

ORIGINAL ARTICLE

Tympanostomy Tubes and Developmental Outcomes at 9 to 11 Years of Age

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ABSTRACT

BACKGROUND

From the University of Pittsburgh (J.L.P., H.M.F., T.F.C., C.A.D., H.E.R., M.K.-L., J.E.J., D.L.S., R.E.O.) and Children's Hospital of Pittsburgh (J.L.P., H.M.F., T.F.C., D.L.P., C.G.S., D.K.C., B.S.B., D.L.S.) — both in Pittsburgh; Stanford University School of Medicine, Stanford, CA (H.M.F.); the University of Texas, Dallas (T.F.C., C.A.D.); the University of California, Riverside (R.E.O.); and the State University of New York at Buffalo, Buffalo (W.E.P.). Address reprint requests to Dr. Paradise at Children's Hospital of Pittsburgh, 3705 Fifth Ave., Pittsburgh, PA 15213, or at jpar@pitt.edu.

Developmental impairments in children have been attributed to persistent middle-ear effusion in their early years of life. Previously, we reported that among children younger than 3 years of age with persistent middle-ear effusion, prompt as compared with delayed insertion of tympanostomy tubes did not result in improved cognitive, language, speech, or psychosocial development at 3, 4, or 6 years of age. However, other important components of development could not be assessed until the children were older.

METHODS

We enrolled 6350 infants soon after birth and evaluated them regularly for middle-ear effusion. Before 3 years of age, 429 children with persistent effusion were randomly assigned to undergo the insertion of tympanostomy tubes either promptly or up to 9 months later if effusion persisted. We assessed literacy, attention, social skills, and academic achievement in 391 of these children at 9 to 11 years of age.

RESULTS

Mean (\pm SD) scores on 48 developmental measures in the group of children who were assigned to undergo early insertion of tympanostomy tubes did not differ significantly from the scores in the group that was assigned to undergo delayed insertion. These measures included the Passage Comprehension subtest of the Woodcock Reading Mastery Tests (mean score, 98 ± 12 in the early-treatment group and 99 ± 12 in the delayed-treatment group); the Spelling, Writing Samples, and Calculation subtests of the Woodcock-Johnson III Tests of Achievement (96 ± 13 and 97 ± 16 ; 104 ± 14 and 105 ± 15 ; and 99 ± 13 and 99 ± 13 , respectively); and inattention ratings on visual and auditory continuous performance tests.

CONCLUSIONS

In otherwise healthy young children who have persistent middle-ear effusion, as defined in our study, prompt insertion of tympanostomy tubes does not improve developmental outcomes up to 9 to 11 years of age. (ClinicalTrials.gov number, NCT00365092.)

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DURING THE PAST FOUR DECADES, INVESTIGATORS have reported that conductive hearing loss associated with persistent otitis media in young children can result in long-term impairment of their development.^{1,2} To prevent or minimize developmental impairment, official guidelines have until recently recommended that young children in whom middle-ear effusion has persisted for as long as 3 months³ or 4 months⁴ undergo myringotomy with insertion of tympanostomy tubes in order to clear the effusion and restore hearing acuity to a normal level.

In 1991, because evidence regarding the developmental effects of otitis media early in life was inconclusive,² and because of the lack of evidence that insertion of tympanostomy tubes in children with persistent middle-ear effusion affects their development favorably, we began a study to address those issues. Previously, we reported that prompt as compared with delayed insertion of tympanostomy tubes before 3 years of age in study participants who had persistent effusion did not have a favorable effect on their cognitive, language, speech, or psychosocial development at 3, 4, or 6 years of age⁵⁻⁷; on their phonological memory at 4 or 6 years of age^{6,7}; or on their auditory processing skills at 6 years of age.⁷ However, it remained uncertain whether developmental effects that were not present or could not be measured reliably by 6 years of age might emerge or become discernible as the children grew older. Of particular interest were domains of development previously reported by others to be unfavorably affected by persistent otitis media early in life — literacy,⁸⁻¹¹ attention,¹¹⁻¹⁶ and academic achievement.^{14,17}

On what basis might adverse outcomes in those domains be expected? To develop literacy, children must learn to isolate phonemes within words and match them to letter sounds to form representations of written words, tasks that may require finer discrimination among speech sounds than does the development of oral language. Accordingly, it seems possible that children who had prolonged periods of hearing loss early in life but whose oral language development remained unaffected would nonetheless encounter difficulty later with reading or spelling. That difficulty might contribute to other learning difficulties, and those in turn, to problems in behavior. Similarly, if children had been receiving decreased, distorted, or inconsistent auditory signals when they were younger, they might have tuned out sound and

become inattentive and distractible, and these effects might first come into play in the classroom and first be measurable objectively as the children grew older. Finally, both learning difficulties and impaired attention would be likely to limit children's academic achievement. We describe here our findings concerning literacy, auditory processing, attention, behavior, social skills, and academic achievement in the children in our study at 9 to 11 years of age.

METHODS

GENERAL PROCEDURES

Our study included two main components. In one component, children with persistent middle-ear effusion were randomly assigned to undergo either prompt insertion of tympanostomy tubes or delayed insertion if the effusion persisted. In the other component, we examined the relationship between the cumulative duration of effusion and later developmental outcomes in a subgroup of children who did not meet the randomization criteria regarding the persistence of effusion. We have described the study procedures in detail previously.^{2,5-7} From June 1991 through December 1995, we enrolled 6350 healthy infants who were 2 to 61 days of age at Children's Hospital of Pittsburgh, Mercy Hospital of Pittsburgh, and six pediatric group practices in the Pittsburgh area. The study was limited to children whose only household language was English. The study was approved by the review boards of the two hospitals, and we obtained written informed consent from one or both parents or guardians of each enrolled infant.

