

TEXAS CHILDREN'S HOSPITAL
EVIDENCE-BASED OUTCOMES CENTER
First Febrile Urinary Tract Infection (UTI)
Evidence-Based Guideline

Definition: The presence of a pure growth of more than 100,000 colony-forming units (cfu) of bacteria per milliliter of urine in a patient with clinical signs and laboratory values suggestive of UTI (positive urinalysis required). Lower counts of bacteria may be clinically important, especially in boys and specimens obtained by catheterization or suprapubic aspiration. (1,2)

Pathophysiology: The disease is usually caused by a bacterial infection. *Escherichia coli* is the most common bacterial species identified. Other common gram negative species include *Klebsiella*, *Proteus*, *Enterobacter*, and *Citrobacter*. Gram positive species include *Staphylococcus saprophyticus* and *Enterococcus*. Pyelonephritis results from bacterial infection of the kidney.

Inclusion Criteria (1-3)

- 1 month - 12 years
- Prepubertal children
- First episode of UTI
- Febrile

Exclusion Criteria (1-3)

- Afebrile
- Conditions in which immunity may be compromised (e.g., transplant recipient [solid organ or hematopoetic], chronic renal insufficiency/kidney disease)
- Known major genitourinary anomalies
- Toxic-appearing
- Sepsis with shock or meningitis
- PICU or NICU 3/4 admission
- Extended-spectrum beta-lactamase (ESBL) producing bacteria
- Other severe comorbid conditions

Differential Diagnosis

Renal abscess	Discitis
Kidney stones	Trauma
Sacroiliitis	Fever
Vertebral osteomyelitis	Gastroenteritis
Appendicitis	Vaginitis/Urethritis

Diagnostic Evaluation: Children with urinary tract infections have a risk of progressing to septic shock. Clinicians should immediately refer to the Septic Shock guideline and intervene rapidly if patient has toxic appearance, ill appearance, altered mental status, and/or compromised perfusion with abnormal vital signs.

Vital Sign Changes of Sepsis (4)

Age	Heart Rate	Resp Rate	Systolic BP	Temp (°C)
0d - 1m	>205	>60	<60	<36 or >38
>1m - 3m	>205	>60	<70	<36 or >38
>3m - 1y	>190	>60	<70	<36 or >38.5
>1y - 2y	>190	>40	<70 + (age in yr x 2)	<36 or >38.5
>2y - 4y	>140	>40	<70 + (age in yr x 2)	<36 or >38.5
>4y - 6y	>140	>34	<70 + (age in yr x 2)	<36 or >38.5
>6y - 10y	>140	>30	<70 + (age in yr x 2)	<36 or >38.5
>10y - 13y	>100	>30	<90	<36 or >38.5
>13y	>100	>20	<90	<36 or >38.5

Signs and Symptoms of Shock (4)

Exam Abnormalities	
Peripheral Pulses	Decreased or weak Bounding
Capillary Refill (central vs. peripheral)	≥3 sec Flash (<1 sec)
Skin	Mottled, cool Flushed, ruddy, erythroderma (other than face) Petechiae below the nipple, any purpura
Mental Status	Decreased, irritability, confusion, inappropriate crying or drowsiness, poor interaction with parents, lethargy, diminished arousability, obtunded

Clinical history, physical examination, and labs are used to diagnose UTI.

History: Assess for

- Urinary symptoms (incontinence, lack of proper stream, withholding maneuvers, frequency, urgency, dysuria)
- Previous UTIs
- Vesicoureteral reflux (VUR)
- Previous undiagnosed febrile illnesses
- Family history of frequent UTIs, VUR, and other genitourinary abnormalities
- Constipation
- Sexual history

Physical Examination

Complete routine vital signs including blood pressure

Assess for

- Toxic appearance, irritable
- Fever
- Disinterested in feeding
- Lethargic
- Poor tone (floppy)
- Poor perfusion
- Sluggish capillary refill
- Tachycardia or bradycardia
- Tachypnea or apnea
- Sunken fontanelle
- Dry mucous membranes
- Jaundice
- Vomiting
- Suprapubic tenderness
- Abdominal/Flank tenderness
- Abdominal mass
- Failure to thrive

