Febrile UTIs in Practice

AAP Guidelines and New Evidence

Jennifer Chapman, MD — Emergency Medicine
Kavita Parikh, MD, MSHS — Hospitalist Medicine
Shilpa Patel, MD, MPH — Emergency Medicine

June 15, 2016

Future of Pediatrics Conference

Children's National

No Disclosures

Children's National

Learning Objectives

1) To review the 2011 AAP Guidelines
2) To review recent evidence in the management of febrile UTIs in children
3) To apply the guidelines and recent evidence

Case 1:	Case 2:	Case 3:
5 month old male	7 week old female	2 yo female with recurrent UTI

Case 1

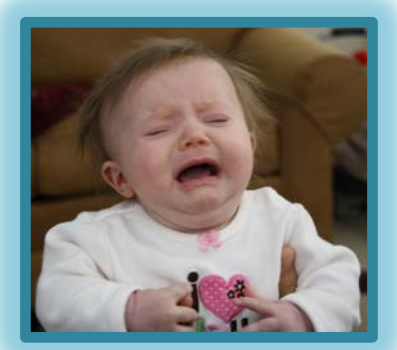
- 5 mo Caucasian, circumcised, male
- T40 for 48 hours
- Well-appearing with defervescence and no localizing signs on exam
- Last immunizations 3 weeks ago

Do we test?

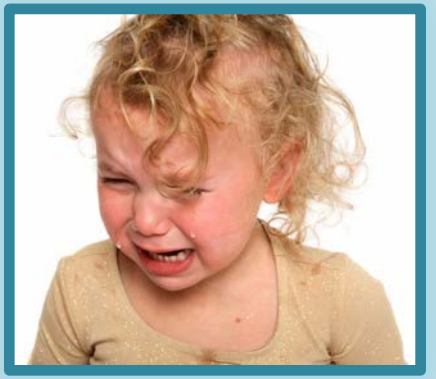
What is the risk of UTI in febrile children?

Does it differ by age, gender, or race?

>



>

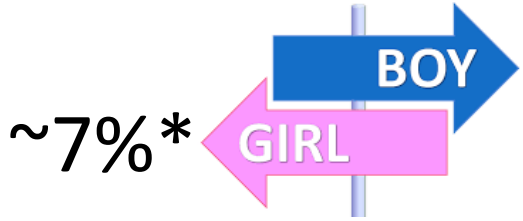


AGE

Risk Factors for UTI

GENDER

RACE



~7%*

~2%*

*Age 3- 12 months

Circumcised ~1 %

NOT Circumcised ~ 6%

Infant GIRLS : Individual Factors

- Race: White
- Age: <12 months
- Temperature: ≥39°C
- Fever: ≥2 days
- Absence of another source of infection

Probability of UTI	# of Factors Present
≤1%	No more than 1
≤2%	No more than 2

Infant BOYS: Individual Factors

- Race: Nonblack
- Temperature: ≥39°C
- Fever: >24 hours
- Absence of another source of infection

Probability of UTI	# of Factors Present	
	Circumcised	
	No	Yes
≤1%	*	No more than 2
≤2%	None	No more than 3

American Academy of Pediatrics
DEDICATED TO THE HEALTH OF ALL CHILDREN™

Kenneth B. Roberts, MD, FAAP
AAP Webinar

Infant GIRLS : Individual Factors

- Race: White
- Age: <12 months
- Temperature: ≥39°C
- Fever: ≥2 days
- Absence of another source of infection

Probability of UTI	# of Factors Present
≤1%	No more than 1
≤2%	No more than 2

Infant BOYS: Individual Factors

- Race: Nonblack
- Temperature: ≥39°C
- Fever: >24 hours
- Absence of another source of infection

Probability of UTI	# of Factors Present	
	Circumcised	
	No	Yes
≤1%	*	No more than 2
≤2%	None	No more than 3

American Academy of Pediatrics
DEDICATED TO THE HEALTH OF ALL CHILDREN™

Kenneth B. Roberts, MD, FAAP
AAP Webinar

How do we make the diagnosis?

- 10K?
- 50K?
- 100K?
- LE? Nitrites? WBC count?

How do we test?

- Urinalysis
- Urine Culture
- Bag vs Catheter

GUIDELINE

American Academy of Pediatrics
DEDICATED TO THE HEALTH OF ALL CHILDREN™

Diagnosis = Positive Culture + Positive UA:

