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Clinical Practice Guideline for the Diagnosis and Treatment of Urinary Tract Infection in Children From 8 Days to 5 Years of Age

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abstract

Urinary tract infection (UTI) is one of the most common bacterial infections in infants and young children, with a prevalence of 7% in infants with fever. This clinical practice guideline (CPG) provides an update of the literature and clinical recommendations of the 2011 American Academy of Pediatrics (AAP) CPG on diagnosing and managing UTI in infants and children. It is designed to provide guidance for pediatricians and other pediatric clinicians on the diagnosis and management of UTIs in infants and children 8 days to 5 years of age and is intended for use in children with low medical complexity across a variety of settings. The CPG is accompanied by 3 technical reports to further elucidate the data that guided the development of recommendations and to establish criteria for the diagnosis of UTI. The Grading of Recommendations Assessment, Development, and Evaluation (GRADE) approach was used to assess the certainty of the evidence and formulate recommendations and good practice statements, including GRADE evidence-to-decision frameworks, which were reviewed by internal and external contributors. The CPG provides 8 Key Action Statements (2 strong and 6 conditional clinical recommendations, ranging from low to very low certainty of evidence) and 4 Good Practice Statements regarding medical evaluation of suspected UTI, management of UTI specific to antibiotic treatment, and imaging modalities and prevention strategies for structural abnormalities, including vesicoureteral reflux, and bowel and bladder dysfunction evaluation and treatment.

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KEY ACTION STATEMENT LIST

Key Action Statements and Remarks	Good Practice Statements
Key Action Statement 1: In medically noncomplex children ages 2 mos to 24 mos with fever without an identified source and in children ages 2 to 5 y with symptoms suggestive of urinary tract infection (UTI [eg, dysuria, new-onset urinary urgency or frequency]), the AAP Guideline Panel suggests medical evaluation for UTI[a] within 72 h of symptom onset rather than a longer period of observation (conditional recommendation, low certainty of evidence). Remark 1 for Key Action Statement 1: Although evaluation within 72 h is generally appropriate, pediatricians and other pediatric clinicians should expedite assessment in children at higher risk for pyelonephritis or kidney injury—for example, those with known structural genitourinary abnormalities (such as hydronephrosis or vesicoureteral reflux), a history of prior febrile UTI, or symptoms consistent with pyelonephritis (such as flank pain). Remark 2 for Key Action Statement 1: Although this Key Action Statement focuses on medically noncomplex children, the same principle of timely evaluation applies to medically complex children who may be at increased risk for renal sequelae and may warrant more urgent assessment.	

Key Action Statement 2: In children with UTI[a], the AAP Guideline Panel suggests a shorter course of antibiotic therapy (≤7 d) rather than a longer (>7 d) course of antibiotic therapy (conditional recommendation, low certainty of evidence).
Remarks for Key Action Statement 2:
• Low-risk children
  ○ The panel suggests a 3- to 5-d course of antibiotics for children 2 y and older with no known underlying anatomic abnormalities of the urinary tract presenting with nonfebrile UTI with referred urinary symptoms suggestive of cystitis (specifically urinary urgency and incontinence, dysuria, or urinary frequency).
  ○ The Panel suggests a 5- to 7-d course of antibiotics for children ages 2 mos to 24 mos with UTI.
• The panel suggests a 5- to 7-d course of antibiotics for children 2 y and older with no known underlying anatomic abnormalities of the urinary tract presenting with signs and symptoms concerning for pyelonephritis (eg, fever ≥102.2° F).
• High-risk children
  ○ A more prolonged antimicrobial course (>7 d) may be provided for infants age 8 d to 2 mos; children with underlying anatomic genitourinary abnormalities; children who have associated bacteremia; or children who do not respond (with resolved or resolving signs and symptoms) to their initial antimicrobial course.	

Key Action Statement 3A: In children ages 8 to 28 d in whom a UTI has been diagnosed,[a] the AAP Guideline Panel suggests parenteral antibiotics with early transition to oral following clinical improvement rather than parenteral antibiotics alone (conditional recommendation, very low certainty of evidence). Key Action Statement 3B: In children older than 28 d and younger than 5 y with UTI,[a] the AAP Guideline Panel recommends oral antibiotics rather than parenteral or sequential antibiotics requiring hospitalization (strong recommendation, very low certainty of evidence). Remarks for Key Action Statement 3B: • The panel defines sequential antibiotics as initial parenteral antibiotics that are subsequently transitioned to oral. • In children older than 28 d who are able to tolerate oral antibiotics and who do not otherwise require hospitalization, outpatient therapy is encouraged.	

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Key Action Statements and Remarks	Good Practice Statements
• Examination of the evidence suggests equivalent outcomes between oral and parenteral/sequential antibiotics with regard to outcomes of renal scarring and short-term recurrence of infection (ie, treatment failure). The use of parenteral antibiotics is, however, associated with several undesirable outcomes, including hospitalization, pain from intravenous (IV) catheter placement, potential for extravasation injury, increased cost, and potential complications associated with peripherally inserted central catheter (PICC) lines, which include infection and clotting. This constellation of harms associated with parenteral antibiotics warrants a strong recommendation against their routine use. • Should pediatricians and other pediatric clinicians have concerns about the ability of families to promptly obtain oral antibiotics from an outpatient pharmacy, a single dose of parenteral antibiotics may be given prior to transition to oral antibiotics.	
Key Action Statement 4: In children younger than 5 y in whom a first febrile UTI has been diagnosed,[a] the AAP Guideline Panel recommends performing renal and bladder ultrasonography (RBUS), rather than not performing RBUS, to detect structural abnormalities or findings associated with vesicoureteral reflux (VUR), not to detect VUR itself (strong recommendation, low certainty of evidence of the clinical impact of the detected abnormalities on RBUS, low certainty of evidence for ultrasonographic detection of VUR). Remark for Key Action Statement 4: Although RBUS is the standard of care for detection of congenital or structural anomalies, there is low certainty about the frequency of RBUS detecting a clinically important anomaly. The AAP Guideline Panel believes, however, that identifying infrequent RBUS abnormalities benefits the proportion of patients who are ultimately identified.	
Key Action Statement 5A: The AAP Guideline Panel suggests against routine voiding cystourethrography (VCUG) after a first febrile UTI[a] in children younger than 5 y who have normal RBUS (conditional recommendation, high certainty of evidence of test accuracy, low certainty of evidence of overall effect). Remark for Key Action Statement 5A: It is an option to perform VCUG after the first febrile UTI in specific subpopulations (eg, age <1 mo; infectious agent other than *Escherichia coli*; circumcised males; atypical/complicated course including septic shock/intensive care unit (ICU) admission; or limited follow-up reliability) with subspecialty consultation for abnormal results. Key Action Statement 5B: The AAP Guideline Panel suggests offering VCUG in: children with clinically relevant abnormalities detected on RBUS after a first febrile UTI,[a] all children younger than 2 y with a second febrile UTI, and children 2 y or older with a second febrile UTI and no alternative explanatory risk factors (conditional recommendation, high certainty of evidence of test accuracy, low certainty of evidence of overall effect). Remark for Key Action Statement 5B: In children with VUR and underlying anomalies of the renal tract that increase risk for both UTI and renal scarring, pediatricians and other pediatric clinicians are encouraged to partner with the family and provide educational resources to assist with early future detection, treatment, and prevention of UTI.	
Key Action Statement 6[b]: In children with low-risk VUR, the AAP Guideline Panel suggests against using routine continuous antibiotic prophylaxis (CAP) (conditional recommendation, low certainty of evidence). Remarks for Key Action Statement 6: • The panel defines low-risk VUR as a child having *both* a lower-grade VUR (I–II) *and* no presence of bowel and bladder dysfunction (BBD) (excluding functional constipation), per the Rome criteria. • The panel recognized, through comprehensive evidence review, that grade III VUR spans an unclear risk category. CAP is a reasonable option for patients with grade III VUR for patients and caregivers who place a higher value on the uncertain reduction in the risk of infections and a lower value on minimizing exposure to antibiotics. • For children with high-risk VUR, CAP is an option. The panel defined high-risk VUR as the presence of *any* of the following:	Good Practice Statement: All decisions regarding use of CAP should occur as part of a shared decision-making process with families, given the uncertainty over risks and benefits in individual patients. Good Practice Statement: Whenever possible, in children with VUR and/or underlying anomalies of the urinary tract that increase risk for UTI and renal scarring, referral to pediatric urology and/or nephrology is recommended for shared decision making and discussion of all management options, including observation, treatment of BBD, antibiotic prophylaxis, and surgical management options. When in-person access to pediatric urologists and nephrologists is limited, virtual consultations, including e-consults and telehealth, can enhance access and specialist involvement. Good Practice Statement: VUR management may include observation, CAP, endoscopic injection, and ureteral reimplantation; selection among options is encouraged to be in collaboration with pediatric urology or pediatric nephrology via shared decision making.

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Key Action Statements and Remarks	Good Practice Statements
○ Grade IV or grade V VUR ○ Intrarenal reflux ○ Demonstrated renal scarring/nephropathy ○ Renal/ureteral structural or cortical abnormalities ○ Recurrent pyelonephritis ○ Bacteremia resulting in intensive care unit admission ○ BBD (excluding functional constipation) • Patients with high-risk VUR and other high-risk urologic abnormalities that are not covered in clinical practice guideline (CPG) should be referred to a pediatric urologist or nephrologist.	
	Good Practice Statement for BBD: In children with UTIs, pediatricians and other pediatric clinicians should evaluate for and treat BBD to decrease the risk of future UTIs. BBD, including constipation, is a substantial risk factor for recurrent UTIs. Assessment of BBD can be conducted via a basic history and physical examination and by using simple screening tools,[1] with consideration of subspecialty referral for children who do not respond to typical constipation and behavioral voiding management. When in-person access to pediatric urologists and nephrologists is limited, virtual consultations, including e-consults and telehealth, can enhance access and specialist involvement.

[a] Criteria for diagnosis of UTI is defined in Table 1: Definition of High-Probability in Children with Low Medical Complexity.

[b] The purpose of Key Action Statement (KAS) 6 is to provide risk stratification and management of children to front-line pediatricians and other pediatric clinicians where immediate consultation or access to pediatric urology may not be readily available. All nephrologists and urologists on the Panel did not support all aspects of the KAS, as it does not address the comprehensive management of VUR, whereas the majority of the Panel deemed the KAS to align with the scope of this guideline. Although clinical perspectives differed among the panel members, nephrology and urology representatives agreed that the KAS guidance is a reasonable starting point for the initial management of the child with VUR while awaiting consultation with subspecialists.

I. INTRODUCTION

Urinary tract infection (UTI) is one of the most common bacterial infections in infants and young children, with a prevalence of 7% in infants with fever.[2] Despite its prevalence, however, the diagnosis and management of UTI in infants and young children remains controversial. This clinical practice guideline (CPG) provides an update of the literature and clinical recommendations, rather than a reaffirmation, of the 2011 American Academy of Pediatrics (AAP) CPG on diagnosing and managing UTI in infants and children.[3]

The CPG also provides a larger age range for recommendations for pediatric patients, expanding from the previous age range of 2 months to 2 years, to now address children from 8 days to 5 years of age. It is designed to assist with the diagnosis and management of UTI in infants and children 8 days to 5 years of age. The CPG is intended for use in children with low medical complexity across a variety of settings (including offices, emergency departments [EDs], and hospitals) by all providers who treat infants and children, including children with neurodevelopmental disabilities (NDDs) and intellectual and developmental disabilities (IDDs). Children who have complex urologic and/or medical conditions (such as immunosuppression) should be referred to subspecialty care for evaluation.

This CPG is not intended for use in children who are medically complex; therefore, it excludes children with neurogenic bladder, immune compromise, extreme prematurity, known congenital anomalies of kidney and urinary tract, major congenital anomalies of other organ systems, multisystem disease, and/or other major chronic illness.

Three accompanying technical reports (TRs) support this guideline. Two TRs further elucidate the data and analyses that guided these clinical recommendations.[4,5] In addition, a third TR ("Urinary Tract Infection Diagnosis—A Companion to the American Academy of Pediatrics' 2026 Clinical Practice Guideline on the Diagnosis and Management of Urinary Tract Infection: Technical Report") establishes criteria for a diagnosis of UTI.[6] Table 1 defines high-probability UTI in children with low medical complexity.

Diagnosis can be exceptionally challenging in some patients and is complicated by ongoing controversy in the literature and the lack of widely accepted laboratory tests that, in isolation, confirm UTI.[6] When to test for UTI and when to treat are determined by many factors, including history (which includes risk factors such as a past history of UTI), symptoms, examination findings, and results of urinalysis (UA) (in real time) and urine culture (which is available later).

Symptoms may be vague in young children and in those with impaired communication skills. In addition, it is possible that a child who does not meet "laboratory criteria" for UTI may have one—while a child who does meet the traditional criteria for UTI may not have one. In addition, although future laboratory indicators may emerge, there is currently no widely accepted "gold standard" to replace the combination of clinical suspicion and an evidence-based approach to testing.[7]

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TABLE 1. Definition of High-Probability UTI in Children With Low Medical Complexity[6,a]

Age	Likely Initial Diagnosis of UTI (Culture Results Pending)	UTI Once Culture Results Are Obtained		
		Markers of Inflammation	Culture Results	Urine Collection Method for Culture
0 to <2 mo	≥5 WBCs/hpf OR ≥trace LE	≥5 WBCs/hpf OR ≥trace LE (any collection method)	≥10 000 CFUs/mL of a pathogenic organism	Catheter or suprapubic aspiration
2 mo to 5 y	≥10 WBCs/hpf OR ≥+2 LE	≥5 WBCs/hpf OR ≥+1 LE (any collection method)	≥10 000 CFUs/mL of a pathogenic organism	Catheter
			≥100 000 CFUs/mL	Clean catch

Abbreviations: CFU, colony-forming unit; hpf, high-powered field; LE, leukocyte esterase; WBC, white blood cell.

[a] The urinalysis (UA) thresholds should be regarded as decision support anchors rather than absolute rules. Their diagnostic utility is determined by pretest probability, as both positive and negative predictive values are strongly influenced by baseline risk. When pretest probability is high (eg, an ill-appearing infant), even with an equivocal UA, pediatricians and other pediatric clinicians may reasonably obtain a urine culture and consider empiric management while awaiting culture results, with prompt reassessment to guide subsequent care. Conversely, when pretest probability is low (eg, a well-appearing child without focal findings), an equivocal UA has greater value in excluding infection, and empiric treatment may not be indicated unless additional risk factors emerge.

The difficulty of distinguishing asymptomatic bacteriuria (ASB) and UTI further complicates efforts to develop a gold standard for diagnosing pediatric UTI.[8] Both the lack of a widely accepted gold standard for diagnostic criteria and diagnostic criteria's variability within the literature challenge the interpretation of testing modalities' sensitivity and specificity. The accompanying report on UTI diagnosis aims to clarify UTI testing and diagnosis.[6]

In prior guidelines, CPG panels (hereafter referred to as panels) identified at-risk infants who are in need of UTI testing using retrospective cohort data. This approach led to the use of race as a factor in stratifying UTI risk. The current panel unanimously concluded, however, that the use of race in assessing UTI risk in infants is likely to be confounded by unmeasured factors among underserved populations, resulting in noncausal associations. The panel felt that it was essential to remove race-based considerations of UTI diagnosis and treatment.

Overall, with respect to the panel deliberation process, the panel recognized that there were differing viewpoints, particularly in areas where evidence was mixed or inconclusive. A minority, including the representatives from urology and nephrology, did not support all aspects of this guideline. The final decisions regarding the content of key action statements (KASs) and remarks were made by majority vote. Key areas of disagreement are noted within the document.

The panel recognizes that further research may enhance our understanding of these recommendations and anticipates that future revisions will be necessary based on our evolving understanding of the complexity of UTI diagnosis and management.

II. METHODOLOGY

The panel assessed the certainty of the supporting evidence and developed and graded the recommendations following the Grading of Recommendations Assessment, Development, and Evaluation (GRADE) approach.[9–12] The overall guideline development process—including funding of the work, panel formation, management of conflicts of interest, internal and external review, and organizational approval—was guided by AAP policies and procedures. The process is intended to meet the criteria of the National Academies of Medicine (formerly the Institute of Medicine) and the Guidelines International Network recommendations for trustworthy guidelines.[13–16]

Guideline Panel Composition, Process, and Support

Panel Formation and Management of Conflicts of Interest

The AAP established a formalized process for receiving and vetting proposals from multiple vendors to streamline the systematic review (SR) of evidence to inform this CPG. Once the vendor selection process was complete, the Evidence Foundation was selected as the contracted consultant organization responsible for conducting this SR. The Evidence Foundation is a registered 501(c)(3) nonprofit organization with the mission of supporting organizations in the development of evidence-based guidelines using the GRADE approach.

The AAP appointed a multidisciplinary panel of subject matter experts to develop the CPG's clinical recommendations. The panel members included the following roles: chair, vice-chair, hospitalists, primary care pediatricians, caregiver representative, and subspecialists in infectious disease, emergency medicine, nephrology, urology, radiology, and critical care. From 2022 to 2025, the panel members participated in a series of virtual monthly meetings and an in-person meeting at AAP headquarters to prioritize clinical questions, review evidence, and formulate recommendations.

Each member of the panel completed an online conflict of interest form, ensuring transparency and integrity

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throughout the process. The AAP's Conflict of Interest Management Advisory Committee reviewed all submitted disclosures and determined that there were no conflicts that would preclude any of the panel members' participation in the guideline development process prior to approval by the AAP Board of Directors. The AAP has neither solicited nor accepted any commercial involvement in the development of the content of this publication. All CPGs are funded by the AAP.

Scope of the Review

The intended audience of these guidelines includes health care professionals caring for children who may have a UTI, including pediatricians, primary care clinicians, emergency and urgent care providers, other clinicians, caregivers, and policy makers. The intended beneficiaries of the guideline recommendations are children between 8 days and 5 years of age who have suspected or diagnosed UTI and their caregivers. SRs were conducted and reported according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) standards.[17] For a full description of the methods and results of the SRs, refer to the accompanying TRs.[4,5]

Guideline Objectives

CPGs from the AAP are primarily intended to help pediatricians and other pediatric clinicians make management decisions about diagnostic and treatment alternatives. Other purposes are to inform policy, education, and advocacy and to articulate future research needs. Although this CPG makes recommendations about evidence-based care, the practice of medicine dictates tailoring care to individual patients and families. Clinicians must make decisions on the basis of the clinical presentation of each individual patient. This decision making ideally occurs through a shared process that considers the patient's and caregiver's values and preferences with respect to the anticipated outcomes of the chosen option. Decisions may be constrained, however, by the realities of a specific clinical setting and local resources, including but not limited to institutional policies, time limitations, and availability of treatments. These guidelines may not include all appropriate methods of care for the clinical scenarios described. As science advances and new evidence becomes available, recommendations may need to be updated. Following this CPG's recommendations cannot guarantee successful outcomes in all situations.

Statements about the underlying values and preferences of the patients and their caregivers, as well as qualifying remarks accompanying each recommendation, are its integral parts and serve to facilitate more accurate interpretation. They should never be omitted when recommendations from these guidelines are quoted or translated.

Population, Intervention, Comparator, and Outcome (PICO) Questions

The panel prioritized the questions to be addressed in this guideline through a series of online, anonymous surveys (SurveyMonkey Inc, San Mateo, California; available at: www.surveymonkey.com).[18] The list of prioritized questions is provided in Table 2. The panel also prioritized additional background questions to be addressed in the CPG narrative to inform its development of a new definition of UTI (see accompanying TR[6]).

Search Strategy

The research team conducted 8 systematic searches to answer the prioritized PICO questions. Search strategies, including the databases and time period searched and the search terms, are described in the accompanying TRs.[4,5] In brief, the searches were restricted to studies published in the English language from January 1, 2008 (coinciding with the end date of the database search for the 2011 AAP UTI CPG) through August 5, 2023. A hand-search was performed of the reference lists for the 2011 AAP UTI CPG[3] and TR[20] to identify relevant references published prior to 2008. Searches were calibrated with input from panel members, who identified key studies for each PICO question. Additionally, during each meeting when evidence was discussed, panel members were asked to bring forward any additional studies that may fulfill the eligibility criteria.

Eligibility Criteria

Descriptions of the eligibility criteria applied during study selection are provided in the accompanying TRs.[4,5] In brief, studies were included if they described a pediatric population with suspected UTI or diagnosed UTI undergoing testing or treatment with an intervention of interest. Narrative reviews, case reports, and noncomparative observational studies were excluded.

Study Selection

Titles, abstracts, and full texts were screened in duplicate and conflicts were discussed and resolved through consensus. During screening, researchers searched for additional evidence related to health equity and costs to address these criteria within the GRADE evidence-to-decision (EtD) framework; these studies were tagged for future reference and excluded.

Data Extraction

The study characteristics and results were extracted into a standardized and piloted form via Google Sheets (Google,

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TABLE 2. Prioritized PICO Questions

Question	Research Process	Outcome
What clinical variables (history and physical examination) are associated with an increased risk of UTI?	SR; update of 2011 AAP UTI CPG	Narrative description of evidence
In children with suspected UTI, should clinicians instruct parents to seek prompt medical evaluation for symptoms suggestive of UTI (fever or dysuria) versus observation for symptom progression?	SR; update of 2011 AAP UTI CPG	KAS
In children with suspected UTI, after urine has been obtained, what is the test accuracy of all elements of all of the following modalities of urine testing for a positive urine culture: • Dipstick nitrates • Dipstick leukocyte esterase • Dipstick RBC count • Dipstick aggregate results spun • Dipstick aggregate results unspun • Dipstick by manufacturer • Gram stain • WBC count • RBC count • Urine appearance (eg, cloudy) • Laboratory UA	SR; update of 2011 AAP UTI CPG	Narrative description of evidence and new UTI definition[6]
In children with suspected UTI after urine (unspun) has been obtained, what is the test accuracy of WBC count + dipstick leukocyte esterase vs CFU count?	Combined with question #2	Narrative description of evidence and new UTI definition[6]
In children without pyuria, should clinicians obtain a urine culture vs no urine culture?	SR; update of 2011 AAP UTI CPG	Narrative description of evidence and new UTI definition[6]
In children with suspected UTI, should bag UA + urethral catheterization (sequential collection) be used versus urine catheterization alone?	SR; update of 2011 AAP UTI CPG	Adoption of recommendation from AAP febrile infant CPG[19] and narrative discussion
In children being treated for UTI, should a shorter course (<7 d) of antibiotics versus a standard course (≥7 d) be used?	SR; update of 2011 AAP UTI CPG	KAS
In children being treated for UTI, should antibiotics be administered via an oral route alone versus a parenteral or sequential (parenteral followed by oral) route?	SR; update of 2011 AAP UTI CPG	KAS
In children with a diagnosis of their first UTI, should RBUS vs no testing be used for the detection of reflux?	SR; update of 2011 AAP UTI CPG	KAS
In children with a diagnosis of recurrent UTI, should RBUS vs VCUG be used for the detection of reflux?	SR; update of 2011 AAP UTI CPG	Narrative discussion
In children with a diagnosis of their first UTI, should VCUG vs no testing be used for the detection of reflux?	SR; update of 2011 AAP UTI CPG	KAS
In children with positive RBUS, should CeVUS vs VCUG be used for the detection of reflux?	SR; update of 2011 AAP UTI CPG	Narrative discussion
In children with VUR, should continuous antibiotic prophylaxis (CAP) vs no CAP be used?	SR; update of 2011 AAP UTI CPG	KAS and GPS
Should children with history of UTI (ie, risk factors that would lead them to being considered for UTI prophylaxis) with clinical signs and symptoms of BBD receive prophylactic UTI treatment plus BBD treatment or BBD treatment alone?	SR; update of 2011 AAP UTI CPG	GPS

Abbreviations: AAP, American Academy of Pediatrics; BBD, bowel and bladder dysfunction; CeVUS, contrast-enhanced voiding urosonography; CFU, colony-forming units; CPG, clinical practice guideline; GPS, Good Practice Statement; KAS, Key Action Statement; RBC, red blood cell; RBUS, renal bladder ultrasound; SR, systematic review; UA, urinalysis; UTI, urinary tract infection; VCUG, voiding cystourethrography; WBC, white blood cell.

Mountain View, California; available at: https://docs.google.com/spreadsheets). Data extraction was performed by 1 member of the research team and reviewed by a second member. Conflicts were resolved through discussion and consensus.

Risk of Bias Assessment

Risk of bias (RoB) was assessed using the Cochrane Collaboration's RoB tool for randomized trials (RoB 2.0) and Risk of Bias in Non-randomized Studies of Interventions (ROBINS-I) tool for nonrandomized studies

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and the Quality Assessment of Diagnostic Accuracy Studies 2 (QUADAS-2) tool for test accuracy studies.[21–24]

Certainty Assessment

The certainty in the body of evidence (also known as quality of the evidence or confidence in the estimated effects) was assessed for each outcome of interest following the GRADE approach. Judgments about overall certainty were based on the following domains: RoB, inconsistency, indirectness, risk of publication bias, presence of large effects, dose-effect relationship, and an assessment of the effect of plausible residual and opposing confounding. The certainty was categorized into 4 levels: high, moderate, low, or very low.[25]

Data Synthesis and Analysis

When possible, data were synthesized quantitatively using random-effects meta-analysis. All statistical analyses were conducted using Cochrane Review Manager (RevMan) software (RevMan [Computer program], Version 5.4, The Cochrane Collaboration, 2020). For test accuracy reviews, statistical pooling was completed using OpenMeta[analyst]. In situations when quantitative synthesis was not possible because of heterogeneity in study designs and/or populations, data were synthesized and reported narratively. Researchers prepared a GRADE evidence profile for each PICO question using the GRADEpro Guideline Development Tool (GRADEpro GDT [Software], McMaster University and Evidence Prime, 2024; available at: https://gdt.gradepro.org). The evidence profiles summarized the results of the SRs, including effect estimates and certainty in the evidence.

Formulating Recommendations/Key Action Statements

The GRADE EtD framework facilitates the transparent combination of evidence with additional considerations such as patient and caregiver values, resource utilization (eg, required resources, cost-effectiveness), health equity, acceptability, and feasibility.[26,27]

The panel's respective clinical leads reviewed draft EtD tables before they were presented to the full panel; these leads contributed clinical context, identified additional indirect evidence, and facilitated panel discussions.

During a 2-day, in-person meeting (preceded by online communication and virtual meetings about the body of evidence), the panel developed recommendations (also referred to as key action statements [KASs]) based on discussion of the evidence profiles and EtD assessment criteria. For each recommendation, the panel took an individual perspective and voted on judgments for the following criteria: priority of the problem; magnitude of desirable and undesirable effects; values; the balance of benefits and harms; resource requirements; cost-effectiveness; and the impact on health equity, acceptability, and feasibility. Panel members nominated options for voting; final judgments were decided based on a majority vote of 80% of the panel members. A quorum of panel members (12 or more of the 15 voting members) was required for votes on all decisions.

