Circumcision status and risk of sexually transmitted infection in young adult males: An

analysis of a longitudinal birth cohort

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Abstract

Objective: Previous research suggests that male circumcision may be a protective factor against the acquisition of sexually transmitted infections (STI); however, studies examining this question have produced mixed results. The aim of the current study was to examine the association between circumcision status and STI risk using a longitudinal birth cohort study.

Methods: Data were gathered as part of the Christchurch Health and Development Study, a 25-year longitudinal study of a birth cohort of New Zealand children. Information was obtained on: a) the circumcision status of males in the cohort prior to age 15 years; b) measures of self-reported STI from ages 18-25; and c) childhood, family and related covariate factors.

Results: Being uncircumcised had a statistically significant bivariate association with self-reported STI, (OR 2.66; 95%CI: 1.17 to 6.11). Adjustment for potentially confounding factors, including number of sexual partners and unprotected sex, as well as background and family factors related to circumcision, did not reduce the association between circumcision status and reports of STI (OR 3.19; 95% CI: 1.32 to 7.75). Estimates of the population attributable risk suggested that universal neonatal circumcision would have reduced rates of STI in this cohort by 48.2% (95%CI: 17.7% to 60.9%).

Conclusions: These findings suggest that uncircumcised males are at greater risk of acquiring STI than circumcised males. Male circumcision may reduce the risk of STI acquisition and transmission by up to one-half, suggesting substantial benefits accruing from routine neonatal circumcision.

There have been ongoing debates and controversies about the role of neonatal circumcision as a public health measure to protect the future health of males (1-10). These issues were examined in a review of the evidence conducted by the American Academy of Pediatrics (11). This review concluded that, while the existing scientific evidence demonstrated potential benefits of neonatal circumcision, this evidence was not sufficient to form the grounds for routine neonatal circumcision. For these reasons, the policy statement concluded "In circumstances in which there are potential benefits and risks, yet the procedure is not essential to the child's current well being, parents should determine what is in the best interests of the child" (p. 691). The report also made it clear that it was important that parents were informed adequately about the risks and benefits of circumcision.

One focus of the AAP review was upon the role of circumcision in decreasing risks of sexually transmitted infection (STI). The report pointed to the fact that evidence for circumcision reducing risks of sexually transmitted infection (STI) was "complex and conflicting" (p. 691). A range of studies that have examined the role of circumcision status in STI risk have concluded that circumcision protects males from acquiring STI. For example, a number of studies have noted that rates of HIV infection are lower in circumcised men (12-21), with some researchers suggesting that this is due to a particular vulnerability to the HIV virus in the cells of the male foreskin (16, 22, 23). Similarly, other studies have found that circumcised men are at lower risk of contracting syphilis (21, 24-29) and genital ulcerative disease (14, 15, 21, 30-35). However, the evidence is mixed for other STI. There is conflicting evidence regarding whether circumcised men may be at lower risk for gonorrhea (24, 25, 36-40). Similarly, while some studies have failed to find evidence to suggest that circumcision protects against Chlamydia (15, 24, 25, 36, 39), other studies have shown a link between circumcision and a lower risk of Chlamydia (37, 41, 42). There is little evidence to suggest that circumcision reduces the risk of genital warts (40, 43).

One major difficulty in drawing conclusions about the relationship between circumcision status and STI risk is the existence of limitations in the evidence base. Alanis and Lucidi (1), in a

review of the medical evidence regarding circumcision, pointed out a number of these limitations, including a paucity of prospective cohort studies of STI risk, and the absence of longitudinal data on the relationships between circumcision and risks of STI over the life course.

