Supplementary Appendix

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

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(PDF updated September 22, 2021)

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Table S1. Two-Year Primary and Secondary Outcomes, According to Treatment Assignment.*

Outcome Measure or Patient Characteristic	Tympanostomy-Tube Group (N=129)	Medical-Management Group (N=121)	All Children (N=250)	Estimated Between-Group Difference (95% CI); P Value†
Two-year occurrence of episodes of acute otitis media				
No. of episodes; no. of child-yr‡	384; 259.5	378; 242.6	762; 502.1	
Yr 1 and 2 combined-rate per child-yr§	1.48 (0.08)	1.56 (0.08)	1.52 (0.08)	0.97 (0.84 to 1.12); P = 0.66
Year 1	1.94±0.12	2.20±0.14	2.07±0.13	
Year 2	1.06±0.09	0.97±0.09	1.01±0.09	
Age at enrollment				
6-11 mo (n=91)	1.87±0.14	2.08±0.15	1.97±0.15	
12-23 mo (n=137)	1.34±0.10	1.34±0.10	1.34±0.10	
24-35 mo (n=22)	0.82±0.18	0.64±0.19	0.73±0.18	
Exposure to other children¶				
Not exposed (n=48)	1.51±0.17	1.53±0.19	1.52±0.18	
Exposed (n=202)	1.47±0.08	1.57±0.09	1.52±0.09	
Otitis media with effusion at randomization				
No (n=156)	1.47±0.09	1.59±0.11	1.53±0.10	
Yes (n=94)	1.49±0.13	1.52±0.12	1.50±0.13	
Estimated risk for recurrences of acute otitis media				
Probably lesser (n=135)‖	1.28±0.10	1.56±0.10	1.42±0.10	
Probably greater (n=115)	1.67±0.11	1.56±0.13	1.62±0.12	
Frequency distribution of episodes of acute otitis media, yr 1 and 2 combined**				
No. of episodes–no. of children/total no. (%)				
0	17/108 (16)	12/100 (12)	29/208 (14)	
1-2	41/108 (38)	41/100 (41)	82/208 (39)	
3-4	24/108 (22)	29/100 (29)	53/208 (26)	
≥5	26/108 (24)	18/100 (18)	44/208 (21)	
Range-no. of episodes	0 - 13	0 - 16	0 - 16	
Principal clinical feature of episodes of acute otitis media				
No. of episodes (%)				
Tympanic membrane bulging	86 (26)	248 (74)	334 (50)	0.34 (0.26 to 0.44)

Otorrhea	250 (74)	85 (26)	335 (50)	
Estimated severity of episodes of acute otitis media††				
No. of episodes (%)				
Probably nonsevere	180/336 (54)	168/333 (50)	348/669 (52)	
Probably severe	156/336 (46)	165/333 (50)	321/669 (48)	0.91 (0.76 to 1.09)
Treatment failure-no.of children/total no. (%) ‡‡				
Had failure	56/124 (45)	74/120 (62)	130/244 (53)	0.73 (0.58 to 0.92)
Did not have failure	68/124 (55)	46/120 (38)	114/244 (47)	
Total days with otitis-related symptoms or signs-no. of days per yr (range)				
Tube otorrhea§§	7.96±1.10 (0 to 81)	2.83±0.78 (0 to 76)	5.44±0.70 (0 to 81)	5.21 (2.60 to 7.82)
Other symptoms of acute otitis media	2.00±0.29 (0 to 17)	8.33±0.59 (0 to 35)	5.11±0.38 (0 to 35)	-6.32 (-7.55 to -5.10)
Total days of antimicrobial treatment-no. of days per yr (range)	8.76±0.94 (0 to 119)	12.92±0.90 (0 to 56)	10.80±0.67 (0 to 119)	-4.50 (-6.82 to -2.18)
Probable side-effects of antimicrobials-No. of children (%); no. of events				
Protocol-defined diarrhea	21 (16); 43	34 (28); 59	55 (22); 102	0.67 (0.44 to 1.03)
Diaper dermatitis	25 (19); 46	33 (27); 56	58 (23); 102	0.79 (0.51 to 1.22)
Child and parent QOL assessments				
Score on the Otitis Media-6 Survey¶¶	1.50±0.03	1.55±0.03	1.52±0.02	-0.05 (-0.13 to 0.02)
Score on the Otitis Media-6 Survey–children's overall QOL‖ ‖	8.45±0.07	8.37±0.07	8.42±0.05	0.06 (-0.13 to 0.24)
Score on the Caregiver Impact Questionnaire***	10.82±0.53	10.93±0.55	10.87±0.38	-0.04 (-1.55 to 1.47)
Score on the Caregiver Impact Questionnaire–caregivers' overall QOL‖ ‖	8.55±0.06	8.50±0.06	8.53±0.04	0.03 (-0.14 to 0.20)
Parental satisfaction with treatment assignment†††	4.64±0.10	4.43±0.13	4.54±0.08	0.25 (-0.06 to 0.56)
Use of medical resources other than trial visits-no. of parent reports/no. of parental questionnaires (%)	738/1635 (45)	672/1628 (41)	1410/3263 (43)	1.07 (0.98 to 1.18)
No. of health care encounters (%)	824 (100)	761 (100)	1585 (100)	
Hospital admission	9 (1)	3 (0)	12 (1)	2.77 (0.73 to 10.52)‡‡‡
Emergency department	123 (15)	97 (13)	220 (14)	1.21 (0.86 to 1.72)
Urgent care	81 (10)	75 (10)	156 (10)	1.01 (0.72 to 1.43)
Primary care provider	468 (57)	469 (62)	937 (59)	0.93 (0.87 to 1.00)
Other§§§	143 (17)	117 (15)	260 (16)	1.15 (0.90 to 1.48)
Use of non-medical resources-no. of reported occurrences/no. of parental questionnaires (%)¶¶¶				
Missed work owing to child's illness	286/1635 (17)	256/1628 (16)	542/3263 (17)	1.11 (0.88 to 1.41)
Special childcare arrangements owing to child's illness	231/1635 (14)	195/1628 (12)	426/3263 (13)	1.15 (0.89 to 1.48)