The panel agreed on the recommendations (including direction and strength), remarks, good practice statements (GPSs), and knowledge gaps through discussion and voting. The final guidelines, including recommendations, were reviewed and approved by all members of the panel.

Interpretation of Strong and Conditional Recommendations/Key Action Statements

The panel members engaged in diverse discussions and healthy debate regarding the interpretation of evidence, which necessitated compromise in formulating the recommendations. The recommendations (ie, KASs) are labeled as "strong" or "conditional" according to the GRADE approach. The words "the Guideline Panel recommends" are used for *strong* recommendations, and the words "the Guideline Panel suggests" are used for *conditional* recommendations. Table 3 provides the interpretation of strong and conditional recommendations for patients, clinicians, policy makers, and researchers.

Discordant Recommendations

In rare instances, low- or very low-certainty evidence may lead to strong recommendations. In those situations, the panel followed guidance by the GRADE Working Group, which is outlined in 5 paradigmatic situations described in Table 4.[11] Although discordant recommendations are rare, certain clinical topics may yield multiple discordant recommendations because of the research landscape around specific populations or conditions. For example, evidence of harms may be more readily available than evidence of benefits.

Differences Between Recommendations and Good Practice Statements

Unlike recommendations (ie, KASs), GPSs are used in instances in which a formal GRADE assessment would be unnecessary. GPSs are often informed by indirect evidence, usually when the net benefit of an action is obvious, widely agreed upon, and critical for clinical care.

The GRADE Working Group proposed that GPSs be developed when the following criteria are met: 1) the statement is clear and actionable; 2) the statement is necessary for clinical practice (ie, "without the guidance, clinicians might fail to take the appropriate action"); 3) there is a large and unequivocal net benefit from the patient's perspective when implementing the GPS; 4) conducting an SR would be an inefficient use of the panel's resources and time; and 5) there is a well-documented, clear, and explicit rationale connecting the indirect evidence.[28] Therefore, unlike recommendations, GPSs are not assigned a certainty of

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TABLE 3. Interpretation of Strong and Conditional Recommendations[11]

Implications for:	Strong Recommendation	Conditional Recommendation
Patients	Most individuals in this situation would want the recommended course of action, and only a small proportion would not.	The majority of individuals in this situation would want the suggested course of action, but many would not. Decision aids may be useful in helping patients to make decisions consistent with their individual risks, values, and preferences.
Clinicians	Most individuals should follow the recommended course of action. Formal decision aids are not likely to be needed to help individual patients and clinicians make decisions consistent with their values and preferences.	Different choices will be appropriate for individual patients; clinicians must help each patient arrive at a management decision consistent with his or her values and preferences. Decision aids may be useful in helping individuals to make decisions consistent with their individual risks, values, and preferences.
Policy Makers	The recommendation can be adopted as policy in most situations. Adherence to this recommendation according to the guideline could be used as a quality criterion or performance indicator.	Policy making will require substantial debate and involvement of various interest holders. Performance measures should assess whether decision making is appropriate.
Researchers	The recommendation is supported by credible research or other convincing judgments that make additional research unlikely to alter the recommendation. On occasion, a strong recommendation is based on low or very low certainty of evidence. In such instances, further research may provide important information that alters the recommendations.	The recommendation is likely to be strengthened (for future updates or adaptation) by additional research. An evaluation of the conditions and criteria (and the related judgments, research evidence, and additional considerations) that determined the conditional (rather than strong) recommendation will help identify possible research gaps.

evidence nor a strength of recommendation and are presented as ungraded recommendations.

Document Review

Before beginning the peer review process, the CPG underwent a comprehensive evaluation using a plagiarism detection software, in accordance with the AAP's protocol for new policies.

Internal and External Peer Review

The CPG went through a comprehensive, rigorous peer review process. External organizations and internal councils, sections, and committees were invited to review the embargoed manuscript and provide comment. They were afforded 30 days for review, per AAP process. Reviewers were invited to inform the panel of any general or substantive comments for consideration.

A total of 37 internal and external peer review entities were invited to provide comments on the draft CPG, corresponding TRs, and Implementation Toolkit.

The following AAP committees were invited to participate in as peer reviewers: the Committees on Child Health Financing; Hospital Care; Infectious Diseases; Medical Liability and Risk Management; Native American Child Health; Pediatric Education; Pediatric Emergency Medicine; Practice and Ambulatory Medicine; and Coding and Nomenclature.

The following AAP sections were invited to participate as peer reviewers: the Sections on Administration and Practice Management; Emergency Medicine; Epidemiology, Public Health and Evidence; Infectious Diseases; Minority Health, Equity, and Inclusion; Nephrology; Radiology; Surgery; Urgent Care Medicine; and Urology.

The following AAP councils were invited to participate as peer reviewers: the Councils on Children With Disabilities; Clinical Information Technology; Community Pediatrics; and Quality Improvement and Patient Safety.

The following additional internal AAP entities were invited to participate as peer reviewers: FamilY Partnerships Network; Partnership for Policy Implementation; Payer Advocacy and Advisory Committee; Pediatric Acute and Critical Care Network; Pediatric Medical Subspecialties; Pediatric Primary Care Quality Network; Pediatric Surgical Specialties; and the AAP Chief Health Equity Officer.

Finally, the following external organizations were also invited to participate as peer reviewers: the American Academy of Family Physicians; American Association of Pediatric Urologists; American College of Emergency Physicians; American Society of Pediatric Nephrology; Societies for Pediatric Urology; and American Urological Association.

The panel received more than 340 comments from 25 internal and external peer review groups that responded to the request to review. These remarks were thoughtfully

TABLE 4. GRADE's Paradigmatic Situations for Discordant Recommendations

Life-threatening situation with low or very low certainty of benefit
Low or very low certainty of benefit with high or moderate certainty of harm
Low or very low certainty of benefit with high or moderate certainty of reduced harm or reduced cost
High certainty of equivalence between options with low or very low certainty of harm or cost
Potential catastrophic harm

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considered by the panel, which addressed them prior to finalizing the CPG.

Organizational Approval

The AAP's extensive organizational approval process began following peer review. Conflict of interest disclosures were obtained again prepublication to confirm that no conflicts existed that might impact authorship. AAP staff senior leadership reviewed all documents and provided comments for clarification and/or improvement. Following revision of the manuscript, the full AAP Board of Directors reviewed the drafts, which were then sent to the AAP Executive Committee for review and approval.

III. KEY ACTION STATEMENTS

The KASs included in this CPG are intended to optimize patient care; they are neither mandatory nor intended as standards of care. The panel acknowledges the inherent need for clinical judgment and shared decision making between clinicians and patients and their caregivers on the basis of many factors, not just the certainty of the evidence, which may cause some level of deviation from the CPG's recommendation. Clinical decisions may be influenced by the specific conditions and circumstances of a health care setting and resource availability, including organizational policies, time restrictions, and treatment availability. This CPG might not address every potential method of care for the described clinical situations. New research evidence may eventually require updates to these KASs. Furthermore, adhering to this CPG does not guarantee successful outcomes.

The values and preferences of patients and caregivers and associated remarks related to each recommendation are essential and aid the accurate interpretation of the KASs. They should always be included when the KASs are cited or translated.

IV. RISK FACTORS

IV. (A) Clinical Variables Associated With Increased Risk of UTI

Consideration and diagnosis of UTI in children begins with a focused history and physical examination. In children, UTI symptoms are often nonspecific or vague and are even more challenging in very young children and those who cannot communicate the commonly considered UTI symptoms of dysuria, urgency, and frequency.[29]

Children with UTI may present with various signs and symptoms that are influenced and vary by age and development. In infants and some medically complex children who are unable to reliably communicate symptoms, initial indications of UTI may include fever in isolation or with other symptoms (eg, fussiness, poor feeding, jaundice, vomiting, or diarrhea.)[30–33] In addition, children with underlying neurologic problems and/or children with chronic medical conditions may present with hypothermia in addition to fever. In severe cases, children may present with sepsis and/or septic shock.

Differential diagnosis is guided by knowledge of the historical risk factors that increase the likelihood of UTI, allowing the provider to appropriately determine which patients need additional testing to confirm diagnosis of UTI.

Through the systematic search, the panel identified 99 studies that described a population of children with UTI. Of those, 55 studies only provided the prevalence of variables of interest in populations with UTI; 9 studies only examined risk factors that were not of interest to the panel; and 35 provided adjusted or unadjusted estimates of UTI risk based on variables of interest to the panel.

For comparisons in which both adjusted and unadjusted estimates were reported, the panel relied solely on the adjusted estimates, drawing on evidence from 31 studies.[29–61] The exception to this rule was fever, for which both estimates were reported, because the unadjusted risk estimates at various temperature thresholds did not have corresponding adjusted counterparts.

Age

Nine studies reported on adjusted risk estimates for age.[29–31,36,37,39,47,52,57] Unpooled adjusted estimates suggest that younger children are at higher risk for UTI than older children.

Sex and Circumcision

Seventeen studies reported on adjusted risk estimates for sex and circumcision.[30,31,35–39,41,43,44,47,48,54,58–60,62] Gender-based risk is dependent on both age and, for young boys, circumcision status. Unpooled adjusted evidence from 14 studies suggests that the risk of UTI is higher in girls compared with boys,[30,31,35,36,43,44,47,48,54,55,58–60,63] which may likely be because of anatomical differences between girls and boys. Additionally, unpooled adjusted evidence from 5 studies suggests that circumcised boys have a reduced risk of UTI compared with uncircumcised young boys.[37–39,59,60] Uncircumcised boys have an increased risk of UTI compared with girls, however.[31,58]

Fever

Five studies reported on unadjusted[30,31,34,43,61] and adjusted[43] risk estimates for fever. Unpooled evidence suggests that the risk of UTI is higher in children who have a fever than those without fever and higher in children with fever without a source than in those with fever from an identified source.[30,31,34,43,61] Additionally, evidence suggests that children who have 1 febrile UTI are at an increased risk of recurrent febrile UTI, compared with children who have nonfebrile UTI.[43]

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Bowel and Bladder Dysfunction and Constipation

Six studies reported on adjusted risk estimates for bowel and bladder dysfunction (BBD) and constipation.[36,41,43,45,53,56] The risk of UTI is higher in children with a history of lower urinary tract dysfunction (LUTD) and BBD, including constipation.[41,56] Assessment of urination and stooling patterns is critical in children of all ages being assessed for UTI.

Prior UTI

Three studies reported on adjusted risk estimates for prior UTI.[39,42,45] Multiple studies have demonstrated an increased risk of UTI among children with a history of previous UTI compared with children without a history of previous UTI (unpooled estimate).

Other Clinical Variables

Additional studies reported on risk estimates of UTI for other clinical variables. Evidence suggests that the following increase the risk of UTI in children: discontinued continuous antibiotic prophylaxis after less than 1 year,[47] urine color/scent,[40] daytime urinary incontinence,[54] abnormalities on imaging,[36,41,42,45,47,49–51,53,54,58,59,62] and preterm birth.[35]

Current antibiotic prophylaxis[41,59] and feeding approaches, such as the addition of breastfeeding,[30,31,35,46] decrease the risk of UTI. The panel did not identify evidence on risk estimates of UTI for the following clinical variables: maternal/family history of UTI, age at toilet training, hypothermia, and hygiene history.

A few additional considerations are worth noting. Constipation, often distinct from BBD, is a common and modifiable risk factor. Neurologic conditions affecting bladder emptying (eg, spina bifida), catheterization or urologic instrumentation, immunosuppression or chronic illness (eg, chronic kidney disease, diabetes), and a family history of VUR may also increase risk.

The use of evidence-based online calculators, such as UTICalc, may be a convenient clinical method of assessing multiple variables to estimate risk for UTI in the clinical setting.[64]

Additional details regarding estimating the likelihood of UTI in a specific patient are available in Supplemental File Table 1.

V. EVALUATION OF SUSPECTED UTI

V.(A) Prompt Medical Evaluation vs Observation for Symptom Progression

Key Action Statement 1: In medically noncomplex children ages 2 months to 24 months with fever without an identified source and in children ages 2 to 5 years with symptoms suggestive of UTI (eg, dysuria, new-onset urinary urgency or frequency), the AAP Guideline Panel suggests medical evaluation for UTI within 72 hours of symptom onset rather than a longer period of observation (conditional recommendation, low certainty of evidence).

Remark 1 for Key Action Statement 1: Although evaluation within 72 hours is generally appropriate, pediatricians and other pediatric clinicians should expedite assessment in children at higher risk for pyelonephritis or kidney injury—for example, those with known structural genitourinary abnormalities (such as hydronephrosis or vesicoureteral reflux), a history of prior febrile UTI, or symptoms consistent with pyelonephritis (such as flank pain).

Remark 2 for Key Action Statement 1: Although this Key Action Statement focuses on medically noncomplex children, the same principle of timely evaluation applies to medically complex children who may be at increased risk for renal sequelae and may warrant more urgent assessment.

Summary of the Evidence

With respect to the effect of prompt medical evaluation vs observation for symptom progression, the panel identified 11 studies: 4 randomized controlled trials (RCTs)[65–68] and 7 observational studies.[69–75] For this analysis, because the "intervention" could not be randomized, the panel treated all studies as if they were nonrandomized studies; none of the participants were randomized to different durations of fever before treatment. The study populations included children with a diagnosis of UTI, febrile UTI, and pyelonephritis.

Multiple durations of prompt and delayed evaluation after experiencing fever before children received treatment were used across the included studies. Two studies classified prompt and delayed evaluation as ≤24 hours and >24 hours, respectively.[65,72] Three studies classified prompt evaluation as <72 hours or ≤3 days and delayed evaluation as >72 hours, ≥3 days, or ≥4 days.[67,71,74] Two studies assessed multiple periods of prompt evaluation compared with 1 delayed evaluation period.[66,69]

Four other studies reported prompt evaluation vs delayed evaluation according to the average or median number of days of fever before treatment or therapeutic delay.[68,70,73,78] All 11 studies reported on renal scarring. For additional information, please refer to the AAP "Clinical Practice Guideline: Evaluation and Management of Well-Appearing Febrile Infants 8 to 60 Days Old."[19]

Benefits

Pooled estimates from 6 studies suggests that relatively earlier evaluation (<72 hours of fever and/or symptoms) may result in less renal scarring compared with relatively later evaluation (>72 hours of fever/symptoms without treatment) (relative risk [RR], 0.68; 95% CI, 0.57 to 0.82).[65–67,69,72,74] Evidence from other nonrandomized studies could not be pooled because of primary study

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authors reporting the odds ratio (OR) for renal scarring[70,71] or not presenting a risk estimate for renal scarring stratified by duration of fever,[70,71,73] but these studies showed consistent results.

Harms

No included studies reported on the harms of relatively earlier vs relatively later evaluation. However, the panel discussed that, given a 5% to 10% prevalence of UTI in children with fever without a source, prompt medical evaluation could cause an overall increase in number of hospital evaluations and unnecessary procedures (eg, urinary catheterization in young children and lab testing) and increase the rates of false-positive results and unnecessary treatment (eg, unnecessary exposure to antibiotics).

Overall, there is low certainty of evidence due to critical concerns about risk of bias from lack of control for potential confounding variables. There are also concerns with possible selection bias, possible misclassification of the exposure (time to treatment), and loss to follow-up.

Additional details regarding the results informing this recommendation are available in Supplemental File Table 2 and the accompanying TR.[5]

Other EtD Criteria and Considerations

In children with febrile UTIs, delay in evaluation and subsequent delay in treatment of UTI may increase the risk of acute renal lesions and renal scarring. (Scarring may vary depending on age, number of febrile UTIs, presence of vesicoureteral reflux, infection severity, and delay in antibiotic initiation.) Delay in evaluation and treatment can have long-term implications of increasing the risk of chronic kidney disease, hypertension, and eventual renal failure/end stage renal disease.[76–78] Evidence of this risk over the years has been contradictory, however.[79,80]

Although this CPG discusses fever as a presentation, this conversation would not be complete without providing the definition of "fever." Fever (temperature >100.4 °F, taken rectally) is a physiologic immunologic response, an element of the human inflammatory response. Fever and human temperature can vary by time of day; differences are related to how and where temperature is taken.[81]

The panel agreed that parents and other caregivers would prefer to avoid disease progression and renal scarring in their children and, thus, place a higher value on decreasing the risk of scarring. Additionally, the panel acknowledges that subspecialists typically see more complex children and/or children with adverse outcomes of missed or delayed treatment of UTI, such as renal scarring and/or avoidable hospitalization from clinical deterioration. Generalists, however, may place higher value on avoiding cost and invasive interventions in otherwise healthy children. Furthermore, it is also possible that a subset of children may present with more severe disease progression while waiting to be evaluated, thus emphasizing that the acceptability of prompt medical evaluation may vary across interest holders.

Evaluation can highlight existing disparities. These disparities include families who lack access to a primary care provider or pediatric care, those who reside in rural areas with restricted access to medical facilities, and families who have low socioeconomic status and might not have dependable transportation for prompt medical assessments.

The panel recognized that these recommendations may not universally apply to all children with UTI. Children with UTI without a fever and no history of prior UTI are at lower risk of scarring and/or for progression to severe disease than younger children with a febrile UTI or children with known anatomic problems. When considering prompt evaluation of children, it remains unknown whether reduction of a single scar leads to any long-term implications or whether risks increase with accumulation of scarring with more instances of UTI.

The optimal timing of intervention to minimize renal scarring for all children remains uncertain. Given the inclusion of a varied population of patients (broad age range and comorbidities) in the studies noted above, safe duration of observation before evaluation of patients who have anatomical abnormalities (eg, VUR) or prior history of UTI needs further study. The panel recommended that optimal timing of medical evaluation is within 72 hours, keeping in mind the large population of both healthy as well as at-risk children to which this recommendation is applicable. The panel agreed that the evaluation can safely take place in the child's medical home (primary care office) or a less-acute setting like a pediatric urgent care setting rather than an ED. The panel's use of "optimal timing of medical review" applies to children without significant renal or urologic conditions.

Additional details regarding the EtD framework for this recommendation are available in Appendix Table 1.

V.(B) Best Testing Modality for Diagnosis of UTI

Summary of the Evidence

The diagnosis of UTIs in children remains complex, despite decades of research aimed at establishing clear diagnostic criteria. Although UTIs are prevalent among children, determining their true prevalence is difficult because of varying diagnostic standards and the lack of a gold standard for diagnostic criteria. The lack of a gold standard is driven both by false-positive results due to collection techniques and by the fact that some infants and children have ASB that will spontaneously clear without therapy.[82–84] Although younger children are more likely to need catheterization, the likelihood of success in obtaining a urine sample is more important than the patient's age in determining the modality for obtaining the urine. For the most part, recommendations related to BBD apply to the toilet-trained

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population. For general approaches to obtaining samples, see Table 1.

UTI definitions are important to minimize both overtreatment and undertreatment, thus optimizing antibiotic use. Controversies include whether pyuria (presence of white blood cells [WBCs] in urine) should be a diagnostic criterion and how to define a "positive" urine culture.[6] Current challenges in defining UTI are compounded by ongoing updates in evidence, requiring pediatricians and other pediatric clinicians to adapt to new data.

Accurately diagnosing UTI involves distinguishing it from ASB and contamination. A key component is a positive urine culture; however, interpreting a positive culture can be challenging. A positive culture may indicate a true UTI, ASB, or contamination. In this context, infants, who cannot express symptoms, are particularly susceptible to misdiagnosis, because fever from other causes can be mistaken for UTI, leading to potential overtreatment and missed alternative diagnoses.

UA is typically used for initial screening for UTI. Critical UA components include leukocyte esterase (LE) and urinary WBCs, which indicate inflammation. Although pyuria may suggest UTI, it can also be present in other conditions. A UA with evidence of pyuria is associated with a higher probability of UTI, but false-negative and false-positive results can occur (see the TR on UTI diagnosis[6]).

For accurate diagnosis, the updated guidelines suggest specific thresholds for pyuria: 5 WBCs per high-powered field (hpf) or trace LE for infants younger than 2 months, and 10 WBCs/hpf or +2 LE for infants and children 2 months or older (see Table 1). These WBC counts reflect an unspun vs centrifuged urine sample.

These thresholds aim to balance sensitivity and specificity in UTI diagnosis as well as degree of tolerance of false-negative and false-positive results based on likely severity of illness.[6] If the laboratory test results do not distinguish between 5 and 10 WBC/hpf, clinical judgment should drive decision making. In addition, because automatic cell counter and urine dipsticks have variable accuracy, clinical suspicion should be considered when evaluating children with suspected UTI.

Nitrites have a low sensitivity but a high specificity for bacteria in the urine.[85] They do not demonstrate inflammation in the urinary tract, however; therefore, they are not useful in distinguishing ASB from UTI.[6]

Urine culture remains the reference for confirming UTI. The 2011 CPG from the AAP recommended a 50 000 colony-forming unit (CFU)/mL cutoff for catheterized samples.[3] Recent evidence, however, suggests that lowering this cutoff to 10 000 CFU/mL for a single organism will improve sensitivity without a clinically significant decrease in specificity.[86] For clean catch samples, the cutoff remains at 100 000 CFU/mL due to higher contamination rates. Cultures with multiple organisms or non-uropathogens typically indicate contamination. Typical uropathogens include *Escherichia coli, Proteus* species, *Klebsiella* species, and other gram-negative organisms; *Enterococcus* species; and, rarely, other gram-positive organisms.[87,88]

Imaging, such as dimercaptosuccinic acid (DMSA) scans, can help assess renal involvement but is not routinely used because of its limitations and availability. Although these scans can identify pyelonephritis, they are not essential for acute diagnosis and are primarily used for research and to detect renal scarring.[75,89,90]

Information about test modalities not discussed in this CPG is provided in the accompanying TR.[6]

Controversies persist, particularly regarding how robust the induction of pyuria is in UTIs not caused by *E coli* and the impact of novel diagnostic techniques. Ongoing research seeks to refine UTI definitions and improve diagnostic accuracy.[83,91,92]

A summary of results of test accuracy from different indices of the UA is available in Supplemental File Tables 3, 4, and 5.

V.(C) Use of Bag Urinalysis and Urethral Catheterization vs Urine Catheterization Alone

The panel initially prioritized the clinical question about whether, in children with suspected UTI, bag UA and urethral catheterization (sequential collection) vs urine catheterization alone should be used, because sequential urine collection is common. Differences in sampling techniques may impact sensitivity and specificity of testing and may have a significant impact on the duration of patient care in offices, EDs, and other health care facilities. Additionally, previous research has shown that sequential collection may reduce catheterization rates in infants who cannot supply a clean-catch urine.[93] For catheter/suprapubic aspiration (SPA) specimens, ≥10 000 CFUs/mL of a single uropathogen confirms UTI when UA criteria are met; for clean-catch, ≥100 000 CFUs/mL remains the threshold due to higher contamination risk.

After consideration of the literature, however, the panel voted not to formulate a KAS regarding this practice, although sequential collection may be useful in many settings. The panel discussed that sequential collection requires time for urine to accumulate again in the bladder after voiding, which may negatively impact patient care in facilities with necessarily shorter visits or the need for rapid turnover of care. Another important consideration was that there may be differences in cost associated with both diagnostic strategies of obtaining urine from infants.[94]

Further, the panel agreed that this clinical question was effectively addressed for young infants in the AAP "Clinical Practice Guideline: Evaluation and Management of Well-Appearing Febrile Infants 8 to 60 Days Old."[19] In KAS 4 of that CPG, the panel recommended that, "Clinicians should obtain urine specimen by catheterization or SPA of bladder

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for urinalysis and, if urinalysis result is positive, for culture or should obtain urine specimen by bag, spontaneous void, or stimulated void for urinalysis and, if urinalysis is positive, obtain a catheterization or SPA specimen for culture (Evidence Quality: A; Strong Recommendation)."[19]

VI. MANAGEMENT

VI.(A) Length of Antibiotic Administration

Key Action Statement 2: In children with UTI, the AAP Guideline Panel suggests a shorter course of antibiotic therapy (≤7 days) rather than a longer (>7 days) course of antibiotic therapy (conditional recommendation, low certainty of evidence).

Remarks for Key Action Statement 2 (see Box):

- Low-risk children
  - The panel suggests a 3- to 5-day course of antibiotics for children 2 years and older with no known underlying anatomic abnormalities of the urinary tract presenting with nonfebrile UTI with referred urinary symptoms suggestive of cystitis (specifically urinary urgency and incontinence, dysuria, or urinary frequency).
  - The panel suggests a 5- to 7–day course of antibiotics for children 2 months to 24 months of age with UTI.
- The panel suggests a 5- to 7-day course of antibiotics for children 2 years and older with no known underlying anatomic abnormalities of the urinary tract presenting with signs and symptoms concerning for pyelonephritis (eg, fever ≥102.2 °F).
- High-risk children
  - A more prolonged antimicrobial course (7–14 days) may be provided for infants 8 days to 2 months of age, children with underlying anatomic genitourinary abnormalities, children who have associated bacteremia, or children who do not respond (with resolved or resolving signs and symptoms) to their initial antimicrobial course.

Box: Summary of Remarks for KAS 2

Patient	Age	Clinical Findings	Antibiotic Duration
Low risk	2–5 years	Nonfebrile UTI	3–5 days
Low risk	2–24 months	Febrile UTI	5–7 days
Low risk	>2 years	Febrile UTI and clinical pyelonephritis	5–7 days
High risk	8 days – 2 months	Febrile UTI	7–14 days
High risk	>2 months	Febrile UTI and known genitourinary abnormalities or bacteremia or poor clinical response	7–14 days

Summary of the Evidence

The role of antibiotic treatment for UTI is to eliminate the acute infection, prevent complications, and reduce the likelihood of renal damage. The panel agreed that delineating the shortest and safest antibiotic course is necessary to reduce the risk of harm associated with prolonged antibiotics.

The panel evaluated 12 RCTs that compared a short (<7) vs prolonged (≥7 days) course of antibiotics in children with UTI 2 months to 18 years of age with a proven urine culture or diagnosis of UTI.[95–106] There was variability in the antibiotic used and the duration of treatment. Of the included studies, 1 study each used amoxicillin,[98] amoxicillin-clavulanic acid,[102] cefuroxime,[100] nalidixic acid,[105] and trimethoprim (TMP).[63] Two studies prescribed nitrofurantoin,[97,99] and 3 studies used TMP.[99,101,105] Two studies used multiple antibiotics across the study population.[95,106]

Additionally, primary study authors compared slightly different durations of antibiotic treatment in which a shorter course ranged from 2 to 5 days and a longer course ranged from 7 to 14 days. Ten studies reported on the rate of recurrent UTI (rUTI) within 30 days of treatment, 3 reported on adverse events (AEs), and 4 reported on resistant rUTI.

