Circumcision and Risk of Sexually Transmitted Infections in a Birth Cohort

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Objective To determine the impact of early childhood circumcision on sexually transmitted infection (STI) acquisition to age 32 years.

Study design The circumcision status of a cohort of children born in 1972 and 1973 in Dunedin, New Zealand was sought at age 3 years. Information about STIs was obtained at ages 21, 26, and 32 years. The incidence rates of STI acquisition were calculated, taking into account timing of first sex, and comparisons were made between the circumcised men and uncircumcised men. Adjustments were made for potential socioeconomic and sexual behavior confounding factors where appropriate.

Results Of the 499 men studied, 201 (40.3%) had been circumcised by age 3 years. The circumcised and uncircumcised groups differed little in socioeconomic characteristics and sexual behavior. Overall, up to age 32 years, the incidence rates for all STIs were not statistically significantly different—23.4 and 24.4 per 1000 person-years for the uncircumcised and circumcised men, respectively. This was not affected by adjusting for any of the socioeconomic or sexual behavior characteristics.

Conclusions These findings are consistent with recent population-based cross-sectional studies in developed countries, which found that early childhood circumcision does not markedly reduce the risk of the common STIs in the general population in such countries. *(J Pediatr 2008;152:383-7)*

Although there is now compelling evidence that male circumcision can reduce the risk of men heterosexually acquiring human immunodeficiency virus infection,[1-3] there are conflicting reports on whether it does so for other sexually transmitted infections (STIs) that are common in developed countries. Although a number of large population-based cross-sectional studies have found no difference in the rate of self-reported STIs by circumcision status,[4-6] a recent report from a birth cohort found that circumcision was protective, and the authors conjectured that universal circumcision could reduce by one-half the rate of STIs in young adults.[7] The results of this study have been questioned on the basis of small sample size,[8,9] measurement error,[8] and potential confounding factors.[10] Although the authors responded to these criticisms, they concluded there was a need for further research to clarify the issues.[11]

We have previously reported from our birth cohort that early circumcision did not protect men from herpes simplex virus type 2 infection, the most common cause of genital herpes, up to age 26 years.[12] In that analysis, we also reported that the rate of self-reported STIs to that age did not vary by circumcision status, but this was not analyzed in detail. Here we report more detail of the analysis up to age 26 years and extend the study to examine the relationship between early childhood circumcision and self-reported STIs up to age 32 years.

METHODS

We studied subjects in the Dunedin Multidisciplinary Health and Development Study, a longitudinal study of a cohort born in Dunedin, New Zealand, between Apr 1, 1972, and Mar 31, 1973. The sample was first followed up at 3 years of age when 1037 (535 male) of 1139 eligible children were seen.[13] Subsequently they were assessed biannually until the age of 15 years, then at 18, 21, and 26 years and most recently at 32 years in 2004 to 2005. Wherever possible, those no longer living in Dunedin returned for the assessment even when overseas.

At the assessment at 3 years of age, the mothers were asked whether their sons had been circumcised, and if so, at what age. At ages 21, 26, and 32 years, participants were asked about STIs experienced with a computer-presented questionnaire. At age 21 years,

IRR	Incidence rate ratio	STI	Sexually transmitted infection

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they were queried about STIs ever, and at ages 26 and 32 years about STIs since the earlier assessment. Participants who reported having an STI were asked to indicate the condition from a list of the common STIs. When the condition was not listed, they could write its name or indicate what symptoms had been present. Men were classified as having had a bacterial STI when they reported chlamydia, gonorrhea, syphilis, or nonspecific urethritis, and they were classified as having had a viral STI when they reported genital herpes or genital warts. When either of these viral infections were mentioned at >1 assessment, only the first was recorded. When candida (or thrush), pubic lice, and scabies were reported they were not included, because they may not have been sexually acquired.[14]

Questions about sexual behavior, mostly based on the 1990 British National Survey of Sexual Attitudes and Lifestyles,[15] also were asked. This included asking about any same sex-contact (up to age 21 years) and since the previous assessment (at ages 26 and 32 years); the number of opposite- and same-sex partners ever (at all ages), and since the previous assessment (at ages 26 and 32 years); and the frequency of condom use (never, sometimes, usually, or always) in the previous 12 months at all 3 ages. At age 21 years, information was sought on first heterosexual intercourse.

