Does This Child Have a Urinary Tract Infection?

Nader Shaikh, MD, MPH
Natalia E. Morone, MD, MSc
John Lopez, MD
Jennifer Chianese, MD, MSc
Shilpa Sangvai, MD, MPH
Frank D'Amico, PhD
Alejandro Hoberman, MD
Ellen R. Wald, MD

Context Urinary tract infection (UTI) is a frequently occurring pediatric illness that, if left untreated, can lead to permanent renal injury. Accordingly, accurate diagnosis of UTI is important.

Objective To review the diagnostic accuracy of symptoms and signs for the diagnosis of UTI in infants and children.

Data Sources A search of MEDLINE and EMBASE databases was conducted for articles published between 1966 and October 2007, as well as a manual review of bibliographies of all articles meeting inclusion criteria, 1 previously published systematic review, 3 clinical skills textbooks, and 2 experts in the field, yielding 6988 potentially relevant articles.

Study Selection Studies were included if they contained data on signs or symptoms of UTI in children through age 18 years. Of 337 articles examined, 12 met all inclusion criteria.

Data Extraction Two evaluators independently reviewed, rated, and abstracted data from each article.

Data Synthesis In infants with fever, history of a previous UTI (likelihood ratio [LR] range, 2.3-2.9), temperature higher than 40°C (LR range, 3.2-3.3), and suprapubic tenderness (LR, 4.4; 95% confidence interval [CI], 1.6-12.4) were the findings most useful for identifying those with a UTI. Among male infants, lack of circumcision increased the likelihood of a UTI (summary LR, 2.8; 95% CI, 1.9-4.3); and the presence of circumcision was the only finding with an LR of less than 0.5 (summary LR, 0.33; 95% CI, 0.18-0.63). Combinations of findings were more useful than individual findings in identifying infants with a UTI (for temperature >39°C for >48 hours without another potential source for fever on examination, the LR for all findings present was 4.0; 95% CI, 1.2-13.0; and for temperature <39°C with another source for fever, the LR was 0.37; 95% CI, 0.16-0.85). In verbal children, abdominal pain (LR, 6.3; 95% CI, 2.5-16.0), back pain (LR, 3.6; 95% CI, 2.1-6.1), dysuria, frequency, or both (LR range, 2.2-2.8), and new-onset urinary incontinence (LR, 4.6; 95% CI, 2.8-7.6) increased the likelihood of a UTI.

Conclusions Although individual signs and symptoms were helpful in the diagnosis of a UTI, they were not sufficiently accurate to definitively diagnose UTIs. Combination of findings can identify infants with a low likelihood of a UTI.

JAMA. 2007;298(24):2895-2904 www.jama.com

CLINICAL SCENARIOS

Case 1

The parents of a 14-month-old female infant report that she has been fussy with rectal temperatures of up to 39.8°C for the past 2 days. Her past medical history is unremarkable and her immunizations are up to date. She has been taking fluids without vomiting. On examination, she appears well and has no identifiable source for the fever.

Case 2

A 5-year-old boy presents with complaints that "it hurts when I pee." He has no other symptoms. On examination, he is afebrile and circumcised.

In this article, we assess whether clinicians can accurately diagnose urinary tract infections (UTIs) by using information from the history and physical examination.

WHY IS THIS QUESTION IMPORTANT?

Urinary tract infections account for 0.7% of all pediatric office encounters and 5% to 14% of pediatric emergency department visits in the United States.[1] If not detected and treated promptly, a UTI can lead to renal scarring, hypertension, and end-stage renal disease.

Children suspected of having a UTI should have a urine specimen collected that is free from contami-

Author Affiliations: Departments of Pediatrics (Drs Shaikh, Lopez, Chianese, and Hoberman) and Internal Medicine (Dr Morone), University of Pittsburgh School of Medicine, Pittsburgh, Pennsylvania; Department of Pediatrics, Ohio State University School of Medicine, Columbus (Dr Sangvai); Department of Mathematics, Duquesne University, Pittsburgh, Pennsylvania (Dr D'Amico); and Department of Pediatrics, University of Wisconsin School of Medicine and Public Health, Madison (Dr Wald).

Corresponding Author: Nader Shaikh, MD, MPH, Department of Pediatrics, Children's Hospital of Pittsburgh, 3705 Fifth Ave, Pittsburgh, PA 15213-2583 (nader.shaikh@chp.edu).

The Rational Clinical Examination Section Editors: David L. Simel, MD, MHS, Durham Veterans Affairs Medical Center and Duke University Medical Center, Durham, North Carolina; Drummond Rennie, MD, Deputy Editor.

Table 1. Pooled Prevalence of UTI in Infants by Age and Sex

	Male Infants		Female Infants		
	<3 mo	3-12 mo	<3 mo	3-12 mo	>12-24 mo
No. of studies	8	2	8	2	1
Prevalence of febrile UTI, % (95% CI)	8.7 (5.4-11.9)	2.2 (1.3-3.1)	7.5 (5.1-10.0)	7.2 (5.5-8.9)	2.1 (1.2-3.6)

Abbreviations: CI, confidence interval; UTI, urinary tract infection.

nating flora. This often involves either catheterization of the urethra or suprapubic aspiration, both of which can be viewed as relatively invasive procedures. Accordingly, it is important to use all available clinical information to select children who are likely to benefit from diagnostic testing.

Definition of a UTI

Recovery of any organisms from a suprapubic specimen, at least 50 000 colony-forming units per milliliter (CFUs/mL) from a catheterized specimen,[2] or at least 100 000 CFUs/mL from a clean-catch specimen is considered significant bacteriuria. The presence of at least 10 white blood cells per microliter from an unspun specimen examined using a counting chamber or at least 5 white blood cells per high power field from a centrifuged specimen constitutes significant pyuria. The presence of significant bacteriuria and pyuria in a symptomatic child constitutes a UTI. Common uropathogens include *Escherichia coli* (accounting for approximately 85% of UTIs in children), *Klebsiella*, *Proteus*, *Enterobacter*, *Citrobacter*, *Staphylococcus saprophyticus*, and *Enterococcus*. Positive cultures obtained using perineal bags are more likely to represent contamination than a true UTI.[3] A UTI can involve the kidney parenchyma (pyelonephritis), the bladder (cystitis), or both.

Differential Diagnosis

Infants (herein defined as ages 0-24 months) can present with fever as the sole manifestation of a UTI.[4,5] Among febrile infants with no other identifiable potential source for fever on physical examination (eg, acute otitis media, acute gastroenteritis, upper respiratory tract infection), the differential diagnosis frequently includes viral infection, UTI, and occult bacteremia. The probability of UTI (7%)[6] exceeds the probability of occult bacteremia among fully immunized children (<1%).[7,8]

Among verbal children (2-18 years) with urinary symptoms, the differential diagnosis includes urinary calculi, urethritis, sexually transmitted infection, dysfunctional elimination,[9] and diabetes. In girls, the differential also includes nonspecific vulvovaginitis and the presence of a vaginal foreign body.

