalence of HIV (Cotonou, Benin and Yaoundé, Cameroon), and two with a high prevalence of HIV (Kisumu, Kenya and Ndola, Zambia). We believe that the differences in prevalence between these four cities were due to differences in rate of spread of HIV rather than differences in time since the start of the epidemics. In each of the four cities, a random sample was taken of about 2000 adults aged 15–49 years. Consenting men and women were first interviewed about their socio-economic background and sexual behaviour. The questionnaire on sexual behaviour also included a section on characteristics of any non-spousal partners in the past 12 months. Men were interviewed about their circumcision status, age at circumcision, symptoms suggestive of a STI in the past 12 months, and health-seeking behaviour for STIs.

After the interview, men and women were asked to provide a blood sample, which was tested for HIV, herpes simplex virus type 2 (HSV-2) and syphilis, and a urine sample, which was tested for gonorrhoea and chlamydial infection by DNA amplification techniques. Men underwent a genital examination to confirm the reported circumcision status and to check for any signs of STI (mainly genital ulceration and urethral discharge). The circumcision status was recorded as 'circumcised', 'not circumcised' or 'uncertain circumcision status'. Nineteen men in Cotonou and one man in Ndola and in Kisumu had uncertain circumcision status and were excluded from the analyses.

All data were double-entered and validated in EPI-INFO version 6.04a (CDC, Atlanta, Georgia, USA). Further data cleaning, and data analysis was carried out with SPSS version 8.0 for Windows (SPSS, Inc, Chicago, Illinois, USA). The analyses presented in this paper are restricted to men who reported that they had ever had sex. The proportions of men who were circumcised and the age at circumcision were compared across the four cities. For each city, the association between circumcision and HIV infection was explored. Where the power was sufficient, multivariate regression analyses were conducted. The following variables were considered as potential confounding factors: socio-demographic characteristics (age, educational attainment, occupation, religion, ethnic group, travel in the past 12 months), sexual behaviour (age at first sexual intercourse, marital status, lifetime number of sex partners, number of non-spousal partners in the past 12 months, one-off sexual contacts or contacts with a sex worker in the past 12 months), and other STIs (HSV-2 infection, syphilis, gonorrhoea and chlamydial infection). Variables were selected for inclusion in the logistic regression model using the forward stepwise procedure. Variables that were associated with HIV infection at a significance level of 0.15 or less were entered into the model. In the final model, only those variables were retained that were associated with HIV infection at a significance level of 0.05 or less.

To exclude the possibility that the lower risk of HIV infection in circumcised men is due to the fact that their partners are less HIV infected than the partners of uncircumcised men, estimates were made of the HIV prevalence in spousal and in non-spousal partners of both groups of men. The reported characteristics of non-spousal partners (ethnic group, age and marital status) were compared between circumcised men and uncircumcised men. Using the distribution of these characteristics and the data on HIV infection in women who reported non-spousal partnerships in the past 12 months, the prevalence of HIV infection was estimated in the non-spousal partners of men. As for the spouses, the comparison was made between spouses of HIV-negative circumcised men and HIV-negative uncircumcised men.

Results

Prevalence of circumcision in the four cities and its association with HIV infection

Table 1 presents the numbers of men who were interviewed and the numbers who were examined, in each city. In Cotonou and Yaoundé, there was excellent agreement between interview reports of being circumcised and clinical examination, but almost all men who

Table 1. Circumcision status as reported by men and as ascertained by clinical examination

	Cotonou	Yaoundé	Kisumu	Ndola
Total number of men interviewed	1021	973	829	720
Number of men who had had sex	894	882	765	642
Number of sexually active men who were examined	767	784	568	512
% of men who reported being circumcised and were confirmed circumcised on clinical examination	723/729 (99.2%)	755/761 (99.2%)	148/164 (90.2%)	41/56 (73.2%)
% of men who reported not being circumcised and were confirmed not circumcised on clinical examination	1/18 (5.6%)	1/22 (4.5%)	394/402 (98.0%)	448/453 (98.9%)

Table 2. Circumcision status as ascertained by clinical examination and prevalence of HIV infection by circumcision status

