Identifying Children Likely to Benefit From Antibiotics for Acute Sinusitis

A Randomized Clinical Trial

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Introduction :

* Acute sinusitis is one of the most common indications for antibiotic use in children.

* The large overlap between symptoms of acute sinusitis and viral upper respiratory tract infection suggests that certain subgroups of children being diagnosed with acute sinusitis, and subsequently treated with antibiotics, derive little benefit from antibiotic use.

Objective :

To assess if antibiotic therapy could be appropriately withheld in prespecified subgroups by comparing treatment with amoxicillin and clavulanate potassium vs matching placebo in children aged 2 to 11 years meeting clinical criteria for the diagnosis of acute sinusitis.

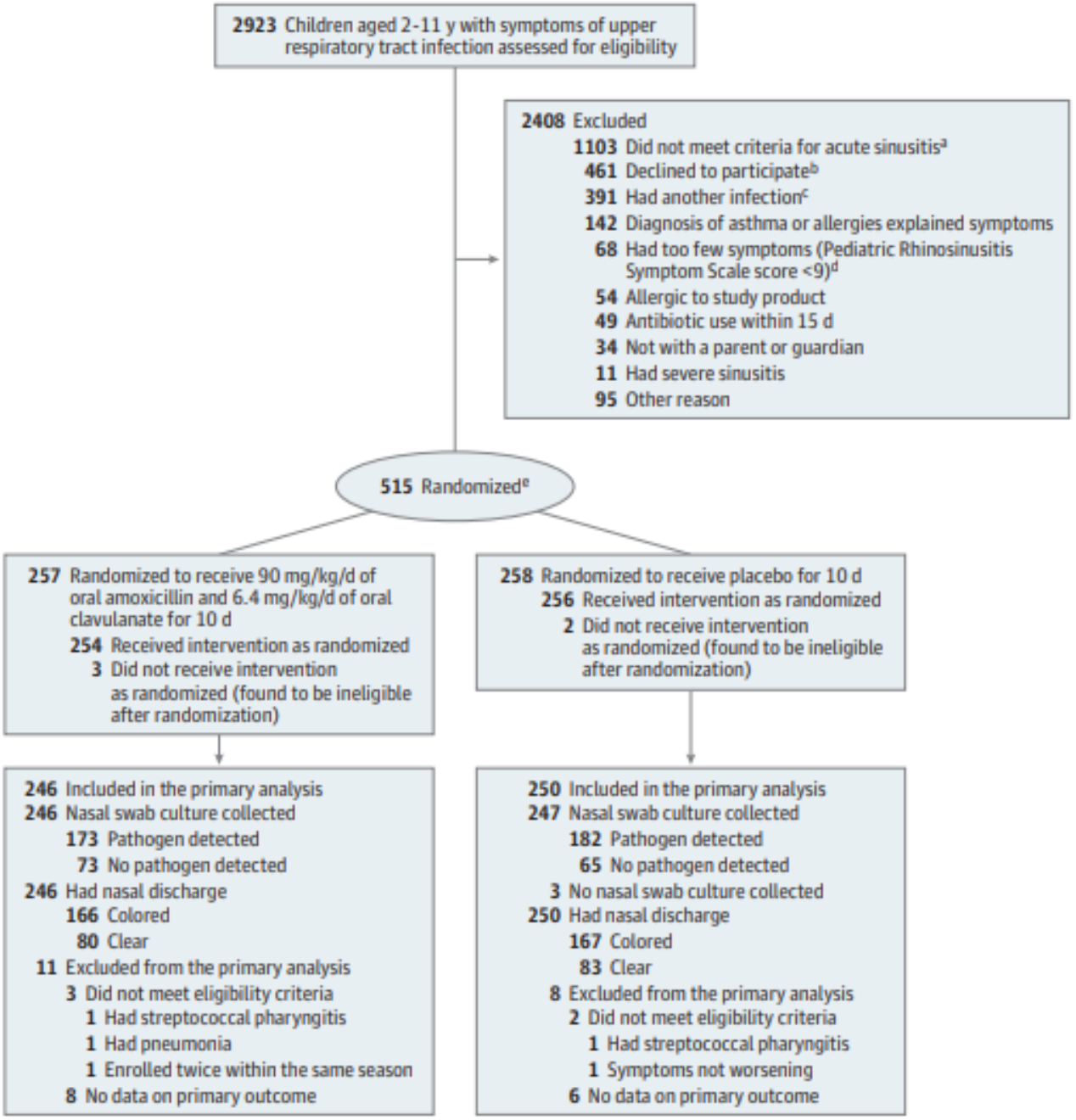
Methods :