In this paper we report the results of a 25-year longitudinal study of a cohort of over 500 New Zealand born males. The aims of this study are to examine the extent to which circumcision status (circumcised, uncircumcised) was related to subsequent risks of STI. This study makes two important contributions to the understanding of linkages between circumcision status and risks of subsequent STI. First the longitudinal nature of the study makes it possible to examine linkages between circumcision status and risks of infection over the life course. In contrast, much previous research in this area has focussed on cross-sectional data gathered at a particular point in time (1). Second, the study had available a large number of social, family and individual factors that could be used as covariates in the analysis. This availability of prospectively-collected covariates is of importance to the extent that there have been ongoing suggestions that the apparent medical benefits of circumcision may reflect factors that are correlated with circumcision and associated with increased risks of STI (e.g. (37)). More generally, the aims of this paper were to examine the extent to which circumcision status was related to risks of subsequent STI when due allowance was made for longitudinally-assessed confounding factors.

Methods

The data were gathered over the course of the Christchurch Health and Development Study (CHDS), a longitudinal study of a birth cohort of 1265 children born in the Christchurch (New Zealand) urban region in mid-1977. This cohort has been studied at birth, 4 months, 1 year and annual intervals to age 16 years, and again at ages 18, 21 and 25 years. The present analyses were based on the male cohort members assessed at ages 4 months, 1 year, 21 years, and 25 years for whom full information on circumcision status and sexually transmitted infections was available.

This sample size was n=510, representing 80% of the cohort of 635 male participants. All data were collected only on the basis of signed consent from research participants. The study had ethical approval from the Canterbury Ethics Committee.

Circumcision status

Circumcision status was assessed though parental report at age four months and through medical records collected at one year of age. Parents were questioned at the age four month assessment as to whether their child had been circumcised. On the basis of this questioning, 26.1% (N = 130) of the males in the sample were classified as having been circumcised. In addition, medical records were collected at each assessment that included a record of whether the child had been circumcised in hospital. On the basis of these records, an additional 24 males were classified as having been circumcised prior to age 15, providing a total of 154 circumcised males (30.2% of the sample).

Self-reported sexually transmitted infections, ages 18-21 and 21-25

At ages 21 and 25, cohort members were questioned about a range of sexual activities and practices they had engaged in since the previous assessment, and the consequences of these activities and practices, including whether they had been diagnosed with a sexually transmitted infection (STI) at any time since the previous assessment. Cohort members who responded "yes" were then asked to provide details of the infection, including the age at which it was contracted, the type of STI contracted (i.e. according to a formal medical diagnosis), and the treatment (if any) provided. Fourteen cohort members (2.7%) reported a medically-diagnosed STI at the age 21 assessment, and 34 cohort members (6.6%) reported an STI at the age 25 assessment. Six (1.2%) cohort members reported STI at both the age 21 and 25 assessments.

The details provided of the self-reported STI were as follows: 22 cases (52.4% of cases) were reported to have been Chlamydia, 13 (31.0% of cases) were reported to have been genital warts, 4 (9.5% of cases) were reported to have been genital herpes, 2 (4.8% of cases) were reported

to have been gonorrhea, 5 (11.9% of cases) were reported as non-specific urethral infections, and one case (2.4%) was described as a co-occurrence of genital herpes and genital warts. There were no self-reported cases of HIV infection, syphilis, or genital ulcerative disease amongst the cohort members.

Covariate factors

The regression models (see Statistical Analysis, below) employed a series of observed covariate factors that were abstracted from the study data base and were selected on the basis that they were: (a) theoretically relevant predictors of STI risk; or (b) known on the basis of prior analysis to be associated with measures of sexual behavior in this cohort. These measures are described below.

Self-reported number of sexual partners ages 21 and 25

At ages 21 and 25 years, participants were questioned about aspects of their sexual behavior over the interval since the previous assessment. We asked the following questions: (1) how many sexual partners have you had during the last year?" (2) "Since you turned (age at previous assessment) how many sexual partners of the opposite sex have you had (including the past year)?" (3) "How many partners of the same sex have you had since you were (age at last assessment)?" These data were used to obtain an estimate of the total number of sexual partners reported by the participants for each of the intervals 18-21 years and 21-25 years. On average, participants reported a mean of 5.4 partners during the interval ages 18-21 and a mean of 7.6 partners during the interval ages 21-25.

