ORIGINAL ARTICLE

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

D Singh-Grewal, J Macdessi, J Craig

....

See end of article for authors' affiliations
....

Correspondence to:
Jonathan Craig, Centre for Kidney Research, Clinical Sciences Building, Locked Bag 4001, Westmead NSW 2145, Sydney, Australia; jonc@health.usyd.edu.au

Objective: To undertake a meta-analysis of published data on the effect of circumcision on the risk of urinary tract infection (UTI) in boys.

Data sources: Randomised controlled trials and observational studies comparing the frequency of UTI 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.

Methods: Two of the authors independently assessed study quality using the guidelines provided by the MOOSE statement for quality of observational studies. A random effects model was used to estimate a summary odds ratio (OR) with 95% confidence intervals (CI).

Results: Data on 402 908 children were identified from 12 studies (one randomised controlled trial, four cohort studies, and seven case–control studies). Circumcision was associated with a significantly reduced risk of UTI (OR = 0.13; 95% CI, 0.08 to 0.20; p<0.001) with the same odds ratio (0.13) for all three types of study design.

Conclusions: Circumcision reduces the risk of UTI. Given a risk in normal boys of about 1%, the number-needed-to-treat to prevent one UTI is 111. In boys with recurrent UTI or high grade vesicoureteric reflux, the risk of UTI 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%. Assuming equal utility of benefits and harms, net clinical benefit is likely only in boys at high risk of UTI.

C ircumcision is the commonest surgical procedure carried out on children.[1] Neonatal circumcision rates vary widely between different cultures, with rates as high as 64%[2] in North America, between 10% and 20% in Australia,[3] and far lower rates in Europe and Asia.[2]

Boys have been circumcised for thousands of years and circumcision plays 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),[4–6] sexually transmitted diseases,[7] penile cancer,[8] and phimosis,[9] and a reduction in the incidence of human papilloma virus related cervical cancer in female sexual partners.[10]

The overall complication rate of circumcision is between 2% and 10%,[11 12] and most complications are minor.[11 13 14] While haemorrhage is the most frequent acute complication, infection, glandular ulceration, urethral fistula formation, and penile amputation can also occur.[11] Long term complications include meatal stenosis and poor cosmetic results.[11]

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.[2 3 15]

Lack of a clear consensus on the magnitude of the benefits of circumcision may reflect the variability in the different methods used to search and critically appraise the available reports.[16] 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 male subjects of all ages.

METHODS

All steps of the review, including literature search, data extraction, and data analysis, were carried out independently by two of us (JM and DSG) without blinding to authorship. Resolution of discrepancies was by consensus and the involvement of the 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 before assessment. When more than one report of the same data was found, data were extracted only from the paper containing the most complete data.

Study selection

All studies examining the effect of male circumcision on UTI were included. The population of interest was male 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 2×2 contingency table to be constructed, so that the odds of UTI in the circumcised group could be compared with those in the uncircumcised group.

....

Abbreviations: CONSORT, consolidated standards for reporting trials; MOOSE, meta-analysis of observational studies in epidemiology; UTI, urinary tract infection

Data extraction

Randomised studies were assessed using the guidelines provided by the CONSORT statement.[17] 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.[18] The quality of studies identified 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 confounding variables.

Data synthesis

Statistical analysis was done with Review Manager (version 4.2).[19] 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 (that is, randomised controlled trial, cohort study, or case–control study) and then an overall OR was calculated across all study types if no heterogeneity was present.

Consistency of the intervention effects across studies was evaluated using the Cochran Q statistic for heterogeneity with $n-1$ degrees of freedom and an α of 0.05. This method calculates a χ^2 statistic, with $p < 0.05$ suggesting that the observed variation in the OR is unlikely to be a result of chance alone.[20] 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.[20] 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

The study selection process is outlined in fig 1. From 2166 titles and abstracts retrieved, 12 fulfilled the inclusion criteria (one randomised trial, four cohort studies, and seven case–control studies).

