Absolute and relative accuracy of rapid urine tests for urinary tract infection in children: a meta-analysis

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CRD summary
This review assessed rapid urine tests for the diagnosis of urinary tract infection in children and concluded that no one test could identify all urinary tract infections without urine culture, but Gram-stain microscopy was the best single test. Dipstick tests should be considered positive if either leucocyte esterase or nitrite was positive. These conclusions are likely to be reliable.

Authors' objectives
To assess whether rapid urine tests were sufficiently sensitive to rule out urinary tract infection in children, without the use of urine culture, and to compare the accuracy of rapid tests with that of microscopy.

Searching
MEDLINE and EMBASE were searched for articles from their inception to July 2009, and full details of the search strategy were provided in an online appendix. The bibliographies of the primary studies and reviews were screened for additional articles. No language restrictions were applied, but retrieved articles in Hebrew, Turkish, Japanese, and Finnish were excluded because translators were not available.

Study selection
Studies comparing one or more rapid test for the diagnosis of urinary tract infection with the reference standard of urine culture, in children (18 years old or younger) were eligible for inclusion. Included studies were required to report sufficient data to construct two-by-two contingency tables with the numbers of true-positive, false-negative, false-positive, and true-negative test results.

The tests assessed in the included studies, alone or in various combinations, were: dipstick nitrite, dipstick leucocyte esterase, microscopy white-cell count, microscopy unstained bacterial count, and microscopy Gram-stained bacterial count.

Two reviewers assessed studies for inclusion.

Assessment of study quality
Quality assessment, based on the Quality Assessment of Diagnostic Accuracy Studies (QUADAS) tool, was conducted by two reviewers. The QUADAS assessed criteria for the spectrum of patients, participant selection, reference and index test methods, verification biases, test independence and interpretation, clinical setting, and handling of missing data and uninterpretable test results. Some design features specific to the setting were also assessed: the test threshold (index test and reference standard) and the use of sample centrifugation.

Data extraction
Two reviewers extracted two-by-two contingency data from each study and used these to calculate the sensitivity, specificity, and diagnostic odds ratio. Where data were reported for more than one diagnostic threshold, those for the threshold used by most of the other studies were used.

The units for microscopy white-cell count were standardised to cells per microlitre, using Stansfield's conversion, from cells per high-power field.

Methods of synthesis
Where five or more studies reported data for the same test, summary receiver operating characteristic (SROC) curves were generated using a hierarchical model. Covariates were added to the model to investigate whether the test accuracy,
the diagnostic threshold, or the shape of the SROC curve was affected by study quality. Only those results that were consistent before and after the removal of a potentially influential study were reported.

Studies comparing two or more index tests with the reference standard, in the same population, were used preferentially to assess the relative accuracy of the index tests. For these analyses, the hierarchical SROC model included test type as a covariate.

For studies reporting full two-by-two data for the index tests used in combination, the potential gain from using combined tests, compared with one test alone, was assessed; two combination rules were used, either positive, where the combined result was positive if either component test was positive, and both positive, where the combined result was positive only where both components were positive.

Results of the review
Ninety-five studies, with 95,703 children and 94,664 urine samples, were included in the analyses. Fifty-three studies (73,085 urine samples) reported data for multiple tests, allowing the estimation of relative test performance. Study quality was variable: 68 studies were conducted in children who were not representative of those in whom the test would normally be used in practice; 37 studies did not report the reference standard methods; and 20 reported no details of the index test methods; few studies reported details of blinding for the interpretation of results. The definition of a positive test was highly heterogeneous, with seven thresholds reported for white-cell count, five for bacterial microscopy, and three for leucocyte esterase.

Microscopy: For Gram-stained bacteria, the summary estimate of sensitivity was 91% (95% CI 80 to 96) and the specificity was 96% (95% CI 92 to 98; 17 studies; 12,530 children). For unstained bacteria, the sensitivity was 88% (95% CI 75 to 94) and the specificity was 92% (95% CI 83 to 96; 22 studies; 54,088 children). For white-cell count, the sensitivity was 74% (95% CI 67 to 80) and the specificity was 86% (95% CI 82 to 90; 49 studies; 66,937 children).

Dipstick: A positive leucocyte esterase test alone gave a sensitivity of 79% (95% CI 73 to 84) and a specificity of 87% (95% CI 80 to 92; 30 studies; 12,954 children). A positive nitrite test alone gave a sensitivity of 49% (95% CI 41 to 57) and a specificity of 98% (95% CI 96 to 99; 46 studies; 62,671 children). The combination of either leucocyte esterase or nitrite positive gave a sensitivity of 88% (95% CI 82 to 91) and a specificity of 79% (95% CI 69 to 87; 15 studies; 6,492 children). The combination of both leucocyte esterase and nitrite positive gave a sensitivity of 45% (95% CI 30 to 61) and a specificity of 98% (95% CI 96 to 99; 13 studies; 5,751 children). There was evidence that the diagnostic odds ratio varied significantly with the threshold used to define a positive test, for both nitrite (p=0.008) and leucocyte esterase (p=0.004).

The ranges of sensitivity and specificity estimates were reported for other test combinations. On the basis of data from studies assessing multiple tests, microscopy for Gram-stained bacteria had a higher accuracy than other laboratory tests with relative diagnostic odds ratios: compared with unstained bacteria of 8·7 (95% CI 1·8 to 41·1), compared with white-cell count of 14·5 (95% CI 4·7 to 44·4), and compared with nitrite of 22·0 (95% CI 0·7 to 746·3).

Authors' conclusions
No rapid urine test was sufficiently sensitive to identify all children with urinary tract infection without the need for a urine culture, but if resources allowed, microscopy with Gram stain should be used as a single rapid test. Dipstick tests should be considered positive if either leucocyte esterase or nitrite was positive.

CRD commentary
The review clearly stated its research objective and defined appropriate inclusion criteria before searching. A number of sources were searched for relevant studies, with no apparent restrictions. Measures were taken, throughout the review process to minimise the potential for error and bias, and the methodological quality of the included studies was appropriately assessed and considered in the analyses and interpretation of the results. The analytic methods were appropriate and were applied to provide relevant information on the alternative clinical diagnostic pathways.

The authors' conclusions reflected the data presented and are likely to be reliable.
Implications of the review for practice and research

**Practice**: The authors stated that the detection of bacteria in urine by microscopy with Gram staining was the best single test and, if it was available locally and reported rapidly, it was the only test that would need to be done to guide the empirical treatment of children using antibiotics. A count of white cells in urine by microscopy was no better than the dipstick tests and should not be used. The dipstick test should be interpreted as positive if either leucocyte esterase or nitrite is positive.

**Research**: The authors did not specify any recommendations for future research.

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