

Supplementary Appendix

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

Supplement to: Hoberman A, Paradise JL, Rockette HE, et al. Treatment of acute otitis media in children under 2 years of age. N Engl J Med 2011;364:105-15.

AOM-SOS (Version 3.0)*

We are interested in finding out how your child has been doing. For each question, please place a check mark in the box corresponding to your child's symptoms. Please answer all questions.

	No	A Little	A Lot
Over the past 12 h, has your child been tugging, rubbing, or holding the ear(s) more than usual?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Over the past 12 h, has your child been crying more than usual?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Over the past 12 h, has your child been more irritable or fussy than usual?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Over the past 12 h, has your child been having more difficulty sleeping than usual?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Over the past 12 h, has your child been less playful or active than usual?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Over the past 12 h, has your child been eating less than usual?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Over the past 12 h, has your child been having fever or feeling warm to touch?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

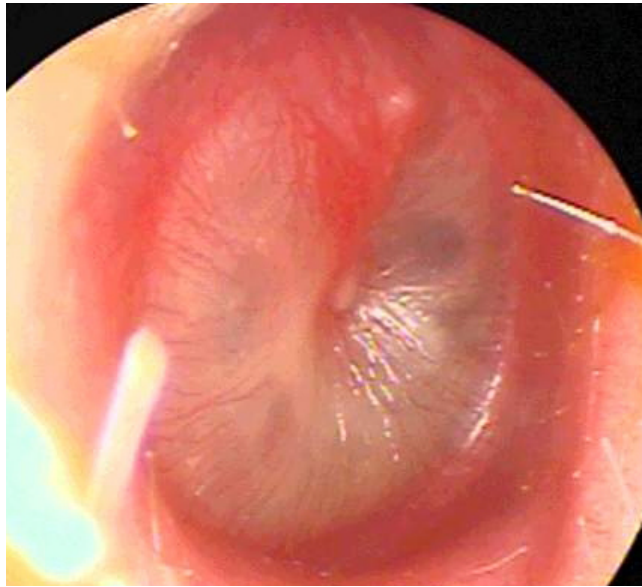
LEGENDS FOR FIGURES

Figure 1. Acute Otitis Media – Severity of Symptoms scale

Figure 2. Slight bulging of the tympanic membrane.

Figure 3. Moderate bulging of the tympanic membrane.

Figure 4. Marked bulging of the tympanic membrane.





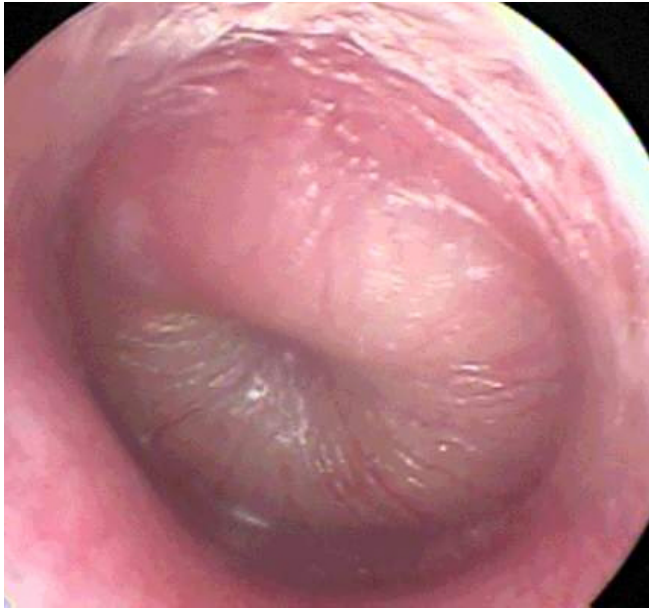


Table 1. Clinical Failure Rates According to Study Group, Age, and Time of Visit.*

Age Group and Time of Visit	Amoxicillin-Clavulanate Group (N = 144)	Placebo Group (N = 147)	P Value
	no. of children experiencing clinical failure / no. of children in age group (%)		
Ages 6 to 11 mo			
At or before Day 4-5	2/83 (2)	20/77 (26)	<0.001
At or before Day 10-12	9/82 (11)	41/76 (54)	<0.001
Ages 12 to 17 mo			
At or before Day 4-5	1/34 (3)	8/41 (20)	0.08
At or before Day 10-12	4/34 (12)	21/40 (52)	<0.001
Ages 18 to 23 mo			
At or before Day 4-5	2/26 (8)	6/27 (22)	0.15
At or before Day 10-12	10/26 (38)	11/27 (41)	0.93
Total (6 to 23 mo)			
At or before Day 4-5	5/143 (3)	34/145 (23)	<0.001
At or before Day 10-12	23/142 (16)	73/143 (51)	<0.001

* Comparisons adjusted for site, history of recurrent AOM and degree of exposure to other children. Data were not available for some children because of missed visits.