Characteristics of the studies included

The characteristics of the studies included are outlined in table 1. All were published between 1987 and 2001. Most originated from North America and relied on hospital inpatient and outpatient data. These 12 studies provided data on 402 908 children and 1953 separate episodes of UTI. Most of the studies included examined UTI in infants. One 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 randomised controlled trial by Nayir[21] was a study of recurrent UTI. Seventy uncircumcised patients with proven UTI were recruited and then randomised 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 six months of parallel follow up was included in the systematic review as the boys randomised to the no circumcision group were circumcised at six months.

Quality of the included studies

For the single randomised trial,[21] follow up was complete and analysis was by intention to treat but no details were provided about 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 employed 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 one year, and in the case–control studies all controls were obtained from hospital based populations (tables 2 and 3).

The confounding variables that were adjusted for included age, socioeconomic status, and ethnicity. Both socioeconomic status and ethnicity were associated with circumcision status in several 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 summarises the results of our meta-analysis.
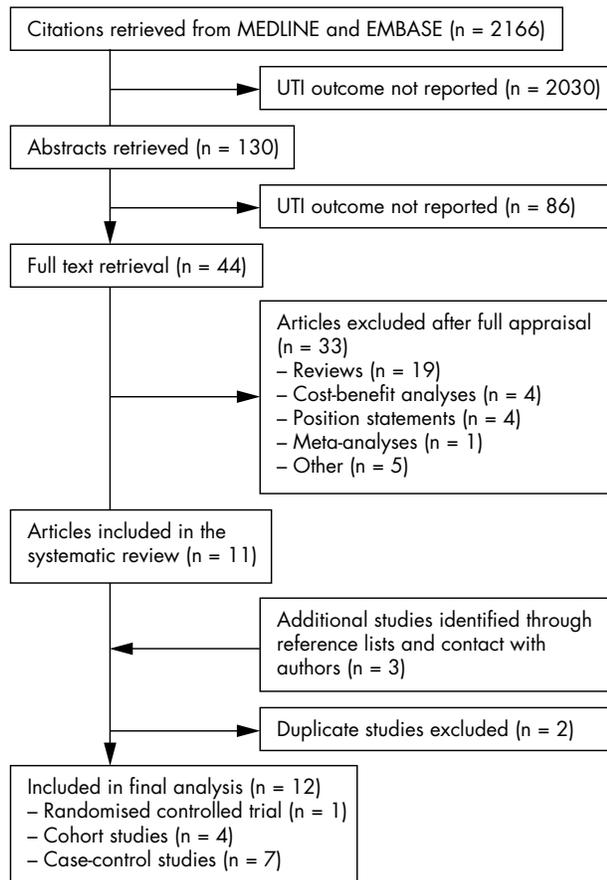
Randomised controlled trial

The randomised study from Nayir[21] had an OR of 0.13 (95% CI, 0.01 to 2.63).

Cohort studies

All four cohort studies[1 5 6 22] showed benefit with a summary OR of 0.13 (95% CI, 0.07 to 0.23). There was significant

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

Table 1 Characteristics of included studies that have examined the effect of circumcision on urinary tract infection in male subjects

Study design	Reference	Year	Country	Setting	n	No of UTI episodes	Age (months, years)
RCT	Nayir[21]	2001	Turkey	Hospital outpatients	70	3	3 months to 10 years
Cohort studies	Schoen et al[22]	2000	USA	Hospital in/outpatient	14 893	154	<1 year
	To et al[1]	1998	Canada	Hospital in/outpatient*	58 434	330	<3 years
	Wiswell and Hachey[6]	1993	USA	Hospital inpatient	107 598	496	<1 year
	Wiswell et al[5]	1987	USA	Hospital inpatient	219 775	610	<1 year
Case–control studies	Craig et al[23]	1996	Australia	Hospital in/outpatient	886	144	<5 years
	Newman et al[24]	2002	USA	Non-hospital outpatients	769	56	<3 months
	Rushton and Majd[25]	1992	USA	Hospital inpatient	86	23	<6 months
	Spach et al[26]	1992	USA	Community sexually transmitted diseases clinic	78	26	Adult
	Crain and Gershel[27]	1990	USA	Hospital outpatient	81	22	<2 months
	Kashani and Faraday[28]	1989	USA	Hospital inpatient	126	17	1 month to 2 years
	Herzog[29]	1989	USA	Hospital outpatient	112	36	<1 year

*Outpatient data not included in analysis as they did not accurately define UTI events.
RCT, randomised controlled trial; UTI, urinary tract infection.

