

Is there a role for antibiotic prophylaxis following UTI?



Kjell Tullus

Consultant Paediatric Nephrologist

Clinical scenarios

- One episode of acute pyelonephritis
- Proven VUR
- Urinary tract malformation
- Recurrent episodes of cystitis

One episode of acute pyelonephritis



- No data exist
- My **opinion**
 - No prophylaxis if US normal
 - Prophylaxis if major dilatation

Clinical scenarios



- One episode of acute pyelonephritis
- **Proven VUR**
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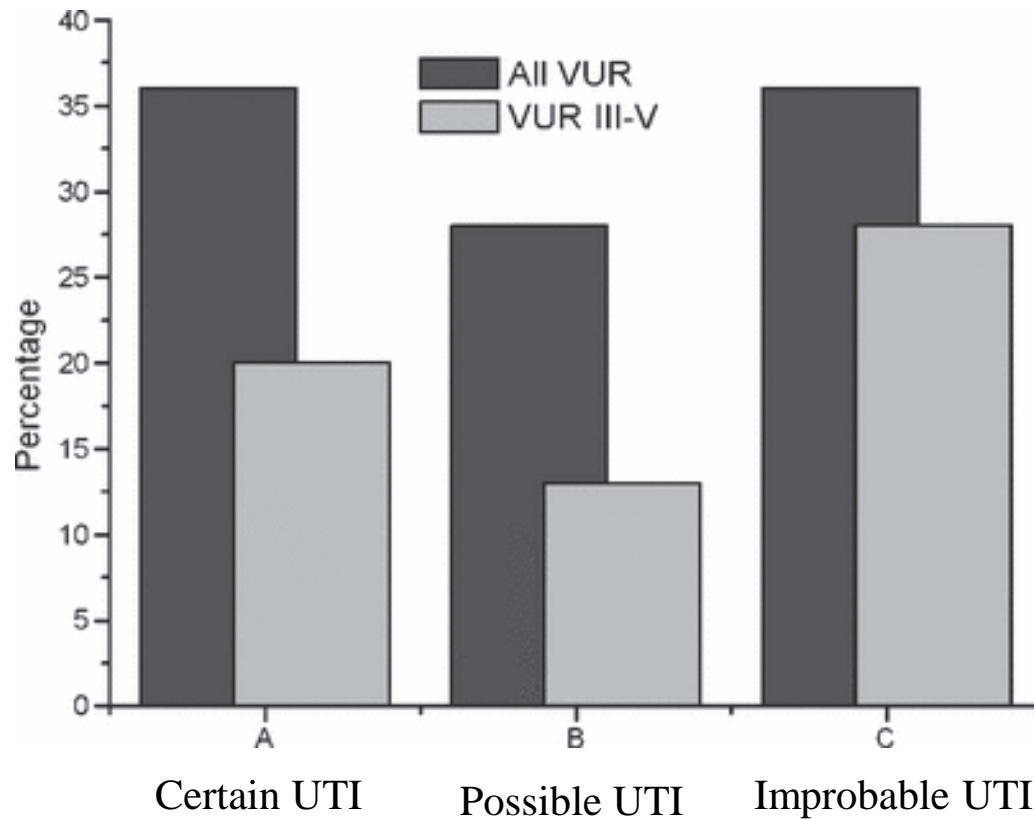
Background on VUR

- What do we **really** know about the importance of VUR?

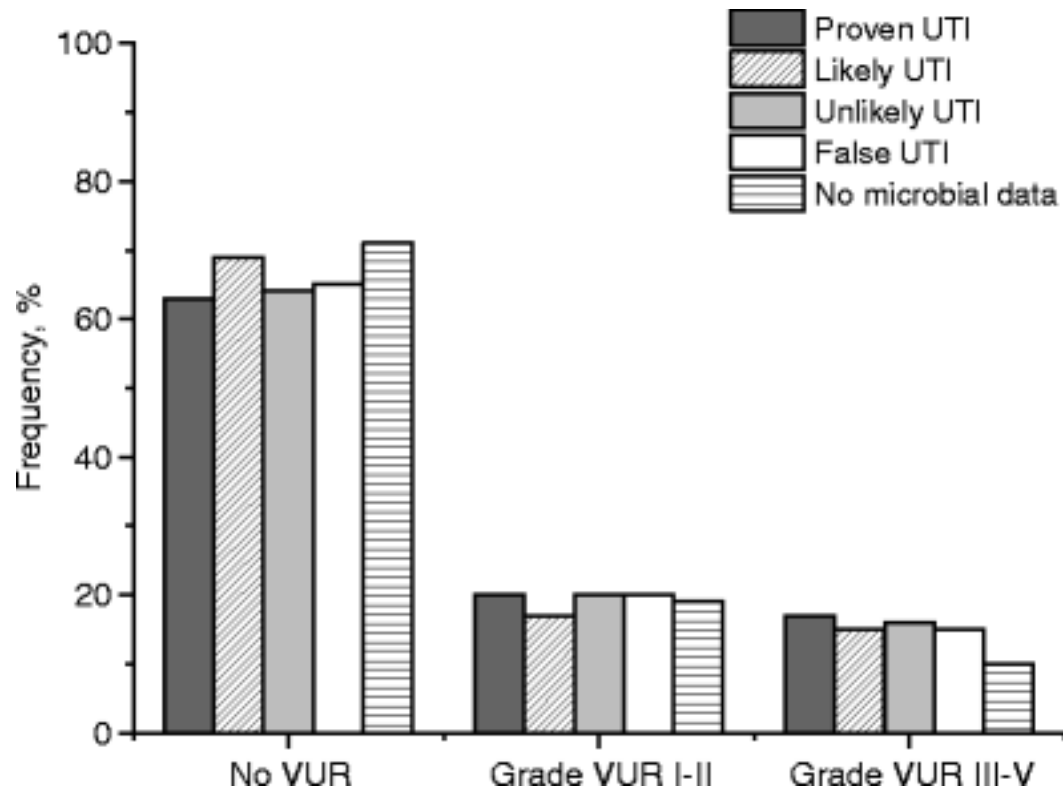
Occurrence of VUR

- Only a few per cent of all children were thought to have VUR
- Recent studies have put that notion question.

