

Supplementary Online Content

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

eTable 1. Diagnosis codes for acute respiratory tract infections

Diagnosis	ICD-9	ICD-10
Acute otitis media	382.00-382.02, 382.4, 382.9	H66.001-H66.019, H66.40-H66.43, H66.90-H66.93
Acute sinusitis	461.0-461.9	J01.00-J01.91
Group A streptococcal pharyngitis	034.0, 462, 463	J02.0-J02.9, J03.00-J03.91

eTable 2. Appropriate antibiotics with classification for treatment of acute respiratory tract infections

Diagnosis	Narrow spectrum antibiotics	Broad spectrum antibiotics
Acute otitis media	Amoxicillin	Amoxicillin-Clavulanate Azithromycin Cefdinir Cefprozil Cefuroxime Axetil
Acute sinusitis	Amoxicillin	Amoxicillin-Clavulanate Azithromycin Cefdinir Cefprozil Cefuroxime Axetil
Group A streptococcal pharyngitis	Penicillin Amoxicillin	Amoxicillin-Clavulanate Azithromycin Cefadroxil Cefdinir Cefprozil Cefuroxime Axetil Cephalexin

eTable 3. Assessment of balance after full matching for clinical outcomes (n=30 086)

		Acute otitis media			Acute sinusitis			Pharyngitis		
		Spectrum			Spectrum			Spectrum		
		Narrow	Broad	Std. Diff	Narrow	Broad	Std. Diff	Narrow	Broad	Std. Diff
Characteristic		n=16437	n=2688		n=3400	n=825		n=5953	n=783	
Age (years, weighted mean)		3.48	3.56	-0.028	6.08	6.41	-0.095	7.6	7.53	0.03
Male		53.2%	53.2%	0.00	52.2%	53.9%	-0.04	49.2%	49.2%	0.00
Race/ethnicity										
	Latino/Hispanic	8.4%	8.6%	-0.01	6.1%	4.6%	0.07	6.2%	5.8%	0.02
	White	61.2%	62.3%	-0.02	67.0%	71.7%	-0.10	65.7%	66.9%	-0.03
	Black	13.2%	11.9%	0.04	9.7%	6.9%	0.10	13.2%	11.3%	0.06
	Other and mixed race	17.3%	17.2%	0.00	17.2%	16.8%	0.01	14.9%	16.0%	-0.03
Public insurance		27.5%	27.5%	0.00	21.5%	18.3%	0.08	24.3%	26.1%	-0.04
Season										
	Winter	40.8%	40.4%	0.01	38.3%	38.6%	-0.01	31.5%	31.5%	0.00
	Spring	25.2%	25.6%	-0.01	18.6%	19.8%	-0.03	34.1%	32.9%	0.02
	Summer	12.9%	12.8%	0.00	13.0%	13.7%	-0.02	15.5%	15.3%	0.00
	Fall	21.0%	21.2%	-0.01	30.1%	28.0%	0.05	18.9%	20.2%	-0.03
Visited urban-teaching practice		89.5%	89.0%	0.02	97.2%	96.9%	0.02	84.1%	84.1%	0.00
Clinician Category										
	Physician with <10 yrs experience	15.0%	15.2%	0.00	10.7%	11.5%	-0.02	16.9%	17.3%	-0.01
	Physician with ≥10 yrs experience	68.0%	67.6%	0.01	78.0%	77.4%	0.02	64.6%	64.0%	0.01
	Nurse	17.0%	17.3%	-0.01	11.3%	11.1%	0.00	18.5%	18.7%	0.00
Prescribed antibiotic ear drops		3.7%	3.7%	0.00						

Note: Numbers are weighted percentages except where otherwise noted. Std diff = standardized difference. Pharyngitis was exactly matched on practice type; AOM was stratified by sex and insurance due to sample size

eTable 4. Odds ratios for clinical outcomes

Outcome	Stratified analysis ^a			Full matched analysis ^b		
	n	OR (95% CI)		n	OR (95% CI)	
Treatment failure, 14 days	22,900	1.02	(0.84, 1.22)	30,086	1.09	(0.90, 1.32)
Treatment failure, 30 days	27,305	1.04	(0.92, 1.18)	30,086	1.08	(0.95, 1.22)
Adverse events, 14 days	23,375	1.36	(1.13, 1.63)	30,086	1.42	(1.17, 1.72)
Adverse events, 30 days	24,333	1.34	(1.14, 1.58)	30,086	1.39	(1.17, 1.66)

Abbreviations: CI, confidence interval; OR, odds ratio

Note: An odds ratio more than 1.0 means that the broad-spectrum antibiotics had a higher risk of the adverse outcome than the narrow-spectrum antibiotics.

^aEstimated using conditional logistic regression, conditioning on the diagnosis clinician strata; analysis dropped patients if a strata did not contain both outcomes (i.e. for these dichotomous outcomes, the strata had to include patients who had the event and patients who did not have the event).