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. When the study by To was 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 differing follow up periods of the studies.

In relation to 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 one month. The three other cohort studies were unable to account for circumcisions undertaken after the neonatal inpatient stay. If there were significant numbers 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 three years compared with a maximum of one year for the other cohort studies. To 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,[23] however, which stratified for age, found no such difference, but was small and may have been subject to type II error.

Table 2 Quality of cohort studies examining the effect of circumcision on urinary tract infection in male subjects

Reference	Definition of UTI	Determination of circumcision status	Exclusion criteria	Follow up	Adjustment for confounding variables		
					Age	SES	Ethnicity
Schoen et al[22]	>10^8/l pure growth in 90% from any means of collection Source unknown in 4% Determined by retrospective database search and confirmed by review of case records of random selection of 52 cases	Inpatients: ICD-9 coding for circumcision in neonatal hospital stay Outpatients: ICD-9 from KPNC database for outpatient circumcision	Patient not within health plan for full duration of study	<1 year	No	No	No
To et al[1]	Inpatients: ICD-9 coding (kidney infection, cystitis, urethritis or urinary tract infection) Outpatients: OHIP data Determined by retrospective database search	The Canadian classification procedure code during the first month of life	Older than 1 month of age at time of circumcision, multiple birth, stillbirth, birth complications and lack of health care number	2–3 years for inpatient cases <1 year for outpatient cases	No	Yes	No
Wiswell and Hachey[6]	Not specified Determined by retrospective database search	US Army patient administration systems and biostatistics activity database	Bag urine specimen, congenital abnormality, or predisposition to UTI (not specified)	<1 year	No	No	No
Wiswell et al[5]	Not specified Determined by retrospective database search	US Army patient administration systems and biostatistics activity database	Congenital abnormality or predisposition to UTI (not specified)	<1 year	No	No	No

ICD-9, International Classification of Diseases, 9th revision; KPNC, Kaiser Permanente Medical Care Program, Northern California, USA; OHIP, Ontario Health Insurance Plan; SES, socioeconomic status.

Table 3 Quality of case–control studies examining the effect of circumcision on urinary tract infection in male subjects

Reference	Definition of UTI	Determination of circumcision status	Exclusion criteria	Origin of controls	Adjustment for confounding variables		
					Age	SES	Ethnicity
Newman et al[24]	Bag urine or clean catch $\geq10^7/l$ CSU $\geq2\times10^6/l$ SPA $\geq10^4/l$	Standard questionnaire	No fever >38°C or urine collected at presentation Uncertain circumcision status	Patients presenting to non-hospital outpatients with a fever	No	No	No
Craig et al[23]	CSU/SPA $\geq10^6/l$ MSU $\geq10^8/l$	Direct questioning of parents or direct examination	Past history of UTI or urinary tract abnormality; neurological or skeletal abnormality predisposing to UTI	Patients presenting to hospital emergency department for any reason other than those diagnosed with UTI	Yes	No	No
Rushton and Majd[25]	MSU $\geq10^8/l$ CSU $\geq10^7/l$	Cases: ''prospectively'' found but not specified Controls: documentation in medical record but no further details given	Prolonged neonatal hospital admission or uncertain circumcision status	Patients admitted with febrile upper respiratory tract infection. Matched for age, race, and SES	No	Yes	Yes
Spach et al[26]	MSU $>10^6/l$ growth along with one or more symptoms	Examination	No clear exclusion criteria	Patients without bacteriuria presenting to outpatient clinic	Yes	No	Yes
Crain and Gershel[27]	Bag urine $\geq10^4/l$ CSU $\geq10^4/l$ SPA $\geq10^2/l$	Documentation in medical records no further details given	Absence of fever	Patients presenting to hospital with fever and without a discharge diagnosis of UTI	No	No	No
Kashani and Faraday[28]	CSU/SPA $\geq10^8/l$	Documentation in medical record	Urinary tract abnormality, inadequate documentation of specimen type or age <1 month	Patients presenting to outpatients clinics for unrelated reasons	No	No	Yes
Herzog[29]	CSU/SPA $\geq10^7/l$	Documentation in medical record or direct contact with family if unclear in medical records	Anatomical abnormality, past history of UTI, myelodysplasia, uncertain circumcision status or race, and equivocal culture results	Patients who presented to emergency with a febrile illness and had a SPA or CSU which was negative	Yes	Yes	Yes