Information on socioeconomic status and educational achievement was collected on both the study participant himself and his family of origin. Childhood socioeconomic status was based on the occupation of the participant's parents from birth to age 15 years by using the New Zealand Elley Irving scale.[16,17] Adult socioeconomic status was derived from his current or most recent occupation at age 32 years, classified by using the New Zealand Socio-Economic Index.[18] The highest educational qualification of the mother was collected at the age 3-year assessment and grouped as "low" for a high school qualification or less, "medium" for a post-secondary qualification excluding university, and "high" for a university qualification. The highest educational qualification of the study participant was based on the highest education achieved by age 32 years by using the same groupings.

Analyses were restricted to participants who answered the questions on sexual behavior and had ever had sexual intercourse or same-sex contact and for whom circumcision information was available. STATA software version 9 was used for all analyses. Chi-square tests for independence (with Yates continuity correction for 2-by-2 tables) were calculated to determine the relations between circumcision and measures of socioeconomic status and most measures of sexual behavior. Negative binomial regression was used to evaluate the relationship between circumcision and mean number of sexual partners in each period, with years since first intercourse as exposure. For participants for whom the age of first intercourse was not unavailable at age 21 years, it was estimated on the basis of the first subsequent assessment at which sexual contact was acknowledged (necessary for 87 men).

Incidence rates for STIs by circumcision status were calculated for the whole time up to age 32 years and for the periods up to age 21, between ages 21 and 26, and between ages 26 and 32 years, with years since first intercourse as exposure time. For each period, participants who were assessed and were sexually active by that time were included. For the whole period to age 32 years, events and exposure times from each available period were summed. Incidence rates were calculated for all self-reported STIs, and also for bacterial and viral STIs. Incidence rate ratios (IRRs) and 95% CIs were calculated by using the Poisson regression, comparing participants who had been circumcised and participants who had not been circumcised. The analyses were recalculated adjusting for measures of socioeconomic status and the appropriate measures of sexual behavior for each period 1 at a time and then together when multiple measures were deemed as confounding variables. These were judged to be confounding when adjustment resulted in a 10% change in the point estimate for circumcision or when the confidence intervals changed to include or exclude 1, resulting in a change of significance.[19] Because of the small numbers of reported bacterial and viral STIs in the individual age periods, adjusted rates are only reported for the whole age period up to age 32 years.

Written informed consent was obtained for each assessment, and ethical approval was given by the Otago Ethics Committee for each phase of the study.

RESULTS

Of the original 535 male cohort members seen at age 3 years, 477 (90.7% of survivors) completed the age 21-year assessment of sexual behavior; 490 (93.3% of survivors) completed the age 26-year assessment; and 487 (93.1% of survivors) completed the age 32-year assessment. Overall, 499 men who were sexually experienced and for whom early circumcision information was available attended at least 1 of these assessments.

Of these 499 men, 201 (40.3%) had been circumcised by age 3 years. There were no significant differences in the socioeconomic characteristics of circumcised men and uncircumcised men (Table I). The mean number of sexual partners during the whole period up to age 32 years for circumcised men (1.4 per year) was significantly less than for uncircumcised men (1.7 per year; $P = .047$), but was not consistently lower in the individual age periods. Although circumcised men were less likely to report same-sex contact up to age 21 years ($P = .073$), they did not at older ages or overall.

Overall, 117 of the 499 men (23.4%) reported ever having had an STI up to age 32 years; 23.4% (47/201) of the circumcised men and 23.5% (70/298) of the uncircumcised men. These 117 men reported 165 STIs: genital warts (56), chlamydial infections (46), genital herpes (34), gonorrhea (2), unspecified urethritis (2), and the remaining 25 were unnamed.