^bIn the full matched analysis, children prescribed narrow-spectrum antibiotics were optimally matched to children prescribed broad-spectrum antibiotics based on a propensity score estimated from patient-level and clinical-level characteristics creating matched sets of difference sizes using all children. Odds ratios were estimated using weighted logistic regression.

eTable 5. Clinical outcomes, results stratified by diagnosis

Day 14 outcomes	Diagnosis	Raw, n (%)		Stratified analysis ^a		Matched analysis ^b	
		Broad	Narrow	Risk difference, % (95% CI) ^a		Risk difference, % (95% CI) ^c	
Treatment failure	AOM	124 (4.6)	614 (3.7)	0.6	(-0.3, 1.5)	0.8	(-0.2, 1.7)
	Sinusitis	15 (1.8)	51 (1.5)	-0.1	(-1.1, 0.9)	0.5	(-0.6, 1.6)
	Pharyngitis	8 (1.0)	144 (2.4)	-1.7	(-2.5, -0.9)	-1.3	(-2.2, -0.3)
Adverse events	AOM	125 (4.7)	507 (3.1)	1.4	(0.5, 2.2)	1.8	(0.8, 2.7)
	Sinusitis	11 (1.3)	61 (1.8)	-0.4	(-1.3, 0.6)	-0.4	(-1.3, 0.5)
	Pharyngitis	21 (2.7)	127 (2.1)	0.5	(-0.6, 1.7)	0.1	(-1.1, 1.3)

N: AOM 19125 (2688 broad, 16437 narrow), Sinusitis 4225 (825 broad, 3400 narrow), Pharyngitis 6734 (783 broad, 5953 narrow)

Note: Outcomes for clinical outcomes were identified in the electronic health record. Treatment failure was defined as an in-person or telephone encounter with the same ARTI diagnosis and a new systemic antibiotic prescription. Adverse events were encounter for candidiasis, non-candida rash, vomiting, diarrhea, other/unspecified allergic reaction, and other/unspecified adverse event.

^aIn stratified analysis, contrasts were made within diagnosis and clinician strata. Risk differences were estimated using fixed-effects linear regression (first differencing method); diagnosis clinician strata were included as fixed effects

^bIn the full matched analysis, children prescribed narrow-spectrum antibiotics were optimally matched to children prescribed broad-spectrum antibiotics based on a propensity score estimated from patient-level and clinical-level characteristics creating matched sets of difference sizes using all children. Risk differences were estimated using weighted logistic regression with marginal standardization.

eTable 6. Prospective patient-centered cohort: enrolled and eligible population (n=10,296) - patient characteristics of children included in the final cohort compared to children who were not successfully enrolled

	No. (%)			
	In cohort		Not in cohort	
Characteristic	n=2472		n=7824	
Age yrs, mean (standard deviation)	5.0	(3.5)	4.8	(3.5)
Male	1275	(52)	4049	(52)
Race				
White	1437	(58)	4662	(60)
Black	636	(26)	1486	(19)
Asian	66	(3)	336	(4)
Other	38	(2)	140	(2)
Unknown	295	(12)	1200	(15)
Latino				
Yes	125	(5)	576	(7)
No	2344	(95)	7235	(92)
Unknown	3	(0)	13	(0)
Public insurance	800	(32)	2402	(31)
Visited urban-teaching practice	777	(31)	2066	(26)

Note: race and ethnicity were obtained exclusively from the EHR; in the analysis of the enrolled cohort race/ethnicity was derived from both the day 14-20 interview and the EHR

eTable 7. Prospective patient-centered cohort: Comparison of patient characteristics of children who did and did not complete the 14-20 day interview

	No. (%)			
	Completed both interviews		Missed day 14 interview	
Characteristic	n=2096		n=376	
Age yrs, mean (standard deviation)	4.9	(3.5)	5.1	(3.7)
Male	1086	(52)	189	(50)
Race				
White	1200	(57)	237	(63)
Black	567	(27)	69	(18)
Asian	48	(2)	18	(5)
Other	28	(1)	10	(3)
Unknown	253	(12)	42	(11)
Latino				
Yes	107	(5)	18	(5)
No	1988	(95)	356	(95)
Unknown	1	(0)	2	(1)
Public insurance	709	(34)	91	(24)
Visited urban-teaching practice	681	(32)	96	(26)

Note: race and ethnicity were obtained exclusively from the EHR; in the final cohort race/ethnicity was derived from both the day 14-20 interview and the EHR

eTable 8. Assessment of balance after full matching for PedsQL and sleep disturbance (n=2430)

	Acute otitis media			Acute sinusitis			Pharyngitis		
	Spectrum		Std. Diff	Spectrum		Std. Diff	Spectrum		Std. Diff
	Narrow	Broad		Narrow	Broad		Narrow	Broad	
Characteristic	n=688	n=411		n=414	n=244		n=488	n=205	
Age (years, weighted mean)	2.99	3.03	-0.014	5.9	6.11	-0.06	7.06	7.06	0.00
Male	52.9%	54.5%	-0.03	54.0%	53.9%	0.00	48.2%	48.9%	-0.01
Race/ethnicity									
Latino/Hispanic	9.2%	8.9%	0.01	6.5%	6.9%	-0.02	8.6%	10.1%	-0.05
White	52.3%	52.2%	0.00	76.0%	77.5%	-0.04	56.1%	68.6%	-0.26
Black	30.9%	30.8%	0.00	9.4%	8.2%	0.04	28.2%	13.9%	0.36
Other and mixed race	7.6%	8.2%	-0.02	8.1%	7.3%	0.03	7.2%	7.5%	-0.01
Public insurance	39.2%	39.8%	-0.01	18.7%	17.2%	0.04	36.4%	25.8%	0.23
Season									
Winter	21.7%	24.7%	-0.07	23.1%	22.3%	0.02	19.9%	21.7%	-0.05
Spring	34.8%	31.4%	0.07	21.6%	21.4%	0.00	40.2%	39.2%	0.02
Summer	25.9%	26.2%	-0.01	15.4%	17.9%	-0.07	23.5%	19.9%	0.09
Fall	17.6%	17.7%	0.00	40.0%	38.4%	0.03	16.3%	19.1%	-0.07
Symptoms reported present at diagnosis									
0	22.9%	19.5%	0.08	14.8%	17.6%	-0.07	17.6%	16.1%	0.04
1	35.1%	35.2%	0.00	33.9%	31.0%	0.06	28.8%	27.4%	0.03
≥2	41.9%	45.3%	-0.07	51.3%	51.5%	0.00	53.6%	56.5%	-0.06
Visited urban-teaching practice	41.6%	41.2%	0.01	4.9%	6.4%	-0.07	42.2%	26.0%	0.35
Clinician Category									
Physician with <10 yrs experience	19.6%	18.9%	0.02	15.8%	16.8%	-0.03	23.2%	22.1%	0.03
Physician with ≥10 yrs experience	57.5%	56.8%	0.02	71.4%	71.6%	0.00	55.9%	57.4%	-0.03
Nurse practitioner	22.9%	24.3%	-0.03	12.8%	11.6%	0.04	21.0%	20.5%	0.01
Attends school or day care	70.1%	68.9%	0.03	80.0%	79.7%	0.01	87.6%	86.3%	0.04
Prescribed antibiotic ear drops	7.3%	6.7%	0.02						

