PEDIATRICS®
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Pediatrics 2002;110;7-15
DOI: 10.1542/peds.110.1.7

Tonsillectomy and Adenotonsillectomy for Recurrent Throat Infection in Moderately Affected Children

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ABSTRACT. *Objective.* **In previous clinical trials involving children severely affected with recurrent throat infection (7 or more well-documented, clinically important, adequately treated episodes of throat infection in the preceding year, or 5 or more such episodes in each of the 2 preceding years, or 3 or more such episodes in each of the 3 preceding years), we found tonsillectomy efficacious in reducing the number and severity of subsequent episodes of throat infection for at least 2 years. The results seemed to warrant the election of tonsillectomy in children meeting the trials' stringent eligibility criteria but also provided support for nonsurgical management. We undertook the present trials to determine 1) whether tonsillectomy would afford equivalent benefit in children who were less severely affected than those in our earlier trials but who nonetheless had indications for tonsillectomy comparable to those in general use, and 2) whether, in such children, the addition of adenoidectomy would confer additional benefit.**

Methods. **We conducted 2 parallel randomized, controlled trials in the Ambulatory Care Center of Children's Hospital of Pittsburgh. To be eligible, children were required to have had a history of recurrent episodes of throat infection that met standards slightly less stringent than the standards used in our earlier trials regarding either the frequency of previous episodes or their clinical features or their degree of documentation, but not regarding >1 of those parameters. These reduced standards were nonetheless more stringent than those in current official guidelines, which list "3 or more infections of tonsils and/or adenoids per year despite adequate medical therapy" as an indication for tonsillectomy or adenotonsillectomy. Of 2174 children referred by physicians or parents, 373 met the current trials' eligibility criteria and 328 were enrolled. Of these, 177 children without obstructing adenoids or recurrent or persistent otitis media were randomized to either a tonsillectomy group, an adenotonsillectomy group, or a control group (the 3-way trial), and 151 children who had 1 or more such conditions were randomized to either an adenotonsillectomy group or a control group (the 2-way trial). Outcome measures were the occurrence of episodes of throat infection during the 3 years of follow-up; other, indirect measures of morbidity; and complications of surgery.**

Results. **By various measures, the incidence of throat infection was significantly lower in surgical groups than in corresponding control groups during each of the 3 follow-up years. However, even among control children, mean rates of moderate or severe episodes were low, ranging from 0.16 to 0.43 per year. Adenotonsillectomy was no more efficacious than tonsillectomy alone. Of 203 children treated with surgery, 16 (7.9%) had surgery-related complications of varying types and severity.**

Conclusions. **The modest benefit conferred by tonsillectomy or adenotonsillectomy in children moderately affected with recurrent throat infection seems not to justify the inherent risks, morbidity, and cost of the operations. We conclude that, under ordinary circumstances, neither eligibility criteria such as those used for the present trials nor the criterion for surgery in current official guidelines are sufficiently stringent for use in clinical practice.** *Pediatrics* **2002;110:7–15;** ***tonsillectomy, adenotonsillectomy, tonsillitis, pharyngitis, streptococcal tonsillopharyngits, throat infection, surgical criteria, randomized clinical trial.***

Tonsillectomy remains the most commonly performed major surgical operation among United States children; in 1996, the most recent year for which national data are available, an estimated 287 000 children under 15 years of age underwent tonsillectomy with or without adenoidectomy. Of these, an estimated 248 000 children (86.4%) underwent adenotonsillectomy and an estimated 39 000 children (13.6%) underwent tonsillectomy alone.[1] As an indication for tonsillectomy or adenotonsillectomy, current guidelines of the American Academy of Otolaryngology-Head and Neck Surgery[2] list "3 or more infections of tonsils and/or adenoids per year despite adequate medical therapy."

