Circumcision for the prevention of urinary tract infection in boys: A systematic review of randomized trials and observational studies

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Abstract

Objective: Circumcision is the most frequently performed surgical procedure in boys. This systematic review summarises the existing data about the effect of circumcision on the risk of urinary tract infection in boys.

Data Sources: Randomised controlled trials and observational studies comparing the frequency of urinary tract infection in circumcised and uncircumcised boys were identified from the Cochrane Controlled Trials Register, MEDLINE, EMBASE, reference lists of retrieved articles and contact with known investigators.

Review methods: Two of the authors independently assessed study quality using the guidelines provided by the MOOSE Statement for quality of observational studies.

Results: Data from 402,908 children was identified from twelve studies (one randomised controlled trial, four cohort studies and seven case control studies). A random effects model was used to estimate a summary odds ratio (OR) with 95% confidence intervals (CI). Circumcision was associated with a significantly reduced risk of urinary tract infection (OR 0.13; 95%CI, 0.08-0.20; p<0.001) with the same odds ratio (0.13) for all three study designs.

Conclusion: Circumcision substantially reduces the risk of urinary tract infection. Given a risk of UTI in normal boys of about 1%, the number-needed-to treat to prevent one urinary tract infection is 111. In boys with recurrent urinary tract infection or high-grade vesicoureteric reflux, the risk of urinary tract infection recurrence is 10% and 30% and the numbers needed-to-treat are 11 and 4 respectively. Haemorrhage and infection are the commonest complications of circumcision occurring at rate of about 2% and assuming equal utility of benefits and harms, net clinical benefit is only likely in boys at high risk of urinary tract infection.
Introduction

Circumcision is the commonest surgical procedure performed on children. Neonatal circumcision rates vary widely between different cultures, with rates as high as 64% in North America, between 10% and 20% in Australia and far lower rates in Europe and Asia.

Circumcision has been performed on males for thousands of years and has a significant cultural and religious role in many societies. It is also undertaken on medical grounds with benefits thought to include improved hygiene, a reduced incidence of urinary tract infection (UTI), sexually transmitted diseases, penile cancer, phimosis and reduced incidence of human papillomavirus-related cervical cancer in female sexual partners.

The overall complication rate of circumcision is between 2 and 10% and most complications are minor. While haemorrhage is the most frequent acute complication of circumcision, infection, glandular ulceration, urethral fistula formation and penile amputation can also occur. Long-term complications include meatal stenosis and poor cosmetic results.

Various paediatric societies have developed position statements on circumcision. These statements generally conclude that there is insufficient evidence to recommend routine neonatal circumcision but consider it justified in recurrent balanitis, true phimosis and UTI.

Lack of a clear consensus on the magnitude of the benefits of circumcision may be due to variability in different methods used to search and critically appraise the available literature. As the most frequently cited benefit of circumcision is a reduced incidence of UTI, we have undertaken a systematic review of the available data on the effect of circumcision on UTI in males.

Methods

All steps of the review including literature search, data extraction and data analysis were carried out independently by two authors (JM and DSG) without blinding to authorship. Resolution of discrepancies was by consensus and the involvement of a third author (JC) when necessary.

Data Sources

The Cochrane Controlled Trials Register (Issue 4 November 2002), MEDLINE (1966 to November 2002), and EMBASE (1980 to November 2002) databases were searched.

MEDLINE and EMBASE were searched using “circumcision” as both a text word and Medical Subject Heading (MeSH) term. The search was not limited by language and
bibliographies of identified publications were examined for any relevant material that may have been overlooked. Details of any additional published or unpublished data were sought from authors identified in the literature search.

Following the computerised database search, all titles were screened and abstracts of relevant or possibly relevant articles were reviewed in full. Studies in languages other than English were translated prior to assessment. When more than one publication of the same data was found, data was extracted only from the study with the most complete data.