Note: Numbers are weighted percentages except where otherwise noted. Std diff = standardized difference.

eTable 9. Assessment of balance after full matching for missed school or daycare (n=1901)

	Acute otitis media			Acute sinusitis			Pharyngitis		
	Spectrum		Std. Diff	Spectrum		Std. Diff	Spectrum		Std. Diff
	Narrow	Broad		Narrow	Broad		Narrow	Broad	
Characteristic	n=460	n=306		n=319	n=209		n=420	n=187	
Age (years, weighted mean)	3.37	3.43	-0.019	6.22	6.51	-0.086	7.2	7.26	-0.02
Male	55.1%	56.0%	-0.02	54.8%	53.5%	0.03	48.8%	48.6%	0.00
Race/ethnicity									
Latino/Hispanic	9.3%	7.7%	0.06	7.5%	7.2%	0.01	8.6%	10.0%	-0.05
White	52.3%	52.8%	-0.01	74.4%	78.9%	-0.11	54.5%	67.1%	-0.26
Black	31.3%	30.9%	0.01	10.1%	8.0%	0.07	29.1%	14.8%	0.35
Other and mixed race	7.2%	8.7%	-0.06	8.1%	5.8%	0.09	7.8%	8.1%	-0.01
Public insurance	36.7%	36.7%	0.00	16.1%	16.7%	-0.02	37.1%	28.2%	0.19
Season									
Winter	23.3%	27.8%	-0.10	25.3%	24.5%	0.02	22.0%	24.5%	-0.06
Spring	35.8%	32.8%	0.06	22.7%	22.5%	0.01	44.4%	43.0%	0.03
Summer	22.4%	22.4%	0.00	9.0%	9.5%	-0.02	16.1%	8.9%	0.22
Fall	18.5%	17.0%	0.04	43.0%	43.5%	-0.01	17.5%	23.6%	-0.15
Symptoms reported present at diagnosis									
0	21.0%	19.6%	0.03	15.3%	17.7%	-0.06	18.1%	18.4%	-0.01
1	35.8%	35.6%	0.01	34.0%	32.8%	0.03	28.6%	26.8%	0.04
≥2	43.2%	44.8%	-0.03	50.7%	49.6%	0.02	53.2%	54.9%	-0.03
Visited urban-teaching practice	41.8%	42.6%	-0.02	5.5%	6.7%	-0.05	43.8%	26.7%	0.36
Clinician Category									
Physician with <10 yrs experience	19.1%	19.5%	-0.01	14.2%	15.9%	-0.05	25.5%	23.1%	0.06
Physician with ≥10 yrs experience	59.5%	56.7%	0.06	72.4%	71.6%	0.02	51.8%	55.0%	-0.07
Nurse practitioner	21.4%	23.8%	-0.06	13.3%	12.6%	0.02	22.7%	21.9%	0.02
Prescribed antibiotic ear drops	6.5%	7.0%	-0.02						

Note: Numbers are weighted percentages except where otherwise noted. Std diff = standardized difference.

eTable 10. Assessment of balance after full matching for need additional childcare (n=1891)

	Acute otitis media			Acute sinusitis			Pharyngitis		
	Spectrum		Std. Diff	Spectrum		Std. Diff	Spectrum		Std. Diff
	Narrow	Broad		Narrow	Broad		Narrow	Broad	
Characteristic	n=457	n=305		n=316	n=209		n=417	n=187	
Age (years, weighted mean)	3.48	3.43	0.015	6.27	6.41	-0.04	7.16	7.29	-0.06
Male	54.1%	57.2%	-0.06	54.3%	53.0%	0.02	48.7%	47.9%	0.02
Race/ethnicity									
Latino/Hispanic	9.1%	7.7%	0.05	7.4%	7.4%	0.00	8.5%	9.8%	-0.04
White	52.1%	52.3%	0.00	75.4%	78.0%	-0.06	55.6%	67.4%	-0.24
Black	32.0%	30.8%	0.03	9.2%	8.8%	0.02	28.8%	14.9%	0.34
Other and mixed race	6.8%	9.3%	-0.09	8.0%	5.8%	0.09	7.1%	7.9%	-0.03
Public insurance	37.7%	36.3%	0.03	16.1%	15.2%	0.03	37.1%	28.1%	0.19
Season									
Winter	23.1%	27.7%	-0.11	24.3%	26.2%	-0.04	21.2%	24.6%	-0.08
Spring	36.5%	33.0%	0.07	23.9%	21.2%	0.06	45.3%	43.0%	0.05
Summer	22.7%	22.1%	0.01	9.2%	9.1%	0.00	16.1%	8.9%	0.22
Fall	17.7%	17.2%	0.01	42.6%	43.4%	-0.02	17.5%	23.4%	-0.15
Symptoms reported present at diagnosis									
0	20.8%	19.9%	0.03	14.4%	18.0%	-0.10	18.1%	19.2%	-0.03
1	36.9%	34.8%	0.04	34.5%	31.7%	0.06	28.8%	25.4%	0.08
≥2	42.3%	45.3%	-0.06	51.1%	50.3%	0.02	53.1%	55.4%	-0.05
Visited urban-teaching practice	41.6%	42.7%	-0.02	5.5%	6.8%	-0.06	43.5%	26.8%	0.36
Clinician Category									
Physician with <10 yrs experience	18.7%	19.1%	-0.01	14.0%	16.3%	-0.07	25.5%	22.1%	0.08
Physician with ≥10 yrs experience	59.9%	57.5%	0.05	73.3%	72.2%	0.03	52.5%	56.0%	-0.07
Nurse practitioner	21.4%	23.4%	-0.05	12.7%	11.4%	0.04	22.1%	22.0%	0.00
Prescribed antibiotic ear drops	6.6%	6.9%	-0.01						