The panel acknowledges that some patients may require longer durations; these patients include those at higher risk of complications (eg, those with genitourinary abnormalities or associated bacteremia), infants younger than 2 months of age for whom studies are lacking, and those who do not respond well to antibiotic therapy by the end of the antibiotic course.

The distinction between pyelonephritis and UTI is difficult in children; however, acute pyelonephritis in children older than 2 years may present with higher fever and the finding of costovertebral angle tenderness.

Benefits

Evidence from 10 RCTs suggests that the rate of rUTI was similar between patients receiving a shorter course of antibiotics and those receiving a longer course of antibiotics (RR 0.96; 95% CI, 0.67 to 1.39; low certainty of evidence).[95–102,105,106] Cumulative antibiotic exposure is associated with an increased risk of *Clostridioides difficile* infections[107]; thus, a shortened course is likely to result in decreased risk of *C difficile* infection. Finally, although it is not yet well-studied, multiple associations have been described with an altered microbiome and chronic diseases (eg, asthma, obesity, and autoimmune diseases).

For patients who are treated for a UTI before the culture results are obtained, and when the culture is negative, antibiotics should be discontinued, unless there was pretreatment prior to the culture being taken. For patients who receive empirical antibiotics prior to urine culture results,

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antibiotics should be discontinued if the culture is negative, unless the specimen was obtained after antibiotic exposure.

Harms

Moderate certainty evidence from 3 RCTs also suggests that a shorter course of antibiotic likely results in little to no difference in the risk of AEs compared with a longer course (RR, 0.93; 95% CI, 0.79 to 1.09).[95,100,106] Four RCTs evaluated the risk of resistant rUTI 30 to 80 days after antibiotic completion. Although not statistically significant, a shorter course of antibiotics may result in fewer resistant rUTIs compared with a longer course (RR, 0.56; 95% CI, 0.31 to 1.02; low certainty of evidence).[95,98,103,104]

The panel also discussed evidence suggesting that leftover antibiotics from longer-duration prescriptions may result in improper circulation of antibiotics and future use without an antibiotic prescription.[108] Additional concerns about antimicrobial resistance include the risk that patients and caregivers may stop antibiotic therapy earlier than prescribed if their symptoms resolve.[109–112] Patients who do not improve with a shorter course of antibiotics may, however, require additional visits, testing, and prescriptions, resulting in higher medical expenses.

Overall, the certainty of the evidence is low due to concerns with risk of bias and imprecision.

Additional details regarding the results informing this recommendation are available in Supplemental File Table 6 and the accompanying TR.[5]

Other EtD Criteria and Considerations

The panel judged that there was probably no important uncertainty or variability in how patients and their caregivers value the main outcomes, considering that a shorter course of antibiotic may be preferred and could increase compliance. In addition to accurately diagnosing UTI and considering deescalating when the diagnosis is ruled out,[113,114] antibiotic stewardship opportunities for decreasing duration of antibiotics have been shown to be well-accepted and relatively easy to implement in ambulatory and inpatient settings.[113,115,116]

The panel also noted that longer courses of antibiotics may result in higher medical expenses that might pose a barrier for families who lack insurance. Therefore, a shorter course of antibiotics could result in moderate savings compared with a longer course. On the basis of these factors, the panel agreed that the impact on health equity varies when implementing a recommendation of a shorter course of antibiotics. Specifically, a shorter course may increase equity when considering decreased costs compared with a longer course. Equity may, however, be decreased when considering access to follow-up care and discrepancies in health literacy.

The evidence of benefit from shorter antibiotic therapy is uncertain for all children with UTI, including low-risk children. The panel suggests a shorter course (<7 days) rather than a longer course (≥7 days) of antibiotic therapy for certain subgroups and clinical scenarios: children 2 years and older with no known underlying anatomic abnormalities of the urinary tract presenting with nonfebrile UTI with referred urinary symptoms suggestive of cystitis (specifically urinary urgency and incontinence, dysuria, or urinary frequency); children 2 to 24 months of age with UTI; and children 2 years and older with no known underlying anatomic abnormalities of the urinary tract presenting with a febrile UTI or a UTI with signs and symptoms concerning for pyelonephritis (ie, fever ≥102.2 °F).

Future research is necessary to more accurately estimate the optimal duration of antibiotics for children younger than 2 months.

Additional details regarding the EtD framework for this recommendation are available in Appendix Table 2.

VI.(B) Route of Antibiotic Administration

Key Action Statement 3A: In children 8 to 28 days of age in whom a UTI has been diagnosed, the AAP Guideline Panel suggests parenteral antibiotics with early transition to oral following clinical improvement rather than parenteral antibiotics alone (conditional recommendation, very low certainty of evidence).

Key Action Statement 3B: In children older than 28 days and younger than 5 years with UTI, the AAP Guideline Panel recommends oral antibiotics rather than parenteral or sequential antibiotics requiring hospitalization (strong recommendation, very low certainty of evidence).

Remarks for Key Action Statement 3B:

- The AAP Guideline Panel defines "sequential antibiotics" as initial parenteral antibiotics that are subsequently transitioned to oral.
- In children older than 28 days who are able to tolerate oral antibiotics and who do not otherwise require hospitalization, outpatient therapy is encouraged.
- Examination of the evidence suggests equivalent outcomes between oral and parenteral/sequential antibiotics with regard to outcomes of renal scarring and short-term recurrence of infection (eg, treatment failure). The use of parenteral antibiotics is, however, associated with several undesirable outcomes, including hospitalization, pain from intravenous (IV) catheter placement, potential for extravasation injury, increased cost, and potential complications associated with peripherally inserted central catheter (PICC) lines, which include infection and clotting. This constellation of harms associated with parenteral antibiotics warrants a strong recommendation against their routine use.

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- Should pediatricians or other pediatric clinicians have concerns about the ability of families to promptly obtain oral antibiotics from an outpatient pharmacy, a single dose of parenteral antibiotics may be given prior to transition to oral antibiotics.

Summary of the Evidence

The ideal route to treat UTI in young children has been a focus of multiple research studies, including 4 RCTs[65,67,117,118] and 6 observational studies.[102,119–123]

These studies evaluated the effect of oral vs parenteral or sequential antibiotics in children ages 0 to 16 years in whom a first febrile UTI or acute pyelonephritis is diagnosed. "Standard sequential antibiotics" was defined as 3 days of parenteral antibiotics in 2 studies[65,118] and as 4 days in 2 studies.[117,122]

One RCT[65] and 5 observational studies examined the outcome of rUTI.[119–123] Four RCTs examined the outcome of renal scarring.[65,67,117,118] Two RCTs examined the outcome of AEs.[65,117] The strong recommendation in KAS 3B reflects the balance of benefits and harms (eg, avoidance of hospitalization, intravenous line complications, and cost) despite very low certainty in comparative efficacy, consistent with GRADE when harms clearly outweigh benefits.

Empirical therapy should prioritize narrow-spectrum agents, when appropriate. In noncritically ill, medically noncomplex patients, cefazolin or cephalexin may be preferred if local susceptibility rates exceed 80% to 85%. When susceptibility to cefazolin is adequate (>80%–85% on local antibiograms), first-line therapy may include cefazolin or cephalexin. Alternative options (particularly in the setting of higher resistance rates or intolerance) include ceftriaxone, cefixime, TMP-sulfamethoxazole (SMX), or ciprofloxacin, although the latter options should be selected with caution and be based on local resistance patterns (preferably from a local/regional children's hospital).

Benefits

One RCT suggests that rUTI may be less likely to occur in children receiving oral antibiotics compared with those receiving sequential antibiotics, but the evidence is very uncertain (RR, 0.67; 95% CI, 0.27 to 1.67).[65] Very low certainty evidence from 5 observational studies that could not be pooled also showed consistent results.[119–123]

Additionally, low certainty evidence suggests that there may be a decreased rate of renal scarring in children receiving oral antibiotics compared with parenteral antibiotics (RR, 0.86; 95% CI, 0.68 to 1.10).

Harms

Two RCTs reported on AEs in children receiving oral vs parenteral antibiotics.[65,117] The evidence suggests that oral antibiotics may have little to no effect on gastrointestinal events, but the evidence is very uncertain (risk difference [RD], 0.01; 95% CI, −0.01 to 0.03). Between 0.07% and 4% of the children receiving oral antibiotics required a change in antibiotics because of vomiting.[65,117,118]

The panel also discussed that incomplete antibiotic courses attributable to poor adherence to prescribed medications, which leads to partial treatment, is another potential risk. This was evaluated in 1 study, in which the oral antibiotic was detectable in 85% of children who were assessed.[65] Additional harms, including any potential differential effects between oral and parenteral antibiotics on the gut microbiome, were not assessed in any of the included studies.

Overall, the certainty of the evidence is very low because of issues of risk of bias and imprecision.

Additional details regarding the results informing this recommendation are available in Supplemental File Table 7 and the accompanying TR.[5]

Other EtD Criteria and Considerations

Parenteral antibiotics have classically been considered to be a more reliable option for the treatment of infections compared with oral antibiotics because of their faster time in achieving therapeutic levels and the advantage of ensuring adherence. The panel, however, noted the harms of parental antibiotics, including the requirement for intravenous access and associated potential complications, as well as the need for hospitalization. The panel judged that avoiding these harms was desirable.

An additional concern about the use of oral antibiotics in younger infants is related to absorption of oral antibiotics. A 2019 SR of use of oral antibiotics in neonates from 0 to 28 days of age found that the antibiotics reviewed were able to reach adequate minimal inhibitory concentrations when taken orally by infants.[124] The researchers noted, however, that maximum serum concentrations were achieved later in oral vs parenteral administration. This finding is consistent with the panel's recommendation to initiate therapy with parenteral antibiotics with early transition to oral following clinical improvement in febrile infants between 8 and 28 days to ensure that infants can rapidly reach target serum concentrations. Moreover, this recommendation for febrile children 8 to 28 days of age with suspected/confirmed UTI also aligns with those of the 2021 AAP CPG recommendation on the evaluation and management of well-appearing febrile infants.[19]

The panel, however, highlighted several potential areas where health equity could be impacted when deciding to treat with oral as opposed to parenteral antibiotics. These effects on equity include a differential burden of hospitalization associated with parenteral antibiotic treatment on families with limited financial resources, restricted access to transportation or child care, limited paid leave

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from work, or reduced access to outpatient follow-up as well as concerns about adherence with oral medications. Additionally, 1 study of 2881 children, which assessed the proportion of filled antibiotic prescriptions following ED visits, found that one-third of all prescriptions were unfilled. Further, the authors reported that children from households with limited English proficiency and those lacking insurance had lower rates of filling prescriptions. Additionally, they found that prescription-filling rates varied across different demographic groups, likely reflecting socioeconomic barriers rather than racial identity.[125]

Once prescriptions are filled, adherence with medication instructions is an additional concern. In a prospective trial of 100 children 2 months to 5 years of age, only 11 children received all recommended medication doses.[126] The authors reported an overall adherence of 62% with all recommended medication doses, with only 21% of patients demonstrating complete adherence with the timing of all medication doses. Of note, the authors also reported that providers were unable to predict which patients would not be adherent.

Further research into optimal methods to increase both filling oral medication prescriptions and adherence with prescribed directions is needed, particularly among populations experiencing barriers to medication access, including limited English proficiency, lack of insurance coverage, transportation barriers, and reduced pharmacy access. For patients who are treated outside of their medical home, it is critical that their pediatrician or pediatric clinician be alerted to a diagnosis of UTI made in an acute care or ED setting; this enables the medical home to follow up on laboratory test results and assess the need for follow-up care.

The panel assessed preferential use of oral antibiotics over either parenteral or sequential antibiotics in most children older than 28 days. The panel, however, noted 4 subgroups in which parenteral or sequential antibiotics may be appropriate:

1. Children younger than 28 days: The panel noted limited representation of infants younger than 2 months in the literature and, therefore, generated a distinct Key Action Statement for children 8 days to 28 days of age, in recognition of the rationale for a more conservative approach to this population. The panel recommends a short course of parenteral antibiotics in children 8 days to 28 days of age followed by oral antibiotics.
2. Children with associated bacteremia.
3. Children who are critically ill.
4. Children who are unable to tolerate oral medications.

Additional details regarding the EtD framework for this recommendation are available in Appendix Table 3.

VII. IMAGING

VII.(A) Use of Renal Bladder Ultrasonography vs No Testing to Diagnose Structural Abnormalities, VUR-Associated Findings

Key Action Statement 4: In children younger than 5 years in whom a first febrile UTI is diagnosed, the AAP Guideline Panel recommends performing renal and bladder ultrasonography (RBUS), rather than not performing RBUS, to detect structural abnormalities or findings associated with VUR, not to detect VUR itself (strong recommendation, low certainty of evidence of the clinical impact of the detected abnormalities on RBUS, low certainty of evidence for ultrasonographic detection of VUR).

Remark for Key Action Statement 4: Although RBUS is the standard of care for detection of congenital or structural anomalies, there is low certainty about the frequency of RBUS detecting a clinically important anomaly. The panel believes, however, that identifying infrequent RBUS abnormalities benefits the proportion of patients who are ultimately identified.

Summary of the Evidence

Thirty studies reported on the diagnostic test accuracy of RBUS in detecting VUR[1] (all grades) after first febrile UTI.[55,127–155]

Three studies reported diagnostic test accuracy of RBUS in detecting VUR after recurrent UTI in children.[148,156,157]

The majority of the panel discussion, however, concerned the sensitivity of RBUS as a screening test for structural abnormalities. Only VUR-associated imaging abnormalities, not VUR itself, are detected by RBUS. These findings are not present commonly with VUR irrespective of grade; thus, RBUS that does not identify other structural anomalies does not rule out VUR. The panel judged RBUS as inaccurate to identify VUR after the first febrile UTI (pooled sensitivity: 0.50; 95% CI, 0.42 to 0.58); pooled specificity was 0.71 (95% CI, 0.62 to 0.78) and, after a recurrent UTI (pooled sensitivity: 0.26; 95% CI, 0.23 to 0.28), pooled specificity was 0.79 (95% CI, 0.76 to 0.81).

The panel concluded that RBUS has limited value in detecting VUR because of its limited sensitivity.

Benefits

No research evidence was identified on the desirable effects of RBUS after first UTI. The panel, however, agreed that, although normal RBUS does not rule out VUR, it may still

[1] VUR refers to retrograde flow of urine during voiding from the bladder into the ureters and, in severe cases, the kidneys. VUR is diagnosed most commonly via voiding cystourethrography (VCUG), which entails placement of a catheter through the urethra, instillation of contrast to fill the bladder, and subsequent fluoroscopic evaluation as the bladder contracts. VCUG can also detect other abnormalities of the bladder and urethra.

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have some value with respect to VUR, given that normal RBUS probably reduces the pretest probability of finding high-grade VUR on voiding cystourethrography (VCUG), if one were obtained. Furthermore, RBUS may be best for detecting other structural abnormalities that may require additional investigation/consideration, especially following a febrile UTI. RBUS that does not identify other structural abnormalities does not rule out VUR, but it does effectively rule out the majority of clinically significant structural abnormalities that predispose a patient to subsequent severe or recurrent UTI. Thus, RBUS can provide information that may guide the management of treatment.

A recent SR estimated that approximately 22% (95% CI, 16.8% to 28%) of children of any age will have an abnormality on kidney ultrasonography following a febrile UTI.[158] Additionally, the authors found the pooled prevalence of a clinically important kidney ultrasonography abnormality, defined broadly as "an ultrasonography finding that changed clinical management,"[158] to be 3.1% (95% CI, 0.3% to 8.1%) in children of any age and 4.5% (95% CI, 0.5% to 12%) in children younger than 24 months.

Harms

These results highlight that normal RBUS does not equate to a normally functioning urinary system; additional UTI episodes and their resulting complications are still possible. The accurate identification of structural abnormalities and VUR is important for management implications. Juliano and colleagues investigated the downstream consequences of misclassifying patients after undergoing RBUS. Of 95 patients with normal RBUS, 84 underwent VCUG. Of these 84, 23 of the patients who received VCUG had dilating VUR, 14 had recurrent pyelonephritis, and 7 received surgical intervention.[159]

These results highlight that RBUS may fail to detect structural abnormalities, possibly leading to mismanagement or delayed treatment. On the other hand, the implications of misclassifying patients as having VUR after undergoing RBUS could include an increased rate of unnecessary testing (eg, VCUG), treatment, and stress and fear on the part of the patient and caregiver.

Additional details regarding the results informing this recommendation are available in Supplemental File Table 8 and the accompanying TR.[4]

Other EtD Criteria and Considerations

Children with structural abnormalities that cause urinary outflow obstruction are potentially at risk for severe UTI and recurrent UTI. The panel concluded that RBUS is the preferred test to detect structural urinary tract abnormalities that may require intervention or management by a pediatric urologist. The panel noted that the majority of children may not have a structural abnormality, but the risks and benefits of RBUS tip the balance in favor of performing RBUS to ensure a clinically significant abnormality is not missed following the first febrile UTI.[148]

As mentioned earlier, RBUS does not diagnose VUR. Although urinary tract dilation identified on RBUS can be associated with VUR, the two are poorly correlated. RBUS is used to identify clinically relevant structural abnormalities that may co-occur with, or predispose to, recurrent UTI or renal injury; VUR is detected with VCUG or contrast-enhanced voiding urosonography (CeVUS) when indicated by the CPG.

Hydronephrosis on RBUS often does not require immediate intervention; thus, the recommendation to perform RBUS following a febrile UTI must be tempered with this nuance. In the SR conducted by Yang and colleagues, 78% of the children had an abnormality on RBUS that was not clinically important.[149] For these children, RBUS may result in additional unnecessary testing, parental anxiety, travel and time for initial RBUS and follow-up tests, and subspecialty evaluation. Children who have self-resolving conditions or those who will not have subsequent febrile UTIs will potentially be exposed to unnecessary testing and interventions such as VCUG and prophylactic antibiotics. Additionally, children with limited access to tertiary care (eg, radiology and subspecialists) may have inequity magnified and limited subsequent care options.

Conversely, however, normal RBUS may be very reassuring to caregivers of a child who recently had a serious bacterial infection.

Although no research evidence was identified regarding patient and caregiver values about the main outcomes, the panel remained aligned with the 2011 CPG panel's sentiment that "Because ultrasonography is noninvasive and poses minimal risk, we assume that parents and other caregivers will prefer RBUS over taking even a small risk of missing a serious and correctable condition."[3] Performing RBUS may result in moderate costs compared with not performing RBUS.[160,161]

Another important consideration was the impact of RBUS on health equity. The panel determined the impact would vary depending on access to a medical home, insurance status, etc. For example, by recommending RBUS following a febrile UTI, equity will be increased for children and caregivers who were unable to obtain prenatal imaging.

The majority of EtD discussion revolved around unintended consequences of recommendations of previous guidelines in practice, which may have been misinterpreted as suggesting that RBUS is an effective tool for screening for VUR.[3] The discussion focused on how best to communicate that RBUS should primarily be used to detect clinically significant structural anomalies that would place the child at significant risk of severe UTI and recurrent UTI and/or kidney injury as well as to identify children who are best referred to pediatric urology.

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The panel also contemplated the value of limited sensitivity of RBUS in detecting VUR, as outlined above. This recommendation does not imply that this imaging needs to be obtained during the acute illness; rather, an appropriate medical home/plan should be identified in the acute setting for the patient/family before imaging during initial presentation. An RBUS during the acute phase may be obtained for cases that present with severe or atypical symptoms to rule out a significant abnormality that may affect management.

Additional details regarding the EtD framework for this recommendation are available in Appendix Table 4.

VII.(B) Routine VCUG After a First Febrile UTI

Key Action Statement 5A: The AAP Guideline Panel suggests against routine VCUG after a first febrile UTI in children younger than 5 years with normal RBUS (conditional recommendation, high certainty of evidence of test accuracy, low certainty of evidence of overall effect).

Remark for Key Action Statement 5A: It is an option to perform a VCUG after the first febrile UTI in specific subpopulations (eg, age younger than 1 month, infectious agent other than *E coli*, circumcised males, atypical/complicated course including septic shock/ICU admission, or limited follow-up reliability) with subspecialty consultation for abnormal results.

Key Action Statement 5B: The AAP Guideline Panel suggests offering VCUG in: children with clinically relevant abnormalities detected on RBUS after a first febrile UTI; all children younger than 2 years with a second febrile UTI; and children 2 years or older with a second febrile UTI and no alternative explanatory risk factors (conditional recommendation, high certainty of evidence of test accuracy, low certainty of evidence of overall effect).

Remark for Key Action Statement 5B: In children with VUR and underlying anomalies of the renal tract that increase risk for both UTI and renal scarring, pediatricians and other pediatric clinicians are encouraged to partner with the family and provide educational resources to assist with early future detection, treatment, and prevention of UTI.

Summary of the Evidence

Because VCUG is the reference standard for detecting VUR, the panel assumed 100% accuracy. Recommendations to perform VCUG in patients with UTIs have largely been driven by observed associations between VUR, recurrent UTIs, and renal scarring.[3,162,163] VUR is a relatively common finding, however, and there was controversy within the panel over when and how patients benefit from detection of this condition.

Benefits

No research evidence was identified on the desirable effects of VCUG after first febrile UTI. The panel discussed that, on the whole, VCUG is largely intended to detect VUR but may be useful for detecting other abnormalities as well. Additional benefits include VCUG possibly reducing downstream consequences, such as hospitalization, and alleviating patient and caregiver anxiety about future risk of rUTI.

Harms

The panel considered the undesirable effects of VCUG, which include pain and anxiety that is induced by insertion of the urinary catheter, other aspects of the test (which may lead to provision of anxiolysis or sedation), the possibility of introducing iatrogenic infections, and radiation exposure.[164–166]

Although some of these issues can be mitigated by the use of child life experts, sedation/anxiolysis, CeVUS, and having the procedure performed by experienced pediatric-focused clinicians, such services may not be widely available outside of large pediatric centers. Additional considerations include the possibility of overdiagnosis (eg, detecting abnormalities of uncertain significance) and associated downstream interventions such as the need for repeat VCUG, urology referrals, and continuous antibiotic prophylaxis (CAP).

Overall, the certainty of the evidence of test accuracy of VCUG is high and the overall certainty of the effect is low (because of low certainty of evidence of the test's effects, low certainty of evidence of the management's effects, and low certainty of evidence of the test result management).

Other EtD Criteria and Considerations

In most cases, VCUG is best performed after completion of therapy and in the outpatient setting, following resolution of the acute infection, an approach that avoids performing the test during acute illness. When there is significant concern that the family may not be able to return for follow-up, however, or when there is another urgent need to diagnose anatomic abnormalities, VCUG may be considered during the index hospitalization. EDs are generally not the preferred setting for initiating VCUG, but inpatient testing can be appropriate when continuity of care or timely diagnosis is at risk.

Prior to 2011, the AAP recommended routine RBUS and VCUG for all patients younger than 2 years with a first febrile UTI.[162] The now-retired 2011 AAP CPG on UTI advocated a more restrictive approach and recommended VCUG only for patients with abnormal RBUS and patients with rUTI.[3] These recommendations acknowledged the suboptimal sensitivity of RBUS for detecting VUR but reasoned that VCUG performed after a second UTI would detect clinically relevant cases.

Additional considerations discussed and reviewed by the panel included the possibility that some families might be reassured by a negative VCUG while other families may have heightened anxiety following a VUR diagnosis. Some members of the panel expressed that VCUG could be offered routinely in certain high-risk groups, even if RBUS was

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normal, including infections caused by organisms other than *E coli*, circumcised males, and infants younger than 1 month.

The panel agreed, however, that shared decision making was important when considering VCUG. The panel felt that the impact of this recommendation on health equity was uncertain due to a research gap. Implementing a recommendation for VCUG after first febrile UTI could impact equity in both directions (ie, reducing or increasing), depending on the situation of a patient and their caregiver. For example, delaying VCUG might be problematic for families who face barriers to reliable follow-up, including limited transportation access, unstable insurance coverage, difficulty obtaining time away from work, or limited access to pediatric subspecialty care.

Navigating the balance between promoting health equity and respecting parental decision making can be difficult but it is essential. Caregivers must be offered the opportunity to engage with their child's clinician(s) in equitable and robust conversation, as partners in care, to determine a child's treatment plan. Families benefit from clear and accessible information—whether through pamphlets, videos, or online resources—which help them think through the issues that matter most to them. When creating these materials, it is important to pay close attention to health equity and literacy.[167]

The panel also agreed that VCUG in older children is likely to be more traumatic than it is for younger children. Therefore—given the costs and risks of VCUG, the high number of VCUGs that need to be performed to diagnose 1 case of high-grade VUR, and the lack of convincing evidence that commonly performed interventions for VUR lead to better renal outcomes—the panel judged that VCUG is probably not acceptable to key interest holders, although it is probably feasible to implement. Therefore, the panel suggests against routine VCUG following a first febrile UTI. The panel, however, suggests offering VCUG for patients with abnormalities on RBUS, for children younger than 2 years with a second febrile UTI, and for children 2 years or older with a second febrile UTI and no alternative explanatory risk factors (eg, BBD).

Other risk factors have been associated with VUR in children with UTIs in prior studies. The most consistent of these risk factors is infection with an organism other than *E coli*.[168–170] Many patients with non-*E coli* UTIs will also have abnormal RBUS, which would trigger a VCUG. There are limited data on the prevalence of VUR/high-grade VUR in patients with non-*E coli* UTIs who have had normal RBUS.[168] Because the overall VUR risk in this population is higher, it is an option to obtain a VCUG in all patients with a first febrile UTI caused by an organism other than *E coli*. Additionally, the panel supported performing VCUG for a first febrile UTI in circumcised males (because UTIs are so rare in this population) or infants younger than 1 month (given that such an early presentation may be more indicative of underlying anatomic abnormalities). This approach lacks supportive data from the literature, however. Families should be fully informed about the risks/benefits of VCUG and should participate in the decision-making process.

Additional details regarding the EtD framework for this recommendation are available in Appendix Table 5.

VII.(C) CeVUS vs VCUG to Diagnose VUR

The question of whether to perform CeVUS in lieu of VCUG, when VCUG is indicated, was prioritized by the panel. CeVUS, an emerging imaging technology, is an ultrasonography-based and radiation-free alternative to VCUG for diagnosing VUR. CeVUS is similar to VCUG in that it necessitates a bladder catheter placement with retrograde filling of the bladder over a voiding cycle to try to identify reflux. It differs from VCUG in that it uses ultrasonography instead of fluoroscopy to detect VUR and associated structural abnormalities.[171–173] Some practitioners believe that, when it is available and there is operator expertise, CeVUS may be considered as an alternative to VCUG to assess VUR while avoiding ionizing radiation; local pathways should specify test choice.

