

Current Issues in UTI:

Beyond the Guidelines

PHM 2017

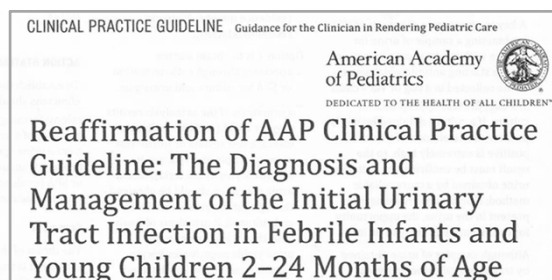
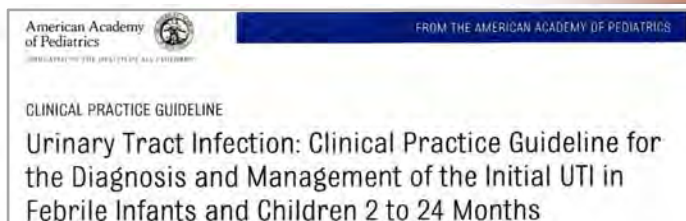
July 21, 2017

Ken Roberts and the PHM UTI All-Star Band:
Mini Wallace, Alan Schroeder, Rick Engel and
Dan Rauch

Disclosures (None)

- We have no relevant financial relationships with the manufacturer(s) of any commercial product(s) and/or provider(s) of commercial services.
- We do not intend to discuss an unapproved/investigative use of a commercial product/device.

AAP Guideline 2011, 2016



Issues Discussed Today

- UTI-related hospitalizations (Rauch)
- 0-2 month olds:
 - UTI-associated bacteremia (Schroeder)
 - UTI-associated meningitis (Wallace)
 - Imaging (Schroeder)
- UTI-related QI (Engel)
- “Loose ends” (Roberts)

Objectives for This Session

- By the end, you will be able to:
 - State changes in the number of UTI-related hospitalizations
 - Raise questions about the significance of UTI-related bacteremia
 - Weigh the risks and benefits for LPs in all infants 0-2 months old with UTI
 - Conclude whether imaging is need for all 0-2 month olds with UTI
 - Recognize the value of QI activities to implement guidelines
 - Include urine SG when interpreting automated urinalyses
 - Pursue the diagnosis of BBD (constipation) by history and physical examination in infants and children with UTI



UTI Hospitalizations

Daniel Rauch, MD, FAAP, FHM
Chief, Division of Pediatric Hospital Medicine
Tufts Medical Center/The Floating Hospital for Children





NATIONAL TRENDS OF UTI HOSPITALIZATIONS

Daniel A Rauch and Ying-hua Liu,
NYU School of Medicine

Background

Oral Versus Initial Intravenous Therapy for Urinary Tract Infections in Young Febrile Children

Alejandro Hoberman, Ellen R. Wald, Robert W. Hickey, Marc Baskin, Martin
Charron, Massoud Majd, Diana H. Kearney, Ellen A. Reynolds, Jerry Ruley and
Janine E. Janosky
Pediatrics 1999;104:79-86

- Studied children 1-24 months with UTI
- Admission and IV abx vs. Outpt with cefixime
- Result – equal efficacy short term and long term

Background

- Cochrane Review
- First published 2003, rev 2007
- “These results suggest that children with acute pyelonephritis can be treated effectively with oral antibiotics (cefixime, ceftibuten and amoxicillin/clavulanic acid) or with short courses (2 to 4 days) of IV therapy followed by oral therapy.”

Background

- UTI is a common cause of admission
 - 9th most common in 2006 (excluding newborn and psych dx)
- UTI treatment has a robust evidence based, non-controversial treatment algorithm

Methods

- Utilized HCUP resources
 - KID - the only dataset on hospital use, outcomes, and charges designed to study children's use of hospital services in the US. Triennial starting 1997. Now includes 38 states.
 - NIS - the largest all-payer inpatient care database that is publicly available in the US. Annual starting 1988
 - HCUPnet - a free, on-line query system based on data from the Healthcare Cost and Utilization Project (HCUP)
 - AHRQ Pediatric Quality indicators
 - PDI 18: UTI Admission Rate

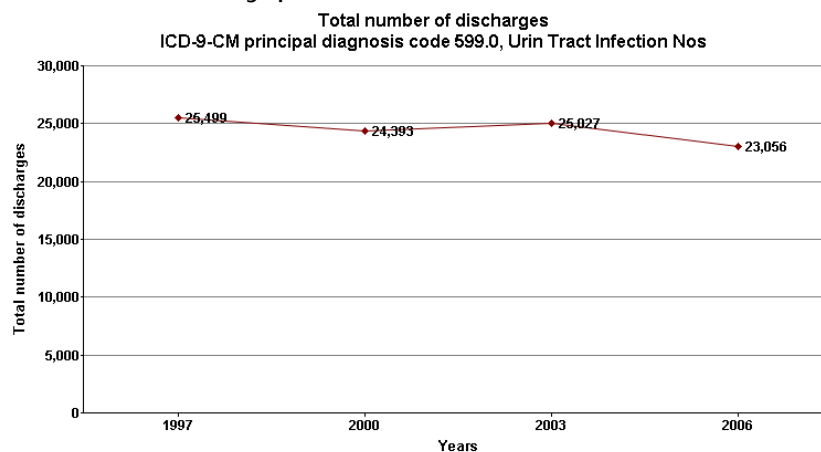
Methods

- Examined:
 - Hospitalization rates for DRG 599.0
 - Length of stay (LOS)
 - Costs

 - 1997-2006

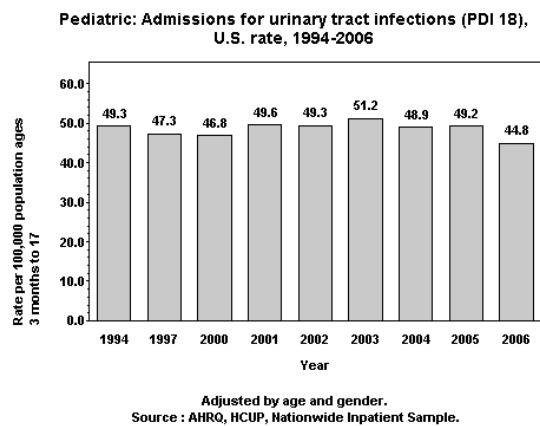
Results

- UTI hospitalizations have not changed significantly over the study period



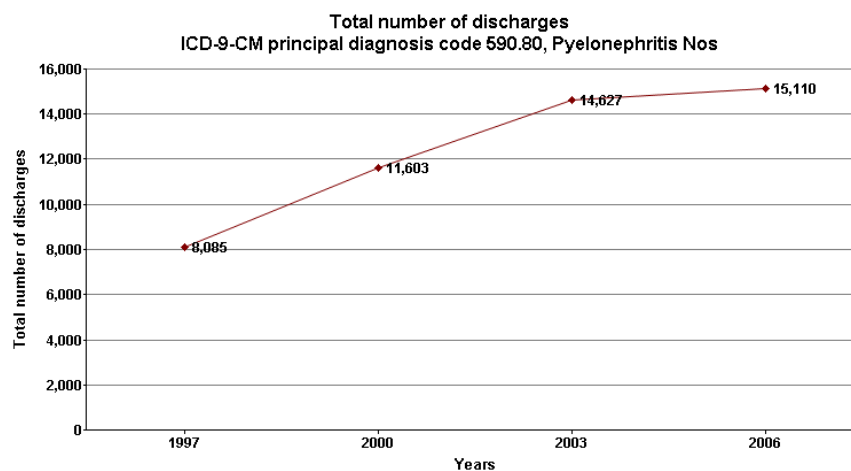
Results

- UTI hospitalization rates have not changed significantly over the study period



Results

- Pyelonephritis rates significantly increased




Results

- UTI Demographics unchanged





Patient distribution by age and sex

	<1	1-4	5-9	10-14	15-17	Boy	Girl
1997	58.1%	20.4%	10.8%	5.2%	5.6%	34.5%	64.5%
2000	57%	21.1%	11.3%	5.6%	5.1%	33.5%	66.5%
2003	58.3%	19.8%	11.2%	5.2%	5.5%	36.5%	62.9%
2006	58.7%	20.5%	10.5%	5%	5.5%	34.6%	64.9%






