ORIGINAL ARTICLE

Short compared with standard duration of antibiotic treatment for urinary tract infection: a systematic review of randomised controlled trials

M Michael, E M Hodson, J C Craig, S Martin, V A Moyer

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

Correspondence to:
Dr E Hodson, Centre for Kidney Research, The Children's Hospital at Westmead, Locked Bag 4001, Westmead, NSW 2145, Australia;
Elisah@chw.edu.au

Accepted 12 March 2002
....

Aims: To compare the effectiveness of short course (2–4 days) with standard duration oral antibiotic treatment (7–14 days) for urinary tract infection (UTI).
Methods: Meta-analysis of randomised controlled trials using a random effects model. Ten trials were eligible, involving 652 children with lower tract UTI recruited from outpatient or emergency departments. Main outcome measures were UTI at the end of treatment, UTI during follow up (recurrent UTI), and urinary pathogens resistant to the treating antibiotic.
Results: There was no significant difference in the frequency of positive urine cultures between the short (2–4 days) and standard duration therapy (7–14 days) for UTI in children at 0–7 days after treatment (eight studies: RR 1.06; 95% CI 0.64 to 1.76) and at 10 days to 15 months after treatment (10 studies: RR 1.01; 95% CI 0.77 to 1.33). There was no significant difference between short and standard duration therapy in the development of resistant organisms in UTI at the end of treatment (one study: RR 0.57, 95% CI 0.32 to 1.01) or in recurrent UTI (three studies: RR 0.39, 95% CI 0.12 to 1.29).
Conclusion: A 2–4 day course of oral antibiotics is as effective as 7–14 days in eradicating lower tract UTI in children.

U rinary tract infection (UTI) is a common condition, occurring in 2% of boys and 8% of girls by 8 years of age.[1] Conventional treatment for UTI is 7–14 days of an antibiotic, chosen on the basis of in vitro sensitivity testing. This results in failure of bacteriuria clearance of 1–3%.[2 3] The potential advantages of short course therapy include improved compliance, decreased antibiotic related side effects, diminished selection of resistant organisms, and cost savings. In adult patients single dose therapy is effective and recommended for uncomplicated UTI.[4 5] In children single dose therapy has not been well accepted because of the higher prevalence of urinary tract pathology and the difficulties in excluding pyelonephritis on clinical features alone. A short course of antibiotics might be as effective as a standard course of 7–14 days and still provide the other benefits of single dose therapy.

Three previous reviews[6–8] involving 8, 14, and 22 trials respectively compared single dose or short course to standard duration antibiotic treatment for lower tract UTI. Two reviews[6 7] did not assess separately the efficacy of single dose and short course therapies and concluded that there was insufficient evidence to justify the use of single dose or short course antibiotic treatment for UTI in children. The third review[8] found no difference in cure rate, based on negative urine cultures taken 4–29 days after enrolment, between short (1–4 days) and standard duration (5 days or more) therapy. However, this review included studies which used different antibiotics in the short and standard treatment duration groups. Moreover, significant heterogeneity among studies was shown, casting some doubt on the validity of combining these data in a meta-analysis. The objective of this systematic review was to summarise the evidence regarding the effects of short course (2–4 days) compared to standard duration (7–14 days) oral antibiotic treatment on the persistence of UTI at the end of treatment and on the recurrence of UTI after treatment.

METHODS
Search strategies
Randomised and quasi-randomised controlled trials were identified from MEDLINE (1966 to February 2001), EMBASE (1988 to February 2001), and the Cochrane Controlled Trials Register (Cochrane Library Issue 1, 2001) without language restriction. The optimally sensitive strategies of the Cochrane Collaboration to identify randomised controlled trials were used for MEDLINE and EMBASE searches.[9 10] They were combined with subject headings and textwords for urinary tract infection and duration of treatment and limited to the paediatric age range (full details available on request). Reference lists of review articles, relevant trials, nephrology textbooks, and abstracts of scientific meetings were also searched. Two reviewers reviewed trials independently for study eligibility and extracted trial data.

Inclusion criteria
Randomised or quasi-randomised trials were selected if they involved children aged 3 months to 18 years with culture proven symptomatic UTI, and compared short term therapy (2–4 days) against standard therapy (7–14 days). To eliminate possible heterogeneity owing to the efficacies of different antibiotics, only studies that used the same antibiotic in both short and standard duration arms were included. The primary outcomes of interest were persisting clinical symptoms at the end of treatment, significant bacteriuria (colony counts ≥10⁴ organisms per ml of urine) at completion of therapy (0–7 days after completing treatment), and recurrent UTI after treatment (10 days or more after completing treatment). Secondary outcomes sought were compliance with medication, development of resistant organisms, costs, and side effects of therapy.

