Supplementary Appendix

This appendix has been provided by the authors to give readers additional information about their work.

Supplement to: The RIVUR Trial Investigators. Antimicrobial prophylaxis for children with vesicoureteral reflux. N Engl J Med 2014;370:2367-76. DOI: 10.1056/NEJMoa1401811

Supplementary Appendix

Table of Contents

The RIVUR Study Investigators: J. Christopher Austin, MD (Oregon Health and Science University, Portland, OR); Sharon M. Bartosh, MD (University of Wisconsin, American Family Children's Hospital, Madison, WI); Louis Bell, MD (Children's Hospital of Philadelphia, Philadelphia, PA); Richard Bellah, MD (Children's Hospital of Philadelphia, Philadelphia, PA); Sonika Bhatnagar, MD, MPH (Children's Hospital of Pittsburgh of UPMC, Pittsburgh, PA); Eileen D. Brewer, MD (Texas Children's Hospital, Houston, TX); Douglas Canning, MD (Children's Hospital of Philadelphia, Philadelphia, PA); Myra A. Carpenter, PhD (University of North Carolina at Chapel Hill, Chapel Hill, NC); Earl Y. Cheng, MD (Ann & Robert H. Lurie Children's Hospital of Chicago, Chicago, IL); Russell W. Chesney, MD (Le Bonheur Children's Hospital, Memphis, TN); Ross Decter, MD (Penn State Milton S. Hershey Medical Center, Hershey, PA); William Robert DeFoor, Jr., MD, MPH (Cincinnati Children's Hospital, Cincinnati, OH); Steven G. Docimo, MD (Children's Hospital of Pittsburgh of UPMC, Pittsburgh, PA); Sahar Fathallah-Shaykh, MD (University of Alabama at Birmingham School of Medicine, Birmingham, AL); Brian Fisher, DO, MSCE (Children's Hospital of Philadelphia, Philadelphia, PA); Barbara Fivush, MD (Johns Hopkins School of Medicine, Baltimore, MD); Arlene C. Gerson, PhD (Johns Hopkins School of Medicine, Baltimore, MD); Saul P. Greenfield, MD (Women and Children's Hospital of Buffalo, Buffalo, NY); Robert Hickey, MD (Children's Hospital of Pittsburgh of UPMC, Pittsburgh, PA); Alejandro Hoberman, MD (Children's Hospital of Pittsburgh of UPMC, Pittsburgh, PA); Anastasia Ivanova, PhD (University of North Carolina at Chapel Hill, Chapel Hill, NC); Ron Keren, MD, MPH (Children's Hospital of Philadelphia, Philadelphia, PA); Bradley P. Kropp, MD, FAAP, FACS (University of Oklahoma Health Sciences Center, Oklahoma City, OK); Ranjiv Mathews, MD (Johns Hopkins School of Medicine, Baltimore, MD); Tej K. Mattoo, MD, DCH, FRCP (UK)

(Wayne State University School of Medicine, Detroit, MI); Gordon McLorie, MD, FRCSC, FAAP (Children's Hospital of Orange County, University of California, Irvine, CA); Daniel R. McMahon, MD (Akron Children's Hospital, Akron, OH); Marva Moxey-Mims, MD (National Institute of Diabetes and Digestive and Kidney Diseases, Bethesda, MD); Milan Nadkarni, MD (Wake Forest University Baptist Medical Center, Winston-Salem, NC); Caleb P. Nelson, MD, MPH (Boston Children's Hospital, Boston, MA); Carrie A. Phillipi, MD, PhD (Oregon Health and Science University, Portland, OR); Hans G. Pohl, MD (Children's National Medical Center, Washington, DC); Mary Ann Queen, MD (Children's Mercy Hospital of Kansas City, Kansas City, MO); Amy Renwick, MD (Alfred I. duPont Hospital for Children, Wilmington, DE); H. Gil Rushton, Jr., MD, FAAP (Children's National Medical Center, Washington, DC); Nader Shaikh, MD (Children's Hospital of Pittsburgh of UPMC, Pittsburgh, PA); Kathy Shaw, MD, MSCE (Children's Hospital of Philadelphia, Philadelphia, PA); Steven J. Skoog, MD, FACS, FAAP (Oregon Health and Science University, Portland, OR); Ming-Hsien Wang, MD (Johns Hopkins School of Medicine, Baltimore, MD); Wayne Waz, MD (Women and Children's Hospital of Buffalo, Buffalo, NY); Lisa Zaoutis, MD (Children's Hospital of Philadelphia, Philadelphia, PA); Theoklis Zaoutis, MD, MSCE (Children's Hospital of Philadelphia, Philadelphia, PA); and Hongming Zhaung, MD, PhD (Children's Hospital of Philadelphia, Philadelphia, PA).