CHANGES IN U.T.I. HOSPITALIZATIONS AFTER 2011 A.A.P. U.T.I. GUIDELINES

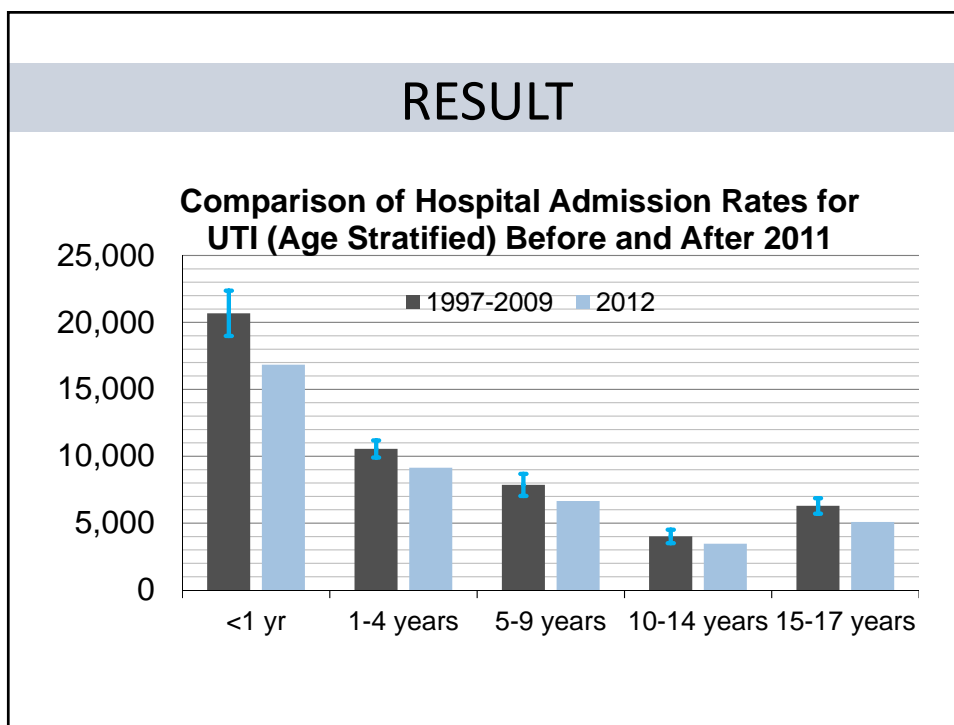
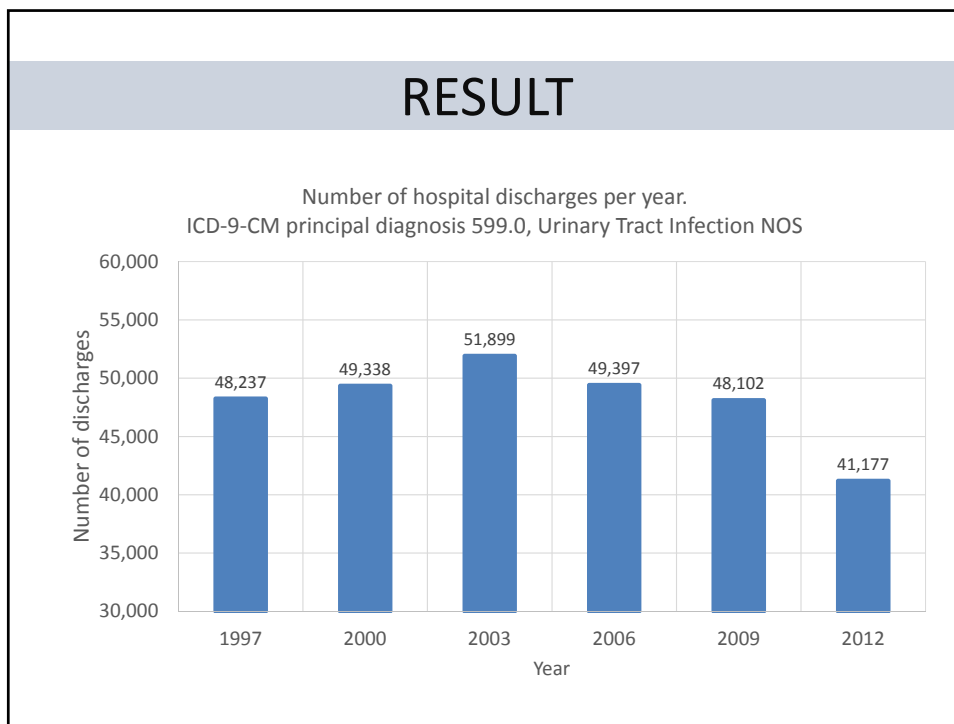
Rauch DA, Courchia B, Ramirez D, Roberts KB

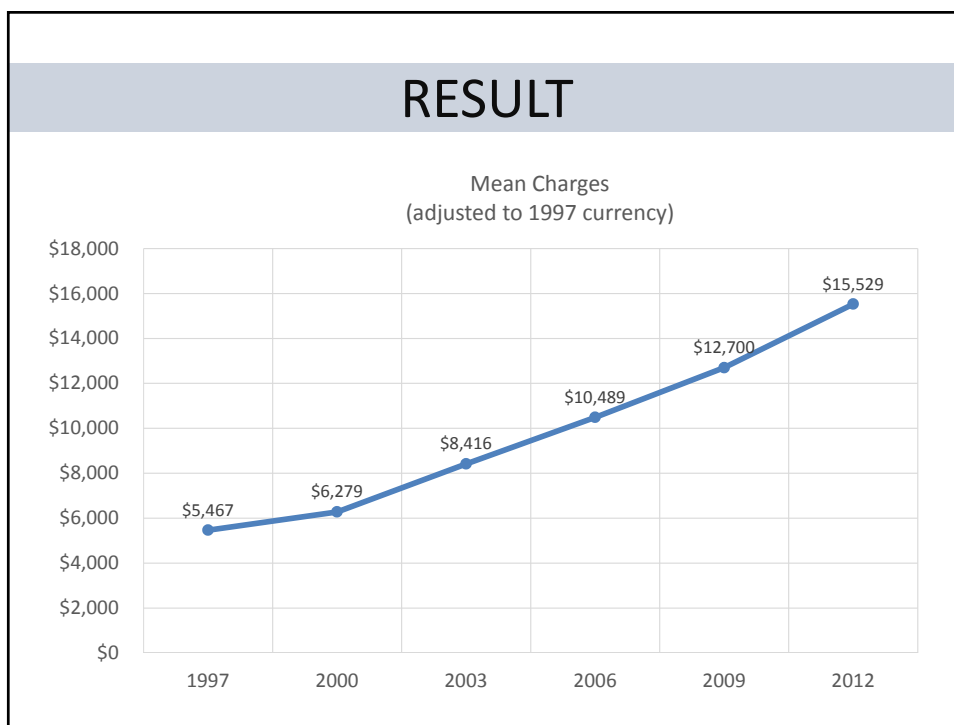
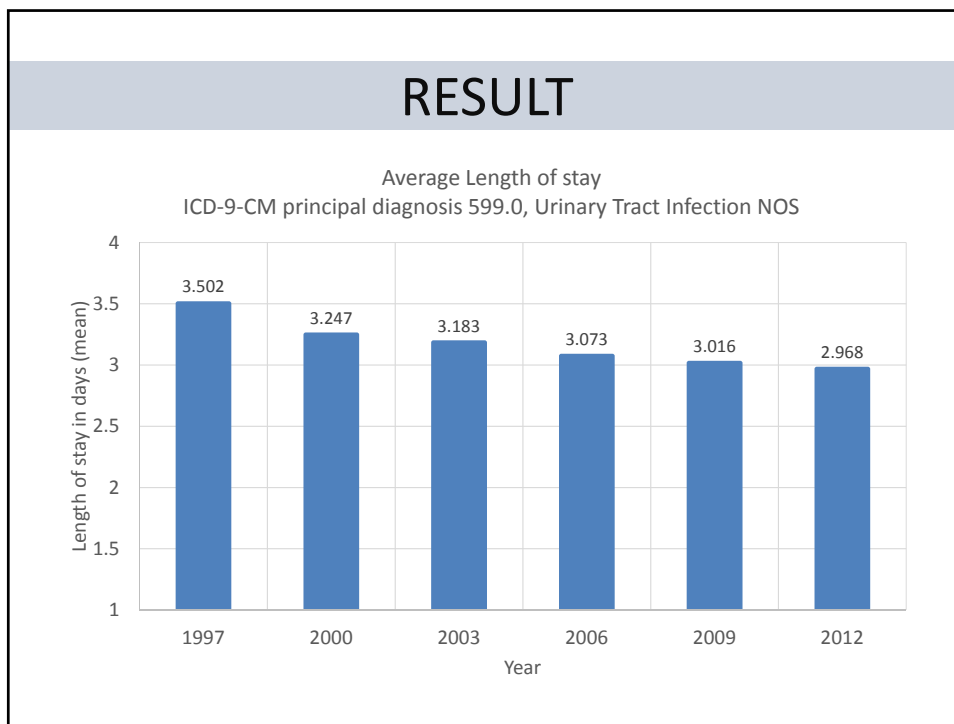





STUDY DESIGN

Discharge volume for CCS principal diagnosis category 159: Urinary tract infection was examined for trends across years by age (as grouped by KID). Changes in length of stay (LOS) and charges corrected for inflation (using <http://data.bls.gov/cgi-bin/cpicalc.pl>) were also examined.