We monitored the children's middle-ear status until they were 3 years of age. We used the term "middle-ear effusion" to encompass all types of otitis media, including acute otitis media and tube otorrhea. We estimated the duration of episodes of effusion on the basis of diagnoses made at hospital or office visits and interpolations for intervals between visits, and we conducted audiometric testing frequently. Hearing was abnormal in approximately half the children with unilateral effusion and in approximately three quarters of those with bilateral effusion.⁵

ELIGIBILITY CRITERIA FOR RANDOMIZATION

Children were eligible to participate in the clinical trial if, between the ages of 2 months and 3 years, they had middle-ear effusion that persisted for 90

days in the case of bilateral effusion or 135 days in the case of unilateral effusion. Children with intermittent effusion for a specified proportion of a longer period were also eligible, as described previously.⁵ For example, children were eligible if they had had bilateral effusion for at least 67% of the preceding 180-day period or unilateral effusion for at least 67% of the preceding 270-day period. A total of 429 children who met one of these criteria and whose parents or guardians gave written informed consent were stratified according to practice site, age (in 6-month categories), and whether the children met the eligibility criteria on the basis of bilateral or unilateral effusion. They were then assigned randomly, within those strata and in balanced blocks of four children, to undergo insertion of tympanostomy tubes either promptly (the early-treatment group) or 6 months later if bilateral effusion persisted or 9 months later if unilateral effusion persisted (the delayed-treatment group). Children for whom consent for randomization was not obtained were treated according to parental choice and followed for the duration of the study. During the first 12 months after randomization, 45% of the children in the delayed-treatment group had middle-ear effusion for more than 50% of the days, as compared with 14% of the children in the early-treatment group.⁵

SUBGROUP OF CHILDREN WHO WERE NOT ELIGIBLE FOR RANDOMIZATION

We randomly selected a subgroup of 241 children to represent the demographic characteristics of the study population as a whole and to represent the spectrum of children ranging from those with no middle-ear effusion to those with a duration of effusion that fell just short of meeting the criteria for randomization. Our objective was to assess the correlations between the duration of effusion in these children and their outcomes and to compare their outcomes with those of the children who underwent randomization. In this subgroup of children, the estimated cumulative duration of middle-ear effusion (unilateral and bilateral combined) ranged from no effusion to 66% of the first year of life and to 45% of the first 3 years of life.²

DEVELOPMENTAL TESTS AND PROCEDURES

We assessed development in the children at the earliest mutually convenient date between their 9th and 12th birthdays and, if possible, when their hearing-level thresholds were 15 dB or less in each

ear at 1000, 2000, and 4000 Hz. Assessments were conducted in a specified order.

We used the following measures to assess literacy: the Woodcock Reading Mastery Tests — Revised, normative updated version,¹⁸ for reading progress; the number of words in a grade-level passage read correctly in 1 minute for oral-reading fluency^{19,20}; and the Spelling and Writing Samples subtests of the Woodcock–Johnson III Tests of Achievement, Standard Battery,²¹ for writing skills. To assess phonological awareness, we used the Elision and Rapid Letter Naming subtests of the Comprehensive Test of Phonological Processing,²² and to assess auditory processing ability, the children’s version of the Hearing in Noise Test.^{23,24} To assess attention, impulsivity, and psychosocial function, we used the Disruptive Behavior Disorders Rating Scale,²⁵ the Child Behavior Checklist,²⁶ the Impairment Rating Scales,²⁷ and the Social Skills Scale of the Social Skills Rating System,²⁸ each completed separately by parents and teachers, and computer-based visual and auditory continuous performance tests.^{29,30} To assess intelligence and academic achievement, we used the Wechsler Abbreviated Scale of Intelligence³¹ and the Calculation subtest of the Woodcock–Johnson III Tests of Achievement, Standard Battery.²¹ The individual assessments are described briefly in Table 1. The examiners and analysts were unaware of the children’s medical histories and treatment-group assignments.

STATISTICAL ANALYSIS

We calculated the duration of middle-ear effusion in children beginning from the age of 2 months. In the randomized clinical trial, to detect differences of 0.33 SD or greater on any outcome measure with a statistical power of 80%, we calculated that we would need to enroll 182 children in each group. Analyses were performed according to the intention-to-treat principle. In the subgroup of children who were not eligible for randomization, the sample of 241 children was sufficient to detect correlations of 0.25, at a power of 91%, between scores on developmental tests and the estimated cumulative proportion of days with middle-ear effusion. Because correlations involving days with bilateral effusion differed little from correlations involving total days with effusion (i.e., bilateral plus unilateral), the reported results are for total days with any effusion.

All scoring of tests and data entries were dou-

Table 1. Developmental Tests and Procedures.