The RIVUR Study Coordinators: Stephanie Clevenger, RN, BSN (University of Alabama at Birmingham School of Medicine, Birmingham, AL); Rachel DeBerardinis (Children's Hospital of Philadelphia, Philadelphia, PA); Julie Denlinger (Cincinnati Children's Hospital, Cincinnati, OH); Whitney Drew (Oregon Health and Science University, Portland, OR); Rebecca Duby (Oregon Health and Science University, Portland, OR); Teresa Falk, LVN, CCRP (Texas

Children's Hospital, Houston, TX); Allyson J. Fried, CPNP (Women and Children's Hospital of Buffalo, Buffalo, NY); Beth Garrett, RN, CCRP (Johns Hopkins School of Medicine, Baltimore, MD); Mary Ann Haralam, CRNP (Children's Hospital of Pittsburgh of UPMC, Pittsburgh, PA); Janelle Jennings, RN, CPN (Children's Mercy Hospital of Kansas City, Kansas City, MO); Jeremy Kaufman (Children's Hospital of Philadelphia, Philadelphia, PA); Diana Kearney, RN, CRCC (Children's Hospital of Pittsburgh of UPMC, Pittsburgh, PA); Kimberly Klipner RN, CCRC (Alfred I. duPont Hospital for Children, Wilmington, DE); Andrea Kuchler (Oregon Health and Science University, Portland, OR); Kathy Lehman (Penn State Milton S. Hershey Medical Center, Hershey, PA); Troy Lubianski, RN, BSN, CCRP (Oregon Health and Science University, Portland, OR); Sabrina Meyer, CPNP (Women and Children's Hospital of Buffalo, Buffalo, NY); Theresa Meyer, MS, RN, CPN (Ann & Robert H. Lurie Children's Hospital of Chicago, Chicago, IL); Ariannah Mirick (Children's Hospital of Philadelphia, Philadelphia, PA); Stacey C. Moyer, MSN, RN (University of Wisconsin Hospital and Clinics, Madison, WI); Allison Parker (Children's Hospital of Philadelphia, Philadelphia, PA); Lena Peschansky, RN, BSN (Wayne State University School of Medicine, Detroit, MI); Lissy Powell (Oregon Health and Science University, Portland, OR); Melissa Reed, RN, BSN (Cincinnati Children's Hospital, Cincinnati, OH); Ilina Rosoklija, MPH (Boston Children's Hospital, Boston, MA); Bruce M. Sprague (Children's National Medical Center, Washington, DC); Katie Tremont (Children's Hospital of Philadelphia, Philadelphia, PA); Lori Triplett, RN (Wake Forest University Baptist Medical Center, Winston-Salem, NC); Kamilah Weems (Children's Hospital of Philadelphia, Philadelphia, PA); Kirk B. Wettengel (University of Oklahoma Health Sciences Center, Oklahoma City, OK); and Ruthie Youssefi RN, MSN, CPNP (Akron Children's Hospital, Akron, OH).

The RIVUR Reference Radiologists: Jeanne S. Chow, MD (Boston Children's Hospital, Boston, MA); Massoud Majd, MD (Children's National Medical Center, Washington, DC); Michael J. Zerin (Wayne State University School of Medicine, Detroit, MI); and Harvey A. Ziessman, MD (Johns Hopkins School of Medicine, Baltimore, MD).

The RIVUR Urinary Tract Infection Classification Committee: Timothy P. Bukowski, MD, William A. Primack, MD, and Richard W. Sutherland, MD (University of North Carolina at Chapel Hill, Chapel Hill, NC).

The RIVUR Central Laboratories: Michael Green, MD, MPH and Karen Barbadora, MT (ASPC) (Children's Hospital of Pittsburgh of UPMC, Pittsburgh, PA); and George J. Schwartz, MD and Paula S. Maier (University of Rochester, Rochester, NY).

Statisticians and staff at the RIVUR Data Coordinating Center (Collaborative Studies Coordinating Center, Department of Biostatistics, University of North Carolina at Chapel Hill) were responsible for data management and statistical analyses.

The RIVUR Data and Safety Monitoring Board: Ana S. Iltis, PhD (Wake Forest University, Winston-Salem, NC); Virginia Keane, MD (University of Maryland, Baltimore, MD); Craig A. Peters, MD (Children's National Medical Center, Washington, DC); Ellen B. Roecker, PhD (University of Wisconsin, Madison, WI); Bruce Slaughenhoupt, MD (University of Wisconsin, Madison, WI); and Howard Trachtman, MD (New York University Langone Medical Center, New York, NY).

RIVUR Inclusion and Exclusion Criteria

Inclusion – child must meet ALL

- Age: 2 months to less than 6 years (72 months) at randomization
- **First or second** urinary tract infection with ≥ 38°C fever **OR** symptoms related to urinary tract documented within ± 24 hours of urinary tract infection work-up (symptoms include dysuria, urgency, frequency, abdominal pain, foul-smelling urine, and in infants, dehydration, hypothermia, and failure to thrive)
- Index urinary tract infection diagnosis occurred within 112 days of randomization
- Pyuria on urine analysis shown in 1 of 3 ways:
  - ≥ 10 WBC/mm^3 **OR**
  - ≥ 5 WBC/HPF **OR**
  - Leukocyte esterase ≥ trace on dipstick
- Culture proven infection with single primary organism:
  - ≥ 50,000 CFU/mL (catheter or aspirated) **OR**
  - ≥ 100,000 CFU/mL (clean void)
- Index urinary tract infection treated for 7+ days with effective drug OR test of cure (negative urine culture) post treatment
- Presence of grade I-IV vesicoureteral reflux in at least one ureter based on radiographic voiding cystourethrogram performed within 112 days after diagnosis of index urinary tract infection