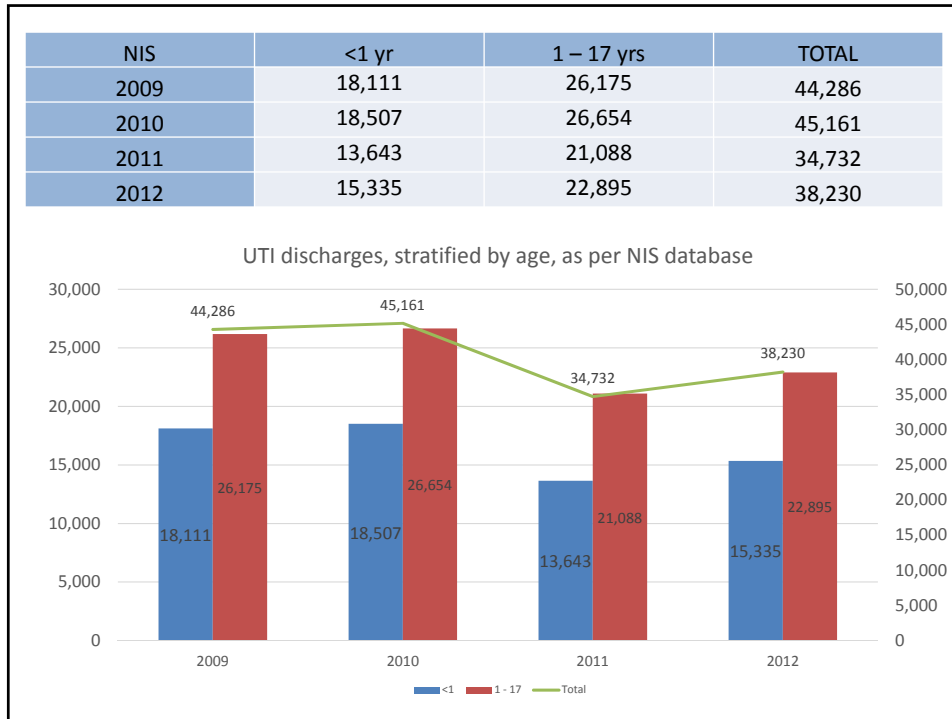


RESULT

Year	Total number of discharges						Mean Charges (adjusted to 1997 currency)	LOS, days (mean)
	Total	<1 year	1-4 yrs	5-9 yrs	10-14 yrs	15-17 yrs		
1997	48,237	20325	10079	8043	3769	6020	\$5,467	3.502
2000	49,338	20114	10746	8222	4239	6016	\$6,279	3.247
2003	51,899	21863	10903	8186	4320	6627	\$8,416	3.183
2006	49,397	21255	10400	7355	3837	6549	\$10,489	3.073
2009	48,102	19930	10601	7467	3875	6229	\$12,700	3.016
2012	41,177	16836	9143	6653	3462	5082	\$15,529	2.968

RESULT

All discharges		Total number of discharges			
		2009	2012	Difference	p-value
		48,102	41,177	-6,925 14.40 %	0.001
Age	<1	19,930	16,836	-3,094 15.52 %	0.0025
	1-4	10,601	9,143	-1,457 13.75 %	0.0054
	5-9	7,467	6,653	-814 10.90 %	0.0212
	10-14	3,875	3,462	-412 10.64 %	0.043
	15-17	6,229	5,082	-1,147 18.42 %	< 0.0001



Comments

- Secular trends of other infectious, non-communicable disease not comparable due to vaccines (pneumonia) or change in organisms (soft tissue infections)
- Coincidence?
 - Fast effect of 2011 AAP Guidelines or 1999 data finally sinking in
 - Data in other dx does show faster and higher uptake of guideline use in hospitalists

Comments

- Can the AAP guidelines be credited for the drop in UTI discharges in light of the significant decrease in EVERY age group?
- What can explain the ever-increasing cost of hospitalization for UTI with more common use of oral antibiotics?

Beatles Songs that Apply

- Let it Pee
- While My Guitar Gently Pees
- Within You Without You
- Tell Me Why
- Help!
- Doctor Robert

UTI and “SBI”

Chapter 77

Urinary Tract Infection

Introduction

Urinary tract infection (UTI) is the most common serious bacterial infection of childhood and is a frequent admitting diagnosis. About 5% of febrile infants younger than 12 months have a UTI, although most can be treated as an outpatient. Indications for inpatient treatment include age younger than 1 to

“SBI” Currently

- UTI vs meningitis
 - UTI many times more common
 - Even in first month: 15-20 times more common
 - Treatment different
 - Prognosis different
 - Downside of delaying dx/rx for a day different

“SBI” Currently

- UTI vs meningitis
 - UTI many times more common
 - Even in first month: 15-20 times more common
 - Treatment different
 - Prognosis different
 - Downside of delaying dx/rx for a day different
- It is time to retire the term “SBI”

So Is a UTI Just a UTI?

- Yes ...

So Is a UTI Just a UTI?

- Yes ... even in the first months of life???

Issues Discussed Today

- UTI-related hospitalizations (Rauch)
- 0-2 month olds:
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 - Imaging (Schroeder)
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- “Loose ends” (Roberts)

Diagnosing bacteremia in UTI: Help you or hurt you?

Alan Schroeder, MD
Stanford University School of Medicine

Case (poor man's audience response)

- 35 day-old female with T 39.1, looks well, no clear source
 - Cath UA: 50 WBC/hpf, 2+LE, neg nitrites; Urine culture sent

Question 1: Who wants a blood culture?

(They have tried twice, unsuccessfully, parents are peeved).

Question 2: Who wants a blood culture?



Case

Blood and urine cultures grow pan-sensitive E coli. At 48 hours of hospitalization, baby is back to baseline.

Question 3: How many more days IV?

- a.) Get 'em home (none)
- b.) 1-2 more for good measure (3-4 days total IV)
- c.) 5-9 days total IV
- d.) 10-14 days total IV

How could a blood culture be beneficial?

Two assumptions

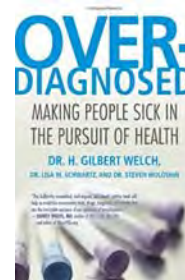
- Bacteremia = more “serious”
- Bacteremia detection → management decisions that are of proven benefit
 - Longer IV abx courses?
 - Longer total abx courses?
 - Different drug? Different dose?
 - Closer follow-up?
 - Imaging?

How could blood culture be harmful?

- Venipuncture → Pain/stress/compromised veins
- Contaminated specimen (13-18% in some series)
 - Additional blood cultures
 - Unnecessary abx (Vanco?)
 - ↑ LOS
 - LP?
- Overdiagnosis/overtreatment

Some overdiagnosis pearls

- Tests can “change management” without benefiting patients
- The detection of abnormalities is not synonymous with patient benefit



Bacteremia in UTI: How common?

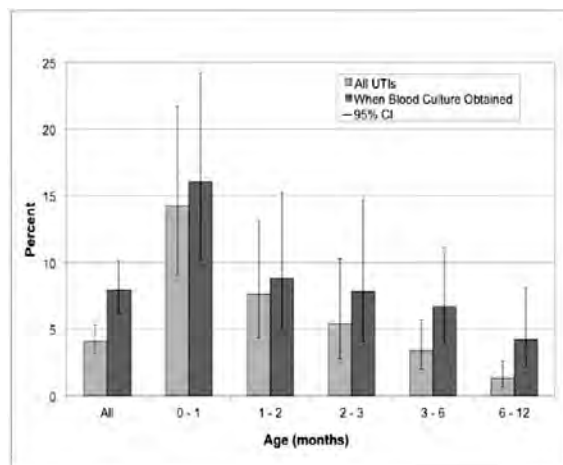


FIGURE 2 Proportion of infants with UTIs who had bacteremia.