Positive culture: ≥50,000 cfu/mL of uropathogen

AND

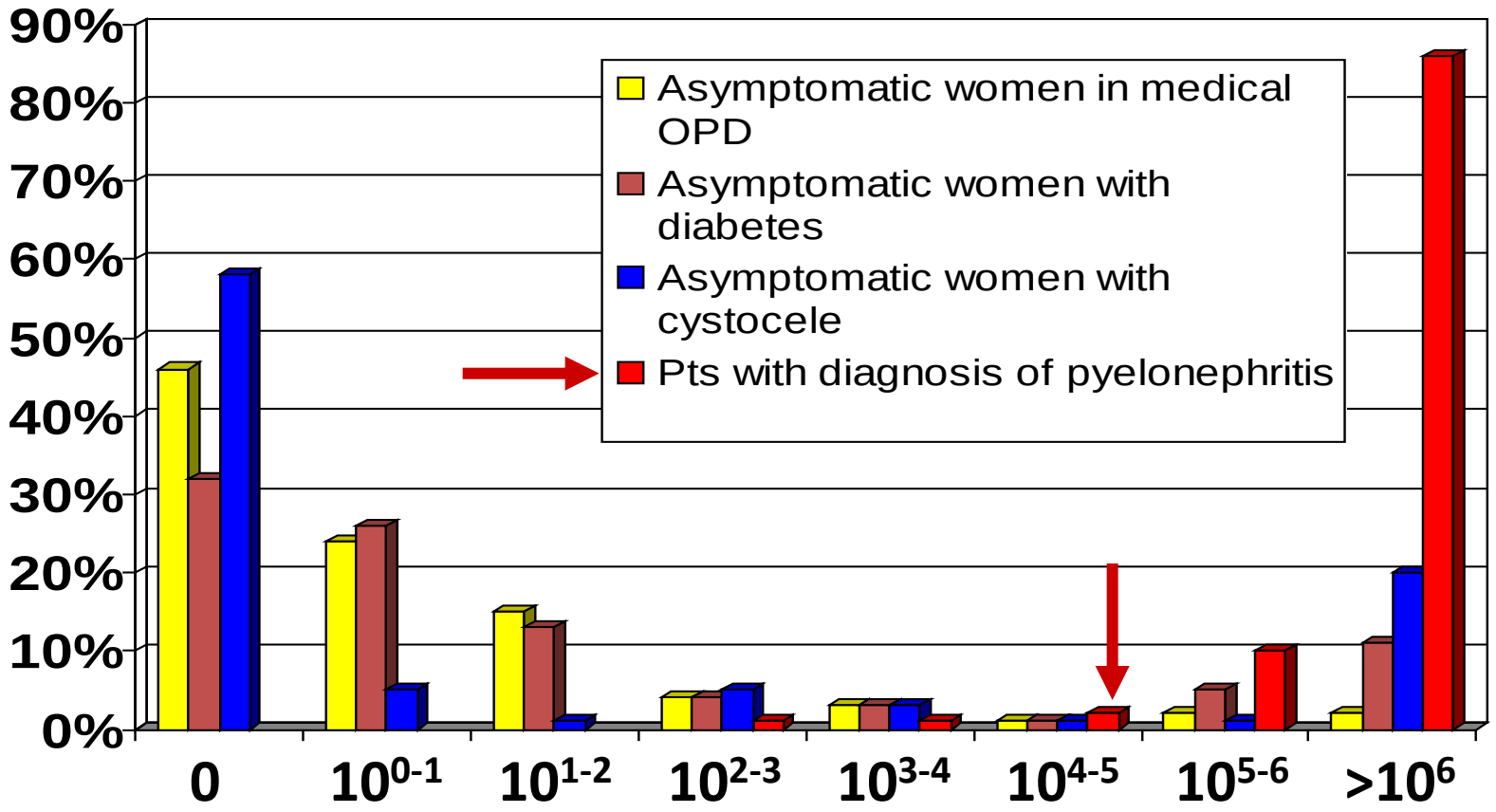
Positive urinalysis

✓Evidence quality: C

✓Recommendation

Children's National™

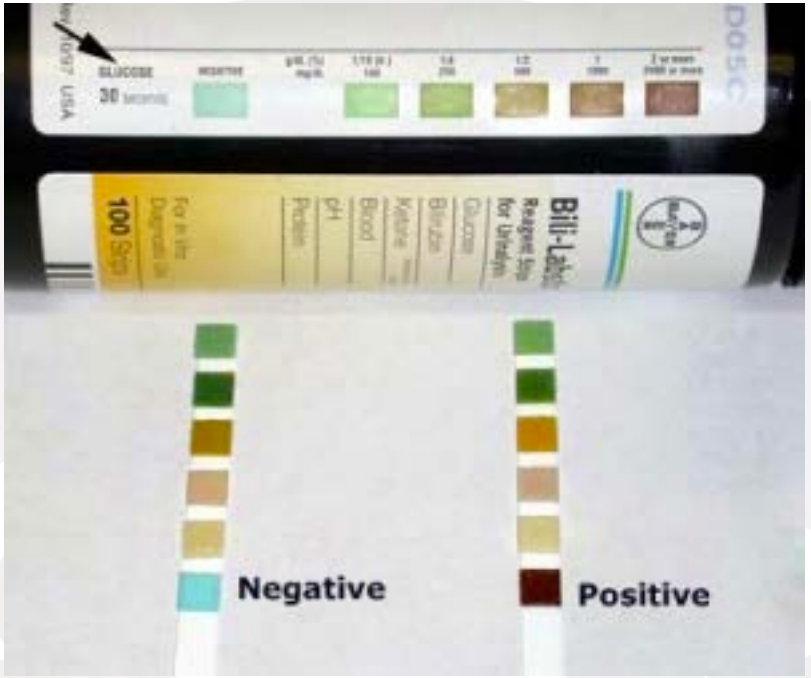
Where Did 100,000 Come From?



Kass E. Asymptomatic infections of the urinary tract. *Trans Assoc Am Phys*. 1956;69:56–64

TESTING

What is a positive UA?



Children's National

Urinalysis suggestive of infection – 2011 Guidelines

TABLE 1 Sensitivity and Specificity of Components of Urinalysis, Alone and in Combination

Test	Sensitivity (Range), %	Specificity (Range), %
Leukocyte esterase test	83 (67–94)	78 (64–92)
Nitrite test	53 (15–82)	98 (90–100)
Leukocyte esterase or nitrite test positive	93 (90–100)	72 (58–91)
Microscopy, WBCs	73 (32–100)	81 (45–98)
Microscopy, bacteria	81 (16–99)	83 (11–100)
Leukocyte esterase test, nitrite test, or microscopy positive	99.8 (99–100)	70 (60–92)

3-24mo
Febrile Boy

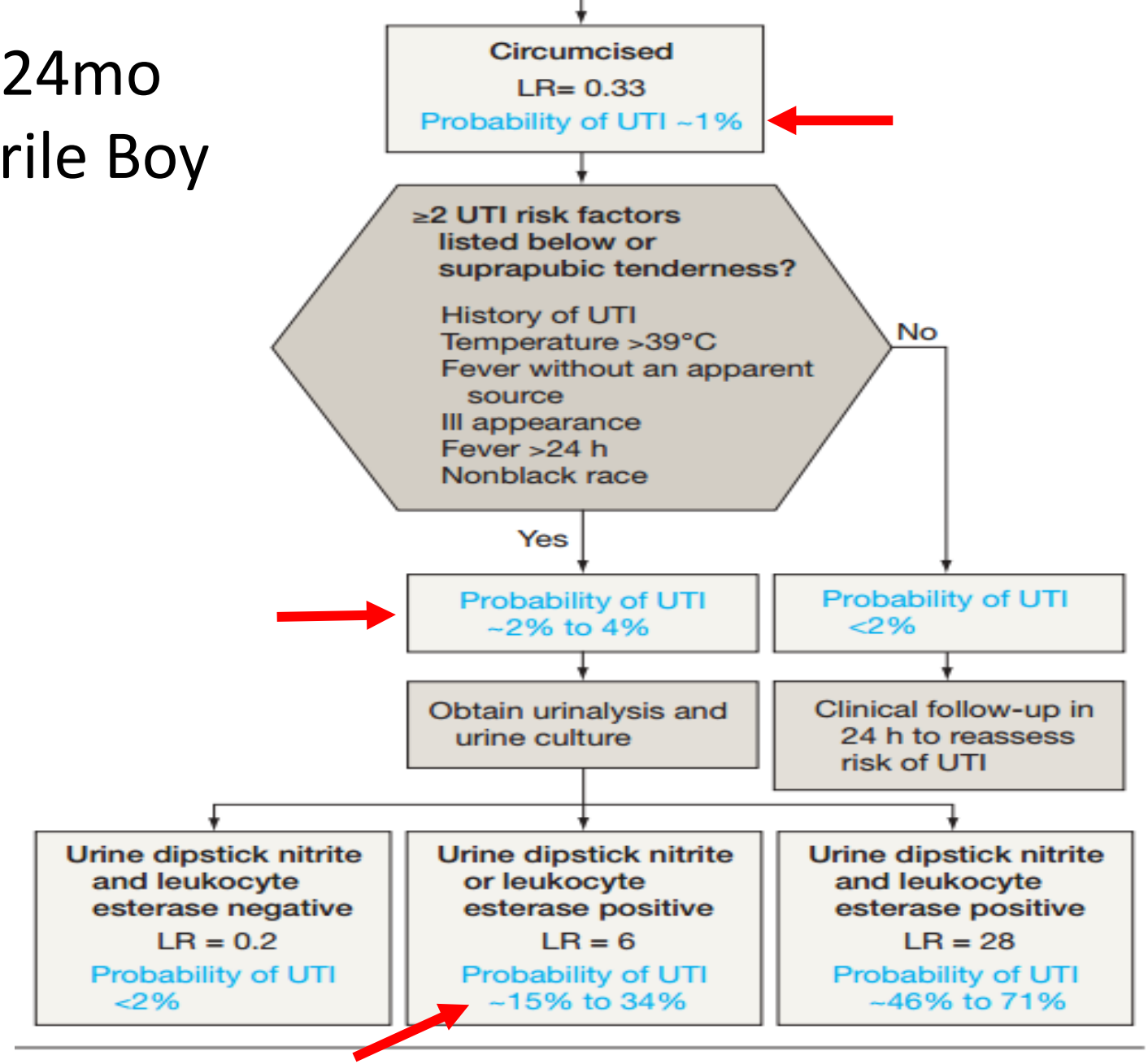


TABLE 4 Urine Culture and UA Results in Infants With Bacteremia and Urine Culture Growth With <50 000 CFU/mL of the Same Organism