Assessment	Description
Woodcock Reading Mastery Tests — Revised, normative updated version	
Word Identification subtest	The child identifies words in isolation.
Word Attack subtest	The child applies phonic and structural analysis to pronounce pseudowords.
Passage Comprehension subtest	The child silently reads one or two sentences with a missing word indicated by a blank space and supplies a word that makes sense.
Oral reading fluency test	The number of words in each of three grade-level passages that a child reads correctly in 1 minute is recorded. The median of the three values is the child's score.
Woodcock-Johnson III Tests of Achievement, Standard Battery	
Spelling subtest	The child spells words from dictation and uses appropriate capitalization and syntax, appropriate plural forms, comparatives, and superlatives.
Writing Samples subtest	The child responds to a brief prompt; items begin with one-word responses and progress to complete sentences of increasing complexity.
Comprehensive Test of Phonological Processing	
Elision subtest	The examiner asks the child to say a word (e.g., "Say 'farm'"), and after the child repeats the word, he or she is asked to say the word again without a specific phoneme (e.g., "Now say 'farm' without saying /f/"). A total of 20 such tasks are presented.
Rapid Letter Naming subtest	The child is asked to name letters that are randomly arranged on a page, and the examiner records the number of seconds required for the child to name all the letters.
Hearing in Noise Test (children's version)	The child repeats a series of seven sentences, one sentence at a time, in a quiet environment and with competing noise at a steady loudness of 65 dB presented by means of a speaker from the front at 0 degrees, from the right at 90 degrees, and from the left at 90 degrees. For each condition, a separate series of sentences is used, and each sentence is presented at increasing levels of loudness until the child can hear and repeat it. For each competing-noise condition, the score is the value obtained by subtracting 65 dB from the average loudness in decibels.
Disruptive Behavior Disorder Rating Scale	A parent and a teacher independently rate the child on 43 items consisting of symptoms of attention deficit-hyperactivity disorder, oppositional defiant disorder, and conduct disorder.
Child Behavior Checklist	A parent and a teacher independently rate the child's overall behavioral and emotional problems by responding to 120 items and scoring each statement as "not true," "somewhat or sometimes true," or "very true or often true." The results are organized into eight specific scales: Withdrawn, Somatic Complaints, Anxious/Depressed, Social Problems, Thought Problems, Attention Problems, Delinquent Behavior, and Aggressive Behavior.
Impairment Rating Scales	With the use of visual-analogue scales, a parent and a teacher independently rate the child's relationships with parents, peers, siblings, and teachers; the effect of any problems on the family; classroom behavior; academic functioning; self-esteem; and overall functioning by marking an "X" on a line. The line for each domain is divided into seven equal parts, and numerical scores (0-6) are assigned to the parent's and the teacher's ratings. Ratings for the individual items correlate highly with ratings for overall functioning.
Social Skills Scale of the Social Skills Rating System	A parent and a teacher independently rate the child on Cooperation, Assertion, and Self-Control, and the parent also rates the child on Responsibility. Items are rated according to perceived frequency (never, sometimes, very often).
Continuous Performance Test	Accuracy, reaction time, inattention, and impulsivity are measured. Scores reflect the numbers of errors of omission and of commission.
Visual	The child watches a computer screen that displays a series of letters. The child presses the space bar on the keyboard when the target letter is preceded by the valid cue, and not under any other circumstances.
Auditory	The child presses the space bar when he or she hears "X" preceded by "A," and not under any other circumstances.
Wechsler Abbreviated Scale of Intelligence	
Vocabulary, Block Design, Picture Arrangement, and Similarities subtests	For each subtest, the number of correct responses is calculated.
Woodcock-Johnson III Tests of Achievement, Standard Battery	
Calculation subtest	The child writes single numbers and adds, subtracts, multiplies, divides, and performs combinations of these basic operations.

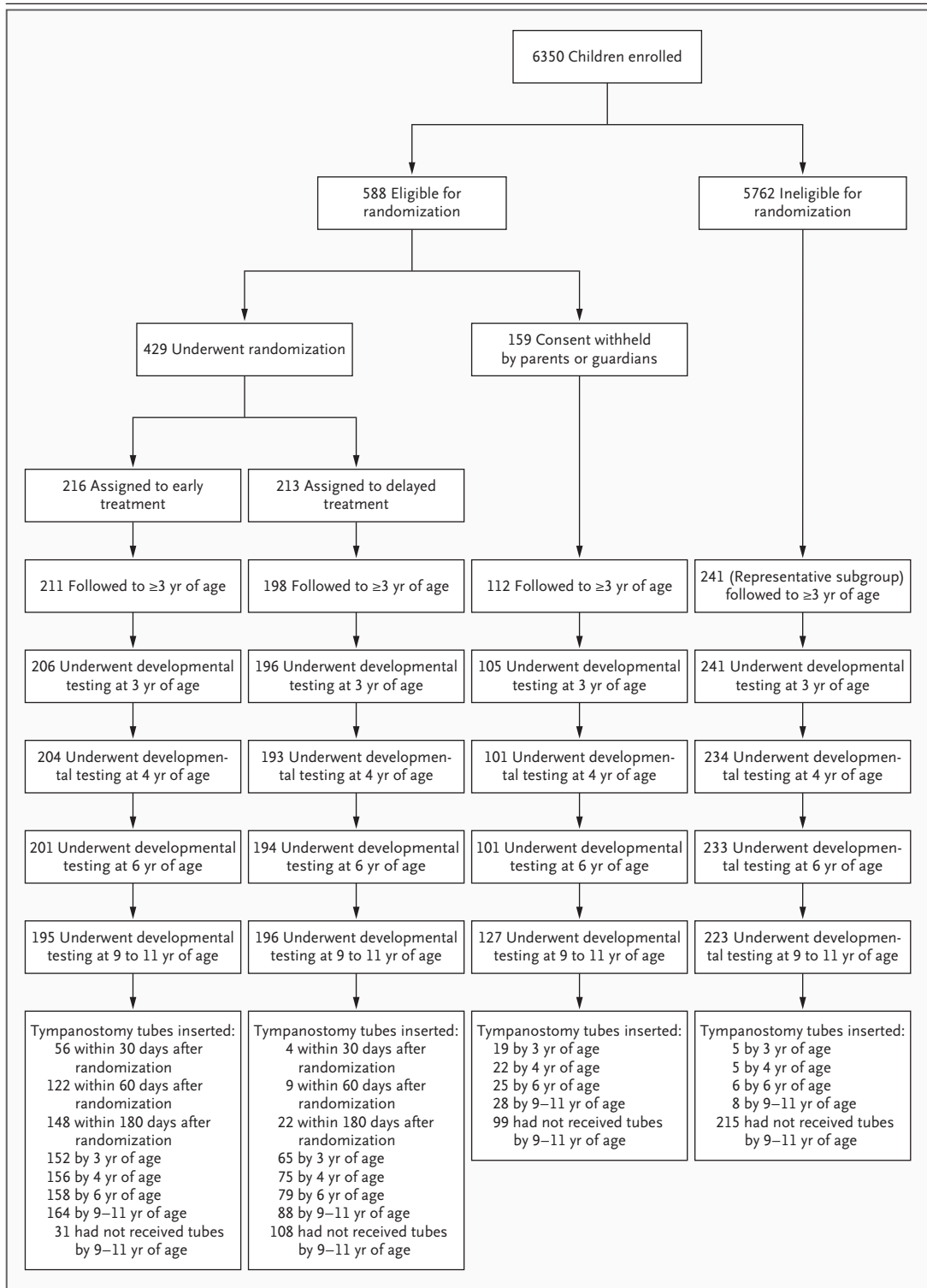


Figure 1. Enrollment, Randomization, and Follow-up of the Children and the Time of Insertion of Tympanostomy Tubes.