Table II shows the incidence rates by circumcision status up to age 32 years and for 3 age periods for all self reported STIs and for bacterial and viral infections separately. Overall, up to age 32 years, for all STIs there were very similar incidence rates, with the IRR equaling 0.96 (95% CI, 0.7-1.3) comparing the uncircumcised with the circumcised men, showing that there was a very slight, but statistically non-

Table I. Socioeconomic characteristics and sexual behavior by circumcision status

	Circumcised, n (%)	Uncircumcised, n (%)	*P* value
Socioeconomic characteristic			
Childhood socioeconomic status (ages 0-15 years)			.959
Low	39 (19.4)	57 (19.3)	
Medium	132 (65.7)	192 (64.9)	
High	30 (14.9)	47 (15.9)	
Maternal education			.334
Low	130 (66)	204 (69.2)	
Medium	57 (28.9)	70 (23.7)	
High	10 (5.1)	21 (7.1)	
Participant's highest qualification (age 32 years)			.699
Low	65 (33)	101 (35.8)	
Medium	90 (45.7)	118 (41.8)	
High	42 (21.3)	63 (22.3)	
Subject's occupational socioeconomic status (age 32 years)			.94
Low	59 (30)	87 (30.7)	
Medium	102 (51.8)	142 (50.2)	
High	36 (18.3)	54 (19.1)	
Sexual behavior			
Age, in years at first intercourse			.463
<15	33 (16.4)	48 (16.1)	
15-17	89 (44.3)	117 (39.3)	
≥18	79 (39.3)	133 (44.6)	
Engaged in same-sex contact*			
Up to age 21	4 (2.4)	17 (6.8)	.073†
Between ages 21 and 26	12 (6.2)	16 (5.8)	.992†
Between ages 26 and 32	9 (4.9)	16 (5.7)	.844†
Up to age 32	17 (9.1)	26 (9.3)	.922†
Condom use "usually" or "always" in previous 12 months‡			
Age 21 assessment	100 (63.3)	144 (60.3)	.614†
Age 26 assessment	79 (42.5)	103 (39)	.523†
Age 32 assessment	44 (24.2)	64 (25.2)	.896†
Mean number of sexual partners per annum			
Up to age 21	2.3	2.1	.287
Between ages 21 and 26	1.5	1.7	.19
Between ages 26 and 32	1.1	1.2	.647
Up to age 32	1.4	1.7	.047
Total	201 (40.3)	298 (59.7)	

Columns may not equal 100 because of rounding.
*Each of the rows refers to the proportion who reported any same sex contact in the period stated.
†Yates continuity correction applied.
‡Each row refers to the proportion "usually" or "always" using condoms in the 12 months before the stated assessment.

significant, lower rate of STIs in the uncircumcised men. This was not changed by >10% by adjusting for any of the socioeconomic or sexual behavior characteristics. For the different age periods, there was no consistent direction of the effects, and the observed differences were not statistically significant. Rates for uncircumcised men were 1.4 times higher in the period up to age 21 years (95% CI, 0.7-2.7), 0.67 times lower in the period 21 to 26 years (95% CI, 0.42-1.1), and 1.2 times higher in the period 26 to 32 years (95% CI, 0.7-2.1). Adjustment for possible confounding factorrs did not appreciably affect the estimates for the IRRs or alter the significance. Examination of possible confounding variables for the types of STIs separately up to age 32 years, suggested the IRR for the bacterial STIs should be adjusted for the number of sexual partners and same sex contact, which resulted in an adjusted IRR of 1.3 (95% CI, 0.69-2.5). It also suggested the IRR for the viral STIs should be adjusted for the number of sexual partners, which resulted in an IRR of 1.0 (95% CI, 0.66-1.6).

