National Collaborating Centre for
Women's and Children's Health

Urinary tract infection in children

diagnosis, treatment and long-term management

Clinical Guideline
August 2007

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Urinary tract infection in children

diagnosis, treatment and long-term management

National Collaborating Centre for Women's and Children's Health

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Evidence tables

August 2007

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Evidence tables should be read in conjunction with the main guideline.

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Abbreviations

APN	acute pyelonephritis
ARR	absolute risk reduction
ASB	asymptomatic bacteriuria
CAT	computed axial tomography
CCT	controlled clinical trial
CER	control event rate
cfu	colony-forming unit
CI	confidence interval
CKD	chronic kidney disease
CRF	chronic renal failure
CRP	C-reactive protein
CT	computed tomography
CUS	cystourethrosonography
CVU	clean voided urine
DES	dysfunctional elimination syndrome
df	degrees of freedom
DMSA	dimercaptosuccinic acid
DOR	diagnostic odds ratio
DRC	direct radionuclide cystography
EDTA	European Dialysis and Transplant Association
eGFR	estimated glomerular filtration rate
EL	evidence level
EQA	external quality assurance
ERF	established renal failure
ESR	erythrocyte sedimentation rate
ESRD	end-stage renal disease
GDG	Guideline Development Group
GFR	glomerular filtration rate
GP	general practitioner
GPP	good practice point
hpf	high power field
HTA	Health Technology Appraisal
ICD	international classification of diseases
IL-1ß	interleukin 1 beta
IL-6	interleukin 6
IM	intramuscular
IQA	internal quality assurance
IQR	interquartile range
IRC	indirect radionuclide cystogram
IV	intravenous
IVP	intravenous pyelogram
IVU	intravenous urogram
LE	leucocyte esterase
LR+	positive likelihood ratio
LR–	negative likelihood ratio
MAG3	mercaptoacetyltriglycine
MCUG	micturating cystourethrogram
MRI	magnetic resonance imaging
NAG	N-acetyl-beta-glucosaminidase
NCC-WCH	National Collaborating Centre for Women's and Children's Health
NHS	National Health Service
NICE	National Institute for Health and Clinical Excellence
NNH	number needed to harm
NNT	number needed to treat

NPV	negative predictive value
NSF	National Service Framework
OR	odds ratio
PCT	primary care trust
PDU	power Doppler ultrasonography
PHLS	Public Health Laboratory Service
pmp	per million population
PPIP	Patient and Public Involvement Programme
PPV	positive predictive value
QALY	quality-adjusted life year
QOF	Quality and Outcomes Framework
RCGP	Royal College of General Practitioners
RCP	Royal College of Physicians
RCPCH	Royal College of Paediatrics and Child Health
RCT	randomised controlled trial
RN	reflux nephropathy
ROC	receiver operating characteristic
RR	relative risk (or risk ratio)
RRT	renal replacement therapy
SD	standard deviation
SIGN	Scottish Intercollegiate Guidelines Network
SPA	suprapubic aspiration
SROC	summary receiver operating characteristic
STING	submucosal Teflon injection
TNF-	tumour necrosis factor alpha
UK	United Kingdom of Great Britain and Northern Ireland
US	ultrasound
USA	United States of America
UTI	urinary tract infection
VCUG	voiding cystourethrogram
VUR	vesicoureteric reflux
VUS	voiding urosonography
WBC	white blood cell
WHO	World Health Organization
WMD	weighted mean difference
WTP	willingness to pay

Evidence tables

Predisposing factors

Bibliographic Information	Study Type & Evidence Level	Aims and comparisons	Number of Patients	Patient characteristics	Follow-up & Outcome Measures	Effect Size	Reviewer comment
Ginsburg CM;McCracken GH; 1982 Apr [116]	Study Type: Case-series Evidence Level: 3	To present clinical and laboratory features of UTI	100 infants 62 boys 38 girls	Infants aged 5 days to 8 months (mean 2.1 months) admitted to one of two hospitals with acute UTI from Mar 1976 to Feb 1981	Number with UTI Age at UTI Symptoms and signs at presentation	Male infants accounted for 75% of UTI cases within the first three months of life compared with 11% of boys who were 3 to 8 months of age. Of the 41 infants who were under 30 days old, 33 (81%) were boys. Symptoms and signs Fever was the most common symptom (in 63%) and symptoms of irritability (55%), had refused feeds (38%), vomiting (36%) and diarrhoea (31%). 67 infants had a fever of 38C and 38 infants had fever of 39C. Abdominal distention and jaundice were only reported in 8% and 7% of patients respectively.	
Kunin CM;Southall I;Paquin AJ; 1960 [117]	Study Type: cross-sectional. Evidence Level: 3	To determine the age, frequency, sex and race distribution of UTI in school aged children Presence of UTI assessed initially by clean catch, confirmed by repeat clean catch and then catheter; UTI defined by 50,000 cfu/ml or more.	n=3057 school children (1647 male, 1410 female)	Participants were from all children enrolled in public, private and parochial schools in a city, 1st through 12th grade (aged approx 6 through 17 yrs), from which 85% 3057/3592) participated in this study One school had black students only (235/260 participated)	No. with ≥100,000 cfu/ml No. with first UTI, by age group No. with UTI for Black females (≥100,000 cfu/ml)	0/1647 boys had >10^5cfu/mL after 2nd clean catch 15/1410 girls continued to have >100,000 cfu/ml after catheterisation 2/15 girls with UTI had had previous UTI (aged 7 and 8) For 6 to 10 age group: 8/772 girls (1.0%); for 11 to 15 age group: 4/495 girls (0.8%); remaining girl was aged between 16-20 yrs. Black females 0.9% (out of 115)	
Biyikli NK;Alpay H;Ozek E;Akman I;Bilgen H; 2004 Feb [118]	Study Type: Case series Evidence Level: 3	To analyse clinical presentation, causative agents, imaging findings and recurrence rates. Clinical presentation only presented in this table (other sections of this paper presented in relevant chapters).	71 neonates with UTI 54/71 (76%) boys and 17/71 (24%) girls	Neonates aged 18.1(±11.2 days) treated for UTI between 1999-2000 at hospital, followed up for at least 6 months, excluded neonates with spina bifida UTI diagnosed as growth of the microorganisms over 10000 cfu/ml in a cateterized urine specimen. Nosocomial UTI defined as a positive urine culture detected 48 hours after admission.	Risk of UTI when pre-term v. not pre-term Assessed by Chi square.	29/71 (41%) were preterm (gestational age 27-37 weeks) 3/71 were small for gestational age Symptoms and signs Signs of sepsis 15/29 (53%) preterm neonates, Hyperbilirubinemia 8/29 (26%) preterm neonate Asymptomatic 6/29 (21%) Hyperbilirubinemia 24/42 (57%) term neonates Signs of sepsis 15/42 (36%) term neonates Asymptomatic in 3/42 (7.1%) The signs of sepsis were: irritability 11/71 (15%)	

Bibliographic Information	Study Type & Evidence Level	Aims and comparisons	Number of Patients	Patient characteristics	Follow-up & Outcome Measures	Effect Size	Reviewer comment
						fever or hypothermia 6/71 (8%) respiratory distress 6/71 (8%) feeding problems 4/71 (5%) vomiting 3/71 (4%) abnormal crying 3/71 (4%) poor weight gain 2/71 (2%) rash 1/71 (1%) Asymptomatic 9/71 (13%)	
Jodal U; 1987 Dec 47	Study Type: Case-series Evidence Level: 3	Study 1 Aims unclear	1177 children with first time symptomatic UTI (952 girls and 225 boys)	Children aged under ten years with first time symptomatic UTI. Bacteriuria definition: At least 10^5 bacteria per ml together with leukocyturia in a midstream sample or bag sample. Any growth on SPA Pyelonephritis definition: Bacteriuria and fever of ≥38.5°C and a microsedimentation rate of ≥25mm per hour or CRP ≥20mg/L Cystitis definition: acute voiding symptoms (dysuria, frequency) with temperature <38.5°C and normal laboratory findings. A child with acute symptoms and bacteriuria that could not be classified was said to have 'unspecified UTI'	Outcome measures: No. with reflux (and grade) No. with scarring No. of symptomatic recurrences No. with pyelonephritis/cystitis	Study 1 225/1177 (19%) boys 952/1177 (81%) girls Boys 133/225 (59%) of UTIs detected in the first year of life 72/225 (33%) had VUR 8/72 (11%) dilated reflux (grade ≥3) 41/225 (18%) had one recurrence 11/225 (5%) had 2 or more recurrences Girls 181/952 (19%) of UTIs detected in the first year of life 315/952 (34%) had VUR (54% between 1-3 years) 25/315 (8%) dilated reflux (grade ≥3) 152/952 (16%) had one recurrence 152/952 (16%) had 2 or more recurrences Scarring 15/278 (5%) children with no reflux had scarring 3/29 (10%) of children with grade 1 reflux had scarring 17/99 (17%) of children with grade 2 reflux had scarring 25/38 (66%) children with grade ≥3 reflux had scarring 25% of the total number of children with scarring did not have reflux. Pyelonephritis 7/141 (5%) children with 0 pyelonephritis episode had scarring 32/366 (9%) of children with 1 pyelonephritis episode had scarring 15/98 (15%) of children with 2 pyelonephritis	

Bibliographic Information	Study Type & Evidence Level	Aims and comparisons	Number of Patients	Patient characteristics	Follow-up & Outcome Measures	Effect Size	Reviewer comment
						episode had scarring 12/35 (35%) of children with 3 pyelonephritis episode had scarring 14/24 (58%) children with ≥4 pyelonephritis episode had scarring	
Zorc JJ;Levine DA;Platt SL;Dayan PS;Macias CG;Krief W;Schor J;Bank D;Shaw KN;Kuppermann N; 2005 [119]	Study Type: Cross-sectional Evidence Level: 3	To identify clinical and demographic factors associated with UTI in febrile infants who are ≤60 days old.	1025 infants	Infants aged from 1 to 60 days (mean 35.5 ± 14.4 days) UTi was defined as growth of a known bacterial pathogen from a catheterised sample at ≥50000cfu/ml or ≥10000cfu/ml in association with a positive dipstick test or urinalysis.	Outcome measures Age ≤28 days Gender Circumcision Ill appearance (YOS>10) Height of fever White race	Factor present, Factor absent, OR (95%CI) Uncircumcised (vs. circumcised male), 62/291vs. 6/262, OR 11.6 (5.0 to 26.6) Max temperature >39°C (vs. <39), 34/209 vs. 57/796, OR2.5 (1.6 to 4.0) Female (vs. circumcised male), 22/439 vs. 6/262, OR 2.2 (0.9 to 5.5) Age <28 days (vs>28 days), 37/334 vs. 54/671, OR 1.4 (0.9 t 2.2) Ill appearing (YOS>10), 4/71 vs. 87/924, OR .6 (0.2 to 1.6) White (vs. other race), 12/259 vs. 79/44, OR 0.4 (0.2 to 0.8) Adjusted OR (Bias-corrected 95%CI) p-value Uncircumcised: 10.4 (4.7 to 31.4) p<0.001 Maximum temperature: 2.4 (1.5 to 3.6) p<0.001 Female: 2.2 (0.9 to 6.6) p=0.10 Age <28 days: 1.6 (0.96 to 2.6) p=0.07 Ill appearing: 0.68 (0.14 to 1.6) p=0.49 White: 0.79 (0.35 to 1.5) p=0.53	
Falcao MC;Leone CR;D'Andrea RA;Berardi R;Ono NA;Vaz FA; 2000 Jan [120]	Study Type: x-sectional. Evidence Level: 3	To analyse the contribution of risk factors to the occurrence of urinary tract infection in full term newborn infants.	61 infants (26 boys, 35 girls).	Infants (gestational age 37 to 42 weeks) presenting with fever (>37.8ºC), weight loss (>10% of birth weight) or non-specific symptoms (feeding intolerance, failure to thrive, hypoactivity, debilitate suction, irritability). In these children another urine sample was collected by SPA to confirm diagnosis. Group I: positive urine culture by urine collection bag, negative on SPA Group II: positive urine culture by urine collection bag, positive on SPA Definition of positive urine sample was 10^5cfu/ml of a single organism for bag collection and any growth on SPA.	Associated infectious pathologies, use of broad spectrum antibiotics, renal and urinary tract malformations, mechanical ventilation, parenteral nutrition and intravenous catheter.	On SPA, 42 infants were culture negative (group I) and a diagnosis of UTI was confirmed in 19 (group II). There were no significant differences between groups for birth weight, sex, asphyxia or membrane rupture time. On presentation there were no differences between the groups for fever (p=0.31), however there were significant differences for weight loss (>10% of birth weight) (p=0.01) and non-specific symptoms (p=0.0004) Group 1 vs. Group 2 (p-value) Birth weight 3399.52 (±418.36) vs. 3171.05 (±515.08) (p=0.07) Sex Male - 16 (38%) vs. 10 (53%) (p=0.28) Female - 26 (62%) vs. 9 (47%) (p=0.28) Asphyxia (Apgar 5'<6) 1 (2.4%) vs. 3 (15.8%) p=0.14 Membrane rupture time ≥24 hours	

Bibliographic Information	Study Type & Evidence Level	Aims and comparisons	Number of Patients	Patient characteristics	Follow-up & Outcome Measures	Effect Size	Reviewer comment
						7 (17%) vs. 5 (26%) p=0.47 Fever (>37.8ºC) 38 (91%) vs. 15 (79%) p=0.31 Weight loss >10% of birth weight 20 (48%) vs. 3 (16%) p=0.01 Nonspecific symptoms 4 (9.5%) vs. 10 (53%) p=0.0004 Risk factors Associated infectious diseases 9 (21%) vs. 12 (63%) p=0.001 RR 3.27 (95%CI 1.51 to 7.04) p=0.0001 Use of broad-spectrum antibiotics 3 (7%) vs. 6 (32%) p=0.02 RR 3.03 (95%CI 1.51 to 6.08) p=0.012 Renal and urinary tract malformations 4 (9.5%) vs. 7 (37%) p=0.01 RR 2.97 (95%CI 1.57 to 5.64) p=0.007 Mechanical ventilation 1 (2%) vs. 4 (21%) p=0.04 RR 2.99 (95%CI 1.61 to 5.53) p=0.029 Parenteral nutrition 1 (2%) vs. 10 (53%) p=0.0006 RR 5.05 (95%CI 2.72 to 9.39) p=0.0009 Intravascular catheter 1 (2%) vs. 5 (26%) p=0.01 RR 3.27 (95%CI 1.84 to 5.83) p=0.009	
Go JMR;Cocjin A;Dee-Chan R; 2005 [121]	Study Type: Case-series Evidence Level: 3	To determine if unexplained and/or excessive jaundice is associated with UTI in infants aged less than 8 weeks of age.	54 infants (22 boys, 32 girls)	All jaundiced , full term (37-42 weeks gestation) infants less than 8 weeks old, born between October 2002 and October 2004. Clinical jaundice was defined as yellowish discolouration of the skin, mucous membranes or sclera. Exclusions: Infants who had previously been evaluated for sepsis and who were treated with intravenous antibiotics, minor infections where jaundice was caused by other known factors.	Detailed questionnaires on prenatal, intrapartum and post-natal events were completed WBC count Serum fractioned bilirubin levels Urinalysis Blood and urine culture	150 infants were born over a two year period, of which 73 presented with jaundice. 19 cases were excluded, 16 because of ABO incompatibility, 2 because of pneumonia and one because of cephalhaematoma. Of the 54 included infants, 5 had UTI and 49 did not. Historical and demographic characteristics Gender (p>0.05) Age (p>0.05) Place of birth (p>0.05) Mode of delivery (p>0.05) Birth weight (p>0.05) Gestational age (p>0.05) Stay at nursery (p>0.05)	

Bibliographic Information	Study Type & Evidence Level	Aims and comparisons	Number of Patients	Patient characteristics	Follow-up & Outcome Measures	Effect Size	Reviewer comment
						Neonatal infection (p>0.05) Mixed feeding Onset of jaundice (p>0.05) Progression Maternal characteristics: Maternal age (p>0.05) Gravidity (p>0.05) Presence of maternal infection (p>0.05) Maternal illness (p>0.05) Infants with UTI vs. infants without UTI, p-value Total bilirubin – 13.38 ± 1.40 vs. 8.91 ± 2.11, p<0.001 Direct bilirubin – 1.38 ± 1.22 vs. 0.28 ± 0.16, p<0.01 Indirect bilirubin – 11.96 ± 1.32 vs. 8.91 ± 2.11, p<0.01	
Hiraoka M;Tsukahara H;Ohshima Y;Mayumi M; 2002 [122]	Study Type: Case control Evidence level: 2-	Distribution of phimosis in boys with first episode of febrile UTI compared with 'healthy' control boys, and male to female ratio of febrile UTI by age and sex.	100 children with febrile UTI (64 boys and 36 girls) and 714 healthy boys	Cases: consecutive children who presented at one hospital with febrile UTI from July 1995 to May 2000 febrile UTI defined as: body temp above 38.5C, ≥50,000 cfu/ml for catheterized urine, one strain, or ≥10^5 cfu/ml for midstream or clean-catch urine Controls: 'healthy' boys, aged 0-3 yrs, uncircumcised. Recruited either at birth or during a health check-up at the same hospital	male:female ratio of first time febrile UTI. Proportion of boys with P0 (external urethral meatus not naturally covered with the prepuce), P1 (prepuce covers external meatus and is fully retractable), P2 (prepuce covers meatus but is only partially retractable), P3 (prepuce covers meatus but retraction does not allow exposure of meatus), or P4 (prepuce covers meatus and is not retractable at all)	From 100 children with febrile UTI, first time infection in 58 boys and 20 girls under age of 7 months male:female ratio of febrile UTI = 5.0; at 1 yr or more ratio = 0.10 85% of boys with febrile UTI under age of 7 months (n=55) had prepuce state P3 or P4; approx 42% of 'healthy' boys under age of 7 months had prepuce state P3 or P4; OR 7.8 (95% CI 3.99 to 15.31)	Unclear why author's chose to report distribution of phimosis only in boys with febrile UTI under 7 months of age Also unclear why author's excluded children between 7 and 11 months old when reporting male:female ratios for first time febrile UTI 95% CI not reported (calculated at NCC-WCH)
Jerkins GR;Noe HN; 1982 Oct [123]	Study Type: Case-series Evidence Level: 3	To identify a group at risk for VUR using awake voiding cystogram	n=104 siblings of patients with VUR (67 female, 37 male)	Siblings were from 78 white patients (60 female and 18 male) with VUR (regardless of UTI history) and were aged 3 months to 15 years	No. of siblings with VUR No. of siblings with VUR by age group No. with VUR with history of UTI	34/104 (32.7%) sibs (25 female (37.3%), 9 (24.3%) male) found to have VUR 16/49 (32.7%) sibs aged 0 to 3 years had VUR 9/23 (39.1%) sibs aged 4-6 years had VUR 9/32 (28.1%) sibs aged 7 years or older had VUR Of 34 with VUR, 6 (17.6%) had history of UTI and 25 (73.5%) had no history of UTI	Impossible to make such a conclusion without context of a comparison group, i.e., these siblings are at much higher risk than who? Among 34 with VUR, 31 had either a history or no history of UTI. Although the remaining 3 patients had a history of abnormal voiding patterns, it was unclear why their UTI status was ignored. Would also be useful to know how many in group without

Bibliographic Information	Study Type & Evidence Level	Aims and comparisons	Number of Patients	Patient characteristics	Follow-up & Outcome Measures	Effect Size	Reviewer comment
							VUR had history of UTI for comparison. No. of siblings with unilateral and bilateral VUR not reported.
Ataei N;Madani A;Esfahani ST;Kejbafzadeh A;Ghaderi O;Jalili S;Sharafi B; 2004 [124]	Study Type: Case-series Evidence Level: 3	To assess number of VUR cases in siblings of patients with VUR by voiding cystourethrogram (VCUG)	40 siblings (25 female, 15 male) of patients with VUR	Siblings were from 34 patients with VUR (irrespective of history of UTI) and ranged from 6 months to 12 years in age. Sibs were screened from Oct 1994 to Feb 2003	No. sibs with VUR No. of VUR with history of UTI	17/40 (42.5%) sibs with VUR Of 17 with VUR, 5 (29.4%) had history of symptomatic UTI bilateral in 6/17 and unilateral in 11/17 siblings	
Singh-Grewal D;Macdessi J;Craig J; 2005 [125]	Study Type: Systematic review / meta-analysis Evidence Level: 2++	To undertake a meta-analysis of published data on the effect of circumcision on the risk of UTI in boys.	Data on 402,908 boys were identified from 12 studies.	Boys of any age where the intervention was circumcision and UTI was the outcome. Only studies that provided a 2x2 table were included so that odds of UTI could be calculated.	Outcome: UTI	RCT – One RCT had an OR of 0.13 (95%CI 0.01 to 2.63) Cohort studies – All four cohort studies showed benefit with a summary OR of 0.13 (95%CI 0.07 to 0.23), however there was significant heterogeneity between studies (x^2 = 82.48, df = 3, p<0.001). When the one outlying study was excluded, the heterogeneity was not significant (p=0.64) Case-control – All 7 case-control studies included showed benefit with a combined OR of 0.13 (95%CI 0.07 to 0.23). There was no significant heterogeneity between studies (x^2 = 8.15, df = 6, p = 0.2) All studies – The summary OR across all study types was 0.13 (95%CI 0.08 to 0.20). There was no significant heterogeneity observed between study types (x^2 = 0.16, df = 2, p = 0.9), however significant heterogeneity was observed the individual studies (x^2 = 90.63, df = 11, p<0.0001) owing to the inclusion of the cohort studies. Without this study there was no significant heterogeneity (x^2 = 10.92, df = 10, p<0.4). The odds of a circumcised boy having a UTI are about 0.1 when compared with uncircumcised boys. While circumcision is shown to be protective against UTI, the risk-benefit of circumcision is not easily quantifiable. The study concludes that while circumcision substantially reduces the risk of UTI, routine circumcision should not be considered. Circumcision has a potential role in boys with past history of recurrent UTI, or with high grade VUR, as the benefits in these cases may outweigh the risk of complications	
Schoen EJ; Colby CJ;Ray GT; 2000 Apr [126]	Study Type: Cohort Evidence level: 2++	Effect of circumcision, performed before discharge after birth or during newborn period, on UTI	1996 cohort: n= 28,812 infants 1997 cohort (for incidence study): n= 20,587 infants	All children born at 12 facilities that were a part of the Kaiser Permanente Medical Care Program of Northern California; n=14,893 were male infants in the 1996	Follow-up period: For 1997 incidence study, 12 months. Outcome Measures: Number circumcised (%)	Of 14,893 male infants born in 1996, 9668 (64.9%) were circumcised In 1996, 446 UTI cases were diagnosed (292 female, 154 male) in infants <1yr old Median age at diagnosis was 2.5 months for	

Bibliographic Information	Study Type & Evidence Level	Aims and comparisons	Number of Patients	Patient characteristics	Follow-up & Outcome Measures	Effect Size	Reviewer comment
				cohort	Number of UTI before 1 year Median age at hospitalisation for UTI Incidence of UTI	uncircumcised male, 4.5 months for circumcised male, and 6.5 months for female infants Incidence of UTI in first year of life 1:47 for uncircumcised male, 1:455 for circumcised male, and 1:49 for female infants; OR for uncircumcised compared with circumcised = 9.1 (95% CI 5.2 to 15.7)	
Wiswell TE;Geschke DW; 1989 Jun [127]	Study Type: Cohort Evidence level: 2+	Retrospective review of hospital records for complications related to circumcision status in first month of life.	136,086 boys	All boys born in US army hospitals from Jan 1980 to Dec 1985	No. circumcised No. of complications in first month of life No. of UTI; association between UTI and circumcision by chi square	100,157 (73.6%) circumcised; 35,929 (26.4%) uncircumcised 193 (0.19%) complications in 193 circumcised boys, including 20 UTI, 5 concomitant cases of bacteremia, 83 haemorrhage, 0 deaths 88 (0.24%) complications in 88 uncircumcised boys, all UTI, 32 concomitant cases of bacteremia, 2 deaths association between UTI and circumcision significant at p<0.0001	Results may be an underestimate of actual frequency of adverse sequelae in both circumcised and uncircumcised boys; minor complications may not have been indexed in records, lesser problems may have been treated on outpatient basis, some children may have been admitted to civilian hospitals No chi square value reported
Wiswell TE;Smith FR;Bass JW; 1985 [128]	Study Type: Cohort Evidence level: 2+	Records of infants who were hospitalised during the first year of life for UTI were reviewed to document incidence of UTI in first year of life	5261 infants (2759 female, 2502 male)	Medical records of all infants born between 1982 and 1983 at an army medical centre. UTI defined as $\geq 10^5$ cfu/ml, one strain, by SPA or catheter	No. evaluated for UTI No. with diagnosed UTI No. males circumcised Mean age at time of diagnosis Associations tested using chi square	400/5261 (7.6%) infants evaluated for UTI 41/5261 (0.78%) infants diagnosed with UTI: 13 female 4 circumcised male 24 uncircumcised male incidence of UTI in males higher than in female (p<0.01) incidence of UTI in uncircumcised higher than in circumcised (p<0.001) 1919/2502 (76.7%) males circumcised female age: 2.5 mo circumcised male: 1.4 mo uncircumcised male: 1.7 mo age range: 10 days to 11 months; 34/41 (83%) were <3mo	
Wisell TE;Enzenauer RW;Holton ME;Cornish JD;Hankins CT; 1987 [129]	Study Type: Cohort. Evidence level: 2+	Records of infants who were hospitalised during the first year of life for UTI were reviewed to document incidence of UTI in first year of life	427698 infants (207923 female, 219775 male)	All infants born between 1975 and 1984 in US army hospitals UTI defined as $\geq 10^5$ cfu/ml, one strain, by SPA or catheter.	No. of UTI by gender No. males circumcised No. of UTI by circumcision status	Females: 1051/207923 (0.51%) with UTI, males: 610/219775 (0.28%) with UTI; chi square = 143.5, p<0.001 173663/219775 (79%) males circumcised UTI in circumcised: 151/173663 (0.09%), UTI in uncircumcised: 459/46112 (99.5%); chi square = 1086.43, p< 0.001	Chi square and p-value calculated by NCC-WCH
To T;Agha M;Dick PT;Feldman W; 1998 Dec 5 [130]	Study Type: Cohort Evidence level:	Circumcision and subsequent risk of UTI (defined by ICD-9 codes	Hospital discharge data on 69,100 boys	Born to residents of Ontario between 1 April 1993 and 31 March 1994; n=30,105 circumcised within	Follow-up period: From birth until first UTI or until 31 March 1996.	1 month probability of hospital admission for UTI (per 1000 person-yrs): 0.34 for circumcised and 1.54 for uncircumcised; relative risk 4.5, 95% CI 2.4 to	

Bibliographic Information	Study Type & Evidence Level	Aims and comparisons	Number of Patients	Patient characteristics	Follow-up & Outcome Measures	Effect Size	Reviewer comment
	2++	for infections of the kidneys, cystitis, urethritis, other unspecified UTI)		first month of life, n=38,995	Outcome Measures: Hospital admission for UTI during the 2-3 years of follow-up NNT	8.4 1 year probability of hospital admission for UTI (per 1000 person-yrs): 1.88 for circumcised and 7.02 for uncircumcised; relative risk 3.7, 95% CI 2.8 to 4.9; 195 circumcisions needed to prevent 1 hospital admission for UTI in first year of life 3 year probability of hospital admission for UTI (per 1000 person-yrs): 2.96 for circumcised and 8.75 for uncircumcised; relative risk 3.0, 95% CI 2.4 to 3.8	
Craig JC;Knight JF;Sureshkumar P;Mantz E;Roy LP; 1996 [131]	Study Type: Case-control Evidence level: 2+	The association between circumcision and risk of UTI and whether this association is independent of age	n=144 circumcised boys with UTI and n=742 controls	Cases: boys, aged <5 years, presenting with symptomatic UTI, with no previous history of diagnosed UTI, from pediatric department of children's hospital from Mar 1993 to Dec 1994 UTI defined as: for SPA or catheter, growth >10^6 cfu/L, one strain; for midstream, >10^8 cfu/L, one strain; PLUS, symptoms and/or signs of UTI Controls: all boys, aged <5 years, without UTI, presenting at the same department in the same hospital as the case boys for one month (Apr) in 1995	No. circumcised, chi square Median age, Mann-Whitney U Association between circumcision and UTI by age, chi square and odds ratio Breslow-Day test for homogeneity	47/742 (6.3%) controls circumcised, 2/144 (1.4%) cases circumcised; chi square = 5.6, p=0.02 median age = 21 months for controls, 5.8 months in cases; p<0.001 under 1 yr: chi square = 3.9, p=0.05; OR 0.3, 95% CI 0.06 to 1.1 1 yr and older: chi square = 2.2, p=0.1; OR 0.2, 95% CI 0.01 to 3.7 combined OR (mantel-haenszel) = 1.8 , 95% CI 0.05 to 0.70; homogeneity, p = 0.4	Statistics vary from what is calculated by NCC-WCH on STATA using numbers provided in paper, e.g. one set of 95% CI presented in paper did not include the OR and was recalculated at NCC-WCH Study did not confirm that controls had no UTI using microbiology
Herzog LW; 1989 [132]	Study Type: Case-control Evidence level: 2+	Association between UTI and circumcision in boys aged < 1year and investigation of whether ethnic, racial or socio-economic factors play a role	n=36 boys with UTI and n=76 controls	From all 211 boys <1 yr old who had urine culture done in ER at one children's hospital for 1985 and 1986, cases were those who had SPA or catheter yielding >10^5 cfu/ml, one strain Controls were patients with negative SPA or catheter culture, i.e., <1000 organisms/ml Infants whose circumcision status could not be determined (n=1 case and n=29 controls), those whose race could not be determined (n=13 controls), those with previous UTI anatomic problems or equivocal results (n=59) were excluded	No. circumcised Mean age Differences in circumcision by age, race, and type of insurance	0/36 cases circumcised, 52/76 (68%) controls circumcised; p<0.0001 3.7 months for cases, 4.5 months for controls; p not significant Also no differences between cases and controls in ethnic group or type of medical insurance Cases less likely to be circumcised if <3mo (p<0.0001) and if >3mo (p<0.0001) Cases less likely to be circumcised among Hispanics (p=0.02), blacks (p<0.001) and whites (p=0.0003) cases less likely to be circumcised for all types of insurance (all p ≤ 0.01)	Abstract mentions no significant difference between cases and controls by ethnic group but this result is not reported in the results section of the paper. Note small sample size.
Marild S;Hansson S;Jodal U;Oden A;Svedberg K; 2004 Feb [133]	Study Type: Case-control Evidence level: 2+	Association between breastfeeding and the risk of first time febrile UTI and the dose-response of protective effect of duration of breastfeeding assessed by interview and	n= 200 consecutive children with UTI (89 male, 111 female) and n=336 controls (147 male, 189 female)	Cases: children age 0-6 yrs presenting with first-time symptomatic UTI in two paediatric departments Inclusion criteria: fever of >38.4°C within 24 hr of diagnosis plus bacteriuria; bacteriuria defined as	Duration of exclusive breastfeeding at time of interview Risk of UTI when breastfed v. not breast fed, difference in risk of UTI between girls and	Mean duration of breastfeeding (wks± SD): girl cases: 16±9.2 girl controls: 18±9.2 boy cases: 11±8.9 boy controls: 12±8.4	Confidence intervals for all results not provided, in particular, provided for overall, but not individual groups No measures to control for recall bias mentioned in the

Bibliographic Information	Study Type & Evidence Level	Aims and comparisons	Number of Patients	Patient characteristics	Follow-up & Outcome Measures	Effect Size	Reviewer comment
		questionnaire		one of the following: for SPA, growth of any cfu/ml, one strain; for midstream samples, growth ≥10^5 cfu/ml, one strain; for bag urine, two separate specimens with growth ≥10^5 cfu/ml, same strain in both specimens. Controls: aimed for 2 per case, enrolled consecutively; no history of previous UTI or urinary tract anomalies; matched for gender and age and registered at same hospital of case.	boys, and risk of UTI in relation to duration of breastfeeding assessed by Poisson regression risk of UTI in first two years of life after weaning	Non-breastfed compared with breastfed: Overall: risk of UTI increased 2.3 times (95% CI 1.56 to 3.39) Girls: risk of UTI increased 3.78 times Boys: risk of UTI increased 1.63 times Longer duration of exclusive breastfeeding significantly reduced probability of UTI; the protective effect of exclusive breastfeeding was strongest right after birth for girls and then decreased until 7 months. In boys, protective effect was less marked and constantly decreased as age increased. Risk of UTI increased rapidly if breastfeeding discontinued after 2 months; lower risks of UTI were observed with weaning after 7 months breastfeeding.	study methods Study did not confirm that controls had no UTI using microbiology
Nuutinen M;Huttunen N;Uhari M; 1996 [134]	Study Type: Case-control Evidence level: 2+	Risk of contracting UTI according to different nappy types used prior to first UTI diagnosis	n = 196 children with UTI (104 female, 92 male) and n=196 controls (104 female, 92 male)	Cases: children who were 'nappy age' and used nappies day and night presenting with first UTI in one of 2 children's hospitals from 1987 to 1994 Inclusion criteria: for SPA, growth of any cfu/ml; for two subsequent clean voided urine samples, growth ≥10^5 cfu/ml, same strain in both specimens. Controls: children who were hospitalised for some other reason, matched for gender and age	Outcome Measures: Odds of UTI	Disposable: 0.95, 95% CI 0.62 to 1.46 super absorbent: 1.04, 95% CI 0.69 to 1.57 washable cotton: 1.00, 95% CI 0.46 to 2.16 No significant differences in nappy habits were reported (including daily number of nappies used, number of defecations per day, frequency of buttock washes, daily time spent without a nappy, and occurrence of nappy rash)	Study did not confirm that controls had no UTI using microbiology - although this does not affect the study outcome as the null hypothesis was not rejected. No measures to control for recall bias mentioned in the study methods
Hoi LV;Sarol JN;Uriarte RD;Tadoy SA; 2000 [135]	Study Type: Case-control Evidence level: 2-	Face-to-face interviews, validated by interview with parents	n =23 children with UTI and n=23 controls; 60.9% female, 39.1% male	Cases: out-patient children aged 6-12 (mean 8.63yrs) with UTI from 4 tertiary hospitals from Sept 1998 to Sept 1999 UTI determined by: for midstream urine, growth of at least 10^5 cfu/ml, one strain, or medium to high growth as identified by aerobic method Controls: selected soon after case was identified, included children presenting with any disease or condition other than urinary diseases and selected hygiene-related diseases	Outcome Measures: Previous history of UTI Increased risk of UTI associated with urination, defecation, washing and bathing habits Association between UTI and age group, school enrolment history of UTI, presence of preschooler in the same household and holding of urination examined in multivariate analysis	21.7% of cases had previous history of UTI compared with 4.3% of controls No increased risk of UTI was observed for bathing habits (daily v. less than daily), urinary frequency (less than 5 times/day or 5+ per day), holding urine during the day (yes or no), permission to urinate at school (during break v. whenever), washing after urination (yes or no), washing after defecation (yes or no), direction of washing (from behind v. from front), or use of soap during washing (yes or no) In multivariate analysis: Adjusted OR 6.18 (95% CI 1.04 to 54.60) for age group and 5.78 (95% CI 1.01 to 51.02) for school enrollment; all other variables NS	Did not specify whether controls were matched for age and gender Did not specify if controls were selected from the same hospital as case Number excluded or declined to participate not specified Small sample size resulted in wide confidence intervals Study did not confirm that controls had no UTI using microbiology No measures to control for recall bias mentioned in the study methods
Hansen A;Hansen	Study Type: x-	Questionnaires to	1557 children (823	1557/2780 (56%) questionnaires	No. reporting previous UTI	75/823 (9.1%) girls and 20/728 (2.7%) boys reported	Major limitation of study is the

Bibliographic Information	Study Type & Evidence Level	Aims and comparisons	Number of Patients	Patient characteristics	Follow-up & Outcome Measures	Effect Size	Reviewer comment
B;Dahm TL; 1997 [136]	sectional. Evidence Level: 3	investigate the potential correlation between UTI and voiding habits (denominators vary due to incomplete questionnaires)	female, 728 male, 6 without gender identification)	from children aged 6 to 9 years old from 77 schools.	No. reporting more than one previous UTI Frequency of micturation Micturation habits compared by chi-square for females only (number of boys too small)	previous UTI 27/75 (36%) girls and 4/20 (20%) had had more than one previous UTI. No significant difference in frequency of micturation between children with and without prior history of UTI (median number voidings for all children = 5/day) Symptoms and signs Micturation habits in previous UTI v. no UTI: bed wetting, 19/75 v. 90/723, p = 0.002 day wetting, 22/75 v. 93/723, p <0.0002 does not reach toilet, 30/75 v. 202/723, p=0.03 prolonged voiding, 25/75 v. 129/723, p<0.002 poor stream, 22/75 v. 114/723, p<0.003 staccato voiding, 23/75 v. 126/723, p<0.006 able to void again, 24/75 v. 1252/723, p<0.002 straining, 13/75 v. 62/723, p=0.02 manual compression of abdomen, 13/75 v. 53/723, p<0.003 encopresis, 10/75 v. 43/723, p=0.03	low response rate: 56% Study design subject to recall bias, e.g., inflated numbers due to parents of children with wetting problems being more likely to respond. Statistical test for frequency of micturation not reported.