Risk Factors For UTI (5)

Girls

- Age younger than 12 months
- Temperature of at least 102.2°F (39°C)
- Fever lasting at least two days
- Absence of another source of infection

Boys

- Temperature of at least 102.2°F (39°C)
- Fever lasting more than 24 hours
- Absence of another source of infection
- Uncircumcised

Laboratory Tests (6,7)

Urinalysis is positive if the sample is positive for leukocyte esterase (LE) or nitrites or microscopy is positive if WBC (≥5 WBCs per high-power field) or bacteria. UTI is unlikely (<0.3%) if the urinalysis is negative.

Sensitivity and Specificity of Urinalysis Components (1,8-10)

Consider empiric treatment until culture results are available.

	Sensitivity	Specificity	*LR +	*LR -
Dipstick	70%	98%	35	0.3
Dipstick & Micro	80%	64%	2.2	0.3
Dipstick & Micro				
0-1 mos	82%	92%	10	0.2
>1-3 mos	82%	94%	13	0.07
Bag LE	76%	84%	4.75	0.29

If nitrites are positive, diagnosis of UTI is very likely.

*LR+: a positive test increases the odds that a patient has the disease by this factor

LR-: a negative test decreases the odds that a patient has the disease by this factor

Positive Urine Culture (1,3)

Catheterization/Suprapubic Aspiration	≥50,000 cfu/mL
Midstream Clean Catch	≥100,000 cfu/mL

Urine specimens should be processed as expediently as possible. If the specimen is not processed promptly, then it should be refrigerated to prevent the growth of organisms. Urine specimens with ≥3 different colony types above the threshold will not be evaluated.

Critical Points of Evidence*

Evidence Supports

- Obtain a urine specimen via transurethral catheterization in non-toilet trained children and via midstream clean catch for toilet trained children. (11-16) – Strong recommendation, moderate quality evidence
Remarks: The diagnosis of UTI cannot be established reliably through culture of urine collected in a bag. (7)
- For rapid diagnosis of UTI, utilize LE and nitrite testing. (15,17-24) – Strong recommendation, moderate quality evidence
- Administer oral antibiotics to toilet trained children and/or children >60 days who are tolerating PO. (25-29) – Strong recommendation, moderate quality evidence
- Administer oral antibiotics and consider outpatient management for non-toilet trained children and/or children 31-60 days who meet the following criteria: no elevated inflammatory markers, tolerating PO, wellhydrated, not tachycardic, adequate transportation, ability to follow up with PCP within 24-48 hours. (25-31) – Weak recommendation, low quality evidence
- Utilize short-course IV antibiotics followed by oral antibiotics (once afebrile and feeding adequately) in children who require admission. (25-29) – Strong recommendation, low quality evidence
- The health benefits of newborn male circumcision outweigh the risks and that the procedure's benefits justify access to this procedure for families who choose it (per the AAP's Circumcision Policy Statement). (32-35) – Strong recommendation, moderate quality evidence

Evidence Against

- Do not routinely administer prophylactic antibiotics to infants/children with their first febrile UTI with a normal renal ultrasound. (36-42) – Strong recommendation, moderate quality evidence
- Do not administer prophylactic antibiotics to infants/children with Grades I-III vesicoureteral reflux. (36-42) – Weak recommendation, moderate quality evidence

Evidence Lacking/Inconclusive

- No evidence addressing whether the diagnostic accuracy of RUS is affected if taken within two days after UTI diagnosis versus several days after diagnosis.