	Cotonou	Yaoundé	Kisumu	Ndola
% circumcised	741/748 (99.1%)	777/784 (99.1%)	156/567 (27.5%)	46/511 (9.0%)
% HIV-positive[a]				
Circumcised	27/735 (3.7%)	35/775 (4.5%)	14/141 (9.9%)	11/44 (25.0%)
Uncircumcised	0/7 (0%)	1/7 (14.3%)	96/361 (26.6%)	117/450 (26.0%)
Odds ratio (95% confidence interval)	51 (0 to > 100)	0.3 (0.03–2.4)	0.3 (0.2–0.6)	1.0 (0.5–1.9)
Power (%) to detect a twofold difference in HIV prevalence between circumcised men and uncircumcised men	9	11	91	48

[a] The total figures of men who were and were not circumcised do not tally with the figures in the top row because not all men were tested for HIV.

said they were not circumcised were in actual fact circumcised. In Kisumu and Ndola, there was very good agreement between reports of not being circumcised and clinical examination (> 95% agreement). Men who said they were circumcised, however, misreported their circumcision status in 9.8 and 26.8% of cases, respectively. In the further analyses, the differentiation between circumcised men and uncircumcised men was made based on the clinical examination results.

In Cotonou and Yaoundé, the two low HIV prevalence cities, almost all men were circumcised (Table 2). In these cities, almost all men (> 99%) reported being circumcised before becoming sexually active. In Ndola, only 9.0% of men were circumcised, of whom 87% (34/39) were circumcised before their first sexual experience. In Kisumu, 27.5% of men were circumcised, of whom 83% (120/145) were circumcised before they became sexually active. The median age at circumcision was 4 years in Cotonou and Yaoundé, 11 years in Kisumu and 10 years in Ndola. The proportion of men circumcised after the age of 20 years was 0.0% in Cotonou and Ndola, 0.1% in Yaoundé, and 8.3% in Kisumu.

In each of the four cities, circumcision is practised primarily out of cultural preference rather than because of religious affiliation. In Cotonou and Yaoundé, circumcision is practised by all ethnic groups. In Kisumu only 10% of Luo men, the predominant ethnic group, were circumcised compared with 85% of men belonging to other ethnic groups (mainly Luya). In Ndola, 4–5% of men belonging to the two main ethnic groups, Bemba and Nyanja, were circumcised compared with 24% of men belonging to the other ethnic groups. Of the circumcised men in Cotonou, Yaoundé and Kisumu, approximately 13% were Muslim; in Ndola, this proportion was 7%.

Table 2 presents the HIV prevalence in men by circumcision status. In Kisumu, the prevalence of HIV infection was significantly lower in circumcised men (9.9%) than in men who were not circumcised (26.6%). In Cotonou and Yaoundé, there were seven uncircumcised men, of whom none and one, respectively, were HIV seropositive. In Ndola, the prevalence was about the same in the two groups. Figure 1 presents the HIV prevalence in the different ethnic groups in the four cities by the proportion of men who are circumcised. The HIV prevalence is negatively correlated with the proportion of men who are circumcised (Spearman correlation = –0.85, $P = 0.000$, $n = 14$).

In Kisumu, the prevalence of HIV infection was 5.5% in men who were circumcised before first sexual intercourse, 26.1% in men who were circumcised after age at first sex, and 26.6% in uncircumcised men. The difference in prevalence between men who were circumcised before and after first sexual intercourse was statistically