**Study Selection**

All studies examining the effect of circumcision of males on UTI were included. The population of interest was males without any age restriction and the intervention evaluated was circumcision. Diagnosis with UTI was the only outcome investigated. Studies were included only if they provided sufficient information for a two by two contingency table to be constructed, so that the odds of UTI in the circumcised group could be compared with those of the uncircumcised group.

**Data Extraction**

Randomised studies were assessed using the guidelines provided by the CONSORT Statement. Aspects of study design including allocation concealment, blinding, follow-up, outcome measurement, and analysis by intention-to-treat were assessed.

Quality assessment for observational studies was carried out using the guidelines provided by the MOOSE Statement. The quality of identified studies was assessed according to the study setting, completeness and duration of follow-up, validity and completeness of exposure and outcome ascertainment, comparability of the control group, and adjustment for known confounders.

**Data Synthesis**

**Statistical analysis was done with Review Manager (version 4.2)**

An odds ratio (OR) with 95% confidence interval (CI) was calculated for each individual study and a summary OR using a random effects model was first calculated for subgroups based on study type (i.e. randomised controlled trial, cohort study or case control study) and then an overall OR calculated across all study types if no heterogeneity was present.

Consistency of the intervention effects across studies was evaluated using the Cochran’s Q statistic for heterogeneity with \( n-1 \) degrees of freedom and an \( \alpha \) of 0.05. This method calculates a chi squared statistic, with \( p<0.05 \) suggesting that the observed variation in the OR is unlikely to be due to chance alone. The \( I^2 \)-statistic was calculated as an estimate of the percentage of the variability in the OR due to heterogeneity rather than chance with an \( I^2 \) of greater than 50% indicating significant heterogeneity. Heterogeneity between and within subgroups, and between individual studies when
combined, was assessed. Possible sources of heterogeneity included study type, setting, study population and follow-up.

There were insufficient studies to construct a funnel plot to assess for publication bias.

Results

Literature search (Figure 1)
From 2166 titles and abstracts retrieved twelve fulfilled the inclusion criteria (one randomized trial, four cohort studies and seven case control studies).

Characteristics of included studies (Table 1)
All of the included studies were published between 1987 and 2001. Most originated from North America and relied on hospital inpatient and outpatient data. These twelve studies provided data from 402,908 children and for 1,953 separate episodes of UTI. Most of the included studies examined UTI in infants. One study included adults and four others included boys beyond the first year of life. Studies generally reported episodes of UTI rather than patients with UTI and only one reported recurrent episodes of UTI in individual patients.

The single randomized controlled trial by Nayir \(^{21}\) was a study of recurrent UTI. Seventy uncircumcised patients with proven UTI were recruited and then randomized into circumcision and non-circumcision groups. UTI was defined as a positive urine culture with \(>10^8/L\) pure growth from a bag or clean catch specimen in the presence of urinary symptoms. The presence of urinary tract abnormality was the only exclusion criterion. Although this trial ran for 12 months, only the 6 months of parallel follow-up was included in the systematic review as the boys randomized to the no-circumcision group were circumcised at 6 months.

Quality of included studies
For the single randomised trial \(^{21}\), follow-up was complete and analysis was by intention to treat but no details were provided regarding the method of randomisation, concealment of allocation, or blinding. No demographic details other than age were available for comparison between the two groups.

The quality of these studies the case control and cohort studies was variable, with variable UTI definitions used and different methods used to ascertain circumcision status and UTI outcome. Exclusion criteria and adjustment for confounding also varied among the studies. Only one of the cohort studies followed patients beyond 1 year and in the case control studies, all controls were obtained from hospital-based populations (Tables 2 and 3).

The confounders adjusted for included age, socioeconomic status and ethnicity. Both socioeconomic status and ethnicity were associated with circumcision status in a number
of studies but there was no evidence of an association between these factors and UTI outcome between the circumcised and uncircumcised groups.