Symptoms and signs

Bibliographic Information	Study Type & Evidence Level	Aim of Study	Number of Patients	Population Characteristics	Follow up & Outcome measures	Effect size	Reviewer Comment
Craig JC;Irwig LM;Knight JF;Sureshkumar P;Roy LP; 1998 Apr [137]	Study Type: Case-series Evidence Level: 3	To describe the demographic and clinical features of children with symptomatic UTI	n=305 children (169 male, 135 female) with UTI	Children aged <5 years presenting consecutively at the emergency hospital of a children's hospital with first documented symptomatic UTI from 1993 to 1994 UTI defined as: for SPA or catheter, >10^6cfu/L, one or two strains; for midstream urine > 10^7 cfu/L, one or two strains; for bag urine, >10^8 cfu/Land urinary white cell count >100 x 10^6/L	Age and gender of children with UTI Frequency of clinical features of children presenting with UTI	Males (n=169) with UTI: 0 to 1 yr: 127 (75.1%) 1 to 2 yrs: 13 (7.7%) 2 to 3 yrs: 12 (7.1%) 3 to 4 yrs: 7 (4.1%) 4 to 5 yrs: 10 (5.9%) Females (n=135) with UTI: 0 to 1 yr: 68 (50.3%) 1 to 2 yrs: 26 (19.3%) 2 to 3 yrs: 19 (14.1%) 3 to 4 yrs: 15 (11.1%) 4 to 5 yrs: 7 (5.2%) Symptoms (from n=304): History of fever, 242 (79.6%) Axillary temp >37.5, 181 (59.5%) Irritability, 159 (52.3%) Anorexia, 148 (48.7%) Malaise/lethargy, 135, (44.4%) Vomiting, 127 (41.8%) Diarrhoea, 63 (20.7%) Dysuria, 45 (14.8%) Offensive urine, 40 (13.2%) Abdominal pain, 40 (13.2%) Frequency, 29 (9.5%) Macroscopic haematuria, 20 (6.6%)	
Ginsburg CM;McCracken GH; 1982 Apr [116]	Study Type: Case-series Evidence Level: 3	To present clinical and laboratory features of UTI	100 infants 62 boys 38 girls	Infants aged 5 days to 8 months (mean 2.1 months) admitted to one of two hospitals with acute UTI from Mar 1976 to Feb 1981	Frequency of symptoms and signs	Age distribution Male infants accounted for 75% of UTI cases within the first three months of life compared with 11% of boys who were 3 to 8 months of age. Of the 41 infants who were under 30 days old, 33 (81%) were boys. Symptoms and signs Fever was the most common symptom (in 63%) and symptoms of irritability (55%), had refused feeds (38%), vomiting (36%) and diarrhoea (31%). 67 infants had a fever of ≥38°C and 38 infants had fever of ≥39°C. Abdominal distention and jaundice were only reported in 8% and 7% of patients respectively.	
Burbige KA;Retik	Study Type:	To present clinical and	83 boys	Boys aged 2 weeks to 14 years treated	Age and gender of	Age distribution	No definition of fever

Bibliographic Information	Study Type & Evidence Level	Aim of Study	Number of Patients	Population Characteristics	Follow up & Outcome measures	Effect size	Reviewer Comment
AB;Colodny AH; 1984 [138]	Case-series Evidence Level: 3	laboratory features of UTI		at a children's hospital with first time UTI. (mean age unknown) UTI defined as >100,000 cfu/ml.	children with UTI Frequency of clinical features of children presenting with UTI Frequency of symptoms and signs	Of the 83 boys, 25% were ≤1 year old and half were < 6 years old. The incidence of urinary tract abnormalities was distributed evenly through the group. Symptoms Fever 40/83 (48%) and the only presenting sign in 25%. Irritative bladder syndromes 23/83 (28%) Abdominal or flank mass 11/83 (13%) Enuresis 7/83 (8%) Gross haematuria 6/83 (7%)	
Messi G;Peratoner L;Paduano L;Marchi AG; 1988 [50]	Study Type: Case-series Evidence Level: 3	To present clinical and laboratory features of UTI and to determine incidence of UTI	223 children (38 males, 185 females)	Children aged 0-14 years presenting with symptomatic UTI and treated at a hospital. UTI was defined as two consecutive urine cultures yielding >10^5cfu/ml of the same bacteria and microscopic examination yielding more then 10leukocytes/mm^3	Presenting symptoms Number with UTI Number with cystitis Number with pyelonephritis Number with VUR Renal scarring Urinary tract malformations	64/223 (29%) aged >1 year 63/223 (28%) aged 1-4 years 96/223 (43%) aged 5-14 years Symptoms and signs Fever 144/223 (64.6%) Dysuria and frequency 92/223 (41.2%) Gastrointestinal symptoms 42/223 (18.8%) Haematuria 24/223 (10.8%) Failure to thrive 14/223 (6.3%) Jaundice 2/223 (0.9%)	
Smellie JM;Ransley PG;Normand IC;Prescod N;Edwards D; 1985 Jun 29 [98]	Study Type: Other Case-series Evidence Level: 3	Factors surrounding the development of renal scars	120 children	Children aged 2 weeks to 12 years who had an intravenous urograms and a UTI seen between 1960 and 1982. New scars were defined as the development of a caliceal deformity with thinning of the overlying renal parenchyma in an area of kidney considered to be normal in the previous urogram. Exclusions: solitary, duplex or horseshoe kidneys, kidney stones, mechanical or neuropathic or postoperative obstruction. Definition of UTI not reported.		Scars developed in 87 kidneys of 74 children (8 boys, 66 girls) New scars 58/74 (78%) of children had normal kidneys initially; unilateral scarring in 46, bilateral in 12 Progressive scars 13/74 (18%) had unilateral scarring initially and developed additional scars 3/74 children had bilateral scarring initially and developed additional scars All children with scarring had UTI 61/74 (82%) due to E. coli. Presenting symptoms: fever (57/74) 77% abdominal or loin pain (34/74) 46% chronic constipation (16/74) 21% uncoordinated voiding with residual urine (8/74) 11% 67/74 (91%) children had reflux, new scars developed with all grades of reflux. However there was a greater tendency for scaring to occur in more severe reflux. 51% of the children who developed scarring had previously had a UTI.	
Honkinen	Study Type:	To assess the clinical	134 children (82	Children aged 7 days to 9.5 years	Age and sex	Age distribution:	Some of the

Bibliographic Information	Study Type & Evidence Level	Aim of Study	Number of Patients	Population Characteristics	Follow up & Outcome measures	Effect size	Reviewer Comment
O;Jahnukainen T;Mertsola J;Eskola J;Ruuskanen O; 2000 Jul [52]	Cross-sectional Evidence Level: 3	characteristics of bacteremic UTI in children.	girls, 52 boys) located from all 36 Finish hospitals and 25 microbiological laboratories, between 1985 and 1994 Comparison group 134 age and sex matched from children hospitalised for blood culture negative symptomatic UTI	(median 0.125 years) with serious bacteremic UTI. Inclusion criteria were symptoms of acute illness such as fever, irritability, vomiting or dysuria; bacterial growth ≥10^5 in one midstream urine or in two urine bag samples; growth of identical pathogen both in the blood and in the urine cultures; first known urinary tract infection; and no known urinary tract abnormality or other severe underlying disease. 29 children had a history of UTI or urinary tract abnormality or other severe underlying disease. 7 children were under 1 week old and analysed separately	distribution of bacteremic UTI Symptoms and signs Laboratory findings Microbiological findings	89/134 (66%) 1 week - 3 months; 61/89 (69%) of youngest age group were boys) 30/134 (22%) 3 to 11 months 16/134 (12%) ≥ 12 months <u>Symptoms and signs</u>: No. with Bacteraemic UTI (%) v No. with Nonbacteraemic UTI (%) Fever 124 (92%) v 121 (90%) Irritability 81 (60%) v 75 (56%) Abnormal crying 46 (34%) v 41 (30%) Vomiting 22 (16%) v 18 (13%) Lethargy 35 (26%)v 41 (30%) Feeding problems 27 (20%) v 13 (10%) Abdominal pain 10 (7%) v 4 (3%) Dysuria 2 (1%) v 4 (3%) Convulsions 5 (4%) v 0 (0%) Only feeding problems were reported more often in bacteremic patients (20% vs. 10 %, p = 0.02). The duration of the preceding fever showed no difference between the two study groups (mean, 1.9 ± 1.9 vs. 1.8 ± 1.7 days, respectively). In patients ≥ 12 months old (n = 17), fever had lasted 2.7 ± 2.1 days in non-bacteremic patients vs. 1.7 ± 1.5 days in bacteremic patients (p = 0.11). No difference was found in the mean values for the highest temperature on admission (39.4 ± 0.5 vs. 39.1 ± 0.5ºC). Two of the patients in both study groups were afebrile (body temp. < 38.0ºC).	Children included in this study may have been included in the study Ref ID 1068
Nayir A; 2001 Dec [139]	Study Type: Cross-sectional Evidence Level: 3	To present clinical characteristics of UTI and to determine whether circumcision decreases the risk of significant bacteriuria and prevents recurrence. By patient interview.	88 boys	Boys aged 3 months to 10 years (mean age 30.3 months ± 26.6 months) with first time symptomatic UTI referred to a paediatric nephrology department. Boys with existing uropathies were excluded. Bacteriuria defined as growth of a single urinary pathogen at 10^5cfu/ml. Urine was collected by bag in 47/88 (53%) of boys and by mid-stream in 41/88 (47%)	Age distribution of UTI Symptoms and signs	Age distribution 47/88 (53%) aged >2 years 23/88 (26%) aged 2-5 years 18/88 (20%) aged <5 years <u>Symptoms and signs</u> Fever <38.5°C 42 (48%) Fever >38.5°C 21 (24%) Vomiting and/or diarrhea 19 (22%) Dysuria/frequency 30 (34%) Enuresis 6 (7%) Suprapubic discomfort 10 (11%) Abdominal pain 16 (18%) Flank pain 4 (5%) Malodorous urine 2 (2%)	Only presenting symptoms of this RCT presented here. See recurrence evidence tables for full review.
Smellie JM;Normand IC;Katz G; 1981 [67]	Study Type: Case-series Evidence Level: 3	To examine the clinical features of children presenting with UTI to determine whether there	744 children, 179 boys and 565 girls	Children aged 0 to 12 years treated in a paediatric department with bacteriologically proven UTI. All children were investigated with	Age distribution of UTI Symptoms and signs	<u>Age distribution</u> 145/744 (19%) aged >1 year 35/744 (5%) aged 1-2 years	Definition of UTI not provided.

Bibliographic Information	Study Type & Evidence Level	Aim of Study	Number of Patients	Population Characteristics	Follow up & Outcome measures	Effect size	Reviewer Comment
		were any differences between those with and those without VUR		intravenous urography (IVU) and MCUG.	No. with VUR	210/744 (28%) aged 2-4 years 249/744 (33%) aged 5-8 years 105/744 (14%) aged 9-12 years 246 (33%) with VUR 498 (67%) without VUR Symptoms and signs Fever 312/744 (42%) Abdominal or loin pain 231/744 (31%) Enuresis 135/354 (38%) – only in children <5 years VUR compared to no VUR Fever 174/498 (35%) without VUR 140/246 (57%) with VUR (p=0.0004 NCC calculated) Abdominal pain 144/498 (29%) without VUR 86/246 (35%) with VUR	
Dickinson JA; 1979 May 19 [45]	Study Type: Case-series Evidence Level: 3	To present clinical features of UTI and determine incidence in a rural area.	14 children with UTI (5 boys and 9 girls) Derived from a total population of 2879 (1446 boys and 1433 girls) Over an 18 month period	Children aged under 15 years attending a semi-rural GP practice. Infection diagnosed if bacterial counts in three consecutive samples exceeded 100000/ml by mid-stream or bag collection. 2 cultures completed in the GP surgery, and a confirmation culture at a laboratory.	Age distribution of UTI Symptoms and signs Frequency of clinical features of children presenting with UTI	156/2879 children presenting with symptoms of UTI, all were investigated (radiological investigations not reported) 14 of whom were found to have bacteriologically confirmed UTI. Incidence of urinary tract infection was 1.7 per 1000 boys at risk per year and 3.1 per 1000 girls. 2 boys and 4 girls presented with dysuria and frequency, 2 girls 1 boy with abdominal pain, one girls with haematuria and one boy with failure to thrive	Criteria to suspect UTI unclear. Symptoms only, or bacterial confirmation? Unclear whether the 156 sent for 'investigation' had urinalysis only, or had further investigations.
Hallett RJ;Pead L;Maskell R; 1976 Nov 20 [141]	Study Type: Case-series Evidence Level: 3	To present clinical and laboratory features of UTI in boys.	73 boys with suspected UTI 51 healthy controls.	Boys aged 2-12 years presenting to a GP clinic with suspected UTI (n=73) and healthy controls (n=51). Definite infection 10^8 organisms/L of a single organism Probable infection 10^7 organisms/L of a single organism Doubtful infection 10^7 organisms/L of mixed organisms. Matched for age and social class.	No. with UTI Presenting symptoms No. of recurrent infections.	49/73 definite infection 12/73 probable infection 12/73 doubtful infection Boys with definite or probable infection (n=61) 26/61 (43%) aged 2-5 years 35/61 (57%) aged 5-12 years Symptoms and signs Presenting symptoms in 49 boys with definite infection. Enuresis 22 (45%) Dysuria/frequency 40 (82%) Haematuria 10 (20%) Fever 13 (26%)	Term 'recurrence' is not defined. No indication of time periods or organisms involved. Not all boys were followed up for the same length of time. Large range of follow-up times and no median/mean time reported.

Bibliographic Information	Study Type & Evidence Level	Aim of Study	Number of Patients	Population Characteristics	Follow up & Outcome measures	Effect size	Reviewer Comment
						Abdominal pain 17 (35%) Balanitis 10 (20%) Similar distribution of symptoms in boys with probable and doubtful infections.	
Brooks D;Houston IB; 1977 Nov [140]	Study Type: Case-series Evidence Level: 3	To present the clinical findings of a study investigating children with UTI in general practice.	38 children (12 boys and 26 girls)	Children aged under 15 years presenting to a single GP practice with symptomatic UTI Bacteriuria defined as >10^5cfu/ml in a clean catch urine sample.	Frequency of clinical features of children presenting with UTI	Dysuria 27/38 (71%) Loin pain/tenderness 5/38 (13%) Vauge abdominal pain 12/38 (32%) Fever 8/38 (21%) Offensive urine 7/38 (18%) Enuresis 9/38 (24%) Daytime incontinence 2/38 (5%) Haematuria 1/38 (3%) Rigor 1/38 (3%)	
Winberg J;Andersen HJ;Bergstrom T;Jacobsson B;Larson H;Lincoln K; 1974 [42]	Study Type: Case-series Evidence Level: 3	To describe the epidemiology, clinical features of children with UTI	521 children (419 girls and 90 boys)	Children aged 0-16 treated at a children's hospital or maternity unit for symptomatic UTI.	No. with UTI No. with fever	Almost all infants had fever, except neonates in whom only 42% had fever. After the first year of life, fever became less common. 1 – 12 months 179/186 (96%) 1-3 years 70/96 (73%) 3-10 years 120/200 (60%) 10-16 years 19/41 (46%) E.coli 83% of girls and 85% of boys under one year 60% of girls and 33% of boys aged 1 to 16 years. 57% of girls and 83% of boys in neonates(p=0.016) Proteus 33% of boys and 0% of girls over one year of age staphlycoccus albus 30% of girls and 12% of boys Recurrence Analysed in 419 girls 2 months to 1 year 53/124 (43%) 53 (43%) with fever, 0 without fever 1 to 3 years 33/87 (38%) 24 (28%) with fever, 9 (10%) without fever. 3 to 11 years 78/187 (42%) 51 (27%) with fever, 27 (14%) without fever. 11 to 16 years 4/21 (19%)	

Bibliographic Information	Study Type & Evidence Level	Aim of Study	Number of Patients	Population Characteristics	Follow up & Outcome measures	Effect size	Reviewer Comment
						3 (14%) with fever, 1 (5%) without fever. Overall 54% of the recurrences occurred within three months, 46% during the following 9 months.	
Hoberman A;Chao HP;Keller DM;Hickey R;Davis HW;Ellis D; 1993 Jul [14]	Study Type: Cross-sectional Evidence Level: 3	To determine the prevalence of UTI in febrile infants with and without source of fever	945 infants with febrile illness.	Febrile infants, aged 1 yr or less, seen in emergency who had urine culture results from Feb 1990 to Jan 1991 fever defined as rectal temp >=38.3C or axillary temp >=37.4C (in ER or in previous 24 hrs) UTI: all by bladder cath; >=10,000 cfu, single organism	Prevalence of UTI	50/945 (5.29%) febrile infants had UTI By fever source: 1/62 unequivocal 15/429 possible 34/454 no source p = 0.02 for possible v. no source	

Urine collection

Bibliographic Information	Study type & Evidence level	Study Aims	Number of patients & prevalence	Population Characteristics	Intervention & comparison	Effect size	Reviewer comment
Rao S;Bhatt J;Houghton C;Macfarlane P; 2004 Aug 144	Study Type: RCT Evidence level: 1+	To evaluate a modified urine collection pad method for its ability to reduce heavy mixed growth bacterial contamination of urine collection pad samples in young children with suspected urinary tract infection.	68 children (37 single pads, 37 replaced pads)	Febrile children under 2 years old admitted to an acute medical ward with suspected UTI.	Children were randomised into two groups: a single urine collection pad that was left in the nappy until a sample had been obtained; or a urine collection pad that was replaced every 30 munited until a sample was obtained. Alarm sensors were placed in all urine collection pads. Urine was aspirated from the urine collection pads using a 20ml syringe and taken immediately to a lab for culture. UTI was defined as pure growth of a single organism >105cfu/ml.	80 children were recruited (42 in the single urine collection pad and 38 in the replaced urine collection pad), and urine collection failed in 12 children (5 single pad, 7 replaced pad) mainly because of faecal soiling of the pad and were excluded from the analysis. Baseline characteristics of the groups were similar with respect to age, however there were significantly more boys in the single pad group (25/37 vs. 13/31, p=0.034)) 3/68 (4%) children had a UTI. Single urine collection pad vs. replaced pad, p-value. UTI (>105cfu/ml) – 2/37 vs. 1/38 Mixed growth (>105cfu/ml) – 10/37 vs. 1/31 Mixed growth (<105cfu/ml) – 3/37 vs. 2/31 No growth – 22/37 vs. 27/31	
Waddington P;Watson A; 1997 145	Study Type: Cohort Evidence level: 2+	To evaluate the ease of application and reliability of different urine collection bags.	50 children (33 boys, 17 girls)	Children attending a children's clinic. No other details provided.	Intervention: The nurses first cleaned the genital area with warm tap water and cotton wool balls before applying the bag.	Hollister U-bags were used in 18 boys and 7 girls, while Urinicol bags were used in 15 boys and 10 girls. 8/25 Hollister u-bags leaked compared to 0/25 Urinicol bags (p<0.01)	
Al-Orifi F;McGillivray D;Tange S;Kramer MS; 2000 146	Study Type: Cohort Evidence level: 2+	To compare the risks of contaminated culture results and consequent adverse clinical outcomes in urine specimens obtained by urine collection bag compared to catheterisation.	7584 urine samples were collected from 4632 children.	Children ≤24 months who had a urine culture obtained by either urine collection bag or catheterisation between January 1993 and December 1995 at an emergency department or an outpatient unit. Negative: <103cfu/ml in a bag specimen, 102cfu/ml in a catheter specimen Positive: ≥104 cfu/ml in a bag specimen, ≥103cfu/ml in a catheter specimen Contaminated: two or more organisms cultured, or when a single organism was cultured in a concentration intermediate between a positive and negative.	Intervention: Bag urine cultures were obtained by Hollister U-bag after the perineum was cleansed with antibacterial soap and tap water. In the outpatient centre the bag was replaced after 30 minutes, while in the emergency department it was not. Catheter specimens were only collected in the emergency department after cleansing with iodinated soap and sterile water	7584 urine cultures 42.1% infants <6 months 25.9% infants between 6 and 11 months 31.9% from children between 12 and 24 months Bag specimens Emergency department: 2597 Outpatients: 2530 Catheter specimens Emergency department: 2457 Contamination Collection method: 54.4% bag vs. 9.0 catheter (p<0.001) Sex: 38.7% male vs. 29.2% female (p<0.001) Age: 31.4% <12 months vs. 38.7% 12-24 months (p<0.001) Leukocyte esterase: 32.3% positive vs. 33.7% negative (not significant) Odds Ratio (adjusted for age, sex and leukocyte esterase test) was 13.3 (95%CI 11.3 to 15.6) and when limited to the first urine culture in each child was OR 13.6 (95%CI 11.1 to 16.7)	

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McKUNE I; 1989 [147]	Study Type: Cohort Evidence level: 2+	To compare the contamination rates between bag and clean-catch urine collection methods.	46 urine samples (23 from each of two wards)	Children under 2 years old in one of two inpatient wards. No other details reported Exclusions: Children receiving antibiotic therapy and known to have gross renal abnormalities. Positive specimens: >105cfu/ml Inadequate specimens: When the specimen could not be interpreted No growth Urine contaminated with faecal bacteria	Intervention: In Ward A, the child's genitalia was washed with soap and water and urine samples were collected in a sterile foil bowl. In ward B soap and water was used, followed by cleansing with sterile water and drying with cotton wool balls and urine collection bags, either Hollister U-bags or Simcare bags were applied.	46 urine samples (23 from each ward) were obtained; in ward A 44 attempts were made to obtain 23 urine samples, 18 of which were obtained in one hour or less. A parent was involved in 33 of the 44 attempts. Of the 11 times a nurse was involved, total time taken was 3 hours 25 minutes, however for 2 hours 15 minutes, nurses were also feeding the infants, therefore extra time taken overall was one hour 10 minutes. No specimens were contaminated In ward B 28 attempts were made to obtain 23 samples. The urine collection bags were in place for 15 minutes to 4 hours 10 minutes, with an average time of one hour 25 minutes. 11 specimens were contaminated with faecal bacteria.	
Kozer E;Rosenbloom E;Goldman D;Lavy G;Rosenfeld N;Goldman M; 2006 Jul [148]	Study Type: RCT Evidence Level: 1+	To compare the severity of pain during SPA with pain during trans-uretrhral catheterisation in infants younger than 2 months.	51 infants (31 boys, 20 girls)	Infants 0-2 months of age presenting to an emergency department with fever (rectal temperature >38C) and requiring a urina culture between April 2004 and April 2005. Exclusions: Premature birth, previous sepsis workup or other painful procedures, anomaly of the urogenital system or abdominal wall or had a known allergy to local anaethetic.	Pain outcomes were measured on three scales: 1. The nurse and one of the child's parents were asked to rank the infants pain on a 100-mm visual analog scale (VAS where 0 means no pain and 10 means worst possible pain) 2. The upper part of the infants body was video-taped during the procedure and one investigator assigned a point score according to the Douleur Aigue di Nouveaune (DAN) neonatal actue pain scale from 0 no pain, to 10 maximal pain based on three parameters; facial expression, limb movement, and vocal expression. 3. The same investigator measured the duration of the cry from the beginning of the procedure until the cry had stopped for at least 5 seconds.	Baseline characteristics Male/female – 17/10 vs. 14/10, p=0.78 Age (±sd) in days – 27.7 (±14.8) vs. 36.5 (±12.3), p=0.007 Weight (±sd) in kgs - 4.03 (±1.2) vs. 4.37 (±0.8), p=0.25 Pain Assessment SPA vs. catheter, difference between SPA and catheter (95%CI of the difference) DAN, mean (±sd) - 7.0 (±1.9) vs. 4.5 (±2.1), 2.5 (1.4 to 3.7) VAS by a parent, mean (±sd) mm – 63 (±27) vs. 46 (±26), 16.8 (1.8 to 31.8) VAS by nurses, mean (±sd) mm - 63 (±18) vs. 43 (±25), 19.6 (7.4 to 31.8) Duration of cry, mean (±sd) s – 62.9 (±26) vs. 49.7 (±35.7), 13.2 (4.3 to 30.7)	
Chu RWP;Wong Y;Luk S;Wong S; 2002 [149]	Study Type: RCT Evidence level: 1+	To determine the optimal method of SPA, the success rate of real time ultrasound-guided SPA compared with conventional SPA and factors associated with success.	30 infants randomly allocated to group A (for real-time ultrasound guided SPA) and 30 infants to group B (Blind SPA with prehydration protocol).	60 infants aged under 12 months were randomised to SPA. 30 infants in ultrasound guided group (19 boys, 11 girls) 30 infants in control group (8 boys and 22 girls) There were no significant differences in the age of infants (5.2 ± 3.4 months in ultrasound group vs. 4.2 ± 3.1 months in control group) p>0.05. In 36 infants (15 in group A and	Infants in group A were not deliberately given any fluid before the first attempt For infants in group A undergoing ultrasound-guided aspiration, the bladder was scanned with an ultrasound scanner and bladder dimensions recorded. The bladder volume was calculated and aspiration wa performed if the bladder volume was estimated to be greater than 3ml. If the baldder volume was less than 3ml, a milk or juice feed was given and ultra-sound inspection repeated every 10-15 mins.	Overall success rates Ultrsound guided 26/30 (87%) 24/30 (80%) in the control group (p<0.05). First attempt Ultrasound success 18/30 (60%); failure 10/30 (33%); voided before attempt 2/30 (7%) Control success 18/30 (60%); failure 12/30 (40%) Equally successful in both groups (p>0.05) Second attempt Ultrasound: success 26/30 (60%); failure 2/30 (7%); voided before attempt 1/30 (3%)	In control group Prehydration protocol used and bladder dullness demonstrated before SPA attempted. This may explain the differences between this study and others. In ultrasound guided group SPA was attempted

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				21 in group B) SPA was performed because fever with positive urinalysis results. In 24 infants (15 in group A and 9 in group B) their previous bag urine sample was culture positive with mixed organisms or doubtful colony counts. No patient had clinical signs of dehydration.	Infants in group B were given 102 ± 47 ml of fluid before the first attempt at SPA which was performed after an interval of 25 ± 16 mins. For patients in group B undergoing conventional SPA, the infant had their nappy changed to ensure the recent voiding would be noticed and received a milk or juice feed. After 15 mins, the presence of the bladder was confirmed by light percussion and SPA was performed.	Control: success 6/30 (20%); failure 6/30 (20%) Third attempt Ultrasound: success 1/30 (3%); failure 0; no parental consent 1/30 (3%) Control: no parental consent 6/30 (20%) Urine collected by catheterisation Ultrasound: 4 (13%) Control: 6 (20%) Ultrasound guided group Bladder depth in mm (mean ± SD) Successful attempts vs. unsuccessful attempts 28 ± 11 vs. 21 ± 5 (p<0.01) Calculated volume (ml) 17 ± 13 vs, 8 ± 6 (p<0.01) Bladder length 32 ± 12 vs. 23 ± 9 (p<0.05) Transverse width 33 ± 9 vs. 29 ± 5 (p>0.05) Control group No differences between successful attempts and failed attempts (time from last feed, amount of last feed, time from last void). Bladder dullness was demonstrated by light percussion 23/24 successful attempts vs. 8/18 failed attempts (OR 29.0, p<0.001)	regardless of the bladder volume.
Kiernan SC;Pinckert TL;Keszler M; 1993 Nov [150]	Study Type: RCT Evidence level: 1+	To determine whether ultrasound guidance is useful to localise the position of the bladder and to increase the amount of urine obtained.	53 neonates	Neonates requiring SPA randomly assigned to an ultrasound-guided, or conventional urine aspiration between July and December 1991. 28 in the ultrasound-guided group 25 controls	Controls: No attempt at aspiration were made within 30 minutes of voiding. Ultrasound-guided: Neonates were scanned with a portable ultrasound scanner equipped with a 5MHz head. Both longitudinal and transverse views of the bladder were obtained. If the bladder measured at least 1x1cm SPA was attempted. Three passes at different angles (90,60 and 120 degrees) were attempted while the needle remained under the skin in both groups.	Weight distribution and the level of operator training between the groups was similar. Success at first attempt Ultrasound 26/28 (93%) Control 7/25 (28%) p=0.001 Overall success (two attempts) Ultrasound 27/28 (96%) Control 15/25 (60%) p=0.003 Volume of urine obtained (ml) Ultrasound 2.1 ± 1.2 Control 1.3 ± 0.9 p=0.029 Number of passes	

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						Ultrasound 1.7 ± 1.0 Control 4.4 ± 2.0 p=0.001 Procedure time (seconds) Ultrasound 53 ± 59 Control 60 ± 40 p=0.600	
Gochman RF;Karasic RB;Heller MB; 1991 [151]	Study Type: RCT Evidence level: 1+	To determine whether portable ultrasound could improve the success rate of SPA in a paediatric ED.	66 children, 35 randomised to ultrasound (22 boys, 13 girls), 31 to no ultrasound (18 boys, 13 girls)	Children aged 0 to 15 months (median 1 month) old requiring urine collection by SPA between January and July 1989. 82% of children were less than 2 months old. No child was considered significantly dehydrated. SPA was considered successful if any urine was aspirated Bladder was considered full if both anterioposterior and transverse maximum diameters were 2cm or more, and empty if either diameter was less than 2cm.	All SPAs were performed by two clinicians. Neither investigator had any formal training in ultrasound technique. Ultrasound group Underwent scanning immediately following clinical evaluation. The ScanMate II ultrasound scanner (a portable scanner) was used. If the bladder was full SPA was attempted, if empty, the bladder was rescanned 30 mins later. If the bladder remained empty SPA was not attempted and bladder catheterisation was performed. No ultrasound SPA perfoemed immediately after the clinical evaluation, provided the child had not voided in the past 30 mins, nor had a wet diaper at the time of evaluation. If the child had recently voided, SPA was delayed for 30 mins. Patients who either failed the SPA or wet a diaper during the waiting period underwent catheterisation.	No significant differences between the groups in terms of age, weight or gender. 82% of children were less than 2 months old 2/66 full bladders identified by bladder percussion. Ultrasound Full bladder visualized in 16/35 (46%) after 30 minute waiting period an additional 3 patients met the criteria for full bladder 19/35 (54%). 15/19 (79%) of SPA attempts were successful. In 3/4 unsuccessful SPA attempts, catheterisation yielded ≥5ml of urine. 16/35 bladders remained empty on 2nd ultrasound scan and 15/16 had ≥5ml of urine was collected on catheterisation. No ultrasound 14/35 underwent SPA immediately and 17/35 had SPA performed after a 30 minute waiting period. 16/31 (52%) SPA attempts were successful In 11/15 unsuccessful SPA attempts, catheterisation yielded ≥5ml of urine. The success rate for the ultrasound group was significantly higher then for the controls (p=0.04) Operator efficiencies - increasing success rate over time (p=0.03) Ultrasound accurately detected the presence of urine in 19/21 children and the absence of urine in 25/29.	Randomisation by random number tables Allocation concealment not described. Blinding not possible
McGillivray D;Mok E;Mulrooney E;Kramer MS; 2005 Oct[153]	Study Type: diagnostic Evidence Level: III	To compare the validity of the urinalysis on clean-voided bag versus catheter urine specimens using catheter culture as the gold standard	303 children (102 boys, 201 girls)	Non-toilet-trained children under 3 years old who presented to a children's emergency hospital between June 2000 and December 2001. Inclusion: Fever without source (>39C) or any fever >48 hours duration and males under 6 months or females under 12 months, uncircumcised boys of	Bag urine (collected first) A positive dipstick was defined as the presence of greater than a trace (Ca15/mm^3) leukocyte esterase or a positive nitrite result. The catheter urine culture was considered positive if it yielded >10^3cfu/ml or >10^6cfu/ml of a single pathogenic organism.	Only children with bag and catheter urine specimens were evaluated. 54/303 (18%) were under 90 days old. 82 of the catheter cultures were positive. Dipstick in paired bag vs catheter specimens (2 age groups) Sensitivity Overall: Bag 85% (78% to 93%) vs. catheter 71% (61% to 81%) p=0.003	No way of knowing how many children did not have a catheter sample (ie. Only had a bag sample and therefore were not analysed)

Bibliographic Information	Study type & Evidence level	Study Aims	Number of patients & prevalence	Population Characteristics	Intervention & comparison	Effect size	Reviewer comment
				any age, past history of UTI or abnormal renal anatomy. Another group of children without fever were also included if they were Ill-appearing without identifiable focus of infection or infants under 3 months exhibiting signs or symptoms of UTI (dysuria, foul-smelling urine, change in urine colour) or had unexplained abdominal pain. Exclusions: children requiring urgent medical attention, children already receiving antibiotics		≤90 days: Bag 69% (44% to 94%) vs. catheter 46% (19% to 73%) p=0.248 >90 days: Bag 88% (81% to 96%) vs. catheter 75% (65% to 86%) p=0.016 Specificity Overall: Bag 62% (56% to 69%) vs. catheter 97% (95% to 99%) p<0.001 ≤90 days: Bag 61% (46% to 76%) vs. catheter 100% (93% to 100%) p<0.001 >90 days: Bag 63% (56% to 70%) vs. catheter 97% (94% to 99%) p<0.001 Dipstick and microscopy in paired bag vs catheter specimens (2 age groups) Sensitivity Overall: Bag 95% (90% to 100%) vs. catheter 83% (74% to 91%) p=0.004 ≤90 days: Bag 77% (54% to 100%) vs. catheter 62% (35% to 88%) p=0.480 >90 days: Bag 99% (96% to 100%) vs. catheter 87% (78% to 95%) p=0.013 Specificity Overall: Bag 45% (38% to 52%) vs. catheter 95% (92% to 98%) p<0.001 ≤90 days: Bag 54% (38% to 69%) vs. catheter 100% (92% to 100%) p<0.001 >90 days: Bag 43% (35% to 50%) vs. catheter 94% (90% to 98%) p<0.001 Dipstick in paired bag vs catheter specimens (boys and girls, 2 age groups) Sensitivity Boys overall: Bag 86% (74% to 99%) vs. catheter 69% (52% to 86%) p=0.131 Boys ≤90 days: Bag 73% (46% to 99%) vs. catheter 45% (16% to 75%) p=0.248 Boys >90 days: Bag 94% (84% to 100%) vs. catheter 83% (66% to 100%) p=0.617 Girls overall: Bag 85% (75% to 95%) vs. catheter 72% (60% to 84%) p=0.023 Girls ≤90 days: Bag 50% (0% to 100%) vs. catheter 50% (0% to 100%) p=1 Girls >90 days: Bag 86% (77% to 96%) vs. catheter 73% (60% to 85%) p=0.023 Specificity	

Bibliographic Information	Study type & Evidence level	Study Aims	Number of patients & prevalence	Population Characteristics	Intervention & comparison	Effect size	Reviewer comment
						Boys overall: Bag 86% (78% to 94%) vs. catheter 99% (96% to 100%) p=0.027 Boys ≤90 days: Bag 100% (79% to 100%) vs. catheter 100% (79% to 100%) p=1 Boys >90 days: Bag 83% (73% to 93%) vs. catheter 98% (95% to 100%) p=0.027 Girls overall: Bag 51% (43% to 59%) vs. catheter 97% (94% to 100%) p<0.001 Girls ≤90 days: Bag 41% (22% to 59%) vs. catheter 100% (89% to 100%) p<0.001 Girls >90 days: Bag 53% (44% to 62%) vs. catheter 96% (92% to 99%) p<0.001 Dipstick in paired bag vs catheter specimens in toilet trained children (n=249) aged >90 days using different colony counts Sensitivity 103cfu/ml: Bag 88% (81% to 96%) vs. catheter 75% (65% to 86%) p=0.016 104cfu/ml: Bag 93% (87% to 100%) vs. catheter 81% (73% to 90%) p=0.046 105cfu/ml: Bag 96% (90% to 100%) vs. catheter 83% (74% to 91%) p=0.077 Specificity 103cfu/ml: Bag 63% (56% to 70%) vs. catheter 97% (94% to 99%) p<0.001 104cfu/ml: Bag 61% (54% to 68%) vs. catheter 94% (91% to 97%) p<0.001 105cfu/ml: Bag 59% (52% to 65%) vs. catheter 90% (86% to 94%) p<0.001	
Schroeder AR;Newman TB;Wasserman RC;Finch SA;Pantell RH; 2005 Oct [154]	Study Type: diagnostic Evidence Level: II	To determine predictors of urethral catheterisation in febrile infants and to compare bag and catheterised urine test performance characteristics.	From a larger study (Febrile Infant Study) involving 219 practices, 3066 infants were enrolled, 1482 had both urinalysis and culture, 1384 who had urine collected by catheter or bag and were evaluated.	Children aged under 93 days with temperature of 38°C or higher who underwent urinalysis and urine culture. For SPA, at lease 100 cfu/ml, for catheter 20000 cfu/ml, for bag and clean catch at least 100000 cfu/ml	Urine collection bags compared to catheterisation.	Bag LE sensitivity: 76% LE Specificity: 84% N sensitivity: 25% N specificity: 98% Catheter LE sensitivity: 86% LE Specificity: 94% N sensitivity: 43% N specificity: 99% Further analysis of 54 patients who had false positive results for LE on bag urinalysis. Of the children who were also tested for nitrites, 4/1 (8%) had positive results. Of children who were also tested for urine white blood cell	

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						counts 9/47 (19%) had more than 10 WBC/hpf. If children who had urine samples with positive LE and positive nitrite reasuls, more than 10 WBC/hpf, or ambiguous culture results are considered to be positive for UTI, the difference between the methods in specificity for LE is still significant. (bag 89%, catheter 95%, p<0.001) Likelihood ratios for urine WBC counts, by urine collection method. Bag 0-2 WBC/hpf – 0.6 3-5 WBC/hpf – 1.1 6-10 WBC/hpf - 0 11-20 WBC/hpf - 7 >20 WBC/hpf – 13.5 ROC curve (95%CI) – 0.71 (0.61 to 0.82) Catheter 0-2 WBC/hpf – 0.2 3-5 WBC/hpf – 1 6-10 WBC/hpf – 3.7 11-20 WBC/hpf – 23.9 >20 WBC/hpf – 26.3 ROC curve (95%CI) – 0.86 (0.82 to 0.91) The area under the ROC curve for urine WBC counts and UTI was higher in children with catheter samples than in those with bag samples (0.86 vs. 0.71, p=0.01).	
Liaw LCT;Nayar DM;Pedler SJ;Coulthard MG; 2000 [155]	Study Type: Cohort Evidence Level: 2+	To assess contamination rates and parents preferences for collecting urine at home.	44 parents collecting urine from 29 boys and 15 girls	Infants aged 1 to 18 months	Pads were placed inside the nappy and checked every 10 minutes until wet, then urine aspirated with a syringe. Bags were applied and inspected every 10 mintues and removed to decant urine. Clean catch samples were collected in a sterile bottle. Samples were immediately instilled on dipslides with sterile swab sticks.	Parents preferred using the pad first, the bag second and the clean catch method third. Seven samples from pads, eight from bags and one from clean catch had contamination. Nine samples from 5 children grew >10^5 coliforms/ml suggesting infection, however these were excluded by sterile samples collected on the same day in hospital. Parents found pads and bags easy to use and preferred them to the clean catch method. The pad was considered comfortable, whereas the bag was distressing, particularly on removal often leaking and leaving red marks. Some found extracting the urine from the pad or emptying the bag awkward. Most parents complained that the clean catch method was time consuming and often messy and nine parents gave up after prolonged attempts.	No information about why children needed urine collected. Volunteer sampling method so not representative of the population. All urine was collected on the same day, so likely bias to the the methods not used first.