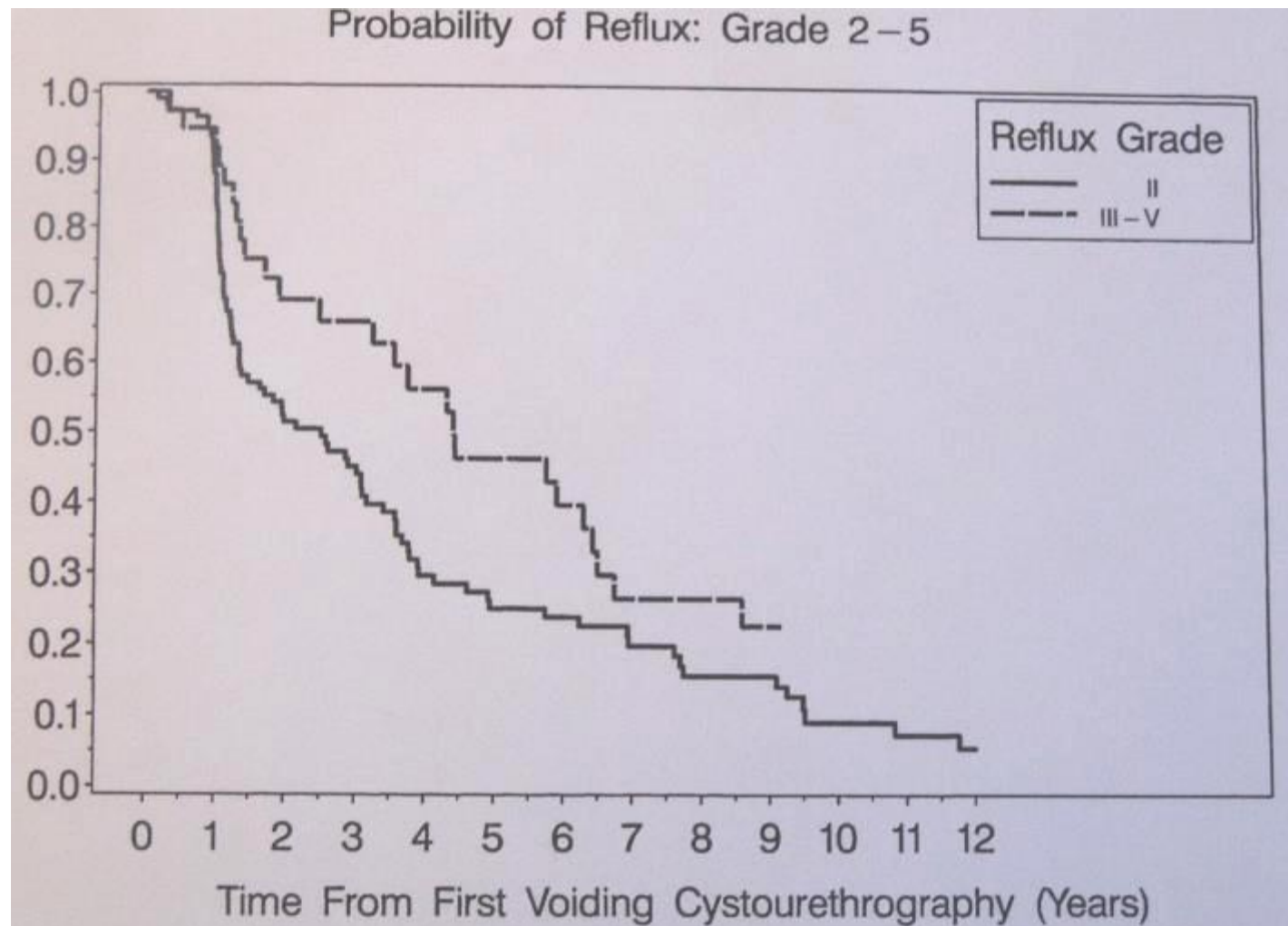
Occurrence of VUR in 347 children



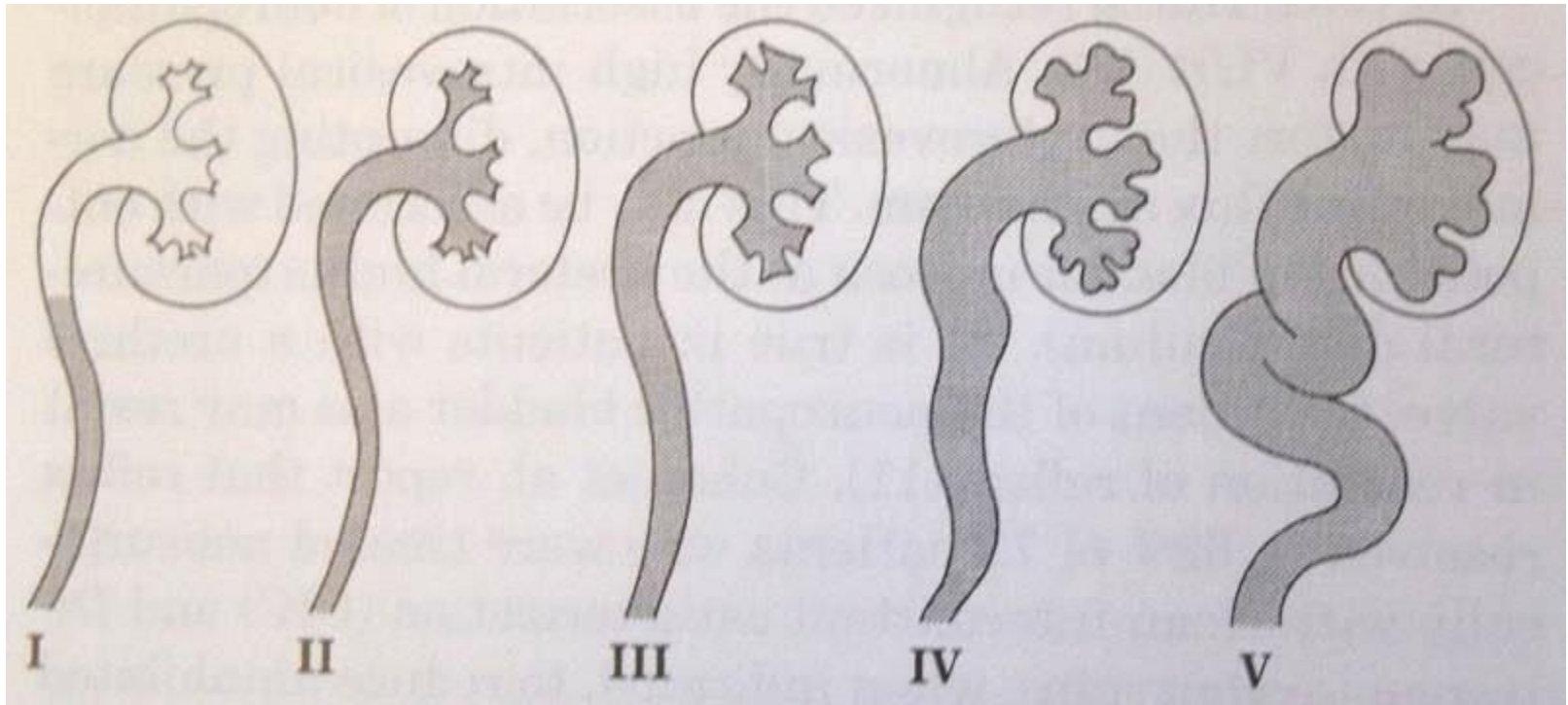
Occurrence of VUR in 1185 children



Natural history of VUR

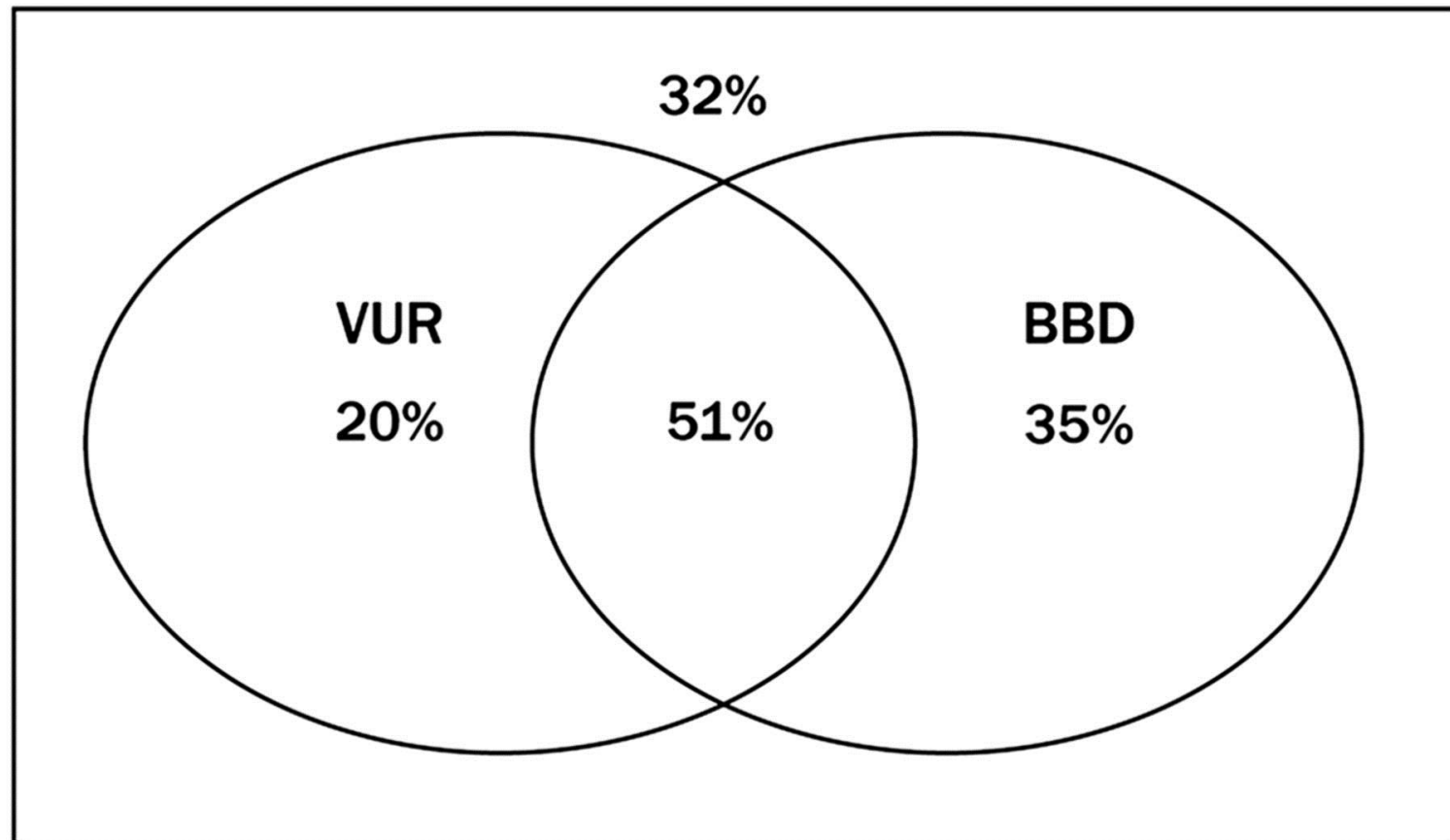


VUR grading



Incidence of recurrent UTIs