Prevalence of a UTI

The prevalence of a UTI among children with symptoms suggestive of a UTI can be used as an estimate of baseline risk. In a meta-analysis,[6] we determined the pooled prevalence of UTI in children by age and sex from 18 pediatric studies. Among infants presenting with fever without an identifiable source on examination, the overall prevalence of a UTI was 7.0% (95% confidence interval [CI], 5.5%-8.4%), but varied from 2.1% to 8.7% based on age and sex (TABLE 1). Among verbal children with urinary symptoms, the prevalence of UTI was 7.8% (95% CI, 6.6%-8.9%).

Examination for the Symptoms and Signs of a UTI

The duration and height of fever should be ascertained. Temperatures higher than 38.0°C are considered significant and temperatures higher than 39.0°C are usually regarded as high fever. In verbal children, the presence of dysuria (painful urination), frequency, urgency, incontinence, fever, abdominal pain, suprapubic discomfort, back pain, and vaginal/penile discharge should be elicited.

Children should be examined thoroughly to determine whether a source can be found to explain the fever. The external genitalia should be carefully examined to rule out any gross anatomic abnormalities, skin lesions, frank discharge, or foreign body. In male infants and children, circumcision status should be noted. Suprapubic tenderness, which suggests cystitis, should be assessed by palpation over the suprapubic region while the patient is supine. Costovertebral angle tenderness, which suggests upper urinary tract involvement (pyelonephritis), is assessed with the patient in the sitting position. The angle formed by the junction of the lower edge of the rib cage and the vertebra is firmly tapped with the side of the hand.

METHODS

We searched the medical literature to determine the accuracy and precision of clinical examination in children suspected of having an acute symptomatic UTI. We searched MEDLINE and EMBASE databases for articles published between 1966 and October 2007, with a search strategy similar to that used by other authors in this series. Search terms included *urinary tract infection, cystitis, pyelonephritis, diagnostic tests, physical examination, sensitivity, specificity, prevalence, incidence, circumcision, irritability, suprapubic tenderness, vomiting, diarrhea, frequency, dysuria, incontinence, pain, costovertebral tenderness, fever, pyrexia, lethargy, symptoms, signs, physical examination,* and *medical history taking* (FIGURE 1). This computerized search was supplemented with a manual review of bibliographies of all articles meeting inclusion criteria, 1 previously published systematic review,[3] 3 commonly used clinical skills textbooks, and contact with 2 experts in the field. Two of the authors (N.S. and J.L.) independently screened the titles and abstracts (when available) of the search results. Full-text articles that could con-

tain data regarding signs and symptoms of UTI were retrieved. Two of the authors (N.S. and N.E.M.) independently reviewed, rated, and abstracted data from each article.

We applied explicit a priori inclusion and exclusion criteria. Articles were included if they contained original prospective data on the accuracy or precision of history or physical examination findings in diagnosing acute culture-proven UTI in children through age 18 years. Articles in languages other than English that met our inclusion criteria were translated to English and reviewed as above. Articles were excluded that only evaluated adults. In an effort to focus on the signs and symptoms of UTI in the general pediatric population, we excluded studies that enrolled only a narrow spectrum of children with UTI. Thus, studies that enrolled only children with asymptomatic bacteriuria (bacteriuria without pyuria or symptoms) or children in high-risk subgroups (severely malnourished, premature, sexually abused, and those with genitourinary or neurological abnormalities or with nosocomial infections) were excluded. We also excluded articles in which inclusion was based on the presence of symptomatic illnesses other than UTI or fever (febrile seizures, infectious diarrhea, bronchiolitis). Case series (<10 patients) and case-control studies were excluded. Articles that contained insufficient or incomplete data to allow calculation of likelihood ratios (LRs) for signs or symptoms of acute UTI were excluded.

Because bedside tests are often used to confirm the diagnosis of UTI, a second objective was to demonstrate how to integrate information from the patient's signs and symptoms with information from the urinalysis. Accordingly, we searched for articles examining the role of bedside urinalysis in the diagnosis of UTI. A recent high-quality meta-analysis was found that examined the accuracy of urinalysis in diagnosing UTI in children.[10,11]

Quality Assessment of Included Articles

Two authors (N.S. and N.E.M.) independently assessed the methodological quality of the included articles using criteria adapted from other authors in this series. Disagreements were resolved by discussion. Level 1 articles included those with an independent blind comparison of signs or symptoms with a reference standard (positive urine culture from a suprapubic, catheterized, or midstream specimen) among a large number (≥200) of consecutive patients suspected of having a UTI. Level 2 articles were similar to level 1 studies but included a smaller number of patients (<200). Level 3 studies were similar to level 1 and level 2 studies except that enrollment of patients was not consecutive. In level 4 studies, in addition to the selection bias present in level 3 studies, the sample was further restricted to the obvious presentations of the target condition. Level 5 studies were similar to level 4 studies but used a reference standard of uncertain validity.

Data Analysis

We used published data from the reported studies that met our inclusion criteria to calculate summary LRs. Five authors provided us with additional raw data from their studies (see "Additional Contributions" section).

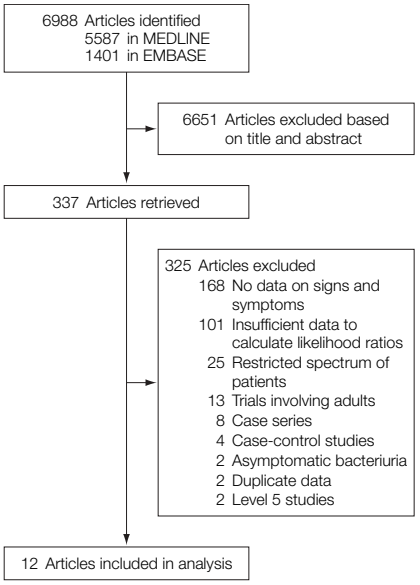
Eight studies enrolled infants aged 0 to 24 months who presented with fever. Of these, 4 enrolled only young infants (0-3 months). Except for ill appearance, all the other signs and symptoms had LRs that were similar across studies that enrolled younger and older infants. Accordingly, we pooled LRs across all 8 studies for all findings except ill appearance.

Two studies enrolled mostly verbal children with urinary symptoms. Although some infants were included in these studies, only data on genitourinary symptoms were reported. Data from these studies were grouped and analyzed together.

Two of the smaller studies included almost equal proportions of infants and verbal children.[12,13] We allocated data from these studies based on the finding being evaluated; symptoms of abdominal pain and foul-smelling urine were placed with data from verbal children, and irritability, vomiting, diarrhea, and jaundice were grouped with data from infants.

A random effects model was used to generate conservative summary measures when data on the sign or symptom was available from 3 or more studies. MetaWin version 2.0 (Sinauer Associates, Sunderland, Massachusetts) was used for the data analysis. In the development of algorithms, we chose a cutoff of 2% as the threshold probability that would trigger further diagnostic testing. This value was based on a previous survey of practicing pediatricians[5] and our clinical judgment. The posterior probabilities of UTI were calculated from the prevalence and LR using Bayes theorem.