**Association between circumcision and UTI (Figure 2)**

**Randomised controlled trial**
The randomised study from Nayir \(^2^1\) had an OR of 0.13 (95% CI 0.01, 2.63).

**Cohort studies**
All four cohort studies \(^1^, ^5^, ^6^, ^2^2\) showed benefit with a summary OR of 0.13 (95% CI 0.07, 0.23). There was significant heterogeneity between the cohort studies \((\chi^2 = 82.48, df=3, \ p<0.001)\) with the study by To et al \(^1\) being the outlier. With the study by To et al \(^1\) excluded the heterogeneity between cohort studies was non-significant \((\chi^2 = 0.88, df=2, \ p=0.64)\).

The reasons for the observed heterogeneity are uncertain but may reflect varying methods of circumcision and UTI ascertainment, and the follow-up periods of the studies.

**Circumcision status:** To et al \(^1\) were able to access information regarding circumcision beyond the neonatal period and excluded subjects circumcised after the age of 1 month. The three other cohort studies were unable to account for circumcisions undertaken after the neonatal inpatient stay. If there were a significant number of circumcisions carried out beyond the neonatal inpatient period, these studies would underestimate UTI occurrence in the circumcised group and thus result in misclassification.

**Follow-up duration:** The study by To \(^1\) extended follow-up to as long as 3 years compared to a maximum of 1 year for the other cohort studies. To \(^1\) showed a progressive reduction in the protective effect of circumcision on UTI with increasing age. Thus, the inclusion of older subjects may have contributed to the difference in results. The Craig study \(^2^3\), however, which stratified for age, found no such difference, but was small and may have been subject to Type II error.

**UTI diagnostic criteria:** The Wiswell studies \(^5^, ^6^\) did not specify diagnostic criteria for defining UTI, while the To et al study \(^1\) used International Classification of Disease, 9\(^{th}\) Revision and Ontario Health Insurance Plan data coding and the Schoen study \(^2^2\) used laboratory data. These differing definitions of UTI are an unlikely source of variability in the results.

To \(^1\) was also the only study to account for repeat episodes of UTI in individual patients and showed that the contributory effect of these repeat episodes was minimal. The other studies recorded the overall number of UTI episodes rather than the number of patients with UTI.

**Case control studies**
All seven case control studies \(^2^3^\text{-}^2^9\) included showed benefit with a combined OR of 0.13 (95% CI 0.07, 0.23). There was no significant heterogeneity between the studies within this group \((\chi^2 = 8.15, df=6, \ p=0.2)\).
All studies
The summary OR across study types when all three were combined was 0.13 (95% CI 0.08, 0.20). There was no significant heterogeneity between the three subgroups ($\chi^2=0.16$, df=2, p=0.9). However, significant heterogeneity was observed between the individual studies ($\chi^2=90.63$, df=11, p<0.00001) due to the inclusion of the To study 1. Without To 1 there was no significant heterogeneity observed between the remaining studies ($\chi^2=10.92$, df=10, p<0.4).

Discussion

The odds of UTI in circumcised boys is about 0.1 when compared with uncircumcised boys. This represents a reduction in odds of nearly 90%.

What is striking from these results is the level of homogeneity in the effect across a variety of settings and the three different study designs. An OR of 0.13 reflects a substantial reduction and makes residual confounding an unlikely source of the observed association.

The temporal and biological plausibility of circumcision (by modifying preputial colonisation 28 and thus decreasing the potential sources of bacteria causing UTI) adds weight to the association being a genuine effect of circumcision on UTI. However, colonisation may also increase the risk of contamination of bag urine collections leading to false positive urine cultures in uncircumcised boys. The method of urine collection was poorly defined or included bag urine collections in a significant number of the studies included in this systematic review 1,5,6,22,23,27, potentially overestimating the rate of UTI in the uncircumcised group. In the remaining studies, clean catch urine or suprapubic tap was the method of urine collection and the favorable odds ratio was maintained even when the above bias was minimized.