Organism	*n*	Urine Culture Growth, CFU/mL			UA Result			
		<10K	10–25K	25–50K	Pyuria >3 WBC/HPF	Any Bacteria	Any LE	Any Nitrites
E coli	12	1	7	4	11/12	10/11[a]	12/12	2/12
GBS	5	4	1	0	1/5	0/4[a]	0/5	0/5
Enterococcus faecalis	1	1	0	0	0	ND	0	0
GAS	1	1	0	0	ND	ND	0	0

GAS, Group A *Streptococcus*; ND, not done.

[a] Denominators reflect that not all infants had UA bacteria results.

Schroeder et al. Pediatrics 2015

TESTING

Is there only 1 way

Pediatrics

June 2016

Two-Step Process for ED UTI Screening in Febrile Young Children: Reducing Catheterization Rates

Jane M. Lavelle, Mercedes M. Blackstone, Mary Kate Funari, Christine Roper, Patricia Lopez, Aileen Schast, April M. Taylor, Catherine B. Voorhis, Mira Henien, Kathy N. Shaw

Children's National

Bag UA appropriate to screen for UTI

- Single center, ED based QI study
- Two step process to screen for UTI
  - Bag UA →

    IF Udip + (mod/lg LE OR nitrites) → Ucath + Abx
- 6mo-24 mo with concern for UTI
- No difference in culture positivity rates
- No difference in return visits
- No difference in length of stay

Lavelle et al. Pediatrics 2016

DIAGNOSIS

TESTING

Culture >50K
AND
UA (+LE/nitrates OR WBC)

Two step method, using bag UA to screen is appropriate

American Academy of Pediatrics
DEDICATED TO THE HEALTH OF ALL CHILDREN™

FROM THE AMERICAN ACADEMY OF PEDIATRICS

CLINICAL PRACTICE GUIDELINE

Urinary Tract Infection: Clinical Practice Guideline for the Diagnosis and Management of the Initial UTI in Febrile Infants and Children 2 to 24 Months

SUBCOMMITTEE ON URINARY TRACT INFECTION, STEERING COMMITTEE ON QUALITY IMPROVEMENT AND MANAGEMENT

KEY WORDS
urinary tract infection, infants, children, vesicoureteral reflux, voiding cystourethrography

ABBREVIATIONS
SPA—suprapubic aspiration
AAP—American Academy of Pediatrics
UTI—urinary tract infection
RCT—randomized controlled trial
CFU—colony-forming unit
VUR—vesicoureteral reflux
WBC—white blood cell
RBUS—renal and bladder ultrasonography
VCUG—voiding cystourethrography

The recommendations in this report do not indicate an exclusive course of treatment or serve as a standard of medical care. Variations, taking into account individual circumstances, may be appropriate.

All clinical practice guidelines from the American Academy of Pediatrics automatically expire 5 years after publication unless reaffirmed, revised, or retired at or before that time.

www.pediatrics.org/cgi/doi/10.1542/peds.2011-1330
doi:10.1542/peds.2011-1330
PEDIATRICS (ISSN Numbers: Print, 0031-4005; Online, 1098-4275).

COMPANION PAPERS: Companions to this article can be found on pages 572 and e748, and online at www.pediatrics.org/cgi/doi/10.1542/peds.2011-1818 and www.pediatrics.org/cgi/doi/10.1542/peds.2011-1332.

abstract

FREE

OBJECTIVE: To revise the American Academy of Pediatrics practice parameter regarding the diagnosis and management of initial urinary tract infections (UTIs) in febrile infants and young children.

METHODS: Analysis of the medical literature published since the last version of the guideline was supplemented by analysis of data provided by authors of recent publications. The strength of evidence supporting each recommendation and the strength of the recommendation were assessed and graded.

RESULTS: Diagnosis is made on the basis of the presence of both pyuria and at least 50 000 colonies per mL of a single uropathogenic organism in an appropriately collected specimen of urine. After 7 to 14 days of antimicrobial treatment, close clinical follow-up monitoring should be maintained to permit prompt diagnosis and treatment of recurrent infections. Ultrasonography of the kidneys and bladder should be performed to detect anatomic abnormalities. Data from the most recent 6 studies do not support the use of antimicrobial prophylaxis to prevent febrile recurrent UTI in infants without vesicoureteral reflux (VUR) or with grade I to IV VUR. Therefore, a voiding cystourethrography (VCUG) is not recommended routinely after the first UTI; VCUG is indicated if renal and bladder ultrasonography reveals hydronephrosis, scarring, or other findings that would suggest either high-grade VUR or obstructive uropathy and in other atypical or complex clinical circumstances. VCUG should also be performed if there is a recurrence of a febrile UTI. The recommendations in this guideline do not indicate an exclusive course of treatment or serve as a standard of care; variations may be appropriate. Recommendations about antimicrobial prophylaxis and implications for performance of VCUG are based on currently available evidence. As with all American Academy of Pediatrics clinical guidelines, the recommendations will be reviewed routinely and incorporate new evidence, such as data from the Randomized Intervention for Children With Vesicoureteral Reflux (RIVUR) study.

CONCLUSIONS: Changes in this revision include criteria for the diagnosis of UTI and recommendations for imaging. *Pediatrics* 2011;128:595–610

Children's National™

Case 1:	Case 2:	Case 3:
5 month old male	7 week old female	2 yo female with recurrent UTI

Case 2

- 7 week old female
- T 38.5
- No other symptoms
- Well appearing

Case 2

- Partial sepsis work-up completed and UA is positive with WBC and mod LE
- Is an LP needed before starting treatment?
- Infant is well appearing and has no other medical history.

Risk of meningitis in a ‘low risk’ 29-60 day old infant with UTI is rare

- Schnadower et. al, Pediatrics 2010
- Retrospective, 20 centers, n=1895
- 29-60 day old with cx proven febrile UTI

Predicting Low Risk

- 4 Factors to Predict Low Risk
  - not clinically ill
  - no underlying disease
  - ANC > 1500
  - band count < 1250

→ consider discharge home after single dose of IV or IM Ceftriaxone with 24 hour follow-up OR short observation period

If any concern for inability to follow-up consider admission

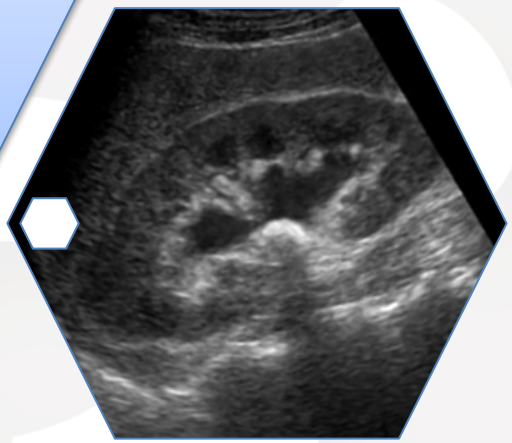
Case 2 -- revised

- Now let's assume our infant is 10 weeks old and has received her 2 mo vaccinations.