Figure 1. Flow Diagram Outlining the Study Selection Process



RESULTS

Study Characteristics

From 6988 articles identified through our iterative search strategy, 337 were not excluded based on the title or abstract. We retrieved and reviewed

the full text of these articles. Twelve articles met all inclusion criteria (TABLE 2).[4,7,12-21] We excluded 2 level 5 studies.[22,23] A total of 8837 children through age 15 years were included in these studies. Studies were published between 1973 and 2006. Fever was the main inclusion criterion in all studies that enrolled infants. The remainder of the studies, all of older children, used a comprehensive list of signs and symptoms; children with any of these signs or symptoms were included. The pooled prevalence of UTI in the 12 included studies was 7.5% (95% CI, 7.0%-8.1%). All studies included in the analysis were level 1 to level 4.

Urine cultures were obtained by bladder catheterization or by suprapubic aspiration in the majority of studies, but a clean-catch specimen or midstream sample was used in 4 studies that included children older than 2 years. In 2 studies,[20,21] bag specimens were used in infants as the initial test for UTI. In both studies, positive bag urine cultures were then confirmed by suprapubic aspiration. In 2 other studies,[16,18] up to 25% of the positive urine specimens were obtained using a bag collected specimen without subsequent confirmation. We included these studies and examined the overall results with and without these studies. Because little difference was observed in the pooled results, we opted to include them in our final analyses. Some of the older articles used a cutoff of 10 000 CFUs/mL (rather than 50 000 CFUs/mL) to define a UTI. We decided to include these articles because the majority of cultures with more than 10 000 CFUs/mL are likely to also have more than 50 000 CFUs/mL.[2] All studies used a threshold of at least 10^4 CFUs/mL for specimens collected by catheterization and at least 10^5 CFUs/mL for clean-catch specimens.

Precision of Symptoms and Signs

One study quantified agreement between the examining physician and the study nurse on historical information and examination findings, by having each patient evaluated by both.[17] Agreement between 200 physician/nurse pairs for historical or physical examination findings, measured by the κ statistic, was fair to good (duration of fever, $\kappa = 0.75$; any urinary symptoms, $\kappa = 0.31$; past history, $\kappa = 0.57$; suprapubic tenderness, $\kappa = 0.38$; and ill appearance, $\kappa = 0.38$).[24,25]

Accuracy of Symptoms and Signs

Febrile Infants Aged 0 to 24 Months. For accuracy of symptoms, a history of

Table 2. Studies Used to Determine the Accuracy of Clinical History and Physical Examination

Source	Quality Level[a]	Setting	No. of Patients With Urine Culture	Age Range	Inclusion Criteria	Method of Urine Collection	Prevalence of UTI, %
Hsiao et al,[7] 2006	1	ED	424	57-180 d	Fever (≥38.0°C)	Urethral catheterization, suprapubic aspiration	9.7
Chen and Baker,[14] 2006	3 (Nonconsecutive)	ED	465	1-24 mo	Fever (≥38.0°C)	Urethral catheterization, suprapubic aspiration, bag specimen (<3% by bag)	13.8
Zorc et al,[15] 2005	1	ED	1005	<2 mo	Fever (≥38.0°C)	Urethral catheterization or suprapubic aspiration	9.1
Musa-Aisien et al,[12] 2003	1	ED	300	1-60 mo	Fever (≥38.0°C)	Clean-catch specimen, suprapubic aspiration	8.7
Struthers et al,[13] 2003	2	Office	110	<6 y	Symptoms of UTI	Clean-catch specimen, suprapubic aspiration	6.4
Newman et al,[16] 2002[b]	4 (Nonconsecutive, up to 25% of urine from bag)	Office	1608	≤3 mo	Fever (≥38.0°C)	Urethral catheterization, suprapubic aspiration, clean-catch specimen, bag specimen	10.4
Shaw et al,[17] 1998	1	Office	2411	Female <2 y Male <1 y	Fever (≥38.5°C)	Urethral catheterization	3.3
Hoberman et al,[4] 1993[c]	1	ED	945	<1 y	Fever (≥38.3°C)	Urethral catheterization	5.3
Crain and Gershel,[18] 1990	3 (Up to 25% of urine from bag)	ED	442	<8 wk	Fever (≥38.1°C)	Urethral catheterization, suprapubic aspiration, bag specimen	7.5
Krober et al,[19] 1985	2	Office	182	<3 mo	Fever (≥38.0°C)	Urethral catheterization	11.0
Dickinson,[20] 1979	2	Office	156	<15 y	Symptoms of UTI	Clean-catch or bag specimens, then suprapubic aspiration	9.0
Heale et al,[21] 1973	1	ED/office	789	<15 y	Symptoms of UTI	Clean-catch or bag specimens, then suprapubic aspiration	9.1

Abbreviations: ED, emergency department; UTI, urinary tract infection.
[a] Methodological quality criteria are described in the "Methods" section. Level 2 studies were similar to level 1 studies but had a sample size of less than 200. Reasons for methodological quality scores lower than level 2 are shown in parentheses.
[b] Although urine cultures were obtained at the physician's discretion, in multivariate analysis only finding (height of fever) increased the odds of obtaining UTI. Accordingly, enrollment was largely independent of the signs and symptoms examined in this article. However, for the reasons mentioned in the table, level 4 was assigned.
[c] Emergency department physicians identified children at risk for UTI based on their clinical suspicion. Investigators approached the remainder of febrile patients who presented during the daytime hours and asked for permission to obtain a catheterized urine specimen. Because enrollment was largely consecutive, level 1 was assigned.

UTI (LR range, 2.3-2.9) and a temperature higher than 40°C (LR range, 3.2-3.3) were the findings most useful for identifying those infants with a UTI (TABLE 3). A temperature higher than 39°C (summary LR, 1.4; 95% CI, 1.2-1.7) and fever duration of more than 24 hours (LR, 2.0; 95% CI, 1.4-2.9) also increased the probability of UTI but were less useful. Children of nonblack race are at increased risk for a UTI (summary LR, 1.4; 95% CI, 1.1-1.8). The relationship between race and UTI could be confounded by differing circumcision rates among racial groups. To control for the potential effect of circumcision on the relationship between race and UTI, we obtained data from the authors of the 6 articles[4,7,14-17] that included data on race and UTI. The relationship between race and UTI persisted even among female infants (positive and negative LRs for nonblack and black female infants were 1.3 [95% CI, 1.1-1.6] and 0.63 [95% CI, 0.41-0.79], respectively). Vomiting, diarrhea, poor feeding, and irritability had both positive and negative LRs with CIs overlapping 1.00 and are therefore not useful in screening for UTI.

For accuracy of signs, the presence of suprapubic tenderness (LR, 4.4; 95% CI, 1.6-12.4) and the lack of circumcision (summary LR, 2.8; 95% CI, 1.9-4.3) were the findings most useful in the diagnosis of UTI (TABLE 4). The presence of another source for fever on examination (eg, acute otitis media, upper respiratory tract infection, or acute gastroenteritis) reduced the probability of UTI only to a small extent (summary LR, 0.69; 95% CI, 0.55-0.80). The presence of circumcision was the only finding that had an LR of less than 0.5 (summary LR, 0.33; 95% CI, 0.18-0.63) and was the most useful finding for identifying male infants who were less likely to have a UTI.