Roman, *Hosp Pediatr* 2015

Assumption 1: bacteremic infants are sicker

Author, journal (year)	Finding
Honkinen, <i>PIDJ</i> (2000)	<ul style="list-style-type: none"> • ↑ feeding problems, CRP • no difference in Tmax or fever duration, WBC, clinical appearance
Schnadower, <i>Pediatrics</i> (2010)	<ul style="list-style-type: none"> • ↑ bands • No difference in clinical appearance
Newman, <i>Arch Ped Adol Med</i> (2002)	<ul style="list-style-type: none"> • No difference in clinical appearance or Tmax
Hoberman, <i>Pediatrics</i> (1999)	<ul style="list-style-type: none"> • ↑ WBC • no difference in Tmax, fever duration, time to defervescence
Roman, <i>Hosp Pediatr</i> (2015)	<ul style="list-style-type: none"> • ↑ % bands • No difference in Tmax, ill appearance
Bachur, <i>Ped Emerg Care</i> (1995)	<ul style="list-style-type: none"> • ↑ % bands • No diff in temp, WBC, ESR, HCO₃

Caveat: We might be comparing "true" UTIs to asymptomatic bacteruria or contamination

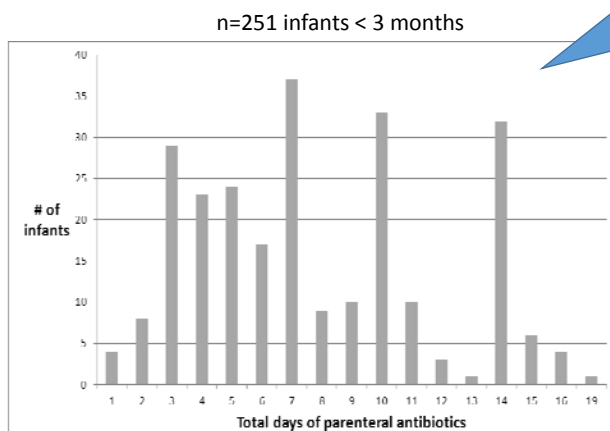
Assumptions

- Assumption 1: bacteremic infants are sicker...meh!

Assumption 2: detection of bacteremia → *beneficial changes* in management

- We know it leads to *changes* in management:
 - Roman, *Hosp Pediatr* 2015: 4.3 days longer IV treatment
 - Honkinen, *PIDJ* 2000: 2.5 days longer IV treatment
 - Brady, *Pediatrics* 2010: higher odds of prolonged IV rx if bacteremic

Are the longer IV courses beneficial?



Schroeder et al, *Arch Dis Child*, 2015

Outcomes excellent, whether you got a FG, TD, or multiple thereof

- No recurrent bacteremic UTI

- 6 recurrent UTI caused by same bug, no association with initial IV duration

Assumptions

- Assumption 1: bacteremic infants are sicker...meh!
- Assumption 2: bacteremia detection → beneficial interventions...meh!

Central assumption that has driven many “standards of care”

Parenteral antibiotics are superior to enteral antibiotics

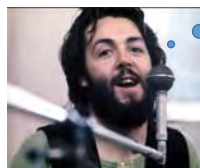
Can someone please show me that sentinel study?! Any study? Bueller?



Closing thoughts

- Blood cultures for well-appearing babies > 1 month with a convincing UA:
 - Probability of harm is high
 - No convincing benefits
- Same probably true for < 1 month, but I'm not quite there yet psychologically
 - Meningitis??

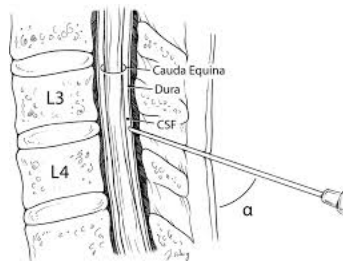
Bacteremia:
Let It Be?



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“To Tap” or “Not to Tap”



Sowdhamini Wallace, DO
Baylor College of Medicine
Houston TX

Little Ones Make Us Worry!

- Hematogenously acquired UTIs?
 - Bacteremia present in 6-10%
- More penetrable blood brain barrier
- Immature immune system
- You may ask...



Evidence for Infants 29 – 60 Days Old

Author, Journal (year)	N	Findings
Thompson, <i>Pediatr Infect Dis</i> (2017)	934	0.2% (n=2; Both with bacteremia)
Tebuegge, <i>PLoS ONE</i> (2011)	304	0% (However, 1 had growth of E. Coli in broth and no pleocytosis-- considered contaminant)
Paquette, <i>Pediatric Emergency Care</i> (2011)	57	1.8% (n=1; E. Coli bacteremia, leukopenia and ill appearance)
Schnadower, <i>Pediatrics</i> (2010)	1609	0.3% (n=2 Definite ABM, 3 Probable)
Adler-Shohet, <i>Pediatr Infect Dis</i> (2003)	85	1.2% (n=1; 7 week old with E. Coli ABM)

10/2,989= 0.3% (95% CI: 0.2%-0.6%)

Evidence for Infants 0-28 Days Old

Author, Journal (year)	N	Findings
Thompson, <i>Pediatr Infect Dis</i> (2017)	803	0.9% (n=7; All cases with bacteremia)
Wallace, <i>J of Pediatr</i> (2017)	236	0.8% (n=2 Probable ABM, 0 Definite ABM)
Bonadio, <i>Pediatr Infect Dis</i> (2014)	100	0% (none pretreated)
Tebuegge, <i>PLoS ONE</i> (2011)	163	1.2% (2 had ABM; Both very ill, irritable and lethargic; 1 additional case with Enterococcus in broth only and considered contaminant)
Zarkesh, <i>Iran J Pediatr</i> (2011)	17	0%
Schwartz, <i>Arch Dis Child</i> (2009)	82	2.4% (2 with E. Coli meningitis)

Evidence for Infants 0-28 Days Old

Author, Journal (year)	N	Findings
Vuillermin, <i>Emerg Med Australasia</i> (2007)	34	0%
Magin, <i>Pediatr Emerg Care</i> (2007)	75	0%
Adler-Shohet, <i>Pediatr Infect Dis</i> (2003)	83	0%
Goldman, <i>CJEM</i> (2003)	70	0%
Syrogianopoulos, <i>Pediatr Infect Dis</i> (2001)	67	0%

14/1,730=0.8% (95% CI: 0.4%-1.4%)



Limitations of the Evidence

- Clinical appearance not always assessed
- Urine collected via non-sterile methods
- Missing LPs/Possible selection bias
- Lack of assessment for antibiotic pretreatment
- Varying definitions of ABM (i.e. Definite vs. Probable)
- Lack of precision surrounding estimates of meningitis

So What Do We Do?

Does every well appearing infant 29-60 days old with grossly positive UA need a LP?



Does every well appearing infant 0-28 days old with positive UA need a LP?



Is there really any harm in doing LPs in all febrile infants with UTI?

It's not always that simple....

- Bloody low volume CSF sample (false negatives)
- Bloody antibiotic pre-treated CSF sample (potential false positives)
- Sterile CSF pleocytosis considered to be “early” bacterial meningitis
- Unable to get CSF sample despite multiple attempts
- Parents refuse LP

Infants 29-60 Days Old

NNT = 333 (95% CI: 166-500)

What is your threshold?

BENEFITS

Under-treatment of ABM
& neurologic sequelae



RISKS

Uninterpretable CSF/Overtreatment
Risks of procedure
Pain
Parental anxiety

Infants 0-28 Days Old

NNT = 125 (95% CI: 71-250)

What is your threshold?

BENEFITS

Under-treatment of ABM
& neurologic sequelae



RISKS

Uninterpretable CSF/Overtreatment
Risks of procedure
Pain
Parental anxiety

Future Directions: *Can Biomarkers Help?*

Eur J Clin Microbiol Infect Dis (2017) 36:281–284

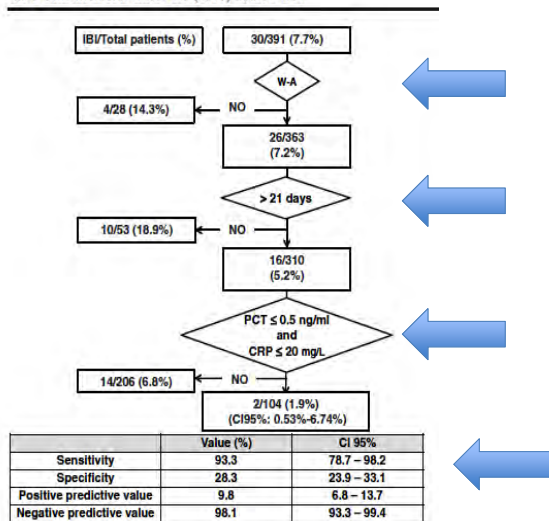


Fig. 1 Performance of predictive model in validation sample

Conclusions

- Remember those NNTs!
- The scale may tip in one direction more than the other depending on patient age, appearance, parental values, and clinical circumstances
- Future directions may include use of laboratory markers to guide the practice for selective LPs

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- “Loose ends” (Roberts)

Diagnosing VUR in UTI: Help you or hurt you?