Recommendations Adopted/Adapted from National Guidelines

- If a clinician assesses a febrile infant with no apparent source for the fever as not being so ill as to require immediate antimicrobial therapy, then the clinician should assess the likelihood of UTI. If the clinician determines the febrile infant to have a low likelihood of UTI, then clinical follow-up monitoring without testing is sufficient (evidence quality: A; strong recommendation). If the clinician determines that the febrile infant is not in a low-risk group, then there are 2 choices.
 - Option 1 is to obtain a urine specimen through catheterization or SPA for culture and urinalysis.
 - Option 2 is to obtain a urine specimen through the most convenient means and to perform a urinalysis. If the urinalysis results suggest a UTI (positive leukocyte esterase test results or nitrite test or microscopic analysis results for leukocytes or bacteria), then a urine specimen should be obtained through catheterization or SPA and cultured; if urinalysis of fresh (less than 1 hour since void) urine yields negative leukocyte esterase and nitrite results, then it is reasonable to monitor the clinical course without initiating antimicrobial therapy, recognizing that a negative urinalysis does not rule out a UTI with certainty. (7)**Remarks:** This recommendation was adopted from the American Academy of Pediatrics - The Diagnosis and Management of the Initial Urinary Tract Infection in Febrile Infants and Young Children 2-24 Months of Age guideline.

- To establish the diagnosis of UTI, clinicians should require both urinalysis results that suggest infection (pyuria and/ or bacteriuria) and the presence of at least 50 000 colony-forming units (cfu) per milliliter of a uropathogen cultured from a urine specimen obtained through transurethral catheterization or SPA. (7)
Remarks: This recommendation was adopted from the American Academy of Pediatrics - The Diagnosis and Management of the Initial Urinary Tract Infection in Febrile Infants and Young Children 2-24 Months of Age guideline.
- Febrile infants with UTIs should undergo renal and bladder ultrasonography (RBUS). Voiding cystourethrography (VCUG) should not be performed routinely after the first febrile UTI; VCUG is indicated if RBUS reveals hydronephrosis, scarring, or other findings that would suggest either high-grade VUR or obstructive uropathy, as well as in other atypical or complex clinical circumstances. (7)
Remarks: This recommendation was adopted from the American Academy of Pediatrics - The Diagnosis and Management of the Initial Urinary Tract Infection in Febrile Infants and Young Children 2-24 Months of Age guideline. VCUG may be indicated with recurrent UTIs when deemed appropriate by the practitioner.
- When initiating treatment, the clinician should base the choice of route of administration on practical considerations: initiating treatment orally or parenterally is equally efficacious. The clinician should base the choice of agent on local antimicrobial sensitivity patterns (if available) and should adjust the choice according to sensitivity testing of the isolated uropathogen (evidence quality: A; strong recommendation). The clinician should choose 7 to 14 days as the duration of antimicrobial therapy (evidence quality B; recommendation). (7)
- Remarks:** This recommendation was adopted from the American Academy of Pediatrics - The Diagnosis and Management of the Initial Urinary Tract Infection in Febrile Infants and Young Children 2-24 Months of Age guideline. A recent study in children with pyelonephritis aged 6 months and older found no difference in outcomes in those treated with shorter (6 to 9 days) vs longer (10 or more days) courses of antibiotics. (7,43)

*NOTE: The references cited represent the entire body of evidence reviewed to make each recommendation.

Condition-Specific Elements of Clinical Management

Urine Specimen for Urinalysis and Culture[†] (7,11-16)

- Non-toilet trained children: transurethral catheterization
- Toilet trained children: midstream clean catch
- If an infant (29 days to 24 months of age) is assessed to have a fever without localizing signs and symptoms and not in need of immediate antibiotics, the clinician should determine risk status for UTI. (7)
- If the infant (29 days to 24 months of age) is assessed to be at low risk for UTI, follow-up without testing is adequate. (7)
- If the infant (29 days to 24 months of age) is assessed to NOT be low risk, proceed with either option below. (7)
 - Option 1 - Obtain a urine specimen through catheterization or SPA for culture and urinalysis.
 - Option 2 - Perform a urinalysis. If the urinalysis results suggest a UTI, then a urine specimen should be obtained through catheterization or SPA and cultured.