Self-reported unprotected sex ages 21 and 25

As part of the assessment at ages 21 and 25 years, participants were questioned about their involvement in incidents of unprotected sex in the previous 12 months. In order to assess sexual activity and unprotected sex, participants were asked how many times they had had sexual intercourse without using a condom, either with an opposite-sex partner or a same-sex partner. For

the purposes of the present analysis, participants were classified as having engaged in unprotected sex during the time interval if they reported having engaged in sex with an opposite-sex partner or a same-sex partner without using a condom on one or more occasions in the past 12 months. Of the male participants, 77% (n = 390) reported having had sex without a condom with either an opposite-sex or same-sex partner.

Maternal age

This was recorded at the time of the survey child's birth.

Maternal education

This was assessed at the time of the survey child's birth using a three point scale which reflected the highest level of educational achievement attained. This scale was: 1 = mother lacked formal educational qualifications (had not graduated from high school); 2 = mother had secondary level educational qualifications (had graduated from high school and may have attended university or the equivalent); 3 = mother had tertiary level qualifications (had obtained a university degree or equivalent qualification).

Family socioeconomic status

This was assessed at the time of the survey child's birth using the Elley-Irving (44) scale of socio economic status (SES) for New Zealand. This scale classifies SES into 6 levels on the basis of paternal occupation, ranging from 1 = professional occupations to 6 = unskilled occupations.

Birth weight

Birth weight was assessed by the recorded weight of the survey child at birth, measured in grams.

Statistical Analysis

The unadjusted association between circumcision and the rate of STI was tested for significance by fitting a random effects logistic regression model to the repeated measures data linking circumcision status to STI risk in the intervals 18-21, 21-25 years. The fitted model was of the form:

$$\text{Logit}(Y_{it}) = B_{0t} + B_1 X_i + \nu_i$$

where logit(Y_{it}) was the log odds of STI for the i-th participant in the t-th time period; X_i was a dichotomous variable representing the individual's circumcision status (circumcised/not circumcised); and ν_i was an individual specific random effect. The intercept term B_{0t} was permitted to vary with time to allow for changes in the base rate of STI between assessment periods. In this model the coefficient B_1 represents the effect of circumcision on STI risk pooled over the assessment periods 18-21, 21-25 years. A test of the significance of the association between circumcision and STI risk was obtained from a Wald chi square test of the hypothesis H_0: $B_1 = 0$. An estimate of the strength of association was provided by the pooled odds ratio (OR) and corresponding 95% CI estimated using the fitting model parameter and SE. The pooled OR was given by exp(B_1).

The associations between STI risk and covariate factors were tested for significance using the chi square test of independence for comparison of percentages and the t-test for independent samples for comparison of means. To adjust the association between circumcision and STI risk for covariates the random effects model above was extended to include covariate factors. The adjusted parameter estimate for circumcision was used to calculate the adjusted OR for risk of STI. The adjusted effect size estimate was used to assess the contribution of circumcision status to the overall rate of STI in the cohort, through calculation of the population attributable risk (PAR) estimate for circumcision (45).

Finally, the above analyses were repeated using only those self-reported cases of Chlamydia as the STI outcome measure (n=22), in order to determine whether there was any specific association between circumcision status and Chlamydia infection.

Results

Associations between circumcision status and sexually transmitted infections

Table 1 shows rates of self-reported STI at ages 18-21 and 21-25 related to circumcision status. The Table shows that at both times uncircumcised males were at increased risk of STI. To estimate the association between circumcision status and rates of STI, a random effects model was fitted to the repeated measures data (see Methods). The estimates from the random effects model showed that uncircumcised males had odds of STI that were 2.66 times higher (95% CI: 1.17 to 6.11; $p < .05$) than circumcised males.

INSERT TABLE 1 HERE

Associations between covariate factors and STI risk (ages 18-25).