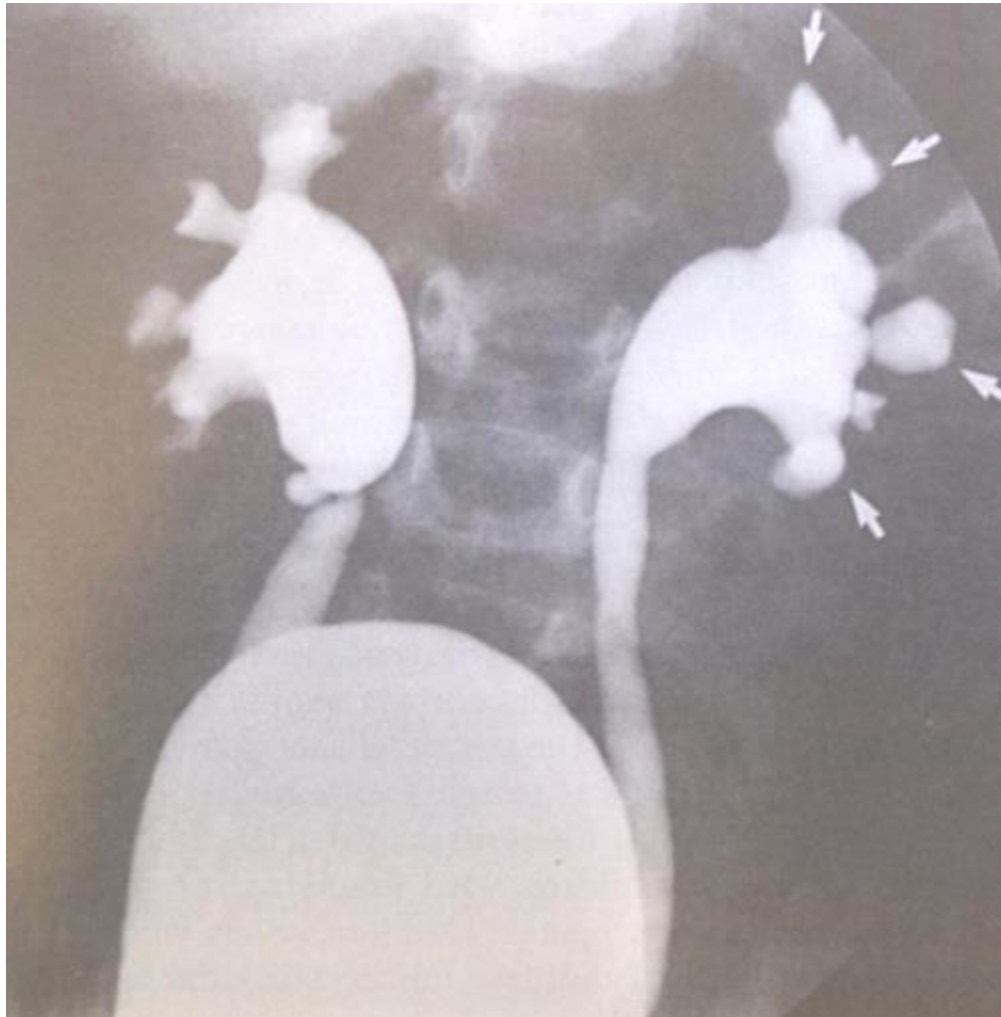
Incidence of Recurrent UTI in Toilet-Trained Children Not on Antimicrobial Prophylaxis



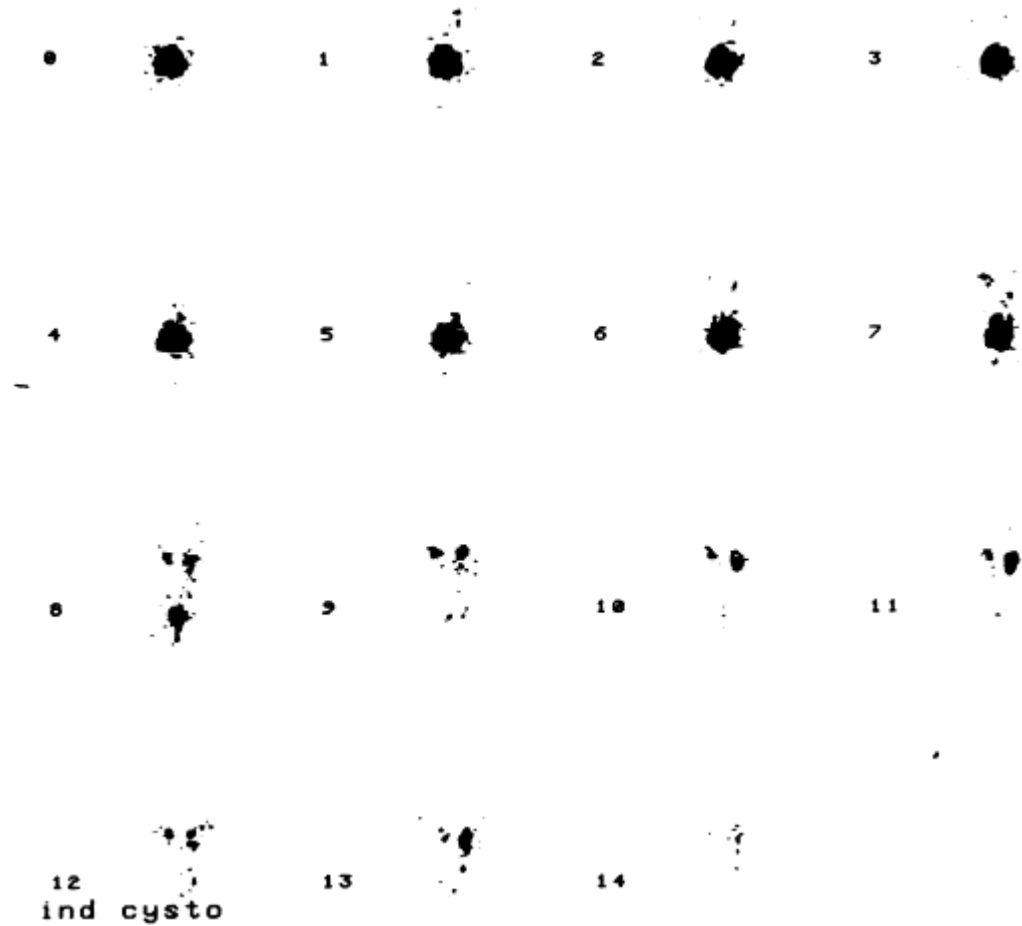
Imaging

- MCUG
- Isotope
 - Indirect
 - Direct
- Ultrasound
 - With contrast
 - Doppler wave measurement