Urine preservation

Bibliographic Information	Study Type & Evidence Level	Study aims	Number of Patients & Characteristics	Intervention	Results	Reviewer Comment
Eriksson I;Lindman R;Thore M; 2002 [156]	Study Type: Comparative Laboratory study Evidence Level: 3	To evaluate a commercial tube prepared with boric acid, sodium formate and sorbitol..	154 patients from eight health centres. Urine samples were collected from consecutive outpatients with suspected acute urinary tract infection. Patients on antibiotics and children below 10 years of age were excluded.	Conventional tubes (styrene tubes 11ml, Cerbo, Sweden) and tubes with bacteriostatic properties (Hemogard Vacutainer (HG) and Becton-Dickinson). Urine was divided into three tubes. One conventional tube was sent to the laboratory by ordinary chilled transport. Another conventional tube and one HG tube were transported to the laboratory without chilling. Cultures were performed upon arrival at the laboratory and then 24, 48 and 72 hours after primary sampling.	Of the 154 patients studied, 144 had positive cultures (>10^6cfu/L) 24 hours after sampling there were no significant differences in bacterial counts between the chilled conventional tubes and the HG tubes at room temperature. However, in the HG tubes a significant change in *enterococcal* counts were noted after 48 hours.	
Lauer BA;Reller LB;Mirrett S;Ferris JA; 1983 Jan [157]	Study Type: Observational Evidence Level: 3	To learn whether or not chemical preservatives in the Becton-Dickinson urine culture kit are useful for the transport of urine for routine urinalysis.	304 women Clean-catch urine specimens were collected from pregnant women visiting an obstetric clinic.	Urine samples were collected in a sterile plastic cup and distributed into a Becton-Dickinson urine culture kit and a sterile glass tube with out preservative.	Of the 304 urine specimens obtained from pregnant women 2% had significant bacteriuria (10^5cfu/ml). There was complete agreement between preserved and unpreserved split samples in the detection of glucose, ketones, bilirubin and blood. Of the 388 women with symptoms of UTI seen in the emergency room or outpatients department 198 (51%) had significant bacteriuria. Urine microscopy revealed a tendency for erythrocyte counts to be diminished after 24 hours at room temperature in unpreserved specimens. Gram stain results of preserved and unpreserved split samples were comparable; staining characteristics were not altered by the preservative.	
Watson PG;Duerden BI; 1977 Jun [158]	Study Type: Observational Evidence Level: 3	To compare methods of preservation with simulated specimens of pooled urine seeded with known concentrations of test organism.	Number of patients/samples unknown Midstream urine was collected from healthy adult males who had not taken antibiotics in the last three days. Urine was collected on a single day and pooled and sterilized.	One strain each of *E.coli, Pseudomonas aeruginosa, Klebsiella aerogenes, Proteus mirabilis, Micrococcus* and *Streptococcus faecalis* were isolated from infected urine. An overnight culture of each test strain in pooled urine was serially diluted to give six simulated specimens of 10, 103, 104, 105, 106 and 107. 1. At room temperature (night time min 14°C, day time max 27°C) 2. In a domestic refrigerator (min 2°C, max 9°C) 3. 0.16g of powdered boric acid dissolved in 9ml of urine to give a 1.8% solution held at room temperature (min 10°C max 28°C). 4. 30% NaCl – 3 PVP solution held at room temperature (min 18°C, max 28°C). 5. A NaCl – PVP solution held at room temperature (min 18°C, max 27°C)	Unpreserved specimens at room temperature Each test strain multiplied rapidly and the surface viable counts showed concentrations of between 107 and 10^8cfu/ml within 72 hours in every specimen. Refrigerated specimens The surface viable counts for all the specimens remained constant for 72 hours. Specimens with 1.8% boric acid The surface viable counts remained constant for 24 hours, but he viable counts of specimens infected with *P.aeruginosa* fell markedly. After 24 hours the viable counts of the *E.coli* specimens, except for the most heavily infected specimen declined. The viable counts of specimens in the *Klebsiella aerogenes*, *Proteus mirabilis*, *Micrococcus* and *Streptococcus faecalis* and the specimen that was most heavily infected with *E.coli* remained constant for 72 hours. Specimens with 9% NaCl – 0.9% PVP There were no differences between the results obtained with PVP of the two molecular weights. The surface viable counts of	Urine only collected from adult males Only used viable counts – rather than culture

Bibliographic Information	Study Type & Evidence Level	Study aims	Number of Patients & Characteristics	Intervention	Results	Reviewer Comment
					all specimens of *E.coli* fell markedly within 24 hours, except the viable count of the most heavily infected specimen which fell more slowly. The viable counts of the most heavily infected *K.aerogenes* remained constant while the other specimens fell more slowly. The strain of *Micrococcus* grew in the specimens however after 24 hours the viable counts remained in the same range that they were in at time zero. The viable counts of *Streptococcus faecalis* specimens remained constant for 72 hours, but the viable counts of all specimens in the Proteus mirabilis and *P.aeruginosa* specimens fell markedly within 24 hours.	
Southern PM;Luttrell B; 1984 Jun [159]	Study Type: Observational Evidence Level: 3	To evaluate the efficacy of collecting urine specimens in Becton-Dickinson tubes and subsequently screening them for bacteriuria with the Abbott MS-2.	312 adults Midstream urine specimens were collected from obstetric outpatients attending a clinic for prenatal care. Some patients had suspected UTI and others were asymptomatic. Urine was collected by mid-stream catch and placed in the Becton-Dickenson tube and another in a screw-cap tube routinely used for transporting urine from the hospital to the laboratory. If samples could not be transported within 20 minutes, the conventional tube was refrigerated. The time necessary for the MS-2 to judge a urine sample positive was recorded for both specimens.	The Abbott MS-2 is an automated system that allows screening of urine specimens for significant bacteriuria.	Of the 312 urine specimens included in the study, 124 were positive for bacteriuria. The median time required for urine specimens to be judged positive by the MS-2 was similar for conventional tube and for Becton-Dickenson tubes (95 and 105 minutes respectively). Bacterial specimen results from conventional tubes did not differ significantly from those from Becton-Dickinson tubes. Culture results from 24 hour delayed samples from the Becton-Dickinson tubes were significantly different in that 40 of the 188 specimens had colony counts in excess of 10^5cfu/ml.	In obstetric population – could be quite different to urine in children.
Raff LJ;Bazzetta K; 1985 [160]	Study Type: Observational Evidence Level: 3	: To determine whether boric acid interferes with the reactions of the Chemstrip LN dipstick.	177 adult patients. Patients included inpatients, outpatients and residents of a nursing centre.	Preliminary study: Specimens negative for leukocyte esterase and nitrite were obtained by multiple mid-stream urine collections into disposable non-sterile urine cups from one asymptomatic volunteer male. Specimens positive for leukocyte esterase and nitrite were prepared by placing Chek-Stix urinalysis control strips in 12ml deionized water, following the manufacturers instructions. The positive and negative samples were then transferred to numbered Sage collection tubes containing boric acid. 21 samples (12 negative and 9 positive) were tested immediately following	Preliminary studies with the LN+ and LN- samples preserved in boric acid demonstrated no evidence of interference with the LN strips immediately after preparation, or after the 2 hour incubation. The dipstick correctly indicated the presence or absence of nitrite and leukocyte esterase in all cases.	Unknown whether these results can be applied to dipsticks in general.

Bibliographic Information	Study Type & Evidence Level	Study aims	Number of Patients & Characteristics	Intervention	Results	Reviewer Comment
				preparation and tested again after 2 hours. Technicians were blind to the composition of each specimen. Main study: 177 consecutive clinical urine specimens preserved in boric acid were evaluated before routine culturing.		
Lauer BA;Reller LB;Mirrett S; 1979 Jul [161]	Study Type: Observational Evidence Level: 3	To evaluate the boric acid-glycerol-sodium formate preservative in the Becton-Dickinson urine culture kit and to evaluate the use of ordinary paper cups for collection of urine.	1000 urine samples sent to a hospital microbiology laboratory. Children and adults with symptoms suggesting UTI and from pregnant women being screened for asymptomatic bacteriuria.	Upon arrival in the laboratory, specimens were refrigerated immediately. Each specimen was cultured 4 times. 1. An initial reference culture 2. A portion of urine was poured into a clean nonsterile paper cup, aspirated into a urine transport tube and recultured immediately. 3. Original specimen paper cup was refrigerated for 18 to 24 hours. 4. Urine transport tube held at room temperature for 18 to 24 hours.	88 of the initial reference cultures were positive (pure growth of 10^5cfu/ml). 82 (93.2%) of the 88 specimens on reference culture were also positive after refrigeration or holding at room temperature in the transport tube for 24 hours. There was one false positive culture from refrigerated urine but none from the transport tube. Mixing urine in the non-sterile container did not introduce detectable contamination.	
Wheldon DB;Slack M; 1977 Jul [162]	Study Type: Observational Evidence Level: 3	To quantitatively investigate the multiplication of contaminant bacteria in urine and attempt to define the duration of delay during which bacterial culture can be expected to give a reliable indication of the presence or absence of urinary infection.	106 patients. Patients attending a health centre and from members of the hospital staff. Individuals with known diabetes, urinary tract abnormalities and those receiving antimicrobial therapy were excluded.	Cultures were performed within one hour of voiding and successive cultures were carried out at 2, 4, 8, 12 and 24 hours after voiding. Throughout the period of sampling, specimens were kept between 19°C and 23°C	Freshly voided urine 14 of the 41 urine samples from males (34%) and 5 of 65 from females (7.7%) had bacterial populations of less than 10^2cfu/ml. None of the urines from males had bacterial counts in excess of 10^5cfu/ml, while four urines from females (6.2%) had counts exceeding 10^5cfu/ml. Multiplication of bacteria Enterococci, E.coli, S albus an group B streptococci were the organisms which most commonly multiplied in urine to give counts in excess of 10^5cfu/ml within 24 hours of voiding. The lag phase was usually short and frequently undetectable. *Enterobacteria* other than *E.coli* were rarely isolated more than 10^2cfu/ml when sampling was carried out but at later samplings showed growth patterns silimar to *E.coli*. All isolates grew exponentially after approximately 8 hours, and most had a lag time of approximately 4 hours.	
Jefferson H;Dalton HP;Escobar MR;Allison MJ; 1975 Nov [163]	Study Type: Observational Evidence Level: 3	To determine the effect of transport delay on the microflora of clinical specimens collected for microbiological analysis.	Number of patients/samples not reported. On a medical ward of a hospital. No other information reported	Clean catch urine specimens were collected from patients on medical wards. Proportions of these specimens were cultures approximately 10 minutes after collection for aerobic organisms. The remainder of each specimen was kept at room temperature until collected by the transportation service.	The time necessary for transportation of the urine specimens ranged from 2 to 5 hours with an average of 4 hours. The results from 100 urine specimens cultured immediately after collection indicated that 71% had colony counts of less than 102; 14% between 104 and 105; and 15% more than 106. After transportation 71% maintained colony counts of less than 102; 9% between 104 and 105; and 20% more than106.	Not enough information to draw any clear conclusions about urine collection. No original N, no information about blinding, no information about patients
De la Cruz E;Cuadra C;Mora JA; 1971 Jul [164]	Study Type: Observational Evidence Level: 3	To study the effect of time, temperature and glucose content on the growth of two initial populations of either *E.coli* or *P.vulgaris* in sterile urine samples.	No information about patients or samples.	All men entering the bathroom of a laboratory were requested to void urine into a two litre flask. The urine collected was sterilized by Seitz filtration not more than three hours after thee flask was left in the bathroom and divided into portions. One of the samples was used for determination of glucose, albumin and pH. The	Urine containing no glucose: The original number of bacteria both in the urines and the controls showed little or no change over time. Populations of *P.vulgaris* remained unchanged at all three temperatures while *E.coli* showed a slight increase over time. Urine containing glucose:	No other studies investigate glucose so not enough information to draw any firm conclusions. No information about the urine samples or the patients they were

Bibliographic Information	Study Type & Evidence Level	Study aims	Number of Patients & Characteristics	Intervention	Results	Reviewer Comment
				remaining urine was stored at 10°C. To strains of *E.coli* and two of *P.vulgaris* were isolated from patients with urinary tract infections.	All bacterial strains studied showed reductions in the populations after two hours of incubation at -10°C and continued to decline at 4 hours and 8 hours. However, there was a steady increase in bacterial numbers with time in the samples incubated at room temperature (25°C) which showed at least 10^5 organisms within 4 hours. The bacterial populations showed almost no change when the incubation temperature was 4°C regardless of bacterial strain.	collected from. Very old study (1971) so laboratory SOPs may have changed (?)
Nickander KK;Shanholtzer CJ;Peterson LR; 1982 Apr [165]	Study Type: Observational Evidence Level: 3	To determine the minimum amount of urine necessary to obtain accurate results with each system.	240 specimens Patients characteristics not reported	The Sage urine culture tube and the Becton-Dickinson culture tube were evaluated by using 30 cultures diluted in urine to 10^5cfu/ml. Both tubes were injected with 1, 2, 3 and 4-5 ml (tube capacity) of urine containing each culture. Specimens were held at 22°C and cultured at 0, 4 and 24 hours.	The Becton-Dickinson urine culture kits were toxic to *E.coli* and *Klebsiella pneumoniae* in specimens containing up to 2ml of urine. The minimum useable amount of urine for reliable results was 3ml. The Sage urine culture tube maintained the number of bacteria in 1 to 4.5ml of urine in 83% of the specimens. However the Sage tube was toxic to *E.coli* when held for 24 hours. Quantitative counts of *enterococci* tended to significantly increase in specimens that contained 2ml or more of urine in either system.	
Lewis JF;Alexander JJ; 1980 [166]	Study Type: Observational Evidence Level: 3	To provide evidence about the validity of overnight refrigeration for quantitative bacteriological evaluation.	Of 414 urine cultures, there were 109 cultures with colony counts of 104 cfu/ml or higher.	Initial urine cultures (less than 2 hours old), compared with refrigerated urine cultures.	Four cultures change from sterile to significant colony count 105 cfu/ml or greater, all of which were S aureus. A single culture changed from 105 cfu/ml to sterile where the organism involved was E.coli. Nine other cultures exhibited some change in colony count of which a number of organisms were involved in the discrepancies.	
RYAN WL;MILLS RD; 1963 May [167]	Study Type: Observational Evidence Level: 3	To determine if bacterial concentrations generally considered insignificant (less than 10,000/ml) many become significant as a result of bacterial multiplication in the urine during refrigeration.	Unknown number of patients/samples Urine obtained from 'normal' males and females – no other information reported.	Following collection (clean catch) the specimens were refrigerated at 5°C for approximately 24 hours. The urine was then pooled, sterilized by pressure filtration and stored at 5°C in 100ml aliquots in sterile bottles. Two bottles were inoculated for each of the bacteria employed and the bottles were placed at 0.5°C, 5°C, 10°C and 15°C. Every 24 hours for 4 days samples of urine from each bottle were cultured.	At 0.5°C, 5°C and 10°C, *E.coli* remained largely unchanged. At 15°C, *E.coli* grew from 12,000/ml immediately after collection to 16,000/ml at 24 hours, 370,000/ml at 48 hours and reached 800,000/ml by 72 hours. Bacterial counts overall remained the most stable in the 5°C group.	

Urine testing

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Deville WL;Yzermans JC;van Duijn NP;Bezemer PD;van der Windt DA;Bouter LM; 2004 Jun 2 [169]	Meta-analysis Evidence level: II	To summarise the available evidence on the diagnostic accuracy of the urine dipstick test, taking into account various pre-defined potential sources of heterogeneity	220 articles of which 72 met inclusion criteria - 17 studied nitrites only, 2 studies leukocyte esterase only and the remaining studies evaluated combinations of both.	Presented results by patient group (pregnant women, elderly, urology, children etc)	Dipstick tests for nitrites and/or leukocytes compared to culture	Accuracy of nitrites was higher in pregnant women (Diagnostic odds ratio = 165) and in elderly people (DOR = 108). Positive predictive values were ≥80% in elderly and in family medicine. Subgroup analysis of diagnostic accuracy found ten studies of nitrite dipstick tests in children. Sensitivity 0.50 (0.42, 0.60), specificity 0.92 (0.87, 0.98) with a DOR 34 (12, 97). Accuracy of leukocyte esterase was high in studies in urology patients (DOR = 267). Sensitivities were highest in family medicine (86%). Negative predictive values were high in both tests in all patient groups and settings except in family medicine. The combination of both test results showed an increase in sensitivity. Accuracy was high in studies in urology patients (DOR = 52), in children (DOR = 46) and if clinical information was present (DOR = 28). Sensitivity was highest in studies carried out in family medicine (90%). Predictive values of combinations of positive test results were low in other situations. Subgroup analysis of accuracy of nitrite and leukocyte esterase dipsticks in combination found nine studies of nitrite dipstick tests in children. Sensitivity 0.83 (0.78, 0.89), specificity 0.85 (0.79, 0.91) with a DOR 46 (23, 95). Using a pre-test probability (prevalence) of 0.20, based on the pooled sensitivities and specificities of the studies, for nitrites, the PPV in children was 61% and the NPV 88%; for leukocyte esterase the PPV in children was 34% and the NPV 88%; for one or both dipsticks positive, the PPV in children was 58% and the NPV 95%; for both dipsticks positive, the PPV in children was 66% and the NPV 87%.	No information about quality assessment including blinding
Doley A;Nelligan M; 2003 Feb [170]	Retrospective case note review Evidence Level: II	To determine if dipstick urinalysis in the paediatric population is an adequate screening tool to exclude UTI..	Records of 6618 paediatric presentations over an 8 month period. 375 patients analysed	Retrospective case-note review of children presenting to a paediatric department. Urine collection was either by bag or clean-catch except in four cases of SPA. Specifically looking at two age groups: 0-2 years and 2-10 years. Positive urine culture was defined as greater than 10^5cfu/ml of an isolated	Bayer Clinitek 50 urinalysis machine using Bayer multistix 10 SG reagent strips compared to culture	The sensitivity of the dipstick in all cases was 92.5% (95%CI 84.3 - 100%), specificity 39.4% (95%CI 34.2 - 44.6%), positive predictive value 15.4% (95%CI 10.8 - 20%) and negative predictive value 97.8% (95%CI 95.3 - 100%). The sensitivity of the dipstick in children aged 0-2 years was 87.5% (95%CI 74.3 - 100%), specificity 39.7% (95%CI 31.5 – 47.9%), positive predictive value 20.4% (95%CI 12.6 – 28.2%) and negative predictive value 94.7% (95%CI 88.9 - 100%). The sensitivity of the dipstick in children aged 2-10 years was 100% (95%CI 100 - 100%), specificity 39.2%	Used in a sample of patients relevant to our population and used valid reference standard. Use of medical records and other retrospective data introduces potential bias. Specificity data low compared with other

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				organism.		(95%CI 32.4 – 46%), positive predictive value 11.0% (95%CI 5.8 – 16.3%) and negative predictive value 100% (95%CI 100 - 100%).	studies. No information about blinding.
Pugia MJ;Sommer RG;Kuo HH;Corey PF;Gopual DL;Lott JA; 2004 Mar [171]	Study Type: Diagnostic Evidence Level: II	To assess the clinical utility of new, pathogen-specific tests to be applied with widely used dipsticks..	1743 patients. 1132 females, 611 males.	Patients with suspected UTI. No information about age of patients.		Combination of leukocyte and nitrite dipsticks gave negative predictive values of 93% for culture-negative samples. Using the same dipsticks on culture positive samples, the positive predictive values were unacceptably low. The false negative rate for leukocyte esterase or nitrite dipstick tests was 5% (80/1743), false positive rate 17% (304), True positive rate 15%(262) and true negative rate 63% (1097). The positive predictive value was 46% and the negative predictive value 93%. The false negative rate for the Immuno-chromatography strip was 10% (168/1743), false positive rate 2% (42), True positive rate 10% (174) and true negative rate 78% (1359). The positive predictive value was 81% and the negative predictive value 89%. The false negative rate for combination leukocyte esterase, nitrite dipstick and immuno-chromatography tests was 11% (190/1743), false positive rate 1% (19), True positive rate 9% (152) and true negative rate 79% (1382). The positive predictive value was 89% and the negative predictive value 88%.	No information about blinding May not be in a suitable group of patients.
Hiraoka M;Hida Y;Mori Y;Tsukahara H;Ohshima Y;Yoshida H;Mayumi M; 2005 [172]	Laboratory study method.. Evidence Level: II	Compared the accuracy in diagnosing significant bacteriruia between quantitative unspun-urine microscopy and the gram-stain	325 urine samples obtained at random from 130 patients	67 males and 63 females aged 3 months to 94 years (mean 37.7 years). 301 mid-stream samples and 24 catheterised samples. 43 samples collected at outpatients and 282 from inpatients. 109 samples from patients being treated with antibiotics 216 from patients without antibiotic treatment.	Gram stain and quantitative unspun urine microscopy compared to culture.	Significant bacteriuria was detected by urine culture in 37 out of 325 urine samples. Unspun-urine microscopy samples in cell-counting chambers were negative in 248 samples, positive in 33 and ambiguous in 44. Ambiguous samples were subjected to oil-immersion microscopy which made it possible to identify rods, cocci, salts or other particles. Overall, unspun-urine microscopy was able to detect bacteriuria in 35 of 37 urine samples with culture-proven significant bacteriuria (sensitivity 94.6%), failing to identify bacilli in two urine samples. Unspun-urine microscopy identified 286 of 288 urine samples with negative culture results (specificity 99.3%) Gram-stain method was able to detect bacteriuria in 33 of 37 urine samples with culture-proven significant bacteriuria (sensitivity 89.2%). Gram-stain method identified 284 of 288 urine samples with negative culture results (specificity 98.6%) Both methods, the unspun microscopy and the Gram stain were similarly reliable when compared with culture.	No blind comparison Two thirds of the patients were being treated with antibiotics.
Ciancaglini E;Fazii P;Sforza GR;	Evidence Level: III	Compared the accuracy of the differential fluorescent	1487 urine samples were	Hospitalised patients and outpatients. Urine collected	Study describes a differential fluorescent staining method which distinguishes Gram	A total of 1487 urine samples were tested. 289 were found to have colony counts greater than 104 cfu/ml;	Blinding, age of patients, reason for

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2004 [173]		staining method and the Gram stain method in screening for bacteriuria compared to conventional culture	tested	using a sterile technique.	positive from Gram negative bacteria in fluorescence compared with conventional culture (greater than or equal to 10^4cfu/ml)	237 yielded a single organism and 52 a mix of two or more organisms. Of the 237 yielding a single organism 224 were detected by the differential fluorescent staining method and 162 by the Gram stain (13 undetected by the differential fluorescent staining method and 75 undetected by the Gram stain). The sensitivity of the differential fluorescent staining method was 94.5% while the sensitivity of the Gram stain was 68.3%. The specificity of the differential fluorescent staining method was 91.6% and the Gram stain 75.8%. The PPV and the NPV of the differential fluorescent staining method were 67.6% and 98.8% respectively and those of the Gram stain 35.9% and 92.3%.	hospitalisation or outpatient visit are all unknown. 'Sterile technique' is not enough information about the urine collection method. Blinding reported between gram-stain and fluorescent preparation, but unknown whether blinding against the reference standard
Winkens R;Nelissen-Arets H;Stobberingh E; 2003 [174]	Evidence Level: II	Assess validity of urine dipslides as performed under daily practice conditions and assessed the influence of the incubation period (24 v 48 hours) on validity	232 patients with 268 episodes of UTI. 83% female, 17% male. Study on the validity of the dipslide performed and judged in general practice under 'non-optimal' conditions.	Patients aged 12 years or older presenting to general practice with a median age of 54 years (range 9-93 years). Five General Practices (16 GPs) all within the same region.	Nitrite test, dipslide and culture were performed. Dipslides with at least 10^5 cfu/ml were considered to reflect a UTI.	The nitrite tests was the initial test in all practices. Of the 268 urine samples a sensitivity of 42% (95%CI 34 to 49%) and a specificity of 95% (95%CI 89 to 98%). The PPV was 93% (95%CI 85 to 98%) and the NPV 50% (95%CI 42 to 57%). The sensitivity of the dipslide in general practice after 24 hours incubation was 73% (95%CI 66 to 80%) and specificity was 94% (95%CI 88 to 98%). The PPV was 95% (95%CI 90 to 98%) and the NPV 68% (95%CI 60 to 76%). As the dipslide is only recommended in the case of a negative nitrite test, when performed after a negative nitrite test the PPV was 92% (95%CI 84 to 98%) and the NPV 73% (95%CI 64 to 81%). Overall the dipslide read under practice conditions performed lower than under optimal conditions.	Blinding unknown.
Scarparo C;Piccoli P;Ricordi P;Scagnelli M; 2002 Jun [175]	Laboratory study Evidence Level: III	To evaluate the UTI diagnostic performance of the DipStreak device with two different chromogenic medium configurations and to compare the performance to that of the reference streak method (calibrated loop).	2000 routine urine samples. 1707 Clean-catch and 262 from indwelling catheter.	876 samples collected from outpatients department and 1124 collected from patients in different departments of the hospital: 161 from Nephrology and kidney transplant unit, 137 from haematology, 101 from geriatrics, 97 from paediatrics, 92 from metabolic diseases, 90 from obstetrics and gynaegology, 89 from intensive care, 82 from urology, 80 from internal medicine, 62 from surgery and 133 from other departments.	Dipstreak device with two different medium formulations - CHROMagar and MacConkey media in one and UriSelect 3 and MacConkey in the other.	In the study comparing Dipstreak (CHROMagar and MacConkey media), Dipstreak (Uriselect 3 and MacConkey media), Uriselect 3 plates and calibrated loop culture, 2000 urine samples were processed and 511 cultures were found to be positive. The CHR dipstreak device, the Uriselect 3 and calibrated loop cultures gave the same detection rate (99.7%). For the direct identification of *E.coli*, *Proteus* and *Enterococcus* isolates, the DipStreak device and Uriselect showed overall sensitivities of 97% and 93.4%. In the second study comparing Dipstreak (Uriselect 3 and MacConkey media), Uriselect 3 plates and calibrated loop culture, 3000 urine samples were processed and 714 cultures were found to be positive. The DipStreak device, the Uriselect 3 and calibrated loop cultures gave detection rates of 99.4%, 99.9% and 99.2% respectively. For the direct identification of *E.coli*, *Proteus* and *Enterococcus* isolates, the	Unspecified patient population No information about blinding. Indwelling catheter, urology and intensive care patients are excluded from the scope. Patients are likely not to be representative of the paediatric population having first line urine tests for suspected UTI.

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						DipStreak device and Uriselect plates showed overall sensitivities of 88.7% and 94.4% respectively	
Huicho L;Campos-Sanchez M;Alamo C; 2002 [176]	Systematic review Evidence level: III	Four aims 1. Summarise the literature on urine screening tests 2. Recall the validity and applicability of the included studies. 3. Perform meta-analysis 4. Identify the test or combination of tests that best predicts the presence or absence of UTI in children..	48 articles evaluated	Children aged 0 to 18 years. Article inclusion criteria: 1. Addressing the usefulness of urinary screening tests in the diagnosis of UTI in children 0-18 years. 2. Original articles. Review papers and letters were excluded. 3. Studies in humans 4. Articles with enough information provided to judge their methodologic quality. 5. Articles with index tests and reference standard (culture) systematically performed in all patients with specification of the sampling technique. 6. Articles with prevalence, sensitivity, specificity, predictive values explicitly stated, or with data presented in such a way that calculation is feasible. 7. Studies that were performed at a hospital or outpatient clinic with medical supervision. Studies performed at home were excluded.	Various urine screening tests compared to culture. Leukocyturia (or pyuria) in uncentrifuged urine. Bacteria and/or leukocytes in uncentrifuged, stained, or unstained urine. Dipstick tests (LE and Nitrite, alone or in combination)	Rapid dipstick tests could not be definitively assessed because of the small number of studies assessing their effectiveness. Bivariate SROC curves showed that pyuria ≥10/hpf and bacteriuria ≥10/hpf had the best diagnostic performance. In multivariate analysis, both remained significant	Quality of primary studies was variable. They grouped together tests which had different cut-off points. Not a particularly helpful study - does not report range of sensitivities/specificitie s for different tests.
Wiwanitkit V;Udomsantisuk N;Boonchalermvich ian C; 2005 [177]	Diagnostic Laboratory study Evidence Level: Ib	Evaluate the diagnostic properties of urine Gram stain and urine microscopic examination for screening UTI and to perform additional cost-utility analysis..	95 urine samples	Samples from suspected UTI cases sent to a University microbiology department. Gram stain was considered positive if presence of ≥1 bacteria/field (x1000). Microscopy was considered positive if the presence of bacteria and pyuria >5 white blood cells or white blood cell clumps/field objective (x400). Urine culture was considered positive if 10^5cfu/ml were present	Gram stain Microscopy compared to culture.	The prevalence of UTI from culture was 54.7% (52 cases). The sensitivity of the Gram stain was 96.2%, specificity 93.0%, positive predictive value 94.3% and negative predictive value 95.2%. False positive was 7.0% and false negative was 3.8%. The sensitivity of the microscopic examination was 65.4%, specificity 74.4%, positive predictive value 75.6% and negative predictive value 64.0%. False positive was 25.6% and false negative was 34.6%. Combining the Gram stain and the microscopic examination, the sensitivity of the was 98.1%, specificity 74.4%, positive predictive value 82.3% and negative predictive value 97.0%. False positive was 25.6% and false negative was 1.9%.	Good information about blinding. Total number of subjects was small. No information about patients (age, gender etc).

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Novak R;Powell K;Christopher N; 2004 May [178]	Evidence Level: II	To determine which urine testing method best identifies UTI in children presenting to a paediatric emergency department.	142 children, 48 boys and 94 girls.	Febrile children under 5 years old who had urine samples collected by catheterisation in an Emergency department. Half of the children were ≤12 months. Samples were transported by pneumatic tube and were analysed within 60 minutes. A positive urine culture was defined as $>10^3$ colonies of a single organism.	Culture Dipstick Sediment examination Unspun leukocyte counts Cyto-centrifuge gram stain	25 cases (17.6%) of UTI were diagnosed by culture, 48% were ≤12 months and 16% were male. Positive leukocyte esterase dipstick had an overall sensitivity of 48% and a negative predictive value of 90%. In children ≤12 months, sensitivity was 42% while in children over 12 months, sensitivity was 53%. Positive nitrite dipstick had an overall sensitivity of 20% and a negative predictive value of 85%. In children ≤12 months, sensitivity was 17% while in children over 12 months, sensitivity was 23%. Positive blood dipstick had an overall sensitivity of 44% and a negative predictive value of 88%. In children ≤12 months, sensitivity was 33% while in children over 12 months, sensitivity was 53%. Positive unspun leukocyte count >10/μl had an overall sensitivity of 68% and a negative predictive value of 92%. In children ≤12 months, sensitivity was 67% while in children over 12 months, sensitivity was 69%. Positive cyto-centrifuge Gram stain had an overall sensitivity of 60% and a negative predictive value of 92%. There was a statistically significant differences between children ≤12 months (sensitivity 42%) and children over 12 months (sensitivity 76%) ($p<0.05$). 2 to 5 or more leukocytes/hpf in sediment had an overall sensitivity of 48% and a negative predictive value of 90%. In children ≤12 months, sensitivity was 42% while in children over 12 months, sensitivity was 53%.	No information about blinding.
Al-Daghistani HI;bdel-Dayem M; 2002 Oct [179]	Evidence Level: III	To compare the performance of leukocyte esterase and nitrite dipstick with the assessment of pyuria by HPF microscopic examination and culture of urine samples in patients with symptoms of UTI.	504 patients, 271 female and 233 male	Patients presenting to a medical centre with symptoms and signs of a UTI. Urine was collected by mid-stream clean-catch.	Dipstick (nitrite and leukocyte esterase) compared to microscopy and culture.	The sensitivity of the leukocyte esterase dipstick was 68.4%, specificity 73.4%, positive predictive value 43.7% and negative predictive value 88.5%. The sensitivity of the nitrite dipstick was 58.9%, specificity 77.8%, positive predictive value 60% and negative predictive value 86.2%. The sensitivity of the microscopic pyuria count was 34%, specificity 86.5%, positive predictive value 43.5% and negative predictive value 81.3%. There was a significant correlation between dipstick results, microscopic examination and urine culture ($p=0.0001$).	No indication of blinding, no indication of age of patients, or exclusion criteria applied.
Arslan S;Caksen H;Rastgeldi L;Uner A;Oner AF;Odabas D; 2002 Mar [180]	Evidence Level: III	To determine the validity of the urinary Gram stain compared with a combination of pyuria plus Gram stain and overall	100 children	Children aged 2 days to 15 years (majority under 5 years) admitted to a Paediatric department between Jan and June 1999 with symptoms	Four tests within the urinalysis (leukocyte esterase, nitrite, microscopy for bacteria, and microscopy for pyuria), urinary Gram stain and urine culture. Complete blood count, peripheral blood smear and ESR	Of the 100 children, 70% had a positive urine culture. The sensitivity of the Gram stain was 80%, specificity 83%, positive predictive value 91% and negative predictive value 64%. The sensitivity of the combination of Gram stain and	No information about blinding Did use a reference standard, but unclear description (used

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		urinalysis..		suggesting UTI. Inclusion criteria; for infants, fever with no apparent source, vomiting, decreased appetite and irritability; for children, abdominal pain and voiding frequency with or without fever; and for older children, dysuria, frequency, urgency and abdominal/flank pain with or without fever. Children receiving antibiotic therapy were excluded. In infants a bag specimen was used, and in toilet-trained children a mid-stream urine sample was used. Cultures were considered positive if the culture showed greater than 100,000 colonies of a single pathogen. Pyuria was considered present if more than 5 WBCs were noted on unstained microscopy and bacteriuria if at least a 'slight' reading was noted at 40x/hpf.	were also analysed.	pyuria was 42%, specificity 90%, positive predictive value 90% and negative predictive value 40%. The sensitivity of the overall urinalysis was 74%, specificity 3.5%, positive predictive value 64% and negative predictive value 5%.	'overall urinalysis' which included culture).
Manoni F;Valverde S;Antico F;Salvadego MM;Giacomini A;Gessoni G; 2002 Oct [181]	Diagnostic Evidence Level: II	Evaluation of the analytical performance of the Sysmex UF-100 cytometer compared to the diagnosis of UTI.	2010 patients	Patients aged between 18 and 78 years (mean 56.4 years) with urine sample submitted to a lab. 1130 (496 males and 634 females) were outpatients and 880 (374 males and 506 females) were inpatients. The majority (90%) of samples were voided urine specimens.	Chemical and physical examination of urine specimen. Dipstick analysis included reagent pads for semi-quantitative assessment of relative density, pH, leukocyte esterase, nitrite, protein, glucose, keytones, urobilinogen, bilirubin and haemoglobin. Microscopic examination Each specimen was centrifuged at 400g for 10 mins. In each specimen at least 20 random microscopic fields were examined at x400 HPF. Culture Samples were inoculated on agar plates by using 0.001ml calibrated loops within 4 hours. After 24 hours cultures were qualified in CLED plates. UF-100 The Sysmex UF-100 is a second-generation automated urine analyser that performs analysis of the formed elements in urine by flow cytometry.	Of the 2010 patients considered, 529 (26.3%) had a UTI. Of the dipstick screening tests (Nitrite and leukocyte esterase dipstick tests) 171 (8.5%) false negatives were observed and 184 (9.2%) false positives. Sensitivity was 0.64 and specificity of 0.88 while PPV was 0.63 and NPV was 0.89. Of the culture tests (bacterial growth on CLED agar) 56 (2.8%) false negatives were observed and 35 (1.7%) false positives sensitivity was 0.89 and specificity of 0.98 while PPV was 0.93 and NPV was 0.89. Of the UF-100 tests 29 (1.4%) false negatives were observed and 102 (5.1%) false positives. Sensitivity was 0.94 and specificity of 0.93 while PPV was 0.83 and NPV was 0.98. The sysmex UF-100 performed more accurately than both the dipstick testing and culture.	No information about blinding to the reference standard

Bibliographic Information	Study type & Evidence level	Study Aims	Number of patients & prevalence	Population Characteristics	Type of test and Reference standard	Sensitivity, Specificity, PPV and NPV	Reviewer comment
Reilly P;Mills L;Bessmer D;Jimenez C;Simpson P;Burton M; 2002 [182]	Diagnostic Evidence Level: III	: To determine if the biochemical results of the urine dipstick could be used to eliminate unnecessary urine cultures	Part One: 843 urine samples Part Two: 6192 urine samples	Urine samples sent to a laboratory for culture. Part one: involved a 3 month retrospective review on urine samples that had both dipstick and culture ordered. Part two: implementation of a policy to screen urine samples having both urinalysis and culture ordered to determine the number of unnecessary urine cultures sent to the lab.	Dipstick compared to culture.	Of the 6192 urine samples processed, 64% (3932) had cultures performed. These were samples which showed positive dipstick and were ordered on physician request, or were not cancelled. 36% (2260) had a negative dipstick and were cancelled. The rate of cancellation appeared consistent at approximately one third when tracked month by month. Of the 3932 samples cultured 22.4% (883) were true positives (positive dipstick and positive culture), while 31.8% (1248) had a positive dipstick but grew organisms that were considered contaminants. False positive results were observed in 1558 (39.6%). Of the samples that showed negative dipstick and were cultured 11 (0.3%) grew a clinically significant pathogen. The study concluded that the biochemical parameters on urine dipsticks can be used as a screen to determine whether or not a urine culture should be performed and implementation of this policy has resulted in the elimination of up to one third of the urine cultures performed in one laboratory	Unsure of the biases in this study -
Bachur R;Harper MB; 2001 [183]	Retrospective medical record review Evidence Level: III	To determine how the sensitivity of the standard urinalysis as a screening test for UTI varies with age and to determine the clinical situation that necessitates the collection of urine culture regardless of the urinalysis result..	37450 children (44% girls) 11089 patients with urine cultures obtained	Children younger than 2 years with fever (≥38°C) seen in an emergency department during a period of 65 months. Cultures were considered positive if $\geq 10^3$ cfu/cl for supra-pubic aspiration, $\geq 10^4$ fo catheterised specimens and $\geq 10^5$ for clean voided specimens. Contaminated specimens were excluded.	All cultures were reviewed for the collection method, isolates and colony units. A urinalysis was considered positive if the presence of one of the following was detected: leukocyte esterase, nitrite, or pyuria.	One study investigated the sensitivity of the standard urinalysis as a screening test for UTI to determine how it varies with age and to determine the clinical situation that necessitates the collection of urine culture regardless of the urinalysis result. The study found that sensitivity of urinalysis was 82% (95%CI 79-84%) and did not vary with age. The specificity of urinalysis was 92% (95%CI 91-92%). The positive likelihood ratios was 10.6 (95%CI 10.0 to 11.2) and the negative likelihood ratio was 0.19 (95%CI 0.18 to 0.20).	Large sample size, although retrospective design does not allow interpretation of why not all patients tested with the reference standard (culture). Blinding not described.

Localisation of UTI by laboratory tests

Bibliographic Information	Study type & Evidence level	Study Aims	Number of patients & prevalence	Population Characteristics	Type of test and Reference standard	Sensitivity, Specificity, PPV and NPV	Reviewer comment
Pecile P;Miorin E;Romanello C;Falleti E;Valent F;Giacomuzzi F;Tenore A; 2004 Aug [185]	Study type: Diagnostic Evidence level: II	To determine the accuracy of procalcitonin measurements in diagnosing acute renal involvement during febrile UTI and in predicting subsequent scars as assessed with DMSA.	100 consecutive children (69 girls and 31 boys) admitted to a peaediatric department between Jan 2000 and Jan 2002 with first episode of febrile UTI	Children 1 months to 13 years (mean 19 months). 66 children were under 1 year. Definition of UTI was positive culture with a single microorganism at ≥10^5cfu/ml from a catheterised or clean voided sample. Patients with previously documented or suspected febrile UTIs were excluded	CRP levels, procalcitonin levels, ESR and leukocyte counts compared to DMSA	Clinical and Laboratory assessments - body temperature - duration of fever - WBC count - CRP level (values of ≥20mg/l were considered abnormal) - ESR - procalcitonin level (values of ≥0.8ng/ml were considered abnormal) Imaging studies - Ultrasound (performed within 3 days) - VCUG (1 month after first infection to detect reflux) - DMSA (5 days after admission). Score of 0 = absence of lesion, 1=uncertain or mild lesion, 2=mild lesion, 3=moderate lesion, 4=severe renal parenchymal lesion (covering >30% of surface area).	Study only showed diagnostic accuracy for the group of patients who scored 2-4 indicating acute pyelonephritis – more significant initial renal damage. The diagnostic accuracy for the group with mild renal damage is unknown. Additionally, only children who scored 2-4 were followed up.
Lin DS;Huang SH;Lin CC;Tung YC;Huang TT;Chiu NC;Koa HA;Hung HY;Hsu CH;Hsieh WS;Yang DI;Huang FY; 2000 Feb [186]	Study type: Diagnostic Evidence level: III	To assess the usefulness of laboratory parameters including peripheral WBC count, CRP, ESR and microscopic urinalysis for identifying febrile infants younger than 8 weeks of age at risk of UTI.	162 febrile children (94 boys, 68 girls)	Febrile infants (rectal temperature >38°C) under 8 weeks old who presented to an emergency department between September 1997 and August 1998 and were hospitalised. Exclusions: Infants who received antibiotics or had a SPA within 24 hours.	History and physical examination and a full evaluation for sepsis including peripheral WBC count, and differential ESR, CRP, blood culture, lumbar puncture, glucose level, protein level, Gram stain, urinalysis and culture. All urine samples were collected by SPA.	All infants had negative blood and CSF cultures. 22/162 (13.6%) had positive urine cultures (4 girls, 18 boys). Hemocytometer WBC counts (≥10 WBC/µl) Sensitivity: 82% Specificity: 94% Accuracy: 92% LR+: 12.7 LR-: 0.19 Standard UA (≥5 WBC/hpf) Sensitivity: 59% Specificity: 93% Accuracy: 88% LR+: 8.3 LR-: 0.44 CRP (>20 mg/L) Sensitivity: 59% Specificity: 90% Accuracy: 86% LR+: 5.9 LR-: 0.45	

Bibliographic Information	Study type & Evidence level	Study Aims	Number of patients & prevalence	Population Characteristics	Type of test and Reference standard	Sensitivity, Specificity, PPV and NPV	Reviewer comment
						ESR (>30 mm/h) Sensitivity: 73% Specificity: 78% Accuracy: 77% LR+: 3.3 LR-: 0.35 Peripheral WBC (>15000/µl) Sensitivity: 36% Specificity: 80% Accuracy: 74% LR+: 1.8 LR-: 0.80	
Benador N;Siegrist CA;Gendrel D;Greder C;Benador D;Assicot M;Bohuon C;Girardin E; 1998 Dec [187]	Study type: Diagnostic Evidence level: III	To measure PCT levels in children with febrile UTI, to compare it to other inflammatory markers and to evaluate it's ability to predict renal involvement as assessed by DMSA.	60 children (17 boys, 43 girls)	Children 1 month to 16 years old (mean age lower UTI 36 months, mean age pyelonephritis 42 months) diagnosed with clinical signs of acute pyelonephritis. Acute pyelonephritis defined as rectal temperature ≥38°C and abdominal pain in older children, or non-specific signs in younger children such as irritability or vomiting. Confirmation by positive urine culture where ≥104cfu/ml for midstream clean voided urine, ≥103 for SPA or catheterisation.	Test: Blood samples were collected on admission for determination of PCT, CRP and leukocyte counts Tests were considered abnormal at: PCT >0.6µg/L CRP >10mg/L DMSA was performed within 5 days of admission. Lesions were graded in 5 categories: 0 – absence of lesion (lower UTI) 1 – very mild (defect covering<5% surface area) 2 – mile (defect covering 5% - 10% surface area) 3 – moderate (defect covering 10% - 30% surface area) 4 – severe renal parenchymal lesions (defect covering >30% surface area)	Age (months) – 36 ± 9 vs. 42 ± 8, p=0.350 Sex (female/male) – 14/9 vs. 29/8, p=0.140 Leukocyte count (mm3)– 10939 ± 834 vs. 17429 ± 994, p=0.0001 PCT (µg/L) – 0.38 ± 0.19 vs. 5.37 ± 1.9, p<0.0001 CRP (mg/L) – 30.3 ± 7.6 vs. 120.8 ± 8.9, p<0.0001 When inflammatory markers were correlated with severity of renal lesions ranked by DMSA, PCT was significantly correlated (p<0.0001) however CRP was of borderline significance (p=0.032). CRP Sensitivity: 100% Specificity 26.1% PCT Sensitivity: 70.3% Specificity: 82.6%	
Gurgoze MK;Akarsu S;Yilmaz E;Godekmerdan A;Akca Z;Ciftci I;Aygun AD; 2005 [188]	Study type: Diagnostic Evidence level: III-	Compared serum levels of proinflammatory cytokines and procalcitonin in children with acute pyelonephritis and with lower tract UTI to establish whether they could be used as a marker in distinguishing acute pyelonephritis.	76 children (48 girls, 28 boys)	Children aged 2 to 144 months (mean age 39.6 ± 33.8 months). All children had been diagnosed with UTI by clinical findings (fever, nausea/vomiting, appetite, dysuria, nonspecific abdominal pain) and laboratory analysis (10^5cfu/ml midstream sample or 10^3cfu/ml in a catheterised sample).	Test: Blood sample (before initiating antibiotic treatment) DMSA Reference test:	34 children (20 girls and 14 boys) had acute pyelonephtritis (mean age 43.4 months) and 42 children (28 girls and 14 boys) had lower UTI (mean age 34.6 months). PCT (at 0.5ng/ml) Sensitivity 58% Specificity 76% CRP (at 20mg/l Sensitivity 94% Specificity 58% IL-ß1 (at 6.9pg/ml)	Study did not provide numbers so no sensitivities/specificitie s could be checked. Evidence level - so should be excluded if other quality studies are found.