* Plus-minus values are means ±SE. Three additional secondary outcome measures—the occurrence of otorrhea, protocol-defined diarrhea, and medication-related diaper dermatitis—were also considered to be adverse events. CI denotes confidence interval, and QOL quality of life.

† Estimates for rates and percentages are based on risk ratios; estimates for continuous outcomes are based on least-squares means. Estimates are adjusted for trial site, age at enrollment, and exposure or nonexposure to other children, unless noted otherwise. P-values are provided only for the primary outcome and for the frequency distribution of episodes of acute otitis media. There was no adjustment for multiple comparisons across the secondary outcomes; results are reported with point estimates and 95% confidence intervals; the confidence intervals are not adjusted for multiple comparisons and should not be used to infer definitive treatment effects.

‡ Values for the number of episodes are rounded to the nearest whole number. The measure "child-years" comprises both full-year and fractional-year experiences, the latter a consequence of withdrawal or loss to follow-up of some children. For each child with incomplete 2-year follow up, we imputed the total number of episodes of acute otitis media using multivariate imputation by chained equations with 50 imputations. For the tympanostomy-tube group, 231.1 of the 259.5 child-years (89%) that are listed represented actual experience; corresponding values for the medical management group were 222.6 of 242.6 (92%). Values for the remaining child-years were imputed.

§ This was the primary outcome measure. The values shown reflect multivariate imputation. Before imputation, the values were 1.45±0.08 in the tympanostomy-tube group and 1.50±0.08 in the medical-management group.

¶ Exposure to other children was defined as exposure to at least three children for at least 10 hours per week.

‖ Risk of recurrences of acute otitis media was categorized, with the use of a 16-point scale, as probably lesser (<8 points) or probably greater (≥8 points), on the basis of the following known or presumed risk factors: early age of onset of acute otitis media, numerous or frequent previous episodes of acute otitis media, receipt of multiple courses of antibiotic treatment (suggesting a higher risk of acute otitis media caused by resistant pathogens), eligibility for enrollment first evident during warm-weather months, parental characterization of previous episodes of acute otitis media as severe, eligibility for enrollment despite nonexposure to other young children, extreme tympanic membrane bulging during previous episodes of acute otitis media, most previous episodes of acute otitis media in both ears, and a high score on the Acute Otitis Media Severity of Symptoms scale during screening, at enrollment, or both (details are provided in protocol version 3).