Exclusion – if child meets one or more

- If child < 6 months old, gestational age <34 weeks
- Index urinary tract infection diagnosis more than 112 days prior to randomization
- Vesicoureteral reflux diagnosed or treated between 1st and 2nd urinary tract infection
- History of more than two urinary tract infections prior to randomization
- Index urinary tract infection not successfully treated
- Greater than two organisms present on index urinary tract infection urine culture
- Second organism present at >10,000 CFU/mL
- Consent not obtained OR inability to complete protocol
- Allergy to trimethoprim-sulfamethoxazole
- Grade V vesicoureteral reflux in either ureter
- Co-morbid urologic anomalies: hydronephrosis, ureterocele, urethral valve, solitary or profoundly small kidney, multicystic dysplastic kidney, neurogenic bladder pelvic kidney or fused kidney.
- History of other renal injury/disease
- Any bladder or renal surgeries
- Congenital or acquired immunodeficiency
- Underlying anomalies or chronic diseases that could potentially interfere with response to therapy such as gastrointestinal conditions (malabsorption, inflammatory bowel disease), liver/kidney failure or malignancy
- Complex cardiac disease
- Family history of anaphylactic reaction to sulfa

RMUR Randomized Intervention for Children with Vesicoureteral Reflux

Scoring for Bladder and Bowel Dysfunction

ID NUMBER:								FORM CODE: DVQ VERSION: A 9/16/06	Contact Occasion		SEQ #	

Participant Name: _____

A. Child Response with Parent Help:

During the past month:	Almost never	Less than ½ the time	About ½ the time	Almost every time	Not applicable
1. When I peed it hurt.	A	B	C	D	N
2. I tried to hold only my pee by crossing my legs, squatting, or doing a pee dance.	A	B	C	D	N
3. When I had to pee, I could not wait	A	B	C	D	N
4. I had to push to pee.	A	B	C	D	N
5. I went to the bathroom to pee only once or twice per day.	A	B	C	D	N
6. I wet my underwear with pee during the day.	A	B	C	D	N
7. When I wet myself with pee, my underwear was soaked.	A	B	C	D	N
8. I had to push for my bowel movements to come out.	A	B	C	D	N
9. I usually did not have a bowel movement every day.	A	B	C	D	N

B. Parent/Guardian Response:

10. During the past month, has your child experienced any stressful events, such as: a new baby, a new school, home problems (divorce/death), a new home, abuse (sexual/physical), school problems, or serious accident/injury? ..... Y N

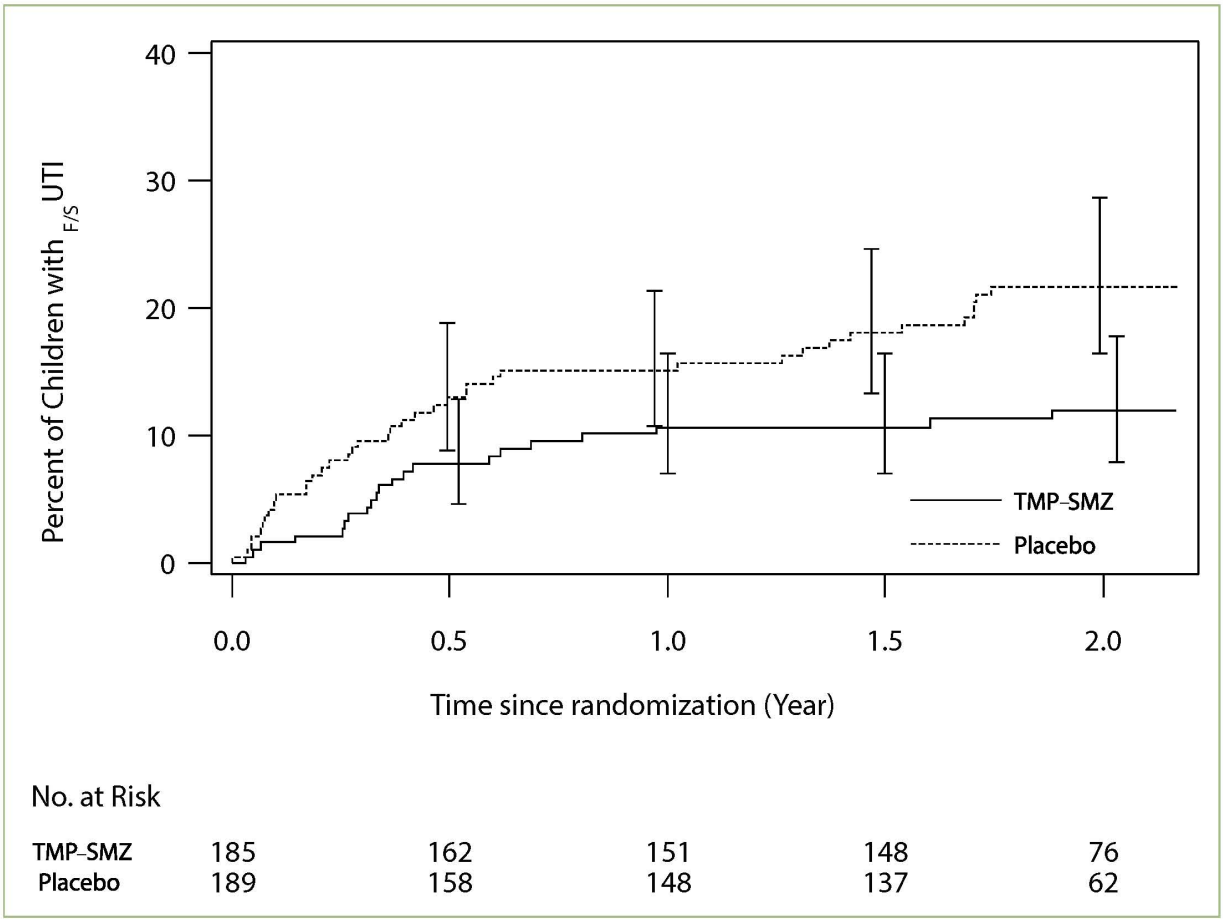
C. Calculation of Bladder and Bowel Dysfunction Score[1]:

The score is the sum of items 1 through 9 where an A = 0 points, B = 1 point, C = 2 points and D = 3 points. Additionally, if Y is selected for Item 10, 3 points are added to the score.

Score = Number of B responses (Item1-9)
+ 2 X Number of C responses (Item1-9)
+ 3 X Number of D responses (Item1-9)
+ 3 (If item 10=Y)

For items 1-10, if 3 or more items are blank or have the value of "N" (Not applicable) then the score is equal to missing.

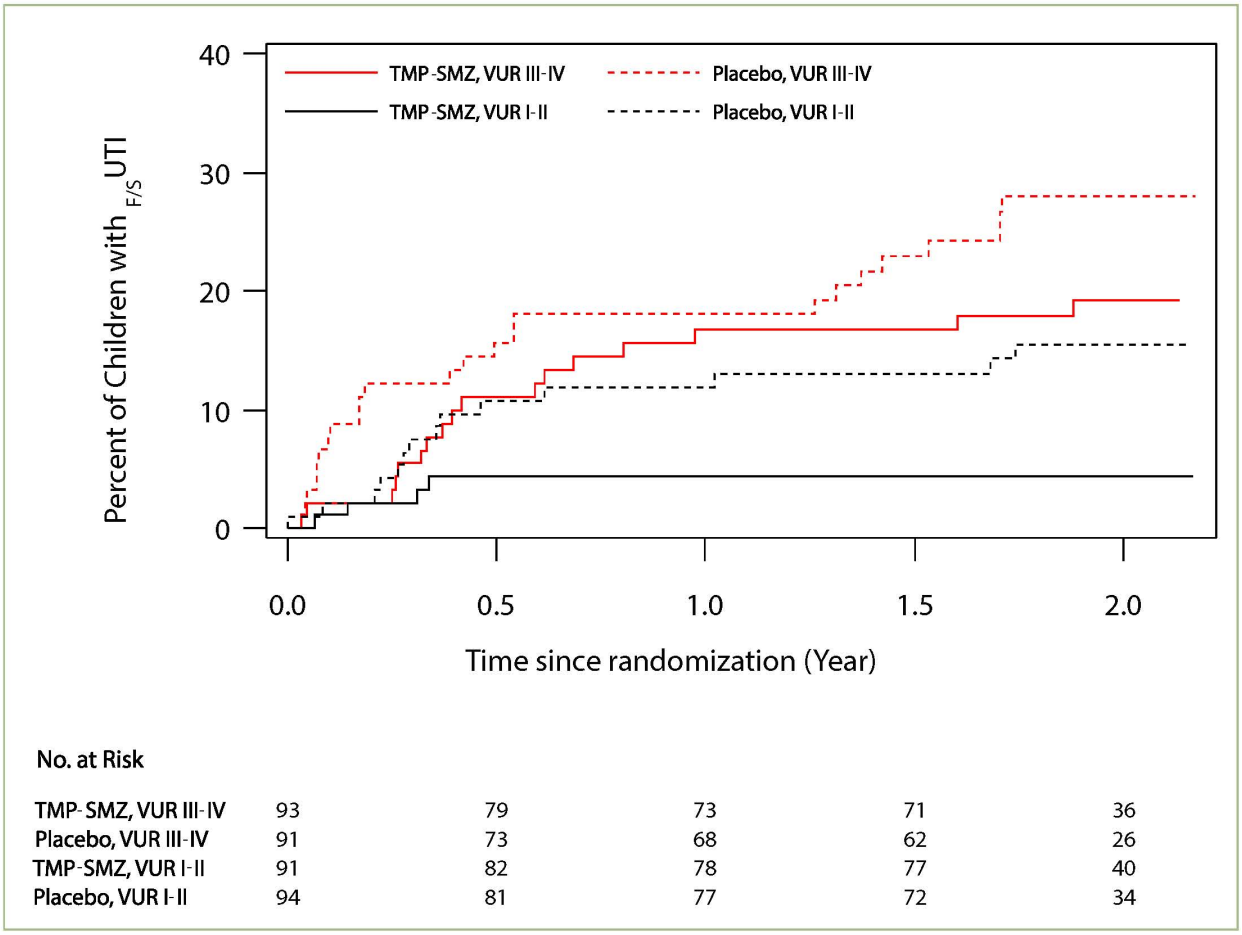
Figure S1. Time to First Recurrent Febrile or Symptomatic Urinary Tract Infection for Children Less Than 2 Years of Age with a First Febrile Urinary Tract Infection by Treatment Group