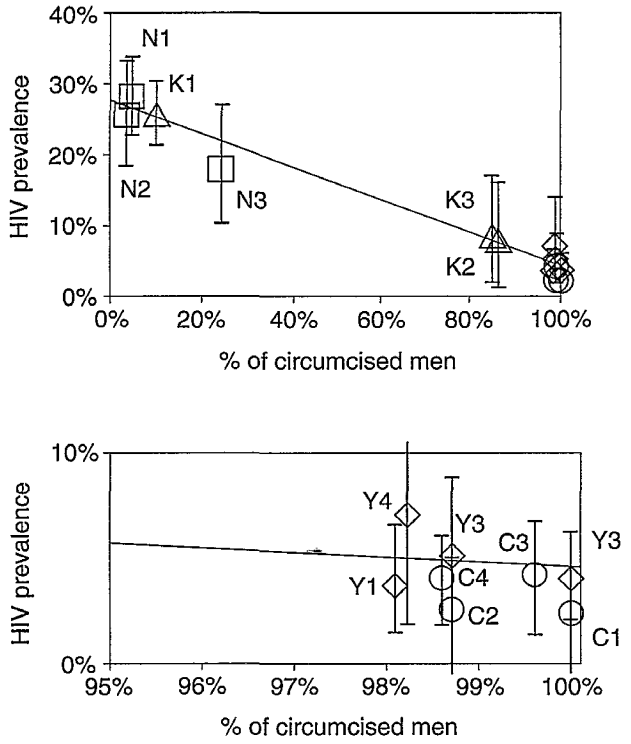

Fig. 1. HIV prevalence versus proportion of circumcised men in each ethnic group of men (see text) in Cotonou (A), Yaoundé (H), Kisumu (B) and Ndola (G). In each figure, the regression line has been drawn. The ethnic groups are: in Ndola: N1, Bembas; N2, Nyanjas; N3, others; in Kisumu: K1, Luos; K2, Luyas; K3, others; in Yaoundé: Y1, Bassas & bakokos; Y2, Pahouins; Y3, Bamilekes; Y4, others; in Cotonou: C1, Ninas; C2, Gouns; C3, Fons; C4, others.

significant ($P = 0.007$). In Ndola, one of the five men who were circumcised after age at first sex was HIV infected, compared with 20.5% (8/39) of the men who were circumcised before first sexual intercourse. In the further analyses, the circumcised men include all men who were circumcised regardless of the age at which it was performed.

Kisumu was the only city where the power was sufficient to allow multivariate analysis of circumcision as a risk factor for HIV infection (Table 2).

Male circumcision as a protective risk factor for HIV infection in Kisumu

In Kisumu, circumcised men were less likely to have had their first sexual experience before age 15 than men who were not circumcised; they had a higher educational attainment and were more likely to have a full-time job (Table 3). Luo men were under-represented among circumcised men, as circumcision is traditionally not practised by the Luo. Almost all Muslims were circumcised. There were no statistically significant differences between circumcised men and uncircumcised men in marital status, lifetime number of sex partners, number of non-spousal partners in the past 12 months, one-off sexual contacts and contacts with sex workers in the past 12 months, alcohol consumption and condom use. However, circumcised men had less HSV-2 infection and syphilis, and were less likely to report an episode of STI in the past 12 months than men who were not circumcised.

Table 3 also presents the odds ratios (OR) for HIV infection associated with circumcision status, stratified on each of the variables used in the comparison between circumcised men and uncircumcised men. In these stratified analyses, there was no evidence for confounding of the protective effect of male circumcision by any of these variables. There was also no significant interaction.

Table 4 presents the results of the univariate analysis of risk factors for HIV infection, in all men and in Luo men only. Apart from circumcision status, the following socio-demographic and behavioural variables were significantly associated with risk of HIV infection: age, marital status, lifetime number of sex partners, number of non-spousal partners in the past 12 months, alcohol consumption and occupation. Men with HSV-2 infection or syphilis and men who reported STI symptoms in the past 12 months were significantly more likely to be HIV infected. In the logistic regression model including the socio-demographic and behavioural variables circumcision status, marital status and alcohol consumption were independent risk factors for HIV infection (Table 5). After adding the STI variables to the model, marital status was no longer significantly associated with HIV risk. Circumcision status, alcohol consumption, HSV-2 infection and history of STI symptoms in the past 12 months remained independent risk factors for HIV infection. The results were similar for all men and for Luo men only: in the final model including the STI variables, the OR was 0.26 [95% confidence interval (CI) = 0.12–0.56] and 0.21 (95% CI = 0.06–0.78), respectively.

Information was available on 329 non-spousal partners of uncircumcised men and 133 non-spousal partners of men who were circumcised. Table 6 compares a few characteristics of these partners, who were used to estimate the prevalence of HIV among the partners of both groups of men. Circumcised men tended to have older partners and were less likely to have Luo partners than uncircumcised men. The estimated prevalence of HIV infection among the partners of both groups of men was the same (32%).

Data were available on 117 spouses of HIV-negative men in Kisumu. Of the spouses of circumcised men, 9.7% (3/31) were HIV infected, whereas 18.6% (16/86) of spouses of uncircumcised men were HIV infected. The difference was not statistically significant ($P = 0.2$).