** Analysis (chi-square) was limited to children with at least 23 months of follow-up.

† † The current American Academy of Pediatrics clinical practice guideline regarding the management of acute otitis media refers to children with "severe signs or symptoms" as those with "moderate or severe otalgia or otalgia for at least 48 hours or temperature 39°C (102.2°F) or higher."[1] In an effort to simulate that definition, we used scores on two items of the five-item Acute Otitis Media – Severity of Symptoms (AOM-SOS) scale, version 4.0,[2] in which parents are asked to rate symptoms, as compared with their child's usual state, as "none," "a little," or "a lot," with corresponding scores of 0, 1, and 2. We categorized episodes of acute otitis media as "probably severe" if the parent described the child as having had moderate or severe otalgia ("a lot" of ear tugging; i.e., a score of 2), a temperature 39°C or higher, or an AOM-SOS scale score of more than 6 (range, 0 to 10, with higher scores indicating greater severity of symptoms) on Day 1.[1,3]

‡‡ Protocol criteria for determination of treatment failure are described in protocol version 3. This analysis concerns the 244 children with follow-up of any duration; 6 children were not evaluated beyond the enrollment visit. Of the children who had treatment failure, the failure was attributed to the occurrence of frequent episodes of acute otitis media in all 56 children in the tympanostomy-tube group and in 55 of the 74 children in the medical-management group. Of these 55 children, 35 underwent tympanostomy-tube placement and 20 did not. The mean time from randomization to tympanostomy-tube placement in these 35 children was 5.17 months. In the remaining 19 children, the episode-frequency criterion for treatment failure was not met, but treatment failure was instead ascribed to the children's receipt of tympanostomy-tube placement at parental request. The mean time from randomization to tympanostomy-tube placement in these 19 children was 2.51 months. Seven of these 19 children had had no episodes of acute otitis media after randomization; were these 7 children to be excluded from the analysis, the risk of treatment failure would still be lower in the tympanostomy-tube group than in the medical-management group.

§ Three children in the tympanostomy-tube group and two in the medical-management group received placement of an ear wick in treating refractory tube otorrhea.

¶¶ Otitis Media-6 Survey was scored with the use of an ordinal response scale from 1 (no problem) to 7 (greatest problem).[4]

‖ ‖ Children's and parents' overall quality of life was scored with the use of an ordinal response scale from 0 (worst quality of life) to 10 (best quality of life).

*** Scoring on the Caregiver Impact Questionnaire was expanded to a continuous response scale from 0 (no effect on caregiver) to 100 (greatest effect).[5]

† † † Parental satisfaction with the child's treatment assignment was assessed on a five-point scale, with higher numbers indicating greater satisfaction.

‡‡‡ Unadjusted estimates provided due to sparse data.

§ § Eleven children in the tympanostomy-tube group and two children in the medical-management group underwent a second tympanostomy-tube placement procedure after intervals ranging from 191 to 553 days from the first procedure. Eight children in the tympanostomy-tube group and two children in the medical-management group underwent adenoidectomy with or without tonsillectomy, procedures not contemplated in the study protocol.

¶¶¶ Shown is the number of instances in which parents reported missing work or the need for special childcare arrangements for at least 1 day.

Table S2. Antimicrobial Resistance among Nasopharyngeal or Throat Specimens Collected Under Varying Circumstances from Children, According to Treatment Assignment.*