Previously, we conducted parallel randomized and nonrandomized clinical trials of the efficacy of tonsillectomy, under certain circumstances combined with adenoidectomy, in children we considered severely affected with recurrent episodes of throat infection.[3] Eligibility for the trials depended on a history of recurrent episodes that met stringent standards in each of 4 categories: frequency of occurrence, clinical features, treatment, and documentation. The frequency standard required the occurrence of 7 or more episodes in the preceding year, 5 or more episodes in each of the 2 preceding years, or 3 or more episodes in each of the 3 preceding years.

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This work was presented, in part, at the combined annual meeting of the American Pediatric Society and the Society for Pediatric Research, Baltimore, MD, May 4–7, 1992.
Received for publication Dec 3, 2001; accepted Apr 3, 2002.
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The clinical-features standard required each episode to have been characterized by 1 or more of the following: oral temperature of at least 38.3°C; cervical lymphadenopathy (enlarged [>2 cm] or tender cervical lymph nodes); tonsillar or pharyngeal exudate; or a positive culture for group A β-hemolytic streptococcus. Episodes with 1 or more of these clinical features were termed "counting" episodes. The treatment standard required that antibiotics had been administered in conventional dosage for proved or suspected streptococcal episodes, and the documentation standard required that each episode and its qualifying features had been substantiated by contemporaneous notation in a clinical record. Children with histories that met all standards except documentation were followed prospectively, and those in whom 2 observed episodes of throat infection occurred, with patterns of frequency and clinical features consistent with the initial history, were considered eligible for the trials.

Those trials showed tonsillectomy to have been efficacious for 2 years, and possibly for a third year, in reducing the number and severity of subsequent episodes of throat infection, although many of the children treated nonsurgically improved spontaneously.[3] The degree of benefit in surgically treated children seemed sufficient to justify tonsillectomy in children with throat infection histories comparable to those of the children in the trials. However, the results did not address either the efficacy of tonsillectomy in children who were less severely affected than those we studied but who had indications for tonsillectomy comparable to those in general use, or whether, in such children, the addition of adenoidectomy to tonsillectomy would confer additional benefit. We conducted 2 parallel randomized, clinical trials to address those questions.

METHODS

Recruitment of Participants, Evaluation, and Eligibility

The present trials were conducted at Children's Hospital of Pittsburgh between April 1982 and March 1994, and were approved annually by the hospital's Human Rights Committee. Participants were recruited from among hospital outpatients and from among children referred by community practitioners or directly by parents. Details have previously been reported regarding initial evaluation of children, study exclusion criteria, and procedures regarding informed consent and surgery.[3–6] Specifically excluded from the present trials were children who met the eligibility criteria of our earlier tonsillectomy trials[3] and children judged to require prompt removal of large tonsils or adenoids because of obstructive symptoms.

To be eligible for the trials, children were required to be 3 to 15 years of age and to have had a history of recurrent episodes of throat infection (ie, tonsillitis, pharyngitis, or tonsillopharyngitis) that met standards slightly less stringent than the standards used in our earlier trials regarding either the frequency of previous episodes or their clinical features or their degree of documentation, but not regarding >1 of these parameters. The reduced standards are shown in detail in the Appendix. The standard in our earlier trials regarding the treatment of previous throat infection episodes was retained in the present trials.

Randomization, Trials, and Treatment Groups

Of 2174 children evaluated, 373 met eligibility criteria for the present trials either initially or after periods of observation (Fig 1). Of these, 45 were not enrolled because their parents withheld consent for them to be assigned randomly. The remaining 328 children were stratified into 2 history-related categories—those in whom either the frequency or the clinical features of previous episodes were below the levels required for eligibility in our earlier trials, and those in whom only documentation of previous episodes was below the required level—and further stratified into 3 age categories—3 and 4 years, 5 and 6 years, and 7 to 15 years. Children who had no apparent indications for adenoidectomy (obstructing adenoids or histories of recurrent or persistent otitis media) were assigned randomly, within history and age categories and in balanced blocks of 3 children, to 1 of 3 treatment groups: tonsillectomy, adenotonsillectomy, or control (the 3-way trial). Children who had 1 or more such indications were assigned randomly, within history and age categories and in balanced blocks of 4 children, to 1 of 2 treatment groups: adenotonsillectomy or control (the 2-way trial). Assignments were made by designated nonclinical staff members using separate, computer-generated random number lists. Parents were advised that children assigned to nonsurgical treatment could subsequently receive surgery at parental request provided that the children continued to meet trial eligibility criteria.