Alan Schroeder, MD
Stanford University School of Medicine

Case

- 2 week-old female, uncomplicated E coli UTI (without bacteremia), normal prenatal US

Question 1: Who wants an RBUS?

Scenario 1 → RBUS is normal

Question 2: Who wants a VCUG?

Scenario 2 → RBUS has “trace pelviectasis”

Question 3: Who wants a VCUG?



Value of RBUS

- Commonly “positive” (~25-50%, higher in young infants)
- Abnormalities of *questionable* significance >> abnormalities of *real* significance
- Non-invasive, no radiation
- False + risk may be higher earlier

Concession

- The sensitivity of RBUS for abnormalities found on VUCG is **LOW!**
 - 4-55%, depending on thresholds of “abnormal” [Nelson, *Pediatrics* 2014]
 - But NPV almost always in high 90’s
 - Important to avoid “false negative confusion”
 - 1-NPV vs 1-sensitivity
 - What are we “missing”?

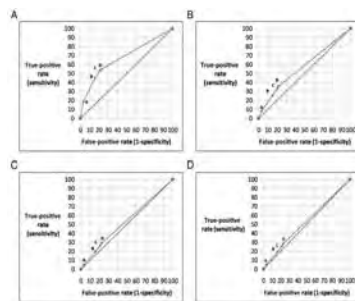


Table 2. Outcomes of Patients With First-Time Febrile Urinary Tract Infection (UTI) During the Prealgorithm and Postalgorithm Periods

Outcome	Prealgorithm Group (n=98)	Postalgorithm Group (n=103)	Risk Ratio (95% CI) ^a
First UTI, No. (%)			
VCUG	97 (99.0)	13 (12.6)	0.13 (0.08-0.21)
Renal US	97 (99.0)	69 (67.0)	0.68 (0.59-0.78)
Recurrent UTI (within 6 mo of first), No. (%)	7 (7.1)	8 (7.8)	1.08 (0.41-2.89)
VUR identified, No. (%)			
Grade 4-5	2 (2.0)	3 (2.9)	1.43 (0.24-8.36)
Grade 1-3	19 (19.4)	0 ^b	...
Prophylactic antibiotic use, No. (%)			
Until VCUG	69 (70.4)	2 (1.9)	0.03 (0.01-0.11)
Indefinitely	26 (26.5)	3 (2.9)	0.11 (0.03-0.35)
None	3 (3.1)	98 (95.1)	31.1 (10.2-94.8)
Subsequent urine cultures per patient, No. (95% CI)	0.3 (0.2-0.5)	0.4 (0.3-0.6)	...

Schroeder, *Arch Ped Adol Med* 2011

These 19 babies
all got...more
VCUGs

Treating VUR

- Very little data on < 2 months
- Prophylactic antibiotics prevent UTI! (at the expense of a high NNT)
 - **But... their efficacy is not modified by the presence or degree of VUR**
 - RIVUR & PRIVENT
 - And... they don't reduce scarring
 - And... they increase the risk of resistance

Except

- Prophylaxis and endoscopic injection superior to surveillance in reducing recurrent UTI and scarring for grades III-IV
 - In girls only (n=~40 pts per group)



VCUG/VUR

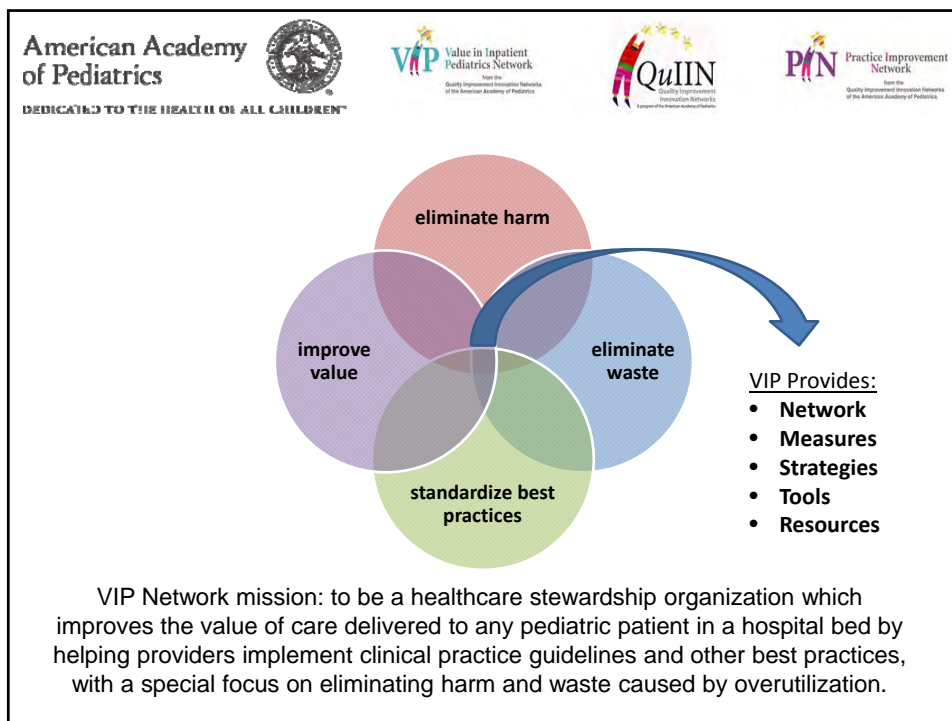
- Reasons why < 2 months might be considered apart from 2-24 months:
 - If we can actually prevent UTIs, more “value” in preventing UTIs in young infants
 - But then it makes more sense to use prophylaxis for *any* UTI in this age group
 - And it makes sense to avoid something (VCUG) that might *cause* UTI
 - Surgical/obstructive problems more likely?
 - Wallace, *AJR* 2015: no cases obstruction in infants < 2 months with normal RBUS
 - Chang, *Hosp Pediatr* 2016: one case of missed PUV

Summary thoughts

- Perplexing that we have spent so much time thinking about and studying how best to screen for something that we don't know how to treat
- US is a poor screening test for "abnormal" but does decrease post-test probability of really bad things
- Not clear why imaging considerations wouldn't apply to < 2 months
 - Think about PUV in boys

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Quality Improvement for children hospitalized with Urinary Tract Infection: Q-UTI