Note: Numbers are weighted percentages except where otherwise noted. Std diff = standardized difference.

eTable 11. Assessment of balance after full matching for patient-reported adverse events (n=2085)

		Acute otitis media			Acute sinusitis			Pharyngitis		
		Spectrum		Std. Diff	Spectrum		Std. Diff	Spectrum		Std. Diff
		Narrow	Broad		Narrow	Broad		Narrow	Broad	
Characteristic		n=582	n=340		n=353	n=211		n=425	n=174	
Age (years, weighted mean)		2.96	3.05	-0.032	5.88	6.11	-0.065	6.97	7.05	-0.04
Male		52.4%	51.7%	0.01	52.9%	55.4%	-0.05	50.2%	49.4%	0.02
Race/ethnicity										
	Latino/Hispanic	10.3%	9.8%	0.02	6.9%	7.7%	-0.03	9.5%	9.7%	-0.01
	White	48.8%	52.0%	-0.07	76.0%	76.3%	-0.01	53.7%	67.5%	-0.28
	Black	32.6%	29.8%	0.06	9.6%	9.3%	0.01	29.3%	14.0%	0.38
	Other and mixed race	8.4%	8.5%	0.00	7.5%	6.7%	0.03	7.5%	8.8%	-0.05
Public insurance		41.1%	39.9%	0.03	18.9%	19.1%	-0.01	39.1%	27.2%	0.26
Season										
	Winter	22.5%	25.6%	-0.07	22.5%	22.4%	0.00	19.7%	23.3%	-0.09
	Spring	34.3%	30.0%	0.09	21.2%	21.4%	-0.01	41.9%	39.2%	0.06
	Summer	25.4%	26.4%	-0.02	15.5%	17.0%	-0.04	22.2%	20.0%	0.05
	Fall	17.8%	17.9%	0.00	40.8%	39.1%	0.04	16.1%	17.5%	-0.04
Symptoms reported present at diagnosis										
	0	23.5%	20.1%	0.08	13.5%	15.8%	-0.07	19.2%	16.5%	0.07
	1	34.5%	36.0%	-0.03	31.2%	29.9%	0.03	27.9%	26.7%	0.03
	≥2	42.0%	43.8%	-0.04	55.4%	54.2%	0.02	52.9%	56.8%	-0.08
Visited urban-teaching practice		43.2%	41.0%	0.05	5.5%	6.9%	-0.06	43.1%	28.0%	0.32
Clinician Category										
	Physician with <10 yrs experience	19.6%	18.5%	0.03	15.5%	15.0%	0.02	24.2%	22.3%	0.05
	Physician with ≥10 yrs experience	57.3%	55.8%	0.03	72.4%	72.2%	0.00	54.7%	56.8%	-0.04
	Nurse practitioner	23.1%	25.8%	-0.06	12.2%	12.8%	-0.02	21.1%	20.9%	0.00
Attends school or day care		71.7%	71.6%	0.00	78.5%	78.9%	-0.01	88.9%	86.2%	0.08
Prescribed antibiotic ear drops		6.9%	6.6%	0.01						

Note: Numbers are weighted percentages except where otherwise noted. Std diff = standardized difference.

eTable 12. Assessment of balance after full matching for persistent symptoms at day 3 (n=1775)

	Acute otitis media			Acute sinusitis			Pharyngitis		
	Spectrum		Std. Diff	Spectrum		Std. Diff	Spectrum		Std. Diff
	Narrow	Broad		Narrow	Broad		Narrow	Broad	
Characteristic	n=504	n=329		n=232	n=144		n=392	n=174	
Age (years, weighted mean)	2.95	3.03	-0.028	6.21	6.72	-0.141	7.19	7.14	0.02
Male	52.2%	53.0%	-0.02	55.9%	54.6%	0.03	49.3%	51.8%	-0.05
Race/ethnicity									
Latino/Hispanic	8.5%	8.1%	0.02	4.8%	4.7%	0.01	8.4%	7.8%	0.02
White	53.8%	54.3%	-0.01	79.5%	82.0%	-0.06	58.9%	71.5%	-0.27
Black	30.3%	29.8%	0.01	7.6%	6.1%	0.06	26.0%	14.1%	0.30
Other and mixed race	7.4%	7.9%	-0.02	8.0%	7.2%	0.03	6.7%	6.6%	0.00
Public insurance	37.4%	38.9%	-0.03	19.7%	17.7%	0.05	33.4%	25.2%	0.18
Season									
Winter	21.3%	24.9%	-0.09	23.1%	22.5%	0.01	21.5%	21.6%	0.00
Spring	34.2%	34.9%	-0.01	21.7%	19.6%	0.05	39.5%	36.7%	0.06
Summer	26.5%	25.6%	0.02	15.8%	17.6%	-0.05	24.4%	24.4%	0.00
Fall	18.0%	14.6%	0.09	39.4%	40.3%	-0.02	14.6%	17.3%	-0.07
Symptoms reported present at diagnosis									
1	45.5%	43.6%	0.04	10.6%	11.9%	-0.04	35.4%	29.8%	0.12
≥2	54.5%	56.4%	-0.04	89.4%	88.1%	0.04	64.6%	70.2%	-0.12
Visited urban-teaching practice	40.6%	41.2%	-0.01	3.4%	3.5%	-0.01	40.3%	24.4%	0.35
Clinician Category									
Physician with <10 yrs experience	18.9%	19.2%	-0.01	16.5%	18.7%	-0.06	21.3%	22.7%	-0.04
Physician with ≥10 yrs experience	57.7%	57.5%	0.00	72.2%	70.5%	0.04	56.8%	58.0%	-0.02
Nurse practitioner	23.4%	23.3%	0.00	11.3%	10.8%	0.02	21.9%	19.3%	0.06
Attends school or day care	71.8%	72.7%	-0.02	80.2%	78.3%	0.05	87.7%	83.3%	0.13
Prescribed antibiotic ear drops	5.6%	6.0%	-0.02						