Forty-two of the children who returned for developmental evaluation at the age of 9 to 11 years — 3 in the early-treatment group of the randomized clinical trial, 11 in the delayed-treatment group, and 28 in the group for whom consent for randomization was withheld — were lost to follow-up before the age of 3 years or did not undergo one or more of the scheduled evaluations at 3, 4, and 6 years of age.

Table 2. Demographic Characteristics of Children Who Underwent Testing, According to Study Component.*

Characteristic	Randomized Clinical Trial (N=391)	Group for Whom Consent for Randomization Was Withheld (N=127)		Subgroup Not Eligible for Randomization (N=223)
		<i>no. of children (%)</i>		
Location of study site				
Urban area	191 (49)	82 (65)†	51 (23)‡	
Small town or rural	140 (36)	26 (20)	86 (39)	
Suburban	60 (15)	19 (15)	86 (39)	
Sex				
Male	225 (58)	74 (58)	112 (50)	
Female	166 (42)	53 (42)	111 (50)	
Age at time of assessment				
9 yr	180 (46)	75 (59)§	23 (10)‡	
10 yr	187 (48)	45 (35)	165 (74)	
11 yr	24 (6)	6 (5)	35 (16)	
12 yr	0	1 (1)	0	
Race or ethnic group¶				
Black	145 (37)	62 (49)	34 (15)‡	
White	234 (60)	62 (49)	183 (82)	
Other or indeterminate	12 (3)	3 (2)	6 (3)	
Maternal level of education				
At study entry				
Less than high school graduate	51 (13)	24 (19)	20 (9)‡	
High school graduate	308 (79)	93 (73)	156 (70)	
College graduate	32 (8)	10 (8)	47 (21)	
At time of current assessment				
Less than high school graduate	16 (4)	12 (9)	6 (3)†	
High school graduate	308 (79)	97 (76)	153 (69)	
College graduate	65 (17)	18 (14)	64 (29)	
Unknown	2 (1)	0	0	
Health insurance status				
At study entry				
Public	249 (64)	93 (73)	68 (30)‡	
Private	139 (36)	33 (26)	152 (68)	
None	3 (1)	1 (1)	3 (1)	
At time of current assessment				
Public	167 (43)	60 (47)	50 (22)‡	
Private	215 (55)	63 (50)	169 (76)	
None	9 (2)	4 (3)	4 (2)	

* Because of rounding, percentages may not sum to 100.

† P<0.01 for the comparison with the distribution of children who underwent randomization.

‡ P<0.001 for the comparison with the distribution of children who underwent randomization.

§ P<0.05 for the comparison with the distribution of children who underwent randomization.

¶ Race or ethnic group was reported by the parent or guardian.

Table 3. Clinical Characteristics of the Tested Children Who Underwent Randomization.*

Characteristic	Early-Treatment Group (N = 195)	Delayed-Treatment Group (N = 196)
	<i>no. of children (%)</i>	
Year of life during which randomization criteria were met		
First	79 (41)	85 (43)
Second	91 (47)	92 (47)
Third	25 (13)	19 (10)
Laterality and sequence of middle-ear effusion serving as the basis for meeting randomization criteria		
Bilateral		
Continuous	39 (20)	36 (18)
Discontinuous	38 (19)	36 (18)
Unilateral		
Continuous	33 (17)	31 (16)
Discontinuous	85 (44)	93 (47)
Abnormal result of hearing test on ≥ 1 occasion before randomization†		
Yes	160 (82)	138 (70)
No	21 (11)	36 (18)
Results incomplete or not reliable or testing not performed	14 (7)	22 (11)
Percentage of time with bilateral middle-ear effusion in 6-mo period before randomization criteria were met‡		
≤ 25	29 (15)	35 (18)
26–50	81 (42)	69 (35)
51–75	70 (36)	77 (39)
76–99	12 (6)	11 (6)
100	3 (2)	4 (2)

ble-checked. All analyses were performed by the authors with the use of two-tailed tests, with a P value of 0.05 or less considered to indicate statistical significance. We used chi-square tests to evaluate between-group differences in proportions of children. We used analysis of variance to test for differences between mean results, Pearson pairwise correlation analysis to test for correlations, and linear regression analysis to adjust for potentially confounding variables and to test for interactions. We did not adjust for the multiple comparisons performed.

RESULTS

STUDY SAMPLE AND TREATMENT GROUPS

A total of 391 of the 429 children who underwent randomization (91%), 127 of the 159 children whose parents or guardians declined randomiza-

tion (80%), and 223 of the 241 children in the subgroup not eligible for randomization (93%) underwent developmental assessment at 9 to 11 years of age. At the time of testing, 84% of the children in the early-treatment group and 45% of the children in the delayed-treatment group had undergone tube insertion (Fig. 1).

Table 2 shows selected demographic characteristics of the children who underwent assessment. Larger proportions of children in the group that underwent randomization than in the subgroup not eligible for randomization were black, younger than 10 years of age, from urban areas, and from families of lower socioeconomic status (determined on the basis of maternal level of education and type of health insurance). In the randomized clinical trial, there were no significant differences in characteristics between the tested children in the early-treatment group and those in

Table 3. (Continued.)