Table 2 shows the associations between STI risk from ages 18-25 and a number of covariate factors. These factors included measures of social, family, and related background factors measured at birth, and measures of sexual activity in adolescence and young adulthood. The Table shows the following:

1. Risks of STI were unrelated to all measures of childhood social background and birth weight ($p > .10$).

2. Risks of STI were related to both: (a) number of sexual partners ($p < .001$); and (b) engaging in unprotected sex ($p < .05$).

INSERT TABLE 2 HERE

Associations following adjustment for covariate factors

The results in Table 2 raise the possibility that the associations between circumcision status and STI risk were due to the covariate factors associated with STI. To address this issue, the results were adjusted for the covariate factors (number of sexual partners and unprotected sex) using logistic regression. The results of this analysis are summarised in Table 3 which shows the odds ratios between circumcision status and STI risk before and after adjustment for covariate factors. These comparisons make it clear that adjustment for covariates did not decrease, but rather increased the magnitude of the association between circumcision status and STI (B = 1.16, SE = .45, p < .01). After adjustment the odds ratio was 3.19 (95% CI: 1.32 to 7.75). The increase in the odds ratio was due to the fact that those who were circumcised reported a greater number of sexual partners and higher rates of unprotected sex than those who were uncircumcised.

INSERT TABLE 3 HERE

Estimates of the Population Attributable Risk (PAR) of circumcision after controlling for covariates

The results in Table 3 show circumcision status was related to overall risk of STI. To assess the contribution of circumcision status to overall rates of STI, the population attributable risk (PAR) was calculated (see Methods). The PAR estimates the percentage decrease in the overall rate of STI that would be observed if all males in the population were circumcised (45). The PAR for circumcision was 48.2% (95%CI: 17.7% to 60.9%), suggesting that if all cohort members were circumcised the overall rate of STI would reduce by 48.2%.

Supplementary analyses

The analyses conducted above were repeated using a subset of self-reported STI, namely those respondents who reported contracting Chlamydia. The unadjusted associations between circumcision status and reports of Chlamydia were similar to those for overall STI (B = .92, SE = .63, p > .10; OR = 2.50; 95%CI: .73 to 8.53), but were not statistically significant due to the small number of cases of Chlamydia (n = 22). Adjustment for the potentially confounding factors listed above followed the same pattern as overall STI (B = 1.11, SE = .63, p > .05; OR = 3.03, 95%CI: .88 to 10.45).

Discussion

In this paper we have used data gathered over the course of a 25-year longitudinal study to examine the association between neonatal circumcision and risks of sexual transmitted diseases in adolescence and young adulthood. The results of this study suggest that following adjustment for a series of covariate factors, uncircumcised males had odds of subsequent STI that were 3.19 (95% CI: 1.32 to 7.75) times higher than circumcised males. These findings are also consistent with and reinforce the findings of a growing number of studies that have found increased risks of STI amongst the uncircumcised (12-19, 22-28, 30-38, 41, 42).

Estimates of the population attributable risk suggested that circumcision status made a substantial contribution to rates of STI. These estimates suggest that had all members of this cohort been circumcised the overall rate of STI within the cohort would have been reduced by nearly 50%. These estimates are consistent with those presented in other research that has suggested that circumcision may lead to substantial reductions in rates of STI infection. For example, a recent randomized controlled trial of the effects of circumcision on HIV infection by Auvert et al. found that circumcision reduced the risk of contracting HIV by 60% (20). In a re-analysis of these data, Shelton estimated that the protective effect of circumcision in the Auvert et al. study may have been

as high as 76% (46). A study of circumcision status and STI in a US sample (with a circumcision rate of approximately 75%) estimated that circumcision could reduce rates of STI in males by about a third (36). Collectively these results suggest that routine neonatal circumcision may have the potential to reduce current population rates of STI in males by one-third to three-quarters, with the findings of this study being in the middle of these estimates.