Table 1 Characteristics of the trials comparing short with standard duration antibiotic therapy in UTI

First author, Year, Country, Source	Patients entered	Patients evaluated	Inclusion criteria	Antibiotics used	Outcomes	Length of study
Wientzen,[26] 1979, USA, OPD	57	52	Symptomatic UTI. Children with ≥3 UTI in previous year excluded. Age 0.25–16 y. MSU*, SPA†, bag‡ samples.	Amoxycillin 4 days versus 10 days	UTI any time after treatment	12 months
Lohr,[25] 1981, USA, OPD	55	49	Girls with symptomatic UTI. Age 2–18 y. MSU samples.	Nitrofurantoin 3 days versus 10 days	UTI 0–7 days after treatment UTI during next 6 months	6 months
Helin,[24] 1981, Sweden, OPD	43	43	Symptomatic UTI. Age 0.25–16 y. Bag, MSU samples.	Trimethoprim/sulphadiazine 4 days versus 10 days	UTI at end of treatment UTI during next 12 months	12 months
Zaki,[23] 1986, Kuwait, Not stated	55	(a) 26 (b) 29	Symptomatic UTI. Children with UTI in previous 6 months excluded. Age 0.5–13 y. Collection method not stated.	(a) Nalidixic acid 3 days versus 10 days (b) TMP/SMX§ 3 days versus 10 days	UTI 2–3 days after treatment UTI at 1–3 months	3 months
Madrigal,[22] 1988, Costa Rica, OPD	104	90	Symptomatic UTI. Children with recurrent UTI excluded. Age 0.25–12 y. MSU, SPA, catheter urine samples.	TMP/SMX 3 days versus 7 days	UTI 10–12 days after therapy UTI at 28–37 days	44 days
CSG,[21] 1991, Denmark, OPD	333	(a) 96 (b) 78 (c) 90¶	Girls with symptomatic & asymptomatic UTI. Age 1–15 y. MSU samples.	(a) Sulphamethizole 3 days (b) Sulphamethizole 10 days (c) Pivmecillinam 3 days	UTI 1–10 days after treatment UTI at 1 month or more Resistant organisms	80 days
Jojart,[20] 1991, Hungary, Not stated	132	(a) 43 (b) 44	Symptomatic & asymptomatic UTI. Children with UTI >3 months earlier could be re-entered to other therapy. Age 1.5–9 y. Collection method not stated.	(a) Nitrofurantoin 3 days versus 14 days (b) TMP/SMX 3 days versus 10 days	UTI at 28–36 days after treatment	36 days
Gaudreault,[19] 1992, Canada, ED	45	40	Symptomatic UTI. Children with UTI in previous 6 months excluded. Age 2.5–18 y. MSU samples.	Trimethoprim/sulphadiazine 3 days versus 10 days	UTI at end of treatment UTI < 28 days after treatment Resistant organisms	38 days
Johnson,[18] 1993, USA, OPD	48	37	Symptomatic UTI. Age 1–13 y. MSU, SPA, catheter samples.	Amoxicillin/clavulinic acid 3 days versus 10 days	UTI 4 days after treatment UTI 30–47 days after therapy Resistant organisms	33 days
Kornberg,[17] 1994, USA, ED & OPD	38	25	Symptomatic UTI. UTI in last 30 days excluded. Age 2–11 y. MSU, catheter samples.	Cefuroxime 2 days versus 10 days	UTI 3–5 days after treatment UTI at 1–15 months	15 months

*Mid stream urine or clean catch urine collection. †Suprapubic bladder aspiration urine collection. ‡Strap-on bag urine collection. §Trimethoprim/sulphamethoxazole. ¶Third group of study by Copenhagen Study Group not included in results.
OPD, outpatient department; ED, emergency department.