CSU, catheter specimen of urine; MSU, midstream urine; SES, socioeconomic status; SPA, suprapubic aspirate; UTI, urinary tract infection.

UTI diagnostic criteria

The Wiswell studies[5][6] did not specify diagnostic criteria for defining UTI, while the study by To et al[1] used *International Classification of Disease*s, 9th revision and Ontario Health Insurance Plan data coding, and the Schoen study[22] used laboratory data. These differing definitions of UTI are an unlikely source of variability in the results.

The study by To was also the only one 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 included[23–29] showed benefit, with a combined OR of 0.13 (95% CI, 0.07 to 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 to 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) owing to the inclusion of the To study.[1] Without To[1] there was no significant heterogeneity between the remaining studies ($\chi^2 = 10.92$, df = 10, p<0.4).
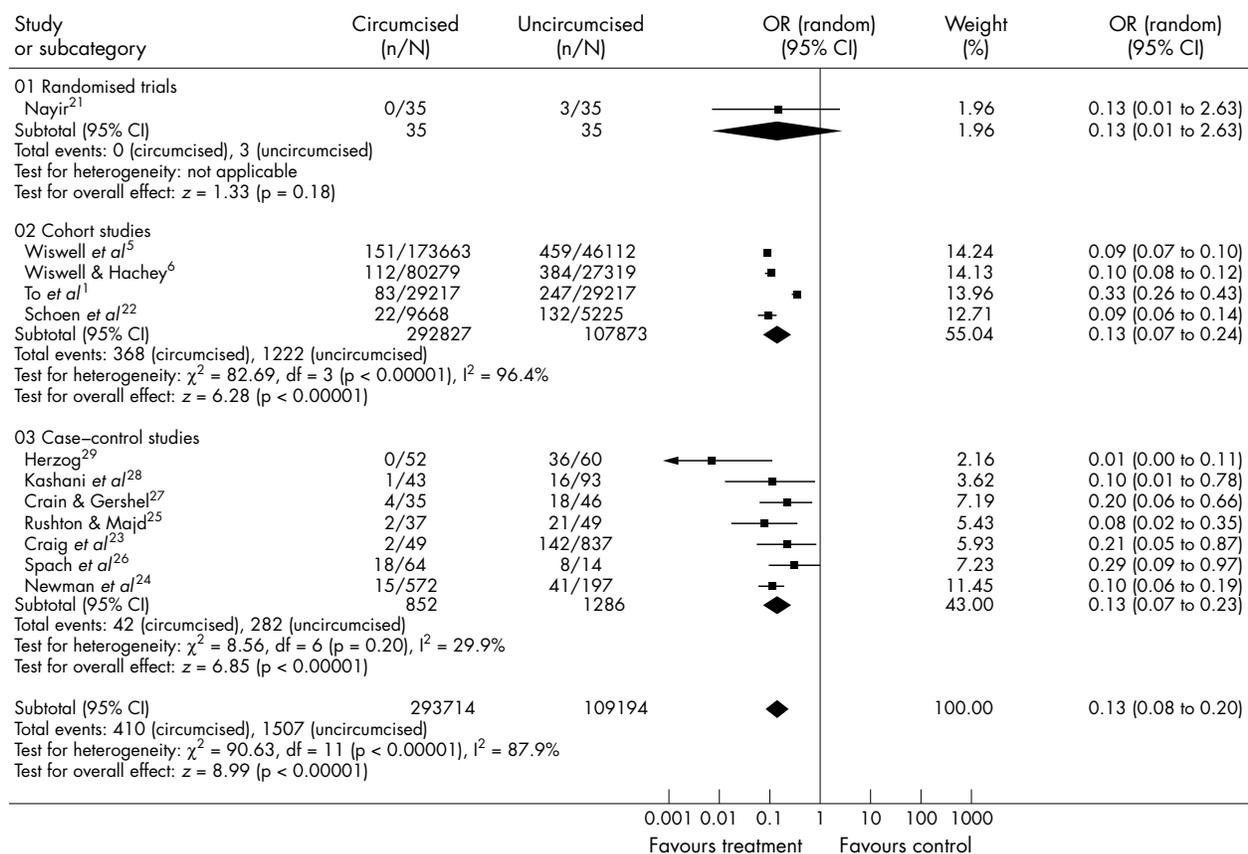
DISCUSSION