How do we treat?

Follow-up?

Do we admit?



Children's National

GUIDELINE

American Academy of Pediatrics
DEDICATED TO THE HEALTH OF ALL CHILDREN™

Oral and IV Antibiotics equally efficacious (2-24 mo)

- ✓ Evidence quality: A
- ✓ Strong recommendation

Take into account:

- ✓ Ability to tolerate oral abx
- ✓ “toxicity”
- ✓ Any concern regarding adherence

Children's National™

GUIDELINE

American Academy of Pediatrics
DEDICATED TO THE HEALTH OF ALL CHILDREN™

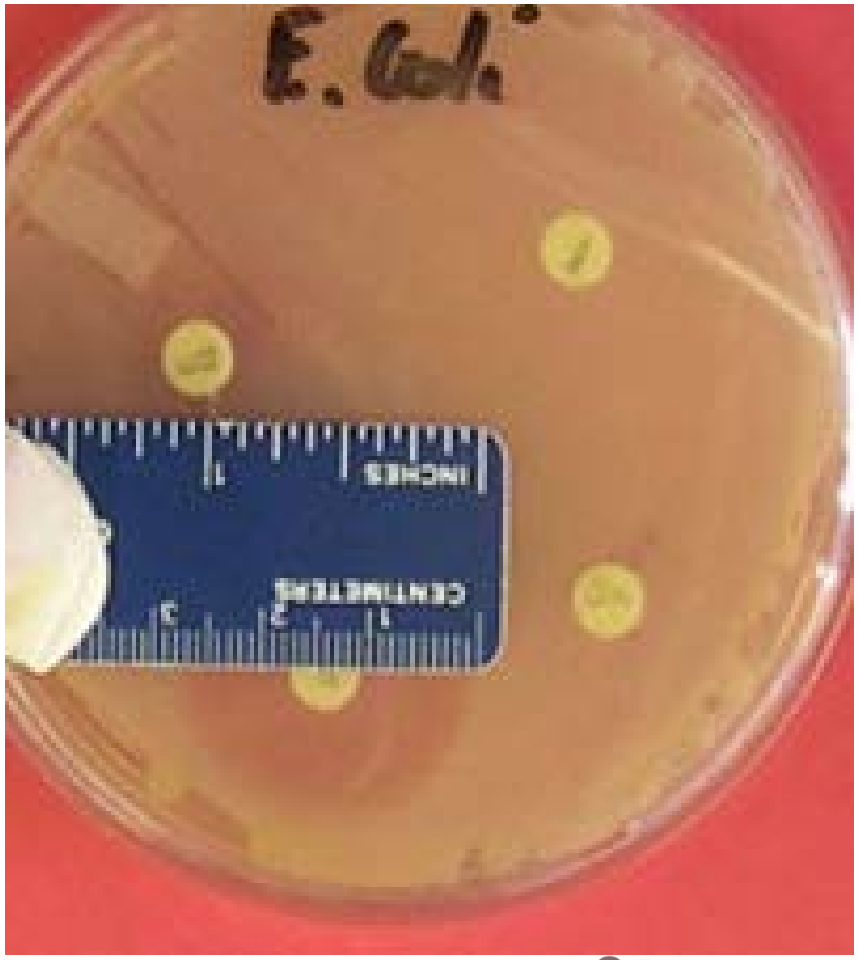
Antibiotic choice based on local sensitivity

- ✓ Evidence quality: A
- ✓ Strong recommendation

Children's National™

Abx of Choice: 2nd -3rd Gen Cephalosporin

- ✓ *Ecoli* (75-90%)
- 60% of *Ecoli* isolates are susceptible to TMP/SMZ
- 41% susceptible to ampicillin
- 93% susceptible to second generation cephalosporins
- ✓ *Enterococcus*
- 100% susceptible to ampicillin
- ✓ *Klebsiella, GBBS…*



2015 CNMC Antimicrobial Susceptibility Data

GUIDELINE

American Academy of Pediatrics
DEDICATED TO THE HEALTH OF ALL CHILDREN™

Duration of Abx: 7-14 days

- ✓Evidence quality: B
- ✓Recommendation

Children's National™

Case 2 -- continued

- Infant is in your office for follow up at 48 hours.
- Doing well, fevers improving.
- Will you complete any imaging for first time UTI?

GUIDELINE

American Academy of Pediatrics
DEDICATED TO THE HEALTH OF ALL CHILDREN™

Renal/Bladder Ultrasound on all infants

✓Evidence quality: C
✓Recommendation

WHY?

- Yield of abnormal findings: 12–16%
- Permanent renal damage (1 year later)
  - Sensitivity: 41%
  - Specificity: 81%

WHEN?

IF ill and not improving then within first 48 hours
IF improving then, if done, better done > 48 hours

Children's National™

DIAGNOSIS

Culture >50K
AND
UA (+LE/nitrates OR WBC)

TESTING

Two step method, using bag UA to screen is appropriate

TREATMENT

Oral = IV
Local resistance
7-14 days

FOLLOW-UP/IMAGING

Follow-up @ 48h
RBUS

Case 1:

5 month old male

Case 2:

10 week old female

Case 3:

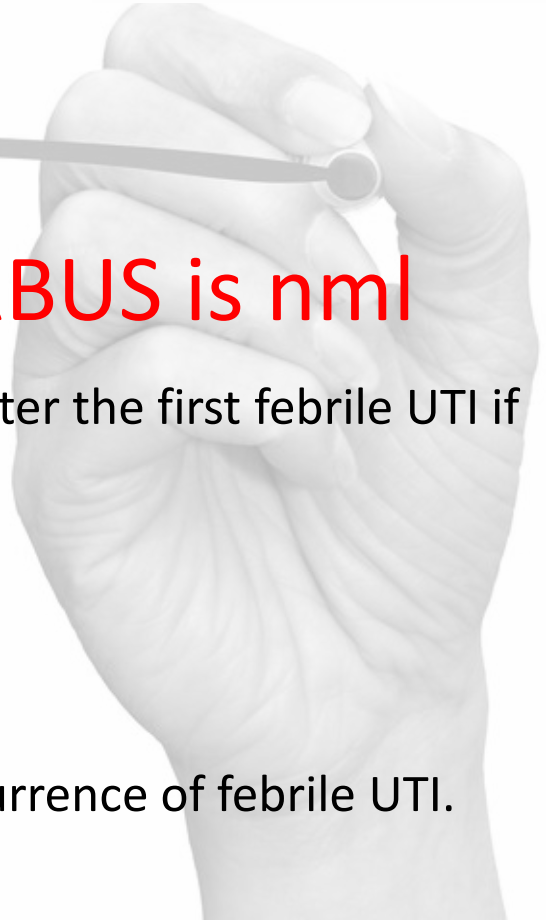
2 yo female with recurrent UTI

Case 3

- 2yo girl with previous febrile UTI in France
- Febrile illness since am
- Do we test?
- Do we image?
- If VUR → What do we do?