- Tolerating oral intake
- Patient/Caregiver discharge teaching completed on:
 - Discharge care
 - Signs and symptoms of concern
 - Risk of recurrence
 - Proper perineal care
 - Documentation of scheduled PCP follow-up

Parent Teaching

- Teach parents to recognize symptoms of UTI
- Clearly explain the course of necessary testing and treatment
- Explain strategies to prevent future recurrence (e.g., adequate hydration, frequent voiding, perineal hygiene, completion of antibiotic course)
- Pediatrician follow-up

Consults/Referrals

- Refer to urology if surgical intervention is being considered and/or if child has VUR.
- Refer to nephrology if child has VUR and associated renal insufficiency, hypertension, abnormal serum chemistries, or renal scarring.

Measures

Structure

- Location of radiologic studies (inpatient or outpatient setting)

Process

- Utilization of the order set(s)
- Frequency of completed radiologic studies
- Time frame to complete radiologic studies

Outcome

- Use of prophylactic antibiotics with documented reflux
- EC visit within 14 days and reason for visit
- Documented use of prophylactic antibiotics
- Length of stay
- Organisms and their resistance patterns
- Rate of positive/negative RUS, radionuclide cystogram, and VCU

Hydration

- IV fluids if not taking oral fluids adequately.

Imaging Studies (1,7)

Age	Imaging Study
1-24 months	Renal ultrasound (RUS) If RUS is normal, a VCUG is not needed.
>24 months	RUS at discretion of physician based on clinical findings

*VCUG may be performed as soon as fever is decreasing and culture-specific antibiotics are in use. There is no need to perform an additional urinalysis if the patient is on appropriate antibiotics.

Admission Criteria

- Unable to tolerate oral fluids (requires IV fluids for hydration)
- Failed outpatient therapy (requires IV antibiotics)

Inpatient Discharge Criteria

- A decreasing trend in daily maximal temperatures combined with physician discretion
- On culture-specific antibiotics

Antibiotic Therapy ⁽⁴⁴⁾

Consider insurance/Medicaid formulary restrictions.

Empirical Oral Therapy - Outpatient			
	Age & Weight Parameters	Dose and Frequency	TCH Formulary
Cefixime	Infants and children ≤45 kg	4 mg/kg/dose PO every 12 h (MAX: 200 mg/DOSE)	Yes
	Children >45 kg and adolescents	400 mg PO every 24 h	
Cefdinir If available, cefixime is the preferred oral antibiotic for the empiric treatment of UTI since it has better pharmacokinetic properties than cefdinir (e.g. urine penetration, and half-life).	Children ≥6 months to 12 years	7 mg/kg/dose PO every 12 h (MAX: 300 mg/DOSE)	Yes
	Adolescents	600 mg PO every 24 h	
Empirical Parenteral Therapy (IV/IM) - Emergency Center or Inpatient			
	Age & Weight Parameters	Dose and Frequency	TCH Formulary
CefTRIAxone NOTE: Not for use in patients receiving Y-site administration of calcium-containing IV fluids with a single lumen or single IV site *Use cefTAZidime as an alternative	Infants and children ≥2 months and adolescents	50 mg/kg/dose IV every 24 h (MAX: 2 grams/DAY)	Yes
CefTAZidime *Use cefTRIAxone as an alternative	Infants, children, and adolescents	50 mg/kg/dose IV every 8 h (MAX: 6 grams/DAY)	Yes
Directed Oral Therapy (Based on Lab Results)			
	Age & Weight Parameters	Dose and Frequency	TCH Formulary
Cefixime	Infants and children ≤45 kg	4 mg/kg/dose PO every 12 h (MAX: 200 mg/DOSE)	Yes
	Children >45 kg and adolescents	400 mg PO every 24 h	
Cefdinir If available, cefixime is the preferred oral antibiotic for the empiric treatment of UTI since it concentrates better in the urine compared to cefdinir.	Children ≥6 months to 12 years	7 mg/kg/dose PO every 12 h (MAX: 300 mg/DOSE)	Yes
	Adolescents	600 mg PO every 24 h	
Amoxicillin	Infants and children <40 kg	13 mg/kg/dose PO every 8 h (MAX: 500 mg/dose)	Yes
	Children and adolescents ≥40 kg	500 mg PO every 8 h	
Trimethoprim and Sulfamethoxazole (TMP/SMX)	Children and adolescents	4 mg TMP/kg/dose PO every 12 h (MAX: 160 mg TMP/dose)	Yes
Directed Parenteral Therapy (IV) - Inpatient (Based on Micro Results)			
	Age & Weight Parameters	Dose and Frequency	TCH Formulary
CeFAZolin	Infants and children	33 mg/kg/dose IV every 8 h	Yes
CefTRIAxone NOTE: Not for use in patients receiving Y-site administration of calcium-containing IV fluids with a single lumen or single IV site *Use cefTAZidime as an alternative	Infants and children ≥2 months and adolescents	50 mg/kg/dose IV every 24 h (MAX: 2 grams/DAY)	Yes