Note: Numbers are weighted percentages except where otherwise noted. Std diff = standardized difference.

eTable 13. Odds ratios for binary patient-centered outcomes

Outcome	Stratified analysis ^a			Full matched analysis ^b		
	n	OR (95% CI)		n	OR (95% CI)	
Missed school or daycare	1418	1.12	(0.84, 1.49)	1901	1.11	(0.87, 1.41)
Required additional childcare	1376	0.99	(0.76, 1.29)	1891	1.07	(0.83, 1.38)
Experienced adverse events	1521	1.75	(1.34, 2.29)	2085	1.82	(1.44, 2.32)
Symptoms present on day 3	1325	1.10	(0.83, 1.47)	1775	1.24	(0.96, 1.59)
Sleep disturbance	1935	1.21	(0.97, 1.52)	2430	1.22	(0.99, 1.52)

Abbreviations: CI, confidence interval; OR, odds ratio

Note: An odds ratio more than 1.0 means that the broad-spectrum antibiotics had a higher risk of the adverse outcome than the narrow-spectrum antibiotics.

^aEstimated using conditional logistic regression, conditioning on the diagnosis clinician strata; analysis dropped patients if a strata did not contain both outcomes (i.e. for these dichotomous outcomes, the strata had to include patients who had the event and patients who did not have the event).

^bIn the full matched analysis, children prescribed narrow-spectrum antibiotics were optimally matched to children prescribed broad-spectrum antibiotics based on a propensity score estimated from patient-level and clinical-level characteristics creating matched sets of difference sizes using all children. Odds ratios were estimated using weighted logistic regression.

eTable 14. Patient-reported outcomes, results stratified by diagnosis

There was limited difference in adverse events by antibiotic spectrum for children diagnosed with sinusitis. After observing this limited difference, we implemented a pooled full-matched analysis with an interaction between exposure and diagnosis. The Wald test of the interaction (two terms) was not significant ($p=0.07$).

Outcome	Raw				Full matched analysis	
	Broad		Narrow		Score or Risk difference (95% CI)	
	<i>n</i>	No. (%)	<i>n</i>	No. (%)		
Acute otitis media						
PedsQL, mean (SD)	411	89.0 (10.6)	668	90.2 (10.1)	-1.4	(-3.0, 0.2)
Sleep disturbance	411	211 (51%)	668	300 (45%)	3.6	(-3.6, 10.8)
Missed school or daycare	306	113 (37%)	460	161 (35%)	2.4	(-6.1, 10.9)
Required additional childcare	305	98 (32%)	457	157 (34%)	3.6	(-4.7, 12.0)
Experienced side effects	340	151 (45%)	582	187 (32%)	17.2	(9.3, 25.2)
Symptoms present on day 3 ^a	329	152 (47%)	504	204 (41%)	7.7	(-0.8, 16.3)
Acute sinusitis						
PedsQL, mean (SD)	244	90.9 (10.2)	414	92.4 (8.6)	-2.1	(-4.2, -0.1)
Sleep disturbance	244	107 (44%)	414	155 (37%)	6.4	(-3.9, 16.7)
Missed school or daycare	209	74 (36%)	319	89 (28%)	3.9	(-6.1, 14.0)
Required additional childcare	209	52 (25%)	316	80 (26%)	-0.5	(-9.5, 8.4)
Experienced side effects	211	49 (23%)	353	78 (22%)	1.9	(-6.3, 10.1)
Symptoms present on day 3 ^a	144	72 (51%)	232	113 (49%)	4.5	(-8.9, 17.8)
Group A Streptococcal pharyngitis						
PedsQL, mean (SD)	205	91.8 (10.5)	488	92.6 (8.8)	-0.5	(-2.3, 1.2)
Sleep disturbance	205	59 (29%)	488	125 (26%)	4.2	(-4.8, 13.2)
Missed school or daycare	187	117 (63%)	420	251 (60%)	1.0	(-9.2, 11.2)
Required additional childcare	187	69 (37%)	417	151 (36%)	0.5	(-10.1, 11.1)
Experienced side effects	174	30 (17%)	425	74 (17%)	14.3	(5.0, 23.6)
Symptoms present on day 3 ^a	174	48 (28%)	392	108 (28%)	1.0	(-8.5, 10.4)

Abbreviations: CI, confidence interval

Note: PedsQL ranges from 0-100 and a higher score indicates a higher health related quality of life. For PedsQL, a score difference less than 0 means that broad-spectrum antibiotics had a lower health-related quality of life score than narrow-spectrum antibiotics. For the other outcomes, a risk difference more than 0 means that the broad-spectrum antibiotics had a higher risk of the adverse outcome than the narrow-spectrum antibiotics.