GUIDELINE

American Academy of Pediatrics
DEDICATED TO THE HEALTH OF ALL CHILDREN™



No VCUG for first febrile UTI if RBUS is nml

VCUG is not recommended to be performed routinely after the first febrile UTI if RBUS is normal.

- ✓ Evidence quality: B
- ✓ Recommendation

Further evaluation should be conducted if there is a recurrence of febrile UTI.

- ✓ Evidence quality: X
- ✓ Recommendation

Children's National™

VUR: To Treat or To Not Treat

Evidence from the RIVUR Trial

Randomized Intervention for
Children with VesicoUreteral Reflux

Children's National

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 JUNE 19, 2014 VOL. 370 NO. 25

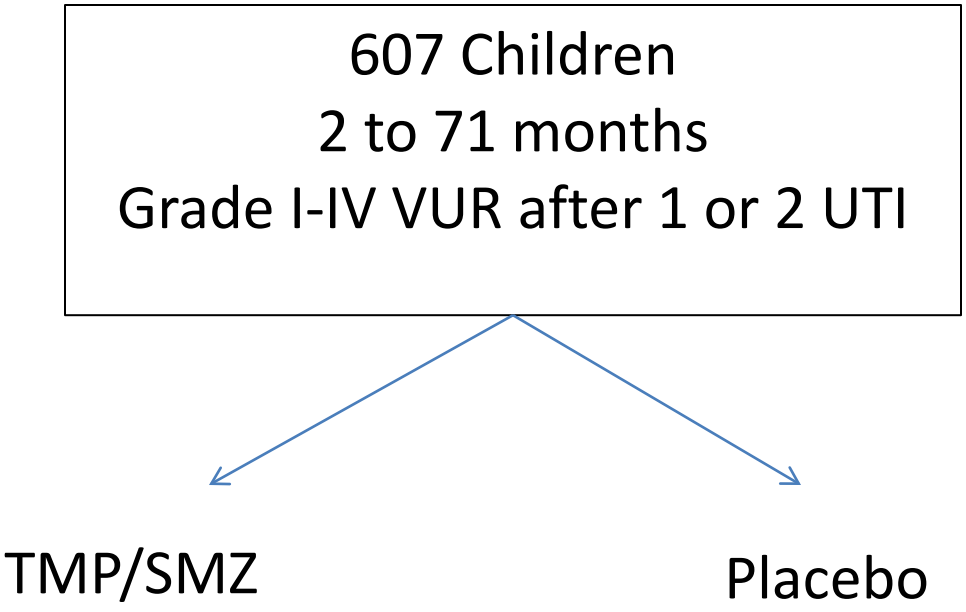
Antimicrobial Prophylaxis for Children with Vesicoureteral Reflux

The RIVUR Trial Investigators*

Children's National

RIVUR Trial

- 2-year randomized, double blind, placebo controlled trial



Patient Characteristics

Median age 12 months

92% girls

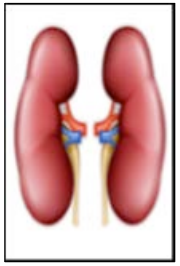
8% boys (63% uncirc)

80% had grades II or III reflux

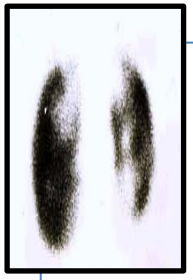
56% BBD

Children's National

Study Outcomes



Recurrent UTI

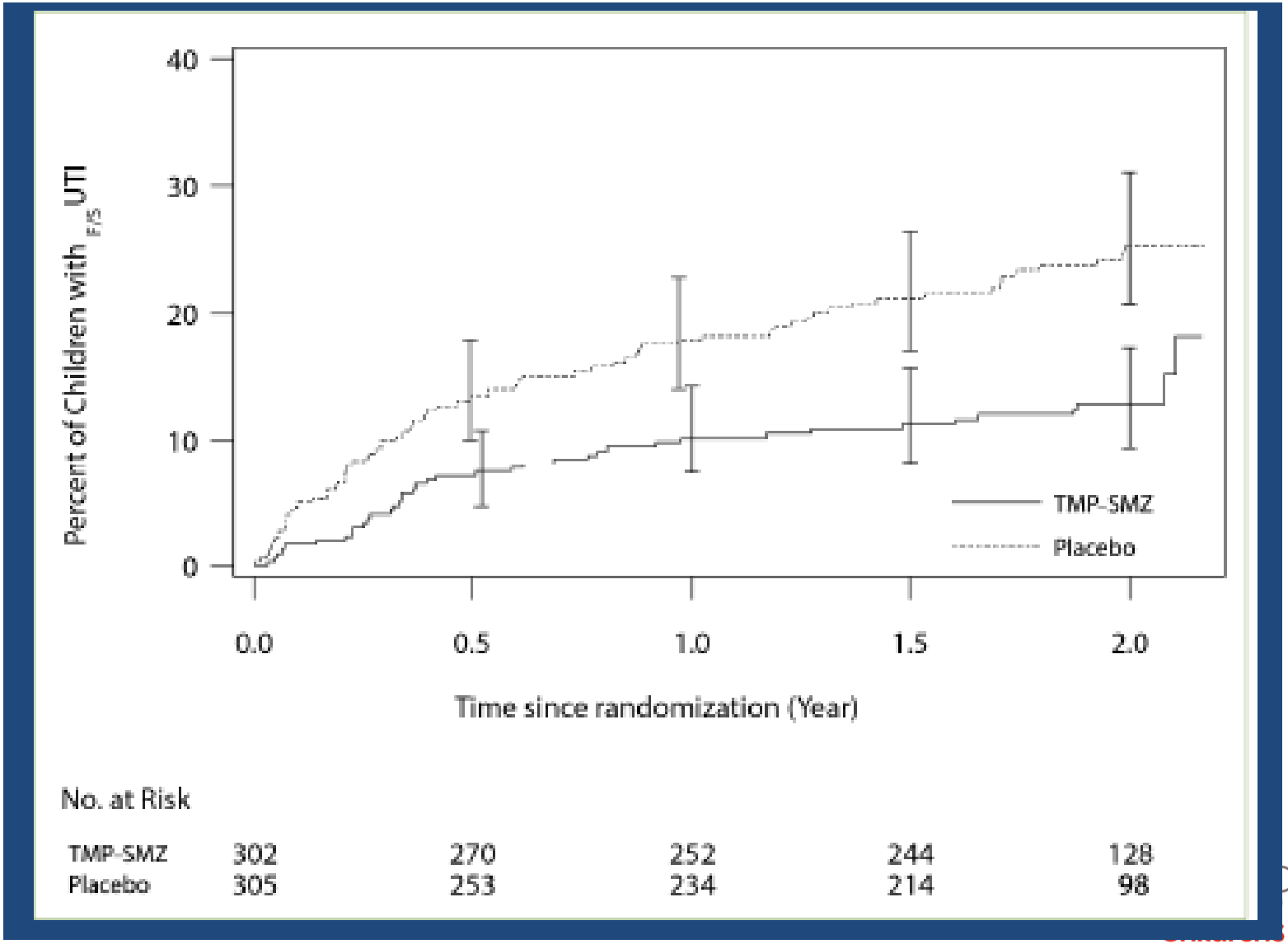


Renal Scarring

Abx Resistance

Children's National

Decreased recurrences of UTI



No Change in Renal Scarring

NO Difference Overall

- Prophylaxis 11.9%, Placebo 10.2% (p=0.55)