CefTAZidime *Use cefTRIAxone as an alternative	Infants, children, and adolescents	50 mg/kg/dose IV every 8 h (MAX: 6 grams/DAY)	Yes
Ampicillin	Infants and children	25-50 mg/kg/dose IV every 6 h (MAX: 100 mg/kg/dose not to exceed 2 grams/dose or 12 grams/DAY)	Yes
Gentamicin	Infants and children Conventional Dosing	2.5 mg/kg/dose IV every 8 h (MAX: 3 mg/kg/dose not to exceed 120 mg/dose)	Yes
	Infants and children Extended-Interval Dosing (Weight Directed)	7.5 mg/kg/dose IV every 24 h	

TCH Evidence-Based Outcomes Center Clinical Algorithm for Children with First Febrile Urinary Tract Infection (UTI)

Abbreviations:
 UA - urinalysis
 LE - leukocyte esterase
 IV - intravenous
 RUS - renal ultrasound
 VCUG - voiding cystourethrogram

Inclusion Criteria

- 1 month - 12 years
- Prepubertal
- First episode of UTI
- Febrile

Exclusion Criteria

- Afebrile
- Conditions in which immunity may be compromised (transplant recipient or chronic renal insufficiency/kidney disease)
- Known major genitourinary anomalies
- Toxic- appearing
- Sepsis with shock or meningitis
- PICU or NICU 3/4 admission
- Extended-spectrum beta-lactamase (ESBL) producing bacteria
- Other severe comorbid conditions