F/SUTI=febrile symptomatic urinary tract infection; TMP-SMZ=trimethoprim-sulfamethoxazole ; No.=number

Subgroup analysis of children less than 2 years of age and enrolled following their first febrile urinary tract infection. Kaplan-Meier estimated cumulative percent of children experiencing a recurrent febrile or symptomatic urinary tract infection for those assigned to trimethoprim-sulfamethoxazole prophylaxis (solid line) and those assigned to placebo (dotted line), with 95% confidence intervals (vertical capped lines) for the corresponding point estimates at 6, 12, 18 and 24 months. Numbers of children at risk at the beginning of indicated time periods are provided. Treatment group comparisons, P-value = 0.015. P-values are based on log-rank test stratified by core site.

Figure S2. Time to First Recurrent Febrile or Symptomatic Urinary Tract Infection for Children Less Than 2 Years of Age with a First Febrile Urinary Tract Infection by Treatment Group and Severity of Vesicoureteral Reflux



F/SUTI=febrile symptomatic urinary tract infection; TMP-SMZ=trimethoprim-sulfamethoxazole; VUR=vesicoureteral reflux; No.=number

Subgroup analysis of children less than 2 years of age and enrolled following their first febrile urinary tract infection. Kaplan-Meier estimated cumulative percent of children experiencing a recurrent febrile or symptomatic urinary tract infection for those assigned to trimethoprim-sulfamethoxazole prophylaxis (solid line) and those assigned to placebo (dotted line) by non-dilating-vesicoureteral reflux grades I and II-(black), and dilating-vesicoureteral reflux grades III and IV-(red) vesicoureteral reflux. Numbers of children at risk at the beginning of indicated time periods are provided. Treatment group comparisons for low grade of VUR (Grade I-II), P-value = 0.019. Treatment group comparisons for high grades of VUR (Grade III-IV), P-value = 0.170. P-values are based on log-rank test stratified by core site.

Table S1. Distribution and Characteristics of all Recurrent Febrile or Symptomatic Urinary Tract Infections

	All Recurrent Febrile or Symptomatic Urinary Tract Infection	
	Trimethoprim-Sulfamethoxazole	Placebo
	N (%)	N (%)
Number of febrile or symptomatic urinary tract infection	60	111
Number of febrile or symptomatic urinary tract infections per child		
0	263 (87)	233 (76)
1	25 (8)	44 (14)
2	9 (3)	20 (7)
3	3 (1)	5 (2)
4	2 (1)	3 (1)
Type of urinary tract infection		
Febrile	21 (35)	23 (21)
Symptomatic	18 (30)	37 (33)
Both	21 (35)	51 (46)
Infecting organism		
Escherichia coli	48 (80)	89 (80)
Klebsiella	4 (7)	6 (5)
Enterococcus	3 (5)	7 (6)
Proteus	0 (-)	4 (4)
Enterobacter	2 (3)	1 (1)
Citrobacter	1(2)	1(1)
Staphylococcus-coagulase negative	0 (-)	2 (2)
Aerobic gram negative enterobacteriaceae	1 (2)	0 (-)
Morganella	1 (2)	0 (-)
Other	0 (-)	1(1)
Hospitalization or emergency room visit in conjunction with febrile or symptomatic urinary tract infection	19 (32)	39 (35)

Table S2. Multivariable Models for First Recurrent Febrile or Symptomatic Urinary Tract Infection

	Model 1	Model 2
	Hazard ratio (95% confidence interval)	**Hazard ratio (95% confidence interval)**
Treatment group (Trimethoprim-sulfamethoxazole vs Placebo)	0.49 (0.33-0.73)	0.44 (0.29-0.66)
Highest grade of baseline vesicoureteral reflux (III-IV vs I-II)	1.90 (1.29-2.79)	1.64 (1.10-2.44)
History of index urinary tract infection (Second vs First)	1.78 (1.03-3.10)	1.95 (1.12-3.41)
Age (6 month increments)	1.07 (1.00-1.13)	Not included
Baseline renal scarring (Scarring vs None)	Not included	3.07 (1.50-6.25)