There have been ongoing debates about the extent to which circumcision may play a protective role in reducing risks of Chlamydia (15, 24, 25, 36, 37, 39, 41, 42). A number of previous studies in this area have failed to find evidence of a protective effect of circumcision in reducing risks of Chlamydia (15, 24, 25, 36, 39). However, the findings of this study produce evidence to suggest benefits of circumcision in reducing rates of Chlamydia. The inconsistent findings on this issue clearly suggest the need for further research to clarify the extent to which circumcision plays a protective role in reducing risks of Chlamydia.

The current study has a number of advantages deriving from the longitudinal design. These include: study of a general population sample; prospective assessment of childhood and family factors; longitudinal assessment of exposure to STI; and statistical control for confounders. However, a potential limitation of this research is that the assessment of STI was based on self report and this is likely to underestimate the true prevalence of these conditions. The prevalence estimates of STI reported in this paper are thus likely to be lower limit estimates of the true but non-observed prevalence of STI. However, while under-reporting of STI may bias estimates of the prevalence of STI downwards, it is unlikely to bias estimates of the association between STI and circumcision, since there is no reason to believe that the reporting accuracy of STI will vary with circumcision status.

Over the last two decades there has been growing opposition to the practice of routine neonatal circumcision on the grounds that the procedure has some risk of severe complications and has relatively few longer-term benefits (47-52). The results of this and other research suggest that this argument may be more finely balanced than critics of circumcision have implied. Specifically,

both during and after infancy, those circumcised appear to experience small but consistent benefits in terms of reduced risks of penile infection in middle childhood (53), urinary tract infection (54-56), and sexually transmitted infections (12-28, 30-38, 41, 42). The common theme of these results is that those circumcised appear to have lower risks of various forms of genital and urinary infection, with these benefits being evident in both childhood and adulthood. As shown in this analysis, the benefits of circumcision for reducing such risks may be quite substantial. The public health issues raised by these findings clearly involve weighing the longer-term benefits of routine neonatal circumcision in terms of reducing risks of infection within the population, against the perceived costs of the procedure.

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Table 1. Associations between circumcision status and STI ages 18-21 and 21-25.

Measure	Circumcision Status		OR (95% CI)
	Circumcised (n = 154)	Non Circumcised (n = 356)	
% Reporting STI at ages 18-21	1.3	3.5	2.68 (.59-12.1)
% Reporting STI at ages 21-25	3.4	8.5	2.61 (.99-6.89)
Pooled estimate of STI risk ages 18-25	4.6	10.4	2.66 * (1.17-6.11)

* Pooled OR estimated from random effects model, Wald χ^2 test of significance of effect of circumcision, $\chi^2 (1) = 5.41$, p<.05

Table 2. Associations between STI risk ages 18-25 and possible covariate factors.

Factor	STI Status Ages 18-25		p^1
	No STI	STI	
Social, Family and Related Background Factors			
% With mother aged <20 years	7.7	9.1	>.70
% Mother had no formal educational qualifications	48.9	47.7	>.80
% In lowest socio-economic status category	18.9	20.5	>.50
Mean (SD) birth weight (in grams)	3397.5 (567.8)	3524.3 (564.2)	>.10
Adolescent & Young Adult Factors			
Mean (SD) number of sexual partners ages 18-25 years	11.7 (15.2)	20.3 (16.5)	<.0001
% Reporting unprotected sex	75.3	88.6	<.05

[1] Mantel-Haenszel χ^2 test for percentages; t-test for independent samples for mean scores.

Table 3. Regression parameters (and standard errors) and odds ratios for the effect of circumcision status on STI risk ages 18-25, before and after covariate adjustment

	Before Adjustment			After Adjustment		
	B	(SE)	OR (95% CI)	B	(SE)	OR (95% CI)
Circumcision status	.98	.42	2.66 (1.17-6.11)	1.16	.45	3.19 (1.32-7.75)