In the full matched analysis, children prescribed narrow-spectrum antibiotics were optimally matched to children prescribed broad-spectrum antibiotics based on a propensity score estimated from patient-level and clinical-level characteristics creating matched sets of difference sizes using all children. Risk differences were estimated using weighted logistic regression with marginal standardization.

^a3 days after diagnosis

eText

Description of patient-centered outcomes

Each patient-centered outcome was assessed one time. Adverse events were assessed at the 2nd interview (14-20 days); the other outcomes were assessed at the first interview (5-10 days).

PedsQL Total Score

PedsQL Parent-Proxy Report Generic Core Scales (age categories: 2-4y, 5-7, 8-12) and Parent Report Infant Scales (age categories: 1-12mos, 13-24) were completed once during the interview conducted 5-10 days after diagnosis and we used the Total Scale Score, a summary score of the 23-item questionnaire. The score can range from zero to 100. Higher scores indicate better health-related quality of life.

Sleep

The PedsQL questionnaire includes one or two questions, depending on age, about sleep. For children <24 months, parents are asked the frequency (never, almost never, sometimes, often, almost always) their child has (1) “difficulty falling asleep” and (2) “difficulty sleeping through the night.” For children ≥2 years, parents are asked the frequency their child has “trouble sleeping.” We categorized children as either without sleep disturbance (“Never” for each sleep question) or with sleep disturbance.

Missed school/daycare and Need for additional childcare

Missed school or daycare and the need for additional childcare (primary or secondary caretaker missed work or daily obligation and/or caretaker had to arrange for additional childcare) was assessed among children who attend school or daycare.

Text from interview guide

Does your child attend school or daycare? Y/N

IF YES:

1. Since your child’s doctor visit on [DAY, DATE], did your child miss any school or daycare because of their [NAME OF INFECTION] (Y/N)?
2. If yes, how much school or daycare was missed?

Since your child’s doctor visit on [DAY, DATE], did you miss any work or another daily obligation (school or other responsibility) because of your child’s [NAME OF INFECTION]?

1. If yes, how much work or other daily obligations were missed?

Is there anyone else in your family or another caregiver that takes care of your child?

1. If yes, did that person miss any work or other daily obligations (school or other responsibility) because of your child’s infection?
2. If yes, how much work or the other daily obligations were missed?

Did you have to arrange for additional childcare (above and beyond what you normally do) because of your child’s infection?

1. If yes, how much additional childcare did you need to arrange?

Adverse events

Adverse events assessed were diarrhea, rash, upset stomach or vomiting.

Text from interview guide

After taking the antibiotic, did your child experience any of the following symptoms?

1. Diarrhea Y/N
 - a. How many bowel movements they had per day
 - b. How many days?
 - c. Did your child need medication attention for the diarrhea?
2. Rash Y/N
 - a. If yes, was the rash in one spot or all over the body?
 - b. If yes, was the rash itchy?
 - c. Did your child need medical attention for the rash?
3. Upset stomach or vomiting Y/N
 - a. If yes, can you estimate how many episodes of vomiting they had per day
 - b. for how many days?
 - c. Did your child need medical attention for the vomiting?

Persistent symptoms

For assessment of persistent symptoms, parents were asked about the presence diagnosis-specific symptoms at diagnosis (AOM: fever, ear pain, decreased appetite; acute sinusitis: fever, face or head pain, runny nose, decreased appetite; Group A streptococcal pharyngitis: throat pain, fever, decreased appetite). If the parent reported the symptom was present at diagnosis, they were asked if and when the symptom resolved. For the outcome of persistent symptoms, we did not include runny nose for acute sinusitis because it is not likely to resolve in 3 days. For this outcome, we excluded children if the parent did not recall these symptoms at diagnosis.

Text from interview guide

Starting from when your child went to the doctor on [DATE OF VISIT] and got [ANTIBIOTIC NAME] for their [NAME OF INFECTION], did your child have any of the following symptoms? [ASK BASED ON CHILD'S DIAGNOSIS]

4. Strep Throat
 - a. Throat pain
 - i. Did your child's throat pain go away?
 - ii. When or what did you child's throat pain stop?
 - b. Fever
 - i. Did your child's fever go away?
 - ii. When or what day did your child's fever stop?
 - c. Decreased appetite (eating less, drinking less than usual)
 - i. Did your child's appetite return to normal?
 - ii. When or what day did your child's appetite return?
5. Pneumonia
 - a. Fever
 - i. Did your child's fever go away?
 - ii. When or what day did your child's fever stop?
 - b. Cough

- i. Did your child's cough go away?
 - ii. When or what day did your child's cough stop?
 - c. Difficulty Breathing
 - i. Did your child's difficulty breathing go away?
 - ii. When or what day did your child's difficulty breathing stop?
 - d. Decreased appetite (eating less, drinking less than usual)
 - i. Did your child's appetite return to normal?
 - ii. When or what day did your child's appetite return?
- 6. Sinusitis
 - a. Fever
 - i. Did your child's fever go away?
 - ii. When or what day did your child's fever stop?
 - b. Face or head pain
 - i. Did your child's face or head pain stop?
 - ii. When or what day did your child's face pain stop?
 - c. Runny nose
 - i. Did your child's runny nose stop?
 - ii. When or what day did your child's runny nose stop?
 - d. Decreased appetite (eating less, drinking less than usual)
 - i. Did your child's appetite return to normal?
 - ii. When or what day did your child's appetite return?
- 7. Ear Infection
 - a. Fever
 - i. Did your child's fever go away?
 - ii. When or what day did your child's fever stop?
 - b. Ear pain
 - i. Did your child's ear pain go away?
 - ii. When or what day did you child's ear pain stop?
 - c. Decreased appetite (eating less, drinking less than usual)
 - i. Did your child's appetite return to normal?
 - ii. When or what day did your child's appetite return?