Surgery, Follow-up, and Definition and Rating of Throat Infection Episodes

All operations were performed or supervised by a study-team otolaryngologist; standard surgical techniques were used.[3,7] Follow-up procedures have been described previously.[3] These included standardized inquiries about day-to-day status biweekly, and standardized clinical assessments by study-team pediatric nurse practitioners and/or pediatricians at 6-week intervals and at the time of acute illnesses. Definition of a throat-infection episode was based on specified criteria that are not presented in full here because of their detail but are available from the authors. Each diagnosed episode was rated "mild," "moderate," or "severe" on the basis of a scoring system whose details are available from the authors. The system involved assigning a score of 0, 1, or 2, with the score increasing as severity increased, to each of 5 elements: the degree of sore throat complaint, the maximum recorded oral temperature, the degree of malaise or reduced activity, the degree of erythema of the tonsils and/or pharynx, and the degree of anterior cervical lymphadenopathy. If the resulting total score totaled 2 or less, the episode was rated "mild"; if 3 to 5, "moderate"; and if 6 or more, "severe."

Management of Throat Infection

Details of management have been described previously.[3] Penicillin V potassium or, in the case of allergy to penicillin, erythromycin, was prescribed in conventional dosage for children with episodes of throat infection that were culture-positive for group A streptococci. For children in whom streptococcal infection persisted or recurred soon after treatment, penicillin was prescribed in larger doses or for longer periods or was administered intramuscularly, or clindamycin, penicillin combined with rifampin, or amoxicillin-clavulanate was prescribed.

Nontrial Comparison Group of More Severely Affected Children

Beginning in 1985, we enrolled and followed according to the present trials' protocol a group of children who met the more stringent eligibility criteria of our earlier trials and who were offered tonsillectomy, but whose parents declined surgery. Our objectives were to determine whether these more severely affected children would develop levels of illness comparable to those of children in the control group of our earlier randomized trial, and also to compare the levels of illness developed by the more affected children with the levels developed by children in the control groups of the present trials.

Statistical Analysis

The primary outcome measure was the occurrence of episodes of throat infection during each of 3 successive follow-up years, categorized according to their clinical features in the same fashion as in our earlier trials.[3] The estimate of sample size for the present trials was 61 children per treatment group. Secondary outcome measures were the occurrence of cervical lymphadenopathy at nonthroat-infection visits, the number of sore-throat days, and the number of days of sore-throat-associated school absence. Except