Bibliographic Information	Study type & Evidence level	Study Aims	Number of patients & prevalence	Population Characteristics	Type of test and Reference standard	Sensitivity, Specificity, PPV and NPV	Reviewer comment
						Sensitivity 97% Specificity 59% IL-6 (at 18pg/ml) Sensitivity 88% Specificity 74% TNF-a (at 2.2pg/ml) Sensitivity 88% Specificity 80%	
Smolkin V;Koren A;Raz R;Colodner R;Sakran W;Halevy R; 2002 [189]	Study type: Diagnostic Evidence level: III-	To evaluate the ability of PCT level to predict renal involvement assessed by DMSA.	64 children (44 girls and 20 boys)	Children aged 2 weeks to 3 years (mean 16.7 ± 8.6 months) admitted to a paediatric department with febrile UTI. Inclusion was confirmed by a positive urine culture. Positive urine culture was defined as any growth on SPA and 10^3cfu/ml on catheterisation.	Test: Reference test: CRP and PCT (on admission) compared to DMSA (performed within 7 days of admission) PCT where a value of >0.5ug/l was considered abnormal CRP where a value of >20mg/l was considered abnormal. DMSA where renal pathology was defined as focal or multifocal perfusion defects or as split renal uptake of less than 45%.	CRP at a cut off value of 20mg/l Sensitivity 100% Specificity 18.5% PPV100% NPV 30.9% PCT at a cut off value of 0.5ug/l Sensitivity 94.1% Specificity 89.7% PPV 97.6% NPV 85.7% The median PCT level was significantly higher in the acute pyelonephritis group (3.41, range 0.36 to 12.4) than the lower UTI group (0.13 range 0.02 to 2.15) p<0.0001.	Study did not provide numbers so no sensitivities/specificities could be checked. Evidence level - so should be excluded if other quality studies are found.

Localisation of infection by imaging tests

Bibliographic Information	Study type & Evidence level	Study Aims	Number of patients & prevalence	Population Characteristics	Type of test and Reference standard	Outcome measures	Sensitivity, Specificity, PPV and NPV	Reviewer comment
Wang Y;Chiu N;Chen M;Huang J;Chou H;Chiou Y; 2005 [191]	Diagnostic study Evidence level III	To compare the renal parenchymal changes seen on US with DMSA in children with acute pyelonephritis and to explore the possibility of detecting the inflammation of APN with US and correlating it with the risk of scarring.	45 children (31 boys and 14 girls)	Children aged 9 days to 10 years old (mean 1.5 ± 0.2 years, median 0.3 years) with febrile UTI who fulfilled criteria for acute pyelonephritis and underwent initial DMSA.	Detecting scarring: Ultrasound and laboratory tests (at the time of hospitalisation) compared to DMSA (performed within one week of hospitalisation)	US assessed as abnormal if one of the following features was observed: parenchymal hyperechogenicity, focal lesion with hyperechogenicity or hypoechogenecity, thickening of the renal pelvis wall, or significant enlargement of the kidney length or width compared to the opposite kidney and compared to the normal range for patient age. Acute DMSA: Acute inflammation was indicated if at least one area of decreased focal or diffuse cortical uptake of DMSA was noted with the renal outline preserved. Follow-up DMSA A small whole renal volume and/or deformation of the renal outlines was considered evidence of previous parenchymal injury. If one or more areas of focal renal cortical defects were consistently associated with defects in the renal outline, a renal scar was diagnosed.	US for detecting APN Sensitivity 49% Specificity 88% PPV 91% NPV 40% (p<0.005, OR 7.1, 95%CI 2.18 to 24.41) CRP >70mg/L for detecting APN Sensitivity 59% Specificity 61% PPV 59% NPV 61% (p=0.13, OR 2.2, 95%CI 0.78 to 6.18) US and CRP combined for detecting APN Sensitivity 36% Specificity 95% PPV 95% NPV 36% (p<0.005, OR 11.9, 95%CI 2.15 to 65.72) US for predicting scarring Sensitivity 59% Specificity 61% PPV 59% NPV 61% (p=0.11, OR 2.3, 95% CI 0.82 to 7.65) CRP >70mg/L for predicting scarring Sensitivity 81% Specificity 74% PPV 78% NPV 77% (p<0.0001, OR 11.9, 95%CI 3.72 to 38.11) US and CRP combined for predicting scarring Sensitivity 52% Specificity 81% PPV 76% NPV 59%	The effects of bias in this study are unknown. Loss to follow up is not explained - for the CRP and low/high risk groups, n=80 where in the US group n=90. Similarly for the follow up DMSA to predict scarring 65 abnormal kidneys were analysed for US while n=58 for CRP and low/high risk groups. This represents more than 10% loss to follow up. The author has been contacted to clarify this. Only children with abnormal initial DMSA were followed-up. This is potentially misleading in terms of scar formation as there is no comparison group and no potential for the false negatives in the initial group to be recognised. This could over-estimate the effectiveness of the test..

Bibliographic Information	Study type & Evidence level	Study Aims	Number of patients & prevalence	Population Characteristics	Type of test and Reference standard	Outcome measures	Sensitivity, Specificity, PPV and NPV	Reviewer comment
							(p<0.01, OR 4.7, 95%CI 1.47 to 14.95)	
Ilyas M;Mastin ST;Richard GA; 2002 [192]	Diagnostic study Evidence level III	First, to correlate the clinical and laboratory manifestations of acute pyelonephritis with the results of DMSA in different age groups. Secondly to compare DMSA renal ultrasonography and VCUG, using DMSA as the gold standard.	222 children (47 boys, 175 girls)	Children aged 2 to 228 months (median age 55 months) Group I – 85 children under 2 years old Group II – 91 children 2 to 8 years old Group III – 46 children over 8 years old Acute pyelonephritis defined as fever (≥38ºC), pyuria (positive leukocyte esterase or ≥10wbc/hpf) and positive urine culture (>105cfu/ml) Exclusions: Renal transplant, Obstructive uropathy, neurogenic bladder, renal calculi, recurrent chronic pyelonephritis.	Renal ultrasound compared to DMSA as gold standard		Group I 41/85 (48%) abnormal DMSA 44/85 (44%) normal DMSA Group II 63/91 (69%) abnormal DMSA 28/91 (31%) normal DMSA Group III 39/46 (85%) abnormal DMSA 7/46 (15%) normal DMSA True positive = 9 False negative = 89 False positive = 0 True negative = 57 Sensitivity: 9% Specificity: 100% PPV: 100% NPV: 39%	Of 163 children, 155 are accounted for in the graph and in the text. Number of false positives not reported in text, however reported in graph as 0. Unsure whether false positive rate is 0 as in graph, or 8 according to text. NCC calculated results, according to numbers in graph.
Halevy R;Smolkin V;Bykov S;Chervinsky L;Sakran W;Koren A; 2004 [193]	Diagnostic study Evidence level II	To evaluate the ability of power Doppler US (a method of colour Doppler sonography) to detect acute pyelonephritis in infants and young children in comparison with DMSA as a reference standard.	62 children (46 girls and 16 boys)	Children aged 2 weeks to 5 years (mean age 21.7 ± 16.6 months) admitted to a paediatric department with febrile UTI (>38°C) Diagnosis of UTI was any growth on SPA and 10^3 on catheter samples.	On admission blood was sampled for leukocytes, ESR and CRP (before antibiotic therapy). Each child was examined with DMSA and PDU (on the same day) within 3 days of admission.	Abnormalities on DMSA Abnormalities on PDU CRP level ESR Leukocyte WBCs	Group 0-1 (none or mild damage) vs. Group 2-4 acute pyelonephritis, p value. Age in months (22.4 ± 17.2 vs. 20.6 ± 15.3, p=0.66) Gender, female/male (19/7 vs. 23/8, p=0.47 CRP level (48.1 ± 39.2mg/L vs 114.9 ± 48.1mg/L, p<0.001) ESR (32 ± 22mm/hour vs 43 ± 16mm/hour, p=0.46) Leukocyte count, cells/mm^3 (16741 ± 5302 vs. 18492 ± 6839, p=0.1512) White blood cells, x10^9/l (14.36 ± 2.9 vs. 16.71 ± 4.1, p=0.06) For detecting acute pyelonephritis, PDU showed: Sensitivity 87% Specificity 92% PPV 93% NPV 86%	No information about blinding. Sampling time period not mentioned.
Bykov S;Chervinsky L;Smolkin V;Halevi R;Garty I; 2003 [194]	Diagnostic study Evidence level Ib	To assess the role of renal power Doppler ultrasonography (PDU) to identify acute pyelonephritis and to determine whether PDU can replace DMSA in the diagnosis of	40 infants (5 boys and 35 girls)	Children/infants aged 1 to 68 months (mean age 25.9 months) hospitalised with a first episode of high fever and bacteriuria and suspected acute pyelonephritis. Children with abnormalities, hydronephrosis and reflux were excluded	All children were examined with PDU and DMSA within the first 3 days after admission. Investigators were blind to the DMSA outcome	No with abnormalities on PDU No with abnormalities on DMSA	PDU was unobtainable in 2 patients, leaving 78 kidneys available for comparison. PDU compared to DMSA for identifying pyelonephritis. Sensitivity 74% Specificity 94% PPV 87% NPV 87%	

Bibliographic Information	Study type & Evidence level	Study Aims	Number of patients & prevalence	Population Characteristics	Type of test and Reference standard	Outcome measures	Sensitivity, Specificity, PPV and NPV	Reviewer comment
		pyelonephritis in children.		Bacteriruia defined as 10^5 cfu/ml from a mid-stream sample or 10^4cfu/ml from a catheter or SPA.			PDU compared to DMSA for identifying renal lesions in patients with acute pyelonephritis (on DMSA) Sensitivity 58%	

Antibiotic treatment for symptomatic UTI

Bibliographic Information	Study Type & Evidence Level	Study Aims	Number of Patients	Patient Characteristics	Intervention & Comparison	Follow-up & Outcome Measures	Effect Size	Reviewer Comments
Dagan R;Einhorn M;Lang R;Pomeranz A;Wolach B;Miron D;Raz R;Weinstock A;Steinberger J; 1992 195	Study Type: RCT Evidence level: 1+	To compare the safety and efficacy of once daily oral cefixime to twice daily oral TMP/SMX for treating acute UTI in children.	94 children enrolled, 76 evaluated 38 received cefixime and 38 received TMP/SMX	Children aged 6 months to 13 years with symptoms of urinary tract infection (confirmed by positive culture). Positive urine defined asmore than 10^5cfu/ml from a clean catch sample, more than 10^3 from catheterisation or SPA. Exclusions: hypersensitivity to beta-lactam antibiotics, sulfa compounds or trimethoprim; children receiving antibacterial medications; children from whom a resistant organism was isolated; underlying anomalies or chronic diseases; children with more than one site of infection; frequent vopmiting not permitting oral therapy.	Intervention: Once daily oral cefixime (8mg/kg) or. Twice daily oral TMP/SMX (8/40mg/kg/day) in divided doses. Treated for 7 to 10 days depending on standard practice within each centre. Comparison: TMP/SMX vs. cefixime.	Follow-up period: 7 to 10 days. Outcome Measures: Urine sterilisation ESR WBC count	Of the original 96 children, 9 had a negative urine culture and a further 9 were Excluded from the study because of poor compliance. Baseline characteristics were similar on enrollment. 28/76 (37%) children were under 3 years of age and one third had history of recurrent UTI. Peripheral white blood cell counts, body temperature and urianalysis returned to normal at the same rate in both groups (data presented in graphs, no numbers provided) ESR on admission Cefixime 44.7±24.6 TMP/SMX 42.4±26.5 ESR 1-2 hours post treatment Cefixime 22.5±11.5 TMP/SMX 20.8±12.8 No failures were observed and relapse occurred in 3 cases within 4 weeks after treatment.	Not enough numbers presented to check whether the calculations are correct - mostly presented as 3D figures. No blinding. 9/94 children were excluded because of poor compliance. This will have an effect on the adverse effects data, which has been omitted for this reason.
Ahmed M;Sloan JE;Clemente E; 2001 196	Study Type: RCT Evidence level: 1-	To determine the comparative safety and efficacy of TMP and TMP/SMX in children with uncomplicated UTI.	125 patients randomised (59 evaluated) 30 TMP 29 TMP/SMX	Children 6 months to 12 years of age (mean age 5.2±0.6 years in TMP children and 5.2±0.7 in TMP/SMX children))with bacteriologically confirmed UTI (>10^5cfu/ml) seen at an outpatients centre.	Intervention: Oral TMP (10mg/kg/day) or TMP/SMX (40mg/kg/day) administered twice daily in divided doses for 10 days. Comparison: TMP monotherapy vs. TMP/SMX combination therapy	Follow-up period: 38-42 days Outcome Measures: Urine steralisation Symptom reduction	No statistically significant differences were found between the two groups. Bacteriological outcome TMP 26/30 (86.7%) TMP/SMX 27/29 (93.1%) p=0.5546 Clinical response TMP 26/30 (86.7%) TMP/SMX 26/30 (86.7%)	Study states that the trial was multi-centre, randomised and investigator-blind, however no further details are available. 125 patients were randomised to treatment, however only 59 were evaluated. Over 50% loss to follow-up with no explanation provided.
Howard JB;Howard JE; 1978 197	Study Type: RCT Evidence level: 1-	To assess the possible superiority of the combination of TMP/SMX over	229 children randomised, 118 evaluated 61 treated with TMP/SFX	Children between 6 months and 10 years with urinary tract infection who could be kept under medical observation for 42 days.	Intervention: TMP/SMX (10-12mg/kg) SMX (50 to 60mg/kg) Both given in three divided doses.	Follow-up period: 42 days Outcome Measures: Clinical and bacteriological cure was defined as the absence	Of the original 229 enrolled, 44 failed to return, in 52 the initial urine culture was negative and 15 did not take the medication. Groups were similar at baseline, however a greater number in the TMP/SMX group had fever (57% vs. 37%, p<0.05) There were no significant differences in responses to therapy at 10	Children were excluded continuously, reducing the power to detect a difference at each point. Started with 229, 44 failed to return, in 52 the

Bibliographic Information	Study Type & Evidence Level	Study Aims	Number of Patients	Patient Characteristics	Intervention & Comparison	Follow-up & Outcome Measures	Effect Size	Reviewer Comments
		SMX alone in treating children with UTI.	57 treated with Sulfamethoxozole alone	Exclusions: chronic or recurrent infection	Comparison: TMP/SMX vs. SMX	of symptoms and signs and sterile culture at 14 day follow up	days in terms of urine steralisation, or adverse effects.	initial urine culture was negative and 15 did not take the medication. Of the remaining 118, 16 did not keep return appointments, 2 did not take the medication, and 1 was not evaluated because of vomiting. There is no way of knowing what the effects of this had on the effectiveness of the oral antibiotics.
Bloomfield P;Hodson EM;Craig JC; 2005 199	Study Type: Systematic review - meta-analysis Evidence level: 1++	To determine the benefits and harms of different antibiotic regimens for the treatment of acute pyelonephritis in children	2612 children in 18 studies 2320 (89%) were assessed for at least one outcome of effectiveness	Children aged 0-18 with proven UTI and acute pyelonephritis treated in either a hospital or outpatients with antibiotics. Diagnosis of acute pyelonephritis required culture of more than 108cfu/L with at least one symptom of systemic illness. Previously diagnosed renal tract abnormalities including VUR were included. Asymptomatic or cystitis were excluded.	Intervention: Parallel RCTs Comparison: Oral therapy vs. short duration IV therapy followed by oral therapy Short duration IV (3-4 days) followed by oral therapy vs. long duration IV The addition of a single does of IV to oral therapy Different dosing frequencies of the same antibiotic	Follow-up period: 3 weeks - 1 year Outcome Measures: Persistent bacteriuria at 48-72 hours. Resolution of clinical symptoms Parenchymal renal damage (on DMSA) Adverse effects	1. Oral therapy vs. IV Time to fever resolution WMD 1.54 (-1.67 to 4.76) Rate of symptomatic recurrence RR 0.67(0.27, 1.67) Rate (RR 1.45 (0.63, 3.03))or size (RR -0.70 (-1.74, 0.34))of renal parenchymal defect on DMSA at 6 months. 2. Short vs. Long duration IV Recurrent UTI within 6-12 months, four trials (RR 1.15 (0.52, 2.51)) Persisting renal parenchymal defects seen on DMSA at 3-6 months, three trials (RR 0.99 (0.72, 1.37)) Adverse effects - gastrointestinal upset (RR 1.29 (0.55, 3.05)) 3. Single dose parenteral and oral vs. oral alone Persistence of bacteriuria (RR 0.77 (0.19, 3.20)) Persistence of clinical symptoms (RR 0.82 (0.24, 2.81)) Total adverse effects (RR 1.37 (0.33, 5.68)) 4. Different dosing regimens Daily parenteral gentamicin or netilmicin v. 8 hour administration. Persisting bacteriuria at 1-3 days(RR 1.98 (0.37, 10.53)) Persisting clinical symptoms (RR 1.98 (0.37, 10.53)) Persisting bacteriuria at one week (RR 2.48 (0.12, 68.57)) Recurrent UTI within 1 month (RR 1.18 (0.33, 4.23)) Time to fever resolution (WMD 2.40 (7.92, 12.72)) 5. Different IV antibiotics IV cefipime to IV ceftazidime: 1 trial involving 299 children (Ref ID 211). There were no significant differences between the groups for bacteriuria (RR 0.12 95%CI 0.01 to 2.16), recurrent infection (RR 0.68 95%CI 0.45 to 3.18), occurrence of unsatisfactory clinical response (RR 0.68 95%CI 0.12 to 4.02) or adverse events (RR 1.41	Quality of included studies was variable with larger, more recent trials having adequate quality.

Bibliographic Information	Study Type & Evidence Level	Study Aims	Number of Patients	Patient Characteristics	Intervention & Comparison	Follow-up & Outcome Measures	Effect Size	Reviewer Comments
							95%CI 0.65 to 3.07). 6.IV cefotaxime to IV amoxicillin/clavulanic acid: 1 trial involving 20 children (Ref ID 138). Two children treated with cefotaxime but none treated with amoxicillin/clavulanic acid had persistent bacteriuria at 48 hours (RR 5.50 95%CI 0.30 to 101.28). Two children treated with cefotaxime but none treated with amoxicillin/clavulanic acid had persistent fever at 48 hours(RR 5.00 95%CI 0.27 to 92.62). Three children treated with amoxicillin/clavulanic but none treated with cefotaxime had gastrointestinal adverse effects (RR 0.14 95%CI 0.01 to 2.45). IV cefotaxime to IV ceftrixone: 1 trial involving 100 children over the age of 24 months (Ref ID 111). There was no significant difference between the groups for bacteriuria (none in either group after 48h), recurrent infection (RR 0.87, 95%CI 0.37 to 2.03 at one month and RR 0.68, 95%CI 0.30 to 1.50) or adverse events (RR 0.67, 95%CI 0.12 to 3.82). aminoglycosides IV isepamicin to IV amikacin: 1 trial involving 16 children compared the (Ref ID 159). There were no significant differences between the groups for bacteriuria (no patient in either group had persistence of bacteriuria after 48 h, 7 days or 30 days) or resolution of fever (mean time same in each group 24h). 7. Single dose vs. longer duration of oral (2 studies) Persistence of bacteriuria (RR 1.73 (0.18, 16.30)) Recurrent UTI with in 6 weeks (RR 0.24 (0.03, 1.97))	
Fischbach M;Simeoni U;Mengus L;Jehl F;Monteil H;Geisert J;Janin A; 1989 200	Study Type: RCT Included in Cochrane review Evidence level: 1+	To compare the efficacy and tolerance of two treatment regimens with tissue penetration	Total 20 participants 10 treated with IV cefotaxime 10 treated with IV amoxycillin /clavulanate	Children above the age of 1 year with urinary tract infection (urinary leukocyte count greater than 10 white blood cell /mm^3 and a bacteriuria greater than or equal to 100,000 colonies/ml, a predominant isolate (more than 80% of the flora), with tissue penetration shown both clinically (poor general condition, lumbar or abdominal pain, temperature above 38.5ºC) and on laboratory tests (ESR greater than 35mm at 1 hour, elevated CRP and orosomucoid)). Children excluded from the study: definite or	Intervention: IV cefotaxime 100mg/kg/day in 4 infusions over 30 min for 14 days versus IV amoxycillin /clavulanate 100mg/kg/day in 4 infusions over 30 min for 7 days followed by oral amoxycillin /clavulanate 50mg/kg/day for 7 days Comparison: treatment vs treatment	Follow-up period: unknown Outcome Measures: Time to defervescence (hours) Sterilization of the urine (0 bacteria/ml)	Time to defervescence ≤ 36 hours: cefotaxime 4/10, amoxycillin /clavulanate 5/10 36-48 hours: cefotaxime 4/10, amoxycillin /clavulanatev 5/10 > 48 hours: cefotaxime 2/10, amoxycillin /clavulanate 0/10 Sterilization of the urine ≤ 48 hours: cefotaxime 7/10, amoxycillin /clavulanate 10/10 48-72 hours: cefotaxime 2/10, amoxycillin /clavulanate 0/10 not obtained: cefotaxime 1/10, amoxycillin /clavulanate 0/10	Small number of participants

Bibliographic Information	Study Type & Evidence Level	Study Aims	Number of Patients	Patient Characteristics	Intervention & Comparison	Follow-up & Outcome Measures	Effect Size	Reviewer Comments
				suspected allergy to β-lactams, antibiotic therapy within the 72h before inclusion in the trial, impaired renal function or post operative infections. 3 participants had a history of congenital abnormalities, 4 has a history of pyelonephritis				
Schaad UB;Eskola J;Kafetzis D;Fishbach M;Ashkenazi S;Syriopoulou V;Boulesteix J;De P;Gres JJ;Rollin C; 1998[201]	Study Type: RCT Included in Cochrane review Evidence level: 1+	To compare the safety and efficacy of cefepime compared to ceftazidime for treating pyelonephritis in children younger than 12 years old.	Total 299 patients 149 in cefepime group 150 in ceftazidime group	≥ 1 month and ≤ 2 years weight at least 3 kg infection requiring hospitalisation, fever at least 38.5 ºC, white blood cell count > 15000 per ml, evidence of pyuria	IV cefepime 50 mg/kg every 8 hours versus IV ceftazidime 50 mg/kg every 8 hours continued until at least 48 hours after having become afebrile, then IV treatment continued or replaced with oral antibiotic therapy (trimethoprim-sulfamethoxazole)	Follow-up period: Follow up at 5-9 days and 4-6 weeks after end of total therapy Outcome measures: Persistent bacteriuria and unsatisfactory clinical response at end of IV therapy and end of antibiotic therapy Recurrent UTI and unsatisfactory clinical response at 5-9 days and 4-6 weeks after end of therapy Adverse effects	Persistence or recurrence of initial pathogen: at end of IV therapy, cefepime 1/111 versus ceftazidine 0/113 (RR 3.05, 95%CI 0.13, 74.16) at end of antibiotic therapy, cefepime 0/96 versus ceftazidine 4/102 (RR 0.12, 95%CI 0.01, 2.16) at 5-9 days after treatment, cefepime 5/95 versus ceftazidine 2/91 (RR 2.37, 95%CI 0.47, 11.91) at 4-6 weeks after treatment, cefepime 1/91 versus ceftazidine 8/97 (RR 0.13, 95%CI 0.02, 1.04) Infection with new pathogen: at 4-6 weeks, cefepime 8/115 versus ceftazidine 7/120 (RR 1.19, 95%CI 0.45, 3.18) Unsatisfactory clinical response: at end of IV therapy, cefepime 2/115 versus ceftazidine 3/118 (RR 0.68, 95%CI 0.12, 4.02) at end of antibiotic therapy, cefepime 2/100 versus ceftazidine 0/102 (RR 5.10, 95%CI 0.25, 104.90) at 5-9 days after treatment, cefepime 2/99 versus ceftazidine 0/100 (RR 5.05, 95%CI 0.25, 103.87) at 4-6 weeks after treatment, cefepime 2/95 versus ceftazidine 8/105 (RR 0.28, 95%CI 0.06, 1.27) Adverse effects: total, cefepime 41/149 versus ceftazidine 37/150 (RR 1.12, 95%CI 0.75, 1.63) drug-related, cefepime 14/149 versus ceftazidine 10/150 (RR 1.41, 95%CI 0.65, 3.07) gastrointestinal, cefepime 10/149 versus ceftazidine 9/150 (RR 1.12, 95%CI 0.47, 2.67) cutaneous, cefepime 3/149 versus ceftazidine 2/150 (RR 1.51, 95%CI 0.26, 8.91) discontinuation due to drug related adverse effects, cefepime 4/149 versus ceftazidine 1/150 (RR 4.03, 95%CI 0.46, 35.61)	
Bakkaloglu	Study Type:	To compare the	100 children	Children aged 2 to 14	Intervention: IV Ceftriaxone	Follow-up period: 4-5	Baseline characteristics were similar between groups.	Results are reported of

Bibliographic Information	Study Type & Evidence Level	Study Aims	Number of Patients	Patient Characteristics	Intervention & Comparison	Follow-up & Outcome Measures	Effect Size	Reviewer Comments
A;Saatci U;Soylemezoglu O;Ozen S;Topaloglu R;Besbas N;Saatci I; 1996 202	RCT Included in Cochrane review Evidence level: 1+	efficacy of ceftriaxone and cefotaxime in childhood pyelonephritis	50 (38 girls and 12 boys) received ceftriaxone 50 (40 girls and 10 boys) received cefotaxime	with complicated or uncomplicated pyelonephritis Pyelonephritis was defined as symptoms and culture showing 10(5) cfu	(50mg/kg once daily) or IV cefotaxime (50mg/kg twice daily) for 10 days Comparison: Treatment vs. treatment	weeks Outcome Measures: Urine steralisation Symptom resolution	45 children had pathological findings on radiological assessment (abdominal ultrasound, IVU and VCUG), 48 in the ceftriaxone group and 42 in the cefotaxime group and were defined as complicated cases. VUR 17 Hydronephrosis 5 Urolithiasis 5 Pelvicalyceal ectasia in 8 Bladder diverticula 4 Other abnormalities 6 Urine sterilisation at 10 days post-treatment Ceftriaxone 42/50 (84%) Cefotaxime 41/50 (82%) Urine sterilisation at 10 days post-treatment Ceftriaxone 42/50 (84%) Cefotaxime 39/50 (78%) Adverse effects in the ceftriaxone group were increased transaminase ALT in one patient, allergic cutaneous reaction in one patient and diarrhea in one patient.. Adverse effects in the cefotaxime group were increased transaminase ALT in one patient and AST in one patient and skin eruptions in three patients.	'overall efficacy' however numbers in table don't relate to the 10 day or 28 day cure rates. For this reason results reported here include 10 day and 28 day data separately.
Kafetzis DA;Maltezou HC;Mavrikou M;Siafas C;Paraskakis I;Delis D;Bartsokas C; 2000 203	Study Type: RCT Included in Cochrane review Evidence level: 1+	To compare the efficacy and safety of isepamicin with amikacin in the treatment of paediatric patients with acute pyelonephritis and to compare blood levels in paediatric patients after administration of the same dosage.	Total 16 patients 10 in isepamicin group 6 in amikacin group	16 patients (10 girls and 6 boys) 10 in isepamicin group 6 in amikacin group Mean age 3 months, range 1 to 84 months. Acute pyelonethritis (fever > 38ºC, and according to age, refusal to feed, vomiting, abdominal pain, lethargy or focal genitourinary signs in a child with laboratory signs of pyuria, leukocytosis, increased C-reactive protein (> 30 mg/ml) an increased erythrocyte sedimentation rate and the isolation of a bacterial pathogen from two samples of clean catch urine at ≥ 100,000	Intervention: IV isepamicin versus IV amikacin 7.5mg/kg bd infusion lasting 30 min, for 10-14 days. Administered solely or in combination with an appropriate antimicrobial agent Comparison: treatment vs treatment	Follow-up period: 30 days following completion of treatment Outcome Measures: Clinical response defined as cure, improvement or failure Relapse defined as reappearance of symptoms and signs of infection following their initial resolution Bacteriological response constituted the primary efficacy endpoint and was defined as either elimination or persistence of the causative pathogen in urine culture. Superinfection was defined as isolation of additional pathogens in	Clinical response defined as cure isepamicin 9/10, amikacin 6/6 elimination of the causative agent but not cure isepamicin 1/10, amikacin 0/6 Relapse - isepamicin 0/10, amikacin 0/6 Bacteriological response pathogens isolated from blood or urine culture - isepamicin 0/10, amikacin 0/6 Superinfection - isepamicin 0/10, amikacin 0/6 Adverse effects - no clinical or laboratory adverse events complicated the course of any patient.	Small number of participants, no power calculation

Bibliographic Information	Study Type & Evidence Level	Study Aims	Number of Patients	Patient Characteristics	Intervention & Comparison	Follow-up & Outcome Measures	Effect Size	Reviewer Comments
				colony-forming units/ml or ≥ 100 colony-forming units/ml from a urine sample obtained by suprapubic aspiration or urethral catheterization before treatment) Patients excluded if they received any antibacterial treatment within four weeks prior to study initiation, a history of intolerance to any aminoglycoside, impaired baseline renal, hearing or vestibular function or were infected with a pathogen resistant to aminoglycosides. Underling disease: 2 patients with hydronephrosisin (one in association with left ureteral stenosis), 1 patient with left double renal pelvis, 1 patient withgrade II vesicourethral reflux and 1 patient with bronchiolitis		repeated urine culture. Adverse effects, graded as mild, moderate, severe, or life-threatening.		
Vilaichone A;Watana D;Chaiwatanarat T; 2001 [204]	Study Type: RCT Included in Cochrane review Evidence level: 1+	Efficicay of treatment for long term outcomes	Total 36 participants 18 in IV ceftriaxone switch to oral ceftibuten group 18 in 10 day IV ceftriaxone group	Age 1 month to 15 years Acute pyelonephritus, 1) fever of more than 38ºC or subnormal temperature in small infants, 2) pyuria (WBC ≥ 5/high power field) and/or bacteriuria (≥ 1 gram negative rod per 10 oil immersion fields in a gramstained uncentrifuged urine), 3) positive urine culture (more than 10000 colony forming unit/cc, single pathogen on midstream clean catch or bag urine) 4) 99mTc-DMSA scan	Intervention: IV ceftriaxone 75mg/kg/day after 24-48 hours after defervescence switched to oral ceftibuten 9 mg/kg/day total duration 10 days (patients discharged after switching to oral antibiotics) versus IV ceftriaxone 75mg/kg/day for 10 days Comparison: short duration IV treatment vs 10 day IV treatment	Follow-up period: 6 months Outcome Measures: Abnormal DMSA at 6 months Recurrent UTI during 6 months Persistent bacteriuria at end of treatment Adverse effects	Abnormal DMSA at 6 months: 12/18 vs 11/18, RR 1.09 95% CI 0.67, 1.79 Recurrent UTI during 6 months: 2/18 vs 1/18, RR 2.00 95% CI 0.20, 20.15 Persistent bacteriuria at end of treatment: 0/18 vs 0/18 Adverse effects: 1/18 vs 0/18, RR 3.00 95% CI 0.13, 69.09	Small study

Bibliographic Information	Study Type & Evidence Level	Study Aims	Number of Patients	Patient Characteristics	Intervention & Comparison	Follow-up & Outcome Measures	Effect Size	Reviewer Comments
				demonstrated cortical defect. Exclusions: age < 1 month, previous UTI, unknown uropathy, allergic to trial antibiotics, renal failure, chronic disease, antibiotics in previous 48 hours				
Benador D;Neuhaus TJ;Papazyan J;Willi UV;Engel-Bicik I;Nadal D;Slosman D;Mermillod B;Girardin E; 2001 205	Study Type: RCT Included in Cochrane review Evidence level: 1+	To compare th prevalence of scarring following initial treatment with antibiotics administered intravenously for 10 or 3 days.	435 children randomised (217 in 3 day IV group and 218 in 10 day IV therapy group) 209 found not to fulfill study criteria (106 in 3 day group and 100 in 10 day) 9 patients dropped out at request of parents (217 in 3 day group and 218 in 10 day)	Age 3 months to 16 years. Mean age younger in 10 day IV therapy group: 1.0 years (range 0.5-3.3) vs 2.4 years (range 0.8-5.6) all other base line characteristics similar. With probable acute pyelonephritis. Exclusion criteria: Age < 3months, history of urinary abnormalities of and hypersensitivity to cephalosporins Randomisation occured before final enrolment, which required a positive initial urine culture and a first scintigraphy showing signs of acute pyelonephritis	Intervention: 3 days IV ceftriaxone 50 mg/kg once daily then 12 days oral cefixime 4 mg/kg twice daily versus 10 days IV ceftriaxone 50 mg/kg once daily then 5 days oral cefixime 4 mg/kg twice daily. At end of treatment all given prophylaxis with co-trimoxazole. Comparison: 3 day IV treatment vs 10 day IV treatment	Follow-up period: 3 months Outcome Measures: Scaring on DMSA at 3 months Recurrent UTI at 3 months	Scaring on DMSA: 9/110 vs 6/110 RR 1.50 95% CI 0.55, 4.07 Recurrent UTI: 40/110 vs 36/110 RR 1.11 95% CI 0.77, 1.60	
Francois P;Bensman A;Begue P;Artaz MA;Coudeville L;Lebrun T;Scheimberg A; 1997 206	Study Type: RCT Included in Cochrane review Evidence level: 1+	To compare the clinical effectiveness and cost of an oral therapy (cefixime) with the parenteral therapy (ceftriaxone) as a support treatment after an initial intravenous (IV) combination therapy in	Total 147 70 in 4 day IV ceftriaxone 77 in 10 days IV ceftriaxone	Age 0.5 -10 years with acute pyelonephritis UTI and fever >38ºC, pyuria, CRP increased Exclusions: previous acute pyelonephritis, organisms resistant to trial antibiotics. Allergy to cephalosporins, B-lactams, aminoglycosides, known uropathology, need for IV antibiotics based on ultrasound, renal failure, immune deficiency, other	Intervention: All received IV ceftriaxone 50 mg/kg/d daily dose and IV netilmicin 6-7.5 mg/kg/d in 3 divided doses for 4 days. Then oral cefixime 4 mg/kg/dose, 2 doses per day for 6 days versus IV ceftriaxone 50 mg/kg/d single daily dose for 6 days Comparison: 4 day IV therapy vs 10 day IV therapy	Follow-up period: 1 month Outcome Measures: Persistant bacteriuria 2 days after end of therapy Recurrent UTI in 20 days after therapy Adverse events	Persistant bacteriuria: 1/63 vs 0/65, RR 3.09 95% 0.13, 74.55 Recurrent UTI: 0/49 vs 2.53, RR 0.22 95% CI 0.01, 4.39 Adverse events:9/67 vs 8/72, RR 1.12 95% CI 0.50, 2.95	Definition of 'success rate' not reported No statistical analyses to take account of potential biases and confounding factors

Bibliographic Information	Study Type & Evidence Level	Study Aims	Number of Patients	Patient Characteristics	Intervention & Comparison	Follow-up & Outcome Measures	Effect Size	Reviewer Comments
		acute pyelonephritis		inflammation.				
Madrigal G;Odio CM;Mohs E;Guevara J;McCracken GH; 1988 207	Study Type: RCT Included in Cochrane review Evidence level: 1+	To evaluate the efficacy of three regimens of TMP/SMX therapy for children with acute uncomplicated UTI.	222 patients enrolled 70 one dose 73 two doses daily for 3 days 79 two doses daily for 7 days	Children aged 3 months to 12 yeaers with suspected or proven acute UTI - diagnostic criteria 100,000 cfu/ml.	Intervention: TMP/SFX One dose Two doses daily for 3 days Two doses daily for 7 days Comparison: Treatment length vs. treatment length	Follow-up period: 28 to 37 days after therapy completion Outcome Measures: Urine steralisation recurrence	There was no difference in bacteriologic cure rates for the single dose regimen (93%) and multidose regimen (96%). The difference in rates of recurrence between single dose (20.5%) and 3 day (5.6%) and 7 day (8%) was statistically significant (p=0.033)	
Noorbakhsh S;Lari AR;Masjedian F;Mostafavi H;Alaghehbandan R; 2004 209	Study Type: RCT Evidence level: 1+	To compare the efficacy of IV aminoglycoside with IV ceftriaxone plus switch therapy to cefixime in children with UTIs	Total 54 30 in ampicillin group 24 in ceftriaxone group	children aged ≤ 10 years with UTI Exclusion criteria: history of serious allergy to study therapy, complete obstruction of the urinary tract, perinephric or intrarenal abscess, any rapidly progressive disease, immune-compromising illness or therapy, the need for concomitant antimicrobials, acute hepatic failure, requirement for peritoneal dialysis or hemodialysis, treatment with a systematic antimicrobial agent for ≥ 24 hours within 72 hours prior to the baseline urine culture, creatinine clearance of < 30 ml/min, aspartate aminotransferase or alanine aminotransferase levels of > 6 times the upper limit of normal, bilirubin or alkaline phosphatase levels of > 3 times the upper limit of normal, absolute neutrophil count of ≤ 1000 per µl, platelet concentration of < 75000 per µl, hematocrit level of <	Intervention: IV amikacin 15 mg/kg daily or gentamicin 3mg/kg daily with ampicillin 100mg/kg daily for 7 to 10 days versus IV ceftriaxone 50mg/kg daily for the first 2 days and then switched to cefixime 8mg/kg daily for 8 days Comparison: threapy vs therapy	Follow-up period: 4-6 weeks post therapy Outcome Measures: Failure of therapy (urine culture of 10,000 colony forming units/ml of any uropathogen present in the admission culture at a concentration of 100,000 colony forming units/ml)	Rate of response (clinically and microbiologically) aminoglycoside 24/30 versus ceftriaxone and switched to cefixine 21/24 (p=0.82)	Poor reporting of results, unsure what outcome 'rate of response' is measuring No power calculation