The unadjusted IRRs comparing the uncircumcised men with the circumcised men who reported any chlamydial infection and any other bacterial infection up to age 32 years were 1.1 (95% CI, 0.62-2) and 2.2 (95% CI, 0.22-21), respectively. For genital herpes and genital warts, the IRRs were 0.64 (95% CI, 0.33-1.3) and 1.2 (95% CI, 0.7-2.1), respectively.

DISCUSSION

The main finding of this study is that in this New Zealand birth cohort we found no evidence to support the

Table II. Relationship between circumcision and incidence of reported sexually transmitted infections

Age period (years)	Circumcision status	Incidence rate (per 1000 person-years)	IRR (95% CI)
All STIs			
Up to age 32	Circumcised	24.4	Ref.
	Uncircumcised	23.4	0.96 (0.7-1.3)
Up to age 21	Circumcised	16.3	Ref.
	Uncircumcised	22.3	1.4 (0.7-2.7)
Ages 21 to 26	Circumcised	39.9	Ref.
	Uncircumcised	26.7	0.67 (0.42-1.1)
Ages 26 to 32	Circumcised	17.7	Ref.
	Uncircumcised	21.5	1.2 (0.7-2.1)
Bacterial STIs			
Up to age 32	Circumcised	6.5	Ref.
	Uncircumcised	7.5	1.1 (0.64-2)
Up to age 21	Circumcised	3.8	Ref.
	Uncircumcised	8	2.1 (0.58-7.9)
Ages 21 to 26	Circumcised	11.7	Ref.
	Uncircumcised	9.6	0.82 (0.37-1.8)
Ages 26 to 32	Circumcised	4.3	Ref.
	Uncircumcised	5.3	1.3 (0.42-3.7)
Viral STIs			
Up to age 32	Circumcised	13.4	Ref.
	Uncircumcised	12.3	0.91 (0.6-1.4)
Up to age 21	Circumcised	12.5	Ref.
	Uncircumcised	12.5	1.0 (0.44-2.2)
Ages 21 to 26	Circumcised	21.3	Ref.
	Uncircumcised	14.7	0.69 (0.37-1.3)
Ages 26 to 32	Circumcised	7.7	Ref.
	Uncircumcised	10.1	1.3 (0.59-2.9)

hypothesis that circumcision has a major protective effect against the STIs commonly experienced there.

Socioeconomic characteristics of the circumcised men and uncircumcised men were similar. Examination of sexual behavior showed that the circumcised men had slightly lower risk behavior—a lower annual number of sexual partners overall up to age 32 years and less same-sex contact up to age 21 years. However, adjustment for potential confounding factors did not raise the point estimate for the relative risk for the uncircumcised men except that for the bacterial STIs for the whole period, but this remained statistically non-significant.

Advantages of this study include that it was prospective and population-based, with a high retention rate. Parental reports at age 3 years of early circumcision were used; mis-reports were unlikely because details of its timing also were asked (87% were undertaken by 1 month of age). Information on later circumcision was not sought; however, this is uncommon in comparison with circumcision in infancy or early childhood. By using the available information on the number of circumcisions performed by age in New Zealand public and private hospitals in the period 1979 to 1992, our best estimate was that 11 more men in the study might have been circumcised before the age of 25 years. If this had occurred, and none of these men who underwent late circumcision had sustained an STI and their sexual behavior did not differ from that of the rest of the sample, there still would not have been a significant difference in the overall rates of STIs. Information about the early childhood socioeconomic environment was obtained, as was information on sexual behavior throughout early adulthood, so that it was possible to explore these as confounding factors. The use of well-validated questions on sexual behavior and the use of a computer to present these questions (with safeguards to protect confidentiality) should have enhanced disclosure.