Measure	Tympanostomy-Tube Group	Medical-Management Group	All Children	Risk Ratio (95% CI)†
	(N=129)	(N=121)	(N=250)	
Children's nasopharyngeal or throat colonization status at enrollment (no. of children)‡	**No. of children with a penicillin-nonsusceptible nasopharyngeal or throat isolate at any follow-up visit/Total no. of children with a nasopharyngeal/throat culture obtained at any follow-up visit (%)§**			
No pathogens (81)	25/37 (68)	24/35 (69)	49/72 (68)	0.96 (0.74-1.24)
Positive only for ≥1 penicillin-susceptible pathogen (69)	22/33 (67)	20/35 (57)	42/68 (62)	1.20 (0.83-1.72)
Positive for ≥1 penicillin-nonsusceptible pathogen (90)	38/43 (88)	34/43 (79)	72/86 (84)	1.10 (0.94-1.29)
Nonsusceptible nasopharyngeal or throat pathogens recovered at acute otitis media visits	**No. of specimens yielding a nonsusceptible pathogen/Total no. of specimens (%)**			
Any nonsusceptible pathogen	66/173 (38)	64/196 (33)	130/369 (35)	1.14 (0.84-1.55)
Nonsusceptible *Streptococcus pneumoniae* only	26/173 (15)	23/196 (12)	49/369 (13)	
β-lactamase positive *Haemophilus influenzae* only	33/173 (19)	34/196 (17)	67/369 (18)	
Nonsusceptible *S. pneumoniae* and β-lactamase positive *H. influenzae*	7/173 (4)	7/196 (4)	14/369 (4)	
Nonsusceptible nasopharyngeal or throat pathogens recovered at routine non-illness visits	**No. of specimens yielding a nonsusceptible pathogen/Total no. of specimens (%)**			
Any nonsusceptible pathogen	116/485 (24)	98/447 (22)	214/932 (23)	1.09 (0.84-1.41)
Nonsusceptible *S. pneumoniae* only	71/485 (15)	54/447 (12)	125/932 (13)	
β-lactamase positive *H. influenzae* only	33/485 (7)	35/447 (8)	68/932 (7)	
Nonsusceptible *S. pneumoniae* and β-lactamase positive *H. influenzae*	12/485 (2)	9/447 (2)	21/932 (2)	
Nonsusceptible nasopharyngeal or throat pathogens recovered at visits for acute otitis media late during respiratory season (Apr-May)	**No. of specimens yielding a nonsusceptible pathogen/Total no. specimens (%)**			
Any nonsusceptible pathogen	16/37 (43)	16/43 (37)	32/80 (40)	1.16 (0.69-1.95)¶
Nonsusceptible *S. pneumoniae* only	5/37 (14)	9/43 (21)	14/80 (18)	
β-lactamase positive *H. influenzae* only	11/37 (30)	5/43 (12)	16/80 (20)	
Nonsusceptible *S. pneumoniae* and β-lactamase positive *H. influenzae*	0/37 (0)	2/43 (5)	2/80 (2)	

Conditional odds ratios‖	**Odds ratio (95% CI)**			
Intermediate or resistant *S. pneumoniae*				
Visit type New acute otitis media episode	0.35 (0.15-0.77)	0.30 (0.13-0.69)	NA	
Routine non-illness	0.45 (0.21-0.94)	0.45 (0.21-0.96)	NA	
Acute otitis media episode during latter part of respiratory season (April-May)	0.35 (0.10-1.31)	0.65 (0.22-1.93)	NA	
β-lactamase positive *H. influenzae*				
Visit type New acute otitis media episode	0.93 (0.49-1.75)	0.75 (0.40-1.39)	NA	
Routine non-illness	0.64 (0.35-1.18)	0.52 (0.29-0.95)	NA	
Acute otitis media episode during latter part of respiratory season (April-May)	1.35 (0.53-3.49)	0.60 (0.21-1.68)	NA	

* Of 1720 specimens obtained, 1539 (89%) were from the nasopharynx and 181 (11%) were from the throat. Throat specimens were obtained mainly from children older than 24 months of age. Pathogens of interest were *S. pneumoniae* and β-lactamase-positive *H. influenzae.*

† Estimates of between-group differences, along with their confidence intervals (CIs) are based on risk ratios. Estimates are adjusted for site, age, and exposure or nonexposure to other children unless noted otherwise.

‡ Analysis restricted to children with at least one follow-up nasopharyngeal or throat culture.

§ The penicillin-nonsusceptible pathogens considered here are penicillin-intermediate and penicillin-resistant *S. pneumoniae* and ß-lactamase-positive *H. influenzae*. Susceptibility to penicillin was defined as follows: susceptible as a minimum inhibitory concentration (MIC) of <0.1 µg/mL; intermediate as an MIC of 0.1 to 1 µg/mL; and resistant as an MIC of >1 µg/mL.

¶ Unadjusted risk ratios provided due to sparse data.

‖ The conditional odds ratio constitutes the odds for a specific treatment group, as compared with the status of that group at randomization, of being colonized at a later time with a nonsusceptible organism conditional on overall carriage of that organism (i.e., both susceptible and nonsusceptible strains) at that time.[6,7] Results are presented without regard to multiple observations in individual children, and are for all visits of a particular type combined.