Table 2 Quality of included trials comparing short with standard duration antibiotic therapy for lower UTI

First author	Allocation concealment	Percent lost to follow up	Blinding of participants and investigators	Blinding of outcome assessment	Intention to treat analysis
Wientzen[26]	Unclear	9	Not stated	Not stated	Not stated
Lohr[25]	Unclear	11	Yes	Not stated	Not stated
Helin[24]	Unclear	0	Not stated	Not stated	Not stated
Zaki[23]	Unclear	0	Not stated	Not stated	Not stated
Madrigal[22]	Unclear	14	Not stated	Not stated	Not stated
CSG[21]*	Yes	21	No	Not stated	Not stated
Jojart[20]	Unclear	34	Not stated	Not stated	Not stated
Gaudreault[19]	Unclear	11	No	Not stated	Not stated
Johnson[18]	Yes	23	No	Not stated	Not stated
Kornberg[17]	Unclear	16	Not stated	Not stated	Not stated

*Copenhagen Study Group of urinary tract infections in children.

Quality assessment

Two reviewers (MM and EH) assessed study quality without blinding to author or source using the criteria of the Cochrane Renal Group. Discrepancies were resolved through discussion. Quality items assessed were allocation concealment, intention to treat analysis, completeness of follow up, and blinding of participants, investigators, and outcome assessment since these may bias the underlying treatment effect.[11]

Statistical analysis

For dichotomous outcomes the relative risks (RR) with 95% confidence intervals (CI) were calculated in RevMan[12] for individual studies and the summary statistics were calculated using a random effects model. The random effects model takes into account between study variability as well as within study variability. A fixed effects model was also used to test the robustness of the analysis and for outliers. Heterogeneity was
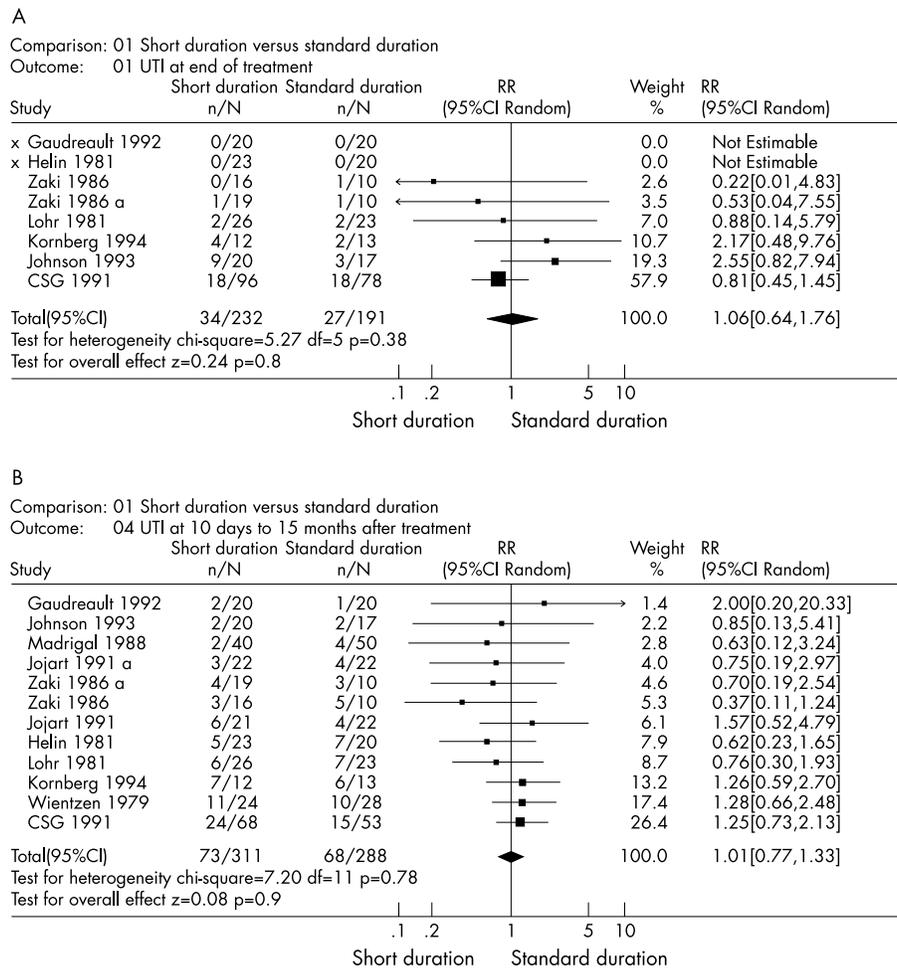
A

Comparison: 01 Short duration versus standard duration
Outcome: 01 UTI at end of treatment