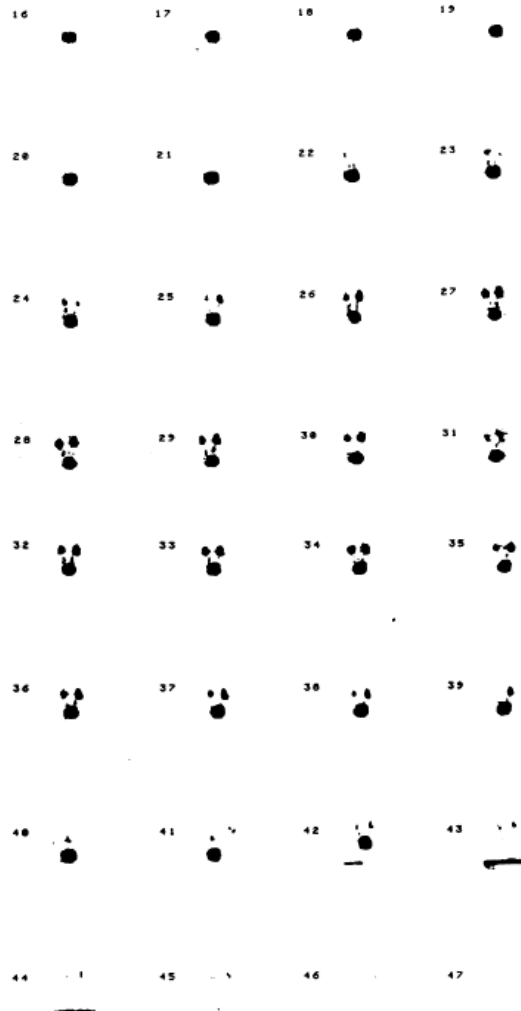
MCUG



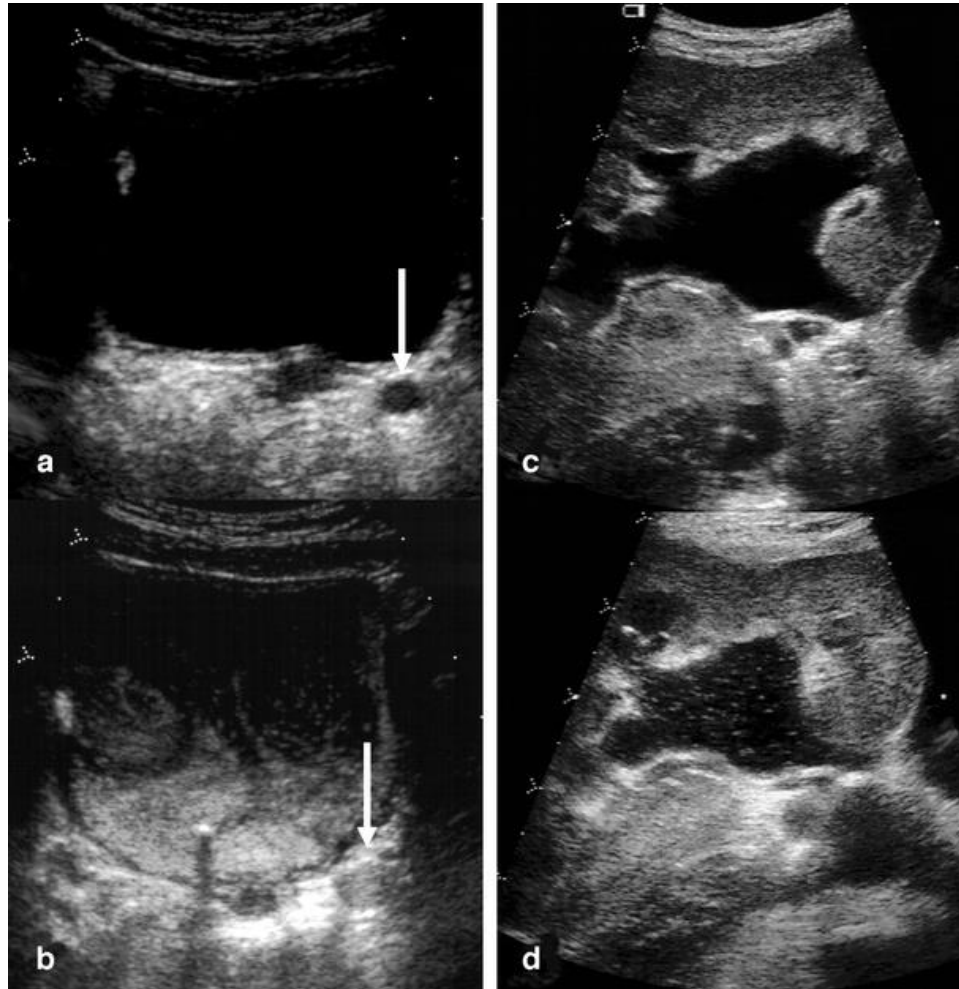
Indirect radionucleotide cystography



Direct radionucleotide cystography



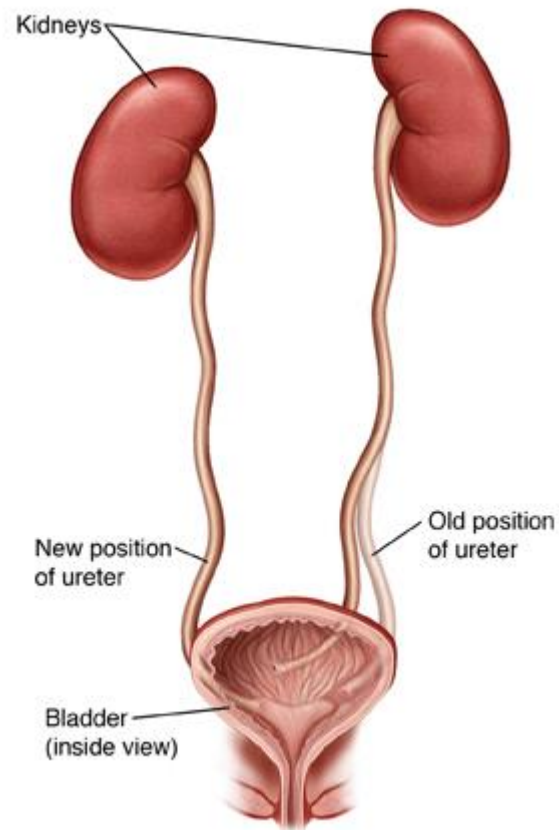
US with contrast



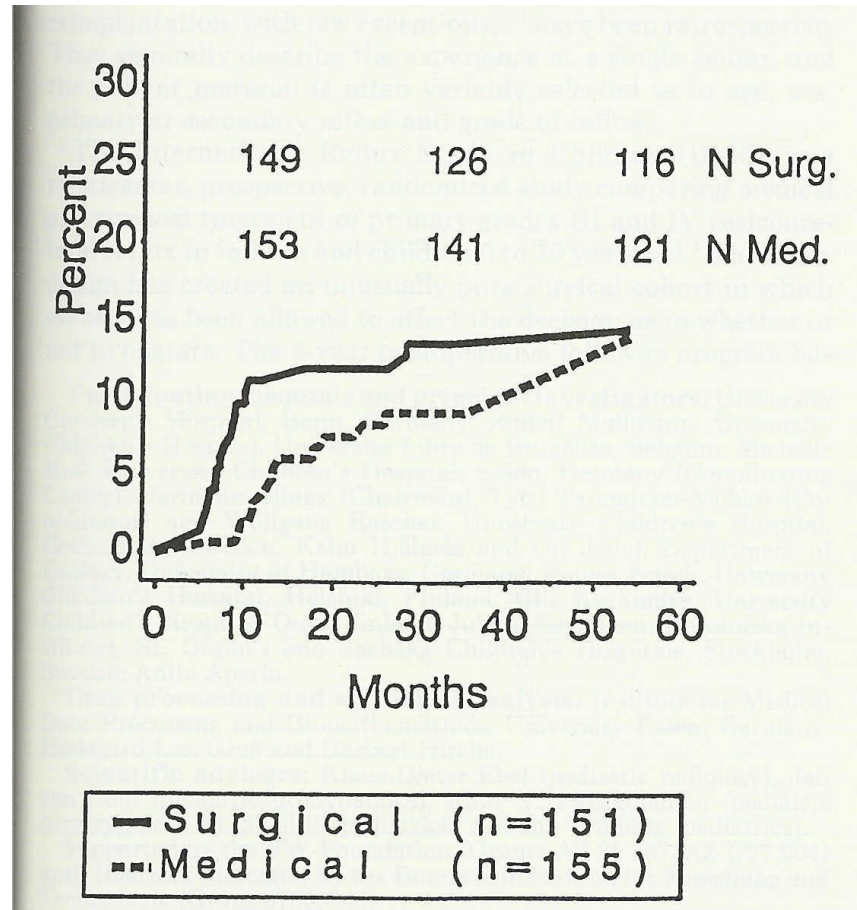
Surgery for VUR

- Methods
- Results

Ureteric reimplantation

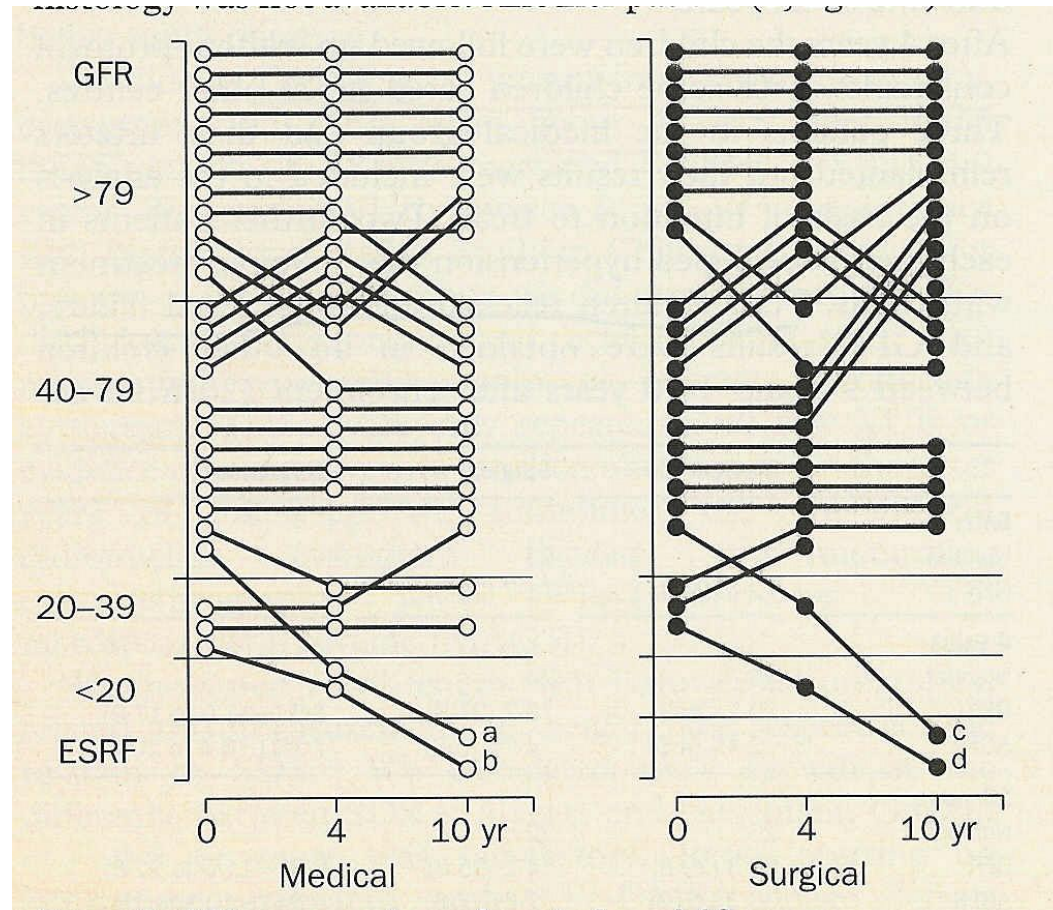


Surgery vs prophylactic antibiotics to prevent new scarring



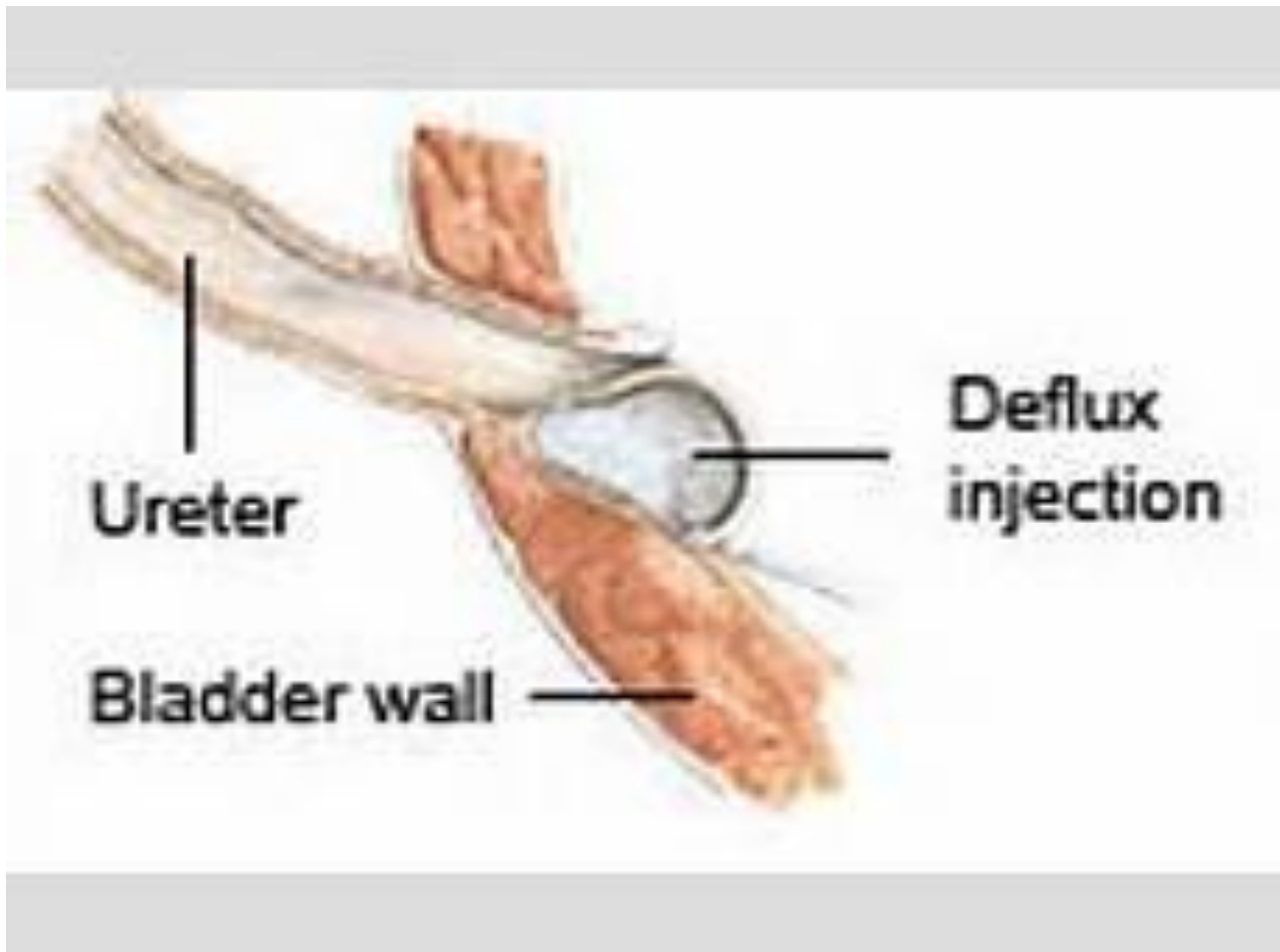
Olbing et al J Urol 1992;148:1653-6

Medical vs surgical 5-year follow-up



Smellie J et al the Lancet 2001;357:1329-34