Characteristic	Early-Treatment Group (N = 195)	Delayed-Treatment Group (N = 196)
	no. of children (%)	
Percentage of time with bilateral middle-ear effusion in 6-mo period before randomization criteria were met, in subgroup of children meeting the criteria on the basis of unilateral effusion†‡		
≤25	29 (25)	34 (27)
26–50	57 (48)	56 (45)
51–75	31 (26)	30 (24)
76–99	1 (<1)	4 (3)
100	0	0
Hearing thresholds at the time of developmental testing at 9–11 yr of age		
Protocol-specified criteria met¶	185 (95)	185 (94)
Protocol-specified criteria not met	10 (5)	11 (6)
Middle-ear effusion status at the time of developmental testing at 9–11 yr of age		
None	182 (93)	186 (95)
Unilateral	11 (6)	9 (5)
Bilateral	1 (<1)	1 (<1)
Indeterminate	1 (<1)	0

* There were no significant differences in characteristics between the two treatment groups. Because of rounding, percentages may not sum to 100.

† On the basis of test results in study children who had no effusion,²⁷ abnormal results of hearing tests were defined as an auditory brain-stem–response threshold exceeding 20 dB hearing level (dB HL) or a pure-tone average exceeding 25 dB HL up to the age of 10 months, exceeding 20 dB HL from 10 to 23 months, and exceeding 15 dB HL from 2 years of age onward.

‡ For the 67 children (27 in the early-treatment group and 40 in the delayed-treatment group) who met the criteria before 9 months of age, the period extended from the age of 61 days (the starting point for data analysis) to the date on which the criteria were met.

§ There were 118 children in the early-treatment group and 124 in the delayed-treatment group.

¶ The criteria consisted of a hearing-level threshold of 15 dB HL or less at 1000, 2000, and 4000 Hz.

the delayed-treatment group or between the 391 children who were tested and the 38 children who were not. Table 3 shows the clinical characteristics of the children who underwent randomization; there were no significant differences between the treatment groups. The mean scores of the participants in the study on 32 of the 48 developmental measures are shown in Table 4. (Only scores for “Total Problems” on the Child Behavior Checklists, not individual scale scores, are shown.)

RANDOMIZED CLINICAL TRIAL

No significant differences in the results favored the early-treatment group over the delayed-treatment group, either before or after adjustment for the children’s sex and age on measures for which normative standard scores were not available. We tested for interactions to determine whether scores on

any of the 48 outcome measures differed in relation to whether the children met the randomization criteria of the study during their first, second, or third year of life; whether they met the criteria on the basis of bilateral continuous middle-ear effusion, unilateral continuous effusion, bilateral discontinuous effusion, or unilateral discontinuous effusion; and, in the 355 children who received hearing tests during one or more episodes of effusion before undergoing randomization, whether one or more of those tests had abnormal results (as defined in Table 3) or showed a pure-tone average threshold of 30 dB or more or 40 dB or more. In 10 of the 240 instances, there were significant interactions; after adjustment for these interactions, no results significantly favored the early-treatment group.

Among the children who underwent random-

Table 4. Scores on Developmental Tests at 9 to 11 Years of Age.*

Test	Randomized Clinical Trial (N = 391)		Children for Whom Consent for Randomization Was Withheld (N = 127)	Subgroup Not Eligible for Randomization (N = 223)
	Early-Treatment Group (N = 195)	Delayed-Treatment Group (N = 196)		
	<i>mean score (no. of children)</i>		<i>mean score (no. of children)</i>	
Literacy				
Woodcock Reading Mastery Tests — Revised, normative updated version [‡]				
Word Identification subtest	98±11 (195)	99±12 (196)	98±12 (127)	101±10 (223)
Word Attack subtest	103±13 (195)	104±14 (196)	103±13 (127)	106±13 (223)
Passage Comprehension subtest	98±12 (195)	99±12 (196)	98±12 (127)	101±10 (223)
Oral reading fluency test [§]				
Children in grade 3	78±36 (37)	87±41 (37)	86±30 (28)	62±11 (2)
Children in grade 4	89±36 (87)	89±38 (97)	92±34 (63)	109±34 (81) [¶]
Children in grade 5	97±36 (54)	102±37 (51)	94±41 (29)	114±36 (115)
Children in grade 6	102±32 (12)	96±43 (9)	93±16 (5)	106±39 (24)
Woodcock-Johnson III Tests of Achievement, Standard Battery				
Spelling subtest	96±13 (194)	97±16 (196)	96±14 (127)	101±12 (223) [¶]
Writing Samples subtest	104±14 (192)	105±15 (195)	103±13 (125)	108±15 (223)
Phonological awareness				
Comprehensive Test of Phonological Processing ^{**}				
Elision subtest	8.6±4.9 (195)	8.7±3.0 (196)	8.9±2.9 (127)	9.2±3.4 (223)
Rapid Letter Naming subtest	9.3±2.5 (193)	9.6±2.4 (196)	9.6±2.4 (127)	10.1±2.6 (223)
Auditory processing				
Children's version of the Hearing in Noise Test ^{††}				
Competing noise from the front (dB)	-0.4±1.7 (195)	-0.6±1.6 (196)	-0.6±1.6 (127)	-0.8±1.5 (223)
Competing noise from the right (dB)	-7.0±3.0 (195)	-7.0±2.4 (196)	-6.7±2.7 (127)	-8.1±2.5 (223) [¶]
Competing noise from the left (dB)	-6.4±2.5 (195)	-6.8±2.5 (196)	-6.5±2.3 (127)	-7.2±2.4 (223) [¶]