Study	Short duration n/N	Standard duration n/N	RR (95%CI Random)	Weight %	RR (95%CI Random)
x Gaudreault 1992	0/20	0/20		0.0	Not Estimable
x Helin 1981	0/23	0/20		0.0	Not Estimable
Zaki 1986	0/16	1/10		2.6	0.22[0.01,4.83]
Zaki 1986 a	1/19	1/10		3.5	0.53[0.04,7.55]
Lohr 1981	2/26	2/23		7.0	0.88[0.14,5.79]
Kornberg 1994	4/12	2/13		10.7	2.17[0.48,9.76]
Johnson 1993	9/20	3/17		19.3	2.55[0.82,7.94]
CSG 1991	18/96	18/78		57.9	0.81[0.45,1.45]
Total(95%CI)	34/232	27/191		100.0	1.06[0.64,1.76]

Test for heterogeneity chi-square=5.27 df=5 p=0.38
Test for overall effect z=0.24 p=0.8

.1 .2   1   5 10
Short duration   Standard duration

B

Comparison: 01 Short duration versus standard duration
Outcome: 04 UTI at 10 days to 15 months after treatment

Study	Short duration n/N	Standard duration n/N	RR (95%CI Random)	Weight %	RR (95%CI Random)
Gaudreault 1992	2/20	1/20		1.4	2.00[0.20,20.33]
Johnson 1993	2/20	2/17		2.2	0.85[0.13,5.41]
Madrigal 1988	2/40	4/50		2.8	0.63[0.12,3.24]
Jojart 1991 a	3/22	4/22		4.0	0.75[0.19,2.97]
Zaki 1986 a	4/19	3/10		4.6	0.70[0.19,2.54]
Zaki 1986	3/16	5/10		5.3	0.37[0.11,1.24]
Jojart 1991	6/21	4/22		6.1	1.57[0.52,4.79]
Helin 1981	5/23	7/20		7.9	0.62[0.23,1.65]
Lohr 1981	6/26	7/23		8.7	0.76[0.30,1.93]
Kornberg 1994	7/12	6/13		13.2	1.26[0.59,2.70]
Wientzen 1979	11/24	10/28		17.4	1.28[0.66,2.48]
CSG 1991	24/68	15/53		26.4	1.25[0.73,2.13]
Total(95%CI)	73/311	68/288		100.0	1.01[0.77,1.33]

Test for heterogeneity chi-square=7.20 df=11 p=0.78
Test for overall effect z=0.08 p=0.9

.1 .2   1   5 10
Short duration   Standard duration

Figure 1 Meta-analyses showing the summary and individual trial relative risks (95% CI) for (A) persistence of urinary tract infection at the end of treatment (8 data sets) and (B) recurrence of infection 10 days to 15 months (12 data sets) after treatment with short duration or standard duration of antibiotics. Trials are shown ordered by study weights. No heterogeneity was shown using Cochran's Q statistic (χ^2). The test statistic Z indicates that there were no significant differences between short and standard durations of antibiotic therapy.
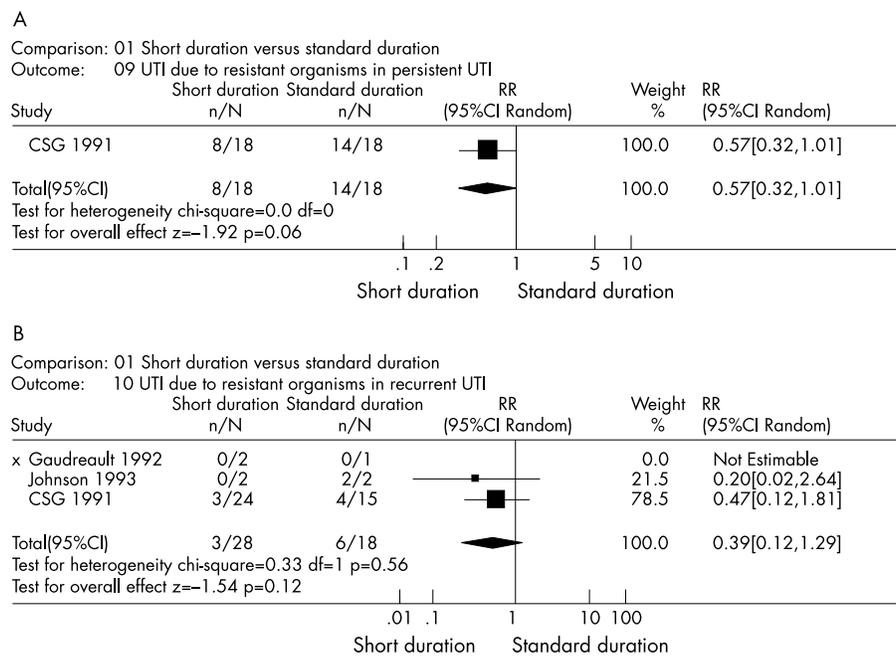
Figure 2 Meta-analyses showing the summary and individual trial relative risks (95% CI) for the number of urinary tract infections (UTI) caused by organisms resistant to the treating antibiotic (A) among persistent urinary tract infections at the end of treatment (1 data set) and (B) among recurrent UTI 10 days to 15 months (3 data sets) after treatment with short duration or standard duration of antibiotics. Trials are shown ordered by study weights.