Bibliographic Information	Study Type & Evidence Level	Study Aims	Number of Patients	Patient Characteristics	Intervention & Comparison	Follow-up & Outcome Measures	Effect Size	Reviewer Comments
				25%, or coagulation tests of >1.5 times the upper limit of normal.				
Baker PC;Nelson DS;Schunk JE; 2001[211]	Study Type: RCT Evidence level: 1+	To determine whether the addition of a single dose of ceftriaxone sodium to a 10-day course of trimethoprim and sulfamethoxazole hastens urine sterilization or resolution of clinical symptoms in febrile children with urinary tract infections	69 Total included in analysis (18/87 drop out, 14 due to no growth in their urine culture, 4 did not return for follow up) 34 treated with IM ceftrixone and oral trimethoprim-sulfamethoxazole 35 treated with oral trimethoprim-sulfamethoxazole only	Aged 6 months to 12 years, temperature > 38.0ºC were diagnosed as having a UTI based on presenting history, physical examination and urinalysis findings. Exclusions: known urologic anomaly, were taking antibiotics, had allergies to study medications, or were clinically unstable. Patients subsequently included in the final study sample if they had a positive urine culture (single organism growth > 100000 colony forming units per high-power field from a clean catch urine specimen or greater than 10000 colony forming units per high-power field from a catheterized urine sample).	IM ceftrixone (1 dose of 50 mg/kg) and oral trimethoprim-sulfamethoxazole (twice daily 5 mg/kg per dose for 10 days) versus oral trimethoprim-sulfamethoxazole only (twice daily 5 mg/kg per dose for 10 days)	Follow up: 48 hours Outcome measures: Treatment failure (microbiological and clinical criteria, persistence of bacterial growth in the follow up urine culture after 48h of treatment or subsequent need for hospital admission) Adverse effects	Treatment failure: 4/34 vs 5/35 p > 0.05 Adverse effects: 4/34 vs 3/35 p = 0.96	
Wallen L;Zeller WP;Goessler M;Connor E;Yogev R; 1983 [210]	Study Type: RCT Included in Keren Meta-Analysis Evidence level: 1+	To compare the effectiveness of a singla intramuscular injection of amikacin sulfate to a 10 day course of sulfisoxazole in treatment of UTI in girls	54 girls 26 received one intramuscular amikacin 28 received 10 oral day sulfisoxazole	Girls aged 1-12 years with suspected UTI and 2 positive cultures. Exclusions: clinical symptoms of pyelonephritis, fever (> 38.3ºC), flank pain, ESR>21mm/hr, antibiotic usage in last week or known urinary tract anomalies	Intervention: Single intramuscular injection of amikacin sulfate compared to 10 day oral sulfisoxazole for the treatment of presumed lower E coli urinary tract infections. Comparison: Treatment vs. treatment	Follow-up period: 3 months. Outcome Measures: Urine steralisation	6/23 receiving IM amikacin and 4/21 receiving oral sulphisoxazole had at least one positive urine culture within 40 days post treatment. Difference no statistically significant (p>0.5)	
Michael M;Hodson EM;Craig JC;Martin S;Moyer VA;	Study Type: Systematic review - meta-analysis Evidence level: 1++	To assess the benefits and harms of short-course compared to conventional therapy for	910 children entered Outcomes evaluated in 652. 168 loss to follow up	Children 3 months - 18 years with culture proven UTI. Excluded children with neurogenic bladders and known urinary tract	Intervention: Antibiotic treatment - RCTs only Comparison: Short v standard duration oral antibiotic therapy	Follow-up period: 33 days - 12 months Outcome Measures: Primary Outcomes - Persisting clinical symptoms at the end of	Significant bacteriuria 8 data sets (RR 1.06, 95%CI 0.64 to 1.76) 0-10 days after completing treatment. Sulphonamides alone or in combination with trimethoprim and other antibiotics - sulphonamide group 4 studies (RR8.80, 95%CI 0.45 to 1.41)	Enrolled both symptomatic and asymptomatic patients Studies included were generally small and included children from a

Bibliographic Information	Study Type & Evidence Level	Study Aims	Number of Patients	Patient Characteristics	Intervention & Comparison	Follow-up & Outcome Measures	Effect Size	Reviewer Comments
2005 198		acute UTI in children.	99 excluded because no long-duration comparison group	abnormalities. RCTs did not specify whether patients were symptomatic or asymptomatic		treatment - Significant bacteriuria (>10,000 organisms/ml) at completion of Rx - Recurrent UTI after Rx (one month or more) Secondary Outcomes - Compliance with medication - Development of resistant organisms - Cost - Side effects	- other antibiotics 4 studies (RR1.72, 95%CI 0.64 to 3.80) Abnormal IVP or MCUG (RR0.99, 95%CI 0.70 to 1.29) But heterogeneity Recurrent UTI 1-15 months FU 10 data sets (RR 0.95, 95%CI 0.70 to 1.29) Recurrent + abnormality (RR0.24 95%CI 0.03 to 1.67) Compliance 3 studies reported satisfactory compliance Resistance urinary pathogens resistant or persistent bacteriuria one study (RR 0.57 95%CI 0.12 to 1.29) Recurrent UTI Three studies (RR 0.39 95%CI 0.12 to 1.29) RRR for resistant organisms 43% for bacteriuria at end of Rx and 61% recurrent.	wide age range. Review looks fine but individual RCTs are a bit dodgy.
Chong CY;Tan AS;Ng W;Tan-Kendrick A;Balakrishnan A;Chao SM; 2003 212	Study Type: RCT Included in Cochrane review Evidence level: 1+	To examine the safety and efficacy of once daily gentamicin treatment ccompared with conventional 8 hourly dosing.	Total 172 (analysed of 210 recruited) 84 in once daily group 88 in three times daily group	Age 1 month to 13 years, (mean age 0.92 ± 1.30 years) with presumed UTI (fever >38ºC with pyuria, >200 white blood cells/ml or foul smelling urine, dysuria, frequency of micturition or loin pain). UTI confirmed on 2 clean catch urines (single organism > 100,000ml) or 1 catheter specimen (single organism >1000/ml) Exclusions: < 1 month of age (or if born prematurely with a corrected age of <24 weeks) history of previous allergy to aminoglycosides, renal impairment with abnormal serum creatinine at baseline or known renal impairment, previous nephrotoxic drugs in the last month,	Intervention: IV gentamicin 5 mg/kg/d given over 1 hour once a day versus IV gentamicin 6 mg/kg/d given over 20-30 minutes three times a day Comparison: once daily treatment vs three times daily treatment	Follow-up period: 3 months Outcome Measures: Persistent bacteriuria (negative urine culture at end of gentamicin treatment) Time to defervescence Nephrotoxicity (increase in creatinine by 50% or more) Renal scar on DMSA scan at 3 months	Persistent bacteriuria: 2/84 vs 2/88, RR 1.05, 95% CI 0.15, 7.27 Time to defervescence: 47.4 ± 34.6 vs 45.0 ± 34.4 RR 2.40, 95% CI -7.90, 12.70 Nephrotoxicity: 1/79 vs 2/80 RR 0.51, 95% CI 0.05, 5.47 Renal scar on DMSA scan at 3 months: 18/75 vs 23/71 RR 0.66 95% CI 0.32, 1.36	

Bibliographic Information	Study Type & Evidence Level	Study Aims	Number of Patients	Patient Characteristics	Intervention & Comparison	Follow-up & Outcome Measures	Effect Size	Reviewer Comments
				concurrent nephrotoxic drugs, known obstructive uropathy, known hearing impairment or abnormal baseline otoacouistic emission.				
Carapetis JR;Jaquiery AL;Buttery JP;Starr M;Cranswick NE;Kohn S;Hogg GG;Woods S;Grimwood K; 2001 213	Study Type: RCT Included in Cochrane review Evidence level: 1+	To determing the safety and efficacy of once daily gentamicin dosing in children with severe UTI	184 children (179 analysed) 90 in once daily group 89 in three times daily group	Age 1 month to 12 years Ill, vomiting and unable to take oral medication reliably. UTI diagnosed by identifying uropathogens in suprapubic aspirate specimens or a pure growth of ≥100000 bacteria/ml in catheter or midstream urine specimens. Exclusions: aminoglycoside hypersensitivity, known gentamicin-resistant organisms, renal impairment, hearing loss, vestibular disease, neutropenia or immunodeficiency	Intervention: once daily IV gentamicin versus three times daily IV gentamicin In both groups gentamicin given as 30 min infusion 7.5 mg/kg for < 5 year olds, 6.0 mg/kg for 5-10 year olds, 4.5 mg/kg for >10 year olds, treatment length varied Comparison: once daily treatment vs three times daily treatment	Follow-up period: Dependent on last day of treatment. Treatment continued until particpants were afebrile for 24h, then oral therapy determined by the antibiotic susceptibility was started Outcome Measures: Cure (resolution of the presenting symptoms and signs without use of other antibiotics Partial resolution Failure (persistence of the original symptoms and signs) Time to fever resolution	Cure 86/90 vs 87/89, RR 0.98, 95% CI 0.93, 1.03 Partial resolution 4/90 vs 2/89 Failure 0/90 vs 0/89 Time to fever resolution: 27 (13.5-47.5) vs 31.0 (9.8-48)h (p = 0.61)	
Vigano A;Principi N;Brivio L;Tommasi P;Stasi P;Villa AD; 1992 Jul 214	Study Type: RCT Included in Cochrane review Evidence level: 1+	To evaluate the efficacy of netilmicin.	150 in total (6 droped out) 74 treated with IM netilmicin 5 mg/kg once daily. 70 were treated with IM netilmicin 2 mg/kg three times a day.	Age 1 month to 12 years with UTI (two urine samples collected by the clean catch method or bladder catheterization containing ≥100,000 colony forming units of gram negative bacteria per ml) symptoms and signs of pyelonephritis (body temperature, ≥ 38.5ºC, erythrocyte sedimentation rate, > 25 mm/l h, C-reactive protein, > 20 μg/ml) Exclusions: hypersensitivity to aminoglycosides, serum creatinine values abnormal for age, presence of ileostomies,	Intervention: IM netilmicin 5mg/kg of body weight once daily versus IM netilmicin 2 mg/kg three times a day Comparison: once daily treatment vs three times a day treatment	Follow-up period: 6 weeks Outcome Measures: Persistant bacteriuria at 7 days and recurrent UTI by 30 days after end of therapy Adverse effects	Persistant bacteriuria at 7 days: 1/74 vs 0/70 Recurrent UTI by 30 days after end of therapy: 5/74 vs 4/70, RR 1.18 95% CI 0.33, 4.23 Adverse effects:hearing impairment 2/20 vs 0/12 increasein serum creatinine2/74 vs 2/70	

Bibliographic Information	Study Type & Evidence Level	Study Aims	Number of Patients	Patient Characteristics	Intervention & Comparison	Follow-up & Outcome Measures	Effect Size	Reviewer Comments
				ureterostomies or neurogenic bladder and a history of signs of deafness				

Cranberry

Bibliographic Information	Study Type & Evidence Level	Study Aims	Number of Patients	Patient Characteristics	Intervention & Comparison	Follow-up & Outcome Measures	Effect Size	Reviewer Comments
Jepson RG;Mihaljevic L;Craig J; 2005 [215]	Study Type: Systematic review - meta-analysis Evidence level: 1++	To assess the effectiveness of cranberries for the treatment of urinary tract infections.	No trials found	Searched for studies	Intervention: Effectiveness of cranberry juice and cranberry products for the treatment of UTI Comparison: No trials found	Follow-up period: Outcome Measures: Outcomes searched were number of symptomatic and asymptomatic UTIs at the end of treatment period.	No trials assessing the treatment of UTIs with cranberry juice were found. Two uncontrolled trials have shown a beneficial effect but no conclusions can be drawn from such studies.	

Factors predicting recurrence

Bibliographic Information	Study Type & Evidence Level	Aim of Study	Number of Patients	Population Characteristics	Interventions	Outcome measures	Results & Comments	Reviewer Comment
Shaikh N;Hoberman A;Wise B;Kurs-Lasky M;Kearney D;Naylor S;Haralam MA;Colborn DK;Docimo SG; 2003 [218]	Study Type: Cohort Evidence level: 2+	To evaluate the relationship between early UTI, VUR and dysfunctional elimination syndrome.	UTI cohort = 123 (115 girls and 8 boys) Comparison cohort = 125 (120 girls and 5 boys)	UTI Cohort: Children aged 4.3 to 10.6 years previously enrolled in a prospective multi-centre UTI treatment trial conducted between 1992 and 1997 who received a diagnosis of febrile UTI before 2 years old. Non-UTI cohort: Children aged 4.3 to 10.6 years identified retrospectively (and randomly) who as part of an evaluation for fever had a negative urinalysis and culture performed during the same period (1992 to 1997). Negative urinalysis: <10 WBC/mm^3 on a haemocytometer in an uncentrifuged specimen. Positive urine culture: At least 10^{4}cfu/ml on catheter sample or 10^{5}cfu/ml on a clean voided specimen. Recurrent UTI: More than one confirmed UTI.	547 questionnaires mailed to eligible subjects (168 in the UTI cohort and 406 in the comparison cohort). 248 completed questionnaires were returned. Questionnaire return rates in the UTI cohort were 73% and in the comparison cohort 31%.	Dysfunctional elimination symptoms were assessed with the dysfunctional voiding scoring system (validated).	The groups were similar with respect to demographic and clinical characteristics. The prevalence of dysfunctional elimination syndrome did not differ between children with UTI and children without (22% vs. 21%, p=0.82). In children with UTI, the prevalence of dysfunctional elimination syndrome did not differ in children with or without VUR (18% vs. 25%, p=0.52). Further analysis using different cut-off values did not yield different results. 31 children had recurrent UTI. Of these 13 (43%) had encopresis (OR 2.5, 95%CI 1.1 to 5.4, p=0.03), 11 (36%) had dysfunctional elimination syndrome (OR 2.2, 95%CI 0.99 to 5, p=0.05) and 17 (55%) had VUR (OR 2.2, 95%CI 0.9 to 5, p=0.07). The only variable that remained significant with recurrent UTI was encopresis (p=0.03).	Inadequate statistical analysis - Included one non-significant variable, and one borderline significant variable in a multivariable model of only 3 variables. Including non-significant variables will make the model more 'fuzzy' although it is unlikely to change the conclusions.
Panaretto KS;Craig JC;Knight JF;Howman-Giles R;Sureshkumar P;Roy LP; 1999 [72]	Study Type: Cohort Evidence level: 2++	Evaluated the risk factors that predispose to recurrent UTI in children and the role of recurrent UTI in renal scarring.	290 children with first UTI	Children (n=133 female, n=157 male), aged under 5 years, presenting at a children's hospital with first time UTI between March 1993 and December 1994 Exclusions: Known predisposing renal, neurological or skeletal causes.	Characteristics of recurrent UTI examined to identify groups at increased risk for recurrent UTI MCUG (at median 29 days, range 5 to 127 days following initial UTI) DMSA (at 7 days, range 0 to 34 days)	Rate of FU No. with VUR at entry No. with fever with UTI at entry No. with recurrence (confirmed with microbiology) Odds ratios (95% CI) Follow-up period: 1 year.	At the initial UTI, VUR was found in 83/290 (29%) of children and renal parenchymal defects in 113/290 (39%). Fever was present in 233/290 (80%) of children at index UTI. At 1 year, 261 (90%) children still in study, 133 girls and 157 boys with median age 1.2 years (range 10 days to 5 years) and at one year follow up was 2.3 years (range 1 to 6 years). 46 recurrent UTI episodes in 34 children - 20 had one recurrence - 14 had two recurrences Gender (OR 1.5, 95%CI 1 to 2.2, p=0.08) Fever (OR 1.2, 95%CI 0.7 to 2, p=0.59)	Study may be insufficiently powered to detect differences between exposed and unexposed groups. Univariate analysis not reported.

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				UTI defined as: for SPA or catheter, >10[6] cfu/l (n=164); for clean catch or midstream, >10[7] cfu/l (n=107); for bag urine, 10[8] cfu/L and white cell count >10[8]/L Recurrent Infection: Recorded as per parental report and documented with confirmatory microbiological analysis.			Age <6 months (OR 2.9, 1.4 to 6.2, p<0.01) VUR (OR 1.3 95%CI 0.6 to 2.5, p=0.50) Dilating VUR (OR 3.6, 95%CI 1.5 to 8.3, p<0.001) Intrarenal VUR (OR 1.3, 95%CI 0.6 to 3.2, p=0.54) Bilateral VUR (OR 1.2, 95%CI 0.6 to 2.3, p=0.6) Abnormal entry DMSA (OR 1.5 95%CI 0.7 to 3.5, p=0.32) VUR was present in 14/34 (41%) with recurrent infection and 65/256 (27%) without recurrent infection. Presence of reflux was not associated with recurrent infection (p<0.05) but the grade of reflux (X2=12.1, p<0.01), bilateral reflux (x2=6.1, p<0.05) and intrarenal reflux (x2=5.2, p<0.05) were significantly associated with recurrence. High grade reflux (grades 3 to 5) was an independent predictor of recurrence (OR 3.6, 95%CI 1.5 to 8.3, p<0.001) Renal parenchymal defects Repeat DMSA was performed in 173 children at 1 year. Recurrent UTI was significantly associated with renal parenchymal defects seen on first UTI (X2=4.6, p<0.05), grade of DMSA abnormality on entry (X2=12.3, p<0.01), DMSA abnormalities at one year (X2=11.5, p<0.001) and renal parenchymal defects at one year (X2=10.1, p<0.001)	
Stauffer CM;van der WB;Donadini R;Ramelli GP;Marchand S;Bianchetti MG; 2004 Apr [219]	Study Type: Case control Evidence level: 2+	To evaluate the role of family history, infrequent voiding, poor fluid intake, functional stool retention and inadequate anogenital hygiene or toilet habits in girls with recurrent UTIs.	90 cases 45 controls	Cases: Girls aged 3.9 to 16 years (median 8.4 years) referred to a nephrology clinic for evaluation of three or more symptomatic UTIs. Controls: Girls aged 4.0 to 14 years (median 7.3 years) none of whom had history of UTI. Controls had: - History of idiopathic childhood nephrotic syndrome cured for 2 years or more (9) - Allergic rhinitis (19) - Treated celiac disease (12) - Tension-type headache (5) Exclusions: first infection under 36 months, asymptomatic infection, adolescents with a history of sexual activity,	Written questionnaire evaluated family history, urinary, bowel and toilet habits, and anogenital hygiene by closed questions. The volume of any intake or urination was recorded for three days by a voiding-drinking diary. Non-invasive urodynamic assessment was completed. The diagnosis of dysfunctional voiding was made in girls with an interrupted urinary stream and unsustained relaxation of the pelvic floor muscles during micturation.	Volume of any intake or urination (by graduated measuring cup) Infrequent voiding (include at least 2 of the following) - habit of passing urine 3 or less times daily - voiding postponement - increased daytime bladder capacity - daytime urinary incontinence Functional stool retention (at least 3 of the following) - 72-hour or more interval between bowel movements - habit of passing small hard stools - history of painful defecation - stool retention on abdominal examination after defecation. Poor fluid intake (from beverage and plain water) Daily fluid intake of less than 600ml/m^2 body surface area	90 cases 60 had a history of lower UTI 30 had history of mixed UTI, upper in 16 and both upper and lower in 14. Family history of UTI (42% of cases v 11% of controls, p<0.001), Behavioural abnormalities (81% v 56%, p<0.01) Infrequent voiding (54% v 24%, p<0.001) Poor fluid intake (53% v 16%, p<0.001) Functional stool retention (30% v 13%, p<0.05) There were no significant differences between cases and controls for anogenital hygiene or toilet habits.	Not clear whether the same exclusion criteria was applied to both cases and controls Participation rates unclear Control selection unclear - don't know where they were selected from or why. No definition of bacteriuria or 'suggestive symptoms'

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				history or findings suggestive of sexual abuse, known urinary tract malformations, neuropathic bladder, moderate to severe mental retardation, disorders of posture or movement, overt encopresis.		or less Inadequate anogenital hygiene or toilet habits (at least 3 of the followint) - underpants frequently contaminated with fecal material at the end of the day - passing toilet paper back to front or using the same piece of paper 2 or more times - use of tight fitting clothes - toilet trained child aged 5 years or less - small children using regular toilets (rather than a potty chair)		
Biyikli NK;Alpay H;Guran T; 2005 Oct [220]	Study Type: Case series. Evidence Level: 3	To survey the incidence of idiopathic hypercalciuria in children with recurrent UTI.	75 children (62 girls, 13 boys)	Children aged 8 years (±2.7 years) with recurrent UTI. Recurrent UTI: two or more episodes of UTI separated for a period by sterile urine culture and symptom-free interval UTI: More than 10^5cfu/ml in mid-stream clean catch urine Hypercalciuria: the average urinary calcuim/creatinine ratio (mg/mg) equal or greater than 0.24 measured in at least 3 random morning urine samples in order to minimize the daily variation, or 24-hour urinary calcium excretion greater than 4mg/kg per day in patients who were found to be hypercalciuric in random urinary excretion of calcium/creatinine ratio (mg/mg).	Ultrasonography for urinary tract abnormalities DMSA for evaluating scar formation	Age at presentation Gender Presenting complaints Family history of urolithiasis Random urinary calcium/creatinine value (measured three times mg/dl) 24-hour calcium excretion (measured by cresolphthalein complexone spectrophotometric method mg/dl) Serum calcium Phosphorus, Electrolytes Blood gas Blood urea nitrogen and creatinine levels	Hypercalciuria was found in 32 children (43%) of whom 23 (72%) were girls and 9 (28%) were boys. (hypercalciuric children vs. normocalciuric children) Mean age (years) 7.2 ± 2.1 vs. 8.7 ± 2.9, p=0.013 Mean calcium/creatinine ratio 0.50 ± 0.21 vs. 0.10 ± 0.04, p=0.01 Voiding dysfunction 20 (63%) vs. 25 (58%) p=0.663 Pain 16 (50%) vs. 29 (67%) p=0.171 Haematuria 11 (35%) vs. 14 (33%) p=0.683 Urolithiasis 2 vs. 0 p=0.064 Family history of urolithiasis 19 (59%) vs. 20 (47%) p=0.414 Predisposing urinary tract abnormality 12 (38%) vs. 8 (19%) p=0.067	
Bratslavsky G;Feustel	Study Type: Case-series.	To evaluate the rate of and	264 infants of whom 119 met the	Children younger than 6 months who had a	Questionnaire administered over the	UTIs (febrile or non-febrile) Duration of breast feeding	16/84 (19%) had at least one febrile UTI after the negative radiographic evaluation.	

Bibliographic Information	Study Type & Evidence Level	Aim of Study	Number of Patients	Population Characteristics	Interventions	Outcome measures	Results & Comments	Reviewer Comment
PJ;Aslan AR;Kogan BA; 2004 Oct [221]	Evidence Level: 3	potential risk factors for recurrent UTI in children with UTI and no abnormality on radiographic evaluation.	inclusion criteria. Follow up data was available for 84 (52 girls and 32 boys)	normal ultrasound and VCUG. Mean age at follow-up 4.8 years (range 2.3 to 7.2 years)	telephone	Type of formula Family history of UTI Neurological problems History of constipation or recurrent fevers Socio-economic status Mean follow-up period 4.4 years (range 1.9 to 7.0 years)	Number with recurrent UTI vs. Number with no recurrent UTI, p-value Breast-feeding (less than 4 months) 13 (81%) vs 39 (57%) p=0.077 Siblings younger than 14 years 12 (75%) vs. 60 (88%) p=0.680 Family history of UTI 9 (56%) vs 29 (43%) p=0.325 Potty training (less than 2 years) 6 (38%) vs 18 (26%) p=0.640 Neurological problems 0 (0) vs. 3 (4%) p=0.687 Undiagnosed fevers 5 (31%) vs 9 (13%) p=0.082 Constipation history 2 (13%) vs. 11 (16%) p=0.714 Residence (live in private house) 12 (75%) vs. 55 (81%) p=0.598 Income less than $50,000 8/13 (62%) vs. 31/57 (54%) p=0.344 Circumcision 2/3 (67%) vs. 17/28 (61%) p=0.841	
Bakker E;Van Gool J;Van Sprundel M;Van Der Auwera JC;Wyndaele J; 2004 [222]	Study Type: Cross-sectional Evidence level: 3	To investigate the possible relationship between recurrent UTI and methods of potty training by comparing the methods used in	4332 questionnaires completed (2215 boys and 2117 girls)	Children completing the last two years of primary school. Mean age of responders was 11.5 ± 0.56 years. Questionnaire given to 5646 and completed by 4332	4332 questionnaires were completed (response rate 77%) and split into three groups 382 (9%) children with a single UTI (99 boys and 283 girls) 132 (3%) children with recurrent UTI (31 boys	No. of UTIs Age at UTI Wetting and soiling Potty training	No differences were observed between the three groups with respect to age. Any UTI Girls vs. boys 18.3% vs. 5.4% (p<0.001) Recurrent UTI group (n=132) 17/31 (51%) boys vs. 21/101 (21%) girls (p<0.001) contracted their first UTI under the age of 2.5 years.	History of UTI not confirmed. This is a major limitation of the study and results should be interpreted appropriately cautiously. P-values not accompanied by actual numbers on 1 occasion – Recurrent UTI

Bibliographic Information	Study Type & Evidence Level	Aim of Study	Number of Patients	Population Characteristics	Interventions	Outcome measures	Results & Comments	Reviewer Comment
		children with and without recurrent UTI.			and 101 girls) 3818 (88%) children who had no history of UTI (2085 boys and 1733 girls).		Daytime wetting (12%) vs. no daytime wetting (2%) (p<0.001) 9/31 (29%) boys with daytime wetting vs. 31/101 (31%) girls. Faecal soiling Recurrent UTI (9.1%) vs. no recurrent UTI (2.5%) Nocturia at least once a week Recurrent UTI 14/132 (10%) vs. No history of UTI 130/3818 (3%) P<0.001 Potty training started before 18 months old Recurrent UTI 21% vs. No history of UTI 31% P<0.05 Reaction of parents when an attempt to void was unsuccessful Kept child on potty until void was obtained Recurrent UTI 9/79 (11%) vs. No history of UTI 89/2567 (3%) P<0.005 Push/strain Recurrent UTI 17 (13%) vs. No history of UTI 263 (7%) P<0.001 Turned on the tap Recurrent UTI 42 (32%) vs. No history of UTI 826 (22%) P<0.001	significantly higher in those with voiding frequency of 10 times or more per day (p<0.02). These have been omitted from the results because they cannot be checked or re-calculated.
Mazzola BL;von Vigier RO;Marchand S;Tonz M;Bianchetti MG; 2003 Jan [223]	Study Type: Case-series. Evidence Level: 3	To evaluate the role of family history, infrequent voiding, poor fluid intake, functional stool retention and inadequate anogenital hygiene or toilet habits in girls with recurrent UTIs.	141 girls	Girls aged 3.9 to 18 years (median 6.5 years) referred to a nephrology clinic for evaluation of three or more symptomatic UTIs. None of the girls had a recent UTI (6 weeks or less). 81 were referred by GPs and 60 referred by paediatricians. Exclusions: first infection under 36 months, asymptomatic infection, adolescents with a history of sexual activity, history or findings suggestive of sexual abuse, known urinary tract malformations, neuropathic bladder, moderate to severe mental retardation, disorders of posture or	Complete history, bowel and bladder questionnaire, physical and neurological examination and urinalysis. A bladder scan measured post-micturation volume The volume of any intake or urination was recorded for three days by a voiding-drinking diary.	Lower tract infection: history of alguria, incontinence, urgency, frequency or suprapubic pain. Upper tract infection: Additional history of chills, fever (rectal body temperature 38.5°C or more) and abdominal or back pain. Volume of any intake or urination (by graduated measuring cup) Infrequent voiding (include at least 2 of the following) - habit of passing urine 3 or less times daily - voiding postponement - increased daytime bladder capacity - daytime urinary incontinence Presumed dysfunctional voiding (including at least 5 of	124/141 (aged 7.8 years range 5.7-10 years) had history of lower tract infection. 17/124 (9.1 years, range 5.7-11) had mixed UTI, upper in 5 and both upper and lower in 12. According to the working definitions no behavioural or functional abnormalities were found in 20/141 (14%) of girls with recurrent UTI. 212 abnormalities were found in 121 girls (aged 8.1 years, range 6-10 years). Two, three or four concomitant abnormalities were found in 66 patients. Girls without abnormalities were significantly younger (5.1 years, range 3.3-7.9 vs. 8.1 years, range 6-10, p<0.05). Girls with dysfunctional voiding (n=25) were significantly older than other girls with abnormalities (n=96) (10.1 years, range 7.6-11, p<0.02 – mean and range for remaining 96 girls not reported). Infrequent voiding 63/141 (45%) Poor fluid intake 60/141 (43%) Functional stool retention 30/141 (21%) Inadequate genital hygiene 27/141 (19%) Dysfunctional voiding 25/141 (18%) Bladder over-activity 7/141 (5%) In micturating cystourethrogram performed in 61 patients. Of the 32 with voiding dysfunction, 13 (41%) were found to have vesicoureteral	Very similar study to study carried out in 2001-2003, but covered 1996-1999. Same inclusion/exclusion criteria and outcome measures. No definition of bacteriuria

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				movement, overt encopresis.		the following) - habit of passing urine 3 or less times daily - voiding postponement - increased daytime bladder capacity - daytime urinary incontinence - diminished sensation of bladder fullness - staccato or fractionated voiding - incomplete bladder emptying Bladder overactivity (at least 3 of the following) - habit of passing urine 7 or more times daily - frequent attacks of imperative urge to void - daytime urge incontinence - hold or squatting maneuvers - reduced daytime bladder capacity Functional stool retention (at least 3 of the following) - 72-hour or more interval between bowel movements - habit of passing small hard stools - history of painful defecation - stool retention on abdominal examination after defecation. Poor fluid intake (from beverage and plain water) Daily fluid intake of less than 600ml/m^2 body surface area or less Inadequate genital hygiene or toilet habits (at least 3 of the following) - underpants frequently contaminated with fecal material at the end of the day - passing toilet paper back to	reflux. Refux was unilateral in 12 (grade I in 4, grade II in 6 and grade III in 2 patients) and bilateral in one case (grade III). Among the 29 remaining patients vesicoureteral reflux was found in 10 (34%). Unilateral in 7 (grade I in 2, grade II in 3 and grade III in 2 patients) and bilateral in 3 patients (one patient each in grade I, II and III)	

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						front or using the same piece of paper 2 or more times - use of tight fitting clothes - toilet trained child aged 5 years or less - small children using regular toilets (rather than a potty chair)		
Ece A;Tekes S;Gurkan F;Bilici M;Budak T; 2005 Aug [224]	Study Type: Case-control Evidence level: 2+	To investigate whether the angiotensin converting enzyme (ACE) and angiotensin II type 1 receptor gene polymorphisms were associated with the renal scar formation secondary to recurrent UTI in children without uropathy. Only baseline data from this study was used.	97 children (81 girls and 16 boys)	97 children with recurrent UTI (16 males and 81 females) aged 6.34 years (± 3.16 years). Exclusions: Underlying primary VUR, neurogenic bladder, bladder dysfunction, lower urinary tract obstruction, renal hypoplasia, ectopic kidney. Definition of UTI: Fever, flank pain, increased ESR, positive CRP, positive urine culture, positive LE or nitrite dipstick. Recurrence at least two attacks of UTI in a patient – cystitis was not regarded as a recurrent UTI.		Age at first UTI Renal scarring (on DMSA performed following 3 month period free from UTI) Number of recurrences Micro-organism isolated	Children with renal scarring vs. children with no renal scarring, p-value Recurrent UTI (6.90 ± 2.45 UTI episodes vs. 3.35 ± 1.48 UTI episodes, p<0.001) Age at initial UTI (2.61 ± 1.52 years vs. 3.52 ± 2.17 years, p=0.040) Age (years) 6.92 ± 3.20 years vs. 6.05 ± 3.15, p>0.05) Gender (male/female) 8/22 vs. 8/59 p>0.05 Micro-organism isolated (*E.coli* /non-*E.coli*) 25/5 vs. 56/11 p>0.05 Follow-up period 3.88 ± 1.97 vs. 3.07 ± 1.86 p>0.05	Only data relevant to the predictors of recurrence was used from this study.
Kropp KA;Cichocki GA;Bansal NK; 1978 Oct [225]	Study Type: Cohort Evidence level: 2-	To investigate the relationship between pinworm infestation and in introital cultures in children with recurrent UTI and those without UTI.	41 girls with recurrent UTI compared to 58 age-matched controls	Cases - 40 girls (mean age 5.5 years) referred for evaluation of at least 2 recurrent urinary tract infections documented by culture. Controls - 62 girls with no history of urinary, vaginal or pinworm infections, seen at a walk-in clinic. Exclusions - one girl in the control group had asymptomatic UTI and was included as a case	Scotch tape test introital swab (at the level of the hymenal ring) Mid-stream urine sample taken	Outcome Measures: Positive scotch tape test Introital enterics urine sample positive	9/41 (22%) with recurrent UTI had a positive scotch tape test compared to 3/58 (5%) of controls 31/41 (75%) of girls with recurrent UTI had a positive introital enterics culture compared to 25/58 (43%) of controls	Patient characteristics not presented, so unclear whether groups are comparable. Causal relationship assumed No statistical analysis attempted.

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				for analysis. Three scotch tape tests were lost or uninterpretable in the control group and were excluded leaving 58 in the control group and 41 in the case group				

Antibiotic prophylaxis

Bibliographic Information	Study Type & Evidence Level	Study Aims	Number of Patients	Patient Characteristics	Intervention & Comparison	Follow-up & Outcome Measures	Effect Size	Reviewer Comments
Savage DC;Howie G;Adler K;Wilson MI; 1975 229	Study Type: RCT Evidence level: 1+	To decide whether prescriptive screening of school age girls is necessary by investigating the effect of antibiotic therapy.	63 girls, 34 in the control group and 29 in the treated group.	Girls aged 5 to 7 years 10 months found to have covert bacteriuria during a screening program of 5 year old girls entering school in 1969 and 1970 in Dundee. Girls were also included who had been detected in 1968 and re-screened in 1969 and 1970. Girls with history of urinary tract infection were excluded.	Intervention: Children with normal IVP and MCUG received 3 months prophylaxis initially and after their first relapse. Later relapses received 6 months prophylaxis. Children with evidence of pyelonephritis and/or VUR received 6 months prophylaxis, and following a relapse, 6-12 months was given. Prophylactic antibiotics were ampicillin, nitrofurantoin or co-trimoxazole. Comparison: Treatment vs. no treatment	Follow-up period: 3 years. Mean period of follow up 44 months (28 to 68 months) Outcome Measures: Persistent infection Recurrent infection Radiological abnormalities Renal growth	PERSISTENT OR RECURRENT INFECTION Treatment group vs. control group Persistent or recurrent infection Within 6 months: 7/29 (24%) 22/32 (69%) ($p<0.01$) Within 12 months: 14/29 (48%) vs. 24/32 (75%) Within 2 years: 20/27 (74%) vs. 27/32 (84%) Infected urine in 3rd year: 11/27 (41%) vs. 19/30 (63%) 4th year: 12/26 (46%) vs. 16/27 (59%) Number of recurrences during years 3 and 4 7/26 (27%) vs. 5/27 (19%) Number of recurrences since diagnosis 6/29 (21%) vs. 3/32 (9%) Treatment group (normal radiology, abnormal radiology) vs. control group (normal radiology vs, abnormal radiology) Persistent or recurrent infection Within 6 months: (16/24 (67%), 6/8 (75%)) vs. (4/18 (22%), 3/11 (27%)) ($p<0.05$) Within 12 months: (18/24 (75%), 6/8 (75%)) vs. (11/18 (61%), 3/11 (27%)) Within 2 years: (20/24 (83%), 7/8 (88%)) vs. (12/18 (67%), 8/9 (89%)) Infected urine in 3rd year: (13/22 (59%), 6/8 (75%)) vs. (8/18 (44%), 3/9 (33%)) 4th year: (11/19 (58%), 5/8 (63%)) vs. (7/18 (39%), 5/8 (63%)) Number of recurrences during years 3 and 4 (4/19 (21%), 1/8 (13%)) vs. (5/18 (28%), 2/8 (25%)) Number of recurrences since diagnosis (3/24 (13%), 0/8 (0%)) vs. (5/18 (28%), 1/11 (9%)) RADIOLOGY 20/29 children in the treatment group were available for radiological investigation 2 years after initial diagnosis, while 30/34 children in the control group were available. Treatment group Normal renal tract (n=17). 16 no change, 0 improved, 1 worse. Pyelonephritis and/or reflux (n=10). 6 no change, 2 improved, 2 worse.	

Bibliographic Information	Study Type & Evidence Level	Study Aims	Number of Patients	Patient Characteristics	Intervention & Comparison	Follow-up & Outcome Measures	Effect Size	Reviewer Comments
							Control group Normal renal tract (n=22). 20, no change, 0 improved, 2 worse Pyelonephritis and/or VUR (n=8). 4 no change, 1 improved, 3 worse. RENAL GROWTH Initial renal length in cm (mean ± sd) Treated, normal radiology (n=26 kidneys) 9.13 ± 0.69 Controls, normal radiology (n=49 kidneys) 9.15 ± 0.81 Treated, abnormal radiology (10 kidneys) 8.9 ± 1.1 Controls, abnormal radiology (11 kidneys) 8.7 ± 1.1 Renal growth in 32 years in cm (mean ± sd) Treated, normal radiology (n=20 kidneys) 0.95 ± 0.58 Controls, normal radiology (n=37 kidneys) 0.67 ± 0.33 Treated, abnormal radiology (7 kidneys) 0.43 ± 0.31 Controls, abnormal radiology (9 kidneys) 0.44 ± 0.41	
Selkon JB;Roxby CM;Sprott MS; 1981 227	Study Type: RCT Evidence level: 1+	To investigate whetner screening programmes can be recommended by showing whether tretment of asymptomatic bacteriuria and progressive scarring can be prevented by prophylaxis.	252 girls, 41 found to have renal involvement at the initial assessment were given prophylaxis, while 211 girls were randomised to receive prophylaxis (n=105) or no treatment (n=106).	Girls aged 4 to 18 years found to have covert bacteriuria during a school screening program between 1968 and 1972 in Newcastle. Bacterial count of 10^5 organisms/ml in at least 2 of the 3 specimens was considered to have significant bacteriuria and was referred to hospital. Girls with history of urinary tract infection were excluded.	Intervention: Initial examination included 6 mid-stream urine samples collected at weekly intervals, IVU and MCUG. Girls found to have initial renal involvement were prescribed prophylaxis for 2 years and each was reviewed on a cse-by-case basis following the two years. Girls in the prophylaxis group were given a 2 year course of either co-trimoxazole, nalidixic acid, ampicillin or nitrofurantoin and treatment was stopped after 2 years if it had been effective in the previous 6 months. If during follow up children randomised to the no treatment group developed symptoms suggesting a UTI and had a positive cultures, 10 day antibiotic treatment was given. Comparison: Treatment vs. no treatment	Follow-up period: All children were seen at 3 and 6 months after the first investigation and then at intervals of 6 months. At the 2 year and 5 year visits, IVU was repeated. MCUG was repeated at the clinicians discretion. Outcome Measures: Natural resolution of bacteriuria Symptomatic UTI Renal growth	No treatment Number becoming abacteriuric at each visit (cumulative total) 1st visit – 5 (5) 3 months – 7 (12) 6 months – 3 (15) 1 year – 7 (22) 2 years – 4 (26) 3 years – 7 (33) 4 years – 9 (42) 5 years – 6 (48) Among the 52 remaining girls, 23 had been given antibiotics at some time during the follow up period either for symptomatic UTI, or for other infections. There were no significant differences in the proportion of girls who became abacteriuric by age. SYMPTOMATIC DISEASE No treatment Acute pyelonephritis = 5 Symptoms suggesting cystitis = 4 A further 9 girls were prescribed antibiotics for pyuria, frequency, haematuria, enuresis or poor kidney growth over the 5 year period. An additional 5 were prescribed antibiotics for other infections. Prophylaxis Acute pyelonephritis = 3 Symptoms suggesting cystitis = 7	Not all girls recruited were randomised. This will over-estimate the treatment effect.