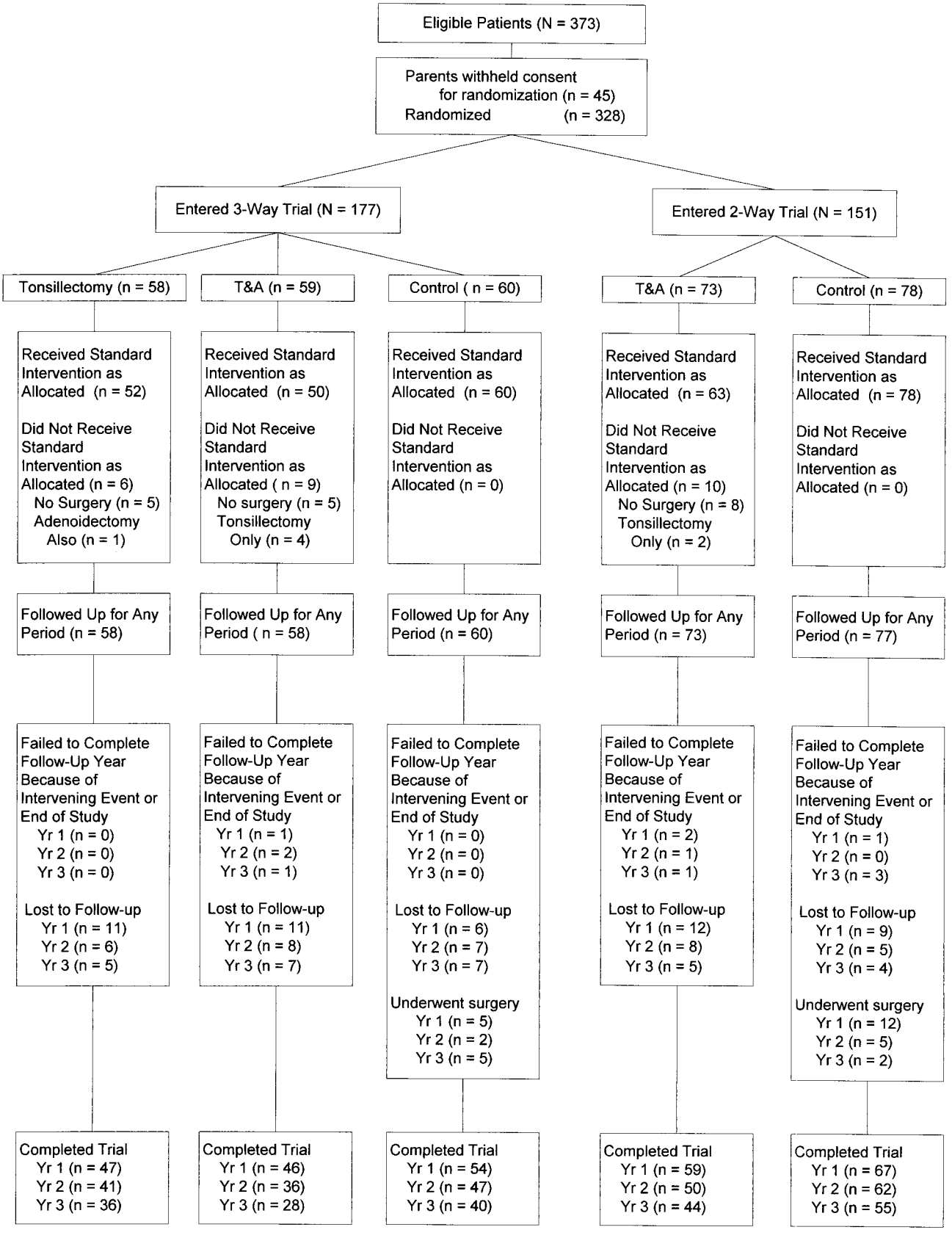

Fig 1. Flow diagram showing progress through the 2 trials. In the 3-way trial, 4 children assigned to undergo adenotonsillectomy were found at operation to have scant adenoid tissue and underwent tonsillectomy only. During follow-up, tonsillectomy was eventually elected for 5 children in the control group, and adenotonsillectomy for 7 children in the control group. Of these 12 children, 3 were lost to follow-up in the third follow-up year. In the 2-way trial, 2 children assigned to undergo adenotonsillectomy underwent tonsillectomy only because of intraoperative bleeding. During follow-up, tonsillectomy was eventually elected for 4 children in the control group, and adenotonsillectomy for 15 children in the control group, 1 of whom had developed a peritonsillar abscess. Of these 19 children, 1, 2, and 4 children were lost to follow-up in the first, second, and third follow-up years, respectively. "Intervening events" refers to the occurrence of other illness or the institution of antimicrobial prophylaxis for nonstudy-related reasons.