Table S3. Distribution of Adverse Events

Adverse Event	Number of Participants with Adverse Events Reported†		Number of Adverse Events Reported‡	
	Trimethoprim-Sulfamethoxazole	Placebo	Trimethoprim-Sulfamethoxazole	Placebo
	N (%)	N (%)	N	N
Any Adverse Event	153 (50.7)	165 (54.1)	414	494
Abscess	0 (-)	1 (0.3)	0	1
Abscess Periodontal	0 (-)	1 (0.3)	0	1
Allergy Reaction	0 (-)	2 (0.7)	0	2
Anomaly Congenital Urogenital	1 (0.3)	1 (0.3)	1	1
Application Site Reaction	2 (0.7)	0 (-)	2	0
Arthralgia	1 (0.3)	0 (-)	1	0
Asthenia	1 (0.3)	0 (-)	2	0
Asthma	0 (-)	7 (2.3)	0	11
Bone Fracture Spontaneous	4 (1.3)	0 (-)	5	0
Breast Enlarge	1 (0.3)	0 (-)	1	0
Bronchiolitis	4 (1.3)	2 (0.7)	6	4
Bronchitis	1 (0.3)	1 (0.3)	1	1
Cellulitis	2 (0.7)	3 (1.0)	2	3
Chills Fever	0 (-)	1(0.3)	0	1
Clubfoot	1 (0.3)	0 (-)	1	0
Colitis	0 (-)	1 (0.3)	0	1
Conjunctivitis	3 (1.0)	1 (0.3)	4	1
Constipation	6 (2.0)	7 (2.3)	7	8
Convulsions	5 (1.7)	4 (1.3)	7	4
Cough Increased	2 (0.7)	2 (0.7)	2	2
Cyanosis	1 (0.3)	0 (-)	1	0
Cystitis	0 (-)	2 (0.7)	0	3
Dehydration	4 (1.3)	6 (2.0)	4	6
Dermatitis Contact	2 (0.7)	0 (-)	2	0
Dermatitis Fungal	6 (2.0)	9 (3.0)	8	15
Diarrhea	11 (3.6)	19 (6.2)	14	27
Dyspepsia	1 (0.3)	1 (0.3)	1	1
Dysphagia	0 (-)	1 (0.3)	0	1
Dyspnea	4 (1.3)	2 (0.7)	4	2
Dysuria	4 (1.3)	7 (2.3)	4	8
Ear Disorder	0 (-)	1 (0.3)	0	1
Ecchymosis	1 (0.3)	1 (0.3)	2	1
Eczema	1 (0. 3)	1 (0.3)	1	1
Enteritis	1 (0.3)	0 (-)	1	0
Erythema Multiforme	0 (-)	1 (0.3)	0	2

(continued)

† More than one adverse event type may be reported for some participants.

‡ More than one adverse event may be listed for some participants, and some participants may have more than one event within an event type.

Table S3. Distribution of Adverse Events

Adverse Event	Number of Participants with Adverse Events Reported†		Number of Adverse Events Reported‡	
	Trimethoprim-Sulfamethoxazole	Placebo	Trimethoprim-Sulfamethoxazole	Placebo
	N (%)	N (%)	N	N
Eye Disorder	0 (-)	2 (0.7)	0	2
Fever	43 (14.2)	55 (18.0)	58	80
Flu Syndrome	0 (-)	4 (1.3)	0	5
Furunculosis	1 (0.3)	0 (-)	1	0
Gastritis	2 (0.7)	0 (-)	2	0
Gastroenteritis	5 (1.7)	5 (1.6)	5	5
Gastrointestinal Disorder	3 (1.0)	0 (-)	4	0
Headache	2 (0.7)	4 (1.3)	2	4
Hemorrhage Gastrointestinal	1 (0.3)	0 (-)	1	0
Hyperglycemia	0 (-)	1 (0.3)	0	1
Hypertension	1 (0.3)	0 (-)	1	0
Hypoglycemia	1 (0.3)	0 (-)	1	0
Ileus	1 (0.3)	0 (-)	1	0
Incontinence Urine	0 (-)	1 (0.3)	0	2
Infection	0 (-)	1 (0.3)	0	1
Infection Bacterial	1 (0.3)	0 (-)	1	0
Injury Accidental	4 (1.3)	7 (2.3)	4	8
Insomnia	2 (0.7)	2 (0.7)	2	2
Kidney Tubular Disorder	1 (0.3)	2 (0.7)	1	2
Laryngitis	12 (4.0)	4 (1.3)	16	7
Leukopenia	3 (1.0)	0 (-)	3	0
Leukorrhea	1 (0.3)	0 (-)	1	0
Lymphadenopathy	0 (-)	1 (0.3)	0	3
Monilia Vagina	1 (0.3)	2 (0.7)	2	2
Nail Disorder	2 (0.7)	0 (-)	2	0
Neoplasm Skin	0 (-)	1 (0.3)	0	1
Nervousness	2 (0.7)	0 (-)	3	0
Oliguria	1 (0.3)	1 (0.3)	1	1
Oral Moniliasis	3 (1.0)	3 (1.0)	3	3
Otitis Externa	1 (0.3)	0 (-)	1	0
Otitis Media	13 (4.3)	24 (7.9)	18	33
Overdose	1 (0.3)	1 (0.3)	1	1
Pain	1 (0.3)	1 (0.3)	1	1
Pain Abdominal	6 (2.0)	2 (0.7)	7	2
Pain Back	0 (-)	1 (0.3)	0	1
Pain Ear	3 (1.0)	1 (0.3)	3	1

(continued)

† More than one adverse event type may be reported for some participants.