analysed using Cochran's Q statistic with an α of 0.1 used for statistical significance. Subgroup analysis was planned based on study quality, patient type (age, finding of abnormal radiological findings), and intervention (type of antibiotic used) as we postulated that the relative treatment effect could vary with these factors.

RESULTS
Trial characteristics
Of 636 titles and abstracts screened, 14 studies were identified by full text review as randomised controlled trials (RCT), which compared short course to standard duration of oral antibiotic treatment. Three studies were subsequently excluded as two[13][14] compared different antibiotics in the short and standard duration groups, and the third[15] compared one day treatment with 10 day treatment. A fourth trial[16] was excluded as significantly more patients (32 of 59) with pyelonephritis were included in the seven day group compared with the three day group (11 of 58) ($\chi^2 = 15.65$, df = 1; p < 0.001), which strongly suggested non-random allocation. Thus ten trials were included in the systematic review.[17–26]

Table 1 summarises trial characteristics. Two trials[20][23] had four arms and were treated as separate trials. Hence there were 12 data sets for analysis. Seven trials[17–19][21][23][24][26] used $\geqslant 10^5$ organisms/ml and three trials[20][22][25] used $> 10^5$ organisms/ml to define UTI. Two trials[17][21] used $< 10^5$ organisms/ml and three trials[18][22][26] used $< 10^4$ organisms/ml to define cure of UTI; the remaining studies[19][20][23–25] did not specify this. All trials included children with previous UTI. In five trials[17][19][21][22][25] urines obtained by strap on bags were excluded. Only one trial[17] recorded persisting symptoms at the end of therapy. Two trials included children with asymptomatic UTI.[20][21] No trial specified whether recurrent UTIs were symptomatic or asymptomatic. All trials excluded children with acute pyelonephritis (diagnosed on the basis of fever of 38°C or above with or without symptoms of loin pain, chills, vomiting, or toxic appearance) or known renal tract abnormalities. Three trials[18][19][21] examined the occurrence of resistant organisms in children with persistent or recurrent UTI.

Study quality
Although 910 children entered the trials, outcomes were evaluated in only 652 children. Trial investigators excluded 168 children from analysis because of loss to follow up, deviation from protocol, non-compliance, or other reasons. Ninety children, who received three days of pivmecillinam, were excluded from the meta-analyses because there was no long duration comparison group.[21] Problems in trial design and reporting were common (table 2). Randomisation was adequately concealed in two studies[18][21]; in the remaining studies sufficient information was not provided to determine whether allocation was adequately concealed.

Study outcomes
As results from random and fixed effects models did not differ, only results from the random effects model are reported. After standard duration therapy, the prevalence of bacteriuria after treatment varied from 0% to 23% (median 10%, mean 14%), while that of recurrent UTI varied from 5% to 50% (median 28%, mean 24%).

There were no significant differences (fig 1) in the frequency of bacteriuria at 0–7 days after completing treatment (eight data sets; RR 1.06, 95% CI 0.64 to 1.76) or in the number of UTIs during 10 days to 15 months follow up (12 data sets; RR 1.01, 95% CI 0.77 to 1.33) between short and standard duration therapy. Analyses comparing different durations of follow up showed no differences in outcomes, so follow up data from 10 days to 15 months were combined. In the one study[17] that reported the outcome of symptomatic UTI, symptoms persisted in three of 12 children treated for two days, but in none of 13 children treated for 10 days. However, the authors did not state at what time during or after treatment this assessment was made.

No significant differences (fig 2) between short and standard duration therapy were found in the number of children with urinary pathogens resistant to the treating antibiotic on in vitro sensitivity analysis in persistent bacteriuria (one study, RR 0.57, 95% CI 0.32 to 1.01; p = 0.06) and in recurrent UTI (three studies; RR 0.39, 95% CI 0.12 to 1.29; p = 0.12).