* This is a multicenter, double-blind, placebo-controlled Randomized clinical trial which was conducted between February 2016 and April 2022 at primary care offices affiliated with 6 US institutions and was designed to evaluate whether symptom burden differed in subgroups defined by nasopharyngeal Streptococcus pneumoniae, Haemophilus influenzae, or Moraxella catarrhalis on bacterial culture and by the presence of colored nasal discharge.

** This Trial included 515 children aged 2 to 11 years diagnosed with acute sinusitis based on clinical criteria

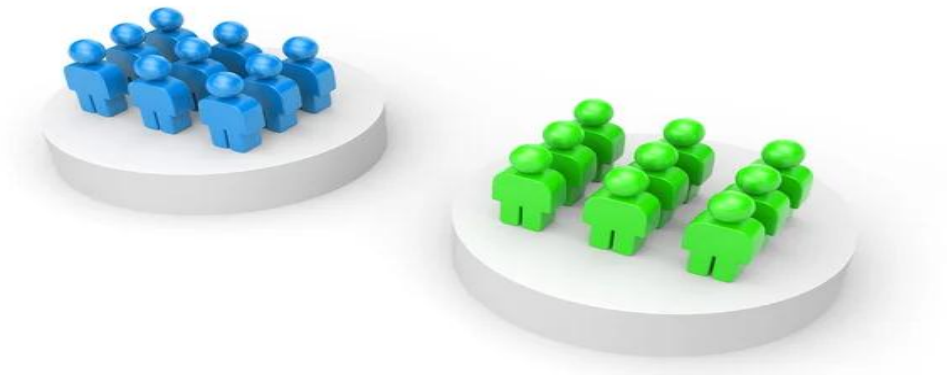
*** An initial score of 9 or greater on the validated Pediatric Rhinosinusitis Symptom Scale (PRSS) was required for inclusion

Figure 1. Enrollment, Randomization, and Follow-Up of Children in a Trial of Antibiotics for Acute Sinusitis



Procedures of The Trial :

* Children were stratified into two groups according to the presence or absence of colored (yellow or green) nasal discharge, in a 1:1 ratio, to receive a 10-day course of either oral amoxicillin (90 mg/kg/d) and clavulanate (6.4 mg/kg/d) (n = 254) or matching placebo (n = 256) .



MAIN OUTCOMES AND MEASURES :

1 / The primary outcome :

was symptom burden based on daily symptom scores on a validated scale **Pediatric Rhinosinusitis Symptom Scale** (PRSS) (ranging from 0 to 40) , completed by parents electronically every evening during the 10 days after diagnosis.

2/ Secondary outcomes : included treatment failure, adverse events including clinically significant diarrhea, generalized rash, and emergence of nonsusceptible S pneumoniae or β-lactamase–positive H influenzae at the time of follow-up and resource use by families

Table 1. Selected Demographic and Clinical Characteristics of Children at Enrollment[a]