Combination of signs and symptoms were more useful than individual findings in identifying children with a UTI (TABLE 5). The presence of high and prolonged fever (>39°C for >48 hours) in the absence of another source for fever on examination increased the probability of a UTI (LR, 4.0; 95% CI, 1.2-13.0). The combination of a temperature less than 39°C and the presence of a potential source for fever (eg, upper respiratory tract infection) was particularly useful (LR, 0.37; 95% CI, 0.16-0.85), especially in a black infant (LR, 0.19). The latter value was used to calculate the posttest probabilities in FIGURE 2 and FIGURE 3 for children with no risk factors for UTI.

Verbal Children. For accuracy of symptoms, the presence of abdominal pain (LR, 6.3; 95% CI, 2.5-16.0), back pain (LR, 3.6; 95% CI, 2.1-6.1), dysuria, frequency, or both (LR range, 2.2-2.8), and new-onset urinary incontinence (LR, 4.6; 95% CI, 2.8-7.6) increased the likelihood of a UTI (TABLE 6). Because the negative LRs for all studied symptoms were more than 0.60, and often approached 1.00, the absence of indi-

Table 3. Diagnostic Accuracy of UTI Symptoms Among Infants Aged 0 to 24 Months

Symptoms by Source	Positive Likelihood Ratio (95% CI)	Negative Likelihood Ratio (95% CI)
Nonblack race		
Hsiao et al,[7] 2006	1.3 (1.2-1.4)	0.05 (0-0.79)
Chen and Baker,[14] 2006	1.2 (1.1-1.3)	0.28 (0.11-0.74)
Zorc et al,[15] 2005	1.0 (0.9-1.1)	0.96 (0.63-1.45)
Newman et al,[16] 2002	1.1 (1.1-1.2)	0.35 (0.18-0.67)
Shaw et al,[17] 1998	3.0 (2.4-3.9)	0.63 (0.51-0.77)
Hoberman et al,[4] 1993	1.3 (1.0-1.5)	0.66 (0.42-1.04)
Summary	1.4 (1.1-1.8)	0.52 (0.29-0.73)
History of prior UTI		
Shaw et al,[17] 1998	2.9 (1.2-7.1)	0.95 (0.89-1.02)
Hoberman et al,[4] 1993	2.3 (0.3-17.4)	0.97 (0.89-1.07)
Temperature >39°C		
Zorc et al,[15] 2005	2.0 (1.4-2.6)	0.78 (0.66-0.91)
Newman et al,[16] 2002	1.6 (1.3-1.9)	0.81 (0.71-0.92)
Shaw et al,[17] 1998	1.2 (1.1-1.3)	0.64 (0.42-0.98)
Hoberman et al,[4] 1993	1.2 (1.0-1.5)	0.66 (0.41-1.06)
Summary	1.4 (1.2-1.7)	0.78 (0.65-0.81)
Temperature >40°C		
Hoberman et al,[4] 1993	3.3 (1.3-8.3)	0.66 (0.35-1.25)
Krober et al,[19] 1985	3.2 (0.7-15.6)	0.93 (0.80-1.08)
Prolonged fever for >24 h		
Newman et al,[16] 2002	2.0 (1.4-2.9)	0.90 (0.83-0.97)
Prolonged fever for >48 h		
Shaw et al,[17] 1998	1.3 (0.8-1.9)	0.95 (0.85-1.06)
Vomiting		
Musa-Aisien et al,[12] 2003[a]	0.43 (0.15-1.26)	1.2 (1.0-1.4)
Newman et al,[16] 2002	0.85 (0.58-1.23)	1.03 (0.96-1.10)
Hoberman et al,[4] 1993	1.1 (0.6-1.9)	0.96 (0.68-1.35)
Summary	0.89 (0.43-1.25)	1.07 (0.88-1.21)
Diarrhea		
Musa-Aisien et al,[12] 2003[a]	0.93 (0.31-2.82)	1.01 (0.87-1.17)
Hoberman et al,[4] 1993	0.64 (0.32-1.26)	1.3 (1.0-1.7)
Poor feeding		
Musa-Aisien et al,[12] 2003[a]	0.75 (0.10-5.50)	1.01 (0.93-1.10)
Newman et al,[16] 2002	0.98 (0.79-1.21)	1.01 (0.89-1.14)
Hoberman et al,[4] 1993	1.00 (0.72-1.39)	1.00 (0.54-1.84)
Summary	0.99 (0.75-1.00)	1.01 (0.99-1.01)
Irritability		
Musa-Aisien et al,[12] 2003[a]	1.8 (0.2-14.0)	0.98 (0.91-1.06)
Hoberman et al,[4] 1993	0.94 (0.72-1.23)	1.26 (0.52-3.04)

Abbreviations: CI, confidence interval; UTI, urinary tract infection.
[a]Included children older than 24 months (median age, 18 months).

vidual symptoms does not substantially reduce the likelihood of a UTI. Offensive urine odor had both positive and negative LRs that crossed 1.00 and is therefore not useful in the diagnosis of a UTI.

For accuracy of signs, we found no data regarding the diagnostic value of individual signs, or combination of findings, in verbal children.

COMMENT

In evaluating pediatric patients with fever or signs and symptoms suggestive of a UTI, the practitioner needs to determine the probability of a serious infection. In our review, we provided practitioners with tools to more accurately estimate the probability of UTI in their patients.

Table 4. Diagnostic Accuracy of Urinary Tract Infection Signs Among Infants Aged 0 to 24 Months

Signs by Source	Positive Likelihood Ratio (95% CI)	Negative Likelihood Ratio (95% CI)
Ill appearance (infants <3 mo)		
Zorc et al,[15] 2005	0.59 (0.22-1.59)	1.03 (0.99-1.08)
Newman et al,[16] 2002	1.1 (0.9-1.3)	0.95 (0.84-1.08)
Ill appearance (infants 3-24 mo)		
Shaw et al,[17] 1998	1.9 (1.5-2.4)	0.68 (0.53-0.88)
Jaundice		
Musa-Aisien et al,[12] 2003[a]	2.1 (0.3-17.4)	0.98 (0.91-1.06)
Suprapubic tenderness		
Shaw et al,[17] 1998	4.4 (1.6-12.4)	0.96 (0.90-1.01)
No other source for fever on examination[b]		
Newman et al,[16] 2002	1.1 (1.0-1.2)	0.55 (0.35-0.86)
Shaw et al,[17] 1998	1.8 (1.3-2.5)	0.80 (0.68-0.95)
Hoberman et al,[4] 1993	1.4 (1.2-1.8)	0.60 (0.40-0.91)
Summary	1.4 (1.1-1.8)	0.69 (0.55-0.80)
Uncircumcised male infants		
Hsiao et al,[7] 2006	4.4 (3.2-6.3)	0.13 (0.03-0.49)
Zorc et al,[15] 2005	1.9 (1.7-2.2)	0.17 (0.08-0.36)
Newman et al,[16] 2002	3.3 (2.7-4.0)	0.35 (0.23-0.54)
Shaw et al,[17] 1998	4.1 (2.2-7.5)	0.69 (0.58-0.82)
Hoberman et al,[4] 1993	3.3 (1.3-8.3)	0.66 (0.35-1.25)
Crain and Gershel,[18] 1990	1.7 (1.3-2.2)	0.35 (0.14-0.86)
Summary	2.8 (1.9-4.3)	0.33 (0.18-0.63)

Abbreviation: CI, confidence interval.
[a] Included children older than 24 months (median age, 18 months).
[b] Other source for fever included illnesses such as upper respiratory tract infection, acute otitis media, and acute gastroenteritis.