‡ More than one adverse event may be listed for some participants, and some participants may have more than one event within an event type.

Table S3. Distribution of Adverse Events

Adverse Event	Number of Participants with Adverse Events Reported†		Number of Adverse Events Reported‡	
	Trimethoprim-Sulfamethoxazole	Placebo	Trimethoprim-Sulfamethoxazole	Placebo
	N (%)	N (%)	N	N
Penis Disorder	0 (-)	1 (0.3)	0	1
Personality Disorder	1 (0.3)	0 (-)	1	0
Pharyngitis	19 (6.3)	14 (4.6)	25	20
Photosensitivity	1 (0.3)	2 (0.7)	1	2
Pneumonia	1 (0.3)	7 (2.3)	1	8
Pyelonephritis	6 (2.0)	11 (3.6)	10	13
Rash	23 (7.6)	23 (7.5)	30	26
Rash Maculo-Papular	3 (1.0)	4 (1.3)	3	6
Rash Pustular	1 (0.3)	1 (0.3)	1	1
Reaction Aggravation	1 (0.3)	0 (-)	1	0
Respiratory Disorder	1 (0.3)	1 (0.3)	1	1
Rhinitis	0 (-)	1 (0.3)	0	1
Serum Glutamic-Oxaloacetic Transaminase Increase	0 (-)	1 (0.3)	0	1
Serum Glutamic-Pyruvic Transaminase Increase	0 (-)	1 (0.3)	0	2
Screaming Syndrome	0 (-)	1 (0.3)	0	1
Sinusitis	3 (1.0)	2 (0.7)	3	5
Skin Discolor	0 (-)	1 (0.3)	0	1
Skin Moniliasis	1 (0.3)	3 (1.0)	1	4
Sputum Increased	1 (0.3)	0 (-)	1	0
Stomatitis	1 (0.3)	0 (-)	1	0
Stomatitis Ulcer	1 (0.3)	0 (-)	2	0
Stridor	0 (-)	1 (0.3)	0	1
Thrombocytopenia	1 (0.3)	0 (-)	2	0
Tooth Caries	0 (-)	1 (0.3)	0	1
Tooth Discoloration	0 (-)	1 (0.3)	0	1
Urgency of Urination	0 (-)	1 (0.3)	0	1
Urinary Tract Disorder	1 (0.3)	1 (0.3)	1	1
Urinary Tract Infection	16 (5.3)	27 (8.9)	24	38
Urine Abnormal	1 (0.3)	0 (-)	1	0
Urticaria	4 (1.3)	4 (1.3)	4	4
Vaginitis	8 (2.6)	3 (1.0)	9	4
Vasodilation	1 (0.3)	0 (-)	1	0
Viral Infection	14 (4.6)	16 (5.2)	14	20
Vomiting	10 (3.3)	9 (3.0)	10	11
Vulvovaginal Disorder	1 (0.3)	0 (-)	1	0
Vulvovaginitis	3 (1.0)	4 (1.3)	3	4

(continued)

† More than one adverse event type may be reported for some participants.

‡ More than one adverse event may be listed for some participants, and some participants may have more than one event within an event type.

Table S3. Distribution of Adverse Events

Adverse Event	Number of Participants with Adverse Events Reported†		Number of Adverse Events Reported‡	
	Trimethoprim-Sulfamethoxazole	Placebo	Trimethoprim-Sulfamethoxazole	Placebo
	N (%)	N (%)	N	N
Other				
Abcess Bacterial	0 (-)	1 (0.3)	0	1
Abrasion	1 (0.3)	0 (-)	1	0
Accidental Ingestion	0 (-)	1 (0.3)	0	1
Acute Upper Respiratory Infection	0 (-)	1 (0.3)	0	1
Atopic Dermatitis	1 (0.3)	0 (-)	1	0
Candida	0 (-)	1 (0.3)	0	1
Choking Sensation	1 (0.3)	0 (-)	1	0
Concussion	0 (-)	1 (0.3)	0	1
Cystoscopy Of Bilateral Ureteral Reimplantation	1 (0.3)	0 (-)	1	0
Cystoscopy With Deflux Injection	0 (-)	1 (0.3)	0	1
Diaper Rash	0 (-)	3 (1.0)	0	3
Dog Bite	1 (0.3)	0 (-)	1	0
Erythema Migrans	0 (-)	1 (0.3)	0	1
Evaluation to Rule Out Fracture	1 (0.3)	0 (-)	1	0
Facial Flushing	0 (-)	1 (0.3)	0	1
Febrile Seizure	1 (0.3)	0 (-)	2	0
Fifths Disease	0 (-)	1 (0.3)	0	1
Foot Injury	0 (-)	1 (0.3)	0	1
Foreign Body In Ear	1 (0.3)	1 (0.3)	1	1
Foreign Body In Esophagus	0 (-)	1 (0.3)	0	1
Foreign Body Sutured In Laceration	0 (-)	1 (0.3)	0	1
Head Injury	1 (0.3)	1 (0.3)	1	1
Ingestion of Foreign Body	1 (0.3)	0 (-)	1	0
Laceration	1 (0.3)	2 (0.7)	1	2
Limping	1 (0.3)	0 (-)	1	0
Lip Laceration	0 (-)	1 (0.3)	0	1
Lyme Disease	1 (0.3)	0 (-)	1	0
Monilia Skin	1 (0.3)	1 (0.3)	1	1
Mouth Laceration	1 (0.3)	0 (-)	1	0
Other	1 (0.3)	0 (-)	2	0
Papular Acrodermatitis	1 (0.3)	0 (-)	1	0
Phimosis/Circumcision	0 (-)	1 (0.3)	0	1
Positive Blood Culture	1 (0.3)	0 (-)	1	0
Pulled Quadricep	1 (0.3)	0 (-)	1	0