The odds of UTI in circumcised boys are 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][30] and thus decreasing the potential source 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 in this systematic review,[1][5][6][22][23][27] thus 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 favourable odds ratio was maintained even when the above bias was minimised.

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

Study or subcategory	Circumcised (n/N)	Uncircumcised (n/N)	OR (random) (95% CI)	Weight (%)	OR (random) (95% CI)
01 Randomised trials					
Nayir[21]	0/35	3/35		1.96	0.13 (0.01 to 2.63)
Subtotal (95% CI)	35	35		1.96	0.13 (0.01 to 2.63)
Total events: 0 (circumcised), 3 (uncircumcised)					
Test for heterogeneity: not applicable					
Test for overall effect: $z = 1.33$ ($p = 0.18$)					
02 Cohort studies					
Wiswell et al[5]	151/173663	459/46112		14.24	0.09 (0.07 to 0.10)
Wiswell & Hachey[6]	112/80279	384/27319		14.13	0.10 (0.08 to 0.12)
To et al[1]	83/29217	247/29217		13.96	0.33 (0.26 to 0.43)
Schoen et al[22]	22/9668	132/5225		12.71	0.09 (0.06 to 0.14)
Subtotal (95% CI)	292827	107873		55.04	0.13 (0.07 to 0.24)
Total events: 368 (circumcised), 1222 (uncircumcised)					
Test for heterogeneity: $\chi^2 = 82.69$, df = 3 ($p < 0.00001$), $I^2 = 96.4\%$					
Test for overall effect: $z = 6.28$ ($p < 0.00001$)					
03 Case–control studies					
Herzog[29]	0/52	36/60		2.16	0.01 (0.00 to 0.11)
Kashani et al[28]	1/43	16/93		3.62	0.10 (0.01 to 0.78)
Crain & Gershel[27]	4/35	18/46		7.19	0.20 (0.06 to 0.66)
Rushton & Majd[25]	2/37	21/49		5.43	0.08 (0.02 to 0.35)
Craig et al[23]	2/49	142/837		5.93	0.21 (0.05 to 0.87)
Spach et al[26]	18/64	8/14		7.23	0.29 (0.09 to 0.97)
Newman et al[24]	15/572	41/197		11.45	0.10 (0.06 to 0.19)
Subtotal (95% CI)	852	1286		43.00	0.13 (0.07 to 0.23)
Total events: 42 (circumcised), 282 (uncircumcised)					
Test for heterogeneity: $\chi^2 = 8.56$, df = 6 ($p = 0.20$), $I^2 = 29.9\%$					
Test for overall effect: $z = 6.85$ ($p < 0.00001$)					
Subtotal (95% CI)	293714	109194		100.00	0.13 (0.08 to 0.20)
Total events: 410 (circumcised), 1507 (uncircumcised)					
Test for heterogeneity: $\chi^2 = 90.63$, df = 11 ($p < 0.00001$), $I^2 = 87.9\%$					
Test for overall effect: $z = 8.99$ ($p < 0.00001$)					

```
        0.001  0.01  0.1    1    10   100  1000
         Favours treatment      Favours control
```