Statistical Considerations Regarding Missing Data

Our analysis of the intention-to-treat population included all randomized children. Study procedures aimed to minimize missing data. For the primary outcome, we calculated rates by dividing the total number of episodes of acute otitis media by the total number of child-years, including fractions of years for children withdrawn or lost to follow-up, thereby incorporating all available follow-up information. The proportions of children withdrawn or lost to follow-up were closely balanced between the two treatment groups, so we considered withdrawal or loss unlikely to constitute an important confounder. For each child with incomplete 2-year follow up, we imputed the number of episodes of acute otitis media using multivariate imputation via chained equations (MICE) with 50 imputations. Covariates in MICE included season, taken as Oct-Jan, Feb-May, and Jun-Sep; age, as children progressed through the 2-year follow-up period; treatment assignment; and selected demographic and clinical characteristics at enrollment, namely site, sex, race, ethnicity, maternal level of education, type of health insurance, exposure to other children, presence or absence of otitis media with effusion at randomization, and estimated risk for acute otitis media recurrences.

Regarding secondary outcomes, when children had missing data for a variable for which we could assign a dichotomous best- or worst-case outcome, we performed a sensitivity analysis, first assuming that such children had a best-case outcome and then, that such children had a worst-case outcome. There were two groups of such secondary outcomes. The first group of secondary outcomes comprised proportions of children categorized respectively as having experienced treatment failure, protocol-defined diarrhea, or diaper dermatitis occasioning the prescription of antifungal treatment. Regarding each of these outcomes we conducted sensitivity analysis, assuming best-case outcome (no treatment failure, no protocol-defined diarrhea, no diaper dermatitis) and worst-case outcome (treatment failure, protocol-defined diarrhea, diaper dermatitis), and we calculated risk ratios. These sensitivity analyses included children who did not complete follow-up for the full 2 years.

The second group of secondary outcomes comprised non-medical resource use and findings of the OM-6 Survey and of the Caregiver Impact Questionnaire (CIQ). According to the study protocol, data concerning non-medical resource use were to have been obtained both at routine visits (every 8 weeks) and at sick visits. Of the 250 enrolled children, 238 had follow-up for at least 8 weeks (121 in the tympanostomy-tube group and 117 in the medical-management group), and 210 children had at least one sick visit (106 in the tympanostomy-tube group and 104 in the medical-management group). For the analysis of non-medical resource use we included only children who had had at least one routine visit or one sick visit following randomization. Data concerning the OM-6 Survey and the CIQ were to have been obtained at least at every other routine visit. For these outcomes we found a relatively low rate of missing forms completed at specified visits (40/3303 [1.2%] for non-medical resource use, 32/1752 [1.8%] for the OM-6, and 31/1732 [1.8%] for the CIQ); no data were imputed for children who did not complete follow-up for the full 2 years. For best-case outcomes, no family member had to miss work; special childcare arrangements were not needed; and scores were 1 on the OM-6-survey, 10 on the OM-6 Quality of Life (QOL), 0 on the CIQ, and 10 on the CIQ QOL. For worst-case outcomes, a family member had to miss work, special childcare arrangements were needed, and scores were 7 on the OM-6 survey, 0 on the OM-6 QOL, 100 on the CIQ, and 0 on the CIQ QOL

Results of these sensitivity analyses (see below Tables S3a-e) were consistent with the complete case analyses, so that the effects of missing data on the conclusions appears minimal. It is important to note that data presented in the sensitivity analyses tables concern, in one case, children (treatment failure, protocol-defined diarrhea, diaper dermatitis; Tables S3a-c), and in the other case, forms completed at specified visits (non-medical resource use, OM-6 and CIQ; Tables S3d-e). Sensitivity analysis was not performed for medical resource use outcomes since best- and worst- case outcomes cannot be readily characterized.

Table S3a. Sensitivity Analysis for Secondary Outcome Treatment Failure.

		Treatment assignment		All
		Tympanostomy-Tube Group	Medical-Management Group	
		N	N	N
Completed 2nd year	**Treatment failure**			
No	**No**	13	10	23
	Yes	8	11	19
Yes	**No**	60	37	97
	Yes	48	63	111

	Treatment assignment				All	
	Tympanostomy-Tube Group		Medical-Management Group			
	N	%	N	%	N	%
Treatment failure (if followed <2 yrs. and no treatment failure, take best case, no failure)						
No	73	56.6	47	38.8	120	48.0
Yes	56	43.4	74	61.2	130	52.0
All	129	100.0	121	100.0	250	100.0

Risk ratio: 0.73 (95% CI; 0.58–0.91); adjusted for site and stratification variables

	Treatment assignment				All	
	Tympanostomy-Tube Group		Medical-Management Group			
	N	%	N	%	N	%
Treatment failure (if followed <2 yrs. and no treatment failure, take worst case, failure)						
No	60	46.5	37	30.6	97	38.8
Yes	69	53.5	84	69.4	153	61.2
All	129	100.0	121	100.0	250	100.0

Risk Ratio: 0.78 (95% CI; 0.64-0.94); adjusted for site and stratification variables

Table S3b. Sensitivity Analysis for Secondary Outcome Protocol-Defined Diarrhea.