***A priori* identification of clinician- and patient-level confounding**

Previous research in this primary care network showed that antibiotic choice varied widely by clinician and that the variability could not be fully explained by differences in patient characteristics.¹ Further, outcomes likely vary by clinician through a variety of mechanisms such as the clinician's, communication skills, office setting, and documentation of clinical outcomes in the EHR. Therefore, it was necessary to account for potential confounding by clinician. Second, antibiotic spectrum may also be a product of patient characteristics. For example, in this primary care network, we previously documented variability in antibiotic prescribing by race, even within clinician.² Outcomes are also likely to be associated with these same patient characteristics. Therefore, it was necessary to account for potential confounding by patient characteristics as well.

1. Gerber JS, Prasad PA, Localio AR, et al. Variation in Antibiotic Prescribing Across a Pediatric Primary Care Network. *J Pediatric Infect Dis Soc.* 2015;4(4):297-304.

2. Gerber JS, Prasad PA, Localio AR, et al. Racial differences in antibiotic prescribing by primary care pediatricians. *Pediatrics.* 2013;131(4):677-684.

Patient and clinician characteristics included in propensity-score models

Retrospective cohort for clinical outcomes (EHR data only)

Age (continuous)

Male

Race/ethnicity (Latino/Hispanic, White, Black, Other and mixed race)

Public insurance

Season (Winter, Spring, Summer, Fall)

Visited urban-teaching practice

Clinician Category (Physician w/ <10 yrs experience, Physician w/ ≥10 yrs experience, Nurse)

Prescribed antibiotic ear drops (for AOM only)

Prospective cohort for patient centered outcomes (EHR and interview data)

*Age (continuous)

*Male

Race/ethnicity (Latino/Hispanic, White, Black, Other and mixed race)

*Public insurance

*Season (Winter, Spring, Summer, Fall)

*Visited urban-teaching practice

*Clinician Category (Physician w/ <10 yrs experience, Physician w/ ≥10 yrs experience, Nurse)

Prescribed antibiotic ear drops (for AOM only)

Symptoms reported present at diagnosis (0, 1, >=2)

Attends school/daycare

*Indicates data obtained from EHR only

Missing responses for patient-centered outcomes

One child did not complete enough questions to receive a PedsQL score. Sleep disturbance, assessed in the PedsQL, was also missing for this one child. Missed school/daycare and required additional childcare were assessed among 1901 children who attended school/daycare. Ten children did not fully respond to the questions about additional childcare. Adverse events, elicited in the 2nd interview, were missing for 346 children (343 lost to follow-up and 3 did not fully respond). Persistence of symptoms was assessed in 1783 children who reported at least one symptom and eight did not fully respond to questions about resolution of symptoms.

Sensitivity analysis account missingness for patient-reported adverse events

For the sensitivity analysis to account for missing responses for the adverse events outcome, missingness was accounted for using inverse probability weighting where weights were generated from logistic regression model for whether the adverse events outcome was observed. These weights were combined with the propensity score weights generated as described previously, but for all patients in this analysis as opposed just those with observed outcome. The final weight was used in the response models described previous to estimate the parameter of interest under a missing at random assumption. We observed results similar to the primary analysis: risk difference 12.9, 95% CI 7.7, 18.0.

Sensitivity analysis to assess potential impact of unobserved confounder for PedsQL and clinical analyses

To assess the potential impact of confounding by unobserved factors, we implemented a formal sensitivity analysis as described by Ding and VanderWeele.³ Using the point estimate of 1.4, the estimated superiority of narrow-spectrum over broad-spectrum antibiotics on the PedsQL quality of life scale in the matched analysis, we investigated the degree of confounding necessary to shift this estimate so that broad-spectrum antibiotics would be superior by 4.0 points in the PedsQL score. A superiority of 4.0 points for broad-spectrum antibiotics would correspond to a clinically meaningful degree of superiority. The minimum strength of association of confounder and

outcome and confounder and choice of antibiotics would correspond to a relative risk of 2.7 for both dimensions of confounder association. Because our analysis was matched for observed patient characteristics, this degree of confounding would have to persist after these adjustments. To the extent that these observed covariates reflect or are proxies for an omitted confounders, a relative risk of 2.7 for residual association is rather strong, and suggests that our finding is robust to omitted patient-level confounders, such as severity of illness that would mask superiority of broad-spectrum antibiotics. The degree of confounding necessary to shift the observed estimate so that broad spectrum would be superior by only 1.0 points remains substantial -- a relative risk of confounder-outcome and confounder-antibiotic association of at least 1.8.

Additional evidence against this source of confounding is the substantial variation across physicians in prescribing of broad-spectrum antibiotics, which points to non-patient factors as an important source of variation and confounding.⁴ But our analysis that controlled for physician factors produced even stronger associations in favor of narrow spectrum antibiotics.

We did the same type of sensitivity analyses for unobserved potential confounders for the clinical outcomes, by use of the concept of the “E-value”, and those results appear in the main text along with a second reference to this approach.⁵

3. Ding P, VanderWeele TJ. Sensitivity Analysis Without Assumptions. *Epidemiology*. 2016;27(3):368-377.

4. Gerber JS, Prasad PA, Localio AR, et al. Variation in Antibiotic Prescribing Across a Pediatric Primary Care Network. *J Pediatric Infect Dis Soc*. 2015;4(4):297-304.