NO Difference in Severe Renal Scarring

- Prophylaxis 4.8%, Placebo 2.6% (p=0.37)

NO Difference in New Renal Scarring

- Prophylaxis 8.2%, Placebo 8.4% (p=0.94)

Children's National

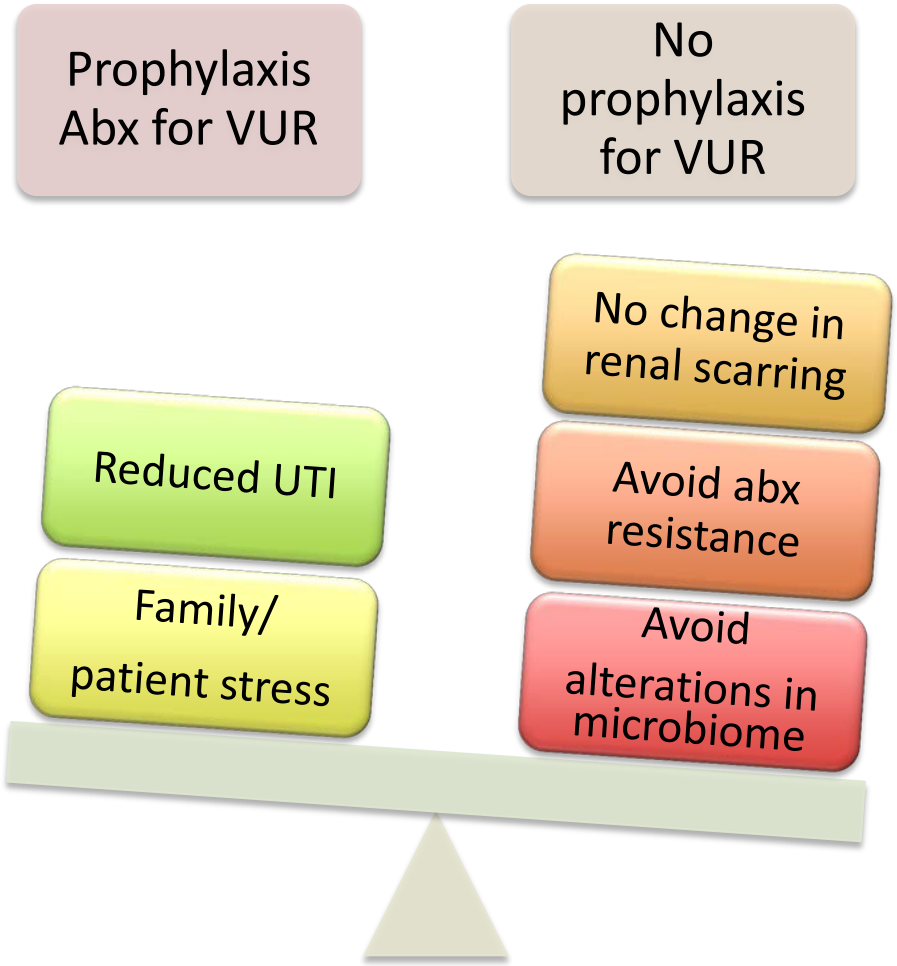
Greater Antibiotic Resistance

- E.Coli from stool culture →
  - Resistance to TMP/SMZ was greater in treatment group, but not statistically significant

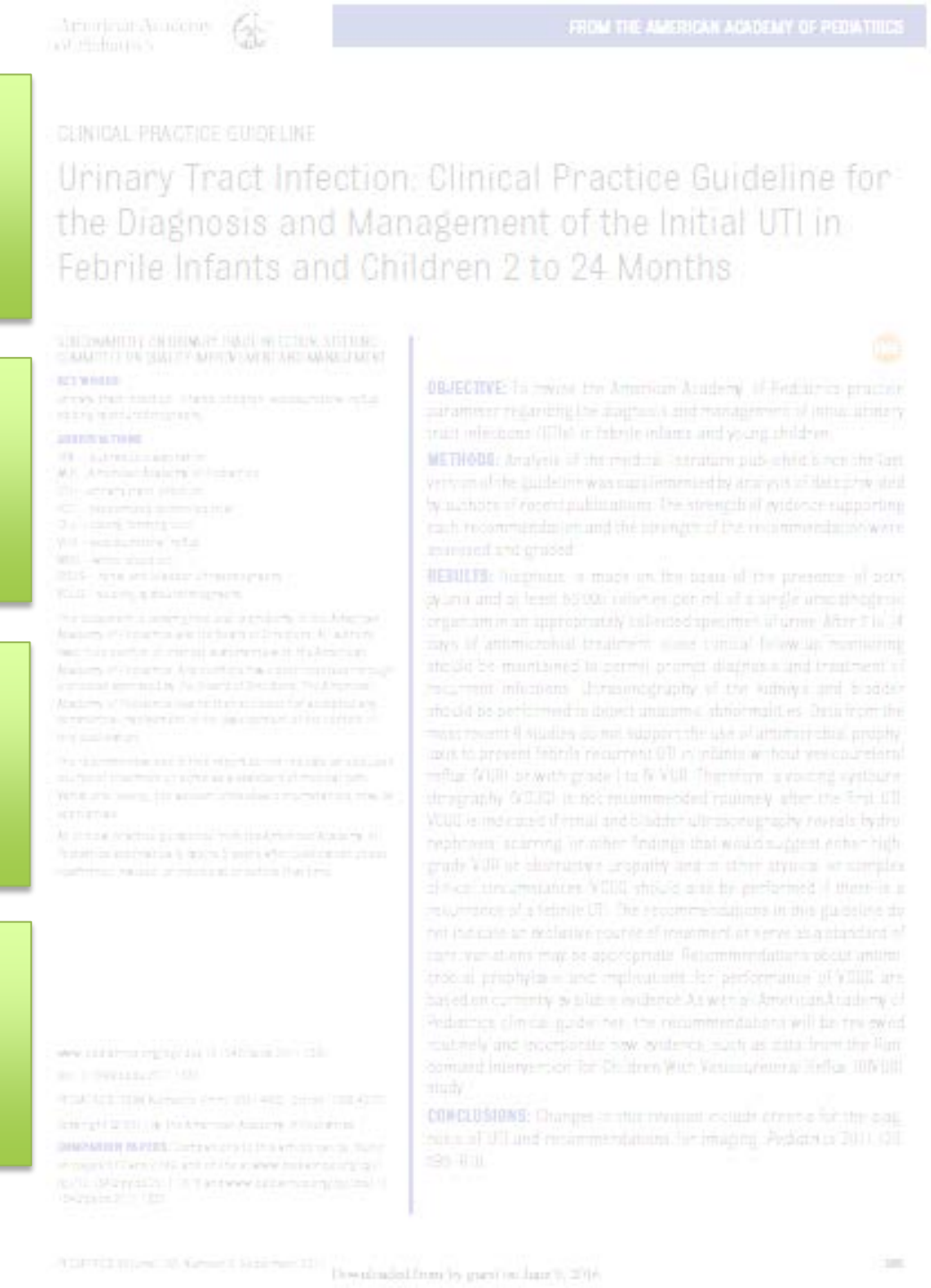
- 1st recurrent UTI with E.Coli →
  - Resistance to TMP/SMZ was greater in treatment group ($p<0.0001$)