Attention, impulsivity, and psychosocial function						
Disruptive Behavior Disorders Rating Scale ^{†††}						
Inattention factor						
Parent's rating	0.70±0.63 (194)	0.65±0.66 (196)	-0.07 to 0.18	0.62±0.61 (126)	0.56±0.59 (223)	
Teacher's rating	0.71±0.74 (190)	0.67±0.75 (192)	-0.11 to 0.19	0.74±0.77 (122)	0.50±0.66 (216)	
Impulsivity and overactivity factor						
Parent's rating	0.67±0.57 (194)	0.57±0.54 (196)	-0.01 to 0.21	0.56±0.51 (126)	0.47±0.44 (223)¶	
Teacher's rating	0.48±0.63 (190)	0.40±0.52 (192)	-0.04 to 0.20	0.50±0.60 (122)	0.30±0.49 (216)	
Oppositional defiant factor						
Parent's rating	0.57±0.58 (194)	0.52±0.53 (196)	-0.06 to 0.16	0.44±0.47 (126)	0.44±0.45 (223)	
Teacher's rating	0.33±0.56 (190)	0.33±0.58 (192)	-0.11 to 0.11	0.43±0.66 (122)	0.23±0.46 (215)	
Child Behavior Checklist ^{§§}						
Total Problems score, parent's rating	51±12 (194)	49±12 (196)¶¶	0.1 to 4.8	48±12 (127)	47±11 (223)	
Total Problems score, teacher's rating	52±11 (189)	50±11 (191)	-0.9 to 3.4	52±12 (123)	47±11 (217)	
Impairment Rating Scales						
Overall functioning, parent's rating	0.82±1.42 (194)	0.68±1.33 (196)	-0.13 to 0.41	0.64±1.21 (127)	0.46±0.98 (233)	
Overall functioning, teacher's rating	2.04±2.24 (190)	1.78±2.19 (192)	-0.18 to 0.70	1.93±2.23 (123)	1.16±1.74 (217)¶¶	
Social Skills Rating System ^{***}						
Social Skills scale, parent's version	96±19 (194)	98±18 (194)	-6.0 to 1.4	98±18 (126)	102±17 (223)	
Social Skills scale, teacher's version	98±13 (184)	99±13 (186)	-4.5 to 0.9	97±14 (120)	102±15 (211)	
Visual Continuous Performance Test ^{†††}						
Inattention	9.7±8.5 (195)	9.5±8.5 (196)	-1.5 to 1.9	10.1±8.6 (127)	7.1±7.4 (223)	
Impulsivity	8.8±16.5 (195)	8.2±15.6 (196)	-2.7 to 3.7	10.1±20.0 (127)	6.1±13.9 (223)	
Auditory Continuous Performance Test ^{†††}						
Inattention	11.1±7.2 (155)	11.4±8.0 (153)	-2.0 to 1.4	11.6±7.3 (100)	8.7±7.0 (128)	
Impulsivity	3.3±8.7 (154)	4.2±12.1 (153)	-3.2 to 1.5	2.3±4.2 (100)	1.7±5.5 (128)	

Table 4. (Continued.)

Test	Randomized Clinical Trial (N = 391)		Children for Whom Consent for Randomization Was Withheld (N = 127)	Subgroup Not Eligible for Randomization (N = 223)
	Early-Treatment Group (N = 195)	Delayed-Treatment Group (N = 196)		
	mean score (no. of children)		mean score (no. of children)	
Intelligence and academic achievement				
Wechsler Abbreviated Scale of Intelligence ^{†††}	96±13 (195)	96±14 (196)	95±15 (127)	101±13 (223)
Calculation subtest of the Woodcock-Johnson III Tests of Achievement, Standard Battery ^{‡‡‡}	99±13 (194)	99±13 (195)	98±12 (127)	104±12 (223)
		95% CI [†]		
		-3.2 to 2.2		
		-2.7 to 2.4		

* Plus-minus values are means ±SD.

† The 95% confidence interval (CI) is for the difference in mean scores (early-treatment group minus delayed-treatment group).

‡ Scores are converted to standard scores according to the child's age. The normative mean standard score is 100±15. Higher scores indicate more favorable results.

§ Scores are not shown for the seven children in grade 2 and the two children in grade 7. Higher scores indicate more favorable results.

¶ P<0.05 for the comparison with the children who underwent randomization (early-treatment and delayed-treatment groups combined) after adjustment for the location of the study site, sex, the level of maternal education, and the type of health insurance.

|| In both subtests, raw scores are converted to standard scores according to the child's age. The normative mean standard score on both subtests is 100±15. Higher scores indicate more favorable results.

** In both subtests, raw scores are converted to standard scores according to the child's age. The normative mean standard score on each subtest is 10±3. Higher scores indicate more favorable results.

†† Higher scores indicate less favorable results. The hearing level in the quiet condition was not a measure of developmental outcome, but the difference in that level between the children who underwent randomization (21.3±3.9 dB) and the children in the subgroup not eligible for randomization (18.7±3.2 dB, P<0.001) might have been reflected in the respective scores of the two groups in the three competing-noise conditions.

‡‡ A parent and a teacher independently rate the child on 43 items consisting of symptoms of attention deficit-hyperactivity disorder, oppositional defiant disorder, and conduct disorder. The items are scored on a four-point scale (0, "not at all"; 1, "just a little"; 2, "pretty much"; 3, "very much") and are averaged for comparison with normative data. For boys 9 or 10 years of age, the normative mean score for the inattention factor is 1.01±0.91; for the impulsivity and overactivity factor, 0.86±0.81; and for the oppositional defiant factor, 0.69±0.77. For boys 11 through 14 years of age, the corresponding values are 1.01±0.96, 0.85±0.88, and 0.73±0.86. Normative data for girls are not available. Higher scores indicate less favorable results.

§§ Scores on each of the eight component scales and a Total Problem score are calculated and converted to T scores. The normative mean T score on each scale and for Total Problems is 50±10. Only the Total Problem scores are shown here. In the parent ratings, there were no significant differences between the early-treatment and delayed-treatment groups on any of the eight individual scales. In the teacher ratings, the score on the Anxious/Depressed scale was higher (i.e., less favorable) in the early-treatment group than in the delayed-treatment group (P<0.05). After adjustment for the location of the study site, sex, the level of maternal education, and the type of health insurance, there were differences between the children who underwent randomization and the subgroup not eligible for randomization in parent ratings on two scales. On the Somatic Complaints scale, scores were higher for the children who were not eligible for randomization than for the children who underwent randomization (P=0.03), and on the Delinquent Behavior scale, scores were higher for the children who underwent randomization than for those who were not eligible for randomization (P=0.02). Higher scores indicate less favorable results.