Table 5. Likelihood Ratios for Combination of Signs and Symptoms in Infants Aged 0 to 24 Months[a]

Source	Symptom Combination	Positive Likelihood Ratio (95% CI)
Shaw et al,[17] 1998	Temperature >39°C for >48 h in a child with no potential source for fever[b]	4.0 (1.2-13.0)
Shaw et al,[17] 1998	Temperature >38°C for >48 h in a child with no potential source for fever[b]	3.6 (1.4-8.8)
Shaw et al,[17] 1998 Hoberman et al,[4] 1993[c]	Temperature >39°C in a child with no potential source for fever[b]	2.0 (1.8-2.4)
Shaw et al,[17] 1998	Temperature >39°C for >48 h	1.7 (0.9-2.9)
Hoberman et al,[4] 1993	Temperature >39°C with a potential source for fever[b]	0.86 (0.50-1.47)
Hoberman et al,[4] 1993	Temperature <39°C in a child with a potential source for fever[b]	0.37 (0.16-0.85)

Abbreviation: CI, confidence interval.
[a] Assuming that race and symptoms are independent, the likelihood ratio for black and nonblack children can be obtained by multiplying the above likelihood ratios by 0.52 and 1.40, respectively.
[b] Other potential sources for fever included illnesses such as upper respiratory tract infection, acute otitis media, and acute gastroenteritis.
[c] Based on combined data from both studies.

Role of Baseline Risk in Diagnosing UTI

In the evidence-based approach, the clinical encounter starts with the estimation of the pretest probability followed by the application of 1 or more diagnostic tests to determine posttest probability. The pretest probability can be estimated from the prevalence of the condition in a population (Table 1).

Role of Symptoms and Signs in Diagnosing UTI

Although certain signs and symptoms (high fever, fever >24 hours, history of a previous UTI, abdominal pain, nonblack race, lack of circumcision, back pain, dysuria, frequency, new-onset urinary incontinence, suprapubic tenderness, and absence of another source of fever on examination) increase the probability of UTI, none in isolation has a sufficiently high LR to allow for a definitive diagnosis of UTI (Figure 2 and Figure 3). For example, the probability of UTI in a child with dysuria (LR, 2.4) is still only approximately 17%. Accordingly, in children, empirical treatment without further evaluation would no doubt lead to overuse of antibiotics. Similarly, none of the signs or symptoms alone had a sufficiently small enough negative LR to allow clinicians to confidently rule out UTI. Nevertheless, in a child with a low baseline probability of UTI, the absence of several key risk factors in combination can decrease the probability of UTI to a point where routine diagnostic testing would no longer be indicated.

Race represents an important factor in determining risk of UTI. Although earlier articles highlighted the increased risk of UTI among white infants, recent articles indicate that the prevalence of UTI among Asian and Hispanic infants is similar to that of white infants.[7,14] Black infants have much lower rates of UTI. We there-

fore chose to categorize race as black and nonblack.

Use of Dipstick Urinalysis in Diagnosing UTI

Dipstick urinalysis supplements clinical information and helps answer the question of whether a child has a UTI. Because delay in treatment has been associated with renal scarring, urinalysis test results should be used to determine whether antimicrobial therapy needs to be initiated immediately.

The most sensitive and specific urinalysis method available—the enhanced urinalysis—involves microscopic examination of an uncentrifuged specimen using a counting chamber.[26] Use of this more sensitive and specific test[10] will minimize inappropriate treatment. However, if an enhanced urinalysis cannot be obtained, dipstick test results may be used to guide treatment decisions.

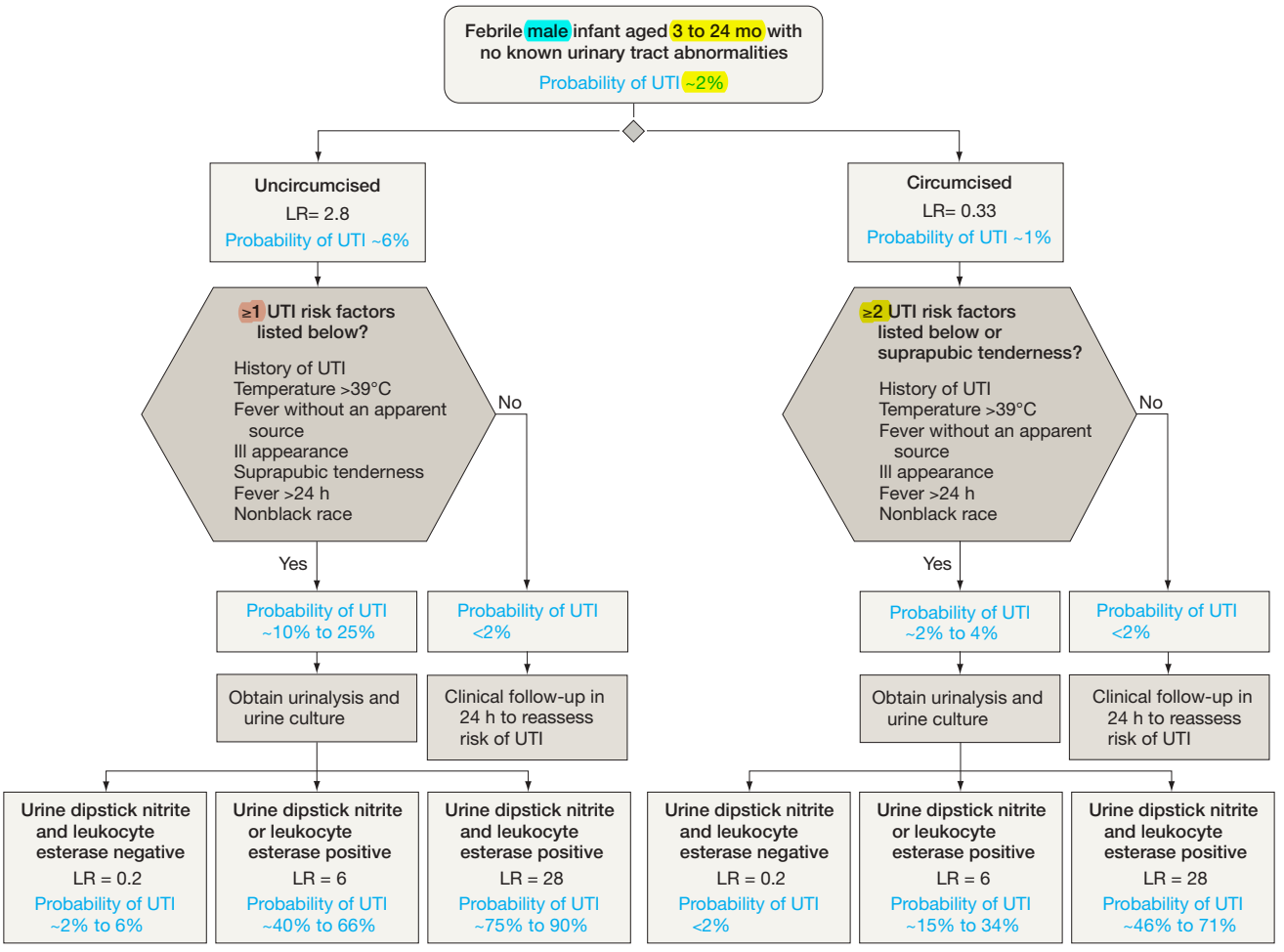
A recent meta-analysis of 70 pediatric studies provides information on the accuracy of dipstick urinalysis.[10] A dipstick test negative for both nitrite and leukocyte esterase had an LR of 0.20 (95% CI, 0.16-0.26). A dipstick test positive for either nitrite or leukocyte esterase had an LR of 6.1 (95% CI, 4.3-8.6). A dipstick test positive for both nitrites and leukocytes had an LR of 28 (95% CI, 17-46).