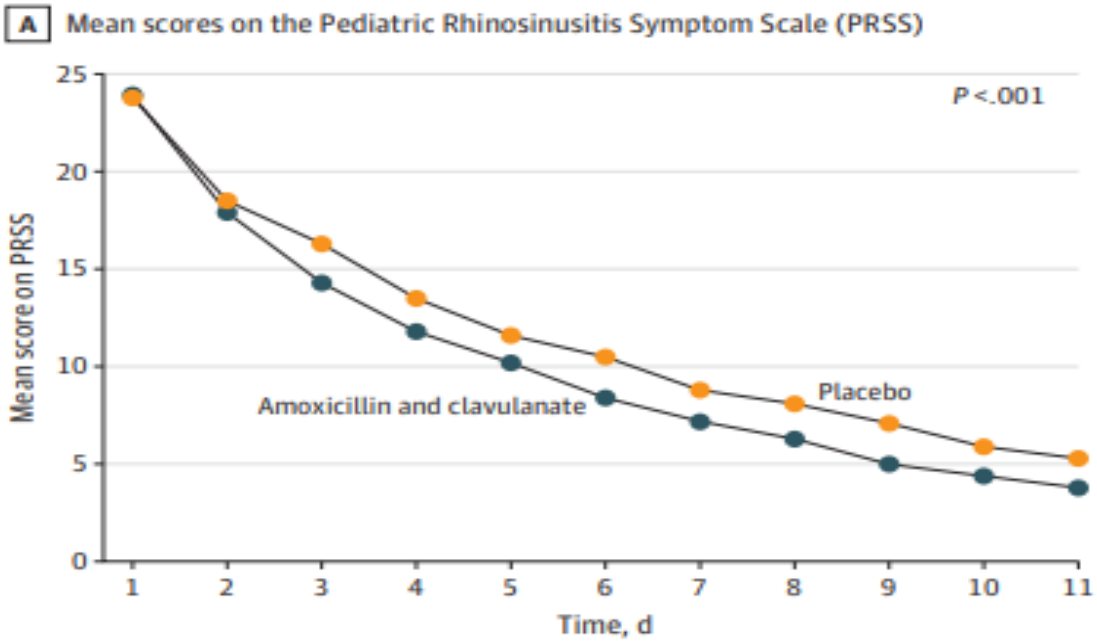
	No. (%)[b]	
	Amoxicillin and clavulanate (n = 254)	Placebo (n = 256)
Age group, y		
2–5	159 (63)	165 (64)
6–12	95 (37)	91 (36)
Age, median (IQR), y	4.9 (3.3–7.3)	5.1 (3.3–7.4)
Sex		
Female	114 (45)	122 (48)
Male	140 (55)	134 (52)
Race[c]		
Asian	5 (2)	5 (2)
Black/African American	91 (36)	88 (34)
More than 1	24 (9)	21 (8)
Native Hawaiian or Other Pacific Islander	1 (<1)	0
Other	5 (2)	6 (2)
White	128 (50)	136 (53)
Ethnicity		
Hispanic or Latino	24 (9)	34 (13)
Not Hispanic or Latino	230 (91)	222 (87)
Primary care office affiliation		
Children's Hospital of Pittsburgh	196 (77)	194 (76)
Kentucky Pediatric and Adult Research	37 (15)	36 (14)
Other[d]	21 (8)	26 (10)
History of allergic rhinitis	78 (31)	80 (31)
History of asthma	46 (18)	48 (19)
Exposure to other children[e]	200 (79)	217 (85)
Fever at any time during the illness	120 (47)	136 (53)
Type of presentation		
Persistent[f]	180 (71)	173 (68)
Worsening[g]	74 (29)	83 (32)
Pediatric Rhinosinusitis Symptom Scale score[h]		
9–15	39 (15)	29 (11)
16–20	43 (17)	49 (19)
21–25	62 (24)	73 (29)
26–30	65 (26)	65 (25)
31–40	45 (18)	40 (16)
Nasal swab culture collected		
Pathogen detected[i]	178 (70)	185 (72)
Streptococcus pneumoniae	66 (26)	77 (30)
Haemophilus influenzae	73 (29)	80 (31)
Moraxella catarrhalis	112 (44)	135 (53)
No pathogen detected	76 (30)	68 (27)
Unknown	0	3 (1)
Colored nasal discharge	171 (67)	169 (66)