Bibliographic Information	Study Type & Evidence Level	Study Aims	Number of Patients	Patient Characteristics	Intervention & Comparison	Follow-up & Outcome Measures	Effect Size	Reviewer Comments
							A further 5 were prescribed antibiotics for other infections. RADIOLOGY Radiology measurements were available for analysis in 91 girls in the prophylaxis group and for 92 in the no treatment group. Follow up data was available from 173 children at 2 years and for 112 at 5 years. Regression analysis showed no differences in renal growth over 5 years between the groups. In children with initially Normal renal tract (n=22). 20, no change, 0 improved, 2 worse Pyelonephritis and/or VUR (n=8). 4 no change, 1 improved, 3 worse.	
Lindberg U;Claesson I;Hanson LA; 1978 [228]	Study Type: RCT Evidence level: 1+	To describe the clinical course of treated or untreated asymptomatic bacteriuria over three years in school aged girls.	116 girls with asymptomatic bacteriuria identified and after exclusion od those with scarring and/or reflux, and then those in whom bacteriuria was eliminated 61 girls were randomised, 31 in the control group and 30 in the treated group.	Girls aged 7 to 15 years found to have asymptomatic bacteriuria during a screening program. Bacterial count of 10^5 organisms/ml was considered to be significant bacteriuria.	Intervention: IVP and MCUG after three years of follow-up. Antibiotic therapy for symptomatic cystitis was 10 day nitrofurantoin and for pyelonephritis sulphafurazole. Prophylaxis was nitrofurantoin. Comparison: Treatment vs. no treatment	Follow-up period: Outcome Measures: Bacteriuria on follow up Symptomatic UTI	27/30 children in the treatment group were followed up for three years. 9/27 (33%) were given long-term prophylaxis because of repeated recurrences; 6/9 continued to have recurrences after 3 years prophylaxis. 13/27 required antibiotic treatment (short-course) for an episode of bacteriuria, and an additional 5/27 required two short courses of treatment, however there were no further recurrences in either group. 30/31 children in the untreated group were followed for 3 years. 9/31 (30%) became spontaneously abacteriuric and none had recurrences. 5/31 (17%) became abacteriuric after penicillin for respiratory infection. 1/30 (3%) had symptomatic pyelonephritis and 1/30 (3%) had dysuria during an episode of measles. 14/30 (47%) remained bacteriuric after three years. Growth of kidneys in these children was normal, there were no signs of scarring. One child developed grade I reflux. There were no significant differences in the number of bacteriuric children in the treatment group (6/27) compared to the untreated group (14/30) at the end of the observation period.	Only half of the original number of girls recruited were randomised. This will over-estimate the treatment effect. Allocation concealment not reported Blinding not reported
Cardiff-Oxford 1978 Apr 29 [226]	Study Type: RCT Evidence level: 1+	To determine the sequeale of covert bacteriuria in girls of school age and whether treatment could prevent any or all of the effects.	208 girls (110 girls treated 98 girls not treated)	Girls identified as having cover bacteriuria for screening study [262] Bacteriuria defined as <10^5cfu/ml in at least 2 consecutive mid-stream samples.	Intervention: Treatment with antibacterial therapy for bacteriuria (usually given co-trimoxazole but also ampicillin, nitrofurantoin, nalidixic acid and pivmecillinam, initally 7 or 14 day course were given but longer courses at discresion of Dr) Controls received no treatment	Follow-up period: from date of first x ray to second four years (± 0.3 years) later. Outcome Measures: time free from infection emergence of symptoms clearence of VUR kidney growth progression of kidney	Bacteriuria at end of study: 17/110 (15%) in treatment girls and 44/98 (45%) in girls with no treatment (chi2=20, p < 0.001) 28/98 (29%) in the treatment group were scarred at the first x-ray 12/110 (15%) in the treatment group were scarred at the first x-ray No new scars were seen in girls who had normal kidneys at the initial x-ray examination Of the girls with scars at the initial x-ray new and/or deepening scars were found in 12/44 (27%). 6/28 (21%) in the girls who received treatment and 6/16 (38%) in the girls who received no treatment.	Allocation concealment not reported. Blinding not reported 7 girls excluded - reason for exclusion unknown. Loss to follow-up was 13% in the treated group and 19% in the control group. This is a 16%

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					During the study period (date of first x-ray till the date of the second, mid-stream urine samples were collected monthly in one health distric (Oxford) and every two months in the other (Cardiff). Comparison: treatment versus control	scars		loss overall. No explanation of whether those lost were similar to the girls followed-up. Did not use intention to treat analysis.
Williams GJ;Lee A;Craig JC; 2001 234	Study Type: Systematic review - meta-analysis Evidence level: 1++	Antibiotics to prevent recurrence	Children under 18 years of age who were at risk of recurrence were included.	Four studies met the inclusion criteria. Trial participants were mostly females aged between six months and 14 years. Three trials investigated antibiotics vs. placebo in children with recurrent UTIs and normal renal tracts from 10-12 weeks One trial compared the effectiveness of nitrofurantoin with trimethoprim over a 6 month period. Brendstrup 1009 Study design: RCT with 6 months follow-up. Participants: 4 boys, 126 girls with a mean age of 7.5 (range 1 to 14 years) UTI: Children with UTI in the previous year. 30 had VUR and 30 had abnormality. Interventions: Nitrofurantoin for 6 months. Trimethoprim for 6 months. Outcomes: Number of repeat infections, adverse events Savage 1975 Study design: Randomised open study, no blinding, follow up 6 months. Participants: Girls aged 5	Intervention: Long-term antibiotics vs. placebo and studies that compared two or more antibiotic regimens. Long-term prophylaxis was defined as antibiotic administered daily for a period of at least two months. Comparison: Antibiotic vs. placebo	Follow-up period: Outcome Measures: Primary outcomes Number of children with repeat symptomatic UTI (confirmed by bacterial growth in the urine) Recurrent UTI (defined as repeat UTI caused by different bacteria to the initial infection) Secondary outcomes Total number of symptomatic recurrent UTIs Adverse reactions to treatment Hospitalisation with UTI UTI with fever	Antibiotic vs. placebo, outcome risk of recurrent UTI Compared to placebo, antibiotics reduced the risk of recurrent UTI (RR 0.36, 95%CI 0.16 to 0.77; RD -46%, 95%CI -59% to -33%) There were no significant differences in the rate of recurrent UTI in control groups (chi2 = 1.29, df = 2, p=0.52) Overall recurrent UTI rate in the placebo group 48/76 (63%), and in the treatment group 15/75 (20%). No reported antibiotic side effects or hospitalisation with recurrent UTI. Antibiotic vs. placebo, outcome quality of the studies Compared to placebo, antibiotics reduced the risk of recurrent UTI in two studies where allocation concealment was unclear or inadequate with no blinding (RR 0.42, 95%CI 0.26 to 0.67; RD -40%, 95%CI -58% to -23%). Risk of recurrent UTI reduced when allocation concealment was adequate with double blinding (RR 0.04, 95%CI 0.0 to 0.67; RD -54%, 95%CI -75% to -34%) Antibiotic vs. placebo, outcome VUR vs. non-VUR One study reported incidence separately. Compared to placebo, antibiotics reduced the risk of recurrent UTI in children without VUR was (RR 0.43, 95%CI 0.25 to 0.73; RD -39%, 95%CI -58% to -20%). In children with VUR the RD was -52% (95%CI -71% to -35%). Antibiotic duration There was a reduction in the risk of recurrent UTI by antibiotics over placebo if the antibiotic was used for 10 weeks, six months or 12 months. There was a similar risk reduction in recurrent UTIs with nitrofurantoin (40%) or cotrimoxazole (43%). Nitrofurantoin vs. Trimethoprim One study investigated compared the effectiveness of nitrofurantoin with trimethoprim over a 6 month period. Nitrofurantoin was more effective in preventing recurrent UTI than trimethoprim (RR 0.48, 95%CI 0.25 to 0.92; RD -18%, 95%CI -34% to -3%). However, patients receiving nitrofurantoin were three times more likely to discontinue the antibiotic due to side effects (nausea, vomiting or stomach ache) than patients receiving trimethoprim (RR 3.17,	Methodological quality of the trials was poor. One trial had inadequate allocation concealment, two did not state the method of randomisation, and two used no blinding at all. None of the studies used intention-to-treat analysis.

Bibliographic Information	Study Type & Evidence Level	Study Aims	Number of Patients	Patient Characteristics	Intervention & Comparison	Follow-up & Outcome Measures	Effect Size	Reviewer Comments
				to 7 years 10 months. UTI: Proven UTI (three consecutive urine samples) 19 had VUR. Interventions: Nitrofurantoin for 10 weeks after acute treatment or Cotrimoxazole twice daily for 10 weeks after acute treatment. Comparison: No treatment for 10 weeks after acute treatment with ampicillin Outcomes: Number of repeat infections Smellie 1978 Study design: Randomised open study, no blinding, follow up 1 year. Participants: 5 boys and 40 girls between 2 and 12 years. UTI: Proven UTI. No children with VUR Interventions: Low dose Cotrimoxazole for 6 to 12 months or Nitrofurantoin for 6 to 12 months. Comparison: No treatment. Outcomes: Number of repeat infections. Stansfield 1975 Study design: Randomised double blinded, follow up 6 months. Participants: 3 boys and 42 girls aged 6 months to 14 years. UTI: Proven UTI (two or consecutive urine samples + pyuria). 10 children had VUR Interventions: Cotrimoxazole for 6			95%CI Side effects of nitrofurantoin may outweigh its prophylactic effects (NNH = 5, 95%CI 3 to 13) compared with trimethoprim (NNT = 5, 95%CI 3 to 33).	

Bibliographic Information	Study Type & Evidence Level	Study Aims	Number of Patients	Patient Characteristics	Intervention & Comparison	Follow-up & Outcome Measures	Effect Size	Reviewer Comments
				months Comparison: Placebo tablets for 6 months Outcomes: Number of repeat infections.				
Wheeler DM;Vimalachandra D;Hodson EM;Roy LP;Smith GH;Craig JC; 2004 235	Study Type: Systematic review - meta-analysis Evidence level: 1++	Anitbiotics for children with VUR	847 children of any age with primary VUR diagnosed by MCUG following a UTI were included in 7 RCTs.	10 studies met the inclusion criteria of the systematic review. Seven trials were included for the review of the guideline. One trial compared prophylaxis with no treatment and is reported in the prophylaxis section of the guideline. Two additional studies compared materials for endoscopic correction of VUR and are outside the scope.	Intervention: Treatments of VUR including surgery (open and endoscopic techniques) and antibiotic prophylaxis of any duration. Comparison:	Follow-up period: Outcome Measures: UTI Renal parehcnymal abnormality	Antibiotic prophylaxis vs. no treatment There was no significant difference between daily antibiotic prophylaxis and no prophylaxis (RR 0.25, 95%CI 0.03 to 1.83) or between three day a week prophylaxis and no prophylaxis (RR 0.46 95%CI 0.10 to 2.00) There were no differences in the risk of renal parenchymal damage between daily antibiotic prophylaxis and no prophylaxis (RR 0.40 95%CI 0.02 to 9.18) or between three day a week prophylaxis and no prophylaxis (RR 0.38 95%CI 0.02 to 8.59).	Birmingham reflux study only enrolled children with dialating reflux (grades 3 to 5). International reflux study only enrolled children with grades 3 to 4 reflux – children with grade 5 were excluded.
Garin EH;Olavarria F;Garcia N;Valenciano B;Campos A;Young L; 2006[71]	Study Type: RCT Evidence level: 1+	Antibiotics for children with and without VUR	Children with VUR (n=113), 55 received prophylaxis, 58 no prophylaxis Children without VUR (n=105), 45 received prophylaxis, 60 no prophylaxis.	Children aged 3 months to 18 years (average 2 years) Inclusion: Documented episode of acute pyelonephritis. Children with fever (>38.5°C), pyuria (<10 white cells per hpf) and significant bacteriuria (>10[5]cfu/ml) underwent DMSA 2 to 7 days following diagnosis of UTI. Those with typical acute pyelonephritis findings on DMSA were included. Acute pyelonephritis defined as focal or diffuse areas of decreased DMSA uptake without evidence of cortical loss. Renal scar defined as decreased uptake associated with loss of the contours of the kidney or cortical thinning with	Intervention: At entry children underwent urinalysis, urine culture, VCUG and renal ultrasound DMSA was obtained at 6 months following febrile UTI. Gentamicin, cefadroxil, cefuroxime, ceftriaxone, or cefotaxime intravenously for 5 to 7 days (standard dose). Oral antibiotics were given to complete a total antibiotic course of 14 days. Children assigned to prophylaxis received either TMP/SMX (1-2mg/kg once daily), or nitrofurantoin (1.5mg/kg once daily) for one year. Children were examined at an outpatient clinic at 3 month intervals. VCUG and ultrasound were repeated at one year. Comparison: Antibiotic vs. no	Follow up period: One year Outcome measures: frequency of UTIs (recurrence) Renal parenchymal damage	Baseline characteristics similar, no significant differences in the median age or gender. The group with VUR who were randomised to receive prophylaxis had a median age of one year older (3 years vs. 2 years) compared to the other groups, but the difference was not significant. In children with VUR there were no significant differences in the grade of reflux. Rates of spontaneous resolution of VUR after one year were 37.5 (grade I), 12.5% (grade II) and 10.3% (grade III). Resolution rates did not differ between groups. <u>Recurrence</u> The incidence of recurrent UTI following pyelonephritis was 20.1%. 17.5 recurrences occurred within the first three months following pyelonephritis, 17.5% between 3 and 6 months, 12% between 6 and 9 months and 53% between 9 and 12 months. The recurrence of pyelonephritis was small (12/218) compared to children who had a recurrence of cystitis or of asymptomatic bacteriuria (32/218). Of the children not receiving prophylaxis 22.4% with VUR had a recurrence compared to 23.3% of children who did not have VUR (p=0.9). Recurrent pyelonephritis was observed in 7 children compared to only one of the children who did not receive prophylaxis (p=0.0291), however in all 7 cases the bacteria showed resistance to the antibiotic used. Of the children receiving prophylaxis, 23.6% with VUR had a recurrence compared to 8.8% of children who did not have VUR. Children with VUR	No intention to treat analysis. Exit criteria stated. Randomisation method not described.

Bibliographic Information	Study Type & Evidence Level	Study Aims	Number of Patients	Patient Characteristics	Intervention & Comparison	Follow-up & Outcome Measures	Effect Size	Reviewer Comments
				decreased volume. Exclusions: Presence of grades 4 or 5 reflux, neurogenic bladder, posterior urethral valves, urinary diversion, bladder diverticulum ureterocele, renal failure and pregnancy. Exit criteria: 2 episodes of pyelonephritis during the year of follow up monitoring, failure to comply with urinary antibiotic prophylaxis and loss to follow-up monitoring.	antibiotic		Prophylaxis 0 asymptomatic 6 cystitis 7 pyelonephritis 42 no recurrence No prophylaxis 3 asymptomatic 9 cystitis 1 pyelonephritis 45 no recurrence Children without VUR Prophylaxis 1 asymptomatic 1 cystitis 2 pyelonephritis 41 no recurrence No prophylaxis 4 asymptomatic 8 cystitis 2 pyelonephritis 46 no recurrence Renal scars 13/218 children developed renal scars during the one year follow up period. There were no differences between those with VUR and those without, nor between those receiving prophylaxis compared to no prophylaxis. Children with VUR 5/55 prophylaxis 2/58 no prophylaxis Children without VUR 2/45 prophylaxis 4/60 without prophylaxis No evidence that VUR increased the likelihood of developing renal scars (p=0.99)	

Prevalence of structural abnormality of urinary tract

Bibliographic Information	Study Type & Evidence Level	Study Aims	Number of patients	Patient Characteristics	Intervention and comparison	Follow-up & Outcome Measures	Effect Size	Reviewer Comments
Biyikli NK;Alpay H;Ozek E;Akman I;Bilgen H; 2004 Feb 118	Study Type: Case series Evidence Level: 3	To analyse the clinical presentation, causative agents, imaging findings and recurrence rates.	71 neonates with UTI	Neonates treated for UTI between 1999-2000 at hospital, followed up for at least 6 months, excluded neonates with spina bifida UTI diagnosed as growth of the microorganisms over 10000 cfu/ml in a cateterized urine specimen. Nosocomial UTI defined as a positive urine culture detected 48 hours after admission.	Intervention: Clinical presentation, causative agents, imaging findings and recurrence rates.	Outcome: Risk of UTI when pre-term v. not pre-term Assessed by Chi square. Follow-up: Mean follow-up 12 months (range 6 months to 36 months)	Mean age at diagnosis: 18.1±11.2 days, follow up for 12±6 months. 54/71 (76%) boys and 17/71 (24%) girls 29/71 (41%) were preterm (gestational age 27-37 weeks) 3/71 were small for gestational age Symptoms and signs Signs of sepsis 15/29 (53%) preterm neonates, Hyperbilirubinemia 8/29 (26%) preterm neonate Asymptomatic 6/29 (21%) Hyperbilirubinemia 24/42 (57%) term neonates Signs of sepsis 15/42 (36%) term neonates Asymptomatic in 3/42 (7.1%) The signs of sepsis were: irritability 11/71 (15%) fever or hypothermia 6/71 (8%) respiratory distress 6/71 (8%) feeding problems 4/71 (5%) vomiting 3/71 (4%) abnormal crying 3/71 (4%) poor weight gain 2/71 (2%) rash 1/71 (1%) Asymptomatic 9/71 (13%) Community acquired 45/71 (63%) and nosocomial 26/71 (37%) Causative agents for community acquired: 44% Escherichia coli, 31% Klebsiella pneumonia, 3% Enterobacter cloacae, 3% Candida albicans, 9% Enterococcus fecalis, 4% Straphylococcus aureus, 3% Group B Streptococcus, 3% Serratia marcessens and 3% Proteus vulgaris. Causative agents for nosocomial: 50% Klebsiella pneumonia, 38% Escherichia coli, 4% Pseudomonas aeruginosa, 4% Proteus vulgaris and 4% Klebsiella oxytoca. Pyria detected in 12/29 (41%) preterm neonates and 29/42 (69%) term neonates 66 neonates who underwent USG scan, 15/66 (23%) had abnormalitys such as renal pelvis dilation, hydronephrosis, or hyperecogenic kidney. VCUG performed in 46 neonates and DMSA scan in 36 neonates. Reflux was found in 7/46 (15%) neonates. 8/36	

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							(23%) showed renal photopenic areas on DMSA. 2 had ureteropelvic junction stenosis and 2 had posterior uretral valve Follow up 20/71neonates had reucurrent UTI, 8/71 had 2 or more recurrences.	
Mazzola BL;von Vigier RO;Marchand S;Tonz M;Bianchetti MG; 2003 Jan 223	Study Type: Case-series Evidence Level: 3	To evaluate the role of family history, infrequent voiding, poor fluid intake, functional stool retention and inadequate anogenital hygiene or toilet habits in girls with recurrent UTIs.	141 girls	Girls aged 3.9 to 18 years (median 6.5 years) referred to a nephrology clinic for evaluation of three or more symptomatic UTIs. None of the girls had a recent UTI (6 weeks or less). 81 were referred by GPs and 60 referred by paediatricians. Exclusions: first infection under 36 months, asymptomatic infection, adolescents with a history of sexual activity, history or findings suggestive of sexual abuse, known urinary tract malformations, neuropathic bladder, moderate to severe mental retardation, disorders of posture or movement, overt encopresis.	Intervention: Complete history, bowel and bladder questionnaire, physical and neurological examination and urinalysis. A bladder scan measured post-micturation volume The volume of any intake or urination was recorded for three days by a voiding-drinking diary.	Lower tract infection: history of alguria, incontinence, urgency, frequency or suprapubic pain. Upper tract infection: Additional history of chills, fever (rectal body temperature 38.5°C or more) and abdominal or back pain. Volume of any intake or urination (by graduated measuring cup) Infrequent voiding (include at least 2 of the following) - habit of passing urine 3 or less times daily - voiding postponement - increased daytime bladder capacity - daytime urinary incontinence Presumed dysfunctional voiding (including at least 5 of the following) - habit of passing urine 3 or less times daily - voiding postponement - increased daytime bladder capacity - daytime urinary incontinence - diminished sensation of bladder fullness - staccato or fractionated voiding - incomplete bladder	124/141 (aged 7.8 years range 5.7-10 years) had history of lower tract infection. 17/124 (9.1 years, range 5.7-11) had mixed UTI, upper in 5 and both upper and lower in 12. According to the working definitions no behavioural or functional abnormalities were found in 20/141 (14%) of girls with recurrent UTI. 212 abnormalities were found in 121 girls (aged 8.1 years, range 6-10 years). Two, three or four concomitant abnormalities were found in 66 patients. Girls without abnormalities were significantly younger (5.1 years, range 3.3-7.9 vs. 8.1 years, range 6-10, p<0.05). Girls with dysfunctional voiding (n=25) were significantly older than other girls with abnormalities (n=96) (10.1 years, range 7.6-11, p<0.02 – mean and range for remaining 96 girls not reported). Infrequent voiding 63/141 (45%) Poor fluid intake 60/141 (43%) Functional stool retention 30/141 (21%) Inadequate genital hygiene 27/141 (19%) Dysfunctional voiding 25/141 (18%) Bladder over-activity 7/141 (5%) In micturating cystourethrogram performed in 61 patients. Of the 32 with voiding dysfunction, 13 (41%) were found to have vesicoureteral reflux. Refux was unilateral in 12 (grade I in 4, grade II in 6 and grade III in 2 patients) and bilateral in one case (grade III). Among the 29 remaining patients vesicoureteral reflux was found in 10 (34%). Unilateral in 7 (grade I in 2, grade II in 3 and grade III in 2 patients) and bilateral in 3 patients (one patient each in grade I, II and III)	Very similar study to [219] carried out in 2001-2003, but covered 1996-1999. Same inclusion/exclusion criteria and outcome measures. No definition of bacteriuria

Bibliographic Information	Study Type & Evidence Level	Study Aims	Number of patients	Patient Characteristics	Intervention and comparison	Follow-up & Outcome Measures	Effect Size	Reviewer Comments
						emptying Bladder overactivity (at least 3 of the following) - habit of passing urine 7 or more times daily - frequent attacks of imperative urge to void - daytime urge incontinence - hold or squatting maneuvers - reduced daytime bladder capacity Functional stool retention (at least 3 of the following) - 72-hour or more interval between bowel movements - habit of passing small hard stools - history of painful defecation - stool retention on abdominal examination after defecation. Poor fluid intake (from beverage and plain water) Daily fluid intake of less than 600ml/m^2 body surface area or less Inadequate genital hygiene or toilet habits (at least 3 of the following) - underpants frequently contaminated with fecal material at the end of the day - passing toilet paper back to front or using the same piece of paper 2 or more times - use of tight fitting clothes		

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						- toilet trained child aged 5 years or less - small children using regular toilets (rather than a potty chair)		
Cascio S;Chertin B;Yoneda A;Rolle U;Kelleher J;Puri P; 2002 236	Study Type: Other Evidence Level: 3	To determine the incidence of urinary tract anomalies in a selected group of infants younger than 8 weeks of age, with no prenatal diagnosis of hydronephrosis who were admitted to the hospital with a documented febrile UTI.	57 infants (42 boys, 15 girls)	Infants younger than 8 weeks who were hospitalised with UTI. Investigation included DMSA and ultrasound within 72 hours of admission to hospital and voiding cystourethrography at least 6 weeks after UTI.			Urinary tract anomalies were detected in 20 (35%) patients. VUR was found in 9 (33%) neonates, 7 girls and 12 boys. DMSA scan was abnormal in 33 (58%) infants; 8 (53%) of girls and 25 (60%) of boys. Renal parenchymal defects were unilateral in 22 patients and bilateral in 11. Focal defects in uptake were detected in 19 (50%) neonate's kidneys with VUR and in 25 (33%) of 76 kidneys without VUR (p>0.05).	
Honkinen O;Jahnukainen T;Mertsola J;Eskola J;Ruuskanen O; 2000 Jul 263	Study Type: Case-series Evidence Level: 3	To assess the clinical characteristics of bacteraemic UTI in children	134 children with serious bacteremic UTI located from all 36 Finish hospitals and 25 microbiological laboratories, between 1985 and 1994 Comparison group 134 age and sex matched from children hospitilised for blood culture negative symptomatic UTI	Children aged 7 days to 9.5 years (median 0.125 years) with serious bacteremic UTI. Inclusion criteria were symptoms of acute illness such as fever, irritability, vomiting or dysuria; bacterial growth ≥105 in one midstream urine or in two urine bag samples; growth of identical pathogen both in the blood and in the urine cultures; first known urinary tract infection; and no known urinary tract abnormality or other severe underlying disease. 29 children had a history of UTI or urinary tract abnormality or other severe underlying disease. 7 children were under 1 week old and analysed separately		Age and sex distribution of bacteremic UTI Symptoms and signs laboratory findings microbiological findings	Age and Sex distribution: 61% boys, 39% girls Age range 7 days to 9.5 years (median 0.125 years) 66% were 1 week to 3 months of age (69% of youngest age group were boys, this male dominance decreased with age) 22% 3 to 11 months 12% ≥ 12 months Annual incidence in Finland of bacteremic UTI in children <16 years of age and without previous UTI infection or underlying disease during the study period was 1.5/100000. Results reported bacteremia patients vs. nonbacteremic patients Symptoms Fever 124 (92%) v 121 (90%) The duration of the preceding fever (mean, 1.9 ± 1.9 vs. 1.8 ± 1.7 days) was not different between groups. Irritability 81 (60%) v 75 (56%) Abnormal crying 46 (34%) v 41 (30%) Vomiting 22 (16%) v 18 (13%) Lethargy 35 (26%)v 41 (30%) Feeding problems 27 (20%) v 13 (10%) p = 0.02 Abdominal pain 10 (7%) v 4 (3%) Dysuria 2 (1%) v 4 (3%) Convulsions 5 (4%) v 0 (0%) Laboratory findings White blood cell count	Some of the Children included in this study may have been included in the study [240]

Bibliographic Information	Study Type & Evidence Level	Study Aims	Number of patients	Patient Characteristics	Intervention and comparison	Follow-up & Outcome Measures	Effect Size	Reviewer Comments
							18.2 ± 7.4 x 109/l (n = 127) vs.19.1 ± 8.2 x 109/l (n = 133) NS Mean CRP on admission 116 ± 67 mg/l (n = 134) vs. 76 ± 56 mg/l (n = 132) p < 0.01. Hyponatremia (sodium concentration ≤ 130 mmol/l) occurred in 9/81 (11%) bacteremic patients and 4/65 (6%) on nonbacteremic patients No differences were found in the mean sodium, potassium or creatinine concentrations Microbiological findings E. coli 114/134 (85%) vs. 125/134 (93%) of the blood culture negative UTIs (p = 0.04). Staphylococcus aureus caused 6 bacteremic infections and 1 nonbacteremic infection. Imaging studies (results available from 132/134 (98%) of bacteremic patients and 134/134 control patients). Urinary tract abnormalities 51% vs. 46% Grade 3-5 vesicoureteral reflux 40 (30%) vs. 22 (16%) Urinary obstruction 12 (9%) vs. 2 (1%) (p < 0.01). Imaging results of 113/114 children with bacteremic urinary infection caused by E.coli. were available. 52/113 (46%) had a urinary tract abnormality 10/113 (9%) later underwent urinary tract surgery. Imaging results of 19/20 children with bacteremic urinary infection caused by bacteria other then E.coli. were available. 17/19 (89%) had a urinary tract abnormality (p < 0.01 when compared to E-coil infections). All of the patients with Staphylococcus aureus, Klebsiella or Enterococcus faecalis had a urinary tract abnormality. 14/19 (74%) later underwent urinary tract surgery (p < 0.01 when compared to E-coil infections). Imaging results of all 124 children with nonbacteremic urinary infection caused by E.coli. were available. 55/124 (44%) had a urinary tract abnormality and 14/124 (11%) later underwent urinary tract surgery. Imaging results of all 10 children with nonbacteremic urinary infection caused by bacteria other then E.coli. were available. 7/10 (70%) had a urinary tract abnormality (p < 0.19 when compared to E-coil infections). 4/10 (40%) later underwent urinary tract surgery (p = 0.03 when compared to	

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							E-coil infections). Neonates The 7 children < 1 weeks were not enrolled in the comparative analysis. 5 boys and 2 girls. Mean CRP on 1st day 118 mg/l (range 23 to 256 mg/l) Mean WBC 12.2 x 10^9/l (range 3.7 to 22.9 x 10^9/l 1/7 was afebrile 3/7 had normal urinary imaging, 2/7 were operated on for urinary obstruction and 1/7 was operated on for grade 4 reflux and 1/7 had grade 2 reflux.	
Ring E;Zobel G; 1988 Jul [77]	Study Type: Other Evidence Level: 3	Intervention: Ultrasonography, voiding cystourethrography and intravenous pyelography were performed in 110/140 (79%) Comparison:	140 with first UTI over a 48 month peroid	140 infants admitted to a paediatric department with suspected first UTI. Bacteriuria was defined as 10^5 cfu/ml collected by catheterisation or SPA and/or white cell count of more than 20x10^6/l. Ultrasonography, voiding cystourethrography and intravenous pyelography were performed in 110. Malformations were diagnosed prenatally in 39 infants.			38 (27%) infants presented during the first month of life and 80 (57%) during the first 3 months. 23 (16%) infants had their first UTI after they were 6 months old. Boys were significantly younger than girls (p<0.01). During the first three months, boys had 69% of all UTIs. After the first three months, females had 63% of all UTIs (p<0.001). The male:female ratio was 2.2:1 during the first three months and 1:1.7 thereafter. Urinary tract malformations were present in 46 infants (42%). There were no significant differences in age or sex among infants with or without malformations. Of the infants with malformations 61% had urinary tract infections before they were 3 months old. VUR accounted for 59% of all malformations and obstructive uropathy for 37%. During the first two months 12 of 17 (70%) of all obstructive uropathies were diagnosed. In contrast, 66% of all patients with VUR had a UTI after they were 2 months old (p<0.05). Urinary tract obstructions were significantly more common in boys (p<0.01). VUR was more common in girls but not significantly so. 46% of all malformations were diagnosed pre-natally.	Ultrasonography, voiding cystourethrography and intravenous pyelography were not performed in all children, however the majority (79%) received the imaging so unlikely to skew results.
Jodal U; 1987 Dec [47]	Study Type: Case-series Evidence Level: 3	Study 1 Aims unclear Study 2 To survey the frequency of bacteriuria in an unselected infant population and to study the interrelation between asymptomatic and symptomatic bacteriuria	Children aged under ten years with first time symptomatic UTI. Bacteriuria definition: At least 105 bacteria per ml together with leukocyturia in a midstream sample or bag sample. Any growth on SPA Pyelonephritis definition: Bacteriuria and fever of ≥38.5°C and a	1177 children with first time symptomatic UTI (952 girls and 225 boys)		Outcome measures: No. with reflux (and grade) No. with scarring No. of symptomatic recurrences No. with pyelonephritis/cystitis	Study 1 225/1177 (19%) boys 952/1177 (81%) girls Boys 133/225 (59%) of UTIs detected in the first year of life 72/225 (33%) had VUR 8/72 (11%) dilated reflux (grade ≥3) 41/225 (18%) had one recurrence 11/225 (5%) had 2 or more recurrences Girls 181/952 (19%) of UTIs detected in the first year of life 315/952 (34%) had VUR (54% between 1-3 years)	

Bibliographic Information	Study Type & Evidence Level	Study Aims	Number of patients	Patient Characteristics	Intervention and comparison	Follow-up & Outcome Measures	Effect Size	Reviewer Comments
			microsedimentation rate of ≥25mm per hour or CRP ≥20mg/L Cystitis definition: acute voiding symptoms (dysuria, frequency) with temperature <38.5°C and normal laboratory findings. A child with acute symptoms and bacteriuria that could not be classified was said to have 'unspecified UTI'				25/315 (8%) dilated reflux (grade ≥3) 152/952 (16%) had one recurrence 152/952 (16%) had 2 or more recurrences Scarring 15/278 (5%) children with no reflux had scarring 3/29 (10%) of children with grade 1 reflux had scarring 17/99 (17%) of children with grade 2 reflux had scarring 25/38 (66%) children with grade ≥3 reflux had scarring 25% of the total number of children with scarring did not have reflux. Pyelonephritis 7/141 (5%) children with 0 pyelonephritis episode had scarring 32/366 (9%) of children with 1 pyelonephritis episode had scarring 15/98 (15%) of children with 2 pyelonephritis episode had scarring 12/35 (35%) of children with 3 pyelonephritis episode had scarring 14/24 (58%) children with ≥4 pyelonephritis episode had scarring Study 2 All girls with asymptomatic bacteriuria were left untreated: Of 3581 newborns in the study population, 94% entered the study and 68% had all three tests at ages two weeks, three months and ten months. Screening bacteriuria (asymptomatic) Girls 0.9% Boys 2.5% Symptomatic UTI Girls 1.1% Boys 1.2% 89/90 infants with bacteriuria had IVU 85/90 had VCUG Reflux Asymptomatic bacteriuria 5/46 (11%) had grades 1 or 2 reflux. Symptomatic UTI 14/39 (36%) had reflux Abnormalities Asymptomatic bacteriuria Symptomatic UTI 5/39 (13%), 1 child had agenesis of one kidney, one had marked pelvo-ureteric stenosis and 3 had	

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							dilated reflux. Clearing of bacteriuria 11 girls with asymptomatic bacteriuria were left untreated and of these 10 (91%) became abacteriuric within 7 months of detection. 34/36 boys were left untreated and within 11 months 27 (79%) became abacteriuric.	
McKerrow W;vidson-Lamb N;Jones PF; 1984 Aug 4 66	Study Type: Case-series Evidence Level: 3	To report the results of investigation and treatment over a five to fifteen year follow up.	Intervention: IVU performed in 550/572 (96%) MCUG performed in 386 where there was suspicion of bladder abnormality.	572 children (399 girls, 173 boys)	Children aged under 13 years with a history of at least one confirmed urinary tract infection who had been referred by their family doctor to a paediatric surgical outpatient clinic	Number with abnormalities	572 children with UTI Abnormalities found in 51% of children with UTI. 6% had scarred kidneys with no evidence of reflux 31% had reflux (24% of ureters) 7.5% had obstructions 48% had cyctourethritis 7% had duplex kidneys 0.9% had deformities Of the ureters with reflux: 53% were initially treated medically, in 84% of these the reflux ceased 53% were operated on, resulting in no further problems in 65%. Late problems developed in 38% of children aged under 5 years and 12% of children aged over 5 years at diagnosis with ureters that had reflux and kidneys showing reflux nephropathy, treated surgically. The problems included repeat operation to correct reflux, nephrectomy because of deteriorating function, ureterosomy, hypertension and renal failure.	Bacteriuria not defined Not all children had an IVU, however the number who did not have one was small.
Burbige KA;Retik AB;Colodny AH; 1984 138	Study Type: Case-series Evidence Level: 3	To present clinical and laboratory features of UTI	83 boys	Boys aged 2 weeks to 14 years treated at a childrens hospital with first time UTI. (mean age unknown) UTI defined as more than 10^5 cfu/ml.	Intervention: VCUG Comparison: n/a Outcomes: Micro-organism isolated Number with abnormality Symptoms		Of the 83 boys, 25% were ≤1 year old and half were < 6 years old. The incidence of urinary tract abnormalities was distributed evenly through the group. A large proportion of gram-positive organisms (49%) while E.coli accounted for only 21% of infections. When the group with gram-positive infection were investigated more closely, it was found that 40% (16 boys) were febrile at presentation. The presence of a foreskin did not alter the culture results in favour of gram-positive organisms, since 5 of the 8 uncircumcised boys had gram-negative organisms on culture. Gram-positive infections were distributed evenly throughout the group with regard to age. 20 patients (24%) Staphylococcus albus, 18 boys (22%) E.coli, 15 boys (18%) Proteus species, 11 (13%) Staphylococcus aureus, 8 (10%) Enterococcus, and less than 5% of each of Klebsiella, Nonhemolytic streptococcus and Pseudomonas. Of the 83 boys, 75% (62 boys) had an abnormality. 46/62 had VUR owing to abnormal ureterovesical junction, 7 had posterior urethral valves, 6 had Ectopic ureterocele (duplex systems) and 5 had Ureteropelvic junction obstruction. Hydronephrosis and/or renal scarring was present in half of	No definition of fever

Bibliographic Information	Study Type & Evidence Level	Study Aims	Number of patients	Patient Characteristics	Intervention and comparison	Follow-up & Outcome Measures	Effect Size	Reviewer Comments
							this group. Surgery was necessary in 58% (48 boys) with the most common procedure being an anti-reflux procedure. Symptoms Fever 40/83 (48%) and the only presenting sign in 25%. Irritative bladder syndromes 23/83 (28%) Abdominal or flank mass 11/83 (13%) Enuresis 7/83 (8%) Gross hematuria 6/83 (7%)	
Ginsburg CM;McCracken GH; 1982 Apr 116	Study Type: Othercase-series Evidence Level: 3	To present clinical and laboratory features of UTI	100 infants (62 boys, 38 girls)	Infants aged 5 days to 8 months (mean 2.1 months) admitted to one of two hospitals with acute UTI from Mar 1976 to Feb 1981	Intervention: Radiography undertaken in 86/100 children Comparison	Frequency of symptoms and signs	Male infants accounted for 75% of UTI cases within the first three months of life compared with 11% of boys who were 3 to 8 months of age. Of the 41 infants who were under 30 days old, 33 (81%) were boys. Symptoms and signs Fever was the most common symptom (in 63%) and symptoms of irritability (55%), had refused feeds (38%), vomiting (36%) and diarrhoea (31%). 67 infants had a fever of 38 C and 38 infants had fever of 39 C. Abdominal distention and jaundice were only reported in 8% and 7% of patients respectively. Abnormalities 26 abnormalities were identified in 18 patients including unilateral and bilateral reflux (grades II to IV); duplication, hydronephrosis and ureteropelvic obstruction. Abnormalities were more common in girls (45%) compared to boys (7%) (p<0.01).	
Smellie JM;Normand IC;Katz G; 1981 67	Study Type: Case-series Evidence Level: 3	To examine the clinical features of children presenting with UTI to determine whether there were any differences between those with and those without VUR	744 children, 179 boys and 565 girls	Children aged 0 to 12 years treated in a paediatric department with bacteriologically proven UTI. All children were investigated with intravenous urography (IVU) and MCUG.	Age distribution of UTI Symptoms and signs No. with VUR		Age distribution 145/744 (19%) aged >1 year 35/744 (5%) aged 1-2 years 210/744 (28%) aged 2-4 years 249/744 (33%) aged 5-8 years 105/744 (14%) aged 9-12 years 246 (33%) with VUR 498 (67%) without VUR Symptoms and signs Fever 312/744 (42%) Abdominal or loin pain 231/744 (31%) Enuresis 135/354 (38%) – only in children <5 years VUR compared to no VUR Fever 174/498 (35%) without VUR 140/246 (57%) with VUR (p=0.0004 NCC calculated)	Definition of UTI not provided.