Dipstick test results should be interpreted while keeping in mind the relatively low pretest probability of UTI and the less than perfect specificity (93%) of the test. Accordingly, if a positive dipstick test result is obtained, it should always be followed up with a confirmatory urine culture. This will allow one to differentiate between a false-positive dipstick test result and a true UTI, and this information will help guide treatment and diagnostic imaging decisions.

Approach to Febrile Infants Younger Than 3 Months

Infants younger than 3 months with a UTI generally present with fever. The prevalence of UTI in this age group in both male and female infants is high. Furthermore, infants

Figure 2. Diagnostic Algorithm for Febrile Male Infants Aged 3 to 24 Months Suspected of Having a UTI



UTI indicates urinary tract infection; LR, likelihood ratio.

with a UTI are more likely than older children to have bacteremia, sepsis, and congenital genitourinary anomalies. Isolation of the causative organism is essential in establishing the correct diagnosis, selecting the proper antimicrobial, and determining the appropriate length of treatment. Accordingly, urinalysis and culture should be considered for all febrile infants younger than 3 months.

Approach to Febrile Male Infants Aged 3 to 24 Months

Febrile uncircumcised male infants aged 3 to 24 months are at relatively high risk for UTI (probability of UTI, approximately 6%), and catheterization should be considered when risk factors for UTI are present (Figure 2).

Febrile circumcised male infants aged 3 to 24 months with a UTI are at low risk for UTI (probability of <1%), and catheterization should be considered when 2 or more signs or symptoms of UTI are present (Figure 2).

Approach to Febrile Female Infants Aged 3 to 24 Months

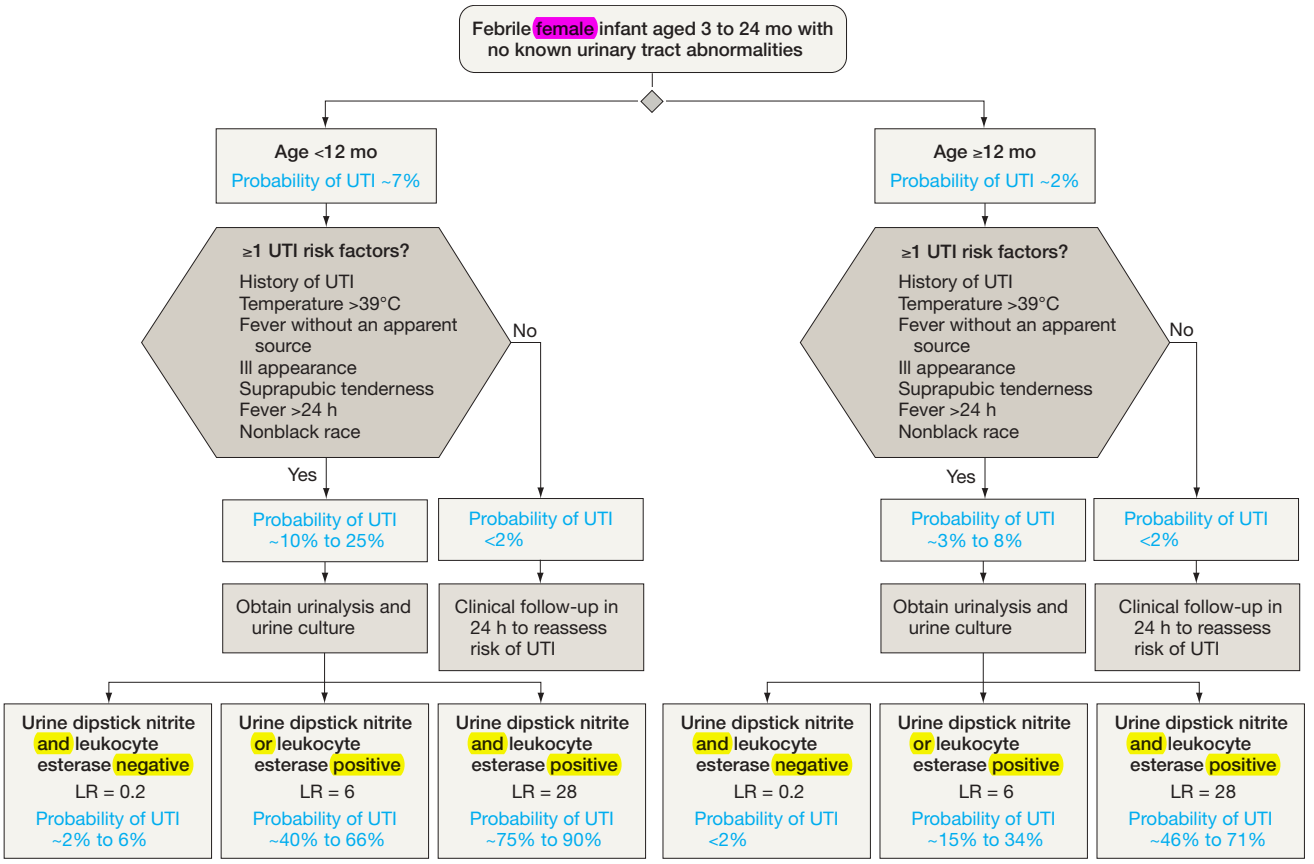
Febrile female infants aged 3 to 12 months with no obvious source for fever on examination have a relatively high risk of UTI (pretest probability of approximately 7%) (Figure 3). Although clinical findings increase the probability of UTI (to 10%-25%), the presence of these findings, individually or in combination, does not rule in the diagnosis. Although the absence of individual findings was not helpful in ruling out UTI, combination of findings can identify infants with a low likelihood of UTI.

Although febrile female infants aged 12 to 24 months are at lower risk for UTI, the presence of any risk factor increases the probability enough to warrant further diagnostic testing (Figure 3).

Approach to Verbal Children

In circumcised male children with nonspecific signs or symptoms (eg, vomiting, diarrhea, chronic enuresis), routine diagnostic testing is not warranted (FIGURE 4). The probability that such a child has a UTI is less than 1%. Circumcised male children with several specific symptoms of UTI (abdominal pain, back pain, dysuria, frequency, high fever, or new-onset incontinence) should have a urine specimen collected for diagnostic testing and re-

Figure 3. Diagnostic Algorithm for Febrile Female Infants Aged 3 to 24 Months Suspected of Having a UTI



UTI indicates urinary tract infection; LR, likelihood ratio.

ceive treatment if the urine culture test results are positive.

