Further investigation of confirmed urinary tract infection (UTI) in children under five years: a systematic review
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CRD summary
This review concluded that there is no evidence to suggest that routine investigation of children with confirmed urinary tract infection (UTI) is effective, and that further research on the effectiveness of investigation of UTI is urgently required. These conclusions are likely to be reliable.

Authors' objectives
To determine the most effective approach to the further investigation of confirmed urinary tract infection (UTI) in children under 5 years of age.

Searching
The authors searched 16 databases (including MEDLINE and EMBASE) from inception to between October 2002 and February 2003 without any language restrictions. The searches were updated in May 2004. In addition, 12 key journals were handsearched, references lists were screened for additional references, and experts in the field were contacted for further published or unpublished material. Full details of the search were reported elsewhere (see Other Publications of Related Interest).

Study selection
Study designs of evaluations included in the review
Controlled trials comparing different imaging strategies and diagnostic cohort studies were eligible for inclusion.

Specific interventions included in the review
Studies were included if they evaluated tests intended to localise the infection, detect reflux, or were used to detect or predict renal scarring. Such tests included clinical features, laboratory-based tests, ultrasound, indirect radionuclide cystography, micturating cystourethrography (MCUG), acute DMSA renal scintigraphy and intravenous pyelography (IVP).

Reference standard test against which the new test was compared
Studies of reflux had to use MCUG as the reference standard; studies with other clinical aims had to use Tc-99 m-DMSA renal scintigraphy as the reference standard (or follow-up of findings from this test in the case of studies to predict renal scarring).

Participants included in the review
Diagnostic cohort studies were included if they included at least 20 children, some of whom were aged 5 years or younger.

Outcomes assessed in the review
Studies were included if they provided patient-based outcomes or sufficient information to construct a 2x2 table to calculate estimates of test performance.

How were decisions on the relevance of primary studies made?
Two reviewers independently selected titles and abstracts, with any disagreements resolved by consensus. One reviewer selected full papers for inclusion and a second reviewer checked their decisions.

Assessment of study quality
The included studies were assessed using the 14-item QUADAS (Quality Assessment of Diagnostic Accuracy Studies)
checklist. One reviewer performed the quality assessment and a second reviewer checked the assessment.

**Data extraction**

One reviewer extracted the data and a second reviewer checked the extraction. The sensitivity, specificity, positive and negative likelihood ratios (LR+ and LR-, respectively), and diagnostic odds ratios were calculated from 2x2 data for each test or test combination.

**Methods of synthesis**

How were the studies combined?
The groups were analysed by clinical aim. Where possible, the LR+ and LR- were pooled using a random-effects model. Where multiple estimates of test performance were presented for the same test, the estimate most clinically similar to other studies was included in the meta-analysis.

How were differences between studies investigated?
The heterogeneity of LRs was assessed using the Q statistic and by visual examination of forest plots. Sensitivity and 1 minus specificity were plotted in receiver operating characteristic space. Where there were sufficient data, heterogeneity was further investigated using regression analysis, with consideration given to sample size, patient age, geographic region, QUADAS items, and also ultrasound technique for the detection of reflux.

**Results of the review**

A total of 73 studies were included in the review: 1 randomised controlled trials (RCT; n=172) and 72 diagnostic cohort studies (number of participants unclear).

**Clinical effectiveness.**

Details of one RCT comparing routine versus selected imaging (using ultrasound and MCUG) were available in abstract form. Routine investigation led to higher rates of imaging (100% versus 21%), identification of reflux and antibiotic prophylaxis, but did not influence the proportion of children with recurrent UTI or the rate of renal scarring after 2 years’ follow-up.

**Diagnostic accuracy.**

In terms of quality, around half the diagnostic cohort studies reported an appropriate patient spectrum or selection criteria. Similarly, around half did not adequately address incorporation bias, disease progression bias or verification bias.

**Localisation of infection.**

Ultrasound (20 studies) gave poor performance both for ruling in (pooled LR+ 3.5, 95% confidence interval, CI: 2.5, 4.8) and ruling out (pooled LR- 0.57, 95% CI: 0.47, 0.68) renal involvement. The clinical and laboratory tests investigated gave varied results and showed poor performance in general: for clinical features (5 studies), the LR+ ranged from 1.1 to 26.6 and the LR- from 0.09 to 0.89; for infection markers (10 studies), the LR+ ranged from 1.0 to 8.8 and the LR- from 0.09 to 1.00; for renal function markers (4 studies), the LR+ ranged from 0.7 to 36.7 and the LR- from 0.02 to 1.51; for immunofluorescence detection of bacteria (1 study), the LR+ was 1.8 and the LR- was 0.55.

**Detection of reflux.**

Standard ultrasound (12 studies) performed poorly (pooled LR+ 1.9, 95% CI: 1.2, 2.9; pooled LR- 0.76, 95% CI: 0.63, 0.93). Contrast-enhanced ultrasound (16 studies) showed much better performance (pooled LR+ 14.1, 95% CI: 9.5, 20.8; pooled LR- 0.20, 95% CI: 0.13, 0.29). Indirect radionuclide cystography (2 studies) showed good LR+ (11.2 and 25.0), but poor LR- (0.41 and 0.68).

**Prediction of renal scarring.**
The diagnostic accuracies of tests evaluated for this clinical aim (clinical, laboratory-based and imaging techniques) were generally poor. The LR+ ranged from 1.1 to 3.1 for four of the studies, with 12.9 for a single evaluation of IVP. The LR- ranged from 0.44 to 0.88.

Detection of renal scarring.

For ultrasound (7 studies), LR+ ranged from 1.3 to 35.9 and LR- from 0.14 to 0.99. For IVP (4 studies), the LR+ ranged from 10 to 171.3 and the LR- from 0.15 to 0.80. For indirect radionuclide cystography (2 studies), the LR+ ranged from 2.1 to 12.6 and the LR- from 0.15 to 0.75.

Authors’ conclusions
There is no evidence to suggest that routine investigation of children with confirmed UTI is effective. Further research on the effectiveness of investigation of UTI is urgently required.

CRD commentary
This was a well-conducted review that answered a well-defined question, searched multiple sources to identify all the relevant evidence, and used appropriate methods to synthesise the included studies and investigate heterogeneity. Validity was assessed using an appropriate published set of criteria, and multiple reviewers were used at each stage of the review in order to minimise the potential for errors and bias. Consequently, the authors’ conclusions are likely to be reliable.

Implications of the review for practice and research
Practice: Baseline renal scintigraphy in children with confirmed UTI, in whom further investigation is planned, may be beneficial in terms of eliminating some children from further invasive investigations. The use of MCUG should be minimised where possible; if evaluation of reflux is considered necessary, contrast-enhanced ultrasound should be considered as an alternative.

Research: Research on the effectiveness (in terms of patient outcomes) of testing at all stages in the investigation of UTI is urgently required. The authors also stated that further research on the accuracy of ultrasound in grading renal scarring is needed.

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Record Status
This is a critical abstract of a systematic review that meets the criteria for inclusion on DARE. Each critical abstract contains a brief summary of the review methods, results and conclusions followed by a detailed critical assessment on the reliability of the review and the conclusions drawn.