Deflux



Deflux



Sting/Deflux

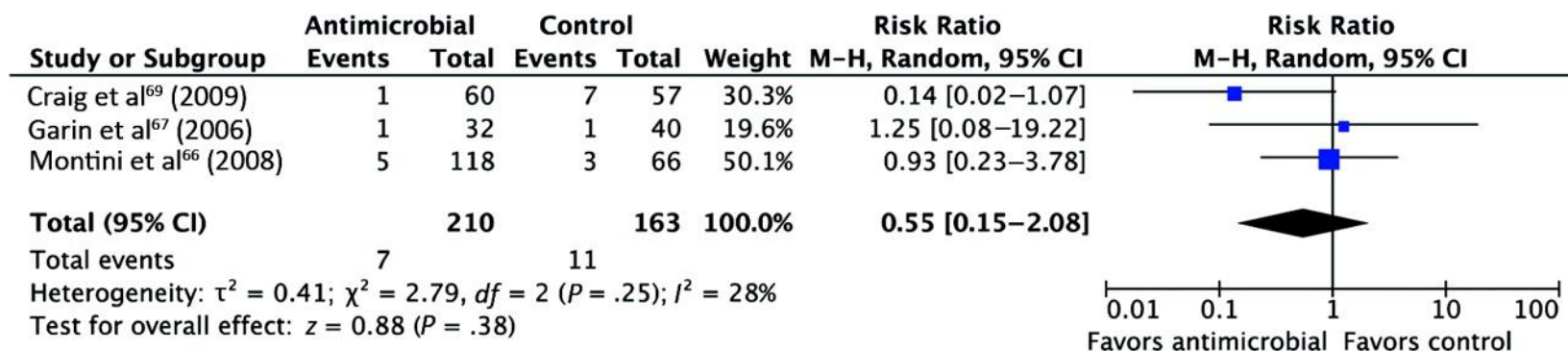
A thick, horizontal yellow brushstroke underline that spans the width of the slide, positioned directly beneath the title.

- Only one study

Prophylactic medications

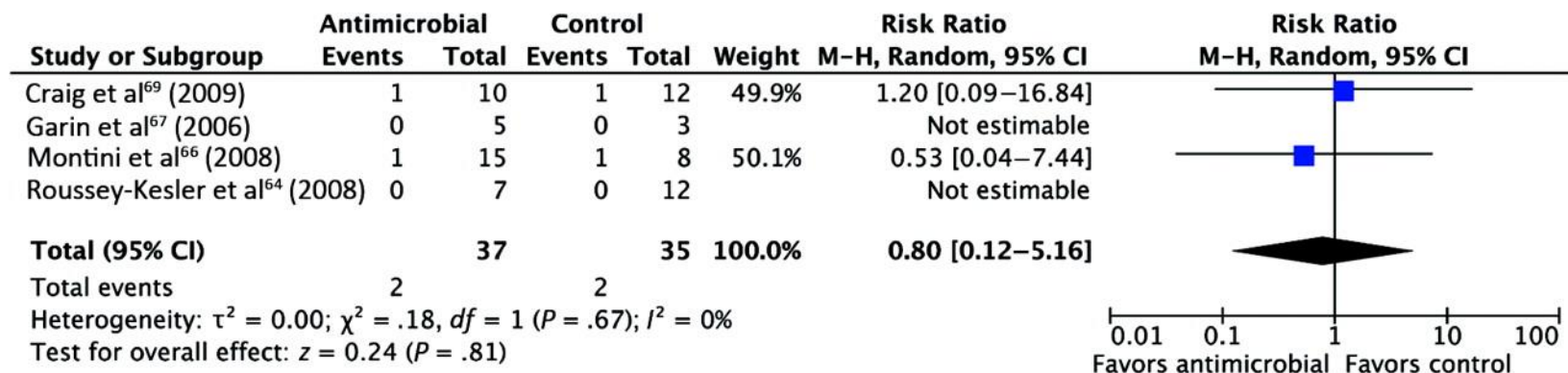
- Surprisingly few and bad studies until recently
- NICE concluded, 10 years ago, that prophylaxis should not be **routinely** recommended

Combined estimates of the effect of antimicrobial prophylaxis on prevention of pyelonephritis in children 2 to 24 months of age without VUR, from random-effects modeling.



