

## Supplementary Appendix

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

Supplement to: Craig JC, Simpson JM, Williams GJ, et al. Antibiotic prophylaxis and recurrent urinary tract infection in children. *N Engl J Med* 2009;361:1748-59.

Supplementary material for on-line publication only

Table 1. Frequency and percentage\* with symptomatic UTI by subgroup

Characteristic	Cotrimoxazole n/N (%)	Placebo n/N (%)	HR (95% CI)	P for interaction <sup>†</sup>	Risk difference (95% CI)
<b>Overall</b>	36/288 (13)	55/288 (19)	0.61 (0.40, 0.93) <sup>^</sup>		6.6 (0.6, 12.6)
<b>Gender</b>					
Female	31/183 (17)	43/186 (23)	0.68 (0.43, 1.08)	0.32	6.1 (-2.1, 14.4)
Male	5/105 (5)	12/102 (12)	0.39 (0.14, 1.09)		7.1 (-0.5, 14.7)
<b>Age group</b>					
< 4 years	18/226 (8)	31/221 (14)	0.53 (0.30, 0.95)	0.48	6.0 (0.1, 11.9)
≥ 4 years	18/ 62 (29)	24/ 67 (36)	0.75 (0.41, 1.38)		6.8 (-9.3, 22.9)
<b>Max VUR Grade</b>					
None	15/119 (13)	17/115 (15)	0.82 (0.41, 1.65)	0.70	1.8 (-7.1, 10.8)
1-2	5/ 57 (9)	8/ 57 (14)	0.58 (0.19, 1.77)		5.4 (-6.4, 17.2)
3-5	9/ 65 (14)	13/ 64 (21)	0.65 (0.28, 1.52)		6.8 (-6.3, 19.8)
Unknown	7/ 47 (15)	17/ 52 (34)	0.39 (0.16, 0.94)		18.5 (1.8, 35.2)
<b>Previous UTIs<sup>‡</sup></b>					
0	13/204 (6)	27/206 (13)	0.46 (0.24, 0.89)	0.59	6.8 (1.0, 12.5)
1	7/ 26 (27)	11/ 35 (31)	0.82 (0.32, 2.12)		4.1 (-19.0, 27.3)
2 or more	15/54 (28)	16/ 44 (38)	0.65 (0.32, 1.32)		9.5 (-9.5, 28.6)
<b>Index UTI</b>					
Sensitive	26/243 (11)	41/236 (19)	0.53 (0.33, 0.87)	0.19	8.1 (1.7, 14.4)
Resistant	10/42 (25)	10/44 (23)	1.02 (0.42, 2.45)		-1.6 (-20.0, 16.8)

\* Percentages are Kaplan-Meier estimates

<sup>†</sup> P for interaction from Cox regression model adjusted for gender, age group and history of >1 UTI (and reflux for VUR only)

<sup>^</sup> For primary endpoint, logrank P=0.02

<sup>‡</sup> Not included: 4 children in cotrimoxazole group and 3 children in placebo group who were known to have had at least one previous UTI, but number unknown

**Table 2. Frequency and percentage\* with UTI with fever by subgroup**

<b>Characteristic</b>	<b>Cotrimoxazole n/N (%)*</b>	<b>Placebo n/N (%)*</b>	<b>HR (95% CI)</b>	<b>P for interaction<sup>†</sup></b>	<b>Risk difference (95% CI)</b>
<b>Overall</b>	19/288 (7)	36/288 (13)	0.49 (0.28, 0.86)		6.1 (1.1, 11.2)
<b>Gender</b>					
Female	16/183 (9)	26/186 (15)	0.58 (0.31, 1.09)	0.30	5.6 (-1.4, 12.5)
Male	3/105 (3)	10/102 (10)	0.28 (0.08, 1.01)		7.1 (0.3, 13.9)
<b>Age group</b>					
< 4 years	11/226 (5)	27/221 (13)	0.37 (0.19, 0.75)	0.17	7.3 (1.9, 12.7)
≥ 4 years	8/ 62 (13)	9/ 67 (15)	0.89 (0.34, 2.31)		2.0 (-10.8, 14.8)
<b>Max VUR Grade</b>					
None	6/119 (6)	14/115 (12)	0.40 (0.16, 1.05)	0.96	6.6 (-0.9, 14.1)
1-2	3/ 57 (6)	6/ 57 (11)	0.46 (0.12, 1.84)		5.5 (-4.9, 15.8)
3-5	7/ 65 (11)	11/ 64 (18)	0.60 (0.23, 1.54)		6.8 (-5.5, 19.1)
Unknown	3/ 47 (7)	5/ 52 (12)	0.56 (0.13, 2.35)		5.5 (-6.7, 17.8)
<b>Previous UTIs<sup>‡</sup></b>					
0	9/204 (5)	23/206 (11)	0.37 (0.17, 0.80)	0.55	6.9 (1.6, 12.1)
1	4/26 (16)	6/35 (18)	0.86 (0.24, 3.06)		1.6 (-18.1, 21.3)
2 or more	5/54 (11)	7/44 (19)	0.50 (0.16, 1.57)		8.5 (-7.2, 24.2)
<b>Index UTI</b>					
Sensitive	14/243 (6)	27/236 (12)	0.47 (0.25, 0.89)	0.74	6.1 (0.9, 11.4)
Resistant	5/42 (14)	9/44 (21)	0.57 (0.19, 1.69)		7.2 (-9.5, 23.8)

\* Percentages are Kaplan-Meier estimates

<sup>†</sup> P for interaction from Cox regression model adjusted for gender, age group and history of >1 UTI (and reflux for VUR only, and index UTI for final model only)

<sup>‡</sup> Not included: 4 children in cotrimoxazole group and 3 children in placebo group who were known to have had at least one previous UTI, but number unknown

### **Safety Monitoring Committee (SMC)**

Three independent members, a methodologist, pediatrician, and nephrologist constituted the SMC. Blinded data for the following secondary outcomes: renal damage, hospitalization with UTI, and febrile UTI were sent to the SMC after every 100 patients recruited. The SMC was required to consider recommending cessation of the trial if the difference in proportions of renal damage and/or hospitalization with UTI at any evaluation was statistically significant ( $P < 0.01$ , 2-sided). The SMC did not receive data on the primary outcome.