Table 3. Comparison between men in Kisumu who are and men who are not circumcised

	Not circumcised, *n* (%)	Circumcised, *n* (%)	Odds ratio (95% confidence interval) for association between HIV and circumcision
Sample	361 (100)	141 (100)	0.30 (0.18–0.55)
Age			
15–19 years	77 (21.3)	20 (14.2)	0.96 (0.10–9.1)
20–29 years	131 (36.3)	66 (46.8)	0.31 (0.12–0.78)
30–39 years	97 (26.9)	39 (27.7)	0.15 (0.05–0.45)
40–49 years	56 (15.5)	16 (11.3)	0.48 (0.12–1.9)
	$P = 0.08$		
Marital status			
Never married	151 (41.8)	59 (42.1)	0.16 (0.02–1.2)
Ever married	210 (58.2)	81 (57.9)	0.30 (0.16–0.59)
	$P = 1.0$		
Age at first sex			
> 14 years	243 (67.3)	108 (77.7)	0.27 (0.13–0.56)
≤ 14 years	118 (32.7)	31 (22.3)	0.31 (0.09–1.1)
	$P = 0.03$		
Number of lifetime partners			
1–3	101 (28.0)	42 (29.8)	0.31 (0.07–1.4)
4–9	154 (42.7)	47 (33.3)	0.38 (0.15–0.95)
> 9	47 (29.4)	52 (36.9)	0.22 (0.09–0.57)
	$P = 0.13$		
Number of non-spousal partners in past 12 months			
0	175 (48.5)	60 (42.6)	0.23 (0.10–0.53)
1	108 (29.9)	49 (34.8)	0.47 (0.17–1.3)
> 1	78 (21.6)	32 (22.7)	0.41 (0.08–1.9)
	$P = 0.46$		
One-off contact or commercial sex in past 12 months			
0	338 (93.6)	131 (92.9)	0.32 (0.17-0.58)
≥ 1	23 (6.4)	10 (7.1)	–
	$P = 0.84$		
Alcohol			
< Once a month	239 (66.2)	122 (62.4)	0.36 (0.16–0.84)
≥ Once a month	122 (33.8)	53 (37.6)	0.21 (0.09–0.52)
	$P = 0.47$		
Education			
No primary	96 (26.6)	29 (20.6)	0.21 (0.05–0.95)
Primary complete	154 (42.7)	47 (33.3)	0.48 (0.20–1.2)
Secondary/higher	111 (30.7)	65 (46.1)	0.23 (0.08–0.61)
	$P = 0.005$		

Continued overleaf

Table 3. Continued

	Not circumcised, *n* (%)	Circumcised, *n* (%)	Odds ratio (95% confidence interval) for association between HIV and circumcision
Occupation[a]			
Full time	77 (21.3)	62 (44.0)	0.31 (0.13–0.74)
Student	58 (16.1)	8 (5.7)	
Other	226 (62.6)	71 (50.4)	0.21 (0.09–0.51)
	$P < 0.001$		
Ethnic group			
Luo	345 (95.6)	45 (31.9)	0.33 (0.13–0.86)
Other	16 (4.4)	96 (61.9)	1.6 (0.18–13.1)
	$P < 0.001$		
Religion			
Christian	309 (85.6)	107 (75.9)	0.33 (0.17–0.64)
Muslim	1 (0.3)	18 (12.8)	
Other	51 (14.1)	16 (11.3)	0.15 (0.018–1.2)
	$P < 0.001$		
Travel in the past 12 months			
< 2 trips	137 (41.9)	43 (33.3)	0.41 (0.16–1.0)
> 1 trip	190 (58.1)	86 (66.7)	0.23 (0.10–0.54)
	$P = 0.11$		
Herpes simplex virus type 2			
Negative	199 (59.4)	96 (72.7)	0.50 (0.16-1.5)
Positive	136 (40.6)	36 (27.3)	0.22 (0.10-0.54)
	$P = 0.0077$		
Syphilis			
Negative	321 (96.1)	135 (100)	0.34 (0.18–0.62)
Positive	13 (3.9)	0 (0)	–
	$P = 0.0024$		
Chlamydial infection			
Negative	340 (97.4)	132 (97.8)	0.28(0.15–0.54)
Positive	9 (2.6)	3 (2.2)	1.8 (0.10–31)
	$P = 1.0$		
Gonorrhoea infection			
Negative	348 (100)	135 (100)	–
Positive	0 (0)	0 (0)	–
Episode of sexually transmitted infection in past 12 months			
No	279 (77.3)	122 (86.5)	0.2 (0.10–0.47)
Yes	82 (22.7)	19 (13.5)	0.89 (0.31–2.6)
	$P = 0.025$		
Frequent condom use with non-spousal partners[b]			
No	141 (82.0)	60 (76.9)	0.33 (0.11–1.0)
Yes	31 (18.0)	18 (23.1)	0.65 (0.11–3.8)
	$P = 0.39$		

[a] Full time, full-time employed; other, includes self-employed, part-time or irregularly employed, looking for a job, being a homemaker.
[b] Frequent condom use, used a condom always or most of the time with all non-spousal partners of the past 12 months.