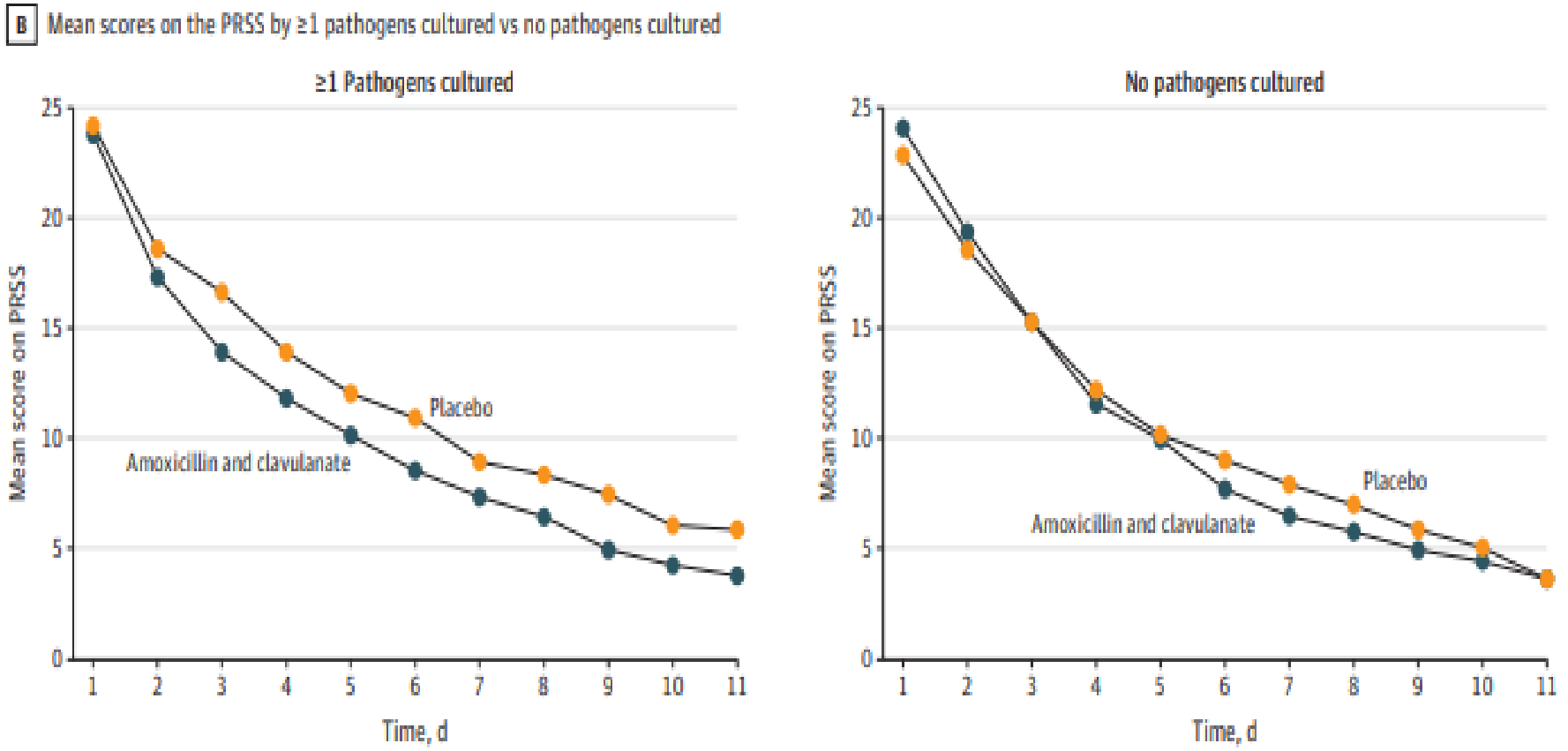
Results :

Most of the 510 included children were aged 2 to 5 years (64%), male (54%), White (52%), and not Hispanic (89%).