The principal weakness of this systematic review is that it is dominated by observational studies of variable quality. The one randomised controlled trial identified had a small sample size and failed to achieve independent statistical significance. However, the point estimate of OR for this randomised controlled trial was identical to that of the other included studies, and our combined result.

Another shortcoming is that the majority of studies measured episodes of UTI rather than the number of patients experiencing UTI. Thus, the prevalence of repeat UTI in these populations is not known and may have biased the observed results if the distribution of patients with repeat UTI was unequal between the two treatment groups. However, as seen in the To study 1, the number of recurrences is likely to be small and an unlikely explanation for the large difference observed between the circumcised and uncircumcised groups.
Existing systematic reviews on the association between circumcision and UTI by Amato in 1992 and Wiswell in 1993 also concluded that circumcision was associated with a protective effect on UTI with ORs of 0.07 (95% CI, 0.06-0.09) and 0.08 (95% CI 0.07-0.09) respectively being obtained. These results imply a more protective effect than our results. This difference may be explained by the fact that we have included a number of additional studies published since the earlier meta-analyses. We also excluded duplicate data from our analysis and have examined heterogeneity between the available data.

While circumcision is protective for UTI, the overall risk-benefit derived from circumcision in preventing UTI is not easily quantifiable as the incidence of important sequelae of UTI (sepsis, permanent renal damage, hypertension and chronic renal failure) are not known. The complication rate of circumcision is documented to be between 2% and 10% and no data is available on the utility of the range of risks and benefits of circumcision. Thus we have used a conservative of circumcision complication of 2% and assumed equal utility for benefits and harms in the following analysis.

Existing studies suggest that from 1% to 2% of boys can be expected to experience a UTI within the first 10 years of life. From the data included in this meta-analysis, the UTI rate in the uncircumcised group was approximately 0.5% and may reflect a shorter follow up period than other studies. Furthermore, studies have shown a recurrence rate of UTI in preschool children of around 10% in the absence of significant urinary tract abnormality. The recurrence rate increases to 30% in children with vesicoureteric reflux of grade 3 and above. We have used these estimates of UTI incidence and circumcision complication rate to construct a table of harms and benefits of circumcision.

This shows that the benefit of circumcision on UTI only outweighs the risk in boys who have had UTI previously and have a predisposition to repeated UTI. As this analysis has used a conservative circumcision complication rate of 2%, if the complication rate was in reality higher the risk benefit analysis may not favour circumcision even in the higher risk populations.

In conclusion, the data we present does not support the routine circumcision of normal boys with standard risk in order to prevent UTI. However, our data suggest that circumcision of boys with higher than normal risk of UTI should be considered. As there is no direct evidence of the effect of circumcision on UTI in this group, confirmation through a randomised trial of circumcision in high-risk patients would be beneficial. Using an OR of 0.2 (the upper limit of the 95% CI of the combined OR found in this study) and a power of 80%, the sample size required to study this hypothesis would be 140 (70 in each treatment arm), assuming a recurrence risk of 10%.

Until this additional information is available, the present data does not support the routine circumcision of males to prevent UTI. However, circumcision should be considered in those with recurrent UTI or significantly increased risk of UTI.
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What this paper adds
While a reduction in the risk of urinary tract infection (UTI) has been reported with circumcision, the magnitude of the benefit remains uncertain. This may be due to variability in different methods used to search and critically appraise the available literature.
The data from this review shows that circumcision substantially reduces the risk of UTI. The data does not support the routine circumcision of normal boys to prevent UTI. This review does, however, suggest that circumcision should be considered in males with a past history of recurrent UTI or high-grade (grade 3 and above) vesicoureteric reflux, as the benefit outweighs the risk of complications in these cases.

Figure Legends

Figure 1
Flow chart outlining study selection process for the effect of circumcision on urinary tract infection.

Figure 2
Meta-analysis of studies examining the effect of circumcision on urinary tract infection in males.
References


Table 1 – Characteristics of included studies that have examined the effect of circumcision on urinary tract infection in males.