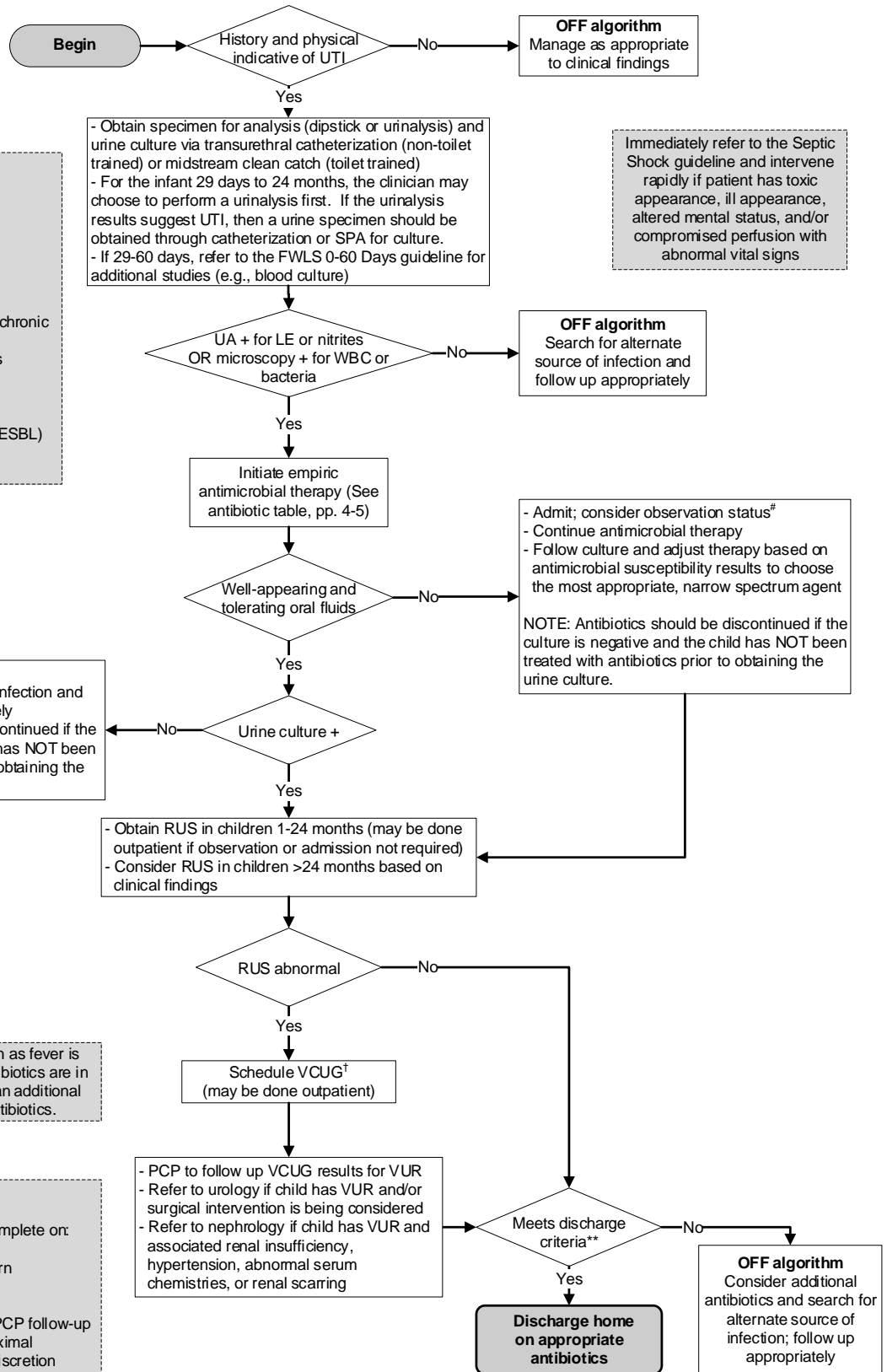
#Admission Criteria

- Unable to tolerate oral fluids (requires IV fluids for hydration)
- Failed outpatient therapy (requires IV antibiotics)

OFF algorithm
 Search for alternate source of infection and follow up appropriately
 NOTE: Antibiotics should be discontinued if the culture is negative and the child has NOT been treated with antibiotics prior to obtaining the urine culture.

****Discharge Criteria**

- Tolerating oral intake
- Patient/Caregiver discharge teaching complete on:
 - Discharge care
 - Signs and symptoms of concern
 - Risk of recurrence
 - Proper perineal care
 - Documentation of scheduled PCP follow-up
- If admitted, decreasing trend in daily maximal temperatures combined with physician discretion



Clinical standards are developed for 80% of the patient population with a particular disease. Each practitioner must use his/her clinical judgment in the management of any specific patient.

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Clinical Standards Preparation

This clinical standard was prepared by the Evidence-Based Outcomes Center (EBOC) team in collaboration with content experts at Texas Children's Hospital. Development of this clinical standard supports the TCH Quality and Patient Safety Program initiative to promote clinical standards and outcomes that build a culture of quality and safety within the organization.