CeVUS has been available in the United States since 2016 and is considered to be a valid alternative method to VCUG according to the American College of Radiology, Society of Pediatric Radiology, European Society of Paediatric Radiology, and European Association of Urology.[174–176]

Most studies comparing VCUG to CeVUS have shown similar sensitivity and specificity for diagnosing VUR with overall good congruence in the grading of VUR.[177–184] In a recent meta-analysis, the overall sensitivity and specificity of CeVUS for diagnosing VUR were 93% and 91%, respectively.[185]

CeVUS is not yet universally available in the United States, especially for children who live in underserved areas. The panel found limited data comparing the available studies and a lack of sufficient evidence in the literature to warrant a KAS regarding this diagnostic approach. Although the decision to obtain or not imaging confirmation of VUR differs by age group, there is no evidence to suggest that age plays a role when deciding between CeVUS and VCUG. This decision is more likely related to availability, practice preferences, and local expertise. Further, the panel felt that the topic was not fully aligned with the scope of the CPG. For these reasons, the panel decided not to proceed with a KAS, despite this methodology potentially holding promise.

VIII. PREVENTION

VIII.(A). CAP for VUR

The purpose of KAS 6 is to provide risk stratification and management of children to front-line pediatricians and

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other pediatric clinicians when immediate consultation or access to pediatric urology may not be readily available. All nephrologists and urologists on the panel did not support all aspects of the KAS, as it does not address the comprehensive management of VUR, whereas the majority of the panel deemed the KAS to align with the scope of this CPG. Although clinical perspectives differed among the panel members, nephrology and urology representatives agreed that the KAS guidance is a reasonable starting point for the initial management of the child with VUR while awaiting consultation with subspecialists.

Key Action Statement 6: In children with low-risk VUR, the AAP Guideline Panel suggests against using routine CAP (conditional recommendation, low certainty of evidence).

Remarks for Key Action Statement 6:

- The panel defines low-risk VUR as a child having *both* a lower-grade VUR (I-II) *and* no presence of BBD (excluding functional constipation), per the Rome criteria.
- The panel recognized, through comprehensive evidence review, that grade III VUR spans an unclear risk category. CAP is a reasonable option for patients with grade III VUR for patients and caregivers who place a higher value on the uncertain reduction in the risk of infections and a lower value on minimizing exposure to antibiotics.
- For children with high-risk VUR, CAP is an option. The panel defined high-risk VUR as the presence of *any* of the following:
  - Grade IV or V VUR
  - Intrarenal reflux
  - Demonstrated renal scarring/nephropathy
  - Renal/ureteral structural or cortical abnormalities
  - Recurrent pyelonephritis
  - Bacteremia resulting in ICU admission
  - BBD (excluding functional constipation)
- Patients with high-risk VUR and other high-risk urologic abnormalities that are not covered in the CPG should be referred to a pediatric urologist or nephrologist.

Good Practice Statement: All decisions regarding use of CAP should occur as part of a shared decision-making process with families, given the uncertainty over risks and benefits in individual patients.

Good Practice Statement: Whenever possible, in children with VUR and/or underlying anomalies of the urinary tract that increase risk for UTI and renal scarring, referral to pediatric urology and/or nephrology is recommended for shared decision making and discussion of all management options, including observation, treatment of BBD, antibiotic prophylaxis, and surgical management options. When in-person access to pediatric urologists and nephrologists is limited, virtual consultations, including e-consults and telehealth, can enhance access and specialist involvement.

Good Practice Statement: VUR management may include observation, CAP, endoscopic injection, and ureteral reimplantation; selection among options is encouraged to be made in collaboration with pediatric urology or pediatric nephrology via shared decision making.

Summary of the Evidence

Intrarenal reflux is the backflow of urine from the renal pelvis/calyces into the renal parenchyma. Multiple RCTs have been performed to evaluate the benefit of UTI prophylaxis in reducing UTI and preventing renal scarring. The panel identified 11 RCTs that included children with VUR to inform this clinical question.[186–196]

Of the 11 studies, 7 prescribed TMP-SMX,[186–189,193–195] and 1 prescribed trimoxazole or amoxicillin-clavulanate.[192]

The remaining studies chose between multiple antibiotics.[188,190,196] Five studies reported on breakthrough UTI.[186–190] Eight studies reported on renal scarring.[186–190,192,193,196] One study reported on improvement in VUR.[191] Additionally, 5 studies reported on AEs[186–188,190,192]; 4 reported on antibiotic-resistant rUTI[186,187,190,194] and 1 on weight gain.[195]

There was inadequate evidence on the benefits of prophylaxis in children without VUR for the panel to make a statement on its utility vs harms.

Consideration of CAP for children with secondary VUR (VUR that is attributable to other anatomic or functional causes) requires referral to a subspecialist. The panel did not consider evidence on secondary VUR; therefore, children with this condition should be referred to a urologist.

In addition, in children with VUR and recurrent UTIs, strong consideration should be made for referral to subspecialist. When in-person access to pediatric urologists and nephrologists is limited, virtual consultations, including e-consults and telehealth, can enhance access and specialist involvement. There was inadequate evidence for the panel to consider the benefits of prophylaxis in children without VUR and make a statement on its utility vs harms.

Benefits

Multiple studies have demonstrated that CAP reduces the risk of breakthrough UTI compared with no CAP (RR, 0.78; 95% CI, 0.60 to 1.03; low certainty evidence).[186–190]

The Panel debated the magnitude and qualifier attributed to this risk reduction. These studies demonstrated that CAP may have little to no difference in renal scarring (RR, 1.09; 95% CI, 0.89 to 1.35, low certainty evidence).[186–190,192,193,196]

The overall effect of CAP for preventing UTI is relatively small, and prevention of 1 UTI requires substantive exposure to antibiotics. In prospective trials, the number needed to treat was 16 children to prevent 1 breakthrough UTI in 2 years.[186–190]

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Additionally, evidence suggests that children who receive CAP may experience an improvement in VUR compared with those who do not receive CAP, but the evidence is very uncertain (RR, 0.83; 95% CI, 0.56 to 1.24).[191]

Harms

CAP for UTI may result in harm to children. Intolerance of prophylaxis regarding side effects such as nausea or diarrhea is similar in children receiving prophylaxis and placebo (RR, 1.06; 95% CI, 0.59 to 1.09, very low certainty evidence).[186–190,192] However, children receiving CAP may be more likely to have resistant rUTI than children receiving placebo (RR, 1.69; 95% CI, 1.15 to 2.47).[186,187,190,194] Furthermore, the number needed to treat to cause 1 resistant rUTI was 26.[186,187,190,194]

Additionally, the burden on caregivers of administering a daily medication and to the child of taking the medication should not be overlooked. Using the number needed to treat above, 5840 to 6205 doses of antibiotics need to be given to prevent 1 UTI. Retrospective cohort studies of nonurologic conditions have linked prolonged antibiotic use to an increased risk of obesity, asthma, and celiac disease.[194–204] In the RIVUR study, however, evidence did not suggest an increased risk of these conditions in children who received CAP compared with those who received placebo. Also, very low certainty evidence from Edmonson and colleagues suggests little to no difference in weight gain (mean difference, 0.04 *z* score lower; 95% CI, 0.2 *z* score lower to 0.12 *z* score higher).[195]

Overall, the certainty of the evidence is very low because of concerns with risk of bias and imprecision.

Additional details regarding the results informing this recommendation are available in Supplemental File Table 9 and Table 10 and the accompanying TR.[5]

Other EtD Criteria and Considerations

Therapy to prevent the sequelae of UTIs is an important goal in managing children with structural abnormalities that increase risk for infection. There is evidence that childhood pyelonephritis may be associated with long-term implications for renal function in adulthood. In a retrospective cohort study of Israeli military recruits, history of pyelonephritis was associated with increased risk of end-stage renal disease.[205] Studies have shown that hypertension occurs more commonly in children, young adults, and adults with renal scarring.[206–208]

Because of the challenges in conducting long-term prospective studies, causality—as opposed to association—between renal scarring, pyelonephritis, and adult renal function has been difficult to establish. In a small, long-term study of infants following their first UTI, with and without unilateral renal scarring, subsequent renal function was similar in the 2 groups 16 to 26 years later. Those with bilateral scarring had a lower overall glomerular filtration rate (GFR) than those without scarring.[209]

Although UTIs are associated with renal scarring, there is likely a complex relationship between UTI and renal scarring. Certainly, infants with underlying urinary tract abnormalities such as VUR are at increased risk of scarring and UTI.[210] Reducing the frequency of UTI, then, would logically prevent long-term renal dysfunction, especially in children with underlying anomalies of the urinary tract.

The recommendation applies to children who are younger than the age range included in most of the studies included in the review. For this reason, caution should be applied when considering the younger age groups—especially for children younger than 60 days.

Because of the complexity of the decision to prescribe CAP and the risk profile associated with this practice, shared decision making and informed consent based on a discussion with family members about the risks and benefits are critical prior to prescription.[211] The differences of opinion among the panel members reflect the significant extent that personal values weigh into the decision to use CAP among patients, families, and physicians. One qualitative study that described parents' attitudes toward the management of VUR found variability in preferences regarding risks and benefits of treatment.[212] The chief parental concerns were whether a method decreases the risk of UTIs, has an acceptable efficacy rate, and is aligned with the family's capabilities.

Personal values allow a person to weigh pros and cons and ultimately lead a practitioner and caregiver to a decision; risk tolerance for each option is a key component of the values in decision making. Some children may find the taste of oral antibiotics unpalatable, which can affect compliance rate.[213]

The panel judged that there are moderate costs associated with CAP compared with no CAP. In relation to cost-effectiveness, cost per quality-of-life-year in children younger than 6 years has been estimated to be more than $100 000 for infants and children with VUR grades I through III.[214] In children with VUR grades IV and V, the estimated cost per quality-of-life-year was lower; however, the number needed to treat was not reduced.[188,214] In the RIVUR study, in which patients were randomly assigned to receive CAP or placebo, patients who received CAP incurred higher overall health care costs ($160 per year, on average).[215]

Although the panel discussed evidence that did not identify differences for demographic profiles of children with UTI in terms of antibiotic prescribing patterns, it acknowledges that the impact on health equity would probably be reduced when implementing a recommendation for CAP, particularly because of patient and caregivers' insurance status and coverage and access to a medical home to receive treatment.

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These considerations ultimately affect the acceptability of CAP. Among key interest holders, evidence suggests that patients and caregivers may have concerns about the need to administer medication daily and monitor AEs and the cost associated with treatment.[212] Furthermore, patient characteristics such as VUR grade may influence the acceptability of CAP.

Additionally, the emergence of resistant organisms from UTI treatment is a global health concern; antimicrobial stewardship protects against emergence of resistant organisms and, thus, has broad implications for public policy and health outcomes.[216] Therefore, pediatricians and other pediatric clinicians may find CAP unacceptable because of the risk of antibiotic resistance.

Additional details regarding the EtD framework for this recommendation are available in Appendix Table 6.

VIII.(B) BBD Evaluation and Treatment

Good Practice Statement: In children with UTIs, pediatricians and other pediatric clinicians should evaluate for and treat BBD to decrease the risk of future UTIs. BBD, including constipation, is a substantial risk factor for recurrent UTIs. Assessment of BBD can be conducted via a basic history and physical examination and by using simple screening tools,[1] with consideration of subspecialty referral for children who do not respond to typical constipation and behavioral voiding management. When in-person access to pediatric urologists and nephrologists is limited, virtual consultations, including e-consults and telehealth, can enhance access and specialist involvement.

Summary of the Evidence

The panel identified 1 observational study[76] and 2 predictive modeling studies[53,217] to inform the comparison of CAP-plus-BBD treatment vs BBD treatment alone in children with a history of UTI and clinical signs and symptoms of BBD.

All 3 studies assessed BBD using the Dysfunctional Voiding Symptom Score (DVSS),[1] which assesses symptoms during the past month. Additionally, 1 study defined BBD as "BBD at baseline" and "BBD over time."[69] Another study noted that the DVSS was administered to "children who received potty training during the follow-up."[218] One study each reported on UTI recurrence,[69] time to UTI recurrence,[53] and UTI-associated new renal scarring.[218]

Benefits

Very low-certainty evidence suggests that children receiving CAP plus BBD treatment may be less likely to experience rUTI compared with children receiving BBD treatment alone (RR, 0.21; 95% CI, 0.08 to 0.56). Additionally, very low-certainty evidence suggests that BBD may be a risk factor for rUTI (hazard ratio, 3.19; 95% CI, 1.24 to 8.21).

Harms

The panel did not identify research evidence reporting on the undesirable effects of CAP plus BBD treatment vs BBD treatment alone. Overall, the certainty of the evidence is very low because of risk of bias, indirectness, and imprecision.

Additional details regarding the results informing this clinical question are available in Supplemental File Table 11 and the accompanying TR.[5]

Other Considerations

BBD in infants and children can result from a range of causes, including neurologic conditions such as neurogenic bladder attributable to spinal cord anomalies, as well as nonneurologic factors like functional constipation that leads to pelvic floor dyssynergia and urinary retention.

BBD is considered to be the association of lower urinary tract dysfunction (LUTD) with bowel dysfunction in an individual patient (including patients with NDD/IDD who do not have other medical issues). LUTD can include symptoms of storage, voiding, and holding maneuvers, pain, and others. Although BBD is formally recognized and defined by the The International Children's Continence Society[219] only in children older than 5 years, clinical patterns of LUTD and bowel dysfunction can be seen in children of all ages. Each condition can exist independently, but they often coexist. In the context of UTI, the incidence of BBD has been shown to be almost 40%[220] to as high as 54%.[221]

Clinical Assessment—History, Scoring Systems, and Testing. The clinical history is the most useful diagnostic tool for BBD. The presence of common symptoms—including urinary frequency (increased or decreased), incontinence (involuntary leakage of urine), urgency, hesitancy, straining, weak or diminished urinary stream, dysuria, intermittency, feeling of incomplete emptying, holding maneuvers, and genital pain—are all symptoms of LUTD. The history can include environmental factors (ie, avoiding toileting at school), potty training conflicts, voiding dysfunction (in children with neurodevelopmental disabilities), and abuse.

To get a clear understanding of a child's bowel and bladder function, it is preferable to ask patients and caregivers symptom-specific questions. Several clinical questionnaires designed to identify pediatric BBD have been reported and can be used to assess the presence and severity of BBD as well as to monitor therapy. These include the DVSS,[1] the Dysfunctional Voiding and Incontinence Scoring System (DVISS),[222] the Pediatric Urinary Incontinence Quality of Life Score (PinQ),[223,224] and the Incontinence Symptom Index-Pediatric (ISI-P).[225]

A prospective comparison of the several indices found that DVISS discriminated best with diagnosis, and the DVSS, DVISS, and ISI-P indices correlated well with

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response to therapy; the PinQ has been validated in several cultural contexts.[226]

Although the diagnosis of complex BBD is best guided by the specialist, more-advanced testing (eg, urodynamics) is not commonly needed. A simple observed void can demonstrate intermittent voiding or a diminished stream. Assessment of bladder capacity and postvoid residual urine volume in the bladder by ultrasonography is noninvasive and can be effective.[227]

Association With Pediatric UTI and VUR. The association of pediatric BBD and UTI has been recognized for several decades.[76,220,228–233] Similarly, the connection of BBD, UTI, and VUR subsequently became solidified and has guided VUR management in the last 2 decades.[234] BBD has been shown to reduce the rate of spontaneous resolution of VUR and is associated with a greater incidence of breakthrough UTI in children receiving antibiotic prophylaxis.[53,235–237] The associations of other negative outcomes of VUR have also been shown to be worsened with BBD, specifically scarring.[45,220]

The literature on BBD and VUR in children is significant; the American Urological Association's clinical guideline on pediatric VUR presents a meta-analysis of the impact of BBD on VUR clinically.[53,235,237]

This association suggests the importance of BBD in the evaluation and care of children with UTI and possible VUR.

Treatment—Behavioral Modifications. The most basic approaches to improve BBD and its complications involve changing the patient behaviors that contribute to BBD. These include establishing a regular voiding schedule for bladder emptying; facilitating more complete bladder emptying with pelvic floor relaxation; improving voiding posture; and establishing tangible improvement goals. These measures can be readily instituted by the general pediatrician and do not require an experienced urotherapist, except in refractory situations.

Efforts to improve constipation are included in these efforts encompassing dietary changes, regular bowel habits, and medications including polyethylene glycol 3350 (Miralax [Bayer HealthCare LLC, Whippany, New Jersey]) as appropriate. Toileting posture can be addressed as well to facilitate more complete bowel emptying.

In children with NDD/IDDs, specialized care may be appropriate.

Treatment—Medical Therapy. There is limited evidence supporting the use of medication in BBD, except for treatment of constipation. In certain patients (best selected by subspecialists), therapy can be aided by anticholinergic medications and alpha-blocking agents.[238,239] Anticholinergics can reduce the degree of bladder instability and urgency that can prompt pelvic floor contractions and impair bladder emptying. It is typically used temporarily to help the child learn more normal bladder patterns. Alpha-blocking agents can facilitate bladder emptying in some children who do not empty well even when voiding appropriately, mostly to reduce the risk of infection attributable to incomplete bladder emptying.

Treatment—Constipation Management. Managing constipation can be critically important in caring for the child with BBD and can require dietary, behavioral, and medical modalities. It should be recognized, however, that simply treating constipation may not solve the bladder and voiding dysfunction issues, which should be addressed as well. Although there are limited objective measures of constipation, the Bristol Stool Scale can be a useful communication and tracking tool.[240]

Referral. Most pediatricians and other pediatric clinicians can effectively manage BBD, as this is largely a behavioral and developmental condition. When complicated by recurrent UTI and in the setting of VUR, referral to a urologist or nephrologist may be appropriate. In a child with clinically significant BBD for whom dietary and behavioral modifications do not improve the condition, referral to pediatric urology can occur for additional escalation of care, including medication and biofeedback. When in-person access to pediatric urologists and nephrologists is limited, virtual consultations, including e-consults and telehealth, can enhance access and specialist involvement.

If the pediatrician or pediatric clinician discovers any evidence of an underlying neurologic condition, such as a sacral dimple or abnormal neurologic examination, additional spinal cord imaging or referral to subspecialists should be considered.

IX. IMPLEMENTATION CONSIDERATIONS

CPGs have been recognized as an essential part of delivering evidence-based medicine to patients by decreasing the gap between available research and bedside clinical care and standardizing clinician practice. Yet, literature describes poor adoption, dissemination, and translation of evidence-based guidelines into clinical practice.[241,242] An SR found that the median proportion of respondents who report adopting and adhering to CPGs is only 36%,[243] with a large variation between different physicians and between different CPGs. It takes an average of 17 years for published research to reach the patient at bedside.[244]

Anticipated barriers to implementation of guidelines for all providers who care for children with UTI in various settings can be categorized at the organizational level, practice and provider level, community level, and patient level. Addressing and anticipating these barriers can make CPG use and acceptance more widespread. An Implementation Toolkit (https://www.aap.org/en/patient-care/urinary-tract-infection-clinical-practice-guideline/)

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has been created in tandem with this CPG to help overcome barriers to its implementation.

Organizational Level

Implementation of evidence-based practice at the organizational level can be described in the context of the safety and quality culture of the organization. Support and time needed to disseminate and adopt this CPG include resources related to dedicated quality improvement personnel[245] and a safety and quality department specifically dedicated to pediatric care.

Practice and Provider Level

Barriers to implementation at the provider level include lack of time and presence of competing priorities, lack of resources, support and incentive, resistance to change, and implicit bias. Evidence indicates that support can be delivered through electronic health record (EHR) support. EHR systems that integrate guidelines and incentivize adoption by coupling with hospital/clinic/Healthcare Effectiveness Data and Information Set quality measures have shown to ease adoption of existing guidelines.[246]

EHRs that incorporate guideline recommendations and make them the default have been shown to change prescribing practices.[247] As part of quality improvement projects, institutions providing direct feedback to practitioners and tracking balancing measures (like treatment failure) have helped to increase practitioner confidence in CPGs, reduce practice variability, and increase CPG adoption.[116,248–251]

Implicit bias in diagnosis and attitudes in prescribing practices that cause inequity have been documented in the literature.[252,253] Racial differences exist in pediatric antibiotic prescribing practices.[254,255] Implicit bias training, as it pertains to health equity, is now part of most hospital annual competencies and should be continued to be offered, because EHR integration and support alone cannot address this bias.

When multiple clinicians are involved in managing UTI, care teams should develop a coordinated plan that is implemented with input from members of the clinical care team, including primary and specialty care clinicians, social and community service providers, and the family and patient. Continuity of care between practice settings should be individualized based on clinical indication, community resources, family preferences, and ability to access care. Communication and definition of roles among all providers and families are needed to clearly delineate responsibility for ordering and reviewing results where applicable, providing follow-up care, and communicating the follow-up care plan with the family. Each family's social and economic needs for follow-up care should be assessed with necessary support arranged from each care setting.

Community Level

An important consideration for the majority of these KASs is that almost half of US children do not have a medical home.[256,257] Appropriate clinical response to antibiotic choice, culture results and sensitivities, follow-up diagnostics like RBUS, and when to perform a VCUG will not occur routinely in the acute care setting. This CPG relies on the provider faced with a child with a UTI to encourage, support, and facilitate, when possible, engagement and communication with a child's medical home or emphasize the importance to limit overuse of acute care settings, unnecessary testing/treatment, or missing opportunities to avoid long-term harm by appropriate implementation of these guidelines especially for the child with recurrent UTIs.

Data show that acute care of children mostly occurs in community health systems and that only a small percentage of children are evaluated at academic institutions.[258] Disparities in equitable health care delivery in rural communities for pediatric patients have also been reported.[259,260] At a time when national trends show decreasing pediatric capacity in most community hospitals,[261] access to high-quality, evidence-based pediatric care must be ensured.[262] With decreasing pediatric volume of patients in these organizations and health systems, decreased level of knowledge and comfort of pediatric patient care is expected to follow. A lack of pediatric-specific equipment and medication are both barriers to CPG dissemination.

The CPG's KASs 3A and 3B recommend early medication transition from parenteral to oral and, in some cases, oral instead of parenteral medication in very young infants. Ensuring the CPG's reach to all places that care for children can impact antimicrobial stewardship. Several tertiary care center claims data studies show inappropriate use of antibiotics at the community level.[263–265] Outreach clinics from tertiary centers, telemedicine, and providing incentives for education at this level can help with CPG adoption.

Patient Level

Research shows that patient education materials on antibiotics and treatment plan can optimize adherence to KASs pertaining to antimicrobial stewardship.[266,267] The literature includes data about caregiver expectation's driving physician practices to vary from the "standard of care."[268,269] Websites such as Choosing Wisely have had long-standing education models for providers on techniques and phrases that help drive effective communication with caregivers.

Implementation considerations and topics for discussion with the caregiver include providing education materials for caregivers about potential benefits and harms of shorter-course antibiotics (KAS 2), oral vs parental antibiotics for UTI (KAS 3A and 3B), recommendation for or against continuous antibiotic prophylaxis (KAS 6A and 6B), and the use of invasive vs noninvasive studies

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investigation after first febrile UTI (KAS 5A and 5B). Furthermore, providing detailed after-care instructions to caregivers for return of care can decrease health disparities in patients without a medical home.

Children and infants with NDD/IDDs may face significant barriers to care, including communication challenges, atypical symptom presentation, and reduced access to timely diagnostic evaluations. All of these barriers can delay recognition and treatment of UTI.

See Figures 1–4 for implementation algorithms.

X. RESEARCH PRIORITIES

Numerous research questions remain unanswered regarding the optimal diagnosis and management of UTIs in infants and children. Several mainstream practices currently considered to be "standard of care" lack robust support in the literature and may inadvertently cause adverse outcomes for patients. The panel has identified areas of needed research, described below.

Diagnosis of UTI

UA thresholds for presumptive treatment of UTI require further study. The goal would be to optimize timely therapy without the provision of unnecessary antibiotic exposure. A better understanding of urine culture CFU thresholds and the pathogenesis of bacterial species will help distinguish between infection and contamination or ASB.

In addition, emerging biomarkers, such as neutrophil gelatinase-associated lipocalin, show promise for the detection of UTI.[7,270] They require further study as a replacement or a complement to point-of-care testing. Kidney or urinary tract epithelial markers of infection may assist with differentiation of active infection and ASB. Although some studies have examined the "2-step" approach to UTI diagnosis (eg, bag UA first, then catheterized urine culture if the bag UA is positive), more data are needed on this approach in infants to ensure that consequential UTIs are not being missed.[93]

Further, there is a pressing need for research into emerging technologies to replace or complement traditional urine cultures, which rely on outdated methodologies. Molecular testing has the potential to be faster and more accurate. Notably, children treated with discordant antibiotics often achieve high cure rates for UTIs, suggesting that current methods for predicting antibiotic efficacy may be inaccurate.[218]

Future research needs include standardized RBUS protocols and consistent definitions across studies, which would strengthen the interpretation and future applicability of the findings. For BBD, future research should be directed at studying younger patient populations and implications in UTI risk reduction with and without CAP.

Finally, adult studies have shown that the oral MV 140 sublingual vaccine (Uromune [Inmunotek SL, Madrid, Spain]) is effective at preventing UTI.[271,272] The panel encourages further research on this approach.

Treatment of UTI

Optimal efficacy of management of UTI in very young infants requires further study. Duration of therapy and efficacy of the oral antibiotic route for bacteremic UTI require further study in infants between 8 days and 2 months of age. Research is needed to guide the optimal duration and selection of antimicrobial therapy for infants and children with UTIs who are cared for in the critical care setting.

Future research should explore the potential value of single-dose antibiotic therapy for simple cystitis in older children who can communicate symptoms well as a way to optimize treatment efficacy and minimize antibiotic exposure.

Understanding of nonantibiotic options for treatment and prevention of UTIs is also needed. More research is needed in translating therapies such as antimicrobial peptides, phages, anti-adhesion molecules, and urinary pH modulation from the bench to the bedside. Therapeutic agents that are used more frequently outside the United States should be compared with agents available in this country (eg, nitroxoline, pivmecillinam, and TMP without SMX).

For future studies, it may also be beneficial to investigate effects of prophylaxis on estimated GFR as an outcome measure.[273] No prospective study has extended past 2 years. Some concerns have been raised that these studies have not been adequately powered to detect renal scarring in children with higher grades of VUR. Additionally, certain subgroups have lower rates of UTI when receiving CAP, depending on the study. For instance, 1 study demonstrated more benefit in boys,[197] but the finding was not seen in other studies.