<table>
<thead>
<tr>
<th>Study design</th>
<th>Author</th>
<th>Year</th>
<th>Country</th>
<th>Setting</th>
<th>N</th>
<th>Number of UTI episodes</th>
<th>Age (months, years)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Randomised controlled trial</td>
<td>Nayir 21</td>
<td>2001</td>
<td>Turkey</td>
<td>Hospital outpatients</td>
<td>70</td>
<td>3</td>
<td>3 months – 10 years</td>
</tr>
<tr>
<td>Cohort study</td>
<td>Schoen et al 22</td>
<td>2000</td>
<td>USA</td>
<td>Hospital in/outpatient</td>
<td>14,893</td>
<td>154</td>
<td>&lt;1 year</td>
</tr>
<tr>
<td></td>
<td>To et al 1</td>
<td>1998</td>
<td>Canada</td>
<td>Hospital in/outpatient</td>
<td>58,434</td>
<td>330</td>
<td>&lt;3 years</td>
</tr>
<tr>
<td></td>
<td>Wiswell &amp; Hachey 6</td>
<td>1993</td>
<td>USA</td>
<td>Hospital inpatient</td>
<td>107,598</td>
<td>496</td>
<td>&lt;1 year</td>
</tr>
<tr>
<td></td>
<td>Wiswell et al 5</td>
<td>1987</td>
<td>USA</td>
<td>Hospital inpatient</td>
<td>219,775</td>
<td>610</td>
<td>&lt;1 year</td>
</tr>
<tr>
<td>Case control study</td>
<td>Newman et al 24</td>
<td>2002</td>
<td>USA</td>
<td>Non-hospital outpatients</td>
<td>769</td>
<td>56</td>
<td>&lt;3 months</td>
</tr>
<tr>
<td></td>
<td>Craig et al 23</td>
<td>1996</td>
<td>Australia</td>
<td>Hospital in/outpatient</td>
<td>886</td>
<td>144</td>
<td>&lt;5 years</td>
</tr>
<tr>
<td></td>
<td>Rushton &amp; Majd 25</td>
<td>1992</td>
<td>USA</td>
<td>Hospital inpatient</td>
<td>86</td>
<td>23</td>
<td>&lt;6 months</td>
</tr>
<tr>
<td></td>
<td>Spach et al 26</td>
<td>1992</td>
<td>USA</td>
<td>Community sexually transmitted diseases clinic</td>
<td>78</td>
<td>26</td>
<td>Adult</td>
</tr>
<tr>
<td></td>
<td>Crain &amp; Gershel 27</td>
<td>1990</td>
<td>USA</td>
<td>Hospital outpatient</td>
<td>81</td>
<td>22</td>
<td>&lt;2 months</td>
</tr>
<tr>
<td></td>
<td>Kashani &amp; Faraday 28</td>
<td>1989</td>
<td>USA</td>
<td>Hospital inpatient</td>
<td>126</td>
<td>17</td>
<td>1 month to 2 years</td>
</tr>
<tr>
<td></td>
<td>Herzog 29</td>
<td>1989</td>
<td>USA</td>
<td>Hospital outpatient</td>
<td>112</td>
<td>36</td>
<td>&lt;1 year</td>
</tr>
</tbody>
</table>

*Outpatient data not included in analysis as it did not accurately define UTI events
Table 2 – Quality of cohort studies examining the effect of circumcision on urinary tract infection in males.