where otherwise indicated, outcome data were derived from children's experiences in whole-year blocks. We analyzed outcome data in both the intention-to-treat and the pragmatic mode.[8,9] All statistical tests were 2-tailed, and we set statistical significance at $P < .05$. We used χ^2 tests to test for differences between proportions, and analysis of variance to test for differences between mean values. In comparing mean percentages of visits, we first applied an arcsine transformation. We compared mean rates of occurrence of episodes of throat infection by assuming a Poisson distribution[10] and applying a generalized linear model.[11] We also assumed a Poisson distribution in calculating 95% confidence intervals for the rates.[12] We summarized times to first occurrence of episodes of throat infection in life-table analyses and compared them using the log rank test.[13,14] For children whose status changed–either through loss to follow-up or, in children assigned to a control group, through receipt of surgery–we used proportional hazards models[15] to compare throat infection rates before the change in status with mean rates in the children's respective treatment groups as a whole during corresponding periods.

RESULTS

Assignment to Treatment Groups, Status Change, Follow-up, Children's Characteristics, and Comprehensiveness of Surveillance

Figure 1 shows the progress of children through the 2 trials. Of the 328 enrolled children, 177 were eligible for the 3-way trial and 151 for the 2-way trial. Eighteen children assigned to surgical treatment groups in the 2 trials were withdrawn by parents without undergoing surgery; 1 participant assigned to control status was withdrawn. Thirty-one control children in the 2 trials eventually underwent surgery at parental request, 12 in the 3-way trial and 19 in the 2-way trial.

Selected demographic and clinical characteristics of children in the 2 trials are summarized in Table 1. These children differed from those whose parents withheld consent for randomization only in that proportionately fewer of the randomized children's parents were executives or professionals (21.3% vs 38%; $P = .02$). By design, none of the children in the 3-way trial had nasal obstruction attributable to large adenoids. Within each trial, there were no statistically significant differences in characteristics between surgical and control groups. Operations were performed within 90 days after assignment in 79% of the children assigned to the tonsillectomy group and 78.8% of the children assigned to the adenotonsillectomy groups. During the 3 whole follow-up years, respectively, the mean numbers of days for which

TABLE 1. Distribution of Children in the 3-Way Trial, the 2-Way Trial, and the Nontrial Comparison Group, According to Selected Demographic and Clinical Characteristics*