Table 4. Association between HIV infection and socio-demographic and behavioural risk factors and sexually transmitted infections among sexually active men in Kisumu: univariate analysis

	OR (95% confidence interval)			OR (95% confidence interval)	
	All men	Luo men only		All men	Luo men only
Age	$P < 0.001$	$P < 0.001$	Occupation	$P = 0.005$	$P = 0.002$
15–19 years	1	1	Full time	1	1
20–29 years	4.4 (1.7–11.5)	6.4 (2.2–19)	Student	0.10 (0.023–0.43)	0.082 (0.19–0.36)
30–39 years	9.4 (3.6–24.7)	13 (4.4–38)	Other	1.1 (0.68–1.7)	1.1 (0.62–1.8)
40–49 years	7.5 (2.7–21.2)	7.2 (2.3–23)			
			Ethnic group	$P = 0.0003$	NA
Marital status	$P < 0.001$	$P < 0.001$	Luo		
Never married	1	1	Other	3.5 (1.8-7.0)	
Ever married	5.8 (3.3–10.2)	5.9 (3.2–10.6)			
			Religion	$P = 0.41$	$P = 0.79$
Age at first sex	$P = 0.9$	$P = 0.65$	Christian	1	1
>14 years	1	1	Muslim	0.42 (0.10-1.9)	1.0 (0.10-9.7)
≤ 14 years	1.0 (0.65–1.6)	0.89 (0.65–1.6)	Other	1.2 (0.67-2.2)	1.1 (0.62-1.8)
Number lifetime partners	$P = 0.001$	$P = 0.004$	Travel in the past 12 months	$P = 0.37$	$P = 0.98$
1–3	1	1	< 2 trips	1	1
4–9	2.6 (1.4–4.7)	2.4 (1.2–4.5)	> 1 trip	0.82 (0.52–1.3)	1.0 (0.62–1.6)
> 9	3.2 (1.7–5.9)	3.0 (1.6–5.9)			
			Circumcision	$P = 0.0001$	$P = 0.02$
Number of non-spousal partners in past 12 months	$P = 0.0001$	$P = 0.0002$	No	1	1
			Yes	0.30 (0.17–0.55)	0.33 (0.13–0.86)
0	1	1			
1	0.46 (0.28–0.76)	0.43 (0.25–0.75)	Herpes simplex virus type 2	$P < 0.001$	$P < 0.001$
> 1	0.31 (0.17–0.59)	0.30 (0.15–0.60)	Negative	1	1
			Positive	9.7 (5.6–17)	11.1 (6.1–20)
One-off contact or commercial sex in past 12 months					
0	$P = 0.08$	$P = 0.14$	Syphilis	$P = 0.04$	$P = 0.09$
≥ 1	0.39 (0.10–1.1)	0.40 (0.12–1.4)	Negative	1	1
			Positive	3.2 (1.1-9.8)	2.6 (0.85-8.0)
Alcohol	$P < 0.001$	$P < 0.001$			
< Once a month	1	1	Chlamydial infection	$P = 0.76$	$P = 0.84$
≥ Once a month	2.5 (1.6–3.8)	2.8 (1.7–4.4)	Negative	1	1
			Positive	1.2 (0.33–4.6)	0.85 (0.17–4.2)
Education	$P = 0.64$	$P = 0.93$			
No primary	1	1	Episode of sexually transmitted disease in past 12 months	$P = 0.006$	$P = 0.03$
Primary complete	1.1 (0.67–1.9)	1.1 (0.61–1.9)	No	1	1
Secondary/higher	0.90 (0.51–1.6)	0.99 (0.53–1.8)	Yes	2.2 (1.2–3.7)	1.9 (1.1–3.5)

NA, Not applicable; OR, odds ratio.