Table 2. Clinical Failure Rates at or before the Day 10-12 Visit, According to Study Group and Demographic and Clinical Characteristics at Entry.*

Characteristic	Amoxicillin-Clavulanate Group	Placebo Group	Odds Ratio (95% Confidence Interval)*	P Value
	no. of children experiencing clinical failure / no. of children in category (%)			
Age at Entry, mo				
6-11	9 / 82 (11)	41 / 76 (54)	0.7 (0.3-1.4)	0.32
12-17	4 / 34 (12)	21 / 40 (52)	0.7 (0.3-1.6)	0.39
18-23	10 / 26 (38)	11 / 27 (41)	Reference	
Sex				
Male	16 / 74 (22)	37 / 77 (48)	1.1 (0.7-1.9)	0.64
Female	7 / 68 (10)	36 / 66 (55)	Reference	
Ethnicity				
Hispanic	3 / 21 (14)	8 / 18 (44)	0.8 (0.3-1.7)	0.53
Non-Hispanic	20 / 121 (17)	65 / 125 (52)	Reference	
Race				
Caucasian	13 / 65 (20)	28 / 63 (44)	Reference	
African-American	10 / 61 (16)	30 / 56 (54)	1.1 (0.6-2.0)	0.64
Other	0 / 16 (0)	15 / 24 (62)	1.1 (0.5-2.4)	0.83
Maternal Education				
Less than high school	3 / 24 (12)	7 / 16 (44)	0.5 (0.2-1.4)	0.20
High school graduate	15 / 89 (17)	45 / 92 (49)	0.7 (0.4-1.3)	0.28
College graduate	5 / 29 (17)	21 / 34 (62)	Reference	
Health insurance status				
Private	7 / 42 (17)	19 / 40 (48)	Reference	
Medicaid	16 / 97 (16)	53 / 101 (52)	1.1 (0.6-2.0)	0.68
None	0 / 3 (0)	1 / 2 (50)	0.6 (0.1-6.2)	0.65

Table 2. Continued

Exposure to other children†

No	10 / 73 (14)	29 / 73 (40)	Reference	
Yes	13 / 69 (19)	44 / 70 (63)	2.3 (1.3-4.1)	0.005

History of recurrent acute otitis media‡

No	18 / 121 (15)	57 / 115 (50)	Reference	
Yes	5 / 21 (24)	16 / 28 (57)	1.5 (0.8-2.9)	0.24

Otalgia at entry

No	9 / 38 (24)	19 / 42 (45)	Reference	
Yes	14 / 104 (13)	54 / 101 (53)	1.0 (0.5-1.7)	0.90

Acute Otitis Media-Severity of Symptom score (AOM – SOS) at entry

≤ 8	9 / 82 (11)	35 / 81 (43)	Reference	
> 8	14 / 60 (23)	38 / 62 (61)	2.2 (1.2-4.0)	0.008

Laterality of acute otitis media

Unilateral	6 / 68 (9)	29 / 70 (41)	Reference	
Bilateral	17 / 74 (23)	44 / 73 (60)	2.0 (1.1-3.7)	0.02

Degree of tympanic membrane bulging (worse ear)

Slight or moderate	12 / 103 (12)	46 / 106 (43)	Reference	
Marked	11 / 39 (28)	27 / 137 (20)	2.3 (1.2-4.4)	0.01

* For each characteristic, odds ratio adjusted for treatment; for each statistically significant characteristic (exposure to other children, AOM-SOS score at entry, laterality of AOM, and degree of tympanic membrane bulging), odds ratio adjusted for treatment and the other three significant characteristics.

† Defined as exposed to at least 3 children for at least 10 hours per week

‡ Defined as ≥3 episodes in 6 months or ≥4 episodes in 1 year

Table 3. Distribution of AOM Pathogens in Nasopharyngeal Cultures According to Study Group and Time of Visit.*

	Amoxicillin-Clavulanate Group			Placebo Group		
	Time of Visit					
	Entry (n=139)	Day 10-12 (n=130)	Day 21-25 (n=128)	Entry (n=143)	Day 10-12 (n=131)	Day 21-25 (n=130)
	no. of children (%)					
<i>Streptococcus pneumoniae</i>	73 (53)	18 (14)	26 (20)	67 (47)	46 (35)	42 (32)
Susceptible (<0.1 µg/mL)	50 (36)	1 (1)	7 (5)†	38 (27)	28 (21)	17 (13)‡
Intermediate (0.1–1 µg/mL)	11 (8)	5 (4)	7 (5)	13 (9)	7 (5)	10 (8)
Resistant (>1 µg/mL)	12 (9)	12 (9)	12 (9)	16 (11)	10 (8)	14 (11)
Sensitivity unknown	0	0	0	0	1 (1)	1 (1)
<i>Haemophilus influenzae</i>	47 (34)	45 (35)	38 (30)	47 (33)	44 (34)	38 (29)
β lactamase - positive	17 (12)	21 (16)	15 (12)	14 (10)	11 (8)	11 (8)
β lactamase - negative	30 (22)	24 (18)	23 (18)	33 (23)	33 (25)	27 (21)
<i>Moraxella catarrhalis</i>	51 (37)	9 (7)	29 (23)†	48 (34)	38 (29)	31 (24)§
<i>Streptococcus pyogenes</i>	2 (1)	0	1 (1)	5 (3)	3 (2)	0
No AOM pathogens	16 (12)	67 (52)	52 (41)	24 (17)	43 (33)	41 (32)

* For the respective pathogens, comparisons are within each treatment group and between time of study entry and Day 21-25. Comparisons adjusted for site, history of recurrent AOM and exposure to other children. For children in whom more than one pathogen was isolated, each pathogen is listed.

† $P \leq 0.001$; ‡ $P = 0.02$; § $P = 0.06$