		Treatment assignment		All
		Tympanostomy-Tube Group	Medical-Management Group	
		N	N	N
Completed 2nd year	**Cumulative # PDD NSAEs**			
No	**0**	20	16	36
	>=1	1	5	6
Yes	**0**	88	71	159
	>=1	20	29	49

	Treatment assignment				All	
	Tympanostomy-Tube Group		Medical-Management Group			
	N	%	N	%	N	%
PDD NSAEs (if followed <2 yrs. and 0, take best case, 0)						
0	108	83.7	87	71.9	195	78.0
>=1	21	16.3	34	28.1	55	22.0
All	129	100.0	121	100.0	250	100.0

PDD denotes protocol-defined diarrhea; NSAE denotes non-serious adverse events

Risk ratio: 0.67 (0.44-1.03); adjusted for site and stratification variables

	Treatment assignment				All	
	Tympanostomy-Tube Group		Medical-Management Group			
	N	%	N	%	N	%
PDD NSAEs (if followed <2 yrs. and 0, take worst case, ≥1)						
0	88	68.2	71	58.7	159	63.6
>=1	41	31.8	50	41.3	91	36.4
All	129	100.0	121	100.0	250	100.0

PDD denotes protocol-defined diarrhea; NSAE denotes non-serious adverse events

Risk ratio: 0.77 (0.56-1.05); adjusted for site and stratification variables

Table S3c. Sensitivity Analysis for Secondary Outcome Diaper Dermatitis.

		Treatment assignment		All
		Tympanostomy-Tube Group	Medical-Management Group	
		N	N	N
Completed 2nd year	**Cumulative # diaper dermatitis NSAEs**			
No	**0**	19	19	38
	>=1	2	2	4
Yes	**0**	85	69	154
	>=1	23	31	54

	Treatment assignment				All	
	Tympanostomy-Tube Group		Medical-Management Group			
	N	%	N	%	N	%
Diaper dermatitis NSAEs (if followed <2 yrs. and 0, take best case, 0)						
0	104	80.6	88	72.7	192	76.8
>=1	25	19.4	33	27.3	58	23.2
All	129	100.0	121	100.0	250	100.0

NSAE denotes non-serious adverse event

Risk ratio: 0.79 (0.51-1.22); adjusted for site and stratification variables

	Treatment assignment				All	
	Tympanostomy-Tube Group		Medical-Management Group			
	N	%	N	%	N	%
Diaper dermatitis NSAEs (if followed <2 yrs. and 0, take worst case, ≥1)						
0	85	65.9	69	57.0	154	61.6
>=1	44	34.1	52	43.0	96	38.4
All	129	100.0	121	100.0	250	100.0

NSAE denotes non-serious adverse event

Risk ratio: 0.80 (0.59-1.10); adjusted for site and stratification variables

Table S3d. Sensitivity Analysis for Secondary Outcome Non-Medical Resource Use.

Worst case outcome (filled with Yes [1]-missed work and special childcare arrangement)	Tympanostomy-Tube Group	Medical-Management Group	Overall	Risk Ratio (95% CI)
	n=1652	n=1651	N=3303	
Has any member of your family had to miss work since the last study visit because your child was sick? no. (%)				
No	1317 (80)	1342 (81)	2659 (81)	1.09 (0.87-1.36)
Yes	303 (18)	279 (17)	582 (18)	
N/A	32 (2)	30 (2)	62 (2)	
If your child was sick, since the last visit, did you have to make special childcare arrangements? no. (%)				
No	1402 (85)	1429 (87)	2831 (86)	1.11 (0.87-1.42)
Yes	248 (15)	218 (13)	466 (14)	
Unknown	2 (0)	4 (0)	6 (0)	

Best case outcome (filled with No [0]-missed work and special childcare arrangement)	Tympanostomy-Tube Group*	Medical-Management Group †	Overall	Risk Ratio (95% CI)
	n=1652	n=1651	N=3303	
Has any member of your family had to miss work since the last study visit because your child was sick? no. (%)				
No	1334 (81)	1365 (83)	2699 (82)	1.12 (0.88-1.41)
Yes	286 (17)	256 (15)	542 (16)	
N/A	32 (2)	30 (2)	62 (2)	
If your child was sick, since the last visit, did you have to make special childcare arrangements? no. (%)				
No	1419 (86)	1452 (88)	2871 (87)	1.15 (0.89-1.49)
Yes	231 (14)	195 (12)	426 (13)	
Unknown	2 (0)	4 (0)	6 (0)	

Table S3e. Sensitivity Analysis for Secondary Analysis Otitis Media-6 Survey and Caregiver Impact Questionnaire.