Female and uncircumcised male children with symptoms suggestive of urinary tract involvement have a baseline UTI probability of approximately 8%.[6] When these children present with specific signs or symptoms of UTI, a urine specimen should be obtained for dipstick testing. Initial management can be guided based on dipstick test result. If positive, a confirmatory urine culture is recommended to guide future management decisions.

Limitations

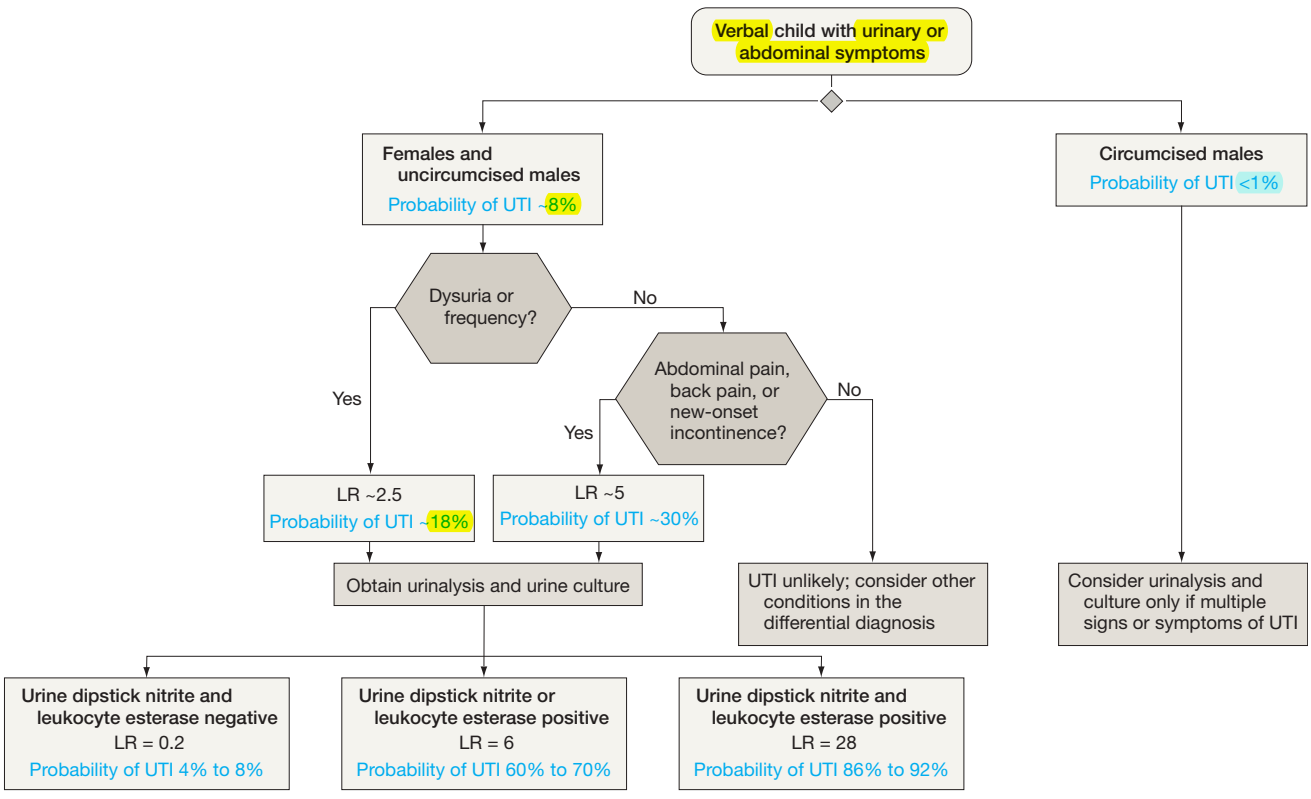
The first limitation relates to how data were pooled. Two articles contained data from both infants and verbal children. We pooled data from these articles with data from articles that included only infants or only verbal children. A second limitation was the lack of specificity regarding how the signs and symptoms were defined or elicited in the original articles. Finally, although nonblack race was associated with UTI, because of the potential risk for confounding and the uncertainties in race labeling, more research is needed to determine the impact of race on UTI risk.

Table 6. Diagnostic Accuracy of Urinary Tract Infection Symptoms Among Verbal Children

Source	Symptoms	Positive Likelihood Ratio (95% CI)	Negative Likelihood Ratio (95% CI)
Musa-Aisien et al,[12] 2003[a]	Abdominal pain	6.3 (2.5-16.0)	0.80 (0.65-0.99)
Heale et al,[21] 1973	Back pain	3.6 (2.1-6.1)	0.84 (0.75-0.95)
Dickinson,[20] 1979	Dysuria/frequency	2.2 (1.1-4.3)	0.71 (0.45-1.13)
Heale et al,[21] 1973	Dysuria	2.4 (1.8-3.1)	0.65 (0.51-0.81)
Heale et al,[21] 1973	Frequency	2.8 (2.0-4.0)	0.72 (0.60-0.86)
Heale et al,[21] 1973	New-onset urinary incontinence (day/night)	4.6 (2.8-7.6)	0.79 (0.69-0.90)
Heale et al,[21] 1973	Offensive urine odor	0.93 (0.34-2.51)	1.01 (0.95-1.07)
Struthers et al,[13] 2003[b]	Offensive urine odor	0.82 (0.34-1.96)	1.2 (0.6-2.4)

Abbreviation: CI, confidence interval.
[a] All children had temperatures higher than 38°C.
[b] Included some nonverbal children.

Figure 4. Diagnostic Algorithm for Verbal Children Older Than 24 Months With Urinary or Abdominal Symptoms



UTI indicates urinary tract infection; LR, likelihood ratio.

SCENARIO RESOLUTION

Case 1

The baseline risk of UTI in the 15-month-old female is approximately 2% (Table 1). Because she has prolonged high fever with no other source on examination (LR, 4.0), her risk of UTI is approximately 7% (Table 5). The clinician decides to obtain a catheterized urine sample for diagnostic testing. A dipstick test result is positive for leukocytes. At this point, because the probability of UTI is substantial (approximately 32%) (Figure 3), treatment with an oral antimicrobial agent is initiated. A telephone call is planned for the following day to ascertain clinical improvement.

Case 2

The baseline probability of UTI in the circumcised male child is less than 1%. Because this patient has dysuria (LR, 2.4) (Table 6), his probability of UTI increases to approximately 2%. A clean-catch urine specimen is obtained revealing trace leukocyte esterase (LR, 6). Given that the probability of UTI is approximately 11% and that the child is afebrile, the clinician decides to await results of the urine culture before initiating antimicrobial therapy.

CLINICAL BOTTOM LINE

Diagnosing a UTI, especially among nonverbal children, challenges physicians because of the nonspecific nature of the presenting signs and symptoms. Although no sign or symptom by itself is diagnostic of UTI in children, the presence of fever with a temperature higher than 40°C, history of a previous UTI, lack of circumcision, abdominal pain, back pain, dysuria, frequency, new-onset incontinence, and suprapubic tenderness increase the baseline likelihood of UTI by 2 to 6 fold. The absence of several key signs and symptoms in combination can be used to identify infants at low risk for UTI.