<table>
<thead>
<tr>
<th>Author</th>
<th>Definition of UTI</th>
<th>Determination of circumcision status</th>
<th>Exclusion criteria</th>
<th>Follow-up</th>
<th>Adjustment for confounders</th>
<th>Age</th>
<th>SES*</th>
<th>Ethnicity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Schoen et al</td>
<td>$&gt;10^9$/L pure growth in 90% from any means of collection. Source unknown in 4%.</td>
<td>Inpatient – ICD-9† coding for circumcision in neonatal hospital stay. Outpatient – ICD-9† from KPNC‡ database for outpatient circumcision.</td>
<td>Patient not within health plan for full duration of study.</td>
<td>&lt;1 year</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>To et al</td>
<td>Inpatients – ICD-9† coding (Kidney Infection, Cystitis, Urethritis or Urinary Tract Infection). Outpatients – OHIP§ data.</td>
<td>The Canadian Classification Procedure Code during the first month of life.</td>
<td>Older than 1 month of age at time of circumcision, multiple birth, stillbirth, birth complications and lack of Health Care Number.</td>
<td>2-3 years</td>
<td>No</td>
<td>Yes</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>Wiswell &amp; Hachey</td>
<td>Not specified.</td>
<td>US Army Patient Administration Systems and Biostatistics Activity database.</td>
<td>Bag urine specimen, congenital abnormality, or predisposition to UTI (not specified).</td>
<td>&lt;1 year</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>Wiswell et al</td>
<td>Not specified.</td>
<td>US Army Patient Administration Systems and Biostatistics Activity database.</td>
<td>Congenital abnormality or predisposition to UTI (not specified).</td>
<td>&lt;1 year</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>No</td>
</tr>
</tbody>
</table>

* SES = Socioeconomic status
† International Classification of Disease 9th Revision
‡ Kaiser Permanente Medical Care Program, Northern California, USA
§ Ontario Health Insurance Plan
Table 3 – Quality of case control studies examining the effect of circumcision on urinary tract infection in males.

<table>
<thead>
<tr>
<th>Author</th>
<th>Definition of UTI</th>
<th>Determination of circumcision status</th>
<th>Exclusion criteria</th>
<th>Origin of controls</th>
<th>Adjustment for confounders</th>
</tr>
</thead>
<tbody>
<tr>
<td>Newman et al 24</td>
<td>Bag urine or clean catch ≥ 10⁷/L CSU† ≥ 2x10⁹/L SPA‡≥ 10⁷/L</td>
<td>Standard questionnaire.</td>
<td>No fever &gt;38°C or urine collected at presentation. Uncertain circumcision status.</td>
<td>Patients presenting to non-hospital outpatients with a fever.</td>
<td>No No No</td>
</tr>
<tr>
<td>Craig et al 23</td>
<td>CSU/SPA 10⁸⁹/L MSUª 10⁷⁹/L</td>
<td>Direct questioning of parents or direct examination.</td>
<td>Past history of UTI or Urinary tract abnormality. Neurological or skeletal abnormality predisposing to UTI.</td>
<td>Patients presenting to hospital emergency department for any reason other than those diagnosed with UTI.</td>
<td>Yes No No</td>
</tr>
<tr>
<td>Rushton &amp; Majd 25</td>
<td>MSU≥ 10⁸/L CSU≥ 10⁷/L</td>
<td>Cases – “prospectively” found but not specified. Controls – documentation in medical record but no further details given.</td>
<td>Prolonged neonatal hospitalization or uncertain circumcision status.</td>
<td>Patients admitted with febrile upper respiratory tract infection. Matched for age, race and SES*.</td>
<td>No Yes Yes</td>
</tr>
<tr>
<td>Spach et al 26</td>
<td>MSU &gt;10⁹/L growth along with one or more symptoms.</td>
<td>Examination.</td>
<td>No clear exclusion criteria.</td>
<td>Patients without bacteruria presenting to outpatient clinic.</td>
<td>Yes No Yes Also adjusted for sexual preference and practices.</td>
</tr>
<tr>
<td>Crain &amp; Gershel 27</td>
<td>Bag urine≥10⁷⁹/L CSU≥ 10⁹⁹/L SPA≥ 10⁷⁷/L</td>
<td>Documentation in medical records no further details given.</td>
<td>Absence of fever.</td>
<td>Patients presenting to hospital with fever and without a discharge diagnosis UTI.</td>
<td>No No No</td>
</tr>
<tr>
<td>Kashani &amp; Faraday 28</td>
<td>CSU/SPA≥ 10⁷⁹/L</td>
<td>Documentation in medical record</td>
<td>Urinary tract abnormality, inadequate documentation of specimen type or age &lt;1 month.</td>
<td>Patients presenting to outpatients clinics for unrelated reasons.</td>
<td>No No Yes</td>
</tr>
<tr>
<td>Herzog 29</td>
<td>CSU/SPA≥ 10⁷⁹/L</td>
<td>Documentation in medical record or direct contact with family if unclear in medical records.</td>
<td>Anatomical abnormality, past history of UTI, myelodysplasia, uncertain circumcision status or race and equivocal culture results.</td>
<td>Patients who presented to emergency with a febrile illness and had a SPA or CSU which was negative.</td>
<td>Yes Yes Yes</td>
</tr>
</tbody>
</table>