Project Chairs

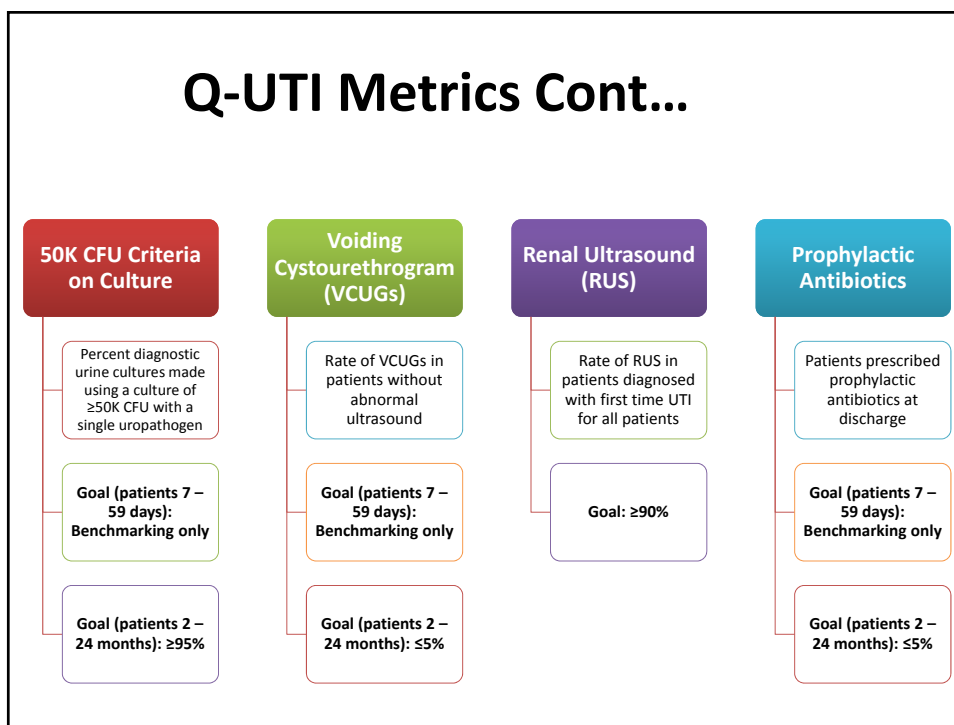
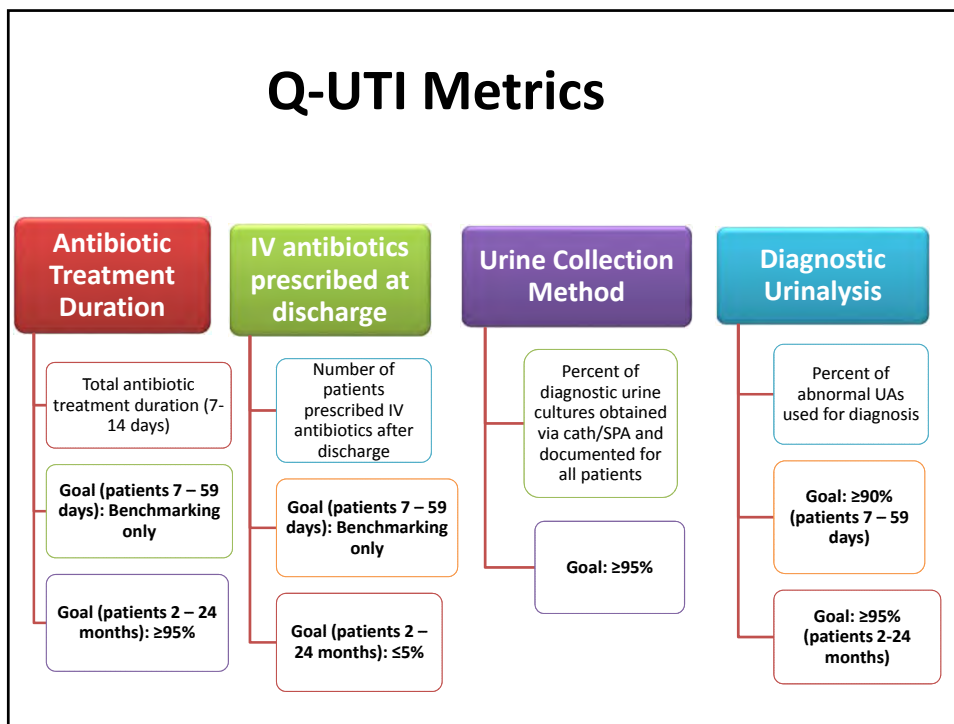
- Richard Engel, MD, FAAP
- Brian Pate, MD, FHM, FAAP

Project Expert Group

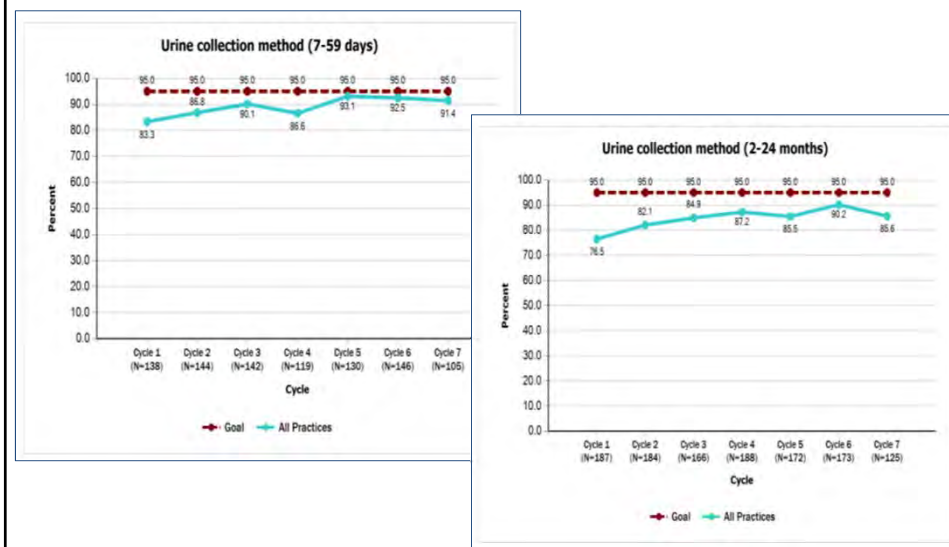
- Matthew Garber, MD, FHM, FAAP
- Chrissy Hrach, MD, FAAP
- Steven Kairys, MD, MPH, FAAP
- Rachel Marek, MD, FAAP
- Katherine O'Connor, MD, FAAP
- Kenneth Roberts, MD, FAAP
- Leticia Shanley, MD, FAAP
- Sowdhamini Wallace, DO, FAAP

AIM:

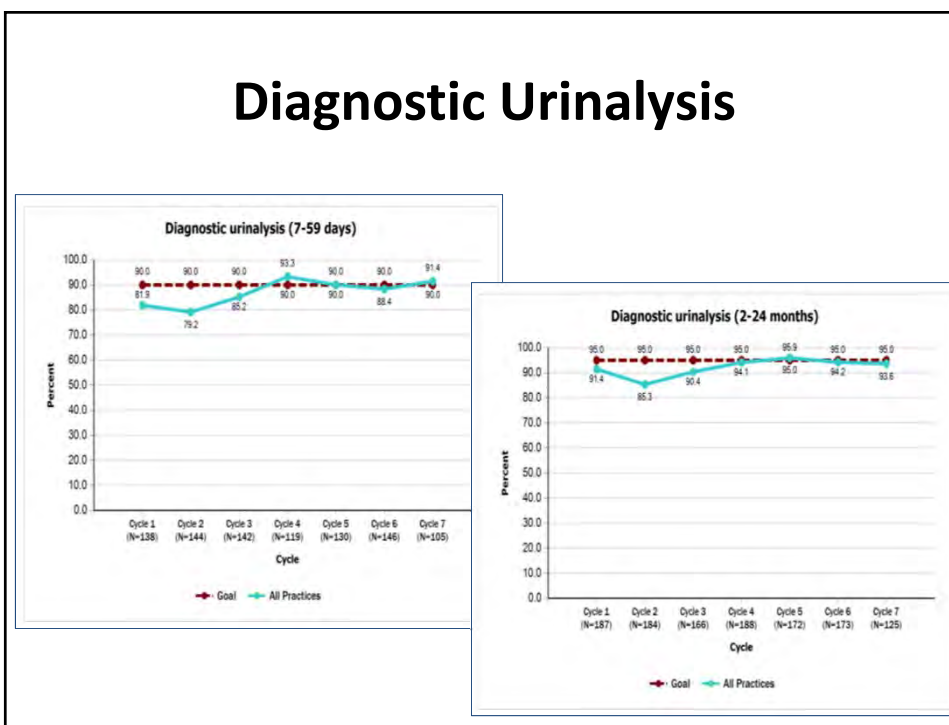
Improve the value of care for children 7 days to 24 months hospitalized because of UTIs in the domains of diagnostic strategy, imaging and treatment based on the recommendations in the 2011 AAP clinical practice guideline on urinary tract infection, as well as other relevant clinical evidence.