Author Contributions: Dr Shaikh had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.
Study concept and design: Shaikh, Lopez, D'Amico, Hoberman.
Acquisition of data: Shaikh, Morone, Lopez, Chianese, Sangvai, Hoberman.
Analysis and interpretation of data: Shaikh, Morone, Sangvai, D'Amico, Hoberman, Wald.
Drafting of the manuscript: Shaikh, Morone, Chianese, Sangvai, D'Amico, Hoberman.
Critical revision of the manuscript for important intellectual content: Shaikh, Morone, Lopez, Chianese, Sangvai, D'Amico, Hoberman, Wald.
Statistical analysis: Shaikh, Lopez, Sangvai, D'Amico.
Administrative, technical, or material support: Shaikh, Lopez.
Study supervision: Shaikh, D'Amico, Hoberman, Wald.
Financial Disclosures: None reported.
Funding/Support: Dr Morone was supported in part by the Roadmap Multidisciplinary Clinical Research Career Development Award grant K12 RR023267 from the National Institutes of Health. The National Institutes of Health had no role in the design and conduct of the study, in the collection, analysis, and interpretation of the data, or in the preparation, review, or approval of the manuscript.
Additional Contributions: Daniel A. Ostrovsky, MD, Duke University, and Molly Berkoff, MD, MPH, University of North Carolina at Chapel Hill, provided critical review of an earlier draft of the manuscript. Five authors (Marc Gorelick, MD, Children's Hospital of Wisconsin,[17] Tom Newman, MD, University of San Francisco,[16] Joseph Zorc, MD, University of Pennsylvania,[4] Allen Hsiao, MD, Yale University,[7] and Lei Chen, MD, Yale University[14]) provided additional raw data from their studies. None of these individuals received any compensation for their contribution.

REFERENCES

1. Freedman AL; Urologic Diseases in America Project. Urologic diseases in North America Project: trends in resource utilization for urinary tract infections in children. *J Urol*. 2005;173(3):949-954.
2. Hoberman A, Wald ER, Reynolds EA, Penchansky L, Charron M. Pyuria and bacteriuria in urine specimens obtained by catheter from young children with fever. *J Pediatr*. 1994;124(4):513-519.
3. Downs SM. Technical report: urinary tract infections in febrile infants and young children: the Urinary Tract Subcommittee of the American Academy of Pediatrics Committee on Quality Improvement. *Pediatrics*. 1999;103(4):e54.
4. Hoberman A, Chao HP, Keller DM, Hickey R, Davis HW, Ellis D. Prevalence of urinary tract infection in febrile infants. *J Pediatr*. 1993;123(1):17-23.
5. Roberts KB, Charney E, Sweren RJ. Urinary tract infection in infants with unexplained fever: a collaborative study. *J Pediatr*. 1983;103(6):864-867.
6. Shaikh N, Morone N, Bost J, Farrell H. Prevalence of urinary tract infection in childhood: a meta-analysis. *Pediatr Infect Dis J*. In press.
7. Hsiao AL, Chen L, Baker MD. Incidence and predictors of serious bacterial infections among 57- to 180-day-old infants. *Pediatrics*. 2006;117(5):1695-1701.
8. Stoll ML, Rubin LG. Incidence of occult bacteremia among highly febrile young children in the era of the pneumococcal conjugate vaccine: a study from a Children's Hospital Emergency Department and Urgent Care Center. *Arch Pediatr Adolesc Med*. 2004;158(7):671-675.
9. Shaikh N, Hoberman A, Wise B, et al. Dysfunctional elimination syndrome: is it related to urinary tract infection or vesicoureteral reflux diagnosed early in life? *Pediatrics*. 2003;112(5):1134-1137.
10. Whiting P, Westwood M, Watt I, Cooper J, Kleijnen J. Rapid tests and urine sampling techniques for the diagnosis of urinary tract infection (UTI) in children under five years: a systematic review. *BMC Pediatr*. 2005;5(1):4.
11. Oxman AD, Cook DJ, Guyatt GH. Users' guides to the medical literature, VI: how to use an overview. *JAMA*. 1994;272(17):1367-1371.
12. Musa-Aisien AS, Ibadin OM, Ukoh G, Akpede GO. Prevalence and antimicrobial sensitivity pattern in urinary tract infection in febrile under-5s at a children's emergency unit in Nigeria. *Ann Trop Paediatr*. 2003;23(1):39-45.
13. Struthers S, Scanlon J, Parker K, Goddard J, Hallett R. Parental reporting of smelly urine and urinary tract infection. *Arch Dis Child*. 2003;88(3):250-252.
14. Chen L, Baker MD. Racial and ethnic differences in the rates of urinary tract infections in febrile infants in the emergency department. *Pediatr Emerg Care*. 2006;22(7):485-487.
15. Zorc JJ, Levine DA, Platt SL, et al. Clinical and demographic factors associated with urinary tract infection in young febrile infants. *Pediatrics*. 2005;116(3):644-648.
16. Newman TB, Bernzweig JA, Takayama JI, Finch SA, Wasserman RC, Pantell RH. Urine testing and urinary tract infections in febrile infants seen in office settings: the Pediatric Research in Office Settings' Febrile Infant Study. *Arch Pediatr Adolesc Med*. 2002;156(1):44-54.
17. Shaw KN, Gorelick M, McGowan KL, Yakscoe NM, Schwartz JS. Prevalence of urinary tract infection in febrile young children in the emergency department. *Pediatrics*. 1998;102(2):e16.
18. Crain EF, Gershel JC. Urinary tract infections in febrile infants younger than 8 weeks of age. *Pediatrics*. 1990;86(3):363-367.
19. Krober MS, Bass JW, Powell JM, Smith FR, Seto DS. Bacterial and viral pathogens causing fever in infants less than 3 months old. *Am J Dis Child*. 1985;139(9):889-892.
20. Dickinson JA. Incidence and outcome of symptomatic urinary tract infection in children. *Br Med J*. 1979;1(6174):1330-1332.
21. Heale WF, Weldon AP, Hewstone AS. Reflux nephropathy: presentation of urinary infection in childhood. *Med J Aust*. 1973;1(23):1138-1140.
22. Hulbert J. Presentation, bacteriological diagnosis and test of cure of urinary tract infection in general practice: report of a trial. *J R Coll Gen Pract*. 1973;23(133):556-560.
23. Pylkkänen J, Vilska J, Koskimies O. Diagnostic value of symptoms and clean-voided urine specimen in childhood urinary tract infection. *Acta Paediatr Scand*. 1979;68(3):341-344.
24. Gorelick MH, Shaw KN. Clinical decision rule to identify febrile young girls at risk for urinary tract infection. *Arch Pediatr Adolesc Med*. 2000;154(4):386-390.
25. Landis JR, Koch GG. The measurement of observer agreement for categorical data. *Biometrics*. 1977;33(1):159-174.
26. Hoberman A, Wald ER, Penchansky L, Reynolds EA, Young S. Enhanced urinalysis as a screening test for urinary tract infection. *Pediatrics*. 1993;91(6):1196-1199.