Table 3 Effects of short and standard duration therapy for UTI based on antibiotics used and associated urinary tract abnormalities

Subgroup	UTI at end of treatment	Recurrence of UTI
Antibiotic type		
Sulphonamide group*	0.80 (0.45 to 1.41)	0.98 (0.65 to 1.46)
Other antibiotics†	1.72 (0.64 to 3.80)	1.04 (0.71 to 1.52)
Imaging studies‡		
Abnormality	0.71 (0.38 to 1.32)§	0.24 (0.03 to 1.67)¶
No abnormality	0.99 (0.12 to 8.56)§	1.42 (0.09 to 21.55)¶

Results presented as relative risk and 95% CI.
*Six studies (339 patients) using sulphonamides alone or in combination with trimethoprim.[19–24]
†Six studies (233 patients) using other antibiotics.[17 18 20 23 25 26]
‡Intravenous pyelogram and/or micturating cystourethrogram.
§Two studies involving 154 children (60 with abnormal imaging).[18 21]
¶One study involving 70 children (12 with abnormal imaging).[22]

However, the summary relative risk reductions for the occurrence of resistant organisms were 43% and 61% for bacteriuria at the end of treatment and recurrent UTI respectively, suggesting a trend towards a fall in the number of children with resistant organisms following short course therapy. Three studies[18 24 25] reported that compliance was satisfactory in both treatment groups, and one study[20] reported that 28% (37/132) were excluded from evaluation because of non-compliance but did not specify the treatment groups. No studies evaluated the costs of the treatment regimens. Adverse effects of antibiotics were not reported in sufficient detail to allow analysis. Of the seven trials[17–19 21 23–25] that reported on adverse effects, only two studies[17 21] reported in which groups the adverse effects occurred. Overall nine children suffered adverse effects: gastrointestinal disturbances (n = 6), dizziness (n = 1), or rash (n = 2).

In subgroup analyses, relative treatment effects with short and standard duration therapy did not differ with sulphonamide containing antibiotics or with non-sulphonamide based antibiotics or between children with and without abnormal renal tracts on imaging after treatment (table 3). Subgroup analysis based on other potential effect modifiers, such as study quality and patient age, was not possible because of the limited numbers of studies available.

DISCUSSION

In children with lower tract UTI there is no significant difference between short and standard duration antibiotic therapy for UTI at the end of treatment or in UTI recurrence rate 10 days to 15 months after treatment.

Although there was no significant difference in the rate of bacteriuria at the end of treatment, the wide confidence intervals of the summary estimate (RR 1.06, 95% CI 0.64 to 1.76)

indicate residual imprecision in the results. Ideally a further adequately powered trial is required. About 1–3% of unselected children treated for symptomatic UTI have UTI after 7–14 days of antibiotic treatment.[2 3] To show a reduction in UTI after treatment from 3% to 2% or from 1% to 0.5% would require 8000 and 10 000 children, respectively, to be enrolled. Such a trial is highly improbable, so how should clinicians decide what treatment duration they should use? The relevance of the residual uncertainty to patient care depends on the risk of persistent infection with standard duration therapy. If the upper and lower limits of the 95% confidence intervals are used to define the best and worst case scenarios in 1000 children with a 1% risk of infection at the end of treatment for their first UTI, four fewer children or eight extra children would have UTI following short duration therapy compared with standard duration—a clinically unimportant difference (table 4). All trials included in this systematic review included children with recurrent UTI; such children are known to be at a higher risk of UTI at the end of treatment compared with children with their first infection.[3] If the risk of infection following treatment is 14% with standard duration therapy, as in the included trials, then 50 fewer or 110 extra children would have UTI following short duration therapy—a difference that is clinically important. In populations with recurrent UTI and a higher risk of UTI at the end of treatment, the possible harms (delay in resolution of symptoms) of not clearing the infection would have to be weighed against the possible benefits (reduced resistance to treating antibiotics, reduced adverse effects of antibiotics, improved compliance, and reduced costs) of using a short course of therapy.