Evaluation of the Renal Tract After UTI

Timing of RBUS requires further study. There is ongoing uncertainty whether early ultrasonography may increase the risk of false-positive results, while delaying the ultrasonography may reduce compliance. Likewise, the indication for early RBUS at the time of diagnosis needs to be better evaluated. Research should focus on optimizing imaging strategies based on age, gender, and genetic risk factors to improve the predictive value of testing.

Management of Urinary Tract Anomalies

Although surgical interventions for VUR are outside the scope of this CPG, additional data on the efficacy of these procedures are needed to refine imaging strategies. RCTs with long-term follow-up could better compare surgical and nonsurgical approaches.

For UTI prophylaxis, studies should examine long-term risks and benefits, including effects on estimated GFR, because radiographic scarring has not been shown to

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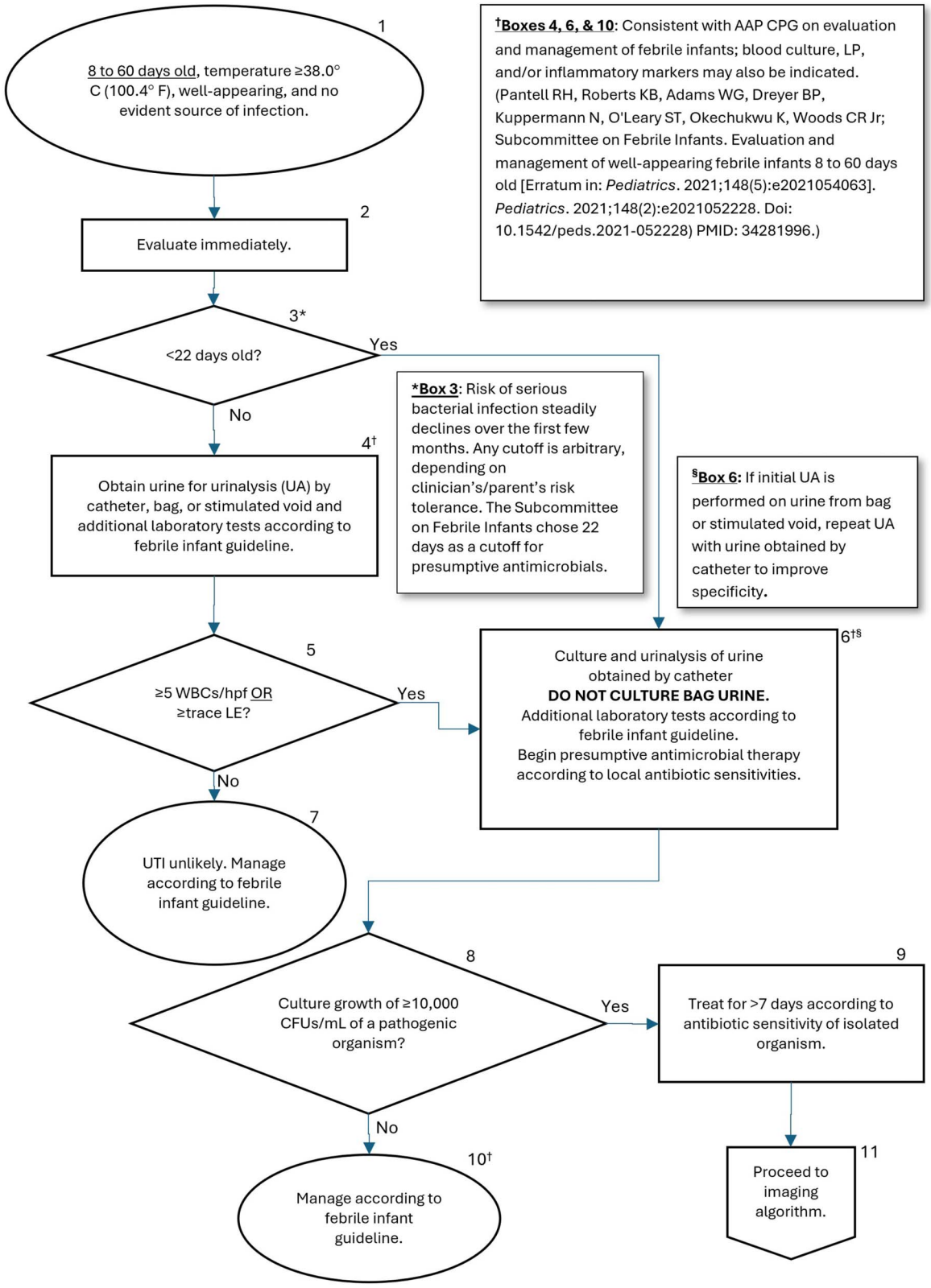


FIGURE 1.
Management of Children With Suspected Urinary Tract Infection (UTI) Ages 8–60 Days.
Abbreviations: AAP, American Academy of Pediatrics; CFU, colony-forming unit; CPG, clinical practice guideline; hpf, high-powered field; LE, leukocyte esterase; WBC, white blood cell.

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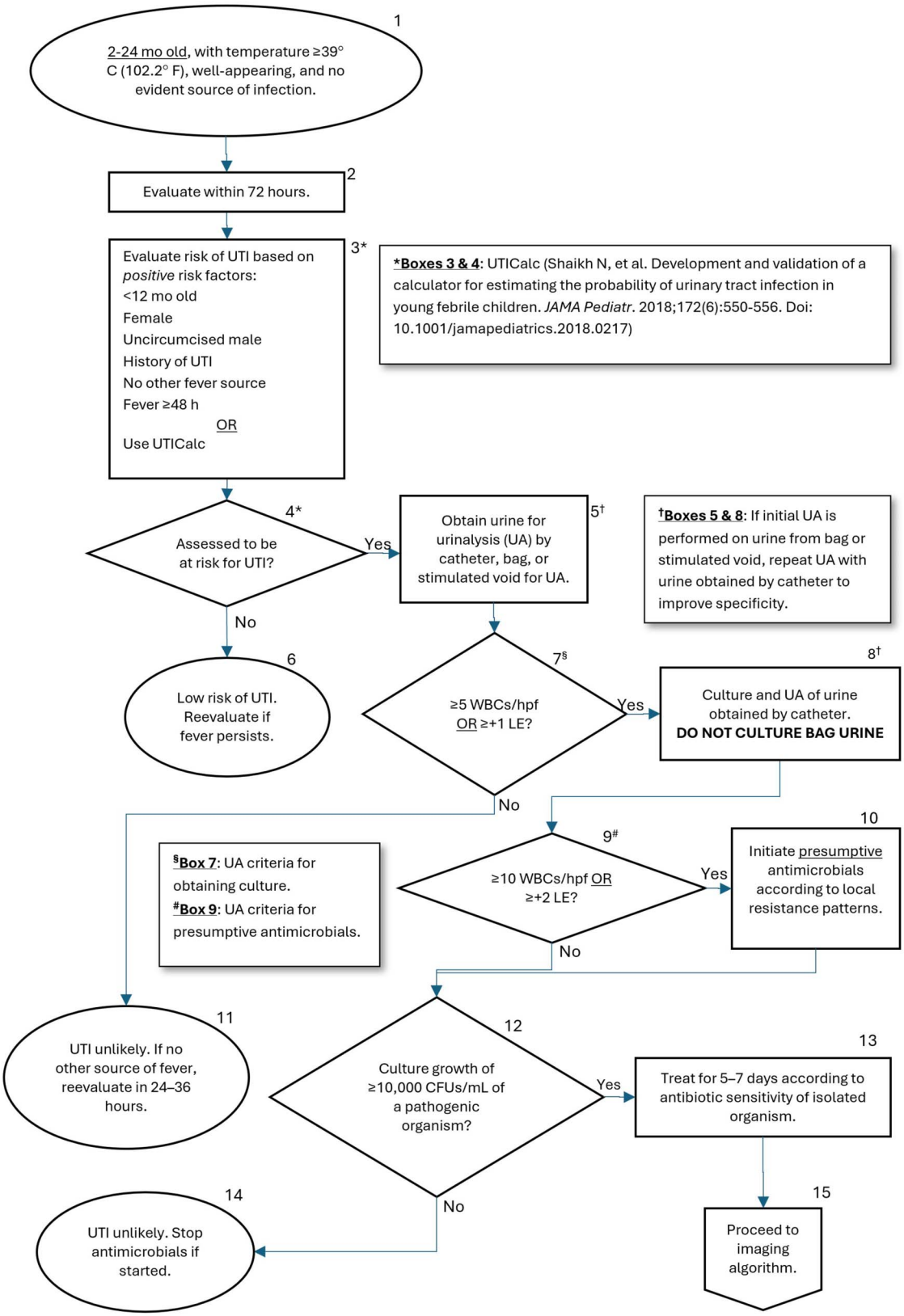


FIGURE 2.
Management of Children With Suspected Urinary Tract Infection (UTI) Ages 2–24 Months.
Abbreviations: CFU, colony-forming unit; hpf, high-powered field; LE, leukocyte esterase; WBC, white blood cell.

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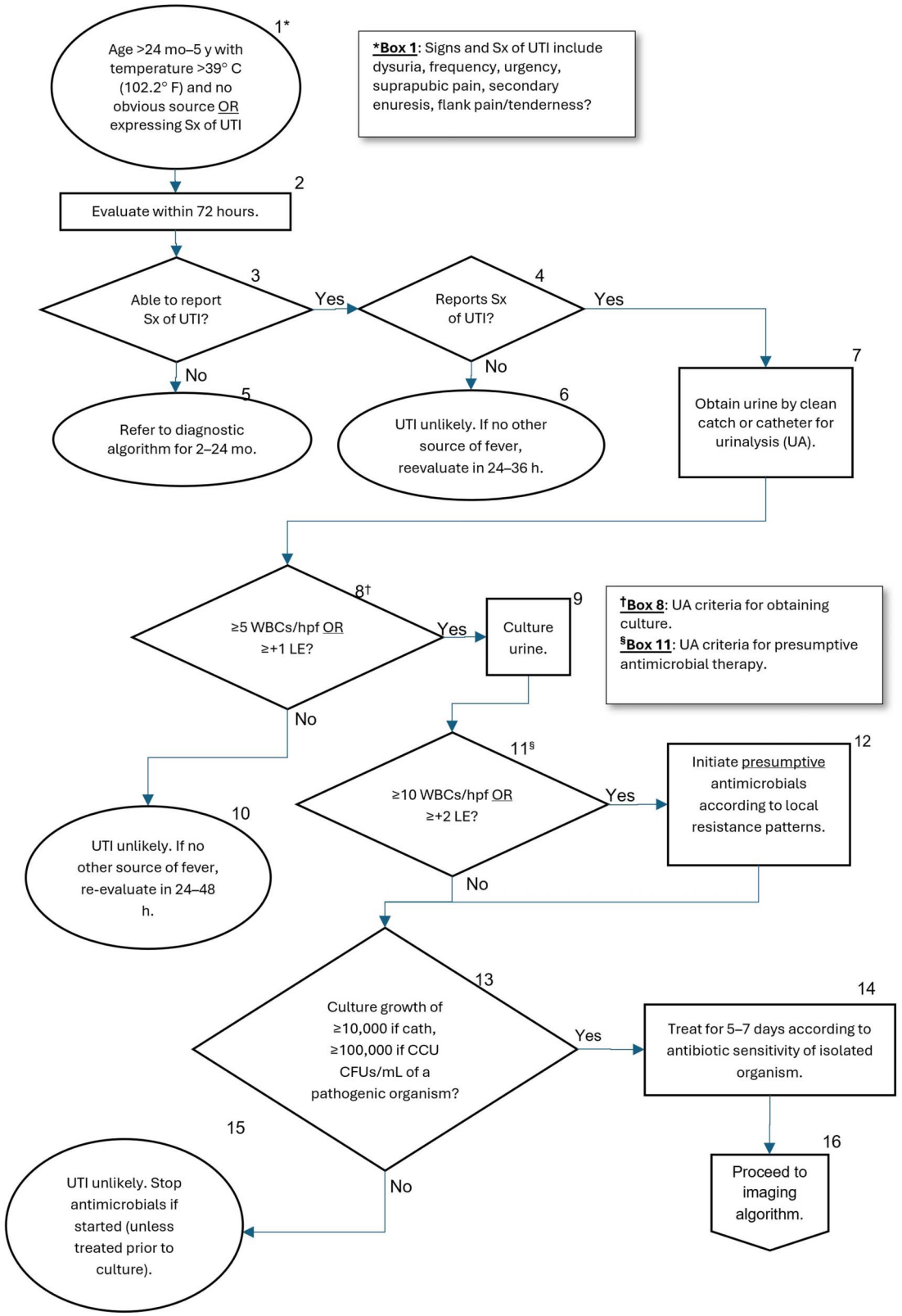


FIGURE 3.
Management of Children With Suspected Urinary Tract Infection (UTI) Ages >24 Months–5 Years.
Abbreviations: cath, catheterization; CCU, clean catch urine; CFU, colony-forming unit; hpf, high-powered field; LE, leukocyte esterase; Sx, symptoms; WBC, white blood cell.

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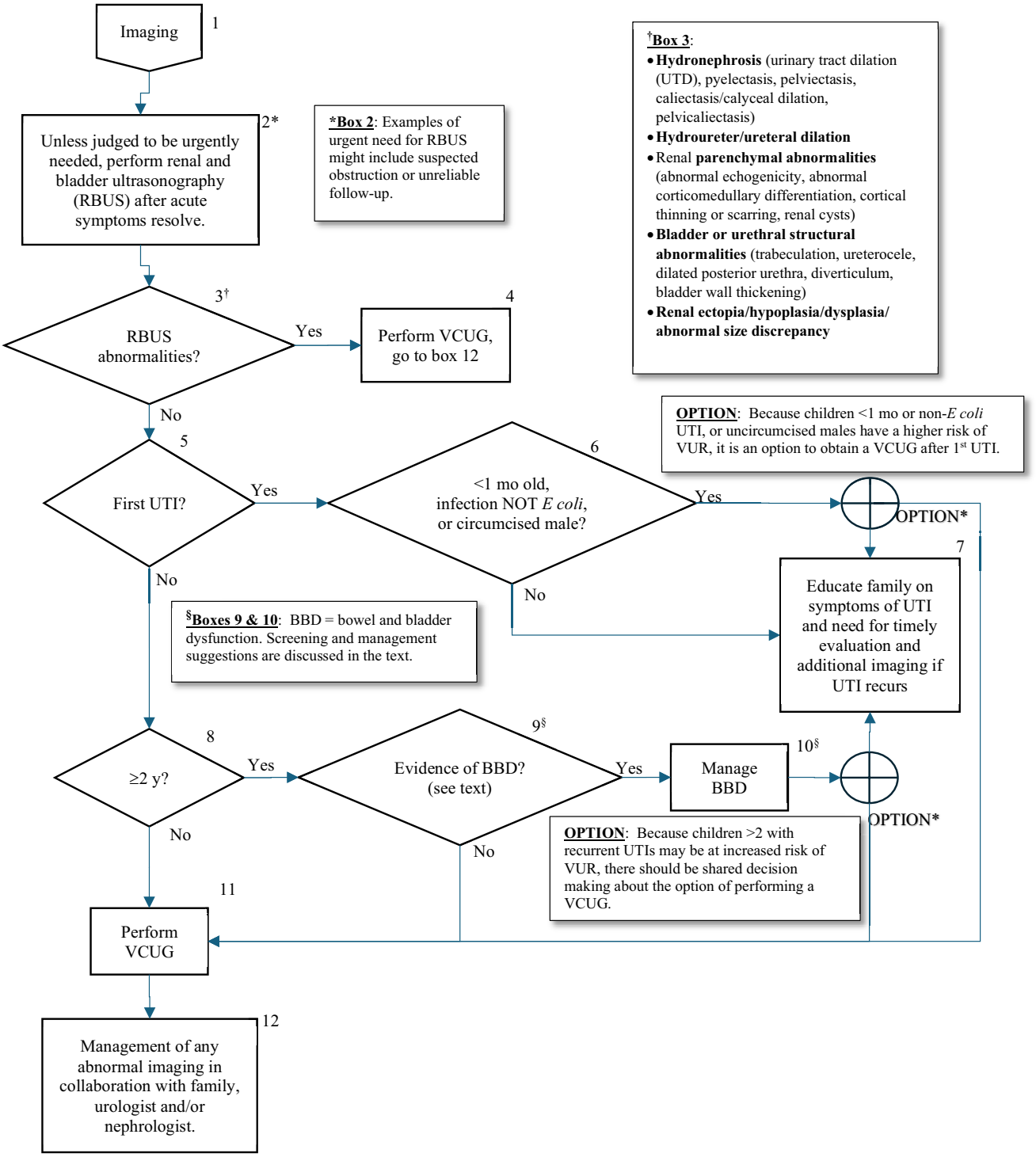


FIGURE 4.
Imaging for Suspected Urinary Tract Infection (UTI).
Abbreviations: VCUG, voiding cystourethrography; VUR, vesicoureteral reflux.

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correlate with renal function.[232,274] Alternatives (such as osmotic laxatives and cranberry juice) require further investigation for at-risk children.[275]

Because of poor interrater reliability on grades of VUR, the panel recommends that research on a more objective VUR grading system should be a priority.

A Call for a National Longitudinal Study

The panel recommends the establishment of a national registry for children with febrile UTIs. This registry would track treatment, VUR presence, renal scarring, recurrent UTIs, and long-term outcomes such as renal function, end-stage renal disease, and hypertension. A large cohort would allow the application of causal reasoning techniques to assess baseline risks and disentangle the roles of therapies, recurrent infections, and VUR in shaping outcomes. Additionally, a biorepository could facilitate retrospective genetic studies to identify risk factors for future screening tools.

XI. CONCLUSION

Although extremely common, pediatric UTIs remain a challenging condition for which to create universal truths to aid pediatricians and other pediatric clinicians. Since the AAP last published a CPG on this topic, an immense amount of work has been done in the field. The panel assessed historic and recent evidence and attempted to provide a refreshed roadmap for pediatricians and other pediatric clinicians faced with a child with either suspected or confirmed UTI.

Each panel member had differing views of the value and weight to place on the potential benefits and potential harms as well as unintended consequences of the CPG. These nuances reflect the different perspectives and experiences as well as goals each clinician, caregiver, and patient face when making care decisions for controversial or vague entities with, at times, conflicting bodies of evidence. The panel used numerous methods to reach consensus on numerous topics, which strengthened this CPG and its implementation by pediatricians and other pediatric clinicians.

This CPG, in no means, supplants the clinical judgment and nuance exhibited by the pediatrician or other clinician. Rather, it is designed to help provide structure and guidance for those who are treating the typical child with UTI. The Key Action Statements and Good Practice Statements within this CPG reflect the uncertainty and nuance still present in diagnosing and managing UTI.

It is also important to be mindful of the growing public health impact of antibiotic resistance and the limited number of antimicrobials to combat infectious diseases. This CPG panel's goal was to help provide a renewed view on this topic and help improve care in all of these arenas.

Much work is still needed to provide a clearer definition of what is and what is not a UTI; the optimal route and duration of treatment; and which patients do, and do not, need additional testing and management.

GUIDELINE PANEL ON DIAGNOSIS AND MANAGEMENT OF UTI

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ABBREVIATIONS

AE: adverse event
AAP: American Academy of Pediatrics
ASB: asymptomatic bacteriuria
BBD: bowel and bladder dysfunction
CPG: clinical practice guideline
CFUs: colony-forming units
CAP: continuous antibiotic prophylaxis
CeVUS: contrast-enhanced voiding urosonography
DVSS: Dysfunctional Voiding Symptom Score
DVISS: Dysfunctional Voiding and Incontinence Scoring System
EHR: electronic health record
EtD: evidence-to-decision
GFR: glomerular filtration rate
GPS: Good Practice Statement
GRADE: Grading of Recommendations Assessment, Development, and Evaluation
HPF: high-powered field
ICU: intensive care unit
ISI-P: Incontinence Symptom Index-Pediatric
IDD: intellectual developmental disability
KAS: Key Action Statement
LE: leukocyte esterase
LUTD: lower urinary tract dysfunction
MOC: maintenance of certification
MIC: minimal inhibitory concentration
NDD: neurodevelopmental disabilities
PinQ: Pediatric Urinary Incontinence Quality of Life Score
PICO: population, intervention, comparator, and outcome
PICC: peripherally inserted central catheter
PRISMA: Preferred Reporting Items for Systematic Reviews and Meta-Analyses
QUADAS-2: Quality Assessment of Diagnostic Accuracy Studies 2
RCT: randomized controlled trial
rUTI: recurrent UTI
RBC: red blood cell
RBUS: renal bladder ultrasonography
RoB: risk of bias
RoB 2.0: risk of bias tool for randomized trials
ROBINS-I: Risk Of Bias In Non-randomized Studies of Interventions
SMX: sulfamethoxazole
SPA: suprapubic aspiration
SR: systematic review
TR: technical report
TMP: trimethoprim
UA: urinalysis
UTI: urinary tract infection
VUR: vesicoureteral reflux
VCUG: voiding cystourethrography
WBC: white blood cell

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Options for the management of significantly relevant financial and intellectual COIs may include removal of a panel member or restrictions on participation such as not voting, abstaining from participating in discussions, or not participating in evidence-based reviews.

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XII. APPENDICES

APPENDIX TABLE 1. EVIDENCE-TO-DECISIONS TABLE FOR PROMPT MEDICAL EVALUATION

Question

Should prompt medical evaluation (<72 hrs) vs observation and evaluation after 72 hrs be used for children <5 yo with fever and symptoms suggestive of UTI?	
POPULATION:	Children <5 yo with fever and symptoms suggestive of UTI
INTERVENTION:	Prompt medical evaluation (<72 hrs)
COMPARISON:	Observation and evaluation after 72 hrs
MAIN OUTCOMES:	Renal scarring; Renal scarring - single study; Renal scarring - mean fever duration
SETTING:	General pediatric practice in collaboration with subspecialists
PERSPECTIVE:	Clinical recommendation – Individual perspective
BACKGROUND:	
CONFLICT OF INTERESTS:	

Assessment

Problem
Is the problem a priority?

JUDGMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ No ○ Probably no ○ Probably yes • **Yes** ○ Varies ○ Don't know	Delay in evaluation and subsequent treatment of UTI may increase the risk of acute renal lesions and renal scarring. The optimal timing of intervention to minimize renal scarring remains uncertain.	Consistent with judgments on prior questions Panel members have noted an abundance of caution among some caregivers/clinicians and a more relaxed approach among others.

Desirable Effects
How substantial are the desirable anticipated effects?

JUDGMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Trivial • **Small** ○ Moderate ○ Large ○ Varies ○ Don't know	Relatively earlier evaluation and treatment (72 hrs or less of fever before treatment) may result in less renal scarring compared to relatively later evaluation and treatment (>72 hrs of fever before treatment). *See Supplemental File Table 2*	Variability in baseline risk based on: • Children w/fever and no history of UTI • Children w/no localizing symptoms • Prior UTI • Age • Known urologic problems (VUR) Panel discussed risk of scarring increasing with increasing duration of fever before treatment Lifelong consequences of scarring Multiple scars/accumulation Proportion of children with UTI out of all children who present with fever Reduction of single scar vs accumulation of scarring Measurement of inflammation vs scarring (acute vs later dimercaptosuccinic acid scan) Decrease in scarring Long term health consequences unknown (hypertension, elevated creatinine, end stage renal disease) Reduction in unnecessary emergency department (ED) visits

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Undesirable Effects
How substantial are the undesirable anticipated effects?

JUDGMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Trivial ○ Small • **Moderate** ○ Large ○ Varies ○ Don't know	*See Supplemental File Table 2*	What are potential undesirable effects? • Increase in overall # of visits for evaluation • Pre-test probability of having a UTI increases over time • Rates of false positives/unnecessary antibiotic exposure • Unnecessary evaluations (catheterization, lab work) • 6 mo vs 4 yr - difference in ability to express symptoms • Children could be evaluated by primary care provider within 3 days - clarify in remarks

Certainty of evidence
What is the overall certainty of the evidence of effects?

JUDGMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Very low • **Low** ○ Moderate ○ High ○ No included studies	We have low certainty in the evidence because of critical concerns about risk of bias from lack of control for potential confounding variables. We also have concerns with possible selection bias, possible misclassification of the exposure (time to treatment), and loss to follow-up.	

Values
Is there important uncertainty about or variability in how much people value the main outcomes?

JUDGMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Important uncertainty or variability • **Possibly important uncertainty or variability** ○ Probably no important uncertainty or variability ○ No important uncertainty or variability		Do values differ about renal scarring? Can we assume that caregivers and children would want to avoid disease progression and renal scarring?

Balance of effects
Does the balance between desirable and undesirable effects favor the intervention or the comparison?

JUDGMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Favors the comparison ○ Probably favors the comparison ○ Does not favor either the intervention or the comparison • **Probably favors the intervention** ○ Favors the intervention ○ Varies ○ Don't know		Children <2 yo with fever without another source and <5 yo with symptoms suggestive of UTI Comparison is between evaluation within 72 hrs vs >72 hrs

Resources required
How large are the resource requirements (costs)?

JUDGMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Large costs • **Moderate costs** ○ Negligible costs and savings ○ Moderate savings	No included studies.	Based on AAP recommendations, this evaluation is from the individual, rather than societal, perspective. No studies were identified addressing this issue. Would resources differ within 72 hrs vs >72 hrs? Does not specifically require ED eval but a shorter time to

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○ Large savings ○ Varies ○ Don't know		evaluation may change practice setting to urgent care/ED vs PCP with implications for resource use Some symptoms may resolve without evaluation/treatment >72 hrs
Certainty of evidence of required resources What is the certainty of the evidence of resource requirements (costs)?		
JUDGMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
○ Very low ○ Low ○ Moderate ○ High • **No included studies**	No included studies.	
Cost effectiveness Does the cost-effectiveness of the intervention favor the intervention or the comparison?		
JUDGMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
○ Favors the comparison ○ Probably favors the comparison ○ Does not favor either the intervention or the comparison ○ Probably favors the intervention ○ Favors the intervention ○ Varies • **No included studies**	No included studies.	
Equity What would be the impact on health equity?		
JUDGMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
○ Reduced ○ Probably reduced ○ Probably no impact ○ Probably increased ○ Increased • **Varies** ○ Don't know		Who could be disadvantaged? Does 72 hrs make a difference? Prompt medical evaluation can increase health care costs, which may be challenging for families who do not have access to health insurance. Some families who live in rural communities and/or those who do not have access to reliable transportation may not be able to access a medical provider for prompt medical evaluation.
Acceptability Is the intervention acceptable to key interest holders?		
JUDGMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
○ No ○ Probably no ○ Probably yes ○ Yes • **Varies** ○ Don't know		Parents and caregivers - likely to be acceptable Providers?
Feasibility Is the intervention feasible to implement?		
JUDGMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
○ No ○ Probably no • **Probably yes** ○ **Yes** ○ Varies ○ Don't know		Comparison of evaluation within 72 hrs vs >72 hrs is not likely to impact feasibility.