Worst case scenarios (filled with '7=OM-6 survey, 0= OM-6 QOL*, 100=CIQ, 0=CIQ OQL')	Tympanostomy-Tube Group	Medical-Management Group	Overall	Estimate (95% CI) Least Square Means
	n=907	n=845	N=1752	Adjusted for site, age, exposure
Otitis Media-6 Survey				
Mean	1.60±0.03	1.64±0.04	1.62±0.03	-0.04 (-0.14 to 0.06)
Otitis Media-6 Survey-Overall child's QOL				
Mean	8.30±0.07	8.22±0.08	8.26±0.05	0.03 (-0.17 to 0.24)
	n=899	n=833	N=1732	
Caregiver Impact Questionnaire Survey				
Mean	12.41±0.66	12.53±0.68	12.47±0.47	0.07 (-1.79 to 1.93)
Caregiver Impact Questionnaire-Overall Caregiver's QOL				
Mean	8.40±0.07	8.34±0.07	8.37±0.05	0.02 (-0.18 to 0.22)

Best case scenarios (filled with '1=OM-6 survey, 10= OM-6 QOL*, 0=CIQ, 10=CIQ OQL')	Tympanostomy-Tube Group	Medical-Management Group	Overall	Estimate (95% CI) Least Square Means
	n=907	n=845	N=1752	Adjusted for site, age, exposure
Otitis Media-6 Survey				
Mean	1.49±0.02	1.54±0.03	1.51±0.02	-0.05 (-0.13 to 0.02)
Otitis Media-6 Survey-Overall Child's QOL				
Mean	8.48±0.06	8.40±0.07	8.44±0.05	0.06 (-0.12 to 0.24)
	n=899	n=833	N=1732	
Caregiver Impact Questionnaire Survey				
Mean	10.63±0.53	10.73±0.54	10.68±0.38	-0.05 (-1.54 to 1.44)
Caregiver Impact Questionnaire-Overall Caregiver's QOL				
Mean	8.58±0.06	8.52±0.06	8.55±0.04	0.03 (-0.14 to 0.20)

AOM-SOS SCALE (VERSION 4.0)

How has your child been doing?

We are interested in finding out how your child has been doing. For each question, please place a check (✓) 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?	❒	❒	❒
Over the past 12 h, has your child been crying more than usual?	❒	❒	❒
Over the past 12 h, has your child been more irritable or fussy than usual?	❒	❒	❒
Over the past 12 h, has your child been having more difficulty sleeping than usual?	❒	❒	❒
Over the past 12 h, has your child been having fever or feeling warm to touch?	❒	❒	❒

OM-6 Survey[4]

Instructions: Please help us understand the impact of ear infections or fluid on your child's quality of life by checking one box [X] for each question below. Thank you.

Physical Suffering: Ear pain, ear discomfort, ear discharge, ruptured ear drum, high fever, or poor balance. How much of a problem for your child during the past 4 weeks?

[ ] Not present/no problem
[ ] Hardly a problem at all
[ ] Somewhat of a problem
[ ] Moderate problem
[ ] Quite a bit of a problem
[ ] Very much a problem
[ ] Extreme problem

Hearing Loss: Difficulty hearing, questions must be repeated, frequently says "what," or television is excessively loud. How much of a problem for your child during the past 4 weeks?

[ ] Not present/no problem
[ ] Hardly a problem at all
[ ] Somewhat of a problem
[ ] Moderate problem
[ ] Quite a bit of a problem
[ ] Very much a problem
[ ] Extreme problem

Speech Impairment: Delayed speech, poor pronunciation, difficult to understand, or unable to repeat words clearly. How much of a problem for your child during the past 4 weeks?