Bibliographic Information	Study Type & Evidence Level	Study Aims	Number of patients	Patient Characteristics	Intervention and comparison	Follow-up & Outcome Measures	Effect Size	Reviewer Comments
							Abdominal pain 144/498 (29%) without VUR 86/246 (35%) with VUR	
Pylkkanen J;Vilska J;Koskimies O; 1981 80	Study Type: Case-series Evidence Level: 3	To identify patients at high risk of renal damage following UTI	Children aged 6 to 24 months UTI defined as: Any bacterial growth from SPA, or 105cfu/ml in 2 consecutive clean-voided urine samples. Pyelonephritis defined as: Rectal temperature ≥39.0C, ESR ≥35mm/h, CRP ≥20ug/ml, decreased renal concentrating capacity (determined by the DDAVP test). Lower tract infection: 2 or less criteria fulfilled Degree of renal parenchyma reduction: Grade 1 - a minor shift of the renal outline Grade 2 - a distinct parenchymal reduction Grade 3 - an almost complete loss of parenchyma corresponding to a deformed calyx group	252 infants and children with first time UTI (271 entered study, 10 moved away and 9 subjects did not comply)	Intervention: IVU to detect renal scarring (performed 2 weeks after the initiation of antibiotic therapy) IVU was repeated at 2 years. MCUG to detect VUR (performed 2-4 weeks after the IVU on patients with suspicion of distending reflux or obstruction at the 14 day check-up).	19/271 (9%) loss to follow-up	164/252 (65%) children had upper UTI 88/252 (35%) children had lower UTI or asymptomatic UTI Abnormalities 26/252 (10%) of all children with UTI had abnormalities (reflux, pelveureteral stenosis, nonobstructive hydronephritis, papilloma of the urinary bladder, ureterocele and sarcoma botryoides of the urinary bladder) 23/164 (14%) of children with upper UTI had abnormalities compared to 3/88 (3%) of children with lower UTI or asymptomatic bacteriuria ($p<0.025$) Reflux (7.9%) 20/252 of all children with UTI had reflux, 3 bilateral and 17 unilateral. 12/252 of all children with UTI (5%) had scarring, and all had upper UTI 8/20 with reflux (40%) had scaring. In children without distending reflux, obstruction of the urinary tract or sarcoma botryoides, 66/237 (28%) had recurrence of UTI in first year and 82/237 (35%) in the first 2 year). 34/237 (14%) had 3rd infection (10/34 (29%) had abnormality)	
Drew JH;Acton CM; 1976 Aug 78	Study Type: Other Evidence Level: 3		905 consecutive infants	SPA was performed in all infants presenting with jaundice of unknown aetiology, failure to gain weight, excessive weight loss, diarrhoea, vomiting, or a clinical picture of sepsis. Diagnosis of UTI was defined as any bacterial growth. After 7 days treatment with antibiotics	Intervention: SPA Radiological investigations Comparison		SPA was performed in 905 infants. 64 were found to have urinary infection, representing 0.5% of all live births during the study eriod. 54 (84%) were males and 10 (16%) were females. 14 (22%) were born before 37 weeks gestation and 50 (78%) were full term infants. 30 (56%) of the male infants and 5 of the 10 (50%) female infants were found to have a radiological abnormality. In 27 of the infants, VUR was the only abnormality present. A further 6 infants were found with hydronephrosis; 3 with obstruction and 3 with megasystems associated with gross reflux.	

Bibliographic Information	Study Type & Evidence Level	Study Aims	Number of patients	Patient Characteristics	Intervention and comparison	Follow-up & Outcome Measures	Effect Size	Reviewer Comments
				infants underwent intravenous pyelography and MCUG.				

Prevalence of vesicoureteric reflux

Bibliographic Information	Study Type & Evidence Level	Study Aims	Number of patients	Patient Characteristics	Intervention and comparison	Follow-up & Outcome Measures	Effect size	Reviewer Comments
Tsai Y;Hsu C;Lin G;Wang C;Cheng C;Huang Y;Yen M;Hsia S;Yan D; 2004 64	Study Type: Cohort Evidence level: 2+	To determine whether renal pelvis dilation on ultrasound was reliable in predicting VUR and to assess the relationship of other clinical information of VUR in children with UTI	114 children (228 kidneys) 79 male 35 female	114 children aged 1-60 months admitted with first episode UTI. Clinical data, renal echo and voiding cystourethrogram results were reported.	Intervention: VCUG Ultrasound	Follow-up period: n/a Outcome Measures: Grade of VUR Renal pelvis size	VUR occurred in 28.9% (33/114) of patients in 20.6% (47/228) kidneys. Severe VUR was observed in 12.3% (14/114) of the patients in 7.9% (18/228) of the kidneys. Unilateral pelvis size greater than 8mm had 2.4 (p=0.049, 95%CI 1.0, 5.9) times greater risk for VUR and 3.7 (p=0.025, 95%CI 1.2, 11.3) times greater risk for severe reflux. The sensitivity in detecting severe reflux was 27.8% and the specificity was 90.5%. The positive and negative predictive values in suggesting severe VUR were 20.0% and 93.6% respectively. The sum of bilateral pelvis sizes greater than 16mm had a greater risk for VUR and severe reflux (4.1 and 4.6 times) and similar specificity a negative predictive value for severe reflux. Age, gender c-reactive proteins, leukocytosis, pyuria and acute pyelonephritis did not show significant relationships to the reflux.	
Chand DH;Rhoades T;Poe SA;Kraus S;Strife CF; 2003 Oct 76	Study Type: OtherCase-series Evidence Level: 3	To determine whether the incidence of VUR differs in children based on age, race and gender and if the incidence and severity of VUR are related to race in girls younger than 7 years presenting for evaluation after UTI.	15,504 patients were included.	Patients 21 years old or younger who had a VCUG or radio-nuclide cystogram performed between Jan 1993 and Dec 2001 at a single hospital.	Intervention: VCUG or RNC	Age, gender Number with UTI Number with reflux	Of the children referred for a VCUG or RNC 9912/15504 (64%) were diagnosed with a UTI. Of these 2927/9912 (29.5%) had reflux. Of the 9912 children who had a VCUG or a nuclide cystogram because of a previous UTI, reflux was significantly less common in black patients, with the odds of a white patient having reflux about three times greater (p<0.001). The incidence of VUR was significantly more common in females and in the youngest age group (>2 years). 2733/8794 (31.1%) white patients with VUR + history of UTI 104/768 (9.6%) black patients with VUR + history of UTI OR 0.34 (p<0.0001) 2724/8776 (31.0%) females with VUR + history of UTI 203/1136 (17.9%) males with VUR + history of UTI OR 0.53 (p<0.0001) 1582/4101 (38.6%) <2 years with VUR + history of UTI 1001/3767 (26.6%) 2-6 years with VUR + history	Results for children aged 0 to 11 years reported. Children aged 12-21 were analysed together and 12-16 year old data could not be extracted separately.

Bibliographic Information	Study Type & Evidence Level	Study Aims	Number of patients	Patient Characteristics	Intervention and comparison	Follow-up & Outcome Measures	Effect size	Reviewer Comments
							of UTI 307/1558 (19.7%) 7-11 years with VUR + history of UTI 37/486 (7.6%) 12-21 years with VUR + history of UTI Of the children who had a VCUG or a nuclide cystogram because of a previous UTI, 38% were younger than 7 years. Girls younger than 7 years were further divided into those younger than 2 years and 2-6 years. VUR incidence was consistently higher and were significantly more likely to have high grade reflux than black girls in white girls.	
Upadhyay J;Bolduc S;Bagli DJ;McLorie GA;Khoury AE;Farhat W; 2003 May 237	Study Type: Case-series Evidence Level: 3	To evaluate the association of dysfunctional voiding with VUR among girls with UTI	114 patients with voiding dysfunction. 58 patients presented with a concomitant UTI	Girls evaluated for symptoms of dysfunctional voiding for at least 6 months.	Intervention: VCUG	Number with VUR	In the 114 patients with dysfunctional voiding symptoms the incidence of concomitant UTI at presentation was 58/114 (51%). Of these 19 (33%) had VUR which was primary in 16 (84%) and secondary with complete ureteral duplication in 3 (16%). All patients were female and VUR was bilateral in 5.	58/114 (50.8%) had a UTI - only analyses on these children were presented.
Zaki M;Mutari GA;Badawi M;Ramadan D;Al deen HE; 2003 Sep 238	Study Type: Case-series Evidence Level: 3	To determine the frequency of VUR and associated kidney involvement among children with first documented febrile UTI	174 children (38 boys and 136 girls)	All consecutive children aged under 12 admitted to two regional hospitals in Kuwait with the diagnosis of first febrile UTI over a 6 year period (June 1995 to June 2001) who had undergone MCUG and DMSA. Positive urine culture defined as 3 urine cultures positive for the same bacterial pathogens by urine collected via catheter, clean-catch or mid-urine stream. All children had: Temperatures of >38.5 ºC Raised ESR (>40mm/h) CRP (>40 mg/l Additionally, all males were circumcised. Exclusions: Children whose parents refused consent for DMSA, neurogenic bladder,	Intervention: DMSA within the first week of initiating treatment MCUG at least one month after diagnosis Comparison: n/a	Prevalence of VUR in children with UTI DMSA scan results Microorganism isolated	VUD 39 (22%) 2/3 of which had grade 1 or 2. there was a higher incidence of VUR in girls than boys (girls: 32/136 (24%) vs boys: 7/38 (18%)) Abnormal DMSA scan results in 59/156 (43%) girls and 4/38 (11%) boys. 1< year (72 children) 34 boys and 38 girls VUD 18/72 (25%) Abnormal DMSA scan results 13/72 (18%) Organisms most frequently isolated *E.Coli* (55 children) followed *Klebsiella spp.*(14 children), *Proteus spp.* (2 children) and *Enterococci* (1 child) 1-5 years (66 patients) 3 boys and 63 girls VUD 12/66 (18%) Abnormal DMSA scan results 35/66 (53%) Organisms most frequently isolated *E. coli* (62 children) followed by *Klebsiella spp.* (2 children) and *Proteus spp.* (2 children) 5 < 12 years (36 patients) 1 boy and 35 girls	

Bibliographic Information	Study Type & Evidence Level	Study Aims	Number of patients	Patient Characteristics	Intervention and comparison	Follow-up & Outcome Measures	Effect size	Reviewer Comments
				and 19 children who were non-Kuaiti Arabs and non-Arab children in order to have a homogeneous racial population.			VUD 9/36 (25%) Abnormal DMSA scan results 15/36 (41%) Organisms most frequently isolated *E. coli* (34 children) followed by *Klebsiella spp.* (1 children) and *Proteus spp.* (1 children)	
Howard RG;Roebuck DJ;Yeung PA;Chan KW;Metreweli C; 2001 Apr 239	Study Type: Case-series Evidence Level: 3	To report the prevalence of VUR and scarring in Chinese children.	93 children identified 65 male 28 female	All children aged under 5 years who presented with a documented UTI between 1994 and 1999 and who underwent a MCUG and DMSA. Scarring defined as: 0 = normal 1 = focal scarring in one region 2 = scarring involving 2 regions 3 = scarring involving 3 regions 4 = generalised reduction in cortical mass	Intervention: DMSA at least 3 months after UTI MCUG at least 6 weeks after UTI	Presence and severity of scarring Number with reflux	The prevalence of VUR was 39% (45% in males and 25% in females) and the prevalence of scarring was 23% (28% in males and 11% in females). Two children had a solitary functioning kidney. VUR was demonstrated in 55 renal units. There was a significant relationship between the degree of scarring and the grade of VUR ($p<0.05$). When renal units were categorised by sex, a significant dependency relationship was seen between the degree of scarring and the grade of VUR for boys ($p<0.05$) but this was not shown to be significant for girls.	
Honkinen O;Jahnukainen T;Mertsola J;Eskola J;Ruuskanen O; 2000 Jul 52	Study Type: Case-series - population surveillance data Evidence Level: 3	To assess the clinical characteristics of bacteraemic UTI in children	134 children with serious bacteremic UTI located from all 36 Finish hospitals and 25 microbiological laboratories, between 1985 and 1994 Comparison group 134 age and sex matched from children hospitilised for blood culture negative symptomatic UTI	Children aged 7 days to 9.5 years (median 0.125 years) with serious bacteremic UTI. Inclusion criteria were symptoms of acute illness such as fever, irritability, vomiting or dysuria; bacterial growth $\geq 10^5$ in one midstream urine or in two urine bag samples; growth of identical pathogen both in the blood and in the urine cultures; first known urinary tract infection; and no known urinary tract abnormality or other severe underlying disease. 29 children had a history of UTI or urinary tract abnormality or other severe underlying disease. 7 children were under 1 week old and analysed separately	Results from imaging studies were available for 132 (98%) of bacteraemic children and all 134 controls. Of the bacteraemic children 112 renal ultrasounds 123 voiding or radionuclide cystourethrograms 77 IVPs Of non bacteraemic children 134 renal ultrasounds 128 voiding or radionuclide cystourethrograms 18 IVPs	Age and sex distribution of bacteremic UTI Symptoms and signs laboratory findings microbiological findings Number with VUR	Age and Sex distribution: 61% boys, 39% girls Age range 7 days to 9.5 years (median 0.125 years) 66% were 1 week to 3 months of age (69% of youngest age group were boys, this male dominance decreased with age) 22% 3 to 11 months 12% ≥ 12 months Annual incidence in Finland of bacteremic UTI in children <16 years of age and without previous UTI infection or underlying disease during the study period was 1.5/100000. Results reported bacteremia patients vs. nonbacteremic patients Symptoms Fever 124 (92%) v 121 (90%) The duration of the preceding fever (mean, 1.9 ± 1.9 vs. 1.8 ± 1.7 days) was not different between groups. Irritability 81 (60%) v 75 (56%) Abnormal crying 46 (34%) v 41 (30%) Vomiting 22 (16%) v 18 (13%)	Some of the Children included in this study may have been included in the study [240]

Bibliographic Information	Study Type & Evidence Level	Study Aims	Number of patients	Patient Characteristics	Intervention and comparison	Follow-up & Outcome Measures	Effect size	Reviewer Comments
							Lethargy 35 (26%)v 41 (30%) Feeding problems 27 (20%) v 13 (10%) p = 0.02 Abdominal pain 10 (7%) v 4 (3%) Dysuria 2 (1%) v 4 (3%) Convulsions 5 (4%) v 0 (0%) Laboratory findings White blood cell count 18.2 ± 7.4 x 109/l (n = 127) vs.19.1 ± 8.2 x 109/l (n = 133) NS Mean CRP on admission 116 ± 67 mg/l (n = 134) vs. 76 ± 56 mg/l (n = 132) p < 0.01. Hyponatremia (sodium concentration ≤ 130 mmol/l) occurred in 9/81 (11%) bacteremic patients and 4/65 (6%) on nonbacteremic patients No differences were found in the mean sodium, potassium or creatinine concentrations Microbiological findings E. coli 114/134 (85%) vs. 125/134 (93%) of the blood culture negative UTIs (p = 0.04). Staphylococcus aureus caused 6 bacteremic infections and 1 nonbacteremic infection. Imaging studies (results available from 132/134 (98%) of bacteremic patients and 134/134 control patients). Urinary tract abnormalities 51% vs. 46% Grade 3-5 vesicoureteral reflux 40 (30%) vs. 22 (16%) Urinary obstruction 12 (9%) vs. 2 (1%) (p < 0.01). Imaging results of 113/114 children with bacteremic urinary infection caused by E.coli. were available. 52/113 (46%) had a urinary tract abnormality 10/113 (9%) later underwent urinary tract surgery. Imaging results of 19/20 children with bacteremic urinary infection caused by bacteria other then E.coli. were available. 17/19 (89%)	

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							had a urinary tract abnormality ($p < 0.01$ when compared to E-coil infections). All of the patients with Staphylococcus aureus, Klebsiella or Enterococcus faecalis had a urinary tract abnormality. 14/19 (74%) later underwent urinary tract surgery ($p < 0.01$ when compared to E-coil infections). Imaging results of all 124 children with nonbacteremic urinary infection caused by E.coli. were available. 55/124 (44%) had a urinary tract abnormality and 14/124 (11%) later underwent urinary tract surgery. Imaging results of all 10 children with nonbacteremic urinary infection caused by bacteria other then E.coli. were available. 7/10 (70%) had a urinary tract abnormality ($p < 0.19$ when compared to E-coil infections). 4/10 (40%) later underwent urinary tract surgery ($p = 0.03$ when compared to E-coil infections). Neonates The 7 children < 1 weeks were not enrolled in the comparative analysis. 5 boys and 2 girls. Mean CRP on 1st day 118 mg/l (range 23 to 256 mg/l) Mean WBC 12.2 x 10^9/l (range 3.7 to 22.9 x 10^9/l 1/7 was afebrile 3/7 had normal urinary imaging, 2/7 were operated on for urinary obstruction and 1/7 was operated on for grade 4 reflux and 1/7 had grade 2 reflux.	
Honkinen O;Lehtonen OP;Ruuskanen O;Huovinen P;Mertsola J; 1999 Mar 20 240	Study Type: Case-series Evidence level: 3	To determine whether an association exists between the bacterial species causing first UTI and abnormal findings in subsequent imaging studies.	1237 Children with positive urine samples.	All children presenting to a hospital with positive urine culture from a sample obtained by SPA (any growth) or catherisation (growth of at least 10000 colony forming unit/ml) between January 1980 to December 1994. Excluded: asymptomatic children, who had been in hospital for more tham 2 day, chronic urinary problems such as neurogenic bladder or no	Intervention: Children with UTI infection underwent: IVP (1980-1983) Ultrasonography (1984-1994) and VCUG (radiographic in boys, nuclear in girls) one to two months after the acute infection. Comparison: Children with first-time UTI caused by E.coli compared to children whose first-time UTI	Outcome Measures: Microbiological results Imaging results	Of the 1237 children with positive urine samples 922 (76%) were obtained by surpapubic aspiration and 295 (24%) by bladder catherisation. Microbiological results: Bacteria cultures were positive for: E.coli 982/1237 (79%) Enteroccus sp. 66/1237 (5.3%) Klebsiella sp. 55/1237 (4.4%) Coagulase negative staphylococcus 47/1237 (3.8%) Proteus sp. 39/1237 (3.2%) Other species 48/1237 (3.9%)	Some of the Children included in this study may have been included in the study Ref ID 996

Bibliographic Information	Study Type & Evidence Level	Study Aims	Number of patients	Patient Characteristics	Intervention and comparison	Follow-up & Outcome Measures	Effect size	Reviewer Comments
				imaging studies were lacking.	was caused by Proteus, Klebsiella, Enterococcus or Coagulase negative staphylococcus		Age and sex matched children whose UTI were caused by E.coli. were compared to children who's UTI was caused by another bacteria: Mean C-reactive protein (mg/l) was the same in the children infected with micro organisms other than E.coil compared with those infected with E. coil. Apart from the children infected with Proteus who had lower mean C-reactive protein levels (23 ± 24 vs. 69 ± 47 mg/l, p < 0.001). Reflux was more common in children infected with Klebsiella and Enterococcus than E-coil (Klebsiella 16/26 vs. 30/92, p < 0.01 and Enterococcus 16/26 vs. 30/92, p < 0.01) but less common in Proteus compared to E. coli. (2/26 vs. 30/92, p < 0.05), and the rate in coagulase negative staphylococcus was no different than E. coil. Operation or injection therapy for reflux was more comment in children infected with Klebsiella, Enterococcus and coagulase negative staphylococcus than E-coil (Klebsiella 10/26 vs. 7/92, p < 0.001, Enterococcus 12/26 vs. 7/92, p < 0.001, and coagulase negative staphylococcus 5/14 vs. 7/92, p < 0.01), and the rate in Proteus was no different than E. coil. Obstruction was more comment in children infected with Klebsiella, Enterococcus and coagulase negative staphylococcus than E-coil (Klebsiella 4/26 vs. 1/92, p < 0.01, Enterococcus 3/26 vs. 1/92, p < 0.01, and coagulase negative staphylococcus 2/14 vs. 1/92, p < 0.05). There were no cased of obstruction in children infected with Proteus. The rate of other abnormalities was not different between the children infected with different microorganisms.	
Sargent MA;Stringer DA; 1995 May 241	Study Type: Case-series Evidence Level: 3	To determine if the frequency of VUR in children referred by paediatric nephrologists and paediatric urologists was different from the frequency observed in children referred by adult urologists, paediatricians and family practitioners.	309 children (192 girls, 117 boys)	Children (aged 1 week - 15 years), having their first VCUG following their first UTI between 1992 and 1993. Exclusions: Children with known VUR, neuropathic bladder, renal or other abnormalities.	Intervention: VCUG	Presence or absence of VUR.	Overall 35/117 (30%) of boys had VUR and 56/192 (29%) of girls had VUR. Children under 1 year Males 19/56 (34%) Females 19/41 (46%) Children under 2 years Males 23/77 (30%) Females 25/57 (44%) Children aged 2-4 years Males 6/19 (32%)	

Bibliographic Information	Study Type & Evidence Level	Study Aims	Number of patients	Patient Characteristics	Intervention and comparison	Follow-up & Outcome Measures	Effect size	Reviewer Comments
							Females 20/63 (32%) Children over 5 years Males 6/21 (29%) Females 11/72 (15%)	
Messi G;Peratoner L;Paduano L;Marchi AG; 1988 50	Study Type: Case-series Evidence Level: 3	To present clinical and laboratory features of UTI and to determine incidence of UTI	223 children (38 males, 185 females)	Children aged 0-14 years presenting with symptomatic UTI and treated at a hospital. 64 infants >1 year, 63 children 1-4 years, 96 children 5-14 years. UTI was defined as two consecutive urine cultures yielding 10^5 or more cfu/ml of the same bacteria and microscopic examination yielding more then 10 leukocytes/mm^3.	VCUG	Number with UTI Number with cystitis Number with pyelonephritis Number with VUR Renal scarring Urinary tract malformations	Symptoms and signs Fever 144/223 (64.6%) Dysuria and frequency 92/223 (41.2%) Gastrointestinal symptoms 42/223 (18.8%) Haematuria 24/223 (10.8%) Failure to thrive 14/223 (6.3%) Jaundice 2/223 (0.9%) Incidence For cystitis, the total incidence per 1000 0-14 year old children in females was 1.08, in males 0.28 and overall 0.67. For pyelonephritis, the total incidence per 1000 0-14 year old children in females was 1.28, in males 0.18 and overall 0.71. Overall, the rate of UTI per 1000 0-14 year old children in females was 2.36, in males 0.46 and overall 1.38. The incidence of VUR per 1000 0-14 year old children in females was 0.41, in males 0.10 and overall 0.25.[50] The distribution of cystitis and pyelonephritis was different between boys and girls. In boys aged less than one year, 4 had cystitis compared to 11 girls and 11 boys had pyelonephritis compared to 38 girls. In boys and girls aged 1 year to 14 years old, 42 boys had cystitis compared to 159 girls and 19 boys had pyelonephritis compared to 162 girls. The incidence of reflux in children with UTI per 1000 children less than one year old was 1.79 in boys and 4.30 in girls. In children between one and four years old the incidence was 0.13 in boys and 0.47 in girls. In children between 5 and 14 years old the incidence was 0.20 in girls and there were no cases for boys.	
Jodal U; 1987 Dec 47	Study Type: Case-series Evidence Level: 3	Study 1 Aims unclear Study 2 To survey the frequency of bacteriuria in an	1177 children with first time symptomatic UTI (952 girls and 225 boys)	Children aged under ten years with first time symptomatic UTI. Bacteriuria definition: At least 10^5 bacteria per ml together with leukocyturia in		Outcome measures: No. with reflux (and grade) No. with scarring No. of symptomatic recurrences	Study 1 225/1177 (19%) boys 952/1177 (81%) girls Boys 133/225 (59%) of UTIs detected in the first year	

Bibliographic Information	Study Type & Evidence Level	Study Aims	Number of patients	Patient Characteristics	Intervention and comparison	Follow-up & Outcome Measures	Effect size	Reviewer Comments
		unselected infant population and to study the interrelation between asymptomatic and symptomatic bacteriuria		a midstream sample or bag sample. Any growth on SPA Pyelonephritis definition: Bacteriuria and fever of ≥38.5°C and a microsedimentation rate of ≥25mm per hour or CRP ≥20mg/L Cystitis definition: acute voiding symptoms (dysuria, frequency) with temperature <38.5°C and normal laboratory findings. A child with acute symptoms and bacteriuria that could not be classified was said to have 'unspecified UTI'		No. with pyelonephritis/cystitis	of life 72/225 (33%) had VUR 8/72 (11%) dilated reflux (grade ≥3) 41/225 (18%) had one recurrence 11/225 (5%) had 2 or more recurrences <u>Girls</u> 181/952 (19%) of UTIs detected in the first year of life 315/952 (34%) had VUR (54% between 1-3 years) 25/315 (8%) dilated reflux (grade ≥3) 152/952 (16%) had one recurrence 152/952 (16%) had 2 or more recurrences <u>Scarring</u> 15/278 (5%) children with no reflux had scarring 3/29 (10%) of children with grade 1 reflux had scarring 17/99 (17%) of children with grade 2 reflux had scarring 25/38 (66%) children with grade ≥3 reflux had scarring 25% of the total number of children with scarring did not have reflux. <u>Pyelonephritis</u> 7/141 (5%) children with 0 pyelonephritis episode had scarring 32/366 (9%) of children with 1 pyelonephritis episode had scarring 15/98 (15%) of children with 2 pyelonephritis episode had scarring 12/35 (35%) of children with 3 pyelonephritis episode had scarring 14/24 (58%) children with ≥4 pyelonephritis episode had scarring Study 2 All girls with asymptomatic bacteriuria were left untreated: Of 3581 newborns in the study population, 94% entered the study and 68% had all three tests at ages two weeks, three months and ten months. Screening bacteriuria (asymptomatic) Girls 0.9%	

Bibliographic Information	Study Type & Evidence Level	Study Aims	Number of patients	Patient Characteristics	Intervention and comparison	Follow-up & Outcome Measures	Effect size	Reviewer Comments
							Boys 2.5% Symptomatic UTI Girls 1.1% Boys 1.2% 89/90 infants with bacteriuria had IVU 85/90 had VCUG Reflux Asymptomatic bacteriuria 5/46 (11%) had grades 1 or 2 reflux. Symptomatic UTI 14/39 (36%) had reflux Abnormalities Asymptomatic bacteriuria Symptomatic UTI 5/39 (13%), 1 child had agenesis of one kidney, one had marked pelvo-ureteric stenosis and 3 had dilated reflux. Clearing of bacteriuria 11 girls with asymptomatic bacteriuria were left untreated and of these 10 (91%) became abacteriuric within 7 months of detection. 34/36 boys were left untreated and within 11 months 27 (79%) became abacteriuric.	
McKerrow W;vidson-Lamb N;Jones PF; 1984 Aug 4 [66]	Study Type: Case-series Evidence Level: 3	To report the results of investigation and treatment over a five to fifteen year follow up.	Intervention: IVU performed in 550/572 (96%) MCUG performed in 386 where there was suspicion of bladder abnormality.	572 children (399 girls, 173 boys)	Children aged under 13 years with a history of at least one confirmed urinary tract infection who had been referred by their family doctor to a paediatric surgical outpatient clinic	Number with abnormalities	572 children with UTI Abnormalities found in 51% of children with UTI. 6% had scarred kidneys with no evidence of reflux 31% had reflux (24% of ureters) 7.5% had obstructions 48% had cyctourethritis 7% had duplex kidneys 0.9% had deformities Of the ureters with reflux: 53% were initially treated medically, in 84% of these the reflux ceased 53% were operated on, resulting in no further problems in 65%. Late problems developed in 38% of children aged under 5 years and 12% of children aged over 5 years at diagnosis with ureters that had reflux and kidneys showing reflux nephropathy, treated surgically. The problems included repeat operation to correct reflux, nephrectomy because of deteriorating function, ureterosomy, hypertension and renal failure.	Bacteriuria not defined Not all children had an IVU, however the number who did not have one was small.

Bibliographic Information	Study Type & Evidence Level	Study Aims	Number of patients	Patient Characteristics	Intervention and comparison	Follow-up & Outcome Measures	Effect size	Reviewer Comments
Pylkkanen J;Vilska J;Koskimies O; 1981 [80]	Study Type: Case-series Evidence Level: 3	To identify patients at high risk of renal damage following UTI	252 infants and children with first time UTI (271 entered study, 10 moved away and 9 subjects did not comply)	Children aged 6 to 24 months UTI defined as: Any bacterial growth from SPA, or 10^5cfu/ml in 2 consecutive clean-voided urine samples. Pyelonephritis defined as: Rectal temperature ≥39.0C, ESR ≥35mm/h, CRP ≥20ug/ml, decreased renal concentrating capacity (determined by the DDAVP test). Lower tract infection: 2 or less criteria fulfilled Degree of renal parenchyma reduction: Grade 1 - a minor shift of the renal outline Grade 2 - a distinct parenchymal reduction Grade 3 - an almost complete loss of parenchyma corresponding to a deformed calyx group	IVU to detect renal scarring (performed 2 weeks after the initiation of antibiotic therapy) IVU was repeated at 2 years. MCUG to detect VUR (performed 2-4 weeks after the IVU on patients with suspicion of distending reflux or obstruction at the 14 day check-up).	Number with UTI Number with abnormalities Number with VUR	19/271 (9%) loss to follow-up 164/252 (65%) children had upper UTI 88/252 (35%) children had lower UTI or asymptomatic UTI <u>Abnormalities</u> 26/252 (10%) of all children with UTI had abnormalities (reflux, pelveureteral stenosis, nonobstructive hydronephritis, papilloma of the urinary bladder, ureterocele and sarcoma botryoides of the urinary bladder) 23/164 (14%) of children with upper UTI had abnormalities compared to 3/88 (3%) of children with lower UTI or asymptomatic bacteriuria ($p<0.025$) <u>Reflux</u> (7.9%) 20/252 of all children with UTI had reflux, 3 bilateral and 17 unilateral. 12/252 of all children with UTI (5%) had scarring, and all had upper UTI 8/20 with reflux (40%) had scaring. In children without distending reflux, obstruction of the urinary tract or sarcoma botryoides, 66/237 (28%) had recurrence of UTI in first year and 82/237 (35%) in the first 2 year). 34/237 (14%) had 3rd infection (10/34 (29%) had abnormality)	
Lindberg U;Claesson I;Hanson LA;Jodal U; 1975 May [242]	Study Type: Case-series Evidence Level: 3	Evaluate the roentgenological findings and relation to pyuria, sedimentation rate, CRP, concentrating capacity and history of earlier infections.	116 schoolgirls with asymptomatic bacteriuria	116 school girls aged 7 to 16 referred to Paediatric Department for further investigation because of at least two positive urine tests detected at urinary screening during 1971-1972 and who presented to the hospital with no symptoms. Positive urine test: more than 10^5cf/ml of the same organism in two consecutive samples. Degree of parenchymal reduction was categorised as: 1 = minor shift of the renal outline 2 = distinct parenchymal	IVP MCUG	Number with reflux Number with scarring Intervention: IVP MCUG	Overall 24/116 (20.7%) with reflux. 11/12 girls with calyceal changes and parenchymal reduction suggestive of previous pyelonephritis had reflux A further 13/104 (11.2%) girls with normal IVPs had reflux. The mean degree of reflux did not differ between the groups with and without parenchymal changes. Five girls had a double collection system (4.3%) and a diverticulum of the urinary bladder was found in 3 girls (2.6%).	

Bibliographic Information	Study Type & Evidence Level	Study Aims	Number of patients	Patient Characteristics	Intervention and comparison	Follow-up & Outcome Measures	Effect size	Reviewer Comments
				reduction 3 = almost complete reduction of parenchyma corresponding to a deformed calys group.				
Kunin CM; 1970 Nov 243	Study Type: Case-series Evidence Level: 3	Reports clinical, bacteriologic and urologic characteristics of the cases detected from population screening.	156 girls identified with persistent bacteriuria	10 year epidemiological study form 1959 to 1969 identified girls with persistent significant bacteriuria. Significant bacteriuria 3 or more consecutive urine cultures containing 10^5 cfu/ml of the same species or serotype of E. coli. Recurrent bacteriuria - reappearance of significant bacteriuria after lowering bacterial counts to ≥1000/ml or within 1 week of completion of therapy.	Intervention: History taking Physical exam IVP Cystogram Comparison: n/a	Number with reflux Number with scarring	Reflux: Total 26/137 (18.9%) Of Caucasian girls (n = 115) Age 5-9: 13/37 (35.1%) 10-14: 8/52 (15.3%) Repair of reflux in 7/26 (27%) girls Follow up cystograms conduced in 16/19 (84%) of the girls who did not have reflux repaired Reflux disappeared in 11/16 (69%)	Upper age limit not reported. Data only extracted for age groups that were clearly defined.

Diagnostic value of imaging tests to detect vesicoureteric reflux

Bibliographic Information	Study type & Evidence level	Study Aims	Number of patients & prevalence	Population Characteristics	Type of test and Reference standard	Outcome measures	Sensitivity, Specificity, PPV and NPV	Reviewer comment
Lai SW;Ng KC; 2003 [264]	Study type: Diagnostic Evidence level: III	Inflammatory parameters for the early detection of VUR in children.	149 with acute pyelonephritis - 123 who had MCUG analysed (48 girls and 75 boys)	Children with documented pyelonephritis at a paediatric department. Children with VUR aged 3.1 ± 3.2 years and children without VUR 1.2 ± 1.4 years. Acute pyelonephritis was diagnosed if DMSA revealed abnormal findings.	MCUG compared to inflammatory markers	No. children with VUR on MCUG Fever >37°C CRP level >0.8mg/dl WBC >11000/mm^3 Neutrophil ratio >80%	Children with VUR had a higher temperature (38.48 ± 0.93 vs 39.00 ± 0.98, p=0.0078) higher CRP level (5.60 ± 5.52 vs 9.26 ± 7.38, p=0.0114) and higher Neutrophil ratio (54.7 ± 16.5 vs 68.5 ± 17.3, p=0.0001) CRP level >0.8mg/dl Sensitivity = 88% Specificity = 11% PPV = 28% NPV 71% Temperature >37°C Sensitivity = 94% Specificity = 10% PPV = 29% NPV = 82% WBC >11,000/mm^3 Sensitivity = 79% Specificity = 26% PPV = 29% NPV = 77% Neutrophil ratio >80% Sensitivity = 35% Specificity = 94% PPV = 71% NPV = 79%	Fever is potentially not a good marker for VUR - anti-pyretic drugs given at home could falsely limit fever on presentation. Numbers reported in the paper for combinations of inflammatory markers could not be reproduced. These numbers are excluded from the review.
Zamir G;Sakran W;Horowitz Y;Koren A;Miron D; 2004 [244]	Study type: Diagnostic Evidence level: II	To assess renal US in the management of young children with first time febrile UTI	255 (63 male, 192 female) children with first time febrile UTI	All children, aged <5 yrs, hospitalised for uncomplicated febrile UTI in a paediatric department from Jan 1999 to Dec 2000 Febrile UTI defined as: SPA any growth; catheter any growth; or midstream, ≥100bacteria/ml and temp ≥ 38.0C	Renal ultrasound (RUS) compared to MCUG	No. with anatomical abnormalities by renal US Sensitivity, specificity, PPV, NPV of RUS v. MCUG for detecting VUR	3/255 (1.2%) with abnormalities: Enlargement of left kidney, 1 child Renal cyst, 1 child Unilateral double collecting system and severe hydronephrosis, 1 child MCUG + - R + 7 26 U S - 36 183 Sensitivity = 16.3% Specificity = 87.6% PPV= 23.5%	

Bibliographic Information	Study type & Evidence level	Study Aims	Number of patients & prevalence	Population Characteristics	Type of test and Reference standard	Outcome measures	Sensitivity, Specificity, PPV and NPV	Reviewer comment
							NPV= 83.2%	
Nakamura M;Shinozaki T;Taniguchi N;Koibuchi H;Momoi M;Itoh K; 2003 [245]	Study type: Diagnostic Evidence level: III	To evaluate the diagnostic potential of voiding urosonography (VUS) compared with MCUG under identical conditions and to evaluate potential reasons for false-negative VUS results.	34 boys and 22 girls - 111 ureterorenal units (one patient with a single kidney was included).	Boys and girls 1 month to 14 years (mean age 2.3 years) with confirmed UTI and follow-up of previously detected VUR.	Simultaneous MCUG and VUS	No with VUR Levovist concentrations	REVIEWER CALCULATED RESULTS See reviewer comments Diagnosing reflux by VUS (compared to the gold standard MCUG) 1 month to 14 years sensitivity 86% specificity 95% PPV 86% NPV 95% Under 24 months sensitivity 73% specificity 98% PPV 92% NPV 93%	Have not explained statistical methods in the paper. The results section assumes that both testing methods are equivalent and does not report the diagnostic accuracy of VUS compared to MCUG. We report in the results the NCC-calculated standard diagnostic calculations. Patient selection method unknown Blinding not possible because procedures performed simultaneously.
Xhepa R;Bosio M;Manzoni G; 2004 [246]	Study type: Diagnostic Evidence level II	To evaluate the diagnostic efficacy of voiding cystourethrosonography in children.	34 patients (22 with VUCG analysed) 21 males and 13 females between 1995 and 1999.	Children aged 2 months to 14 years (mean age 3.9 years) referred to hospital for investigation of VUR because of documented pyelonephritis.	CS/CUS compared to MCUG	Number of children with VUR	22 patients had 45 kidney-ureter units. Sensitivity = 93% Specificity = 44% PPV = 75% NPV = 78% Authors contacted – 2 children had duplex kidneys, one had a single kidney and 19 had normal kidneys = 45 ureter units in 22 patients.	Over a four year period (1995-1999) 22 children were received CS. Over a one month period (Oct 2000) 12 children received CUS. Patient selection criteria not reported in enough detail. Unsure whether CS and CUS are equivalent. Authors reported most results by ureter units which will overestimate effectiveness.
Hansson S;Dhamey M;Sigstrom O;Sixt R;Stokland E;Wennerstrom M;Jodal U; 2004 [265]	Study Type: Diagnostic Evidence Level: Ib	Evaluated the ability of DMSA scintigraphy to predict the presence of dilating VUR in infants with UTI.	303 children (163 boys, 140 girls)	Children seen at the emergency department of a hospital. Boys aged 5 days to 19.9 months (mean age 3.1 months). Girls aged 5 days to 22.6 months (mean age 8.5 months). Children with suspected obstruction on ultrasound were excluded.	DMSA compared to MCUG	Bacteriuria defined as greater than 10^5 cfu/ml on bag, midstream or catheter sample. Renal damage on urography was defined as focal parenchymal reduction with corresponding calix deformation and/or small kidney.	VUR was present in 36/163 (22%) of boys and 44/140 (31%) of girls. At the primary examination 156/303 (55%) of patients had abnormal DMSA. Sensitivity 66% Specificity 54% PPV 40% NPV 82%	

Bibliographic Information	Study type & Evidence level	Study Aims	Number of patients & prevalence	Population Characteristics	Type of test and Reference standard	Outcome measures	Sensitivity, Specificity, PPV and NPV	Reviewer comment
Sukan A;Bayazit AK;Kibar M;Noyan A;Soyupak S;Yapar Z;Anarat A; 2003 [247]	Study type: Diagnostic Evidence level III-	To compare direct radionuclide cystography and MCUG in children with suspected reflux.	25 children with recurrent UTI (13 female, 12 male)	Children on bacterial prophylaxis, aged 1.5 months to 15 yrs, from May 2000 to Jan 2001	To compare DRNC with MCUG in detection of VUR	No with VUR	MCUG + - D + 1 5 R N - 4 14 C Reviewer calculated results Sensitivity = 20% Specificity= 73.7%	One child unaccounted for and reason not explained in text Sensitivity and specificity calculated by authors (71% and 67% respectively) did not match that calculated at NCC-WCH (either by child or by ureter units) although the same numbers that were reported in the results were used. Authors reported most results by ureter units which will overestimate effectiveness.