A / The mean symptom scores were significantly lower in children in the amoxicillin and clavulanate group (9.04 [95% CI, 8.71 to 9.37]) compared with those in the placebo group (10.60 [95% CI, 10.27 to 10.93]) (between-group difference, −1.69 [95% CI, −2.07 to −1.31]).

Figure 2. Symptom Burden Assessed by Mean Score on the PRSS During the First 10 Days of Follow-Up

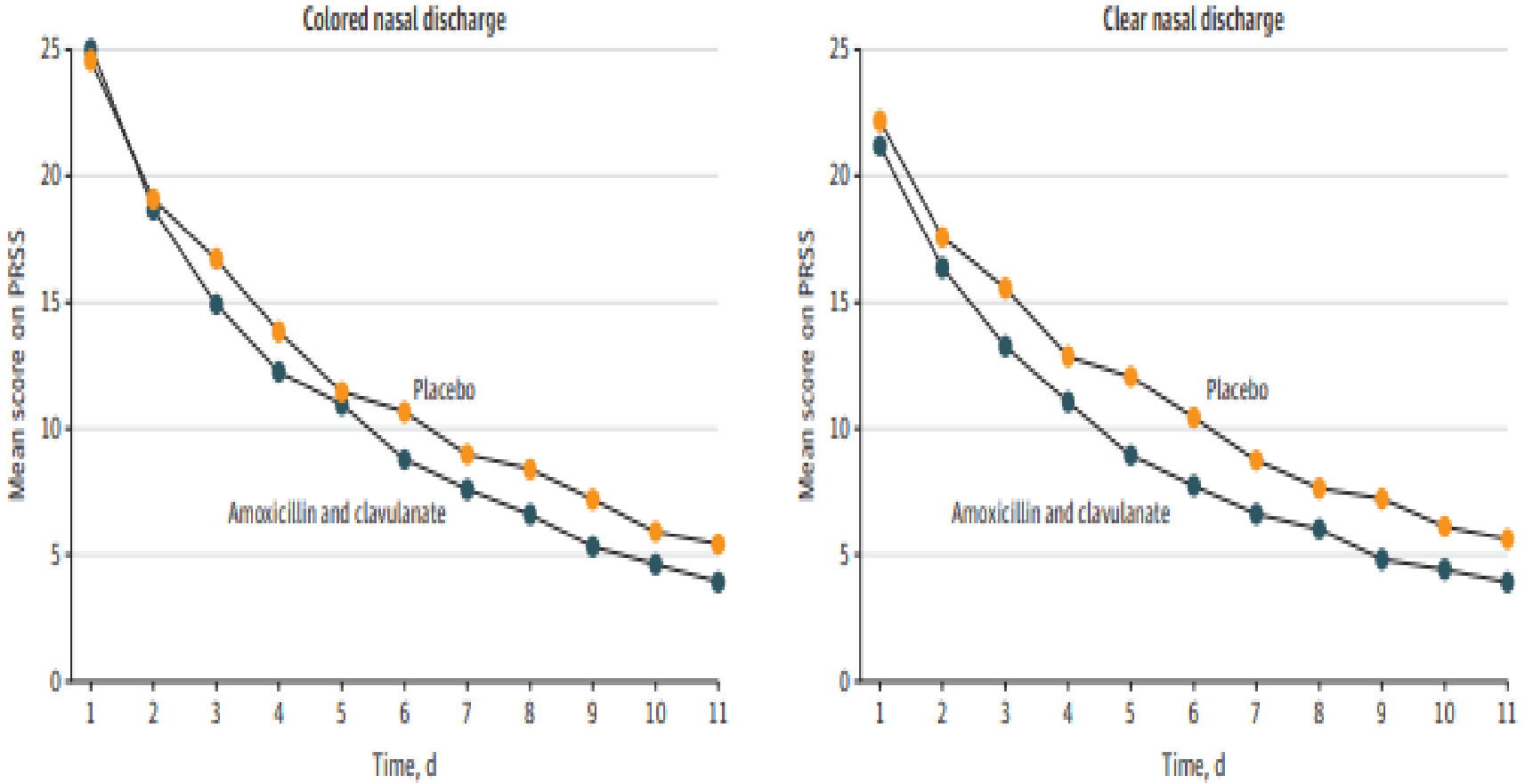




B Children without nasopharyngeal pathogens detected did not benefit from antibiotic treatment as much as those with pathogens detected; the between-group difference in mean symptom scores was −0.88 (95% CI, −1.63 to −0.12) in those without pathogens detected compared with −1.95 (95% CI, −2.40 to −1.51) in those with pathogens detected.

Efficacy did not differ significantly according to whether colored nasal discharge was present (the between-group difference was −1.62 [95% CI, −2.09 to −1.16] for colored nasal discharge vs −1.70 [95% CI, −2.38 to −1.03] for clear nasal discharge; P = .52 for the interaction between treatment group and the presence of colored nasal discharge).

C Mean scores on the PRSS by nasal discharge color



- Compared with children in the placebo group, children in the amoxicillin and clavulanate group were significantly less likely to experience treatment failure, develop acute otitis media, or receive additional systemic antibiotics

- The length of time to symptom resolution was significantly lower for children in the antibiotic group (7.0 days) than in the placebo group (9.0 days) (P = .003)

Table 3. Secondary Outcomes of Efficacy, Safety, and Resource Use Among All Randomized and Eligible Children

Secondary outcomes	No./total (%)		Between-group difference (95% CI)[a]	Risk ratio (95% CI)[a]	*P* value	No. needed to treat or harm (95% CI)[b]