¶¶ P<0.05 for the comparison with the early-treatment group.

||| A score of 3 or higher is considered to be indicative of clinically meaningful impairment.

*** The normative mean standard score is 100±15. Higher scores indicate more favorable results.

††† Normative data are not available. Higher scores indicate less favorable results.

‡‡‡ The normative mean score is 100±15. Higher scores indicate more favorable results.

ization, there were no significant differences in mean scores between those who received tympanostomy tubes before 3 years of age (irrespective of the treatment assignment) and those who did not. There were also no significant differences between the mean scores of children who underwent randomization and those of children for whom randomization was declined.

OBSERVATIONAL COHORT

In the subgroup of children who were not eligible for randomization, unadjusted correlations between the scores on each outcome measure (for oral reading fluency, the two children in grade 3 were excluded) and the cumulative duration of middle-ear effusion in the children during their first, second, and third years of life and their first 2 and first 3 years of life were all less than 0.27. For most children (142 of 235), these correlations were less than 0.10, and for most children (183 of 235), the correlations were nonsignificant. After adjustment for demographic variables, there were significant correlations between the duration of effusion during one or more of the periods considered and scores on 4 of the 19 formal test measures and 16 of the 28 measures based on reports by parents and teachers (data not shown). In each case, a longer duration of effusion was associated with a less favorable score. However, the percentage of variance in scores that was explained by the duration of middle-ear effusion, apart from that explained by the demographic variables, was low, ranging from 1.8% to 6.4% (mean, 3.0%). Also, after adjustment for demographic variables, the scores on 39 of the 47 comparable outcome measures did not differ significantly between the children in the subgroup not eligible for randomization and the children who underwent randomization. Six of the eight exceptions are shown in Table 4; the remaining two exceptions involved scores on individual Child Behavior Checklist scales.

DISCUSSION

We describe follow-up developmental findings in a cohort of children in relation to the cumulative duration of middle-ear effusion before the age of 3 years and receipt or nonreceipt of tympanostomy tubes. In a clinical trial in which the children who had persistent effusion during that age period were assigned randomly to undergo prompt

insertion of tympanostomy tubes or delayed insertion if the effusion persisted, there were no significant differences at 9 to 11 years of age in scores favoring early treatment over delayed treatment on any of the 48 developmental measures we used. For 46 of the measures, the associated 95% confidence intervals afforded assurance that the presence of any difference that was 0.33 SD or larger favoring the early-treatment group would probably have been detected. These findings affirm our observation made when the children were younger. That is, early tympanostomy tube placement as compared with delayed tube placement in the children in whom effusion continued unremittingly did not result in a significant effect on the children's cognitive or psychosocial development or on their phonological and auditory processing skills.^{2,5-7,32} Our findings also extend that observation to include measures of the children's literacy, attention, social skills, and academic achievement.

Among the children in whom the duration of middle-ear effusion did not meet the eligibility criteria for enrollment in the clinical trial, correlations between the duration of effusion during various periods in the first 3 years of life and developmental outcomes were generally weak and not significant — results that are consistent with our findings when the children were younger.^{2,6,7,32} For the significant correlations, the percentage of variance in the results that was explained by the duration of effusion was negligible. Nevertheless, these significant correlations, along with certain outcomes that were better for these children than for the children who underwent randomization, raise the possibility that prolonged effusion had some adverse developmental effects. A more likely explanation for these findings, however, is residual confounding, given the more favorable socioeconomic status of the children in the subgroup that was not eligible for randomization and the fact that low socioeconomic status was a major risk factor both for early-life otitis media in these children³³ and for less than optimal developmental outcomes in children in this and other studies.^{2,6,7,32,34}

Our study included close monitoring of children's middle-ear status throughout their first 3 years of life, a broad array of developmental assessments, and a high rate of follow-up. The consistency of the results in different age periods not only affirms the validity of our findings but also suggests that developmental differences

between the treatment groups will not emerge at later ages.

As we have noted previously,^{2,6,7} our findings cannot be generalized to children who are not otherwise healthy or have disabling conditions such as sensorineural hearing loss or Down's syndrome; to children with longer periods of effusion than those we studied; or to children in whom effusion is consistently accompanied by extreme degrees of hearing loss. However, such children are seen infrequently in general clinical practice.

Given the consistency of our current findings with those reported when the children were younger, we conclude that for otherwise healthy children who are younger than 3 years of age and have asymptomatic middle-ear effusion that is persistent, as defined in our study, prompt insertion of tympanostomy tubes does not improve the developmental outcomes as compared with delayed insertion in children in whom effusion continues unremittingly. Accordingly, in children such as those we studied, watchful waiting for at least 6 additional months when effusion is bilateral and

for at least 9 additional months when effusion is unilateral is the preferred management option. Such conservative management was recommended in a recent practice guideline that cited our findings in children at 3 years of age, but this guideline was formulated before our findings in the children at later ages were reported.³⁵