[ ] Not present/no problem (or not applicable)
[ ] Hardly a problem at all
[ ] Somewhat of a problem
[ ] Moderate problem
[ ] Quite a bit of a problem
[ ] Very much a problem
[ ] Extreme problem

Emotional Distress: Irritable, frustrated, sad, restless, or poor appetite. How much of a problem for your child during the past 4 weeks as a result of ear infections or fluid?

[ ] Not present/no problem
[ ] Hardly a problem at all
[ ] Somewhat of a problem
[ ] Moderate problem
[ ] Quite a bit of a problem
[ ] Very much a problem
[ ] Extreme problem

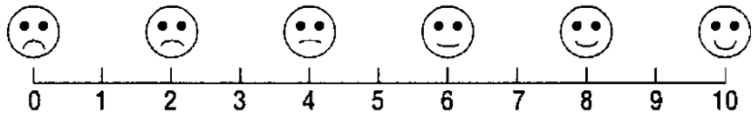
Activity Limitations: Playing, sleeping, doing things with friends/family, attending school or day care. How limited have your child's activities been during the past 4 weeks because of ear infections or fluid?

[ ] Not limited at all
[ ] Hardly limited at all
[ ] Very slightly limited
[ ] Slightly limited
[ ] Moderately limited
[ ] Very limited
[ ] Severely limited

Caregiver Concerns: How often have you, as a caregiver, been worried, concerned, or inconvenienced because of your child's ear infections or fluid over the past 4 weeks?

[ ] None of the time
[ ] Hardly any time at all
[ ] A small part of the time
[ ] Some of the time
[ ] A good part of the time
[ ] Most of the time
[ ] All of the time

Overall, how would you rate your child's quality of life as a result of ear infections or fluid?
(Circle one number)



Worse Possible Quality-of-Life — Half-way Between Worst and Best — Best Possible Quality-of-Life

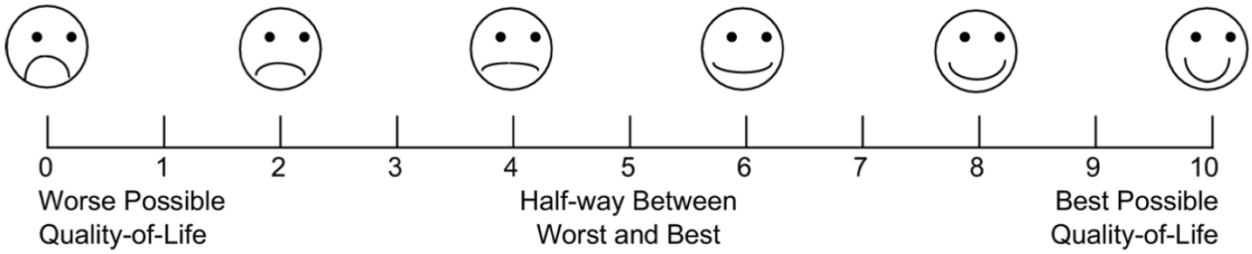
The 6-item health-related quality-of-life survey (OM-6) for chronic and recurrent otitis media.

CAREGIVER IMPACT QUESTIONNAIRE

How often did you or your partner experience the following problems during the past 3 months as a consequence of ear infections or ear fluid in your child? Please circle one number for each question.

	None of the time	Hardly any of the time	A little of the time	Some of the time	A good bit of the time	Most of the time	All of the time
1. Lack of sleep	1	2	3	4	5	6	7
2. Absence from work or education	1	2	3	4	5	6	7
3. Cancelling of family activities, such as trips, play dates, vacations	1	2	3	4	5	6	7
4. Changing daily activities, such as housework, shopping, or time with other siblings	1	2	3	4	5	6	7
5. Feeling nervous, agitated, or irritable	1	2	3	4	5	6	7
6. Feeling helpless or frustrated	1	2	3	4	5	6	7

7. Overall, how would you rate *your* quality of life during the past 3 months as a result of your child's ear infections or fluid (circle one number):



8. Are there other children in your family?

[ ] Yes [ ] No → skip questions 9 and 10

If there are other children in your family, then please indicate to what extent your agree or disagree with the statements below. Please circle one number for each question.

	Strongly agree	Agree	Not certain	Disagree	Strongly disagree
9. Our other children felt neglected or excluded when our child had an ear infection or fluid during the past 3 months	1	2	3	4	5
10. Our other children demanded extra attention when our child had an ear infection or fluid during the past 3 months	1	2	3	4	5

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