Characteristic	3-Way Trial			2-Way Trial		Nontrial Comparison Group ($n = 14$)
	Tonsillectomy Group ($n = 58$)	Adenotonsillectomy Group ($n = 59$)	Control Group ($n = 60$)	Adenotonsillectomy Group ($n = 73$)	Control Group ($n = 78$)	
	Number of Children (%)					
Age (y)						
3–4	8 (13.8)	4 (6.8)	7 (11.7)	13 (17.8)	13 (16.7)	2 (14.3)
5–6	9 (15.5)	13 (22.0)	11 (18.3)	24 (32.9)	26 (33.3)	5 (35.7)
7–15	41 (70.7)	42 (71.2)	42 (70.0)	36 (49.3)	39 (50.0)	7 (50.0)
Sex						
Female	28 (48.3)	39 (66.1)	39 (65.0)	47 (64.4)	43 (55.1)	9 (64.3)
Male	30 (51.7)	20 (33.9)	21 (35.0)	26 (35.6)	35 (44.9)	5 (35.7)
Race						
White	50 (86.2)	55 (93.2)	56 (93.3)	58 (79.5)	67 (85.9)	13 (92.9)
Black/other	8 (13.8)	4 (6.8)	4 (6.7)	15 (20.5)	11 (14.1)	1 (7.1)
Eligibility criteria less stringent than in earlier trials[3] regarding						
Frequency or clinical features of previous episodes	29 (50.0)	32 (54.2)	27 (45.0)	34 (46.6)	36 (46.2)	NA
Documentation of previous episodes	29 (50.0)	27 (45.8)	33 (55.0)	39 (53.4)	42 (53.8)	NA
Infection-free size of tonsils at entry[16]						
1+	4 (6.9)	4 (6.8)	6 (10.0)	1 (1.4)	6 (7.7)	1 (7.1)
2+	28 (48.3)	25 (42.4)	29 (48.3)	31 (42.5)	32 (41.0)	8 (57.1)
3+	23 (39.7)	28 (47.5)	22 (36.7)	34 (46.6)	34 (43.6)	5 (35.7)
4+	2 (3.4)	0 (0.0)	2 (3.3)	6 (8.2)	6 (7.7)	0 (0.0)
Not observed	1 (1.6)	2 (3.4)	1 (1.7)	1 (1.4)	0 (0.0)	0 (0.0)
Nasal obstruction attributable to large adenoids†						
Any	0 (0.0)	0 (0.0)	0 (0.0)	55 (75.3)	58 (74.4)	0 (0.0)
None	58 (100)	59 (100)	60 (100)	18 (24.7)	20 (25.6)	14 (100)
Siblings						
Any	47 (81.0)	47 (79.7)	50 (83)	58 (79.5)	63 (80.8)	10 (71.4)
None	11 (19.0)	10 (16.9)	9 (15)	15 (20.5)	15 (19.2)	4 (28.6)
Unknown	0 (0.0)	2 (3.4)	1 (2)	0 (0.0)	0 (0.0)	0 (0.0)
Parents' socioeconomic status						
Executive or professional	15 (25.9)	10 (16.9)	20 (33)	10 (13.7)	15 (19.2)	4 (28.6)
Other employed	36 (62.1)	39 (66.1)	29 (48)	50 (68.5)	51 (65.4)	7 (50.0)
Disabled, public assistance, unemployed, other	7 (12.1)	10 (16.9)	11 (18)	13 (17.8)	12 (15.4)	3 (21.4)

NA indicates not applicable.
* Because of rounding, percentages may not total 100. None of the within-trial, between-group comparisons were statistically significant.
† Based on combined clinical and radiographic assessment.[17]

TABLE 2. Episodes of Throat Infection According to Trial, Whole Follow-up Year, Type of Episode, and Treatment Group