Pediatrics 2011;128:e749-e770

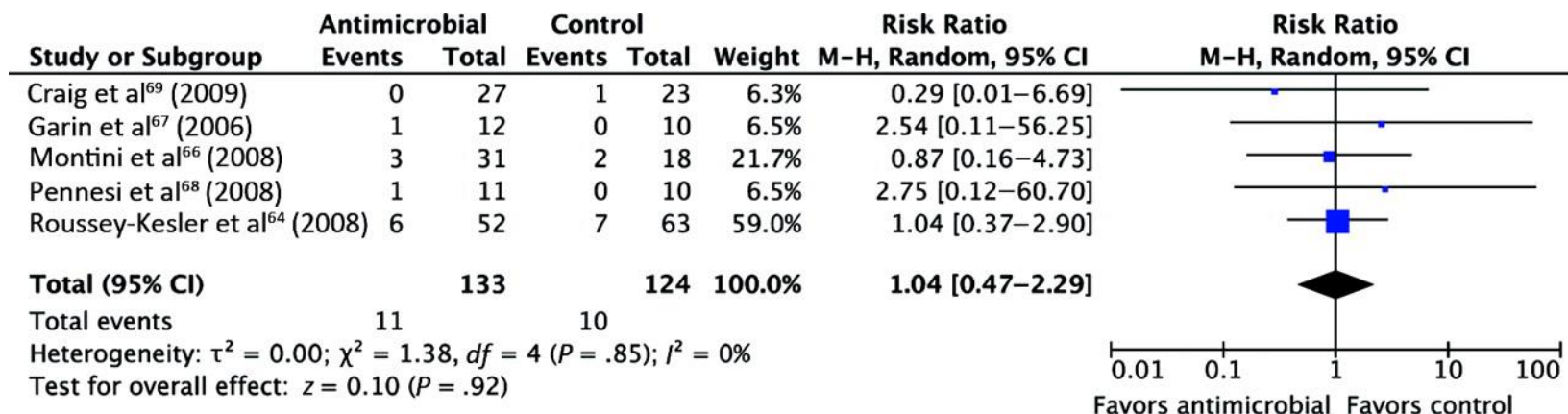
Combined estimates of the effect of antimicrobial prophylaxis on prevention of pyelonephritis in children 2 to 24 months of age with grade I VUR, from random-effects modeling.



Pediatrics 2011;128:e749-e770

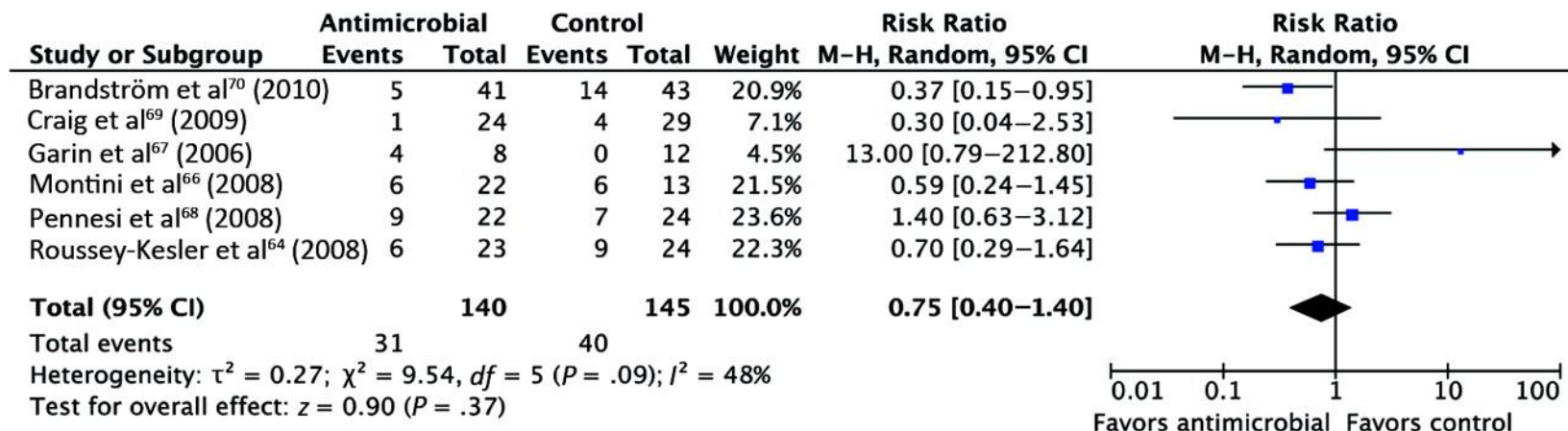
PEDIATRICS®

Combined estimates of the effect of antimicrobial prophylaxis on prevention of pyelonephritis in children 2 to 24 months of age with grade II VUR, from random-effects modeling.



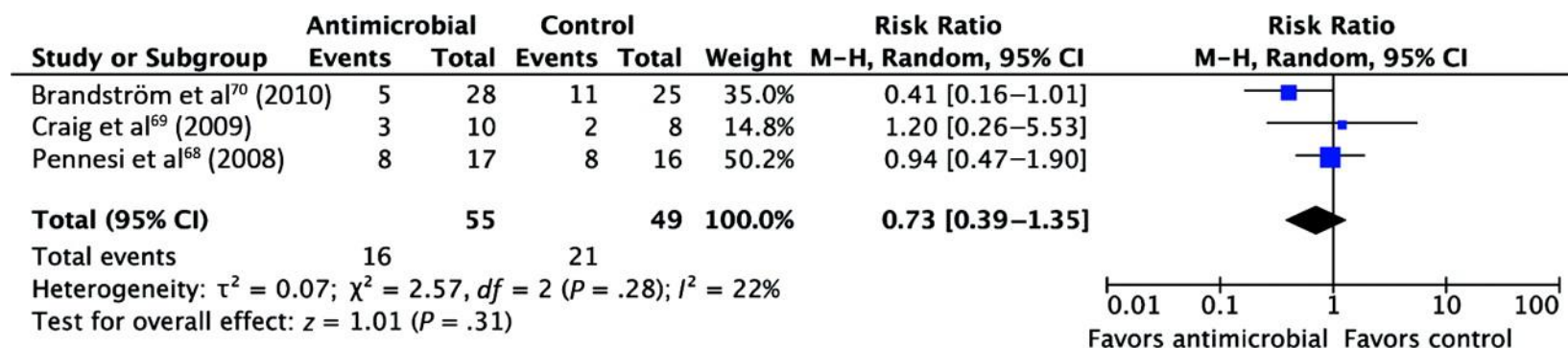
Pediatrics 2011;128:e749-e770

Combined estimates of the effect of antimicrobial prophylaxis on prevention of pyelonephritis in children 2 to 24 months of age with grade III VUR, from random-effects modeling.



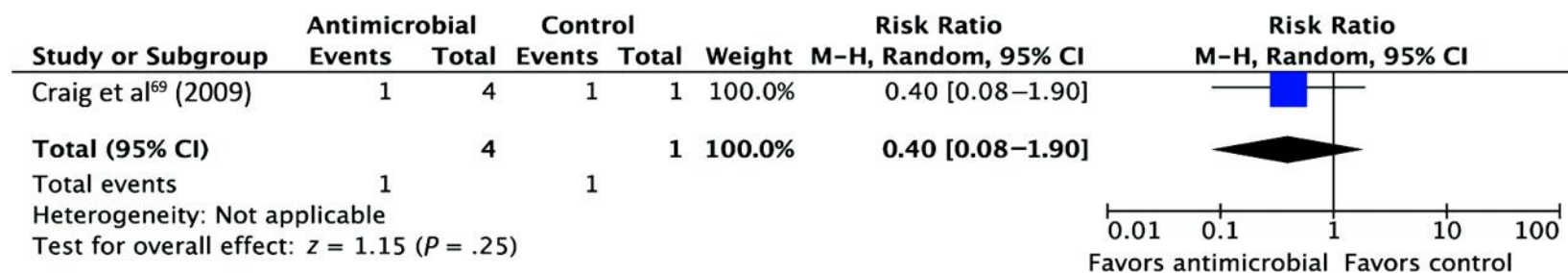
Pediatrics 2011;128:e749-e770

Combined estimates of the effect of antimicrobial prophylaxis on prevention of pyelonephritis in children 2 to 24 months of age with grade IV VUR, from random-effects modeling.



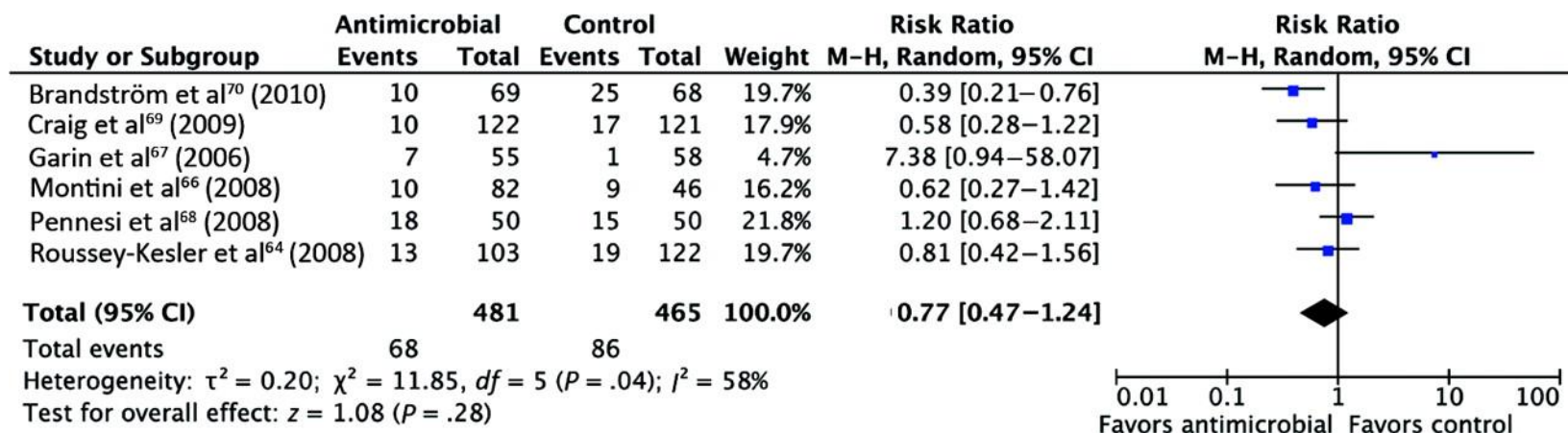
Pediatrics 2011;128:e749-e770

Estimate of the effect of antimicrobial prophylaxis on prevention of pyelonephritis in children 2 to 24 months of age with grade V VUR, from random-effects modeling.