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

controlled trial was identical to that of the other studies included, and to 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[4] and Wiswell in1993[6] also concluded that circumcision was associated with a protective effect on UTI, with ORs of 0.07 (95% CI, 0.06 to 0.09) and 0.08 (0.07 to 0.09), respectively, being obtained. These results imply a more protective effect than we found in our analysis. This difference may be explained by the fact that we included several additional studies[11 21 23 24 26] published

since the earlier meta-analyses. We also excluded duplicate data from our analysis and 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%,[11 12] and no data are available on the relative risks and benefits of circumcision. Thus we have used a conservative estimate of circumcision complications 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.[23 31 32] 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[32 33] have shown a recurrence rate of UTI in preschool children of around 10% in the absence of

Table 4 Benefit versus harm for circumcision in preventing urinary tract infection in boys at different levels of risk for UTI per 1000 boys, assuming a complication rate of 2% and an odds ratio of 0.13

Patient group	Risk of UTI	UTI in uncircumcised (n)	UTI in circumcised (n)	UTI prevented by circumcision (n)	Complications of circumcision (n)
Normal	1%	10	1	9	20
Past UTI	10%	100	13	87	20
High grade VUR	30%	300	39	261	20

OR, odds ratio; UTI, urinary tract infection; VUR, vesicoureteric reflux.

What is already known on this topic

- 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 urinary tract infection
- Lack of a clear consensus on the magnitude of the benefits of circumcision may reflect variability in the different methods used to search and critically appraise the available reports

What this study adds

- Meta-analysis of existing research shows that circumcision substantially reduces the risk of urinary tract infection (UTI)
- The data do not support the routine circumcision of normal boys to prevent UTI
- Circumcision should be considered in boys 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

significant urinary tract abnormality. The recurrence rate increases to 30% in children with vesicoureteric reflux of grade 3 and above.[32][33] We have used these estimates of UTI incidence and circumcision complication rate to construct a table of harms and benefits of circumcision (table 4).

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 were in reality higher the risk–benefit analysis may not favour circumcision even in the higher risk populations.

In conclusion, the data we present do 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 do not support the routine circumcision of boys to prevent UTI. However, circumcision should be considered in those with recurrent UTI or significantly increased risk of UTI.

. . . .

Authors' affiliations
D Singh-Grewal, J Macdessi, Department of Paediatrics and Child Health, The Children's Hospital at Westmead, Sydney, Australia
J Craig, Centre for Kidney Research, The Children's Hospital at Westmead, Sydney, Australia