Self reports of STIs were used, which could have resulted in an underestimate of total rates. For self-reporting to hide a protective effect of circumcision, the men who were uncircumcised would have to have had a higher proportion of STIs unrecognized or unreported. Although unlikely, we explored the possibility with our data on herpes simplex virus-2 seroprevalence at age 32 years[20] and responses to a question asked at age 32 years about whether they had ever had genital herpes. Men who were uncircumcised did not have a higher proportion of unrecognized infections; 60% of the circumcised men and 56% of the uncircumcised men with serologic evidence of herpes simplex virus-2 infection did not report a past infection ($P = .88$). Another disadvantage of using self-reports is that the type of STI might be mis-reported. Although unlikely to result in bias, to avoid this and also because of small numbers and lack of statistical power for individual STIs, we have considered the overall results primarily.

The literature to date suggests that circumcision might give variable protection against STIs depending on the organism. There is now strong observational and trial evidence from Africa that circumcision has a protective effect against heterosexual acquisition of human immunodeficiency virus by men.[1-3] A meta-analysis of observational studies also suggests some protection against syphilis and chancroid.[21] The evidence of protection is less clear for other conditions. Alanis and Lucidi reviewed the topic in 2004 and concluded that although it was possible that circumcision has a small protective effect against gonorrhea, there was little evidence of any protective effect against chlamydial infection or genital warts.[22] Since then there has been 1 study published that examined serologic markers of past *Chlamydia trachomatis* infection among control women in a number of case-control studies of cervical cancer from 5 countries.[23] However, there have been criticisms of this study because of wide differences in the prevalence of circumcision between countries and because there was little power to analyze by individual country.[24] The same study also found a higher rate of detection of human papilloma virus from the penises of uncircumcised men.[25] However, the authors caution that inadequate penile samples might have been taken from the circumcised men.[23] Another study that used more extensive sampling found no difference between the prevalence of human papilloma virus by circumcision status.[26]

Although the best evidence of causation would come from randomized controlled trials, it is unlikely that any will be undertaken to examine this question directly. However, self-reports

of symptoms of other STIs were reported in 1 of the trials undertaken in Africa to investigate the impact of circumcision on HIV acquisition.[3] At follow-up, genital ulcers were significantly less common in the circumcised men (prevalence risk ratio, 0.53; 95% CI, 0.43-0.64), but genital discharge (prevalence risk ratio, 0.84; 95% CI, 0.63-1.11) and dysuria (prevalence risk ratio, 0.97; 95% CI, 0.77-1.21) were not.

There also has been consistency in the results from 3 large population-based cross-sectional studies in developed countries undertaken in the United States, United Kingdom, and Australia that together included >16,000 men.[4-6] All 3 studies used probability sampling and relied on self-reports of STI and circumcision. Similar to our results, none of these studies found a relationship between circumcision and lifetime reports of bacterial and viral STIs.

Although our results are consistent with the lack of a protective effect, they are at variance with the recently published report by Fergusson et al, who, using data from another New Zealand cohort, found that circumcision reduced by more than one-half the risk of any STI up to age 25 years.[11] Because both studies have particular strengths for examining this question, it is important to consider reasons for the discrepant findings. A lower proportion of the Christchurch sample (30.2%)[11] was circumcised than the proportion of our Dunedin sample (40.2%; who were born 5 years earlier). This difference is in keeping with trends in circumcision in New Zealand at the time.[27] This might have introduced a difference in characteristics between the circumcised men and uncircumcised men in the Christchurch compared with the Dunedin cohort, so residual confounding is more likely in the Christchurch analysis. But because adjustment for confounding increased the protective effect found in that study, this is an unlikely explanation. Another difference was that in the Christchurch study only 8.5% of men reported an STI between ages 18 and 25 years, which was less than half the 19.9% reported in our Dunedin study up to age 26 years. The reasons for this are not clear, but possibly the computer-presented questions in the latter study promoted disclosure. Finally, as noted,[8,9] the Christchurch study was a relatively small sample; thus their estimate of the protective effect of circumcision lacks precision, with wide confidence intervals, and is compatible with only a small increase in risk.

Although the reason for the different findings in the 2 cohorts is unclear, when our findings are considered in the context of other recent population-based studies in developed countries, it appears unlikely that circumcision has a major protective effect against common STIs in these populations, although a small effect cannot be ruled out.

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