Pediatrics 2011;128:e749-e770

Combined estimates of the effect of antimicrobial prophylaxis on prevention of pyelonephritis in children with VUR, from random-effects modeling.



Pediatrics 2011;128:e749-e770

Prophylactic medication

Swedish study



- 203 children, 75 boys and 128 girls
- Grade III and IV VUR
- Age 1-2 years
- Treated with
 - Prophylaxis (trimethoprim) n=69
 - Sting (deflux) n=66
 - Surveillance n=68
- 2 year follow-up

Outcome of reflux at 2 years

Swedish study



- Still grade III or IV
 - 60% prophylaxis group
 - 30% deflux group
 - 55% surveillance group
- VUR disappeared
 - 15% prophylaxis group
 - 40% deflux group
 - 20% surveillance group

UTI recurrence at 2 years

Swedish study



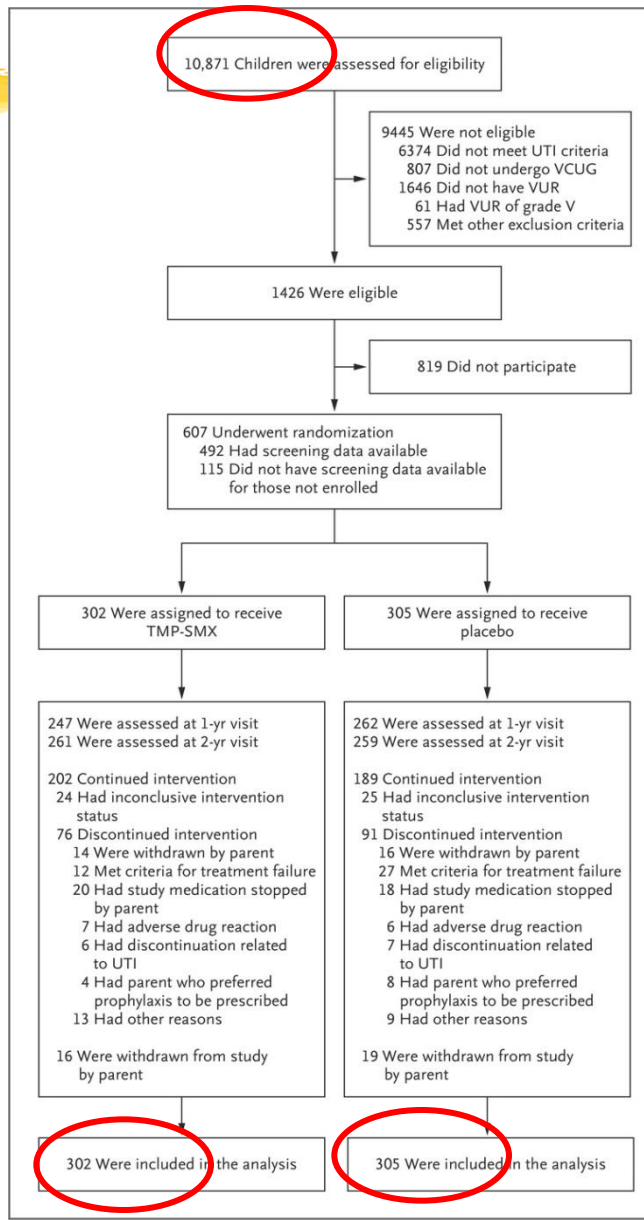
- **Girls**
 - 18% prophylaxis group
 - 22% deflux group
 - 55% surveillance group
- **Boys**
 - 8% prophylaxis group
 - 17% deflux group
 - 4% surveillance group
- **Significant difference for girls but not for boys**

New renal scarring at 2 years

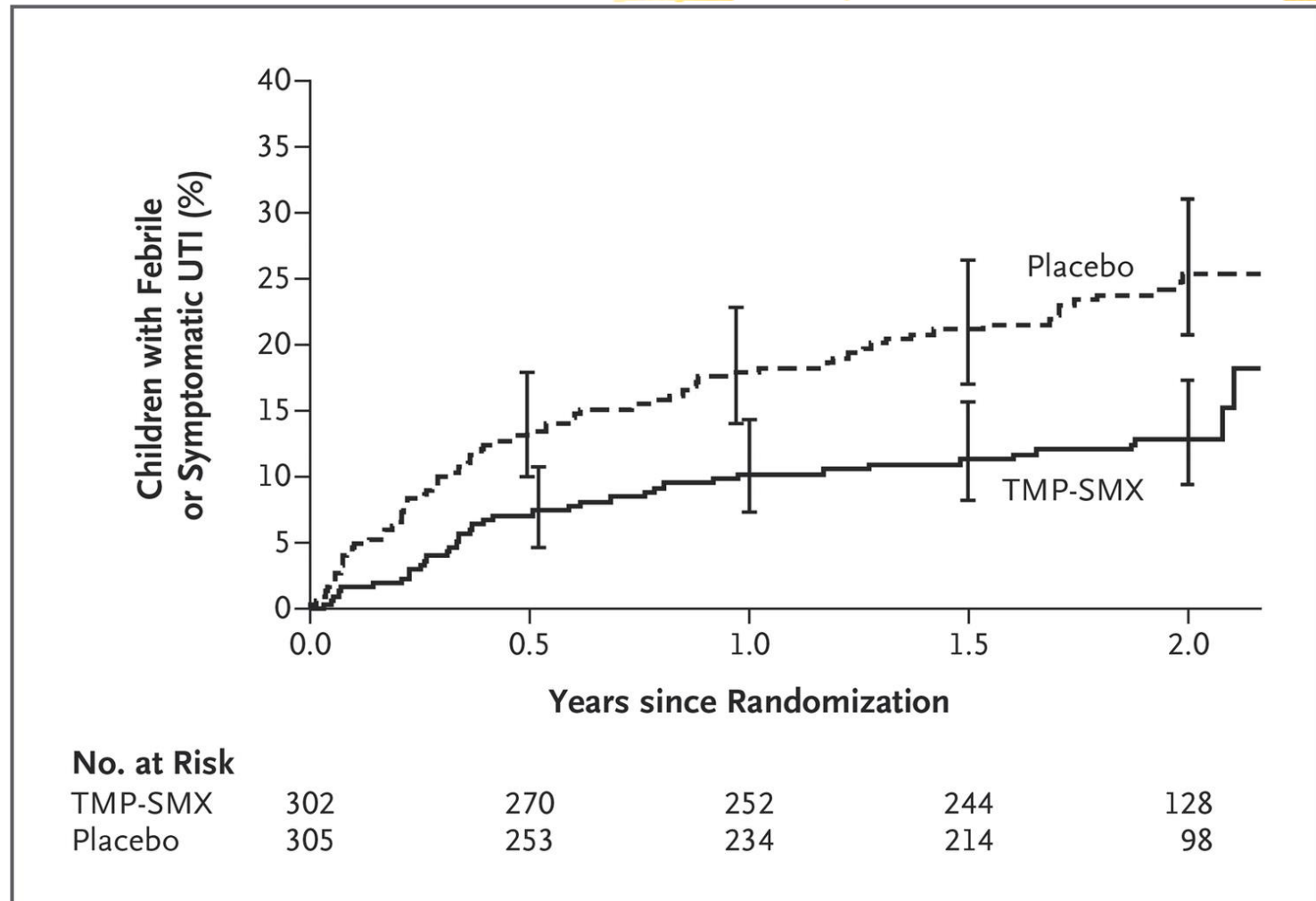
Swedish study

- **Girls**
 - 0 prophylaxis group
 - 4 deflux group
 - 7 surveillance group
- **Boys**
 - 0 prophylaxis group
 - 1 reflux group
 - 1 surveillance group
- **Significant difference for girls but not for boys**