Data on the development of resistant organisms were reported in only three trials. In view of the increasing prevalence in UTI of organisms resistant to commonly used antibiotics,[27] the possible trend towards a reduction in the

Table 4 Estimated risk for UTI 0–7 days following short duration antibiotic therapy in 1000 children, with different risks of UTI (using the summary RR of 1.06; 95% CI of 0.64 and 1.76)

Risk of UTI 0–7 days after standard duration therapy	Number with UTI after standard duration therapy	Effect of treating children with short duration of antibiotics		
		Extra children with UTI after short duration	Fewer children with UTI after short duration (best scenario)	Extra children with UTI after short duration (worst scenario)
1%*	10	1	4	8
3%†	30	2	11	23
14%‡	140	8	50	110

*Data from Craig *et al.*[2]
†Data from Winberg *et al.*[3]
‡Mean rate of UTI, 0–7 days after standard duration therapy from 8 data sets included in meta-analysis.[17–19 21 23–25]

number of children with resistant organisms following short duration therapy needs further study. It was not possible to determine whether short duration therapy offered any reduction in antibiotic related adverse effects. Detailed data on compliance with medications in each treatment group were not provided in any study. No study addressed whether using short course therapy reduced costs.

There are important limitations of this systematic review because of problems with the primary studies. Some information of most relevance to clinical care was not provided in these studies. None of the trials specified the time to symptom resolution after commencement of antibiotics and whether UTI at the end of treatment or UTI recurrence were associated with clinical symptoms. Two trials[20 21] enrolled both symptomatic and asymptomatic patients. Inclusion of these trials did not result in heterogeneity. It is now recommended that school age children with asymptomatic bacteriuria should not be treated with antibiotics as they are not at increased risk of impaired renal growth or deterioration in renal function when untreated,[28 29] but are at increased risk of pyelonephritis following treatment.[29] Children with pyelonephritis or known urinary tract pathology were excluded, so no recommendations on treatment duration can be made for such children, who comprise a large proportion of children under 5 years with UTI.[2 3] Studies were generally small, included children from a wide age range, and were of suboptimal quality. Trials with inadequate allocation or blinding can exaggerate the efficacy of experimental treatment,[11] and meta-analyses of poor quality trials[30] can provide erroneous information on the benefits of therapy. Despite these methodological issues, no significant heterogeneity was shown between study results. Formal testing to exclude publication bias resulting from exclusion of some unpublished trials using funnel plots[31] was not possible because of the small number of studies.

Combining inadequately powered trials in a meta-analysis can improve statistical power. However, this study has still not provided incontrovertible evidence that short duration (2–4 days) is better or worse than standard duration therapy (7–14 days) in eradicating childhood UTI because of residual imprecision. For most children with first UTI, who are at low risk (1–3%) of bacteriuria at the end of treatment with standard duration treatment,[2 3] this statistical imprecision is of doubtful clinical significance. Therefore, based on these data, short duration of treatment is a reasonable option for children with lower tract UTI.

ACKNOWLEDGEMENTS

. . . .

Authors' affiliations
M Michael, E M Hodson, J C Craig, S Martin, Centre for Kidney Research, The Children's Hospital at Westmead, Sydney, Australia
V A Moyer, Center for Clinical Research and Evidence Based Medicine, The University of Texas–Houston Health Science Center, Houston, TX 77030, USA

REFERENCES

1 **Hellstrom A**, Hanson E, Hansson S, et al. Association between urinary symptoms at 7 years old and previous urinary tract infections. Arch Dis Child 1991;**66**:232–4.

2 **Craig JC**, Irwig LM, Knight JF, et al. Symptomatic urinary tract infection in preschool Australian children. J Paediatr Child Health 1998;**34**:154–9.

3 **Winberg J**, Andersen HJ, Berström T, et al. Epidemiology of symptomatic urinary tract infection in childhood. Acta Paediatr Scand 1974;**252**(suppl):1–20.

4 **Ronald AR**, Boutros P, Mourtada H. Bacteriuria localization and response to single dose therapy in women. JAMA 1976;**235**:1854–6.

5 **Philbrick JT**, Bracikowski JP. Single dose antibiotic treatment for uncomplicated urinary tract infection. Less for less? Arch Intern Med 1985;**145**:1672–8.

6 **Shapiro ED**. Short-course antimicrobial treatment of urinary tract infections in children: a critical analysis. Pediatr Infect Dis 1982;**1**:294–7.

7 **Moffatt M**, Embree J, Grimm P, et al. Short-course antibiotic therapy for urinary tract infections in children: a methodological review of the literature. Am J Dis Child 1988;**142**:57–61.