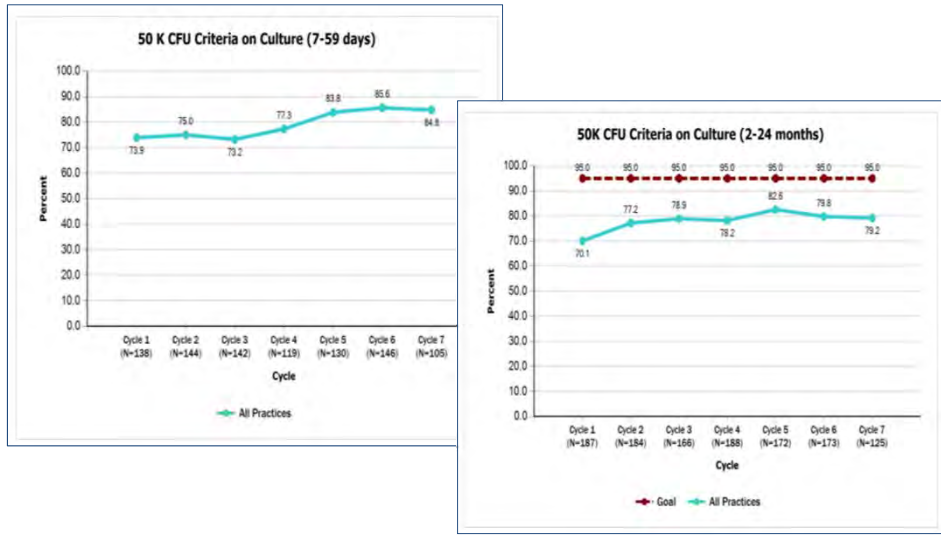
Urine Collection Method



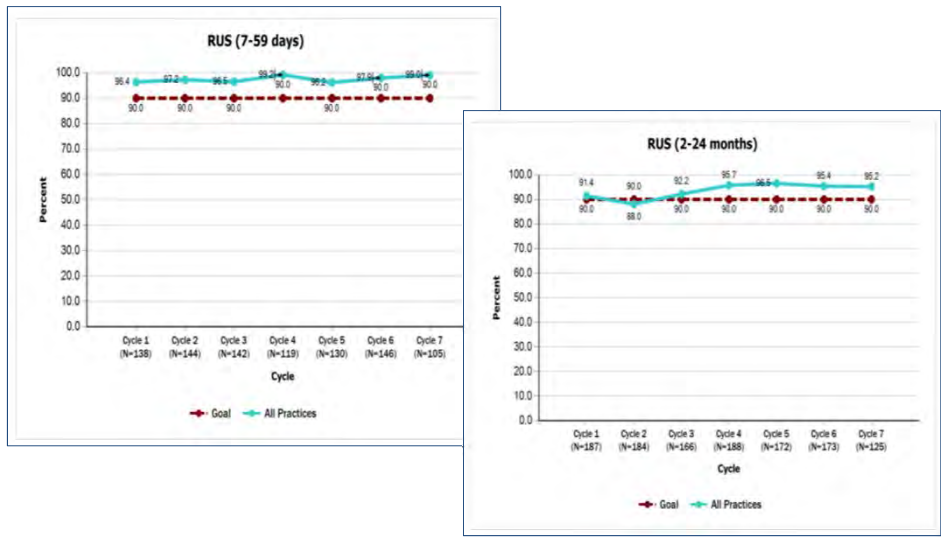
Diagnostic Urinalysis



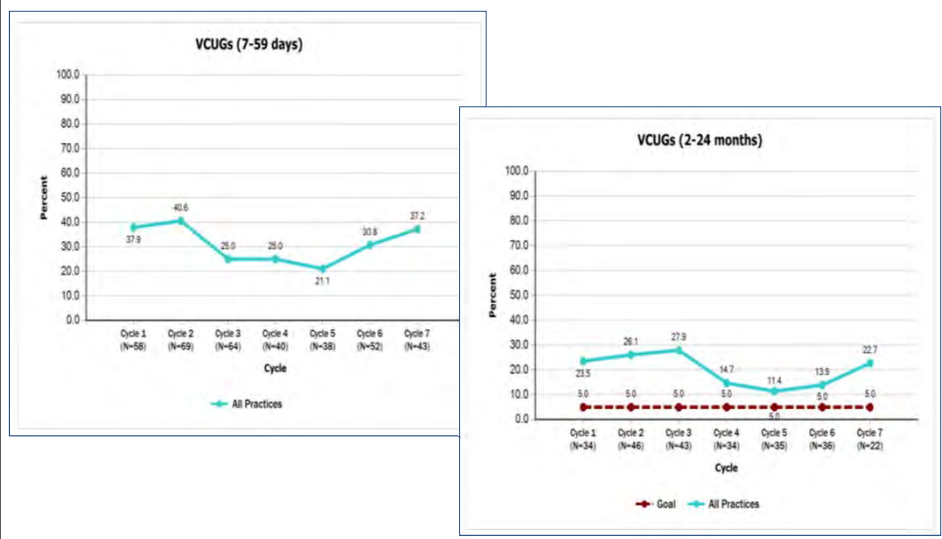
50K CFU Criteria on Culture



RUS



VCUGs



Major Themes

- Baseline data strong, but improvement and/or sustainability demonstrated in all metrics
- Improvement in **Value**
 - Less overdiagnosis
 - 61 more patients correctly diagnosed with cath specimen
 - 84 more patients had positive UA
 - Less overtreatment
 - Fewer VCUG's – relative reduction of 44%
- Low-resource strategies work
- Project successful across 42 diverse hospitals
- Gaps/variability persisted >4yrs after AAP CPG published
 - Baseline data shows: 26% of VCUG's were not indicated; only 75% had appropriate diagnostic urine culture results

Issues Discussed Today

- UTI-related hospitalizations (Rauch)
- 0-2 month olds:
 - UTI-associated bacteremia (Schroeder)
 - UTI-associated meningitis (Wallace)
 - Imaging (Schroeder)
- UTI-related QI (Engel)
- “Loose ends” (Roberts)

“Loose Ends”

1. Diagnosis
 - a. Pyuria
 - b. Colony count
2. Treatment
 - a. “Hours matter” (Really??)
3. Risk
 - a. Underlying abnormality
 - b. Recurrence
 - c. Renal damage/Scarring

Diagnosis: Pyuria--WBCs

- Criterion for WBCs
 - Centrifuged specimen: ≥ 5 WBCs/hpf
 - “Enhanced urinalysis”: ≥ 10 WBCs/mm³
 - Automated urinalysis (Iris): Depends* ...
 - SG ≥ 1.015 : ≥ 6 WBCs/hpf
 - SG < 1.015 : ≥ 3 WBCs/hpf

*Chaudhari, Pediatrics 11/2016

Diagnosis: Pyuria--LE

- Criterion for LE
 - Lavelle (Pediatrics, 2016): \geq Moderate
 - Chaudhari (Pediatrics, 2016): \geq Small
 - Schroeder (Pediatrics, 2015): Any (including Trace)
- Do the differences matter?
 - Sensitivity including trace: 97.6%¹
 - Sensitivity excluding trace: 95.7%¹
 - False positives if include trace: ~6%²
- LE comparable to formal urinalysis

¹Schroeder, Pediatrics, 2015
²Glissmeyer, Pediatrics, 2014

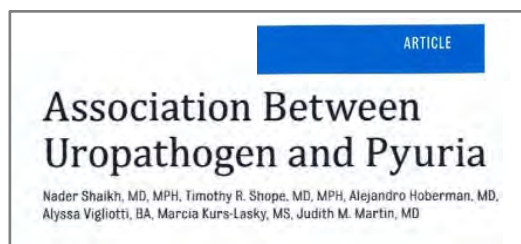
Does Pyuria Matter?

- When quantitative microbiology was introduced for diagnosis of UTI (1950s), pyuria went out of favor as too insensitive
 - Was compared to colony counts in adults with clinical pyelonephritis
 - Noted: Not everyone with $\geq 100,000$ cfu/mL had pyuria
 - But not everyone with $\geq 100,000$ cfu/mL had symptoms, either

Rates of Pyuria with + Culture

- | | Pyuria | No Pyuria |
|-----------------------|--------------|-----------|
| • Sanford (1955): | 86% (adults) | 14% |
| • Hoberman (1995): | 91% | 9% |
| • Swerkersson (2016): | 92% | 8% |
| • Shaikh (2016): | 87% | 13% |
- Rate of UTI in febrile infants ~5%
 - Pos culture/No pyuria among the 5%: ~0.5-0.7%
 - If true UTIs, would miss in 5-7 per 1,000 febrile infants
 - But that's also the rate of asymptomatic bacteriuria

Pyuria: Non E coli Uropathogens



Pediatrics July, 2016

Pyuria: Non E coli Uropathogens

- Shaikh (2016): Non E coli, 15% of organisms, were less likely to cause pyuria than E coli
- BUT “less likely:” They do cause pyuria, just at a lower rate: 77% vs 91%
 - So 23% of 15% = 3% of total were non E coli without pyuria
- Concern, because non E coli also:
 - More likely than E coli to be associated with high grade VUR
 - More likely than E coli to result in scarring
- But are these the non E coli without pyuria?
 - Not known
 - And in animal studies, scars are caused by WBCs—not bacteria (Glaser, Ped Nephrol 1987)

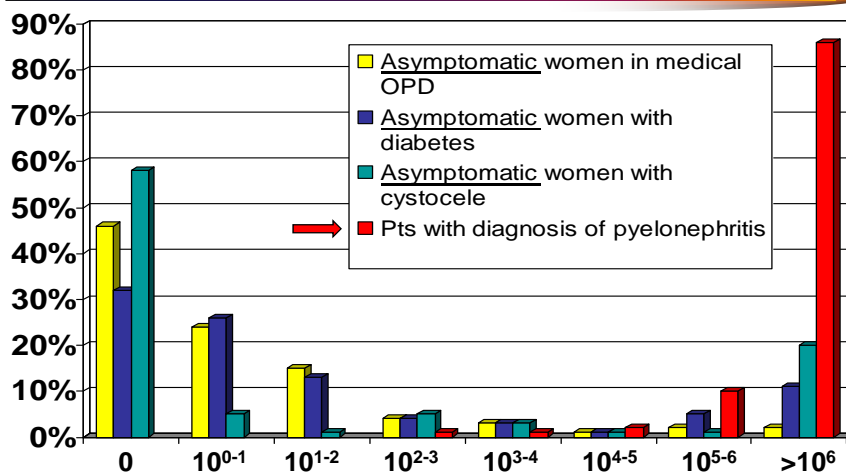
The Future?