	Amoxicillin and clavulanate	Placebo				
Efficacy						
Treatment failure[c]	76/254 (30)	111/256 (43)	−13.3 (−22.0 to −4.7)	0.69 (0.54 to 0.88)	.003	8 (3 to 13)
Received another antibiotic[d,e]	34/251 (14)	66/256 (26)	−11.8 (−18.8 to −4.7)	0.52 (0.36 to 0.76)	<.001	9 (4 to 13)
Development of acute otitis media[d]	0/251	8/256 (3)	−0.03 (−0.05 to −0.01)[f]	0 (0 to 0.48)[f]	.007[f]	32 (11 to 54)
Safety						
Nonsusceptible pathogen at follow-up[g]	19/148 (13)	18/152 (12)	0.4 (−7.0 to 7.8)	1.16 (0.63 to 2.13)	.63	
Clinically significant diarrhea[h]	29/254 (11)	12/256 (5)	6.3 (0.3 to 12.3)	2.40 (1.26 to 4.59)	.005	16 (5 to 26)
Rash	2/254 (0.8)	1/256 (0.4)	0.5 (−2.8 to 3.9)	2.05 (0.19 to 22.37)	.54	
Resource use[i]						
All reports of work missed	39/248 (16)	41/271 (15)	0.8 (−5.4 to 6.9)	1.03 (0.68 to 1.56)	.89	
All health care visits reported	22/248 (9)	38/271 (14)	−5.2 (−10.6 to 0.2)	0.65 (0.40 to 1.05)	.07	
All reports of extra childcare	10/248 (4)	11/271 (4)	0.2 (−3.2 to 3.6)	0.90 (0.36 to 2.25)	.82	

Limitation :

- The target sample size was not reached because the COVID-19 pandemic disrupted enrollment.
- Changes in the gut microbiome due to antibiotic use were not assessed.
- Children with severe sinusitis were excluded.
- This study used clinical history and nationally accepted standards followed by culture of nasopharyngeal specimens, rather than the gold standard of sinus aspiration, to make the diagnosis of acute sinusitis.

Conclusions :

In children with acute sinusitis, antibiotic treatment had minimal benefit for those without nasopharyngeal bacterial pathogens on presentation, and its effects did not depend on the color of nasal discharge. Testing for specific bacteria on presentation may represent a strategy to reduce antibiotic use in this condition.