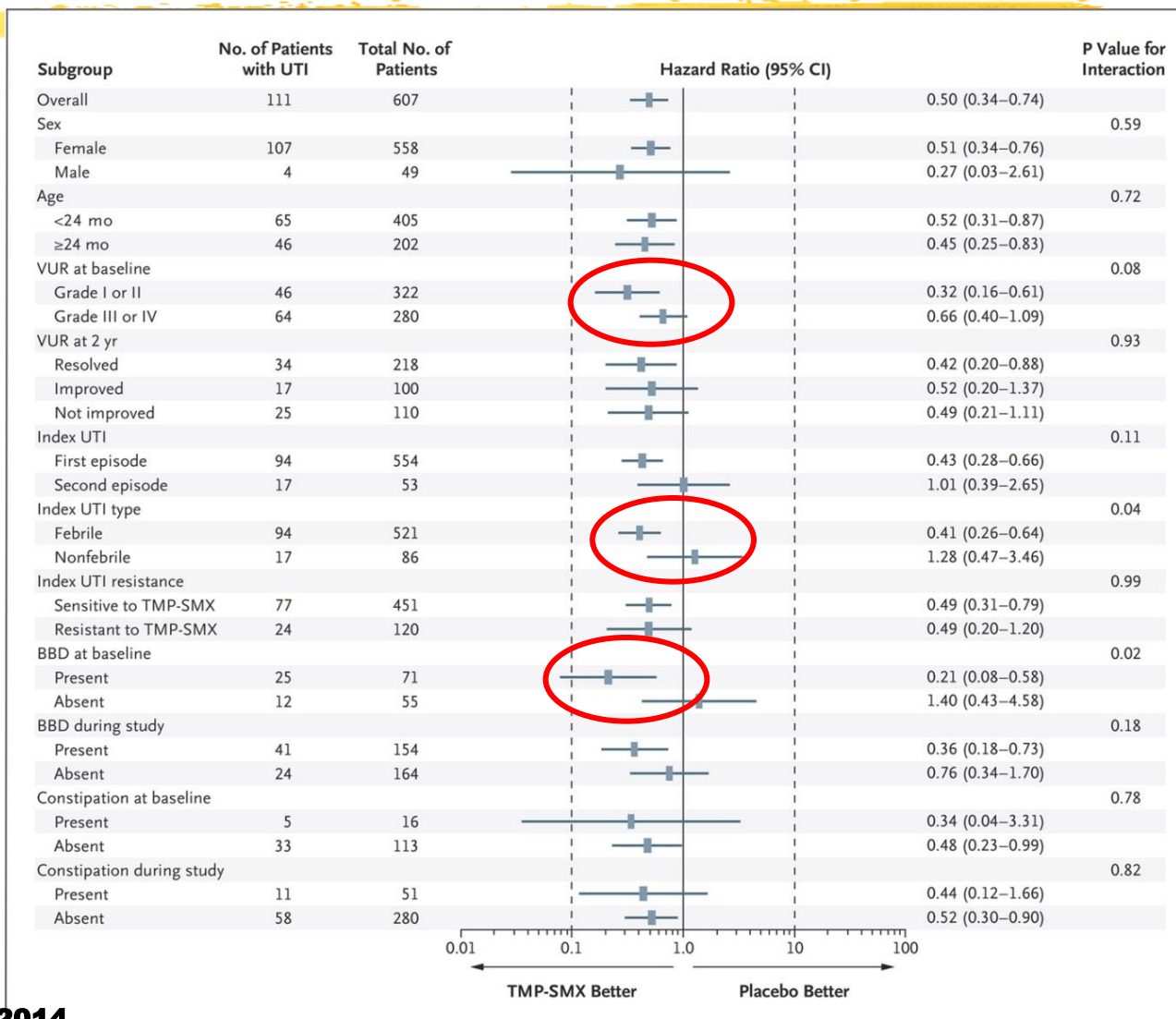
RIVUR Trial



Febrile or symptomatic UTI



Risk for recurrent UTI in subgroups

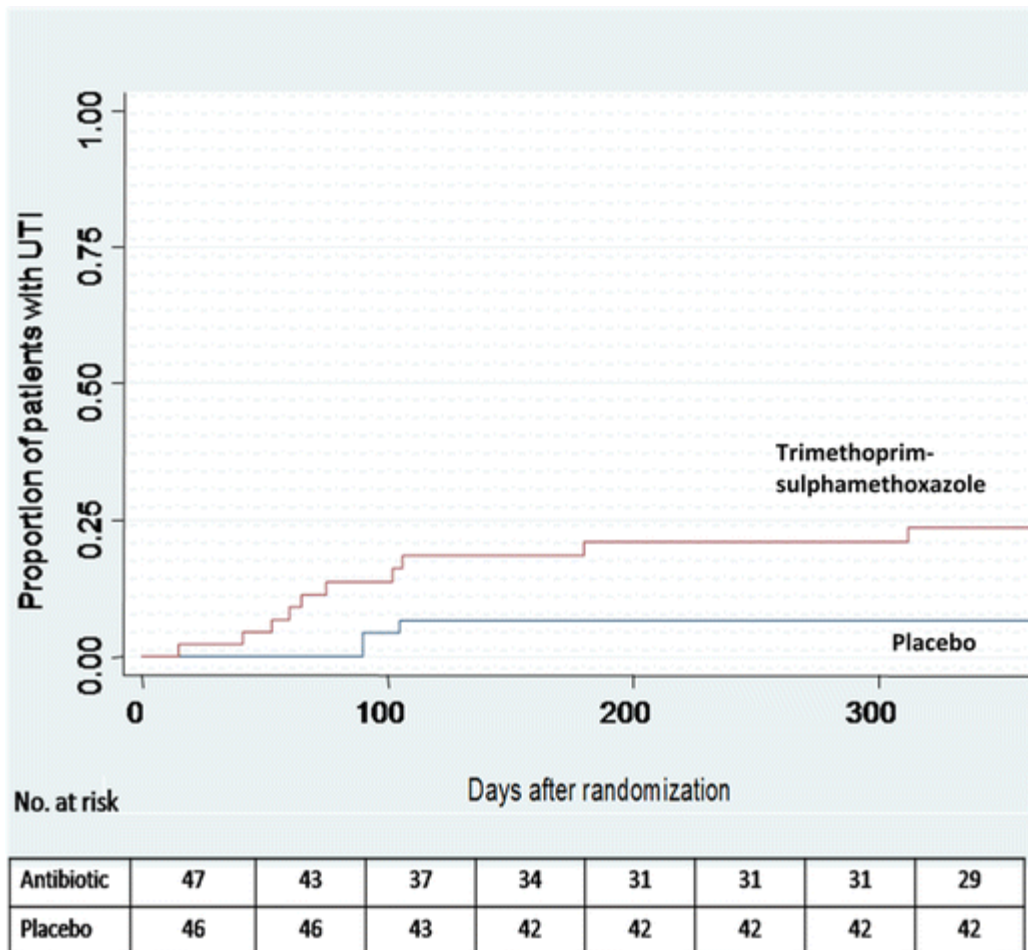


Clinical outcome - scarring

Outcome	Trimethoprim– Sulfamethoxazole <i>no. of children/total no. (%)</i>	Placebo	Absolute Difference in Risk (95% CI) <i>percentage points</i>
Recurrent febrile or symptomatic UTI*			
Children with missing 2-yr data classified as having had an event (intention-to-treat analysis)	77/302 (25.5)	114/305 (37.4)†	11.9 (4.6 to 19.2)
Children with missing 2-yr data classified as not having had an event (intention-to-treat analysis)‡	39/302 (12.8)	72/305 (25.4)§	12.6 (6.1 to 19.0)
Children with missing 2-yr data omitted	39/264 (14.8)	72/263 (27.4)§	12.6 (5.7 to 19.5)
Treatment failure‡¶	14/302 (5.0)	27/305 (9.6)¶	4.5 (0.2 to 8.8)
Renal scarring**			
Overall	27/227 (11.9)	24/235 (10.2)	–1.7 (–7.4 to 4.0)
Severe††	9/227 (4.0)	6/235 (2.6)	–1.4 (–4.7 to 1.8)
New‡‡	18/220 (8.2)	19/227 (8.4)	0.2 (–4.9 to 5.3)
Any cortical defect	29/227 (12.8)	25/235 (10.6)	–2.1 (–8.0 to 3.7)
Antimicrobial resistance			
Resistant <i>Escherichia coli</i> in stool	56/203 (27.6)	41/210 (19.5)	–8.1 (–16.2 to 0.1)
First recurrent febrile or symptomatic UTI with resistant <i>E. coli</i>	19/30 (63.3)§§	11/57 (19.3)	–44.0 (–64.1 to –24.0)
First recurrent febrile or symptomatic UTI with any resistant pathogen	26/38 (68.4)§§	17/69 (24.6)	–43.8 (–61.7 to –25.8)

* Included are 7 children (3 in the trimethoprim–sulfamethoxazole group and 4 in the placebo group) with febrile or symptomatic UTIs that occurred before a missed 2-year visit. Imputation was applied to 38 children in the trimethoprim–

Indian placebo controlled randomised study



Prophylaxis gives increasing resistance



- Increasing non-E.coli 26.9% to 46.9%
- Increasing resistance to
 - Amoxiclav
 - Cotrimoxazole
 - Cefuroxime
 - Ceftriaxome
 - Gentamicin
 - Nitrofurantoin

Summary



- Surgery routinely not better than prophylactic antibiotics
- Give prophylaxis until the age of 2 for boys and 4 for girls
- Surgery in selected cases of antibiotic failure

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- Urinary tract malformation
- Recurrent episodes of cystitis

Urinary tract malformation

- We do not know!
- One important international study ongoing
- My personal **opinion** is that antibiotics does not help
- Circumcision might help

Clinical scenarios



- One episode of acute pyelonephritis
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Recurrent episodes of cystitis

- This is not to protect kidneys
- But to reduce suffering from too many infections
- No good studies
- My **opinion** is that prophylaxis works in selected cases

Summary

- Still many things that we do not know
- Some evidence that it is beneficial in infant boys and girls with VUR grad III and IV
- Might help girls with many recurrent episodes of cystitis