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EBOC Team

Development Process

This clinical standard was developed using the process outlined in the EBOC Manual. The literature appraisal documents the following steps:

1. Review Preparation
 - PICO questions established
 - Evidence search confirmed with content experts
2. Review of Existing Internal and External Guidelines
 - Cincinnati Children's First Urinary Tract Infection in Children ≤12 Years; American Academy of Pediatrics' Urinary Tract Infection: The Diagnosis and Management of Initial UTI in Febrile Infants and Children 2 to 24 Months; Reaffirmation of AAP Clinical Practice Guideline: The Diagnosis and Management of the Initial Urinary Tract Infection in Febrile Infants and Young Children 2-24 Months of Age; National Institute of Health and Clinical Excellence Urinary Tract Infection in Children
3. Literature Review of Relevant Evidence
 - Searched: PubMed, Cochrane Collaboration, CINAHL, Google
4. Critically Analyze the Evidence
 - 13 meta-analyses, 3 randomized controlled trials, and 39 nonrandomized studies
5. Summarize the Evidence
 - Materials used in the development of the guideline, evidence summary, and order sets are maintained in a UTI evidence-based review manual within EBOC.

Evaluating the Quality of the Evidence

Published clinical guidelines were evaluated for this review using the **AGREE II** criteria. The summary of these guidelines are included in the literature appraisal. AGREE II criteria evaluate Guideline Scope and Purpose, Stakeholder Involvement, Rigor of Development, Clarity and Presentation, Applicability, and Editorial Independence using a 4-point Likert scale. The higher the score, the more comprehensive the guideline.

This clinical standard specifically summarizes the evidence *in support of or against* specific interventions and identifies where evidence is *lacking/inconclusive*. The following categories describe how research findings provide support for treatment interventions.

"Evidence Supports" provides evidence to support an intervention.
"Evidence Against" provides evidence against an intervention.
"Evidence Lacking/Inconclusive" indicates there is insufficient evidence to support or refute an intervention and no conclusion can be drawn *from the evidence*.

The **GRADE** criteria were utilized to evaluate the body of evidence used to make practice recommendations. The table below defines how the quality of the evidence is rated and how a strong versus weak

recommendation is established. The literature appraisal reflects the critical points of evidence.

Recommendation	
STRONG	Desirable effects clearly outweigh undesirable effects or vice versa
WEAK	Desirable effects closely balanced with undesirable effects
Quality	Type of Evidence
High	Consistent evidence from well-performed RCTs or exceptionally strong evidence from unbiased observational studies
Moderate	Evidence from RCTs with important limitations (e.g., inconsistent results, methodological flaws, indirect evidence, or imprecise results) or unusually strong evidence from unbiased observational studies
Low	Evidence for at least 1 critical outcome from observational studies, RCTs with serious flaws or indirect evidence
Very Low	Evidence for at least 1 critical outcome from unsystematic clinical observations or very indirect evidence

Recommendations

Practice recommendations were directed by the existing evidence and consensus amongst the content experts. Patient and family preferences were included when possible. The Content Expert Team and EBOC team remain aware of the controversies in the diagnosis/management of first febrile UTI in children. When evidence is lacking, options in care are provided in the clinical standard and the accompanying order sets (if applicable).

Approval Process

Clinical standards are reviewed and approved by hospital committees as deemed appropriate for its intended use. Clinical standards are reviewed as necessary within EBOC at Texas Children's Hospital. Content Expert Teams are involved with every review and update.

Disclaimer

Practice recommendations are based upon the evidence available at the time the clinical standard was developed. Clinical standards (guidelines, summaries, or pathways) **do not** set out the standard of care and are not intended to be used to dictate a course of care. Each physician/practitioner should use his or her independent judgment in the management of any specific patient and is responsible, in consultation with the patient and/or the patient's family, to make the ultimate judgment regarding care.

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Version History

Date	Comments
May 2008	Originally completed
Jan 2012	Updated
Dec 2015	Updated
Aug 2017	Added a note indicating preference of cefixime to cefdinir
Jan 2019	Revised the 'Vital Sign Changes of Sepsis' table, replaced cefotaxime with ceftazidime, and changed the dosing of ceftriaxone
August 2021	Adopted AAP recommendations for imaging, specimen collection, antibiotic duration and diagnosis for UTI; Remainder of content reaffirmed