REFERENCES

1 **To T**, Agha M, Dick PT, et al. Cohort study on circumcision of newborn boys and subsequent risk of urinary-tract infection. Lancet 1998;**352**:1813–16.
2 **American Academy of Pediatrics**. Circumcision policy statement. American Academy of Pediatrics. Task Force on Circumcision. Pediatrics 1999;**103**:686–93.
3 **Royal Australasian College of Physicians**. Paediatrics and Child Health Division. Policy statement on circumcision, 2002, www.racp.edu.au/hpu/paed/circumcision/index.htm#toc.
4 **Amato D**, Garduno-Espinosa J. Circumcision in the newborn child and risk of urinary tract infection during the first year of life. A meta-analysis. Bol Med Hosp Infant Mexico 1992;**49**:652–8.
5 **Wiswell TE**, Enzenauer RW, Holton ME, et al. Declining frequency of circumcision: implications for changes in the absolute incidence and male to female sex ratio of urinary tract infections in early infancy. Pediatrics 1987;**79**:338–42.
6 **Wiswell TE**, Hachey WE. Urinary tract infections and the uncircumcised state: an update. Clin Pediatr 1993;**32**:130–4.
7 **Cook LS**, Koutsky LA, Holmes KK. Circumcision and sexually transmitted diseases. Am J Public Health 1994;**84**:197–201.
8 **Schoen EJ**. The relationship between circumcision and cancer of the penis. Cancer J Clin 1991;**41**:306–9.
9 **Dewan PA**, Tieu HC, Chieng BS. Phimosis: is circumcision necessary? J Paediatr Child Health 1996;**32**:285–9.
10 **Castellsagué X**, Bosch FX, Muñoz N, et al. Male circumcision, penile human papillomavirus infection, and cervical cancer in female partners. N Engl J Med 2002;**346**:1105–12.
11 **Williams N**, Kapila L. Complications of circumcision. Br J Surg 1993;**80**:1231–6.
12 **Kaplan GW**. Complications of circumcision. Urol Clin North Am 1983;**10**:543–9.
13 **Griffiths DM**, Atwell JD, Freeman NV. A prospective survey of the indications and morbidity of circumcision in children. Eur Urol 1985;**11**:184–7.
14 **Harkavy KL**. The circumcision debate. Pediatrics 1987;**79**:649–50.
15 **Canadian Paediatric Society**. Neonatal circumcision revisited. Fetus and Newborn Committee, Canadian Paediatric Society. Can Med Assoc J 1996;**154**:769–80.
16 **Shaneyfelt TM**, Mayo-Smith MF, Rothwangl J. Are guidelines following guidelines? The methodological quality of clinical practice guidelines in the peer-reviewed medical literature. JAMA 1999;**281**:1900–5.
17 **Begg C**, Cho M, Eastwood S, et al. CONSORT statement – improving the quality of reporting of randomized controlled trials. JAMA 1996;**276**:637–9.
18 **Stroup DF**, Morton SC, Olkin I, et al. Meta-analysis of observational studies in epidemiology: a proposal for reporting. Meta-analysis of Observational Studies in Epidemiology (MOOSE) group. JAMA 2000;**283**:2008–12.
19 **RevMan Analyses [Computer program]**. Version 1.0 for Windows. In: Review Manager (RevMan) 4.2. Oxford: The Cochrane Collaboration, 2002.
20 **Higgins JPT**, Thompson SG, Deeks JJ, et al. Measuring inconsistency in meta-analysis. BMJ 2003;**327**:557–60.
21 **Nayir A**. Circumcision for the prevention of significant bacturia in boys. Paediatr Nephrol 2001;**16**:1129–34.
22 **Schoen EJ**, Colby CJ, Ray GT. Newborn circumcision decreases incidence and costs of urinary tract infections during the first year of life. Pediatrics 2000;**105**:789–93.
23 **Craig JC**, Knight JF, Sureshkumar P, et al. Effect of circumcision on incidence of urinary tract infection in preschool boys. J Pediatr 1996;**128**:23–27.
24 **Newman TB**, Bernzweig JA, Takayama JI, et al. Urine testing and urinary tract infections in febrile infants seen in office settings: The Paediatric Research Office Settings' Febrile Infant Study. Arch Pediatr Adolesc Med 2002;**156**:44–54.
25 **Rushton HG**, Majd M. Pyelonephritis in male infants: how important is the foreskin? J Urol 1992;**148**:733–6.
26 **Spach DH**, Stapleton AE, Stamm WE. Lack of circumcision increases the risk of urinary tract infection in young men. JAMA 1992;**267**:679–81.
27 **Crain EF**, Gershel JC. Urinary tract infections in febrile infants younger than 8 weeks of age. Pediatrics 1990;**86**:363–7.
28 **Kashani IJ**, Faraday MS. The risk of urinary tract infection in uncircumcised male infants. Int Pediatr 1989;**4**:44–5.
29 **Herzog LW**. Urinary tract infections and circumcision. A case-control study. Am J Dis Child 1989;**143**:348–50.
30 **Wiswell TE**, Miller GM, Gelston HM, et al. Effect of circumcision status on periurethral bacterial flora during the first year of life. J Pediatr 1988;**113**:442–6.
31 **Hellstrom A**, Hanson E, Hansson S, et al. Association between urinary symptoms at 7 years old and previous urinary tract infection. Arch Dis Child 1991;**66**:232–4.
32 **Winberg J**, Anderson HJ, Bregstom T, et al. Epidemiology of symptomatic urinary tract infection in childhood. Acta Paediatr Scand 1974;**252**(suppl):1–20.
33 **Panaretto KS**, Craig JC, Knight JF, et al. Risk factors for recurrent urinary tract infection in preschool children. J Paediatr Child Health 1999;**35**:454–9.