Children's National

Debate continues



Children's National



DIAGNOSIS

Culture >50K
AND
UA (+LE/nitrates OR WBC)

TESTING

Two step method, using bag UA to screen is appropriate

TREATMENT

Oral = IV
Local resistance
7-14 days
No prophylaxis

FOLLOW-UP/IMAGING

Follow-up @ 48h
Not better - RBUS
VCUG only if abnl RBUS or second UTI

Future Directions

- Due for revision of AAP guidelines
- Novel POC testing; non-invasive testing
- Smart diapers

References

- AAP Clinical Practice Guideline: *Pediatrics.* 2011
  - http://pediatrics.aappublications.org/content/early/2011/08/24/peds.2011-1330
- AAP Webinar by Kenneth Roberts:
  - http://www2.aap.org/pcorss/webinars/pco/AAP%20Webinar_UTI-Roberts-Final.ppt

SUMMARY: 2011 AAP GUIDELINE FOR DIAGNOSIS AND MANAGEMENT OF UTIS IN FEBRILE INFANTS

June 20, 2016

Children's National

- **Inclusion**: Infant 2-24 mo with unexplained fever(> 38C)
  - Rate of UTI: ~5%
  - Rate of scarring higher than older children

- **Exclusion**: neurologic or anatomic abnormality known to be associated with recurrent UTI or renal damage

DIAGNOSIS: 2011 AAP Guidelines	
Specimen collection for urine culture must be catheterization or suprapubic aspiration	Strong
Risk stratification based on bag urinalysis and if positive then catheterize or suprapubic tap for culture	
Diagnosis established with both suggestive of infection: 1. Urinalysis suggestive of infection 2. Culture with >50K CFU	Recommend

Children's National

MANAGEMENT: 2011 AAP Guidelines	
YES – oral and parenteral abx equal efficacy	Strong
YES – 7 to 14 days of antimicrobial therapy	
YES – RBUS: Febrile infants with UTIs should undergo renal and bladder sonography (RBUS) IF ill and not improving then within first 48 hours IF improving then, if done, better done > 48 hours	Recommend
NO – VCUG after first febrile UTI YES – VCUG after second UTI or if abnormal RBUS	
YES – Once documented febrile UTI, instruct parents to return within 48 hours for another febrile illness	

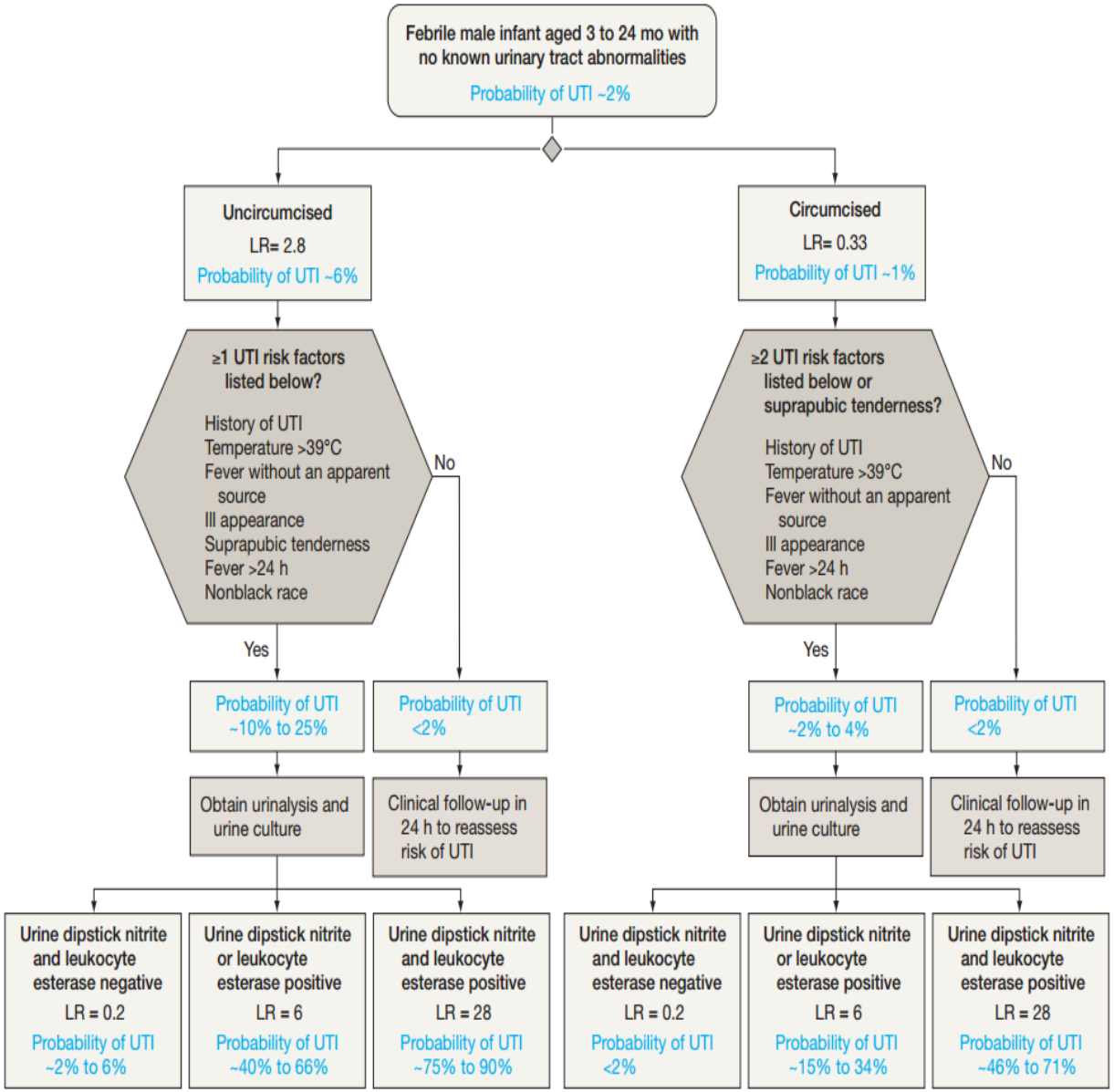
Children's National

Changes from previous UTI Guidelines

- Diagnosis:
  - Abnormal urinalysis + positive culture (need both)
  - Positive culture is >= 50K CFU/mL
  - Assessment of likelihood of UTI
- Treatment:
  - Oral as effective as parenteral
- Imaging:
  - VCUG not routinely recommended after first febrile UTI
- Follow-up:
  - Emphasis on urine testing with subsequent febrile illnesses