Prevalence of renal parenchymal defects

Bibliographic Information	Study Type & Evidence Level	Study Aims	Number of patients	Patient Characteristics	Intervention and comparison	Follow-up & Outcome Measures	Effect Size	Reviewer Comments
Ece A;Tekes S;Gurkan F;Bilici M;Budak T; 2005 Aug 224	Study Type: Case-control Evidence level: 3	To investigate whether the angiotensin converting enzyme (ACE) and angiotensin II type 1 receptor gene polymorphisms were associated with the renal scar formation secondary to recurrent UTI in children without uropathy. Only baseline data from this study was used.	97 children (81 girls and 16 boys)	Children with recurrent UTI aged 6.34 years (± 3.16) Exclusions: Underlying primary VUR, neurogenic bladder, bladder dysfunction, lower urinary tract obstruction, renal hypoplasia, ectopic kidney. Definition of UTI: Fever, flank pain, increased ESR, positive CRP, positive urine culture, positive LE or nitrite dipstick. Recurrence: the existence of at least two attacks of UTI in a patient – cystitis was not regarded as a recurrent UTI.	Children with renal scarring compared to children with no renal scarring	Age at first UTI Renal scarring (on DMSA performed following 3 month period free from UTI) Number of recurrences Micro-organism isolated	Children with renal scarring vs. children with no renal scarring, p-value Recurrent UTI (6.90 ± 2.45 UTI episodes vs. 3.35 ± 1.48 UTI episodes, $p<0.001$) Age at initial UTI (2.61 ± 1.52 years vs. 3.52 ± 2.17 years, $p=0.040$) Age (years) 6.92 ± 3.20 years vs. 6.05 ± 3.15, $p>0.05$) Gender (male/female) 8/22 vs. 8/59 $p>0.05$ Micro-organism isolated (E.coli /non-e.coli) 25/5 vs. 56/11 $p>0.05$ Follow-up period 3.88 ± 1.97 vs. 3.07 ± 1.86 $p>0.05$	Only data relevant to the predictors of recurrence was used from this study.
Jodal U; 1987 Dec 47	Study Type: Case-series Evidence Level: 3	Study 1 Aims unclear Study 2 To survey the frequency of bacteriuria in an unselected infant population and to study the interrelation between asymptomatic and symptomatic bacteriuria	Children aged under ten years with first time symptomatic UTI. Bacteriuria definition: At least 10^5 bacteria per ml together with leukocyturia in a midstream sample or bag sample. Any growth on SPA Pyelonephritis definition: Bacteriuria and fever of ≥38.5°C and a microsedimentation rate of ≥25mm per hour or CRP ≥20mg/L Cystitis definition: acute voiding symptoms (dysuria,	1177 children with first time symptomatic UTI (952 girls and 225 boys)		Outcome measures: No. with reflux (and grade) No. with scarring No. of symptomatic recurrences No. with pyelonephritis/cystitis	Study 1 225/1177 (19%) boys 952/1177 (81%) girls Boys 133/225 (59%) of UTIs detected in the first year of life 72/225 (33%) had VUR 8/72 (11%) dilated reflux (grade ≥3) 41/225 (18%) had one recurrence 11/225 (5%) had 2 or more recurrences Girls 181/952 (19%) of UTIs detected in the first year of life 315/952 (34%) had VUR (54% between 1-3 years) 25/315 (8%) dilated reflux (grade ≥3) 152/952 (16%) had one recurrence 152/952 (16%) had 2 or more recurrences Scarring 15/278 (5%) children with no reflux had scarring 3/29 (10%) of children with grade 1 reflux had scarring 17/99 (17%) of children with grade 2 reflux had scarring 25/38 (66%) children with grade ≥3 reflux had scarring 25% of the total number of children with scarring did not have reflux.	

Bibliographic Information	Study Type & Evidence Level	Study Aims	Number of patients	Patient Characteristics	Intervention and comparison	Follow-up & Outcome Measures	Effect Size	Reviewer Comments
			frequency) with temperature <38.5°C and normal laboratory findings. A child with acute symptoms and bacteriuria that could not be classified was said to have 'unspecified UTI'				Pyelonephritis 7/141 (5%) children with 0 pyelonephritis episode had scarring 32/366 (9%) of children with 1 pyelonephritis episode had scarring 15/98 (15%) of children with 2 pyelonephritis episode had scarring 12/35 (35%) of children with 3 pyelonephritis episode had scarring 14/24 (58%) children with ≥4 pyelonephritis episode had scarring Study 2 All girls with asymptomatic bacteriuria were left untreated: Of 3581 newborns in the study population, 94% entered the study and 68% had all three tests at ages two weeks, three months and ten months. Screening bacteriuria (asymptomatic) Girls 0.9% Boys 2.5% Symptomatic UTI Girls 1.1% Boys 1.2% 89/90 infants with bacteriuria had IVU 85/90 had VCUG Reflux Asymptomatic bacteriuria 5/46 (11%) had grades 1 or 2 reflux. Symptomatic UTI 14/39 (36%) had reflux Abnormalities Asymptomatic bacteriuria Symptomatic UTI 5/39 (13%), 1 child had agenesis of one kidney, one had marked pelvo-ureteric stenosis and 3 had dilated reflux. Clearing of bacteriuria 11 girls with asymptomatic bacteriuria were left untreated and of these 10 (91%) became abacteriuric within 7 months of detection. 34/36 boys were left untreated and within 11 months 27 (79%) became abacteriuric.	
Pylkkanen J;Vilska J;Koskimies O; 1981 [80]	Study Type: Case-series Evidence Level: 3	To identify patients at high risk of renal damage following UTI	Children aged 6 to 24 months UTI defined as: Any bacterial growth from SPA, or 10^5cfu/ml in 2 consecutive clean-voided urine samples. Pyelonephritis defined as: Rectal temperature ≥39.0C, ESR ≥35mm/h, CRP	252 infants and children with first time UTI (271 entered study, 10 moved away and 9 subjects did not comply)	Intervention: IVU to detect renal scarring (performed 2 weeks after the initiation of antibiotic therapy) IVU was repeated at 2 years. MCUG to detect VUR (performed 2-4 weeks after the IVU on patients with	19/271 (9%) loss to follow-up	164/252 (65%) children had upper UTI 88/252 (35%) children had lower UTI or asymptomatic UTI Abnormalities 26/252 (10%) of all children with UTI had abnormalities (reflux, pelveureteral stenosis, nonobstructive hydronephritis, papilloma of the urinary bladder, ureterocele and sarcoma botryoides of the urinary bladder) 23/164 (14%) of children with upper UTI had abnormalities compared to 3/88 (3%) of children with lower UTI or asymptomatic bacteriuria (p<0.025) Reflux (7.9%) 20/252 of all children with UTI had reflux, 3 bilateral and 17 unilateral. 12/252 of all children with UTI (5%) had scarring, and all had upper UTI	

Bibliographic Information	Study Type & Evidence Level	Study Aims	Number of patients	Patient Characteristics	Intervention and comparison	Follow-up & Outcome Measures	Effect Size	Reviewer Comments
			≥20ug/ml, decreased renal concentrating capacity (determined by the DDAVP test). Lower tract infection: 2 or less criteria fulfilled Degree of renal parenchyma reduction: Grade 1 - a minor shift of the renal outline Grade 2 - a distinct parenchymal reduction Grade 3 - an almost complete loss of parenchyma corresponding to a deformed calyx group		suspicion of distending reflux or obstruction at the 14 day check-up).		8/20 with reflux (40%) had scaring. In children without distending reflux, obstruction of the urinary tract or sarcoma botryoides, 66/237 (28%) had recurrence of UTI in first year and 82/237 (35%) in the first 2 year). 34/237 (14%) had 3rd infection (10/34 (29%) had abnormality)	
Shah KJ;Robins DG;White RH; 1978 Mar 92	Study Type: Case-series Evidence Level: 3	To describe children diagnosed as having a UTI and currently attending a renal clinic at a children's hospital.	105 children (23 boys, 82 girls)	Children (52/102 aged under 5 years) who attended a renal clinic during 1974 with recently diagnosed or had a previous UTI. Exclusions: Neurological disorders affecting bladder function, anatomical abnormality. UTI definition: >10^5 ml pathogenic organisms on culture of two midstream urine specimen, or any growth on SPA. Scar definition: the loss of parenchymal thickness associated with distortion of one or more underlying calyces with or without irregularity of the renal outline.	Intervention: At follow up visits Excretory urogram (IVU) were reviewed; renal length measured and presence of scars, pelvicalyceal and ureteric dialation and striations noted. Cystourethrogram (CUG) were also reviewed and the severity of VUR graded.	Grade of reflux Renal scarring	VUR by age 32/105 (30%) Grade III reflux 8/32 under 1 years, 13/32 aged 1-5 years, 11/32 6 years and older 8/105 (8%) Grade II reflux 1/8 under 1 year, 4/8 aged 1-5 years, 3/8 aged 6 years and older 15/105 (14%) Grade II reflux 0/15 under 1 year, 8/15 aged 1-5 years, 7/15 aged 6 years and older Scarring by kidney (n=210 kidneys in 105 patients) 47/105 (22%) Grade III reflux. Of these 37 (79%) scarred 13/210 (6%) Grade II reflux. Of these 5 (38%) had renal scarring 30/210 (14%) Grade I reflux. Of these 6 (20%) had renal scarring 20/210 (10%) no reflux unilaterally. Of these, none had renal scarring 66/210 (31%) no reflux bilaterally. Of these 1 (1.5%) had renal scarring 34/210 Did not have a cystourethrogram. Of these, 0 had renal scarring. No scars v. (grade II + III): x2 = 84.45 (p<0.001) (No scars + grade I) v (grade II + III): x2 = 77.39 (p<0.001) II v III: x2 = 6.06 (p<0.025) Scars initially present which deteriorated	

Bibliographic Information	Study Type & Evidence Level	Study Aims	Number of patients	Patient Characteristics	Intervention and comparison	Follow-up & Outcome Measures	Effect Size	Reviewer Comments
				Deterioration of an existing scar was defined as further parenchymal thinning with or without increased distortion of the underlying calyces, or extension of the scar to previously normal kidney tissue. Grades of reflux I - reflux on filling or micturation into the ureter only II - Reflux on filling or micturation, up to the pelvicalyceal system but without distension III - Reflux on filling or micturation up into the pelvicalyceal system and distending it.			6/105 (4 girls, 2 boys) 5 with grade III reflux (one with grade I) Average follow up time 2.5 years (range 1.1 to 3.8 years) New scars observed at subsequent IVU 5/105 (all girls) 4 with grade III reflux (one with grade II) Average follow up time 3.1 years (range 1.7 to 4.2 years)	
Winberg J;Andersen HJ;Bergstrom T;Jacobsson B;Larson H;Lincoln K; 1974 42	Study Type: OtherObservational Evidence Level: 3	To describe the epidemiology and clinical features of children with UTI	596 consecutive cases of UTI	Children aged 0-16 treated at a children's hospital or maternity unit for symptomatic UTI.			In all children under 11 years of age the annual incidence was 1.1% in boys and 3% in girls. When newborns were excluded, the incidence of UTI in boys was 0.7% and in girls 2.8%.[42] Almost all infants had fever, except neonates in whom only 42% had fever, After the first year of life, fever became less common. 1 – 12 months 179/186 (96%) 1-3 years 70/96 (73%) 3-10 years 120/200 (60%) 10-16 years 19/41 (46%) E.coli was the infecting organism in 83% of girls and 85% of boys under one year and in 60% of girls and 33% of boys aged 1 to 16 years. Boys had a higher frequency of Proteus (33%) over one year of age than girls (0%), while girls were more likely to have staphlycoccus albus over one year of age (30%) than boys (12%). Among neonates, 75% were infected with E.coli, however there were significantly more males (83%) than females (57%) (p=0.016).	
Smellie JM;Poulton A;Prescod NP; 1994 May 7 248	Study Type: Case-series Evidence Level: 3	To review the histories of children with bilateral renal scarring and severe VUR to determine whether an improvement in early management	52 children (24 boys and 28 girls).	Children aged 1-14 years who were already participating in an RCT of medical vs. surgical management of their reflux. All children had a history of UTI with symptoms not always related to the urinary tract.	IVU for detecting renal scarring A - one or two scars B - more than two scarred areas C - generalised parenchymal thinning with deformity of	Delay in diagnosis: if no urine sample was cultured when there was a period of acute symptoms related to the urinary tract; high fever lasting for at least five days; when there were ill defined symptoms (such as abdominal pain) for	Delay in one or more of the criteria in 50/52 children (21 boys and 20 girls). Delay in diagnosis of infection 41/52 Delay in effective treatment 45/52 Delay in diagnosis of reflux without prophylaxis 25/52 Delay in investigation of the urinary tract (by cystography) 33/52 Four children of mothers known to have reflux nephropathy were not investigated until they developed a urinary tract infection. All children in the study had bilateral renal scarring. Among the 11 children without delay in diagnosis the types of scars seen were moderate in 10	Study speculates about many things: 1 The fact that no urine sample was cultured could be for a number of reasons. 2. Delays in receiving cystography investigation may have been patient initiated.

Bibliographic Information	Study Type & Evidence Level	Study Aims	Number of patients	Patient Characteristics	Intervention and comparison	Follow-up & Outcome Measures	Effect Size	Reviewer Comments
		might reduce the risk of scarring			papillae D - a small, poorly functioning, end-stage kidney	at least one month; one or more previous episodes with similar symptoms to those present when the first UTI was diagnosed; delayed bladder control (any daytime wetting at age 5 years or over, or night time wetting at 7 years or over). Delayed or inadequate treatment: More than 4 days between urine collection and antibiotic treatment; low dose prophylaxis had not been prescribed between either treatment of presenting infection and investigation or after the diagnosis of reflux. Delayed or inadequate investigation: When cystography was excluded from the initial investigation; cystography delayed for more than one month in a child not receiving prophylaxis; adequate imaging of the kidneys was omitted; investigation was not performed until after recurrent infection; or family history of VUR or reflux nephropathy was disregarded.	children and severe in 1 child. Among the 24 children in whom there was up to a 6 month delay, 11 had moderate scar types and 13 severe. Among the 17 children in whom there was more than a 6 month delay, 6 had moderate scar types and 11 severe. There was a significant relationship between the type of renal scarring between no delay and a delay of more than 6 months (X2= 6.32, p=<0.01) and also a significant trend (X2= 7.43, df=1, p=<0.001).	There is no way to be sure from clinical notes that these are due to 'inadequate treatment' by a clinician. All children had bilateral reflux which may or may not be related to the initial UTI. There are a number of underlying assumptions that at the time of this study were unknown. What the authors have deemed 'appropriate treatment' may have been acceptable at the time (early 1980's) but is not necessarily supported by evidence. This study has been given a - grade because of the above.

Incidence of new/progressive renal parenchymal defects

Bibliographic Information	Study Type & Evidence Level	Study Aims	Number of Patients &	Patient Characteristics	Intervention and comparison	Outcome measures	Results & Comments	Reviewer Comment
Martinell J;Hansson S;Claesson I;Jacobsson B;Lidin-Janson G;Jodal U; 2000 [97]	Study Type: Case-series follow up. Evidence Level: 3	The relationship between age at first infection, age at detection of renal scarring, occurrence of dilated VUR and attacks of pyelonephritis, and the appearance of lesions during follow up.	107 Females who had been continuously monitered for their first UTI in childhood	Bacteriuria was defined as at least 10^5 cfu/ml in a clean-catch specimen or any growth on SPA. Acute pyelonephritis bacteriuria was required together with fever of at least 38.5°C below the age of 16 years and 38.0°C in older patients	All patients received at least 2 urographies with a mean number of investigations	Median age at first urography 7.1 years (range 0.2 to 16.3 years) and at the last urography 21.7 years (range 14.7 to 36.1 years).	Median age at first urography 4.7 years. Median age at detection of scarring 9.9 years (mean 10.9 years) On first urography scars were seen on 38/107 (36%) unilateral in 31 Bilateral in 7 On last urography 51/107 (48%) with scars Unilateral in 38 Bilateral in 14 Status unchanged in 23 but had deteriorated in 28. In 56/107, no scarring was observed Progression of scarring In 23 with established scars, the degree of scarring remained unchanged during follow up. In 28 there was a progression; 10 developed more severe scars, 5 with unilateral scarring developed new scars in the other kidney, 13 developed new scars in previously normal kidneys. VUR 67/106 (63%) had reflux Of the 51 with renal scarring 42 (82%) had reflux. There was a significant relationship between maximal reflux grade and renal scarring (p<0.001) Risk factors for scarring Grade of reflux (<0.0001), number of pyelonephritis attacks (p<0.0001) and younger age at first recognised UTI (p<0.01) all correlated significantly with scarring	
Naseer SR;Steinhardt GF; 1997 [249]	Study Type: Case series Evidence Level: 3	To characterise patients in whom new renal scars developed while being monitored for UTIs	1426 patients with urinary tract infections	All patients with urinary tract infection, pyelonephritis and reflux identified between 1988 and 1996. Pyelonephritis defined as febrile UTI with flank pain and tenderness New scar defined as new DMSA perfusion defect not seen on the initial DMSA scan.	DMSA 4 months after presenting with UTI Cystogram	Renal scarring	685/1462 (46%) with pyelonephritis 1062/1426 (75%) with reflux (558 bilateral and 504 unilateral. 192 (13.5%) had scarring at initial presentation 31/1426 (2.1%) developed scars, 30 of which were progressive and 1 which was new.	No definition of UTI Selection criteria unclear
Smellie JM;Ransley PG;Normand IC;Prescod N;Edwards D;	Study Type: OtherCase-series Evidence Level: 3	Factors surrounding the development of renal scars	120 children	Children aged 2 weeks to 12 years who had an intravenous urograms and a UTI seen between 1960 and 1982. New scars were defined as	No interventions		Scars developed in 87 kidneys of 74 children (8 boys, 66 girls) New scars 58/74 (78%) of children had normal kidneys initially; unilateral scarring in 46, bilateral in 12 Progressive scars	

Bibliographic Information	Study Type & Evidence Level	Study Aims	Number of Patients &	Patient Characteristics	Intervention and comparison	Outcome measures	Results & Comments	Reviewer Comment
1985 Jun 29 98				the development of a caliceal deformity with thinning of the overlying renal parenchyma in an area of kidney considered to be normal in the previous urogram. Exclusions: solitary, duplex or horseshoe kidneys, kidney stones, mechanical or neuropathic or postoperative obstruction. Definition of UTI not reported.			13/74 (18%) had unilateral scarring initially and developed additional scars 3/74 children had bilateral scarring initially and developed additional scars All children with scarring had UTI 61/74 (82%) due to E. coli. Symptoms presenting symptoms were: fever (57/74) 77% abdominal or loin pain (34/74) 46% chronic constipation (16/74) 21% uncoordinated voiding with residual urine (8/74) 11% 67/74 (91%) children had reflux, new scars developed with all grades of reflux. However there was a greater tendency for scaring to occur in more severe reflux. 51% of the children who developed scarring had previously had a UTI.	
Vernon SJ;Coulthard MG;Lambert HJ;Keir MJ;Matthews JNS; 1997 95	Study Type: Case-series Evidence Level: 3	To determine up to what age children remain at risk of developing a new renal scar from a UTI	429 children (339 girls, 158 boys)	Children with a UTI at age 3 or 4 who had a normal ultrasound scan and a normal DMSA scan. Parents were invited to bring the children back to be re-scanned 2-11 years later.	DMSA	Frequency of new renal scars	No. of infections before original scanning: 3 year-olds 1 127/209 (61%) 2 25/209 (12%) 3 or more 7/209 (3%) Unknown 50/209 (24%) 4 year-olds 1 121/220 (55%) 2 29/220 (13%) 3 or more 16/220 (7%) Unknown 54/220 (25%) Overall (3 and 4 year olds) 1 248/429 (58%) 2 54/429 (13%) 3 or more 23/429 (5.4%) Unknown 104/429 (24%) No. of infections between original scanning and follow up scanning: 3 years-olds 0 128/176 (73%) 1 22/176 (13%) 2 3/176 (2%) 3 or more 23/176 (13%) Infection at repeat scanning 7/176 (4%) 4 year-olds 0 124/179 (69%) 1 8/179 (4%) 2 17/179 (9%)	Not all UTIs were confirmed by a reliable source - although the number is small. Of the 3 year olds 11% were confirmed by both the GP and the parent and 2% were confirmed by the GP alone. Of the 4 year olds 7% were confirmed by both the GP and the parent and 9% were confirmed by the GP alone.

Bibliographic Information	Study Type & Evidence Level	Study Aims	Number of Patients &	Patient Characteristics	Intervention and comparison	Outcome measures	Results & Comments	Reviewer Comment
							3 or more 30/179 (17%) Infection at repeat scanning 24/179 (13%) Overall 3 and 4 years-olds 0 252/355 (71%) 1 30/355 (8.5%) 2 20/355 (5.6%) 3 or more 53/355 (15%) Infection at repeat scanning 31/355 (8.7%) Overall 5/355 (1.4%) children developed scarring in follow-up period and all were girls in the 3 year old group. Of the children who had scarring 2/5 2 UTIs before original scanning 1/5 3 or more UTIs before original scanning 2/5 unknown number of UTIs before original scanning Of the children who had scarring 1/5 had no UTIs between original and follow up scanning 4/5 had three or more UTIs between original and follow up scanning 2/5 had an infection at repeat scanning	
Cardiff-Oxford Bacteriuria study group 1978 Apr 29 226	Study Type: RCT Evidence level: 1-	To determine the effects of covert bacteriuria on renal growth and scarring.	208 girls (110 girls treated 98 girls not treated)	Girls identified as having cover bacteriuria for screening study [55] Bacteriuria defined as <10^5cfu/ml in at least 2 consecutive mid-stream samples.	Intervention: Treatment with antibacterial therapy for bacteriuria (usually given co-trimoxazole but also ampicillin, nitrofurantoin, nalidixic acid and pivmecillinam, initially 7 or 14 day course were given but longer courses at discretion of Dr) Controls received no treatment During the study period (date of first x-ray till the date of the second, mid-stream urine samples were collected monthly in one health	Follow-up period: from date of first x ray to second four years (± 0.3 years) later. Outcome Measures: time free from infection emergence of symptoms clearance of VUR kidney growth progression of kidney scars	Bacteriuria at end of study: 17/110 (15%) in treatment girls and 44/98 (45%) in girls with no treatment (chi2=20, p < 0.001) 28/98 (29%) in the treatment group were scarred at the first x-ray 12/110 (15%) in the treatment group were scarred at the first x-ray No new scars were seen in girls who had normal kidneys at the initial x-ray examination Of the girls with scars at the initial x-ray new and/or deepening scars were found in 12/44 (27%). 6/28 (21%) in the girls who received treatment and 6/16 (38%) in the girls who received no treatment.	7 girls excluded - reason for exclusion unknown. Loss to follow-up was 13% in the treated group and 19% in the control group. This is a 16% loss overall. No explanation of whether those lost were similar to the girls followed-up. Study is given a - rating for this reason. Did not use intention to treat analysis.

Bibliographic Information	Study Type & Evidence Level	Study Aims	Number of Patients &	Patient Characteristics	Intervention and comparison	Outcome measures	Results & Comments	Reviewer Comment
					district (Oxford) and every two months in the other (Cardiff). Comparison: treatment versus control			
Ditchfield MR;Grimwood K;Cook DJ;Powell HR;Sloane R;Gulati S;De Campo JF; 2004 Jun 250	Study Type: Case-series Evidence Level: 3-	To determine the prevalence of renal cortical defects in children 2 years after the child's first recognised UTI and to analyse the relationship of these defects with acute illness variables, primary VUR and recurrent infections.	193 children recruited, 150 followed up.	193 children aged younger than 5 years presenting to the emergency department of a children's hospital with their first (culture proven) UTI Exclusions: Obstructive uropathy, neurogenic bladder. UTI: At least 10^5cfu/ml from a midstream or catheter specimen or any growth from SPA.	Antibiotic treatment VCUG DMSA	VUR (and grade) on VCUG Scarring on DMSA 0=none 1 = possible defects 2 = probable defects 3 = definite defects For analysis defects graded 0 or 1 were considered normal and those graded 2 or 3 were considered abnormal.	Repeat DMSA were performed on 150/193 (78%) children of whom 54 (36%) had grade 3-5 VUR. Those lost to follow-up were younger, had fewer hospitalisations, lower prevalence of VUR and overall, had a significantly lower risk of initial renal cortical defects, either as subjects (X2 = 6.59, p=0.01), or their individual kidneys (X2 = 4.60, p=0.03) 75/150 (50%) had an acute renal cortical defect in 95 kidneys on initial DMSA. 2 years later defects persisted in 20 of the 75 participants. During the study period 15 (10%) children had further UTIs diagnosed. No new defects were detected in the 150 children, including those with recurrent UTI. Prevalence of persistent defects after UTI for all study participants was 20/150 (13.3%, 95%CI 8.3, 19.8) Resolved vs. persistent renal cortical scintigraphic defects, p-value Male 22/55 (40%) vs. 2/20 (10%), p=0.023 Female 33/55 (60%) vs. 18/20 (90%) p=0.004 Age less than 24 months 47/55 (85%) vs. 8/20 (40%) p<0.001 Hospitalisation 37/55 (67%) vs. 9/20 (45%) p=0.10 Reflux grade 2 8/55 (15%) vs. 4/20 (25%) p=0.72 Reflux grades 3-5 10/55 (18%) 6/30 (30%) p=0.34 Recurrent infection 11/55 (20%) vs. 4 (20%) p=1.0	22% loss to follow-up could have a large impact on the results. Those lost to follow-up were younger, ewer hospitalisations, lower prevalence of VUR and overall, had a significantly lower risk of initial renal cortical defects - study results will be over-estimated.

Diagnostic value of detecting renal parenchymal defects

Bibliographic Information	Study type & Evidence level	Study Aims	Number of patients & prevalence	Population Characteristics	Type of test and Reference standard	Outcome measures	Sensitivity, Specificity, PPV and NPV	Reviewer comment
Moorthy I;Wheat D;Gordon I; 2004 [251]	Diagnostic study Evidence level II	The use of ultrasonography in the evaluation of renal scarring.	465 patients (930 kidneys) Number of boys and girls unknown	Children aged 3 months to 16 years with proven UTI who presented to a radiology department and who underwent ultrasound and DMSA on the same day at least 3 months after UTI.	Ultrsonography compared to DMSA (both examinations on the same day)	Focal scarring on DMSA: Diffuse or sharp indentation in contour with thinning of cortex; Any shaped defects with loss of renal volume; Degree of photopenia more commonly severe or absent activity. Diffuse scarring on DMSA: Differential function <45% with homogenous uptake. Focal scarring on ultrasound: Approximation of sinus echoes to cortical surface with or without underlying calyceal dilatation; Irregularity of cortical outline. Diffuse scarring on ultrasound: global cortical thinning; >10% difference in renal length on prone view.	Focal scarring in Kidneys Sensitivity: 5.2% Specificity: 98.3% PPV: 50% NPV: 75.8% Diffuse scarring in Kidneys Sensitivity: 47.2% Specificity: 91.8% PPV: 60.8% NPV: 86.6%	
Wang Y;Chiu N;Chen M;Huang J;Chou H;Chiou Y; 2005 [191]	Diagnostic study Evidence level III	To compare the renal parenchymal changes seen on US with DMSA in children with acute pyelonephritis and to explore the possibility of detecting the inflammation of APN with US and correlating it with the risk of scarring.	45 children (31 boys and 14 girls)	Children aged 9 days to 10 years old (mean 1.5 ± 0.2 years, median 0.3 years) with febrile UTI who fulfilled criteria for acute pyelonephritis and underwent initial DMSA.	Ultrasound and laboratory tests (at the time of hospitalisation) compared to DMSA (performed within one week of hospitalisation)	US assessed as abnormal if one of the following features was observed: parenchymal hyperechogenicity, focal lesion with hyperechogenicity or hypoechogenecity, thickening of the renal pelvis wall, or significant enlargement of the kidney length or width compared to the opposite kidney and compared to the normal range for	US for detecting APN Sensitivity 49% Specificity 88% PPV 91% NPV 40% (p<0.005, OR 7.1, 95%CI 2.18 to 24.41) CRP >70mg/L for detecting APN Sensitivity 59% Specificity 61% PPV 59% NPV 61% (p=0.13, OR 2.2, 95%CI 0.78 to 6.18) US and CRP combined for detecting APN	The effects of bias in this study are unknown. Loss to follow up is not explained - for the CRP and low/high risk groups, n=80 where in the US group n=90. Similarly for the follow up DMSA to predict scarring 65 abnormal kidneys were analysed for US while n=58 for CRP and low/high risk groups. This represents more than 10% loss to follow up. The author has been

Bibliographic Information	Study type & Evidence level	Study Aims	Number of patients & prevalence	Population Characteristics	Type of test and Reference standard	Outcome measures	Sensitivity, Specificity, PPV and NPV	Reviewer comment
						patient age. Acute DMSA: Acute inflammation was indicated if at least one area of decreased focal or diffuse cortical uptake of DMSA was noted with the renal outline preserved. Follow-up DMSA A small whole renal volume and/or deformation of the renal outlines was considered evidence of previous parenchymal injury. If one or more areas of focal renal cortical defects were consistently associated with defects in the renal outline, a renal scar was diagnosed.	Sensitivity 36% Specificity 95% PPV 95% NPV 36% (p<0.005, OR 11.9, 95%CI 2.15 to 65.72) US for predicting scarring Sensitivity 59% Specificity 61% PPV 59% NPV 61% (p=0.11, OR 2.3, 95% CI 0.82 to 7.65) CRP >70mg/L for predicting scarring Sensitivity 81% Specificity 74% PPV 78% NPV 77% (p<0.0001, OR 11.9, 95%CI 3.72 to 38.11) US and CRP combined for predicting scarring Sensitivity 52% Specificity 81% PPV 76% NPV 59% (p<0.01, OR 4.7, 95%CI 1.47 to 14.95)	contacted to clarify this. Only children with abnormal initial DMSA were followed-up. This is potentially misleading in terms of scar formation as there is no comparison group and no potential for the false negatives in the initial group to be recognised. This could over-estimate the effectiveness of the test.
Temiz Y;Tarcan T;Onol FF;Alpay H;Simsek F; 2006 [252]	Diagnostic study Evidence level II	To investigate and compare the efficacy of DMSA and renal ultrasonography in detecting renal scars in children with primary VUR.	62 children (18 boys, 44 girls)	Children aged 6 months to 15 years (mean age 5 years) diagnosed with primary VUR between 1997 and 2003 following a documented UTI. Reflux was bilateral in 29 children and unilateral in 33 children.	DMSA and ultrasound were performed simultaneously.		Of the 90 refluxing units 30 (33%) had grades I to II 37 (41%) had grade III 24 (26%) had grades IV to V DMSA detected renal scars in 32/58 units with bilateral VUR and in 20/33 units with unilateral VUR. Ultrasonography detected scars in 22/58 units with bilateral VUR and in 9/33 with unilateral VUR. Ultrasound did not detect any defects when DMSA was normal. NCC Calculated Unilateral VUR Sensitivity: 69% Specificity: 100% PPV: 100% NPV: 72% Bilateral VUR	.

Bibliographic Information	Study type & Evidence level	Study Aims	Number of patients & prevalence	Population Characteristics	Type of test and Reference standard	Outcome measures	Sensitivity, Specificity, PPV and NPV	Reviewer comment
							Sensitivity: 45% Specificity: 100% PPV: 100% NPV: 54%	
Kavanagh EC;Ryan S;Awan A;McCourbrey S;O'Connor R;Donoghue V; 2005 [253]	Diagnostic study Evidence level Ib	To compare DMSA with MRI for the detection of renal parenchymal defects in children presenting for radiological investigation after a first UTI.	37 children (19 boys and 18 girls)	Children aged 4 months to 13 years (mean 4.5 years) presenting for radiological investigation at a paediatric hospital after a first UTI. MRI and DMSA were performed at the same appointment. Renal scarring was defined as a photopenic focus and contracted contour on DMSA and as a contracted contour or focal defect on MR sequences.	MRI compared to DMSA (undertaken at the same appointment)	Kidney scarring on a kidney-by-kidney basis where each kidney was graded as normal or abnormal for renal scarring. Kidney scarring on a zonal basis where each kidney was divided into 6 zones and each zone was assessed for the presence or absence of renal scarring..	Scarring on a kidney-by-kidney basis Sensitivity 77% Specificity 87% PPV 77% NPV 87% Scarring on a zonal basis Sensitivity 75% Specificity 98% PPV 83% NPV 97%	Three radiologists reported the MRI results blind to results of the DMSA.
Kovanlikaya A;Okkay N;Cakmakci H;Ozdogan O;Degirmenci B;Kavukcu S; 2004 Jan [254]	Study type: Diagnostic Evidence level: II	To compare MRI and DMSA findings in childhood acute pyelonephritis and to determine pyelonephritic foci in the acute phase.	20 children (15 females, 5 males)	Children aged 2 to 14 years (mean age 7.3 ± 3.4 years) with symptoms of dysuria, enuresis, costovertebral pain, fever of <37.5°C and/or a positive urine culture. Exclusions: elevated levels of serum creatinine, allergy to gadopentate dimeglumine, history of haemolysis and claustrophobia.	MRI compared to DMSA - all children underwent investigations within a week in either order.	Pyelonephritic lesions The kidneys were divided into three zones (upper, mid and lower) Acute pyelonephritis was seen as increased signal areas on enhanced images.	Both MRI and RCS demonstrated evidence of lesions in 11 (55%) patients. Sensitivity 91% Specificity 89% PPV 91% NPV 89% No statistically significant difference in lesion detection according to kidney zones between the two methods (p>0.05)	Small number of children limits the usefulness of this study No definition of a positive urine culture.

Surgical intervention for VUR

Bibliographic Information	Study Type & Evidence Level	Study Aim	Number of Patients	Patient Characteristics	Intervention & Comparison	Follow-up & Outcome Measures	Effect Size	Reviewer Comments
Wheeler DM;Vimalachandra D;Hodson EM;Roy LP;Smith GH;Craig JC; 2004 [235]	Study Type: Systematic review - meta-analysis Evidence level: 1++	To evaluate the benefits and harms of different treatment options for primary VUR	847 children of any age with primary VUR diagnosed by MCUG following a UTI were included in 7 RCTs.	10 studies met the inclusion criteria of the systematic review. Seven trials were included for the review of the guideline. One trial compared prophylaxis with no treatment and is reported in the prophylaxis section of the guideline. Two additional studies compared materials for endoscopic correction of VUR and are outside the scope.	Intervention: Treatments of VUR including surgery (open and endoscopic techniques) and antibiotic prophylaxis of any duration. Comparison:	Follow-up period: Outcome Measures: UTI Renal parehcnymal abnormality	Antibiotic prophylaxis vs. surgery and antibiotics, outcome UTI Seven trials compared prophylaxis with surgery and antibiotics with the outcomes of UTI. The frequency of recurrent UTI ranged from 0-42% in the antibiotic only group and from 20-22% in the surgery and antibiotic group. By two years there was no reduction in the risk of UTI in the surgery and antibiotic vs. the antibiotic only group (RR1.07, 95%CI 0.55 to 2.09). By five years there was no significant differences in the risk of UTI between the groups (RR 0.99, 95%CI 0.79 to 1.26) The risk of febrile UTI reported by the European and USA arms of the International reflux study was significantly lower in the surgery and antibiotic groups (8-10%) than in the antibiotic only groups (22%) (RR 0.43, 95%CI 0.27 to 0.70). The overall incidence of symptomatic UTI (reported only by the European arm) showed no significant difference between the groups (RR 0.95, 95%CI 0.67 to 1.35) Antibiotic prophylaxis vs. surgery and antibiotics, outcome renal parenchymal abnormality Seven trials compared prophylaxis with surgery and antibiotics with the outcomes of renal parenchymal abnormality. (see table in text) The risk of renal parenchymal abnormality at 5 years using DMSA was investigated in the European arm of the International Reflux study where no differences	Birmingham reflux study only enrolled children with dialating reflux (grades 3 to 5). International reflux study only enrolled children with grades 3 to 4 reflux – children with grade 5 were excluded.

Bibliographic Information	Study Type & Evidence Level	Study Aim	Number of Patients	Patient Characteristics	Intervention & Comparison	Follow-up & Outcome Measures	Effect Size	Reviewer Comments
							were found between the antibiotic group and the surgery and antibiotic group (RR 0.97 95%CI 0.58 to 1.62). The European and US arms of the International Reflux study differentiated between renal scarring and renal parenchymal thinning on IVP. There were no differences at 5 years (RR 1.28 95%CI 0.84 to 1.94) or at 10 years (RR0.90 95%CI 0.46 to 1.75). There was no significant difference between daily antibiotic prophylaxis and no prophylaxis (RR 0.25, 95%CI 0.03 to 1.83) or between three day a week prophylaxis and no prophylaxis (RR 0.46 95%CI 0.10 to 2.00) There were no differences in the risk of renal parenchymal damage between daily antibiotic prophylaxis and no prophylaxis (RR 0.40 95%CI 0.02 to 9.18) or between three day a week prophylaxis and no prophylaxis (RR 0.38 95%CI 0.02 to 8.59).	

Advice

Bibliographic Information	Study Type & Evidence Level	Aim of Study	Number of Patients & Patient Characteristics	Population Characteristics	Outcome measures	Results & Comments	Intervention	Reviewer Comment
Owen D;Vidal-Alaball J;Mansour M;Bordeaux K;Jones KV;Edwards A; 2003 Oct 260	Study Type: OtherCase-series Evidence Level: 3	To assess parental understanding of UTI in their child and identify any delay perceived in the diagnosis, along with identifying how helpful parents had found any information they had been given	52 parents	Parents of children aged over two years being investigated in one outpatient department following proven UTI between 1998 and 2000. Children were eligible if they had no previous history of renal pathology and had been referred to the outpatient department with proven UTI. All children were new referrals and were at their first clinic visit.	Closed and open questions	Was explanation given about the need to test for UTI? 87% yes, 13% no If so, was the explanation helpful? 83% yes, 17% no Did you receive a leaflet about childhood UTIs? 52% yes, 48% no If so, was the leaflet useful? 100% yes, 0% no Was an explanation given about how to collect urine? 79% yes, 21% no If so was the explanation helpful? 95% yes, 5% no Was it difficult to collect urine? 54% yes, 46% no Which method of urine collection did you prefer or manage? Clean catch 40% Bag 37% Pad 23% Did you receive enough information regarding possible future illness episodes? 80% yes, 20% no Would you know what to do in the event of a repeat episode of UTI? 89% yes, 11% no From this first episode, who requested a urine sample for testing? GP 71% Hospital on admission 8% Health visitor 2% Nurse practitioner 2% Parents themselves 17% On which visit to the clinic was the urine sample requested? First 37% Second 31% Third 14% Fourth 8% Missing 7% Was the sample taken before starting antibiotics? 84% yes, 16% no Content analysis of the qualitative data identified some key themes -Delays in requesting urine samples. Some parents felt	Intervention: Semi-structured questionnaire was given to parents at their first attendance	

Bibliographic Information	Study Type & Evidence Level	Aim of Study	Number of Patients & Patient Characteristics	Population Characteristics	Outcome measures	Results & Comments	Intervention	Reviewer Comment
						there had been a delay between their child becoming unwell and a urine sample being requested. -Difficulties in collection. Mainly around bag collection methods which some parents said produced unnecessary discomfort for their child, while others felt it was difficult to keep the bag in place. -Information. Some parents were happy with the information they received, however the majority requested more information and more detailed advice. -Empowering. Following the initial event, parents in this study seemed to understand more about the diagnosis and felt in a better position to deal with future episodes of UTI in their children. Some parents suggested that their experience taught them what to do in the future. -Organisational problems. A number of parents expressed frustration at organisational aspects in terms of limited GP resources in the weekend, several hospital appointments for investigations and receiving different information from different health care professionals.		
Liaw,L.C.T.; Nayar,D.M.; Pedler,S.J.; Coulthard,M.G. 2000 155	Study Type: Cohort study Evidence level: 2+	To investigate parent's preference on urine collection methods	N=44 Parents,	29 boys, median age 4 months, (1-18 months) Parents of children aged 1 to 18 months volunteered to collect urine at home by pads, bags and clean catch in a rondom order on one day	Parent's preference	Parents' assessments Pad/Bag/Clean Catch Preference order First 21/18/5 Second 19/12/ 13 Third 4/ 14/ 26 Open comments Positive Easy, hygienic, or quick 25/ 24/ 8 Comfortable for child 10/ 3/ 0 Negative Uncomfortable or distressing 1 /26/ 3 Fiddly or messy 9/ 10/ 20 Impractical or time consuming 10/ 0/ 36 Difficult to get urine out of pad 8 Red marks left on skin — /11/ — Too much trouble—gave up (boys) 1 (0)/ 4 (3)/ 9 (5)	Parent's preference assessed	

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Enquiries regarding the above guidelines can be addressed to:

National Collaborating Centre for Women's and Children's Health
27 Sussex Place
Regent's Park
London
NW1 4RG
team@ncc-wch.org.uk

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