- Multiple studies now promoting neutrophil gelatinase associated lipocalin (NGAL) as more sensitive than LE or WBCs by microscopy

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Origin of 100,000 cfu/mL Criterion



*Adapted from Kass E. Trans Assoc Am Phys 1956;69:56-64

Diagnosis: Colony Count

- Problem is defining the “gold standard”
 - Clinical pyelo: Kass (1956): 100,000 cfu/mL
 - Single organism: Hoberman (1995): 50,000 cfu/mL
 - Bacteremic UTI: Schroeder (2015): 10,000 cfu/mL
 - CRP/+Imaging: Swerkersson (2016): 10,000 cfu/mL
 - Primack (unpublished): 10,000– if pyuria and fever
- Many labs don’t specify between 10-100K, so 10,000 cfu/mL would be easier criterion for widespread application than 50,000.

Issues Discussed Today

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Do Hours Matter– Really??

Medscape PEDIATRICS MedPulse

Top Stories

Renal Scarring in Pediatric UTI: Hours Matter

Research

JAMA Pediatrics | Original Investigation

Early Antibiotic Treatment of Febrile Urinary Tract Infection and Renal Scarring

Nader Shalh, MD, MPH; Tq K. Mattoo, MD; Ron Kerem, MD; Anastasia Ivareva, PhD; Gang Cui, MPH; Maria Mosey-Mims, MD; Massoud Majd, MD; Harvey A. Ziesman, MD; Alejandro Hoberman, MD

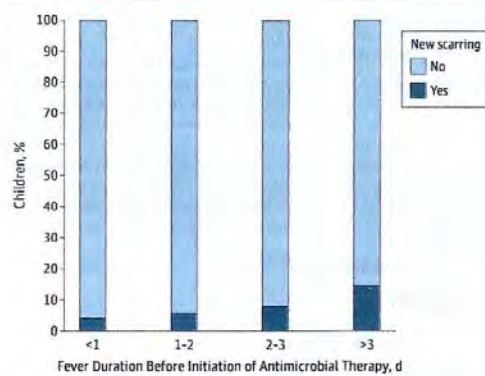
ARTICLE

Early Treatment of Acute Pyelonephritis in Children Fails to Reduce Renal Scarring: Data From the Italian Renal Infection Study Trials

Ian K. Hewitt, MBBS, FRACP; Pietro Zucchetto, MD; Luca Rigon, MD; Francesca Maschio, MD; Pier Paolo Molinari, MD; Lisanna Tomasi, MD; Antonella Toffolo, MD; Luigi Pavanello, MD; Carlo Crivellaro, MD; Stefano Bellato, MD; Giovanni Montini, MD

Do Hours Matter?

Figure. Percentage of Children With New Renal Scarring According to Delay in the Initiation of Antimicrobial Therapy



“Loose Ends”

1. Diagnosis

- a. Pyuria
- b. Colony count

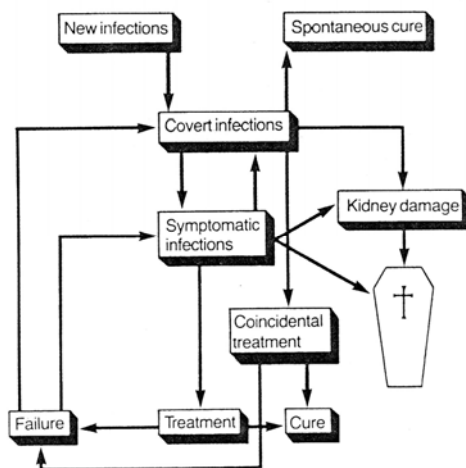
2. Treatment

- a. “Hours matter”-- really??

3. Risk

- a. Underlying abnormality
- b. Recurrence
 - Prophylaxis
 - BBD
- c. Renal damage/Scarring

“Conventional Wisdom” from 1960s



Used with permission from the author

Risk: Underlying Abnormality

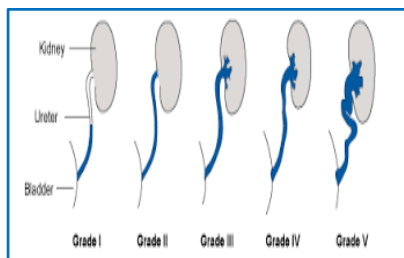
- Anatomic (eg, congenital dysplasia)
 - Major cause of chronic kidney disease; not UTI, VUR
- Population-based: Finland (N = 1,576)
 - “VUR with UTI without structural abnormalities in the kidneys seems not to cause CKD.”
 - “Active treatment of VUR seems not to reduce the occurrence of CKD and, in large prospective follow-up studies, the renal function of patients with VUR has been well preserved.”

Pediatrics 2011;128:840-47

Where Does That Leave Reflux?

- Of infants with febrile UTI:

- No VUR: 65%
- Grade I-II: 22%
- Grade III: 9%
- Grade IV: 4%
- Grade V: 1%



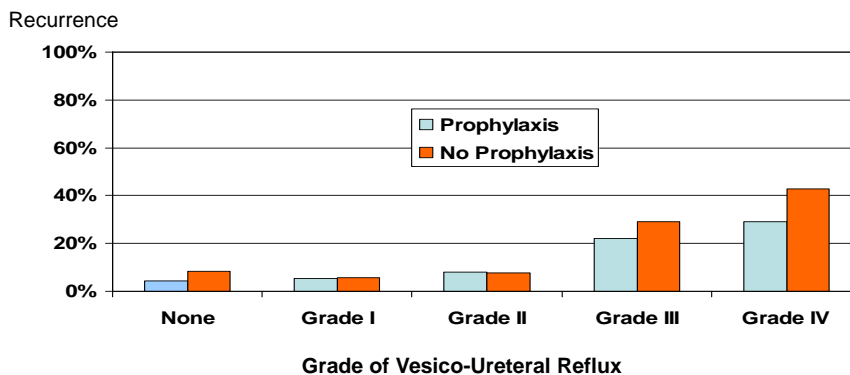
- Low-grade tends to resolve

- High-grade still a concern

- But only 5% have grade IV-V
- 2/3 are identified by abnormal RBUS
- Waters muddied by some adding grade III to “high grade”

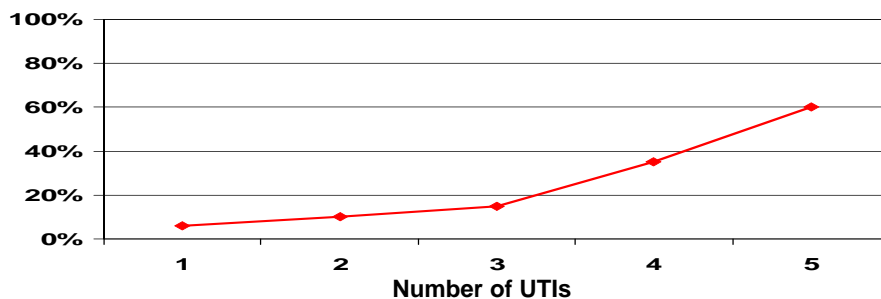
Reflux and Recurrences

- Recurrences more likely with grade IV-V VUR whether prophylaxis given or not



Recurrences

- Best predictor of a recurrence is a recurrence
- What is lost by “watchful waiting”?
 - May incur symptomatic illness with ...
 - An increased risk of scarring



Scarring and Prophylaxis

- Focus of studies of prophylaxis has been on preventing recurrence
- New focus: preventing scarring
 - RIVUR: No benefit (11.9% vs 10.2%)
 - Authors considered trial underpowered to detect difference (N = 607)
 - New meta-analysis*: N = 1427
 - 7 RCTs including RIVUR
 - Conclusion: No benefit

*Pediatrics May, 2017

Where Does That Leave Us?

- BBD: Bowel-bladder dysfunction
 - For practical purposes: constipation
- Old articles from GI clinic note recurrent UTIs stopped when constipation treated
- Brought to light in RIVUR and CUTIE
 - More than half of those old enough to be screened by questionnaire (>2 years)
 - The group that responded best to prophylaxis
 - But no comparison of TMP-SMX to Miralax

Evaluating Risk: Summary

- Imaging: Routine RBUS
 - VCUG *only if* indicated
- History and physical for BBD
 - Relief of constipation by itself may be sufficient to reduce/eliminate recurrences
- Prophylaxis?
 - Possibly, if multiple recurrences
 - Along with Miralax??
 - Duration?

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