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Summary of Judgments

	JUDGMENT						
PROBLEM	No	Probably no	Probably yes	**Yes**		Varies	Don't know
DESIRABLE EFFECTS	Trivial	**Small**	Moderate	Large		Varies	Don't know
UNDESIRABLE EFFECTS	Trivial	Small	**Moderate**	Large		Varies	Don't know
CERTAINTY OF EVIDENCE	Very low	**Low**	Moderate	High			No included studies
VALUES	Important uncertainty or variability	**Possibly important uncertainty or variability**	Probably no important uncertainty or variability	No important uncertainty or variability			
BALANCE OF EFFECTS	Favors the comparison	Probably favors the comparison	Does not favor either the intervention or the comparison	**Probably favors the intervention**	Favors the intervention	Varies	Don't know
RESOURCES REQUIRED	Large costs	**Moderate costs**	Negligible costs and savings	Moderate savings	Large savings	Varies	Don't know
CERTAINTY OF EVIDENCE OF REQUIRED RESOURCES	Very low	Low	Moderate	High			**No included studies**
COST EFFECTIVENESS	Favors the comparison	Probably favors the comparison	Does not favor either the intervention or the comparison	Probably favors the intervention	Favors the intervention	Varies	**No included studies**
EQUITY	Reduced	Probably reduced	Probably no impact	Probably increased	Increased	**Varies**	Don't know
ACCEPTABILITY	No	Probably no	Probably yes	Yes		**Varies**	Don't know
FEASIBILITY	No	Probably no	**Probably yes**	Yes		Varies	Don't know

Type of Recommendation

Strong recommendation against the intervention	Conditional recommendation against the intervention	Conditional recommendation for either the intervention or the comparison	**Conditional recommendation for either the intervention or the comparison**	Strong recommendation for the intervention

Conclusions

Recommendation
Key Action Statement 1: In medically noncomplex children ages 2 months to 24 months with fever without an identified source, and in children ages 2 to 5 years with symptoms suggestive of urinary tract infection (UTI [eg, dysuria, new-onset urinary urgency or frequency]), the AAP Guideline Panel suggests medical evaluation for UTI within 72 hours of symptom onset rather than a longer period of observation (conditional recommendation, low certainty of evidence). Remark 1 for Key Action Statement 1: Although evaluation within 72 hours is generally appropriate, pediatricians and other pediatric clinicians should expedite assessment in children at higher risk for pyelonephritis or kidney injury—for example, those with known structural genitourinary abnormalities (such as hydronephrosis or vesicoureteral reflux), a history of prior febrile UTI, or symptoms consistent with pyelonephritis (such as flank pain). Remark 2 for Key Action Statement 1: Although this Key Action Statement focuses on medically noncomplex children, the same principle of timely evaluation applies to medically complex children who may be at increased risk for renal sequelae and may warrant more urgent assessment.
Justification
Subgroup considerations
Implementation considerations
Monitoring and evaluation
Research priorities
Optimal timing of medical evaluation for children with symptoms suggestive of UTI who also have VUR/prior UTI.

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APPENDIX TABLE 2. EVIDENCE-TO-DECISIONS TABLE FOR ANTIBIOTIC DURATION

Question

Should a shorter course of antibiotic therapy (<7 days) vs a longer course of antibiotic therapy (>7 days) be used for children being treated for UTI?	
POPULATION:	children being treated for UTI
INTERVENTION:	a shorter course of antibiotic therapy (7 days or less)
COMPARISON:	a longer course of antibiotic therapy (>7 days)
MAIN OUTCOMES:	Recurrent UTI (rUTI); Adverse events; Resistant rUTI;
SETTING:	
PERSPECTIVE:	clinical recommendation – individual perspective
BACKGROUND:	
CONFLICT OF INTERESTS:	none

Assessment

Problem
Is the problem a priority?

JUDGMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ No ○ Probably no ○ Probably yes • **Yes** ○ Varies ○ Don't know	Urinary tract infection (UTI) is one of the most common bacterial infections of childhood. Among febrile infants, unwell children in general practice, and older children with urinary symptoms, 6%–8% will have a UTI. Over 30% of children with UTI will have recurrent UTI. Common risk factors for recurrence include vesicoureteral reflux (VUR) and bowel and bladder dysfunction (BBD). Oral antibiotics are effective in many cases. Previous Cochrane reviews suggest that 2–4 days courses are as effective for uncomplicated cystitis as 7–14 days, while single-dose therapy is less effective. Younger and sicker children may require initial intravenous therapy. Kaufman J, Temple-Smith M, Sanci L. Urinary tract infections in children: an overview of diagnosis and management. *BMJ Paediatr Open.* 2019;3(1):e000487	

Desirable Effects
How substantial are the desirable anticipated effects?

JUDGMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Trivial ○ Small • **Moderate** ○ Large ○ Varies ○ Don't know	*See Supplemental File Table 6*	The panel identified and considered the additional benefits of a relatively shorter course of antibiotics when making their judgment: • Lower risk of *Clostridium difficile* infection • Fewer side effects • Less alteration of intestinal biome • Increased adherence

Undesirable Effects
How substantial are the undesirable anticipated effects?

JUDGMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
• **Trivial** ○ Small ○ Moderate ○ Large ○ Varies ○ Don't know	*See Supplemental File Table 6*	The panel decided that no treatment-associated adverse effects of discontinuing antibiotic treatment earlier vs later.

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Certainty of evidence What is the overall certainty of the evidence of effects?		
JUDGMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
○ Very low • **Low** ○ Moderate ○ High ○ No included studies	The certainty of evidence is LOW because of concerns with risk of bias and imprecision.	Studies do not differentiate pyelonephritis from cystitis.
Values Is there important uncertainty about or variability in how much people value the main outcomes?		
JUDGMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
○ Important uncertainty or variability ○ Possibly important uncertainty or variability • **Probably no important uncertainty or variability** ○ No important uncertainty or variability	No research evidence was identified regarding parent/caregiver or patient values about the main outcomes (recurrent UTI, resistant rUTI, adverse events).	Caregivers may prefer shorter antibiotics because of burden associated with antibiotic compliance for a longer period of time. Caregivers may also question clinical efficacy of shorter antibiotics based on older standard of care - not as concerning with a fully informed parent. Shorter course could be perceived as "less treatment" for UTI vs "more treatment."
Balance of effects Does the balance between desirable and undesirable effects favor the intervention or the comparison?		
JUDGMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
○ Favors the comparison ○ Probably favors the comparison ○ Does not favor either the intervention or the comparison • **Probably favors the intervention** ○ Favors the intervention ○ Varies ○ Don't know		DESIRABLE: moderate UNDESIRABLE: trivial CERTAINTY: low VALUES: probably no important uncertainty or variability Panel updated the cutoff for short antibiotics course to 7 days or less (7 days as the ceiling for short course of antibiotics). Additional clarity may be needed to define the short course as the terminology differs across the guideline panel. "If the patient is responding to treatment, do not exceed 7 days."
Resources required How large are the resource requirements (costs)?		
JUDGMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
○ Large costs ○ Moderate costs ○ Negligible costs and savings • **Moderate savings** ○ Large savings ○ Varies ○ Don't know	There were no included studies on the costs of shorter vs longer duration of antibiotics.	The panel considered whether the perspective of resource use differs by the perspective (eg, patient/caregiver, health system, payor); however, the overall decision was to consider a shorter course of antibiotics (less medication) as moderate savings compared with a longer course of antibiotics. The panel identified that the cost of antibiotics does increase by the dose.
Certainty of evidence of required resources What is the certainty of the evidence of resource requirements (costs)?		
JUDGMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
○ Very low ○ Low ○ Moderate ○ High • **No included studies**	There were no included studies on the costs of shorter vs longer duration of antibiotics.	

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Cost effectiveness Does the cost-effectiveness of the intervention favor the intervention or the comparison?		
JUDGMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
○ Favors the comparison ○ Probably favors the comparison ○ Does not favor either the intervention or the comparison • **Probably favors the intervention** ○ Favors the intervention ○ Varies ○ No included studies	There were no included studies on the cost effectiveness of shorter vs longer duration of antibiotics.	Equivalent clinical effectiveness?
Equity What would be the impact on health equity?		
JUDGMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
○ Reduced ○ Probably reduced ○ Probably no impact ○ Probably increased ○ Increased • **Varies** ○ Don't know	No research evidence was identified on the impact of antibiotic duration on health equity.	Are there groups or settings that might be disadvantaged by a recommendation for shorter vs longer antibiotics? Short course could result in a second prescription if they do not improve - revisit, additional pharmacy, cost. Issues around leftover medication. Children experiencing barriers to consistent health care access may not have a medical home for follow-up. Implementation considerations to support providers and patients. Panel identified situations in which equity may be increased by short course: cost. Panel identified situations in which equity may be decreased by short course: access to follow-up care, discrepancies in health literacy. How predictable are equity tradeoffs? Would most children experience increase in equity?
Acceptability Is the intervention acceptable to key interest holders?		
JUDGMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
○ No ○ Probably no • **Probably yes** ○ Yes ○ Varies ○ Don't know	One study (n = 953) examined the acceptability of antibiotic syrups, suspensions, and oral solutions prescribed to pediatric outpatients in France (Cohen 2009). They found that children rated amoxicillin–clavulanate generics as less "satisfactory" than the reference product, with treatment completion rates of 82.3% and 91.7% respectively. Cohen R, de La Rocque F, Lécuyer A, Wollner C, Bodin MJ, Wollner A. Study of the acceptability of antibiotic syrups, suspensions, and oral solutions prescribed to pediatric outpatients. *Eur J Pediatr*. 2009;168(7):851–857	The panel considered the following interest holder groups when considering their judgment on acceptability: • Patients • Parents/caregivers • Providers • Health system • Pharmacists • Antimicrobial stewardship teams Providers may be reluctant to change practice patterns; on the other hand, consciousness about antimicrobial stewardship is increasing. Older literature may overestimate issues with acceptability because attitudes around prescribing have changed over time. One panel member noted, "As a parent of a child who hates taking antibiotics, I'd be thrilled." In instances when patients have previously used longer courses, education and communication between caregiver and provider should occur explaining the change in regimen.

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Feasibility Is the intervention feasible to implement?		
JUDGMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
○ No ○ Probably no ○ Probably yes • **Yes** ○ Varies ○ Don't know	No research evidence was identified on the feasibility of shorter vs longer duration of antibiotics.	Possible reduction in feasibility associated with additional follow-up after shorter course—patients with no medical home will have to follow up in other settings (eg, urgent care). The panel's judgment was based on recognizing that if the treatment options are roughly equivalent clinically, there would not be a difference in necessary follow-up.

Summary of Judgments

	JUDGMENT						
Problem	No	Probably no	Probably yes	**Yes**		Varies	Don't know
Desirable Effects	Trivial	Small	**Moderate**	Large		Varies	Don't know
Undesirable Effects	**Trivial**	Small	Moderate	Large		Varies	Don't know
Certainty of evidence	Very low	**Low**	Moderate	High			No included studies
Values	Important uncertainty or variability	Possibly important uncertainty or variability	**Probably no important uncertainty or variability**	No important uncertainty or variability			
Balance of effects	Favors the comparison	Probably favors the comparison	Does not favor either the intervention or the comparison	**Probably favors the intervention**	Favors the intervention	Varies	Don't know
Resources required	Large costs	Moderate costs	Negligible costs and savings	**Moderate savings**	Large savings	Varies	Don't know
Certainty of evidence of required resources	Very low	Low	Moderate	High			**No included studies**
Cost effectiveness	Favors the comparison	Probably favors the comparison	Does not favor either the intervention or the comparison	**Probably favors the intervention**	Favors the intervention	Varies	No included studies
Equity	Reduced	Probably reduced	Probably no impact	Probably increased	Increased	**Varies**	Don't know
Acceptability	No	Probably no	**Probably yes**	Yes		Varies	Don't know
Feasibility	No	Probably no	Probably yes	**Yes**		Varies	Don't know

Type of Recommendation

Strong recommendation against the intervention	Conditional recommendation against the intervention	Conditional recommendation for either the intervention or the comparison	**Conditional recommendation for the intervention**	Strong recommendation for the intervention
○	○	○	○	○

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Conclusions

Recommendation

Key Action Statement 2: In children with UTI, the AAP Guideline Panel suggests a shorter course of antibiotic therapy (≤7 days) rather than a longer course of antibiotic therapy (>7 days) (conditional recommendation, low certainty of evidence).
Remarks for Key Action Statement 2:
• Low-risk children
  ○ The panel suggests a 3- to 5-day course of antibiotics for children 2 years and older with no known underlying anatomic abnormalities of the urinary tract presenting with nonfebrile UTI with referred urinary symptoms suggestive of cystitis (specifically urinary urgency and incontinence, dysuria, or urinary frequency).
  ○ The panel suggests a 5- to 7–day course of antibiotics for children 2 months to 24 months of age with UTI.
• The panel suggests a 5- to 7-day course of antibiotics for children 2 years and older with no known underlying anatomic abnormalities of the urinary tract presenting with signs and symptoms concerning for pyelonephritis (eg, fever ≥102.2° F).
• High-risk children
  ○ A more prolonged antimicrobial course (>7 days) may be provided for infants 8 days to 2 months of age; children with underlying anatomic genitourinary abnormalities; children who have associated bacteremia; or children who do not respond (with resolved or resolving signs and symptoms) to their initial antimicrobial course.

Justification
Subgroup considerations
Implementation considerations
• Education for parents and practitioners about shorter course • Acknowledge variability in provider acceptability during implementation • To improve feasibility of a shorter course of treatment for patients without a medical home, address with after-care instructions
Monitoring and evaluation
Research priorities
• Studies assessing the effectiveness of antibiotic duration in children <2 months • Future research on the cut off the very short course (3–5 days) for children only over 2 months of age, given they did not include that age range in those RCTs • Data for 3 days, especially in preverbal children (1 year old) • Disaggregated age data and pyelonephritis/cystitis

APPENDIX TABLE 3. EVIDENCE-TO-DECISIONS TABLE FOR ORAL VS PARENTERAL OR SEQUENTIAL ANTIBIOTICS TO TREAT UTI IN CHILDREN

Question

Should oral antibiotics vs parenteral or sequential antibiotics be used for children being treated for UTI?	
POPULATION:	children being treated for UTI
INTERVENTION:	oral antibiotics
COMPARISON:	parenteral or sequential antibiotics
MAIN OUTCOMES:	Recurrent UTI - RCT; Recurrent UTI - NRS; Adverse events; New renal scarring
SETTING:	
PERSPECTIVE:	Clinical recommendation – individual perspective
BACKGROUND:	
CONFLICT OF INTERESTS:	

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Assessment

Problem Is the problem a priority?		
JUDGMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
○ No ○ Probably no ○ Probably yes • **Yes** ○ Varies ○ Don't know	Urinary tract infection (UTI) is one of the most common bacterial infections of childhood. Among febrile infants, unwell children in general practice, and older children with urinary symptoms, 6%–8% will have a UTI. Over 30% of children with UTI will have recurrent UTI. Common risk factors for recurrence include vesicoureteral reflux (VUR) and bladder–bowel dysfunction (BBD). Oral antibiotics are effective in many cases. Previous Cochrane reviews suggest that 2–4 days courses are as effective for uncomplicated cystitis as 7–14 days, while single dose therapy is less effective. Younger and sicker children may require initial intravenous therapy. Kaufman J, Temple-Smith M, Sanci L. Urinary tract infections in children: an overview of diagnosis and management. *BMJ Paediatr Open*. 2019;3(1):e000487	
Desirable Effects How substantial are the desirable anticipated effects?		
JUDGMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
○ Trivial ○ Small ○ Moderate • **Large** ○ Varies ○ Don't know	Studies (NRS) reporting on infants with bacteremic UTI: Desai 2019: aRD: 3% (95% CI: -5.8 to 12.7) Olson 2022: 30-day revisit early oral conversion vs long-course IV therapy aOR: 4.22 (90% CI: 0.83, 21.34). *See Supplemental File Table 7*	A new study (Montini 2023) included in the pooled analysis investigated oral vs sequential antibiotics in a younger population (median 9 months) and found that oral antibiotics were non-inferior to sequential (parenteral to oral) in this group. IV may be standard of care Anticipated hesitancy to use oral regardless of available data 5% threshold proposed for minimal important difference for outcome rUTI Special groups: • <2 months • Bacteremic UTI • Sepsis • No tolerance for PO meds AAP febrile infant guidelines - recommend for IV <28 days https://publications.aap.org/pediatrics/article/148/2/e2021052228/179783/Clinical-Practice-Guideline-Evaluation-and?autologincheck=redirected Research priority: <2 months Panel discussed potential harms of IV/parenteral or sequential therapy - averting these harms is a desirable outcome (see additional considerations about undesirable effects)
Undesirable Effects How substantial are the undesirable anticipated effects?		
JUDGMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
• **Trivial** ○ Small ○ Moderate ○ Large ○ Varies ○ Don't know	A research report from PCORI found that problems from a PICC were common among children receiving intravenous antibiotics in the hospital setting. Side effects also occurred more often with a PICC than with antibiotics taken by mouth. Children with a PICC were more likely to go to the emergency department. They were also more likely to end up back in the hospital. The reason was usually problems from the PICC.	2 studies reported on vomiting leading to treatment discontinuation in the oral antibiotics group. Are any adverse events for oral or sequential/parenteral antibiotics not captured? • Peripheral IV infiltrates • Compliance of oral meds

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	Keren R, Localio R, Rangel S, Shah S, Srivastava R, Hall M. For children discharged after hospitalization for serious bacterial infections, are orally administered antibiotics as effective as antibiotics given intravenously through a PICC? *PCORI Final Res Rep.* 2018; https://doi.org/10.25302/11.2018.CER.526 *See Supplemental File Table 7*	• Gut flora Hospitalization as an undesirable effect • Harms of febrile infant hospitalizations: https://publications.aap.org/hospitalpediatrics/article/8/12/746/26559/Length-of-Stay-and-Complications-Associated-With • https://publications.aap.org/pediatrics/article/111/3/617/79879/Hospital-Reported-Medical-Errors-in-Children https://www.britishjournalofnursing.com/content/pivc-complications/complications-of-peripheral-intravenous-catheters-and-risk-factors-for-infiltration-and-phlebitis-in-children/#:~:text=The%20study%20covered%20244%20patients,8.7%20%25%20and%2015.8%25%20respectively https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5735659/ SR on oral absorption of PO abx in neonates: https://pubmed.ncbi.nlm.nih.gov/31236572/ Research priority: Would note that adverse events/adherence to course should be a research topic as evidence is significantly lacking Special consideration for younger age group: Unsure how neonatal/maturing nephron concentrates antibiotics in urine

Certainty of evidence
What is the overall certainty of the evidence of effects?

JUDGMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
• **Very low** ○ Low ○ Moderate ○ High ○ No included studies	Certainty is very low because of issues with risk of bias and imprecision.	Infants <2 months are not well-represented in the literature

Values
Is there important uncertainty about or variability in how much people value the main outcomes?

JUDGMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Important uncertainty or variability ○ Possibly important uncertainty or variability ○ Probably no important uncertainty or variability • **No important uncertainty or variability**	No studies were identified that described parent or child values related to the outcomes of interest (recurrent UTI, renal scarring, adverse events).	IV antibiotics require hospitalization

Balance of effects
Does the balance between desirable and undesirable effects favor the intervention or the comparison?

JUDGMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Favors the comparison ○ Probably favors the comparison ○ Does not favor either the intervention or the comparison • **Probably favors the intervention – children <2 mos** • **Favors the intervention – children >2 mos**		DESIRABLE: large UNDESIRABLE: trivial CERTAINTY: very low VALUES: no important uncertainty or variability Panel considered additional harms associated with IV administration and hospitalization

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○ Varies ○ Don't know		
Resources required How large are the resource requirements (costs)?"		
JUDGMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
○ Large costs ○ Moderate costs ○ Negligible costs and savings ○ Moderate savings • **Large savings** ○ Varies ○ Don't know	While no studies were identified that described the cost of oral antibiotics vs parenteral/sequential, parenteral antibiotics generally require a hospital admission for administration, which incurs substantial cost.	Cost of hospitalization is substantial Cost of oral antibiotics is minimal
Certainty of evidence of required resources What is the certainty of the evidence of resource requirements (costs)?		
JUDGMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
○ Very low ○ Low ○ Moderate ○ High • **No included studies**	There were no included studies.	
Cost effectiveness Does the cost-effectiveness of the intervention favor the intervention or the comparison?		
JUDGMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
○ Favors the comparison ○ Probably favors the comparison ○ Does not favor either the intervention or the comparison ○ Probably favors the intervention • **Favors the intervention** ○ Varies ○ No included studies	No studies identified.	Health Care Costs and Utilization Project data on hospital costs for children: https://hcup-us.ahrq.gov/reports/statbriefs/sb299-Hospital-Stays-Children-2019.jsp
Equity What would be the impact on health equity?		
JUDGMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
○ Reduced ○ Probably reduced ○ Probably no impact • **Probably increased** ○ Increased ○ Varies ○ Don't know	Parenteral antibiotics via intravenous routes require hospital administration and may cause additional burden to parents/guardians and children who may miss work and school. Antibiotic administration via subcutaneous routes may require time needed to manage multiple administrations of medications over several days. One study (n = 2881) measured the proportion of filled prescriptions following ED visits by children in aggregate and by patient race/ethnicity. They found that a third of antibiotic prescriptions for bacterial infections in the ED are unfilled. Hispanic children and children of other racial/ethnic groups have lower rates of prescription filling compared with non-Hispanic white children. Interpreter use and uninsured status also have lower rates of prescription filling. Berkowitz D, Breslin K, Croskey A, Badolato G, Goyal MK. Racial and ethnic differences in prescription filling after discharge from an urban pediatric emergency department. *Pediatr Emerg Care*. 2022;38(1):e117-e120	There may be inequities associated with IV treatment routes, as differential treatment in the hospital setting may disproportionately affect children and families facing barriers to health care access, transportation, financial resources, or reliable follow-up care. Study on oral antibiotic compliance: https://pubmed.ncbi.nlm.nih.gov/36317476/ Although not specific to antibiotic route, children who are white non-Hispanic, those with English as primary language, those on commercial insurance are more likely to be prescribed broader range, non-first line antibiotics compared with their counterparts for common infections. (Kim C, Kabbani S, Dube WC, et al. Health equity and antibiotic prescribing in the united states: a systematic scoping review. *Open Forum Infect Dis*. 2023;10(9):ofad440; Goyal MK, Johnson TJ, Chamberlain JM, et al; Pediatric Care Applied Research Network (PECARN). Racial and ethnic differences in antibiotic use for viral illness in emergency departments. *Pediatrics*. 2017;140(4):e20170203El Feghaly RE, Sainz LE, Lee BR, et al; For REDUCE (Reducing Differences in

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		Urgent Care Encounters – Antibiotic Choice) Collaborative. Sociodemographic differences in treatment of acute respiratory infections in pediatric urgent cares. *Infect Control Hosp Epidemiol*. 2024 Dec 3:1–9. Doi: 10.1017/ice.2024.196; Nedved AC, Lee BR, Wirtz A, Monsees E, Burns A, Turcotte Benedict FG, El Feghaly RE. Socioeconomic differences in antibiotic use for common infections in pediatric urgent-care centers-A quasi-experimental study. *Infect Control Hosp Epidemiol*. 2023;44 (12):2009–2016). Half of US children do not have a medical home. Impact on access and follow-up. Increased risk of non-adherence may be differential based on socio-economic factors. Hospitalization will likely be more burdensome for families facing financial, transportation, childcare, employment, or follow-up care barriers.

Acceptability
Is the intervention acceptable to key interest holders?

JUDGMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ No ○ Probably no • **Probably yes – children <2 mos** • **Yes – children >2 mos** ○ Varies ○ Don't know	Parenteral administration routes often cause pain for intramuscular injection or IV catheter insertion, and IV administration also may restrict movement during administration and admissions for the duration. Some children may find the taste of oral antibiotics unpalatable. Would some parents and guardians prefer a one-time intramuscular antibiotic shot rather than an oral medication given several times a day over several times a day? One study (n = 953) examined the acceptability of antibiotic syrups, suspensions, and oral solutions prescribed to pediatric outpatients in France (Cohen 2009). They found that children rated amoxicillin–clavulanate generics as less "satisfactory" than the reference product, with treatment completion rates of 82.3% and 91.7%, respectively. Cohen R, de La Rocque F, Lécuyer A, Wollner C, Bodin MJ, Wollner A. Study of the acceptability of antibiotic syrups, suspensions, and oral solutions prescribed to pediatric outpatients. *Eur J Pediatr*. 2009;168(7):851–857 **Antibiotic resistance:** Albaramki 2019 (n = 243) matched children with ESBL-producing bacteria UTI (46%) with controls with non-ESBL-producing bacteria UTI of the same age and gender. They found that potential risk factors for ESBL-UTI were previous use of antibiotics in the last 3 months, previous hospitalization in the last 3 months, history of recurrent UTI, and presence of renal anomalies. There was higher resistance to amoxicillin-clavulanate, amikacin, gentamicin, and quinolones in the ESBL group compared with the control group. Albaramki JH, Abdelghani T, Dalaeen A, et al. Urinary tract infection caused by extended-spectrum β-lactamase-producing bacteria: risk factors and antibiotic resistance. *Pediatr Int*. 2019;61(11):1127–1132	Interest holders: • Providers • Pharmacists • Health system • Patients • Caregivers

Feasibility
Is the intervention feasible to implement?

JUDGMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ No ○ Probably no ○ Probably yes • **Yes** ○ Varies ○ Don't know	No research evidence identified.	Is parenteral administration feasible for all children with UTI? Special groups: • Tube feeding • Intolerance to oral antibiotics • Contraindication

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Summary of Judgments

	JUDGMENT						
PROBLEM	No	Probably no	Probably yes	**Yes**		Varies	Don't know
DESIRABLE EFFECTS	Trivial	Small	Moderate	**Large**		Varies	Don't know
UNDESIRABLE EFFECTS	**Trivial**	Small	Moderate	Large		Varies	Don't know
CERTAINTY OF EVIDENCE	**Very low**	Low	Moderate	High			No included studies
VALUES	Important uncertainty or variability	Possibly important uncertainty or variability	Probably no important uncertainty or variability	**No important uncertainty or variability**			
BALANCE OF EFFECTS	Favors the comparison	Probably favors the comparison	Does not favor either the intervention or the comparison	**Probably favors the intervention (children <2 mos)**	**Favors the intervention (children >2 mos)**	Varies	Don't know
RESOURCES REQUIRED	Large costs	Moderate costs	Negligible costs and savings	Moderate savings	**Large savings**	Varies	Don't know
CERTAINTY OF EVIDENCE OF REQUIRED RESOURCES	Very low	Low	Moderate	High			**No included studies**
COST EFFECTIVENESS	Favors the comparison	Probably favors the comparison	Does not favor either the intervention or the comparison	Probably favors the intervention	**Favors the intervention**	Varies	No included studies
EQUITY	Reduced	Probably reduced	Probably no impact	**Probably increased**	Increased	Varies	Don't know
ACCEPTABILITY	No	Probably no	**Probably yes (children < 2mos)**	**Yes (children > 2mos)**		Varies	Don't know
FEASIBILITY	No	Probably no	Probably yes	**Yes**		Varies	Don't know

Type of Recommendation

Strong recommendation against the intervention	Conditional recommendation against the intervention	Conditional recommendation for either the intervention or the comparison	Conditional recommendation for the intervention	Strong recommendation for the intervention
○	○	○	○	○

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Conclusions

Recommendation
Key Action Statement 3A: In children 8 to 28 days of age in whom a UTI has been diagnosed, the AAP Guideline Panel suggests parenteral antibiotics with early transition to oral following clinical improvement rather than parenteral antibiotics alone (conditional recommendation, very low certainty of evidence). Key Action Statement 3B: In children older than 28 days and younger than 5 years with UTI, the AAP Guideline Panel recommends oral antibiotics rather than parenteral or sequential antibiotics requiring hospitalization (strong recommendation, very low certainty of evidence). Remarks for Key Action Statement 3B: • The panel defines sequential antibiotics as initial parenteral antibiotics that are subsequently transitioned to oral. • In children older than 28 days who are able to tolerate oral antibiotics and who do not otherwise require hospitalization, outpatient therapy is encouraged. • Examination of the evidence suggests equivalent outcomes between oral and parenteral/sequential antibiotics with regards to outcomes of renal scarring and short-term recurrence of infection (eg, treatment failure). The use of parenteral antibiotics is, however, associated with several undesirable outcomes, including hospitalization, pain from IV placement, potential for extravasation injury, increased cost, in addition to potential complications associated with peripherally inserted central catheter (PICC) lines, which include infection and clotting. This constellation of harms associated with parenteral antibiotics warrants a strong recommendation against their routine use. • Should clinicians have concerns about the ability of families to promptly obtain oral antibiotics from an outpatient pharmacy, a single dose of parenteral antibiotics may be given prior to transition to oral antibiotics.
Justification
Subgroup considerations
Implementation considerations
Monitoring and evaluation
Research priorities
• Studies assessing the desirable effects of oral antibiotics vs parenteral or sequential antibiotics in children <2 months • Studies assessing the adverse events and adherence to antibiotics course

APPENDIX TABLE 4. EVIDENCE-TO-DECISIONS TABLE FOR RENAL AND BLADDER ULTRASONOGRAPHY TO DIAGNOSE VESICOURETERAL REFLUX

Question

Should renal and bladder ultrasonography (RBUS) be used to diagnose vesicoureteral reflux (VUR) in children <5 y in whom a first UTI is diagnosed?	
POPULATION:	Children <5 y in whom a first UTI is diagnosed
INTERVENTION:	RBUS
PURPOSE OF THE TEST:	Diagnosis of VUR Diagnosis of any structural abnormalities including VUR
ROLE OF THE TEST:	RBUS may be performed to identify findings that increase suspicion of VUR, or any structural abnormalities
LINKED TREATMENTS:	Antibiotic prophylaxis, surgical or endoscopic correction of VUR, monitoring/surveillance
ANTICIPATED OUTCOMES:	Recurrent UTI, renal scarring
SETTING:	Primary care/general pediatrics
PERSPECTIVE:	Clinical recommendation – Individual perspective
BACKGROUND:	
SUBGROUPS:	N/A
CONFLICT OF INTERESTS:	

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Assessment

Problem Is the problem a priority?		
JUDGMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
○ No ○ Probably no ○ Probably yes • Yes ○ Varies ○ Don't know		
Test accuracy How accurate is the test?		
JUDGMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
○ Very inaccurate • Inaccurate ○ Accurate ○ Very accurate ○ Varies ○ Don't know	**Test accuracy** RBUS Sensitivity: 0.49 (95% CI: 0.42 to 0.57) Specificity: 0.70 (95% CI: 0.64 to 0.76) *See Supplemental File Table 8*	Sensitivity, specificity varies Positive/abnormal result Negative/normal result **What is the accuracy of RBUS to identify any structural abnormalities - including VUR - after first UTI:** • Noninvasive, sensitive, available point-of-care • Best available test for many structural problems • Prenatal RBUS (age consideration)
Desirable Effects How substantial are the desirable anticipated effects?		
JUDGMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
○ Trivial • **Small – performing RBUS for VUR after first UTI** • **Moderate – performing RBUS for any structural abnormality after first UTI** ○ Large ○ Varies ○ Don't know	No research evidence was identified on the desirable effects of RBUS after first UTI.	Age consideration: <2 y, ≥2 y **What are desirable effects of performing RBUS for any structural abnormalities - including VUR - after first UTI?** • There are desirable effects unrelated to VUR: identifying other structural anomalies; judgment would be different considering these effects Regardless of RBUS results, voiding cystourethrography (VCUG) may still be performed Wait time for VCUG; RBUS provides information in the meantime that may guide management or reassure
Undesirable Effects How substantial are the undesirable anticipated effects?		
JUDGMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
○ Trivial ○ Small • **Moderate** ○ Large ○ Varies ○ Don't know	False positive: Rate of recurrent UTI with no intervention (Q10EP) False positive: Children undergo VCUG One study (Juliano 2013) found that out of 95 patients with normal RBUS, 84 underwent voiding cystourethrography. Despite normal RBUS, 23 of 84 patients (24%) had dilating vesicoureteral reflux. Of the 95 patients with normal RBUS 14 (15%) had recurrent pyelonephritis and 7 (7%) went on to surgical intervention. Another study (Oh 2010) of 227 children with a first febrile UTI, therapeutic delay time and presence of reflux were predictive of acute scintigraphic lesion and ultimate scar formation. Another study (Spencer 2012) divided children ages <18 y with febrile UTI (n = 152) into 2 cohorts: those who had a VCUG performed within 1 week of diagnosis (early VCUG cohort) and those who had a VCUG performed more than	Consequences of: • False negative - missed diagnosis of VUR • False positive - unnecessary VCUG, stress/fear, burden of appointments • True positive - overdiagnosis

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	1 week after diagnosis (late VCUG cohort). The incidence and severity of VUR were similar in patients that underwent early and late VCUG testing. Patients who underwent early VCUG testing showed no sign of worsening illness after the test was performed. During the 5-year follow up, these patients did not have higher rates of return emergency department visits or hospital readmission compared with those who received late VCUG testing. Patients who underwent early VCUG testing did not develop signs or symptoms of urosepsis. Furthermore, there were no differences in median maximal temperature before and after early testing. Routh et all reported an effective radiation dose of 0.72 mSV per patient for a top-down (RBUS + VCUG) approach. Juliano TM, Stephany HA, Clayton DB, et al. Incidence of abnormal imaging and recurrent pyelonephritis after first febrile urinary tract infection in children 2 to 24 months old. *J Urol.* 2013;190(4 Suppl):1505–1510 Oh MM, Cheon J, Kang SH, Park HS, Lee JG, Moon du G. Predictive factors for acute renal cortical scintigraphic lesion and ultimate scar formation in children with first febrile urinary tract infection. *J Urol.* 2010;183(3):1146–1150 Spencer JD, Bates CM, Mahan JD, et al. The accuracy and health risks of a voiding cystourethrogram after a febrile urinary tract infection. *J Pediatr Urol.* 2012;8(1):72–76 Routh JC, Grant FD, Kokorowski PJ, et al. Economic and radiation costs of initial imaging approaches after a child's first febrile urinary tract infection. *Clin Pediatr (Phila).* 2012;51(1):23–30	
Certainty of the evidence of test accuracy What is the overall certainty of the evidence of test accuracy?		
JUDGMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
○ Very low • Low ○ Moderate ○ High ○ No included studies	Concerns with inconsistency and imprecision when RBUS is used for diagnosis of reflux.	
Certainty of the evidence of test's effects What is the overall certainty of the evidence for any critical or important direct benefits, adverse effects, or burden of the test?		
JUDGMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
○ Very low ○ Low ○ Moderate ○ High • No included studies		Direct benefit/harm of test - not applicable because this test does not have direct consequences for health
Certainty of the evidence of management's effects What is the overall certainty of the evidence of effects of the management that is guided by the test results?		
JUDGMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
○ Very low • Low ○ Moderate ○ High ○ No included studies	One study (Hannula 2012) found that patients with a renal parenchymal defect on RBUS experienced the following outcomes more often than patients without renal parenchymal defect: • UTI recurrence (18/22 patients [82%] vs 51/128 patients [40%], respectively; difference, 42%; 95% CI, 20%–56%) • Received antibiotic prophylaxis (21/22 patients [95%] vs 77/128 patients [60%], respectively; difference, 35%; 95% CI, 17%–46%)	Downstream health outcomes of VUR treatment (antibiotics, endoscopic correction) VUR prophylaxis certainty of evidence (CoE) + other management pathways Assumption that management proceeds appropriately

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	• Had urinary tract surgery (15/22 patients [68%] vs 27/128 patients [21%], respectively; difference, 47%; 95% CI, 25%–64%) When comparing antibiotic prophylaxis (n = 69), endoscopic injection (n = 66) or surveillance (n = 68) for management of VUR, the Swedish reflux trial found that in girls, UTI recurrence rate was 19% with prophylaxis, 23% with endoscopic treatment, and 57% with surveillance. In boys, there was no difference between treatment groups. New renal damage was seen in 13 girls: 8 under surveillance, 5 in the endoscopic group and none on prophylaxis, and in 2 boys. In 13 children with no or nondilating VUR after 1 injection, dilating VUR reappeared at the 2-year follow up. Hannula A, Perhomaa M, Venhola M, Pokka T, Renko M, Uhari M. Long-term follow-up of patients after childhood urinary tract infection. *Arch Pediatr Adolesc Med.* 2012;166(12):1117–1122 Brandström P, Jodal U, Sillén U, Hansson S. The Swedish reflux trial: review of a randomized, controlled trial in children with dilating vesicoureteral reflux. *J Pediatr Urol.* 2011;7(6):594–600	
Certainty of the evidence of test result/management How certain is the link between test results and management decisions?		
JUDGMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
○ Very low • Low ○ Moderate ○ High ○ No included studies		Is every patient with a diagnosis of VUR going to receive the same treatment?
Certainty of effects What is the overall certainty of the evidence of effects of the test?		
JUDGMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
○ Very low • Low ○ Moderate ○ High ○ No included studies		
Values Is there important uncertainty about or variability in how much people value the main outcomes?		
JUDGMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
• Important uncertainty or variability ○ Possibly important uncertainty or variability ○ Probably no important uncertainty or variability ○ No important uncertainty or variability	No research evidence was identified regarding parent/caregiver or patient values about the main outcomes.	Values around false-negative and false-positive results, recurrent UTI, renal scarring Anxiety about getting a test and not getting a test 2011 CPG: "Because ultrasonography is noninvasive and poses minimal risk, we assume that parents will prefer RBUS over taking even a small risk of missing a serious and correctable condition." The panel made this judgment based on a parent/patient perspective (intended beneficiaries of the recommendation). Caregiver representative noted variability • RBUS has burden of time, transportation, but the test itself is less invasive • Distinction between VUR and general abnormalities may not drive decisions for parents/caregivers; contingent on framing by clinician

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Balance of effects Does the balance between desirable and undesirable effects favor the intervention or the comparison?		
JUDGMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
○ Favors the comparison • Probably favors the comparison – **RBUS for VUR** ○ Does not favor either the intervention or the comparison • Probably favors the intervention – **RBUS for any structural abnormalities in children >2 y/o** • Favors the intervention – **RBUS for any structural abnormalities in children <2 y/o** ○ Varies ○ Don't know		The panel voted to judge this criterion based on toilet training/age. Post-toilet training is when voiding dysfunction/BBD can become apparent.
Resources required How large are the resource requirements (costs)?		
JUDGMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
○ Large costs • Moderate costs ○ Negligible costs and savings ○ Moderate savings ○ Large savings ○ Varies ○ Don't know	One study (Raju 2012) estimated costs to the health care system by averaging per-patient hospital costs as follows. • Ultrasound: $231.31 • Office visit: $64.16 Another study (Routh 2012) estimated costs per-patient and per 100,00 patients as follows: • Ultrasound: $226 per 1yo child • Direct imaging-related costs, per 100,000 patients for a top-down (RUS + VCUG) approach: $82.9 to $105.5 million _____ Raju GA, Marks AJ, Benoit RM, Docimo SG. Models of care for vesicoureteral reflux with and without an end point of reflux resolution: a computer cost analysis. *J Urol.* 2013;189 (6):2287–2292 Routh JC, Grant FD, Kokorowski PJ, et al. Economic and radiation costs of initial imaging approaches after a child's first febrile urinary tract infection. *Clin Pediatr (Phila).* 2012;51(1):23–30	Direct costs (eg, RBUS costs, technician, radiologist) Answered based on costs to an individual patient
Certainty of evidence of required resources What is the certainty of the evidence of resource requirements (costs)?		
JUDGMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
○ Very low ○ Low ○ Moderate ○ High • No included studies		
Cost effectiveness Does the cost-effectiveness of the intervention favor the intervention or the comparison?		
JUDGMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
○ Favors the comparison • Probably favors the comparison ○ Does not favor either the intervention or the comparison	One study found that among children ages 2–24 months after a first febrile UTI, 91 patients would need to be screened with RBUS to prevent 1 recurrent UTI. RBUS increases per quality-adjusted life-years (QALYs) by +0.0002 per patient screened, corresponding to an incremental cost-effectiveness ratio of $803,000 per QALY gained. Typical	

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○ Probably favors the intervention ○ Favors the intervention ○ Varies ○ No included studies	thresholds for cost-effective interventions are below $100,000 per QALY gained. Gaither TW, Selekman R, Kazi DS, Copp HL. Cost-effectiveness of screening ultrasound after a first, febrile urinary tract infection in children age 2–24 months. *J Pediatr*. 2020;216:73–81.e1	
Equity What would be the impact on health equity?		
JUDGMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
○ Reduced ○ Probably reduced ○ Probably no impact ○ Probably increased ○ Increased • Varies ○ Don't know	No research evidence was identified on the impact of RBUS after first UTI on health equity.	Are there groups or settings that might be disadvantaged in relation to the problem or options that are considered? Based on an assumption that recommendation for US will result in adherence Lack of medical home Un- or underinsured Would recommendation for RBUS increase access? Identification of abnormalities may increase equity for children who were not screened for them prenatally (because of disadvantages)
Acceptability Is the intervention acceptable to key Interest holders?		
JUDGMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
○ No ○ Probably no ○ Probably yes • Yes ○ Varies ○ Don't know	No research evidence was identified on the acceptability of RBUS after first UTI to key interest holders.	2011 CPG: "Because ultrasonography is noninvasive and poses minimal risk, we assume that parents will prefer RBUS over taking even a small risk of missing a serious and correctable condition." Other interest holders: • Do not include payers
Feasibility Is the intervention feasible to implement?		
JUDGMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
○ No ○ Probably no ○ Probably yes • Yes ○ Varies ○ Don't know	No research evidence was identified on the feasibility of RBUS after first UTI.	Referral patterns Lack of medical home Lack of structure to collect UTI history

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Summary of Judgments

	JUDGMENT						
PROBLEM	No	Probably no	Probably yes	**Yes**		Varies	Don't know
TEST ACCURACY	Very inaccurate	**Inaccurate**	Accurate	Very accurate		Varies	Don't know
DESIRABLE EFFECTS	Trivial	**Small – performing RBUS for VUR after first UTI**	**Moderate – performing RBUS for any structural abnormality after first UTI**	Large		Varies	Don't know
UNDESIRABLE EFFECTS	Trivial	Small	Moderate	Large		Varies	Don't know
CERTAINTY OF THE EVIDENCE OF TEST ACCURACY	Very low	**Low**	Moderate	High			No included studies
CERTAINTY OF THE EVIDENCE OF TEST'S EFFECTS	Very low	Low	Moderate	High			**No included studies**
CERTAINTY OF THE EVIDENCE OF MANAGEMENT'S EFFECTS	Very low	**Low**	Moderate	High			No included studies
CERTAINTY OF THE EVIDENCE OF TEST RESULT/ MANAGEMENT	Very low	**Low**	Moderate	High			No included studies
CERTAINTY OF EFFECTS	Very low	**Low**	Moderate	High			No included studies
VALUES	**Important uncertainty or variability**	Possibly important uncertainty or variability	Probably no important uncertainty or variability	No important uncertainty or variability			
BALANCE OF EFFECTS	Favors the comparison	**Probably favors the comparison – RBUS for VUR**	Does not favor either the intervention or the comparison	**Probably favors the intervention – RBUS for any structural abnormalities in children >2 y/o**	**Favors the intervention – RBUS for any structural abnormalities in children <2 y/o**	Varies	Don't know
RESOURCES REQUIRED	Large costs	**Moderate costs**	Negligible costs and savings	Moderate savings	Large savings	Varies	Don't know
CERTAINTY OF EVIDENCE OF REQUIRED RESOURCES	Very low	Low	Moderate	High			**No included studies**
COST EFFECTIVENESS	Favors the comparison	**Probably favors the comparison**	Does not favor either the intervention or the comparison	Probably favors the intervention	Favors the intervention	Varies	No included studies
EQUITY	Reduced	Probably reduced	Probably no impact	Probably increased	Increased	**Varies**	Don't know
ACCEPTABILITY	No	Probably no	Probably yes	**Yes**		Varies	Don't know
FEASIBILITY	No	Probably no	Probably yes	**Yes**		Varies	Don't know

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Type of Recommendation

Strong recommendation against the intervention	Conditional recommendation against the intervention	Conditional recommendation for either the intervention or the comparison	Conditional recommendation for the intervention	**Strong recommendation for the intervention**
○	○	○	○	○

Conclusions

Recommendation
Key Action Statement 4: In children younger than 5 years in whom a first febrile UTI is diagnosed, the AAP Guideline Panel recommends performing renal and bladder ultrasound (RBUS), rather than not performing RBUS, to detect structural abnormalities or findings associated with VUR, not to detect VUR itself (strong recommendation, low certainty of evidence of the clinical impact of the detected abnormalities on RBUS, low certainty of evidence for ultrasound detection of VUR). Remark for Key Action Statement 4: Although RBUS is the standard of care for detection of congenital or structural anomalies, there is low certainty about the frequency of RBUS detecting a clinically important anomaly. The panel believes, however, that identifying infrequent RBUS abnormalities benefits the proportion of patients who are ultimately identified.
Justification
Subgroup considerations
Implementation considerations
Monitoring and evaluation
Research priorities

APPENDIX TABLE 5. EVIDENCE-TO-DECISIONS TABLE FOR VOIDING CYSTOURETHROGRAPHY TO DIAGNOSE VESICOURETERAL REFLUX

Question

Should voiding cystourethrography (VCUG) be used to diagnose vesicoureteral reflux (VUR) in children <5 y in whom a first UTI is diagnosed?	
POPULATION:	Children <5 y in whom at least one UTI has been diagnosed
INTERVENTION:	Voiding cystourethrography (VCUG) after first UTI vs VCUG after second UTI
PURPOSE OF THE TEST:	Diagnosis of vesicoureteral reflux (VUR)
ROLE OF THE TEST:	VCUG may follow ultrasonography with findings that increase suspicion of VUR or be ordered regardless of ultrasonography results for diagnosis of VUR
LINKED TREATMENTS:	Antibiotic prophylaxis, surgical or endoscopic correction of VUR, monitoring/surveillance
ANTICIPATED OUTCOMES:	Recurrent UTI, renal scarring
SETTING:	Primary care/general pediatrics
PERSPECTIVE:	Clinical recommendation – individual perspective
BACKGROUND:	
SUBGROUPS:	N/A
CONFLICT OF INTERESTS:	

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Assessment

Problem Is the problem a priority?		
JUDGMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
○ No ○ Probably no ○ Probably yes • **Yes** ○ Varies ○ Don't know		Comparison was decided to be VCUG for first UTI vs VCUG for second UTI. All judgments were based on this comparison.
Test accuracy How accurate is the test?		
JUDGMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
○ Very inaccurate ○ Inaccurate ○ Accurate • **Very accurate** ○ Varies ○ Don't know	*Test accuracy* VCUG is the reference standard; we assumed 100% accuracy for diagnosis of VUR	**Consequences of:** • True positives • False negatives • True negatives • Falst positives 2011 CPG: "there are no clinical or laboratory indicators that have been demonstrated to identify infants with high-grade VUR." VUR prevalence (first UTI): • Grades IV-V: 6% • Grades I-III: 29% • All: 35% VCUG is very accurate in detecting any reflux, but there is variability in the grading
Desirable Effects How substantial are the desirable anticipated effects?		
JUDGMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
• **Trivial** ○ Small ○ Moderate ○ Large ○ Varies ○ Don't know	No research evidence was identified regarding the desirable effects of VCUG for first vs second UTI.	Assumption: comparator is no VCUG after first UTI, not no VCUG ever Assumption: documented UTI per panel definition Assumption: febrile UTI indicates pyelonephritis; decision is based on suspected pyelonephritis Age cutoff options: none, toilet training vs not, 2 y, 2 mo - 14/14 no cutoff for EtD criteria Cognitive development is also a consideration - psychological impact What are other desirable effects? • Rule out VUR (negative VCUG) • May be able to reduce risk of another UTI and downstream consequences, eg, hospitalization • Alleviate anxiety about future risk of another UTI
Undesirable Effects How substantial are the undesirable anticipated effects?		
JUDGMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
○ Trivial ○ Small • **Moderate** ○ Large ○ Varies ○ Don't know	One study (Oh 2010) of 227 children with a first febrile UTI, therapeutic delay time and presence of reflux were predictive of acute scintigraphic lesion and ultimate scar formation. Another study (Spencer 2012) divided children aged <18 years with febrile UTI (n = 152) into 2 cohorts: those who had a VCUG performed within 1 week of diagnosis (early VCUG cohort) and those who had a VCUG performed more than 1 week after	Undesirable effects: • Unnecessary testing • Burden of test: pain, stress, anxiety • Radiation exposure • Overdiagnosis (reflux that would have resolved without treatment)

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	diagnosis (late VCUG cohort). The incidence and severity of VUR were similar in patients that underwent early and late VCUG testing. Patients who underwent early VCUG testing showed no sign of worsening illness after the test was performed. During the 5-year follow-up, these patients did not have higher rates of return emergency department visits or hospital readmission compared to those who received late VCUG testing. Patients who underwent early VCUG testing did not develop signs or symptoms of urosepsis. Furthermore, there were no differences in median maximal temperature before and after early testing. A comparison (n = 111) of spot films vs photofluorography VCUG reported radiation doses between 10.75 mGycm2 (photofluorography DAP in children with mean weight 6.4 kg) to 97.13 mGycm2 (spot film DAP in children with mean weight 12.2 kg). (Malekzadeh 2012) _____ Oh MM, Cheon J, Kang SH, Park HS, Lee JG, Moon du G. Predictive factors for acute renal cortical scintigraphic lesion and ultimate scar formation in children with first febrile urinary tract infection. *J Urol*. 2010;183(3):1146–1150 Spencer JD, Bates CM, Mahan JD, et al. The accuracy and health risks of a voiding cystourethrogram after a febrile urinary tract infection. *J Pediatr Urol*. 2012;8(1):72–76 Malekzadeh M, Bahreyni Toossi MT, Alamdaran SA, Naseri M, Beheshtian A. Comparison between patient dose arising from photofluorographic and standard fluoroscopic voiding cystourethro graphy in children with urinary tract infection [corrected]. *Nephrourol Mon*. 2012;4(3):541–544	• Anxiety associated with diagnosis of VUR and prognosis • Diagnosis of VUR may lead to more aggressive treatment/ management of fever • Infection risk from catheterization

Certainty of the evidence of test accuracy
What is the overall certainty of the evidence of test accuracy?

JUDGMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Very low ○ Low ○ Moderate • **High** ○ No included studies	High certainty of test accuracy from evidence profile	VCUG is the reference standard for diagnosis of VUR

Certainty of the evidence of test's effects
What is the overall certainty of the evidence for any critical or important direct benefits, adverse effects, or burden of the test?

JUDGMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Very low • **Low** ○ Moderate ○ High ○ No included studies		Direct harm: • UTI • Radiation (population vs individual level - assumption is individual) • Psychological harm (post-traumatic stress disorder [PTSD])

Certainty of the evidence of management's effects
What is the overall certainty of the evidence of effects of the management that is guided by the test results?

JUDGMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Very low • **Low** ○ Moderate ○ High ○ No included studies	In children with grade III-IV VUR, when comparing antibiotic prophylaxis (n = 69), endoscopic injection (n = 66) or surveillance (n = 68) for management of VUR, the Swedish reflux trial found that in girls, UTI recurrence rate was 19% with prophylaxis, 23% with endoscopic treatment, and 57% with surveillance. In boys, there was no difference between treatment groups. New renal damage was seen in 13 girls: 8 under surveillance, 5 in the endoscopic group and none on prophylaxis, and in 2 boys. In 13 children with no or nondilating VUR after 1 injection, dilating VUR reappeared at the 2-year follow-up.	Downstream health outcomes of VUR treatment (antibiotics, endoscopy correction) 2011 CPG: "prompt diagnosis and effective treatment of a febrile UTI recurrence may be of greater importance regardless of whether VUR is present or the child is receiving antimicrobial prophylaxis." Consistent with ultrasonography

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	Brandström P, Jodal U, Sillén U, Hansson S. The Swedish reflux trial: review of a randomized, controlled trial in children with dilating vesicoureteral reflux. *J Pediatr Urol.* 2011;7(6):594–600	

Certainty of the evidence of test result/management
How certain is the link between test results and management decisions?

JUDGMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Very low • **Low** ○ Moderate ○ High ○ No included studies		Is every patient with VUR going to receive the same treatment? Practice variation Management of recurrent UTI after VCUG is performed

Certainty of effects
What is the overall certainty of the evidence of effects of the test?

JUDGMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Very low • **Low** ○ Moderate ○ High ○ No included studies		Overall certainty

Values
Is there important uncertainty about or variability in how much people value the main outcomes?

JUDGMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Important uncertainty or variability • **Possibly important uncertainty or variability** ○ Probably no important uncertainty or variability ○ No important uncertainty or variability	No research evidence was identified regarding parent/caregiver or patient values about the main outcomes.	Values around false-negatives/false-positives, recurrent UTI, renal scarring 2011 CPG: "The judgment of parents may come into play, because VCUG is an uncomfortable procedure involving radiation exposure. In some cases, parents may prefer to subject their children to the procedure even when the chance of benefit is both small and uncertain. Antimicrobial prophylaxis seems to be ineffective in preventing recurrence of febrile UTI/pyelonephritis for the vast majority of infants. Some parents may want to avoid VCUG even after the second UTI. Because the benefit of identifying high-grade reflux is still in some doubt, these preferences should be considered. It is the judgment of the committee that VCUG is indicated after the second UTI."

Balance of effects
Does the balance between desirable and undesirable effects favor the intervention or the comparison?

JUDGMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Favors the comparison • **Probably favors the comparison** ○ Does not favor either the intervention or the comparison ○ Probably favors the intervention ○ Favors the intervention ○ Varies ○ Don't know		Accuracy: Very accurate Desirable: Trivial Undesirable: Moderate Certainty of DTA: High Overall Certainty: Low Values: Possibly important uncertainty Subgroups: not applicable

Resources required
How large are the resource requirements (costs)?

JUDGMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Large costs • **Moderate costs**	No research evidence was identified regarding the required resources of VCUG for first vs second UTI.	Direct costs (eg, VCUG costs, technician, radiologist) Individual patient perspective

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○ Negligible costs and savings ○ Moderate savings ○ Large savings ○ Varies ○ Don't know		Odds of undergoing VCUG are decreased after second UTI, but cost of test does not change
Certainty of evidence of required resources What is the certainty of the evidence of resource requirements (costs)?		
JUDGMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
○ Very low ○ Low ○ Moderate ○ High • **No included studies**		
Cost effectiveness Does the cost-effectiveness of the intervention favor the intervention or the comparison?		
JUDGMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
○ Favors the comparison ○ Probably favors the comparison ○ Does not favor either the intervention or the comparison ○ Probably favors the intervention ○ Favors the intervention ○ Varies • **No included studies**	No research evidence was identified regarding the cost-effectiveness of VCUG for first vs second UTI.	Waiting is always more cost-effective EXCEPT for cost of false-negative
Equity What would be the impact on health equity?		
JUDGMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
○ Reduced ○ Probably reduced ○ Probably no impact ○ Probably increased ○ Increased ○ Varies • **Don't know**	No research evidence was identified regarding the impact of VCUG for first vs second UTI on health equity.	Are there groups or settings that might be disadvantaged in relation to the problem or options that are considered? Potential disadvantage for waiting—follow-up may not occur (no-shows) and delays in care may disproportionately affect children and families facing barriers to reliable follow-up, including transportation limitations, inconsistent access to primary care, financial constraints, or difficulty obtaining time away from work. Disparities in access to VCUG Address effects on equity in narrative—may impact equity in both directions depending on the situation Research gap
Acceptability Is the intervention acceptable to key interest holders?		
JUDGMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
○ No • **Probably no** ○ Probably yes ○ Yes ○ Varies ○ Don't know	An anonymous survey to all fellows of the American Academy of Pediatrics Section on Urology showed that given a choice of fluoroscopic voiding cystourethrography, radionuclide cystography, and voiding ultrasonography, fluoroscopic voiding cystourethrography was preferred by 98% and 96% of respondents for initial evaluation of urinary tract infection in males and females, respectively, 96% for assessment of prenatal hydronephrosis, 54% for follow-up of vesicoureteral reflux, 59% for screening siblings, and 63% and 66%, respectively, after open and endoscopic correction of vesicoureteral reflux. Voiding ultrasonography was preferred by less than 10% of respondents	Judgment is based on acceptability of the VCUG test after first UTI compared to VCUG test after second UTI Subset of physicians will find aggressive testing unacceptable Acceptability to caregivers/patients through the diagnostic journey—first vs second UTI Panel noted additional burden (pain, trauma) of performing the test in older children While VCUG is probably acceptable to different interest holders, when comparing VCUG after first vs second UTI, patients and families may find VCUG more acceptable after second UTI

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	in all groups, and radionuclide cystography was preferred by the remainder. Voiding images of the urethra, child-friendliness of staff, sensitivity and accuracy were factors most important in choosing a test. Of the respondents 83% reported full-time access to pediatric radiologists at their primary hospital, although a minority had full-time access to pediatric radiologists at additional institutions. Sedation was used in some or most cases by 29%, rarely by 56% and never by 15% of respondents. Ellison JS, Maxfield CM, Wiener JS. Voiding cystography practices and preferences of North American pediatric urologists. *J Urol.* 2009;182(1):299–305	

Feasibility
Is the intervention feasible to implement?

JUDGMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ No ○ Probably no • **Probably yes** ○ Yes ○ Varies ○ Don't know	No research evidence was identified regarding the feasibility of VCUG for first vs second UTI.	Access to facilities and specialists may vary Infrastructure based on setting

Summary of Judgments

	JUDGMENT						
PROBLEM	No	Probably no	Probably yes	**Yes**		Varies	Don't know
TEST ACCURACY	Very inaccurate	Inaccurate	Accurate	**Very accurate**		Varies	Don't know
DESIRABLE EFFECTS	**Trivial**	Small	Moderate	Large		Varies	Don't know
UNDESIRABLE EFFECTS	Trivial	Small	**Moderate**	Large		Varies	Don't know
CERTAINTY OF THE EVIDENCE OF TEST ACCURACY	Very low	Low	Moderate	**High**			No included studies
CERTAINTY OF THE EVIDENCE OF TEST'S EFFECTS	Very low	**Low**	Moderate	High			No included studies
CERTAINTY OF THE EVIDENCE OF MANAGEMENT'S EFFECTS	Very low	**Low**	Moderate	High			No included studies
CERTAINTY OF THE EVIDENCE OF TEST RESULT/ MANAGEMENT	Very low	**Low**	Moderate	High			No included studies
CERTAINTY OF EFFECTS	Very low	**Low**	Moderate	High			No included studies
VALUES	Important uncertainty or variability	**Possibly important uncertainty or variability**	Probably no important uncertainty or variability	No important uncertainty or variability			

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BALANCE OF EFFECTS	Favors the comparison	**Probably favors the comparison**	Does not favor either the intervention or the comparison	Probably favors the intervention	Favors the intervention	Varies	Don't know
RESOURCES REQUIRED	Large costs	**Moderate costs**	Negligible costs and savings	Moderate savings	Large savings	Varies	Don't know
CERTAINTY OF EVIDENCE OF REQUIRED RESOURCES	Very low	Low	Moderate	High			**No included studies**
COST EFFECTIVENESS	Favors the comparison	Probably favors the comparison	Does not favor either the intervention or the comparison	Probably favors the intervention	Favors the intervention	Varies	**No included studies**
EQUITY	Reduced	Probably reduced	Probably no impact	Probably increased	Increased	Varies	**Don't know**
ACCEPTABILITY	No	**Probably no**	Probably yes	Yes		Varies	Don't know
FEASIBILITY	No	Probably no	**Probably yes**	Yes		Varies	Don't know

Type of Recommendation

Strong recommendation against the intervention	**Conditional recommendation against the intervention**	Conditional recommendation for either the intervention or the comparison	Conditional recommendation for the intervention	Strong recommendation for the intervention
○	○	○	○	○

Conclusions

Recommendation
Key Action Statement 5A: The AAP Guideline Panel suggests against routine VCUG after a first febrile UTI in children younger than 5 years who have normal RBUS (conditional recommendation, high certainty of evidence of test accuracy, low certainty of evidence of overall effect). Remark for Key Action Statement 5A: It is an option to obtain a VCUG after the first febrile UTI in specific subpopulations (eg, age <1 month, infectious agent other than *Escherichia coli*; circumcised males, atypical/complicated course including septic shock/ICU admission, or limited follow-up reliability) with subspecialty consultation for abnormal results. Key Action Statement 5B: The AAP Guideline Panel suggests offering VCUG in: children with clinically relevant abnormalities detected on RBUS after a first febrile UTI, all children younger than 2 years with a second febrile UTI, and children 2 years or older with a second febrile UTI and no alternative explanatory risk factors (conditional recommendation, high certainty of evidence of test accuracy, low certainty of evidence of overall effect). Remark for Key Action Statement 5B: In children with VUR and underlying anomalies of the renal tract that increase risk for both UTI and renal scarring, pediatricians and other pediatric clinicians are encouraged to partner with the family and provide educational resources to assist with early future detection, treatment, and prevention of UTI.
Justification
Subgroup considerations
Implementation considerations
Monitoring and evaluation
Research priorities
• The impact of VCUG for first vs second UTI on health equity.

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APPENDIX TABLE 6. EVIDENCE-TO-DECISIONS TABLE FOR CONTINUOUS ANTIBIOTIC PROPHYLAXIS FOR VESICOURETERAL REFLUX

Question

Should continuous antibiotic prophylaxis vs no continuous antibiotic prophylaxis be used for children with vesicoureteral reflux (VUR)?	
POPULATION:	children with VUR
INTERVENTION:	continuous antibiotic prophylaxis
COMPARISON:	no continuous antibiotic prophylaxis
MAIN OUTCOMES:	Breakthrough UTI (BT UTI) - only VUR; Renal scarring - all studies; Adverse events; Resistant recurrent UTI (rUTI); Weight gain; Improvement in VUR
SETTING:	general pediatric practice in collaboration with subspecialists
PERSPECTIVE:	Clinical recommendation – Individual perspective
BACKGROUND:	
CONFLICT OF INTERESTS:	

Assessment

Problem
Is the problem a priority?

JUDGMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ No ○ Probably no ○ Probably yes • Yes ○ Varies ○ Don't know	Urinary tract infection (UTI) is one of the most common bacterial infections of childhood. Among febrile infants, unwell children in general practice and older children with urinary symptoms, 6%–8% will have a UTI. Over 30% of children with UTI will have recurrent UTI. Common risk factors for recurrence include VUR and bladder–bowel dysfunction (BBD) (Kaufman 2019). VUR results in urine passing retrograde up the ureter. UTIs associated with VUR may be a cause of permanent renal parenchymal damage. Current treatment options include surgical reimplantation of the ureters, long-term antibiotics, endoscopic correction by subureteric injection of a substance, complementary medicines, or a combination of interventions. Although VUR is a common problem in childhood, the optimal management strategy remains a subject of controversy, and practice varies widely (Williams 2019). Kaufman J, Temple-Smith M, Sanci L. Urinary tract infections in children: an overview of diagnosis and management. *BMJ Paediatr Open*. 2019;3(1):e000487 Williams G, Hodson EM, Craig JC. Interventions for primary vesicoureteric reflux. *Cochrane Database Syst Rev*. 2019;2(2): CD001532	Scope of this guideline is not management of reflux (CAP is not the only option) General peds practice - collaboration w/subspecialists https://www.sciencedirect.com/science/article/pii/S0090429511004250 Question is a priority as part of the diagnostic pathway for VUR

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Desirable Effects
How substantial are the desirable anticipated effects?

JUDGMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Trivial • Small ○ Moderate ○ Large ○ Varies ○ Don't know	*See Supplemental File Table 9 and Table 10*	Data on scarring are unclear; no impact, don't know, studies are indirect based on duration of follow-up (too short) Some reduction in BT UTI Assumptions: • Children w/VUR are more likely to have UTI (increasing risk with increasing grade) • Multiple recurrent UTI leads to clinically meaningful renal damage (via scarring) • GFR values • "if you are the child whose recurrent pyelo is prevented by antibiotics, and then VUR resolves, and so you avoid surgery, that is ANYTHING but trivial"

Undesirable Effects
How substantial are the undesirable anticipated effects?

JUDGMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Trivial ○ Small • Moderate ○ Large ○ Varies ○ Don't know	*See Supplemental File Table 9* NNH: 27 children treated to cause 1 resistant UTI	Other effects: increase in allergies, auto-immune disorders, burden of daily antibiotic therapy Impact of rUTI: prescribe a different antibiotic, hospitalization, PICC Patient-level undesirable effects "I see MDR UTIs too, in children not taking prophylaxis. And I think it hard to argue that a child on Bactrim has MDR bacteria due to Bactrim alone - only Bactrim resistance is being selected for..."

Certainty of evidence
What is the overall certainty of the evidence of effects?

JUDGMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Very low • Low ○ Moderate ○ High ○ No included studies	The certainty of evidence is low because of concerns with risk of bias and imprecision.	

Values
Is there important uncertainty about or variability in how much people value the main outcomes?

JUDGMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
• Important uncertainty or variability ○ Possibly important uncertainty or variability ○ Probably no important uncertainty or variability ○ No important uncertainty or variability	One qualitative study (n = 26) described parents' attitudes toward the management of vesicoureteral reflux and found variability in preferences regarding risks and benefits of treatment (Tran 2017). Chief parental concerns were whether a method decreases the risk of UTIs, has an acceptable efficacy rate, and aligns itself with their family's capabilities. Tran GN, Bodapati AV, Routh JC, Saigal CS, Copp HL. Parental preference assessment for vesicoureteral reflux management in children. *J Urol.* 2017;197(3 Pt 2):957–962	• Reducing risk of recurrent UTI • Increasing risk of resistant recurrent UTI - variability in severity of consequences of resistant UTI • Increasing risk of medication side effects • Possible downstream health consequences of daily antibiotics (autoimmune, allergy) Variability based on patient characteristics? eg, VUR grade, dilating vs non-dilating "if you are the child whose recurrent pyelo is prevented by antibiotics, and then VUR resolves, and so you avoid surgery, that is ANYTHING but trivial"

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Balance of effects Does the balance between desirable and undesirable effects favor the intervention or the comparison?		
JUDGMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
○ Favors the comparison ○ Probably favors the comparison ○ Does not favor either the intervention or the comparison ○ Probably favors the intervention ○ Favors the intervention • Varies ○ Don't know		DESIRABLE: small UNDESIRABLE: moderate CERTAINTY: low VALUES: important uncertainty or variability Varies based on values
Resources required How large are the resource requirements (costs)?		
JUDGMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
○ Large costs • Moderate costs ○ Negligible costs and savings ○ Moderate savings ○ Large savings ○ Varies ○ Don't know		Cost associated with ongoing monitoring of antibiotic regimen? Unmeasured costs of daily therapy Direct costs of antibiotic prophylaxis vs no antibiotic prophylaxis Copays may vary based on insurance status Direct costs to patients are higher with treatment; direct costs to insurance are higher with no treatment (complications) Relevant duration of therapy
Certainty of evidence of required resources What is the certainty of the evidence of resource requirements (costs)?		
JUDGMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
○ Very low ○ Low ○ Moderate ○ High • No included studies		
Cost effectiveness Does the cost-effectiveness of the intervention favor the intervention or the comparison?		
JUDGMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
○ Favors the comparison • Probably favors the comparison ○ Does not favor either the intervention or the comparison ○ Probably favors the intervention ○ Favors the intervention ○ Varies ○ No included studies	One study compared the cost per quality-adjusted life-year (QALY) gained in 4 treatment strategies in children aged <6 years diagnosed with VUR after a first UTI, considering these treatment strategies: (1) prophylaxis for all children with VUR, (2) prophylaxis for children with grade III or grade IV VUR, (3) prophylaxis for children with grade IV VUR, and (4) no prophylaxis. Costs and effectiveness were estimated over the patient's lifetime. The investigators found that prophylaxis of children with grade IV VUR costs $37,903 per QALY gained. Treating children with grade III and IV VUR costs an additional $302,024 per QALY gained. Treating children with all grades of VUR costs an additional $339,740 per QALY gained. They concluded that CAP is only cost-effective for children grade IV VUR using $100,000/QALY gained as a threshold for cost-effectiveness (Shaikh 2020). A study to elicit utility scores for VUR from a representative, well-characterized community sample of adults who have been parents (n = 1200) showed that VUR has a mean utility score of 0.82, which indicates that the community perceives this condition to be a substantial burden. For comparison, conditions with similar utility scores include compensated hepatitis B-related	Downstream costs and benefits? eg, prophylaxis prevents surgery in grade IV Varies by grade of reflux Low-grade VUR (I-III) Grade IV - decision to have surgery w/input from panel members; Swedish reflux trial Varies

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	cirrhosis (0.80) and glaucoma (0.82); conditions with higher utilities include neonatal jaundice (0.99) and transient neonatal neurological symptoms (0.95); and conditions with lower utility scores include severe depression (0.43) and major stroke (0.30). Our results suggest that parents consider the burden associated with VUR to be significant and that the impact of the condition on families and children is substantial (Nelson 2015). Palmer and colleagues compared mean costs of the prophylaxis and placebo groups of the RIVUR trial. These estimates incorporated costs of medications, imaging and complications such as pyelonephritis, likelihood of surgery, and loss of work. The authors found that mean costs were higher for treatment vs placebo at $3092 and $2932, respectively. Shaikh N, Rajakumar V, Peterson CG, et al. Cost-utility of antimicrobial prophylaxis for treatment of children with vesicoureteral reflux. *Front Pediatr*. 2019;7:530 Nelson CP, Routh JC, Logvinenko T, Rosoklija I, Kokorowski PJ, Prosser LA, Schuster MA. Utility scores for vesicoureteral reflux and anti-reflux surgery. *J Pediatr Urol*. 2015;11(4):177–182 Palmer LS, Seideman CA, Lotan Y. Cost-effectiveness of antimicrobial prophylaxis for children in the RIVUR trial. *World J Urol*. 2018;36(9):1441–1447	

Equity
What would be the impact on health equity?

JUDGMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Reduced • Probably reduced ○ Probably no impact ○ Probably increased ○ Increased ○ Varies ○ Don't know	Two studies on antibiotic prescribing patterns for common conditions did not identify any differences for demographic profiles of children with UTIs in pediatric urgent care centers (Nedved 2023) or in primary care offices (Gerber 2013). Nedved AC, Lee BR, Wirtz A, et al. Socioeconomic differences in antibiotic use for common infections in pediatric urgent-care centers-A quasi-experimental study. *Infect Control Hosp Epidemiol*. 2023;44(12):2009–2016 Gerber JS, Prasad PA, Localio AR, et al. Racial differences in antibiotic prescribing by primary care pediatricians. *Pediatrics*. 2013;131(4):677–684	Are there groups or settings that might be disadvantaged by a recommendation for prophylaxis vs no prophylaxis? Insurance coverage vs no coverage Medical home/PCP vs no medical home/PCP Prescribing practices may be more aligned with recommendations among disadvantaged populations

Acceptability
Is the intervention acceptable to key interest holders?

JUDGMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ No ○ Probably no ○ Probably yes ○ Yes • Varies ○ Don't know	Some clinicians may be hesitant to prescribe continuous antibiotic prophylaxis in children with VUR given the risk of antibiotic resistance. In a small qualitative study, parents described concerns with maintenance of a daily administration of medication, monitoring of side effects and potential antibiotic resistance, and the costs associated (Tran 2017). Some children may find the taste of oral antibiotics unpalatable. Another study (n = 953) examined the acceptability of antibiotic syrups, suspensions, and oral solutions prescribed to pediatric outpatients in France (Cohen 2009). They found that children rated amoxicillin–clavulanate generics as less "satisfactory" than the reference product, with treatment completion rates of 82.3% and 91.7%, respectively. Finally, a study (n = 5342) of compliance with antibiotic prophylaxis in children VUR found that 40% of VUR patients on AP are compliant, with young age, frequent hospitalization, and specialist visits associated with compliance (Copp 2010). Tran GN, Bodapati AV, Routh JC, Saigal CS, Copp HL. Parental preference assessment for vesicoureteral reflux management in children. *J Urol*. 2017;197(3 Pt 2):957–962	Interest holders: • Physicians (no additional burden, but some may find prophylaxis unacceptable) • Caregivers/patients may perceive a daily med regimen as a burden Patient characteristics (eg, VUR grade, dilating vs nondilating) may influence acceptability of antibiotic prophylaxis

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	Cohen R, de La Rocque F, Lécuyer A, Wollner C, Bodin MJ, Wollner A. Study of the acceptability of antibiotic syrups, suspensions, and oral solutions prescribed to pediatric outpatients. *Eur J Pediatr*. 2009;168(7):851–857 Copp HL, Nelson CP, Shortliffe LD, Lai J, Saigal CS, Kennedy WA; Urologic Diseases in America Project. Compliance with antibiotic prophylaxis in children with vesicoureteral reflux: results from a national pharmacy claims database. *J Urol*. 2010;183(5):1994–1999 **Antibiotic Resistance:** One study (n = 35) conducted RNA gene sequencing of stool samples of children <3 years old who underwent antibiotic treatment during the acute phase of febrile UTI. CAP (TMP-SMX) was initiated in 23 patients with grade III or higher VUR and was not administered in 12 patients without reflux. They found that patients receiving CAP had normal gut microbiota diversity (Akagawa 2020). A sub-analysis of the RIVUR trial (n = 571) evaluated factors associated with TMP-SMX–resistant rUTI. Among those with rUTI, 76% (26/34) of subjects receiving TSP had TMP-SMX–resistant organisms versus 28% (19/67) of subjects receiving placebo. The proportion of TMP-SMX–resistant rUTI decreased over time: in the TSP arm, 96% were resistant during the initial 6 months versus 38% resistant during the final 6 months; corresponding proportions for the placebo arm were 32% and 11%. Among children receiving TSP, 7/55 (13%) with TMP-SMX–resistant index UTI had rUTI, whereas 27/223 (12%) with TMP-SMX–susceptible index UTI had rUTI (aHR 1.38, 95% CI 0.54–3.56). Corresponding proportions in the placebo arm were 17 (26%) of 65 and 50 (22%) of 228 (aHR 1.33, 95% CI 0.74–2.38). Although TMP-SMX resistance is more common among children treated with TSP versus placebo, resistance decreased over time. Among children treated with TSP, there was no significant difference in UTI recurrence between those with TMP-SMX–resistant index UTI versus TMP-SMX–susceptible UTI (Nelson 2016). Another study (n = 129) evaluated children (1 mo - 15 y) with VUR who developed at least one UTI during a 10-year study period. They found that 68 (52.7%) had recurrent UTIs. The rates of susceptibility of E. coli to commonly used antimicrobials were significantly lower in children who developed more than one episode of UTI (Wu 2016). Akagawa Y, Kimata T, Akagawa S, et al. Impact of long-term low dose antibiotic prophylaxis on gut microbiota in children. *J Urol*. 2020;204(6):1320–1325 Nelson CP, Hoberman A, Shaikh N, et al. Antimicrobial resistance and urinary tract infection recurrence. *Pediatrics*. 2016;137(4):e20152490 Wu TH, Huang FL, Fu LS, et al. Treatment of recurrent complicated urinary tract infections in children with vesicoureteral reflux. *J Microbiol Immunol Infect*. 2016;49(5):717–722	

Feasibility
Is the intervention feasible to implement?

JUDGMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ No ○ Probably no ○ Probably yes • Yes ○ Varies ○ Don't know		Is CAP feasible to implement in all children with VUR? Certain grades?

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Summary of Judgments

	JUDGMENT						
PROBLEM	No	Probably no	Probably yes	**Yes**		Varies	Don't know
DESIRABLE EFFECTS	Trivial	**Small**	Moderate	Large		Varies	Don't know
UNDESIRABLE EFFECTS	Trivial	Small	**Moderate**	Large		Varies	Don't know
CERTAINTY OF EVIDENCE	Very low	**Low**	Moderate	High			No included studies
VALUES	**Important uncertainty or variability**	Possibly important uncertainty or variability	Probably no important uncertainty or variability	No important uncertainty or variability			
BALANCE OF EFFECTS	Favors the comparison	Probably favors the comparison	Does not favor either the intervention or the comparison	Probably favors the intervention	Favors the intervention	**Varies**	Don't know
RESOURCES REQUIRED	Large costs	**Moderate costs**	Negligible costs and savings	Moderate savings	Large savings	Varies	Don't know
CERTAINTY OF EVIDENCE OF REQUIRED RESOURCES	Very low	Low	Moderate	High			**No included studies**
COST EFFECTIVENESS	Favors the comparison	**Probably favors the comparison**	Does not favor either the intervention or the comparison	Probably favors the intervention	Favors the intervention	Varies	No included studies
EQUITY	Reduced	**Probably reduced**	Probably no impact	Probably increased	Increased	Varies	Don't know
ACCEPTABILITY	No	Probably no	Probably yes	Yes		**Varies**	Don't know
FEASIBILITY	No	Probably no	Probably yes	**Yes**		Varies	Don't know

Type of Recommendation

Strong recommendation against the intervention	**Conditional recommendation against the intervention**	Conditional recommendation for either the intervention or the comparison	Conditional recommendation for the intervention	Strong recommendation for the intervention
○	○	○	○	○

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Conclusions

Recommendation

Key Action Statement 6: In children with low-risk VUR, the AAP Guideline Panel suggests against using routine CAP (conditional recommendation, low certainty of evidence).
Remarks for Key Action Statement 6:
• The panel defines low-risk VUR as a child having *both* a lower-grade VUR (I-II) *and* no presence of bowel and bladder dysfunction (BBD) (excluding functional constipation), per the Rome criteria.
• The panel recognized, through comprehensive evidence review, that grade III VUR spans an unclear risk category. CAP is a reasonable option for patients with grade III VUR for patients and caregivers who place a higher value on the uncertain reduction in the risk of infections and a lower value on minimizing exposure to antibiotics.
• For children with high-risk VUR, CAP is an option. The panel defined high-risk VUR as the presence of *any* of the following:
  ○ Grade IV or grade V VUR
  ○ Intra-renal reflux
  ○ Demonstrated renal scarring/nephropathy
  ○ Renal/ureteral structural or cortical abnormalities
  ○ Recurrent pyelonephritis
  ○ Bacteremia resulting in ICU admission
  ○ BBD (excluding functional constipation)
• Patients with high-risk VUR and other high-risk urologic abnormalities that are not covered in the CPG should be referred to a pediatric urologist or nephrologist.
Good Practice Statement: All decisions regarding use of CAP should occur as part of a shared decision-making process with families, given the uncertainty over risks and benefits in individual patients.
Good Practice Statement: Whenever possible, in children with VUR and/or underlying anomalies of the urinary tract that increase risk for UTI and renal scarring, referral to pediatric urology and/or nephrology is recommended for shared decision-making and discussion of all management options, including observation, treatment of BBD, antibiotic prophylaxis, and surgical management options. When in-person access to pediatric urologists and nephrologists is limited, virtual consultations, including e-consults and telehealth, can enhance access and specialist involvement.
Good Practice Statement: VUR management may include observation, CAP, endoscopic injection, and ureteral reimplantation; selection among options is encouraged to be in collaboration with pediatric urology or pediatric nephrology via shared decision making.

Justification
Subgroup considerations
Implementation considerations
Monitoring and evaluation
Research priorities

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