Type of Episode*	Treatment Group	3-Way Trial				2-Way Trial			
		Number of Subjects	Number of Episodes per Year		*P* Value†	Number of Subjects	Number of Episodes per Year		*P* Value†
			Range	Mean (95% Confidence Interval)			Range	Mean (95% Confidence Interval)	
Follow-up year 1‡									
All types combined	Tonsillectomy	47	0–7	1.96 (1.58–2.40)	.02	—	—	—	—
	Adenotonsillectomy	46	0–8	1.85 (1.51–2.34)	.001	59	0–6	1.90 (1.56–2.28)	<.001
	Control	54	0–8	2.78 (2.35–3.26)	—	67	0–10	3.60 (3.16–4.08)	—
Counting	Tonsillectomy	47	0–4	0.94 (0.68–1.26)	<.001	—	—	—	—
	Adenotonsillectomy	46	0–2	0.76 (0.54–1.08)	<.001	59	0–4	1.02 (0.78–1.31)	<.001
	Control	54	0–6	1.78 (1.44–2.17)	—	67	0–7	2.22 (1.88–2.61)	—
Group A β-Strep	Tonsillectomy	47	0–4	0.53 (0.34–0.79)	.18	—	—	—	—
	Adenotonsillectomy	46	0–2	0.37 (0.22–0.60)	.005	59	0–2	0.39 (0.25–0.58)	.003
	Control	54	0–4	0.81 (0.59–1.09)	—	67	0–4	0.84 (0.63–1.09)	—
Moderate or severe	Tonsillectomy	47	0–2	0.17 (0.07–0.34)	.62	—	—	—	—
	Adenotonsillectomy	46	0–1	0.09 (0.02–0.23)	.053	59	0–2	0.15 (0.07–0.29)	.003
	Control	54	0–1	0.24 (0.13–0.41)	—	67	0–3	0.43 (0.29–0.62)	—
Follow-up year 2‡									
All types combined	Tonsillectomy	41	0–9	1.59 (1.22–2.02)	<.001	—	—	—	—
	Adenotonsillectomy	36	0–8	1.78 (1.37–2.27)	<.001	50	0–7	1.74 (1.42–2.19)	<.001
	Control	47	0–8	2.85 (2.39–3.38)	—	62	0–8	2.89 (2.48–3.34)	—
Counting	Tonsillectomy	41	0–5	0.78 (0.53–1.10)	<.001	—	—	—	—
	Adenotonsillectomy	36	0–2	0.47 (0.28–0.76)	<.001	50	0–4	0.72 (0.51–1.02)	<.001
	Control	47	0–7	1.70 (1.35–2.12)	—	62	0–6	1.66 (1.36–2.02)	—
Group A β-Strep	Tonsillectomy	41	0–3	0.22 (0.10–0.42)	<.001	—	—	—	—
	Adenotonsillectomy	36	0–1	0.17 (0.06–0.36)	<.001	50	0–3	0.36 (0.22–0.58)	.006
	Control	47	0–4	0.77 (0.54–1.06)	—	62	0–4	0.76 (0.56–1.01)	—
Moderate or severe	Tonsillectomy	41	0–3	0.15 (0.05–0.32)	.07	—	—	—	—
	Adenotonsillectomy	36	0–1	0.06 (0.01–0.20)	.007	50	0–1	0.06 (0.01–0.18)	.002
	Control	47	0–4	0.38 (0.23–0.61)	—	62	0–3	0.31 (0.18–0.48)	—
Follow-up year 3‡									
All types combined	Tonsillectomy	36	0–8	1.19 (0.89–1.66)	<.002	—	—	—	—
	Adenotonsillectomy	28	0–5	1.36 (0.96–1.86)	.01	44	0–7	1.48 (1.17–1.93)	.002
	Control	40	0–5	2.25 (1.90–2.91)	—	55	0–8	2.38 (2.03–2.88)	—
Counting	Tonsillectomy	36	0–2	0.36 (0.02–0.64)	<.001	—	—	—	—
	Adenotonsillectomy	28	0–3	0.46 (0.25–0.79)	<.001	44	0–4	0.39 (0.23–0.63)	<.001
	Control	40	0–4	1.33 (1.05–1.82)	—	55	0–6	1.29 (1.03–1.66)	—
Group A β-Strep	Tonsillectomy	36	0–1	0.17 (0.06–0.37)	<.001	—	—	—	—
	Adenotonsillectomy	28	0–1	0.21 (0.08–0.47)	.003	44	0–1	0.11 (0.04–0.27)	<.001
	Control	40	0–4	0.75 (0.53–1.13)	—	55	0–4	0.71 (0.51–0.99)	—
Moderate or severe	Tonsillectomy	36	0–0	0.00 (0.00–0.11)§	<.001	—	—	—	—
	Adenotonsillectomy	28	0–1	0.11 (0.02–0.31)	.22	44	0–0	0.00 (0.00–0.09)	.002
	Control	40	0–2	0.28 (0.14–0.52)	—	55	0–1	0.16 (0.08–0.32)	—
Follow-up years 1–3‡									
All types combined	Tonsillectomy	36	—	1.55 (1.33–1.82)	<.001	—	—	—	—
	Adenotonsillectomy	28	—	1.63 (1.37–1.93)	<.001	44	—	1.74 (1.54–2.00)	<.001
	Control	40	—	2.77 (2.52–3.13)	—	55	—	2.93 (2.69–3.22)	—
Counting	Tonsillectomy	36	—	0.67 (0.53–0.85)	<.001	—	—	—	—
	Adenotonsillectomy	28	—	0.56 (0.41–0.74)	<.001	44	—	0.68 (0.55–0.84)	<.001
	Control	40	—	1.69 (1.49–1.97)	—	55	—	1.73 (1.54–1.95)	—
Group A β-Strep	Tonsillectomy	36	—	0.29 (0.20–0.41)	<.001	—	—	—	—
	Adenotonsillectomy	28	—	0.20 (0.12–0.32)	<.001	44	—	0.29 (0.21–0.40)	<.001
	Control	40	—	0.82 (0.67–1.01)	—	55	—	0.77 (0.65–0.92)	—
Moderate or severe	Tonsilectomy	36	—	0.09 (0.04–0.17)	.002	—	—	—	—
	Adenotonsillectomy	28	—	0.08 (0.03–0.17)	.003	44	—	0.07 (0.03–0.13)	<.001
	Control	40	—	0.33 (0.24–0.45)	—	55	—	0.28 (0.21–0.37)	—