(continued)

† More than one adverse event type may be reported for some participants.

‡ More than one adverse event may be listed for some participants, and some participants may have more than one event within an event type.

Table S3. Distribution of Adverse Events

Adverse Event	Number of Participants Adverse Events Reported‡		Number of Adverse Events Reported†	
	Trimethoprim-Sulfamethoxazole	Placebo	Trimethoprim-Sulfamethoxazole	Placebo
	N (%)	N (%)	N	N
Reactive Airway Disease	0 (-)	1 (0.3)	0	1
Removal of Staples	1 (0.3)	0 (-)	1	0
Scalp Laceration	1 (0.3)	0 (-)	1	0
Undescended Testis	0 (-)	1 (0.3)	0	1
Upper Respiratory Infection	1 (0.3)	0 (-)	1	0
Ureteral Reimplantation	2 (0.7)	5 (1.6)	6	8
Urinary Reflux	0 (-)	2 (0.7)	0	2
Vesicoureteral Reflux	0 (-)	2 (0.7)	0	3
Viral	1 (0.3)	0 (-)	1	0
Viral Gastroenteritis	0 (-)	1 (0.3)	0	1
Yeast Infection	1 (0.3)	1 (0.3)	1	1

† More than one adverse event type may be reported for some participants.

‡ More than one adverse event may be listed for some participants, and some participants may have more than one event within an event type.

Table S4. Distribution of Discharge Summaries from Hospitalization or Emergency Room Visits

Discharge Distributions[†]	Number of Participants with Indicated Hospitalization or Emergency Room Visits		Number of Indicated Hospitalization or Emergency Room Visits Reported	
	Trimethoprim-Sulfamethoxazole	Placebo	Trimethoprim-Sulfamethoxazole	Placebo
	N (%)	N (%)	N	N
Number of Hospitalizations or Emergency Room Visits	124 (41.1)	148 (48.5)	276	351
Infectious and Parasitic Diseases (001-139)	39 (12.9)	42 (13.8)	49	56
Neoplasms (140-239)	0 (-)	0 (-)	0	0
Endocrine Nutritional and Metabolic Diseases and Immunity Disorders (240-279)	14 (4.6)	10 (3.3)	16	10
Diseases of Blood and Blood-forming Organs (280-289)	3 (1.0)	2 (0.7)	3	2
Mental Disorders (290-319)	0 (-)	0 (-)	0	0
Diseases of the Nervous System and Sense Organs (320-389)	16 (5.3)	34 (11.1)	19	39
Diseases of the Circulatory System (390-459)	0 (-)	0 (-)	0	0
Diseases of the Respiratory System (460-519)	41 (13.6)	45 (14.8)	63	79
Diseases of the Digestive System (520-579)	18 (6.0)	15 (4.9)	23	16
Diseases of the Genitourinary System (580-629)	39 (12.9)	61 (20.0)	70	120
Diseases of the Skin and Subcutaneous Tissue (280-709)	10 (3.3)	11 (3.6)	11	15
Diseases of the Musculoskeletal System and Connective Tissue (710-739)	2 (0.7)	2 (0.7)	3	4
Congenital Anomalies (740-759)	7 (2.3)	1 (0.3)	7	3
Certain Conditions Originating in the Prenatal Period (760-779)	0 (-)	0 (-)	0	0
Symptoms Signs and Ill-defined Conditions (780-799)	71 (23.5)	97 (31.8)	124	167
Injury and Poisoning (800-999)	20 (6.6)	19 (6.2)	26	24
Supplemental Classification (V01-V89, E800-E999)	13 (4.3)	13 (4.3)	14	14

[†]More than one diagnosis may have been listed for some participants, and some participants may have more than one hospitalization or emergency room visit.

References

1. Farhat W, Bagli DJ, Capolicchio G, et al. The dysfunctional voiding scoring system: quantitative standardization of dysfunctional voiding symptoms in children. J Urol 2000;164:1011-5.