5. VanderWeele TJ, Ding P. Sensitivity Analysis in Observational Research: Introducing the E-Value. *Ann Intern Med*. 2017; 167(4):268-74. [PMID: 28693043]

Post-hoc analyses for PedsQL Outcome

Hierarchical model

We fit a 3-level hierarchical model. An important difference from the primary analysis to note: in the propensity score matching approach presented in the paper, matching was done within ARTI diagnosis. For the hierarchical model, we included diagnosis as a factor variable but did not include interaction terms between diagnosis and each covariate. We fit a mixed effects model that included all covariates included in the primary analysis propensity score model as fixed effects, a random intercept for the clinician (n=271), and a random intercept and slope for the practice site (n=27). These random effects will not protect against confounding, although they will address issues of variance. The results of this 3-level model were consistent with the primary analyses presented in the paper (see below). In addition, we found that the likelihood ratio test of the model with 3 random effects compared to the model with only covariates, was not significant (p=0.99), a result that suggests that variance is not an issue in these data.

N=2,430

Score difference (95% CI): -0.93 (-1.77, -0.09)

P=0.030

Exact matching on baseline symptom count category

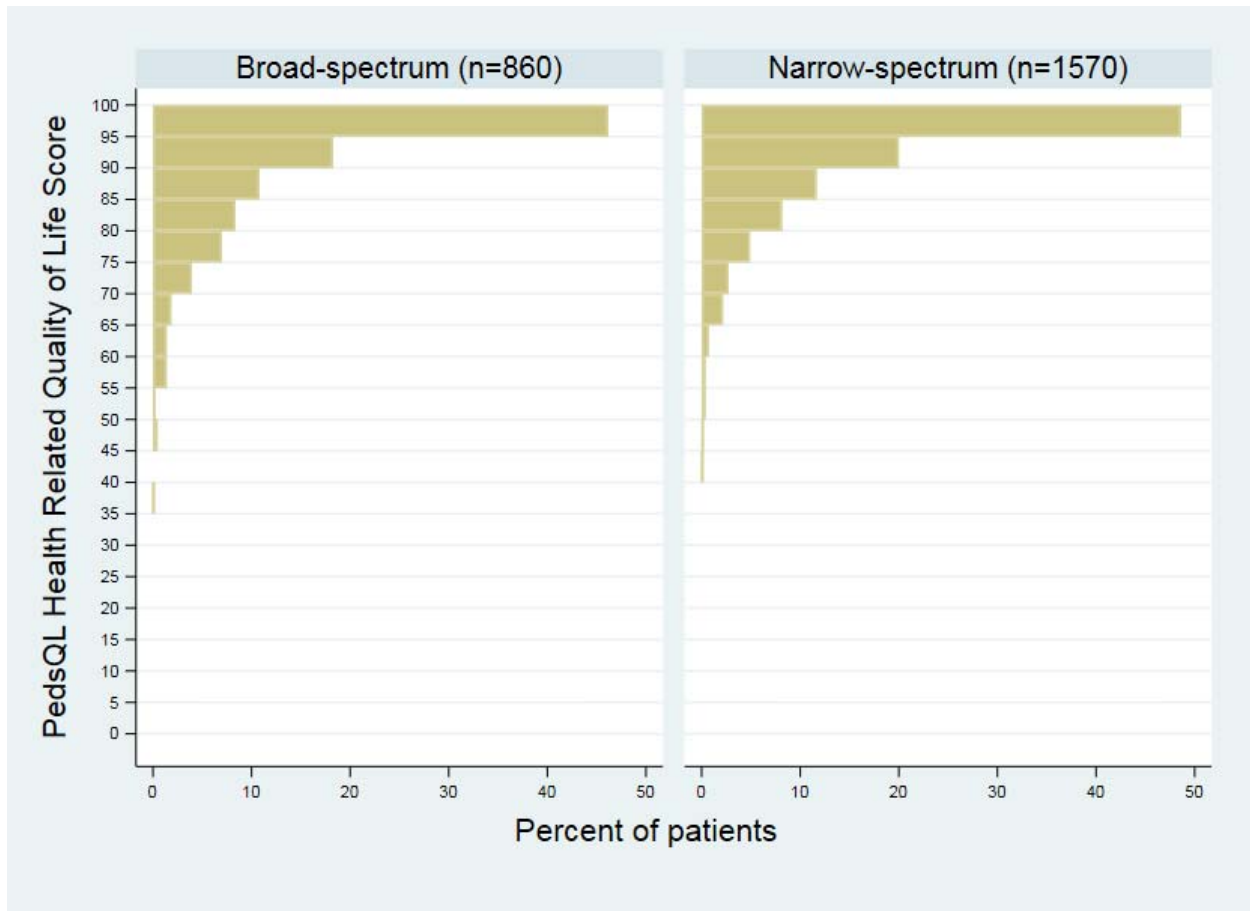
We repeated our propensity score based full matching stratified on diagnosis. In this iteration, we also exactly matched on the symptom count category (0, 1, >2). After matching, we repeated the analysis including everyone (to confirm primary analysis results) and then implemented a response model only including children with at least one parent-reported symptoms and another response model only including children with 2 or more parent-reported symptoms.

Results after full matching with exact match on symptom category

Population	Score difference	95% CI
All children (n=2430)	-1.06	-2.03, -0.09
>0 symptoms (n=1961)	-1.01	-2.13, 0.12
>1 symptoms (n=1162)	-0.54	-2.12, 1.03

Directionally, results of these subset analyses were consistent with the primary analysis, though they are not statistically significant. It is not clear if this is because of loss of power or whether restricting to those children with parent-reported symptoms has reduced a ceiling effect. The magnitude of the score difference is also reduced in the analysis restricted to children with more than 1 symptom reported. These results support the original conclusions that broad-spectrum antibiotics are not better than narrow-spectrum antibiotics for this patient-centered outcome.

eFigure 1. Histogram of PedsQL health related quality of life score (n=2430)



Note: Values in each PedsQL bin are \geq lower limit and $<$ upper limit starting at 0. Each bin is 5 points. PedsQL ranges from 0-100 and a higher score indicates a higher health related quality of life. 18.8% of respondents (16.7% broad and 19.9% narrow) had a score of 100.