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REFERENCES

1. Kavanagh JF, ed. Otitis media and child development. Parkton, MD: York Press, 1986.
2. Paradise JL, Dollaghan CA, Campbell TF, et al. Language, speech sound production, and cognition in three-year-old children in relation to otitis media in their first three years of life. *Pediatrics* 2000; 105:1119-30.
3. 2000 Clinical indicators compendium. Alexandria, VA: American Academy of Otolaryngology-Head and Neck Surgery, 2000.
4. Stool SE, Berg AO, Berman S, et al. Otitis media with effusion in young children. Clinical practice guideline. No. 12. Rockville, MD: Agency for Health Care Policy and Research, July 1994. (AHCPR publication no. 94-0622.)
5. Paradise JL, Feldman HM, Campbell TF, et al. Effect of early or delayed insertion of tympanostomy tubes for persistent otitis media on developmental outcomes at the age of 3 years. *N Engl J Med* 2001; 344:1179-87.
6. Paradise JL, Dollaghan CA, Campbell TF, et al. Otitis media and tympanostomy tube insertion during the first three years of life: developmental outcomes at the age of four years. *Pediatrics* 2003;112:265-77.
7. Paradise JL, Campbell TF, Dollaghan CA, et al. Developmental outcomes after early or delayed insertion of tympanostomy tubes. *N Engl J Med* 2005;353:576-86.
8. Urdike C, Thornburg JD. Reading skills and auditory processing ability in children with chronic otitis media in early childhood. *Ann Otol Rhinol Laryngol* 1992; 101:530-7.
9. Luotonen M, Uhari M, Aitola L, et al. Recurrent otitis media during infancy and linguistic skills at the age of nine years. *Pediatr Infect Dis J* 1996;15:854-8.
10. Kindig JS, Richards HC. Otitis media: precursor of delayed reading. *J Pediatr Psychol* 2000;25:15-8.
11. Bennett KE, Haggard MP, Silva PA, Stewart IA. Behaviour and developmental effects of otitis media with effusion into the teens. *Arch Dis Child* 2001;85:91-5.
12. Hersher L. Minimal brain dysfunction and otitis media. *Percept Mot Skills* 1978; 47:723-6.
13. Feagans L, Sanyal M, Henderson F, Collier A, Applebaum M. Relationship of middle ear disease in early childhood to later narrative and attention skills. *J Pediatr Psychol* 1987;12:581-94.
14. Roberts JE, Burchinal MR, Collier AM, Ramey CT, Koch MA, Henderson FW. Otitis media in early childhood and cognitive, academic, and classroom performance of the school-aged child. *Pediatrics* 1989;83:477-85.
15. Roberts JE, Burchinal MR, Campbell F. Otitis media in early childhood and patterns of intellectual development and later academic performance. *J Pediatr Psychol* 1994;19:347-67.
16. Asbjørnsen A, Holmeffjord A, Reisaeter S, et al. Lasting auditory attention impairment after persistent middle ear infections: a dichotic listening study. *Dev Med Child Neurol* 2000;42:481-6.
17. Teele DW, Klein JO, Chase C, Menyuk P, Rosner BA. Otitis media in infancy and intellectual ability, school achievement, speech, and language at age 7 years. *J Infect Dis* 1990;162:685-94.
18. Woodcock RW. Woodcock Reading Mastery Tests — Revised. Circle Pines, MN: American Guidance Service, 1987.
19. Deno SL. Curriculum-based measurement: the emerging alternative. *Except Child* 1985;52:219-32.
20. Allinder M, Fuchs L, Fuchs D. Curriculum-based measurement. In: Booney VH, ed. Psychological assessment of children: best practices for school and clinical settings. 2nd ed. New York: John Wiley & Sons, 1988:106-29.
21. Woodcock RW, McGrew KS, Mather N. Woodcock-Johnson III tests of achievement. Itasca, IL: Riverside Publishing, 2001.
22. Wagner RK, Torgesen JK, Rashotte CA. Comprehensive Test of Phonological Processing. Austin, TX: Pro-Ed, 1999.
23. Nilsson M, Soli SD, Sullivan JA. Development of the Hearing in Noise Test for the measurement of speech reception thresholds in quiet and in noise. *J Acoust Soc Am* 1994;95:1085-99.
24. Nilsson MJ, Soli SD, Gelnett DJ. Development and norming of a Hearing in

- Noise Test for Children. Los Angeles: House Ear Institute, 1996.
25. Pelham WE Jr, Gnagy EM, Greenslade KE, Milich R. Teacher ratings of DSM-III-R symptoms for the disruptive behavior disorders. *J Am Acad Child Adolesc Psychiatry* 1992;31:210-8. [Erratum, *J Am Acad Child Adolesc Psychiatry* 1992;31:1177.]
26. Achenbach TM. Integrative guide for the 1991 CBCL/4-18, YSR, and TRF profiles. Burlington: University of Vermont Department of Psychiatry, 1991.
27. Fabiano GA, Pelham WE, Waschbusch DA, et al. A practical measure of impairment: psychometric properties of the Impairment Rating Scale in samples of children with attention deficit hyperactivity disorder and two school-based samples. *J Clin Child Adolesc Psychol* 2006;35:369-85.
28. Gresham FM, Elliot SN. Social skills rating system. Circle Pines, MN: American Guidance Service, 1990.
29. Halperin JM, Sharma V, Greenblatt E, Schwartz ST. Assessment of the continuous performance test: reliability and validity in a non-referred sample. *Psychol Assess* 1991;3:603-8.
30. Aylward GP, Brager P, Harper DC. Relations between visual and auditory continuous performance tests in a clinical population: a descriptive study. *Dev Neuropsychol* 2002;21:285-303.
31. Wechsler D. Wechsler Abbreviated Scale of Intelligence manual. New York: Psychological Corporation, 1999.
32. Feldman HM, Dollaghan CA, Campbell TF, et al. Parent-reported language skills in relation to otitis media during the first three years of life. *J Speech Lang Hear Res* 2003;46:273-87.
33. Paradise JL, Rockette HE, Colborn DK, et al. Otitis media in 2253 Pittsburgh-area infants: prevalence and risk factors during the first two years of life. *Pediatrics* 1997;99:318-33.
34. Gottfried AW, Gottfried AE, Bathurst K, Guerin DW, Parramore MM. Socioeconomic status in children's development and family environment: infancy through adolescence. In: Bornstein MH, Bradley RH, eds. Socioeconomic status, parenting and child development. Mahwah, NJ: Lawrence Erlbaum, 2003:189-207.
35. American Academy of Family Physicians, American Academy of Otolaryngology-Head and Neck Surgery, American Academy of Pediatrics Subcommittee on Otitis Media with Effusion. Otitis media with effusion. *Pediatrics* 2004;113:1412-29.

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