* SES = Socioeconomic status  †CSU = Catheter specimen urine  ‡SPA=Suprapublic aspirate
ª MSU = Midstream urine
Table 4 – Benefits versus harms for circumcision in the prevention of UTI* in boys at different levels of risk for UTI* per 1000 boys. Assuming a complication rate of 2% and an OR‡ of 0.13.

<table>
<thead>
<tr>
<th>Patient group</th>
<th>Risk of UTI*</th>
<th>Number of UTI* in uncircumcised</th>
<th>Number of UTI* in circumcised</th>
<th>Number of UTI* prevented through circumcision</th>
<th>Number of complications of circumcision</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal</td>
<td>1%</td>
<td>10</td>
<td>1</td>
<td>9</td>
<td>20</td>
</tr>
<tr>
<td>Past UTI*</td>
<td>10%</td>
<td>100</td>
<td>13</td>
<td>87</td>
<td>20</td>
</tr>
<tr>
<td>High grade VUR</td>
<td>30%</td>
<td>300</td>
<td>39</td>
<td>261</td>
<td>20</td>
</tr>
</tbody>
</table>

* UTI = urinary tract infection  ‡ OR = odds ratio † VUR = vesicoureteric reflux
Citations retrieved from MEDLINE and EMBASE (n = 2166)

- UTI outcome not reported (n = 2036)

Abstracts retrieved (n = 130)

- UTI outcome not reported (n = 86)

Full text retrieval (n = 44)

Articles excluded after full appraisal (n = 33).
- Reviews (n = 19)
- Cost-benefit analyses (n = 4)
- Position statements (n = 4)
- Meta-analyses (n = 1)
- Other (n = 5)

Articles included in the systematic review (n = 11)

- Additional studies identified through reference lists and contact with authors (n = 3)
- Duplicate studies excluded (n = 2)

Included in final analysis (n = 12)
- Randomised controlled trial (n = 1)
- Cohort studies (n = 4)
- Case control studies (n = 7)
Review: Circumcision  
Comparison: 01 UTI  
Outcome: 01 Number of UTI episodes