Male circumcision and HIV in Ndola

In Ndola, there was little difference in the prevalence of HIV infection among men who were circumcised and men who were not (OR = 0.95, 95% CI = 0.46–1.94). There were no differences between both groups of men in terms of socio-economic characteristics and sexual behaviour (data not shown). In contrast to Kisumu, there was also no difference in prevalence of HSV-2 (42% in circumcised men and 40% in uncircumcised men), syphilis (11% in circumcised men and 13% in uncircumcised men), or in the proportion of men who reported a STI episode in the past 12 months (18 and 19%).

When looking at the association between circumcision and HIV infection by marital status, we found that none

Table 5. Multivariate model of the association between circumcision status and HIV among sexually active men in Kisumu

	Odds ratio (95% confidence interval)			
	All men		Luo men only	
	Model without variables related to STI	Model with variables related to STI	Model without variables related to STI	Model with variables related to STI
Circumcision	$P = 0.0000$	$P = 0.0006$	$P = 0.016$	$P = 0.020$
No	1	1	1	1
Yes	0.27 (0.15–0.51)	0.26 (0.12–0.56)	0.29 (0.11–0.79)	0.21 (0.06–0.78)
Marital status	$P = 0.0000$	NE	$P = 0.0000$	NE
Never married	1		1	
Ever married	5.3 (3.0–9.5)		5.1 (2.8–9.4)	
Alcohol	$P = 0.0019$	$P = 0.0021$	$P = 0.0012$	$P = 0.0005$
< Once a month	1	1	1	1
≥ Once a month	2.1 (1.3–3.3)	2.3 (1.4–3.9)	2.3 (1.4–3.8)	2.8 (1.6–5.0)
Episode of sexually transmitted disease in past year	NA	$P = 0.021$	NA	$P = 0.047$
No		1		1
Yes		2.2 (1.1–4.4)		2.2 (1.0–4.6)
Herpes simplex virus type 2	NA	$P = 0.0000$	NA	$P = 0.0000$
Negative		1		1
Positive		8.8 (5.0–16)		10.7 (5.7–20)

STI, Sexually transmitted infection; NE, not entered by the stepwise procedure; NA, not applicable.

Table 6. Comparison of reported characteristics (%) of partners of circumcised men and partners of men who were not circumcised, in Kisumu

	Partners of uncircumcised men ($n = 329$)	Partners of circumcised men ($n = 133$)
Age		
< 15 years	6.7	2.3
15–19 years	64.7	54.1
20–24 years	18.5	24.8
25–29 years	7.9	11.3
> 29 years	2.1	7.5
Marital status		
Never married	82.4	82.3
Now married	9.8	6.4
Past marriage	4.0	5.0
Do not know	3.7	3.7
Ethnic group		
Luo	88.2	58.9
Other	11.8	41.1
Estimated prevalence of HIV	32%	32%

of 18 circumcised, never-married men were HIV infected, whereas the prevalence of HIV infection among uncircumcised, never-married men was 12% (20/167). This difference was not statistically significant ($P = 0.23$). Among men who were married or had been married in the past, the prevalence of HIV infection was 42% (11/26) in circumcised men and 34% (96/282) in uncircumcised men. It seemed that circumcised men were more often married to an HIV-infected woman than uncircumcised men. Of the HIV-negative married men, 3/10 spouses (30%) of circumcised men were HIV infected, compared with 15/135 (11%) of uncircumcised men. Multivariate analysis was carried out on the pooled data of never-married men and men who were married to an HIV-uninfected woman. This gave an OR for HIV infection associated with circumcision of 0.5 (95% CI = 0.1–2.2). This OR was similar to that in Kisumu (OR = 0.3, 95% CI = 0.06–1.5).

Discussion

We found a strong protective effect of male circumcision in Kisumu, Kenya, with an OR of 0.2–0.3. In this city, circumcision is not traditionally practised by the main ethnic group, the Luo, whereas men belonging to other ethnic groups are mostly circumcised. The association

between circumcision and HIV infection persisted after allowing for possible confounding factors, including socio-economic factors, sexual behaviour and other STIs. In addition, we compared the prevalence of HIV infection in spousal and in non-spousal partners of circumcised men and uncircumcised men. According to our estimates, there was no difference in HIV prevalence among non-spousal partners of both groups of men. The data on spouses suggested that circumcised men may less likely be married to an HIV-infected woman, but the twofold difference in HIV prevalence of spouses of HIV-negative men could not explain the three to fivefold difference in odds of HIV infection associated with circumcision.