8 **Tran D**, Muchant DG, Aronoff SC. Short-course versus conventional length antimicrobial therapy for uncomplicated lower urinary tract infections in children: a meta-analysis of 1279 patients. J Pediatr 2001;**139**:93–9.

9 **Dickersin K**, Scherer R, Lefevre C. Identifying relevant studies for systematic reviews. BMJ 1994;**309**:1286–91.

10 **Lefebvre C**, McDonald S. Development of a sensitive search strategy for reports of randomized controlled trials in EMBASE. Paper presented at the Fourth International Cochrane Colloquium, Adelaide, Australia, 20–24 October 1996.

11 **Schulz KF**, Chalmers I, Hayes RJ, et al. Empirical evidence of bias. Dimensions of methodological quality associated with estimates of treatment effects in controlled trials. JAMA 1995;**273**:408–12.

12 **Review Manager (RevMan)**. 4.1 for Windows. Computer Program. The Cochrane Collaboration, Oxford, UK, 2000.

13 **Helin I**. Three-day therapy with cephalexin for lower urinary tract infections in children. Scand J Infect Dis 1984;**16**:305–7.

14 **Khan AJ**, Kumar K, Evans HE. Three-day antimicrobial therapy of urinary tract infection. J Pediatr 1981;**99**:992–4.

15 **McCracken GH Jr**, Ginsburg CM, Namasonthi V, et al. Evaluation of short-term antibiotic therapy in children with uncomplicated urinary tract infections. Pediatrics 1981;**67**:796–801.

16 **Tambic T**, Oberiter V, Delmis J, et al. Diagnostic value of a P-Fimbriation test in determining duration of therapy in children with urinary tract infection. Clin Ther 1992;**14**:667–70.

17 **Kornberg AE**, Sherin K, Veiga P, et al. Two-day therapy with cefuroxime axetil is effective for urinary tract infections in children. Am J Nephrol 1994;**14**:169–72.

18 **Johnson CE**, Maslow JN, Fattler, RN, et al. The role of bacterial adhesins in the outcome of childhood urinary tract infections. Am J Dis Child 1993;**147**:1090–3.

19 **Gaudreault P**, Beland M, Girodias JB, et al. Single daily doses of trimethoprim/sulphadiazine for three or 10 days in urinary tract infections. Acta Paediatr 1992;**81**:695–7.

20 **Jojart G**. Comparison of 3 day versus 14 day treatment of lower urinary tract infection in children. Int Urol Nephrol 1991;**23**:129–34.

21 **Copenhagen Study Group of urinary tract infections in children**. Short-term treatment of acute urinary tract infection in girls. Scand J Infect Dis 1991;**23**:213–20.

22 **Mardigal G**, Odio CM, Mohs E, et al. Single dose antibiotic therapy is not as effective as conventional regimens for management of acute urinary tract infections in children. Pediatr Infect Dis J 1988;**7**:316–19.

23 **Zaki M**, Helin I. Nalidixic acid and trimethoprim/sulphamethoxazole as alternatives for short-term treatment of urinary infections. Ann Trop Paediatr 1986;**6**:205–7.

24 **Helin I**. Short-term treatment of lower urinary tract infections in children with trimethoprim/sulphadiazine. Infection 1981;**9**:249–51.

25 **Lohr JA**, Hayden GF, Kesler RW, et al. Three day therapy of lower urinary tract infections with nitrofurantoin macrocrystals: a randomized clinical trial. J Pediatr 1981;**99**:980–3.

26 **Wientzen RL**, McCracken GH Jr, Petruska ML, et al. Localization and therapy of urinary tract infections of childhood. Pediatrics 1979;**63**:467–74.

27 **Gupta K**, Scholes D, Stamm WE. Increasing prevalence of antimicrobial resistance among uropathogens causing acute uncomplicated cystitis in women. JAMA 1999;**281**:736–8.

28 **Cardiff-Oxford Bacteriuria Study Group**. Sequelae of covert bacteriuria in schoolgirls. Lancet 1978;**1**:889–93.

29 **Hansson S**, Jodal U, Norén L, et al. Untreated bacteriuria in asymptomatic girls with renal scarring. Pediatrics 1989;**84**:964–86.

30 **Moher D**, Pham B, Jones A, et al. Does quality of reports of randomised trials affect estimates of intervention efficacy reported in meta-analyses? Lancet 1998;**352**:609–13.

31 **Egger M**, Davey-Smith G, Schneider M, et al. Bias in meta-analysis detected by a simple graphical test. BMJ 1997;**315**:629–34.