<table>
<thead>
<tr>
<th>Study or sub-category</th>
<th>Circumcised n/N</th>
<th>Uncircumcised n/N</th>
<th>OR (random) 95% CI</th>
<th>/Weight %</th>
<th>OR (random) 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>01 Randomised Trials</td>
<td></td>
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<tr>
<td>Navir [21]</td>
<td>0/35</td>
<td>3/35</td>
<td>1.95</td>
<td>0.13</td>
<td>[0.01, 2.63]</td>
</tr>
<tr>
<td>Subtotal (95% CI)</td>
<td>35</td>
<td>35</td>
<td></td>
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<tr>
<td>Total events: 0 (Circumcised), 3 (Uncircumcised)</td>
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<tr>
<td>Test for heterogeneity: not applicable</td>
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<tr>
<td>Test for overall effect: Z = 1.33 (P = 0.18)</td>
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<tr>
<td>02 Cohort Studies</td>
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<tr>
<td>Schoen et al [22]</td>
<td>22/9668</td>
<td>132/5225</td>
<td>12.71</td>
<td>0.09</td>
<td>[0.06, 0.14]</td>
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<tr>
<td>To et al [1]</td>
<td>83/29217</td>
<td>247/29217</td>
<td>13.95</td>
<td>0.33</td>
<td>[0.26, 0.43]</td>
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<tr>
<td>Wiswell &amp; Hackey [6]</td>
<td>112/80279</td>
<td>384/27319</td>
<td>14.13</td>
<td>0.10</td>
<td>[0.08, 0.12]</td>
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<tr>
<td>Wiswell et al [5]</td>
<td>151/173663</td>
<td>459/46112</td>
<td>14.24</td>
<td>0.09</td>
<td>[0.07, 0.10]</td>
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<tr>
<td>Subtotal (95% CI)</td>
<td>292827</td>
<td>107873</td>
<td></td>
<td>0.13</td>
<td>[0.07, 0.24]</td>
</tr>
<tr>
<td>Total events: 368 (Circumcised), 1222 (Uncircumcised)</td>
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<tr>
<td>Test for heterogeneity: Ch² = 62.59, df = 3 (P &lt; 0.00001), P = 96.4%</td>
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<tr>
<td>Test for overall effect: Z = 6.26 (P &lt; 0.00001)</td>
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<tr>
<td>03 Case Control Studies</td>
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<tr>
<td>Herzog [29]</td>
<td>0/52</td>
<td>36/60</td>
<td>2.15</td>
<td>0.01</td>
<td>[0.00, 0.11]</td>
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<td>Kashani et al [28]</td>
<td>1/43</td>
<td>16/83</td>
<td>3.62</td>
<td>0.10</td>
<td>[0.01, 0.78]</td>
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<tr>
<td>Rushton &amp; Majd [25]</td>
<td>2/37</td>
<td>21/49</td>
<td>5.43</td>
<td>0.08</td>
<td>[0.02, 0.35]</td>
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<tr>
<td>Craig et al [23]</td>
<td>2/49</td>
<td>142/837</td>
<td>5.93</td>
<td>0.21</td>
<td>[0.05, 0.87]</td>
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<tr>
<td>Crain &amp; Gershel [27]</td>
<td>4/35</td>
<td>18/46</td>
<td>7.19</td>
<td>0.20</td>
<td>[0.06, 0.66]</td>
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<tr>
<td>Spach et al [26]</td>
<td>18/64</td>
<td>8/14</td>
<td>7.23</td>
<td>0.29</td>
<td>[0.09, 0.97]</td>
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<td>Newman et al [24]</td>
<td>15/5720</td>
<td>41/197</td>
<td>11.45</td>
<td>0.10</td>
<td>[0.06, 0.19]</td>
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<tr>
<td>Subtotal (95% CI)</td>
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<td>1286</td>
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<td>[0.07, 0.23]</td>
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<tr>
<td>Total events: 42 (Circumcised), 282 (Uncircumcised)</td>
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<tr>
<td>Test for heterogeneity: Ch² = 8.55, df = 5 (P = 0.20), P = 29.9%</td>
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<td>Test for overall effect: Z = 6.85 (P &lt; 0.00001)</td>
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<tr>
<td>Total (95% CI)</td>
<td>293714</td>
<td>109194</td>
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<td>100.00</td>
<td>[0.08, 0.20]</td>
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<tr>
<td>Total events: 410 (Circumcised), 1507 (Uncircumcised)</td>
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<tr>
<td>Test for heterogeneity: Ch² = 90.63, df = 11 (P &lt; 0.00001), P = 87.9%</td>
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<tr>
<td>Test for overall effect: Z = 8.99 (P &lt; 0.00001)</td>
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</tbody>
</table>
Circumcision for the prevention of urinary tract infection in boys: A systematic review of randomized trials and observational studies

Davinder Singh-Grewal, Joseph MaCdessi and Jonathan Craig

Arch Dis Child published online May 12, 2005

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