In Rakai Region, Uganda, the strongest protective effect of circumcision was found in men who were circumcised before age 13 [7]. However in Mwanza Region, Tanzania, the opposite was found, i.e. circumcision after age 14 was protective against HIV infection while circumcision before age 15 was associated with an increased risk of HIV infection [8]. In our study in Kisumu, men who were circumcised before they had their first sexual experience had a lower prevalence of HIV infection than men who were circumcised after they had become sexually active. However, the number of men who were circumcised after their sexual debut was too small to perform a separate multivariate risk factor analysis and to compare the odds ratio for HIV infection in this group with the odds ratio in men who were circumcised before age at first sex.

The prevalence of HSV-2 infection and of syphilis was significantly lower in circumcised men than in uncircumcised men in Kisumu. Analysis of risk factors for HSV-2 infection found circumcision to have a protective effect with an adjusted OR of 0.4 [9]. Indeed, one proposed mechanism to explain the protective effect of circumcision against HIV infection is its protective effect against other STIs, in particular ulcerative STIs [10]. However, when we added HSV-2 and history of STI in the past 12 months to the logistic regression model, the association between circumcision and HIV infection was not weakened as one would have expected if the effect of circumcision were mainly through other STIs. This suggests that, in Kisumu, the protective effect of circumcision is mainly a direct biological effect. Several mechanisms have been proposed to explain this including increased likelihood of abrasions in the presence of a foreskin and the presence of Langerhans cells in the foreskin [11,12].

The data from Ndola are more difficult to interpret. Circumcision is less common and power was limited, but there were some striking differences with Kisumu. In contrast to Kisumu, the prevalence of HSV-2 and of syphilis was the same in circumcised and in uncircumcised men in Ndola. This may suggest that circumcised men in Ndola were more exposed to infected partners. The data on the spouses go in the same direction as they suggest that circumcised men in Ndola were more often married to an HIV-infected woman. When restricting the analysis to men who were never married or men who were married to an HIV-uninfected woman, circumcision showed a protective effect, although it was not statistically significant.

In conclusion, our data on the association between male circumcision and HIV infection at the individual level add to the existing body of evidence for a protective effect of circumcision against the acquisition of HIV infection by men [5]. The main objective of the multicentre study was to try and identify factors that could explain the differences in rate of spread of HIV between different cities in sub-Saharan Africa. We found striking differences in the proportion of men who were circumcised between the low HIV prevalence cities, where almost all men were circumcised, and the high HIV prevalence cities, where the majority of men were uncircumcised. The difference between our study and earlier ecological studies was that we collected data on sexual behaviour and on other STIs in each of the four populations. We found important differences in sexual behaviour between the four cities but they could not by themselves explain the differences in rate of spread of HIV [13]. For instance, the rate of partner change was higher in Yaoundé, one of the low HIV prevalence cities, than in Kisumu and Ndola. We concluded that the differences in rate of spread of HIV were rather due to differences in probability of transmission of HIV during sexual intercourse, and two factors were identified that enhance the probability of transmission in Kisumu and Ndola, i.e. lack of male circumcision and HSV-2 infection [14].

There is considerable evidence that circumcision protects men against the acquisition of HIV infection [5,15] and it is time now to seriously consider male circumcision as a strategy to prevent the spread of HIV [16,17]. Several issues will need to be addressed when considering such intervention. First, the evidence we have so far comes from observational studies of the protective effect of circumcision at the individual level. We need studies on the effect of male circumcision at the population level. The magnitude of this effect is likely to differ from one population to another. Studies on circumcision as a risk factor for HIV infection have found variations in the strength of the association between male circumcision and HIV infection, which may be due to interaction with other STIs or with genital hygiene practices [18]. Second, there are concerns about decrease in safe sexual practices if circumcision is perceived to offer full protection against HIV infection. Finally, there are issues of acceptability, feasibility, cost-effectiveness, safety and evaluation of the intervention. A recent feasibility study found that male circumcision in Kisumu may be accept-

able by non-circumcising populations if presented as a measure to improve genital hygiene [19]. More research of this type is needed, as well as research on how best to promote circumcision. The risks and benefits of promotion of male circumcision will have to be weighed against each other, but we cannot continue to ignore a potentially very effective intervention against HIV.

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