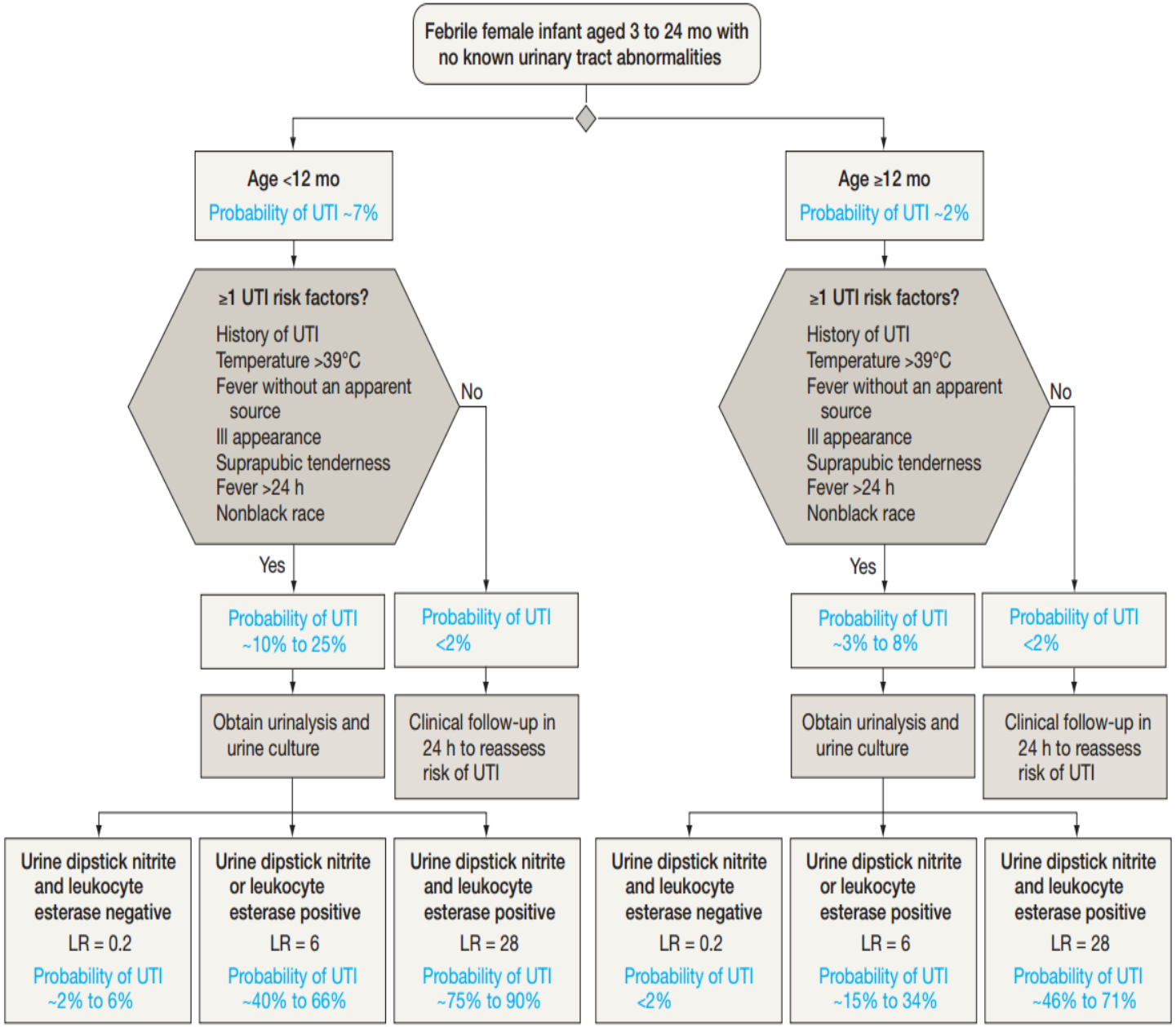
ALGORITHMS

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



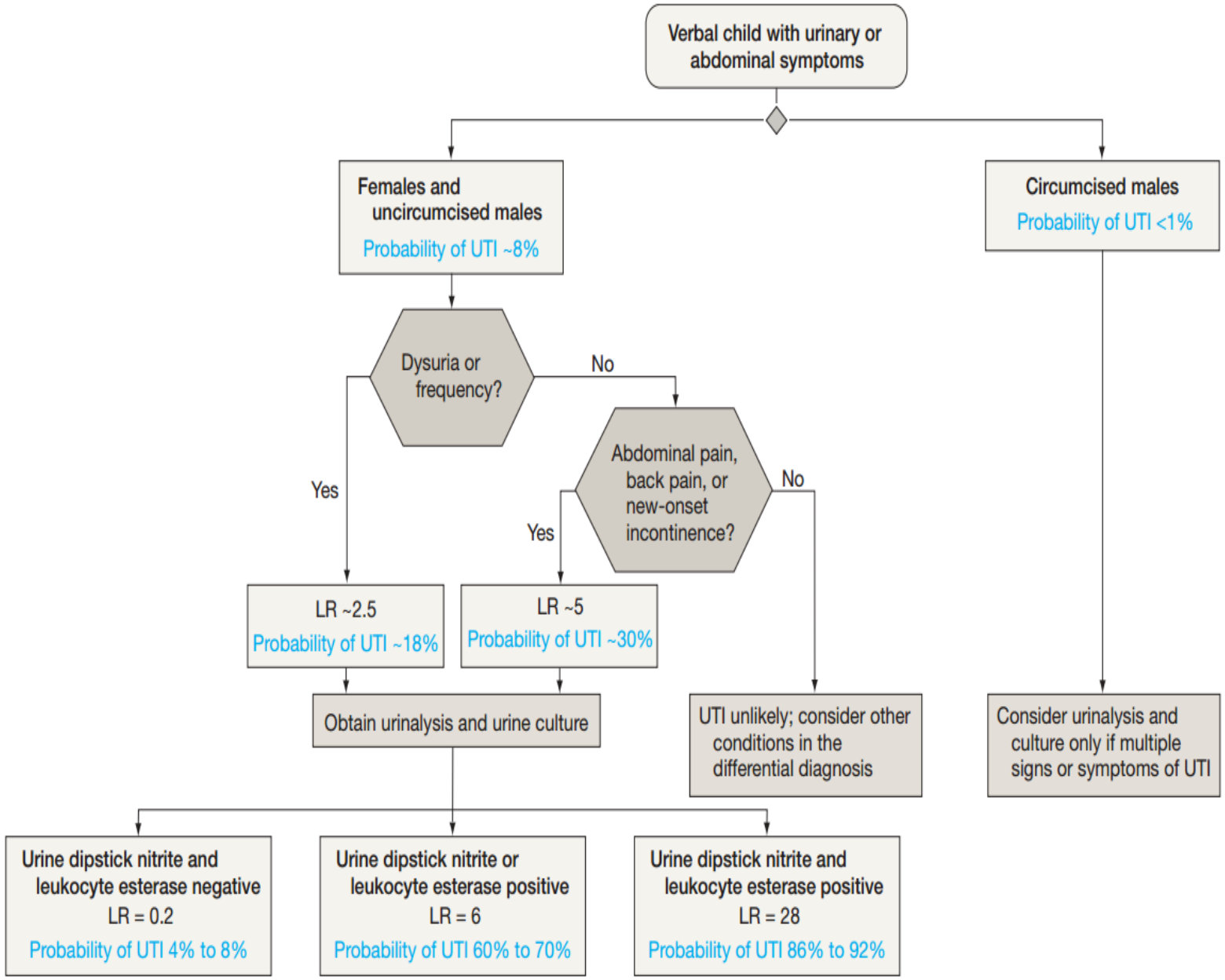
UTI indicates urinary tract infection; LR, likelihood ratio.

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



UTI indicates urinary tract infection; LR, likelihood ratio.

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



UTI indicates urinary tract infection; LR, likelihood ratio.