* Counting episodes were those that met the clinical-features standard of our earlier trials.[3] See text for details. β Strep denotes beta-hemolytic streptococcal.
† *P* values refer to the comparison with the corresponding control group value. Comparisons include adjustment for stratification variables (eligibility criteria and age group) and gender.
‡ Not included in the table are data derived from experiences of less than a whole year (ie, 12 calendar months) of follow-up (although those data are included in analyses described in the text for the 3 follow-up years combined).
§ *P* = .01 for the comparison with the corresponding adenotonsillectomy value. The comparison includes adjustment for stratification variables and gender.

follow-up information concerning daily status was recorded for children in the various treatment groups ranged from 348 to 356. None of the surgical-versus-control differences in these values were statistically significant. The mean numbers of visits per follow-up year ranged from 8.3 to 10.6 in surgical groups and from 9.3 to 11.8 in control groups. Adenotonsillectomy-versus-control differences in these values were significant in the 3-way trial in the first follow-up year (9.3 vs 10.4; $P < .05$) and in the 2-way

trial in the first 2 follow-up years (10.6 vs 11.8; $P = .02$; and 8.9 vs 10.2; $P < .01$).

Occurrence of Observed Episodes of Throat Infection

Data on the occurrence of observed throat-infection episodes in the present trials during children's first, second, and third whole years of follow-up are summarized in Table 2. All results presented are derived from intention-to-treat analyses; pragmatic analyses gave similar results. Consistently in both the 3-way and the 2-way trial, outcomes were significantly more favorable in children in the surgical groups than in children in the corresponding control groups. However, illness rates in children in the control groups were modest, particularly in regard to throat-infection episodes rated as moderate or severe. For example, in the 2 trials, the proportion of children in the control groups in whom any moderate or severe episodes occurred in a given follow-up year ranged from 16% to 30%, and in the children in the 2 control groups, the proportions of all episodes over the 3-year follow-up period that were rated as moderate or severe were 11.3% and 10.5%, respectively. The results of analyses for the 3 follow-up years combined were consistent with the year-by-year results. So also were the results of life-table analyses which, unlike the data summarized in Table 2, incorporated data from fractional-year experiences.

Effects of Status Change and Loss to Follow-up

In both trials, among the control children who eventually underwent surgery, mean rates of throat infection during the follow-up periods preceding the surgery were modestly higher than rates during the corresponding periods in the control groups as a whole, although in no instances were the differences statistically significant. Among children both in surgical groups and in control groups who were lost to follow-up, rates of throat infection during the follow-up periods preceding the loss did not differ appreciably from the corresponding rates in the respective treatment groups as a whole.

To assess the potential impact of these events, we performed sensitivity analyses using extreme assumptions concerning throat infection rates that might have prevailed throughout the 3-year follow-up period had these events not occurred. Specifically, to each control child who underwent surgery we applied that child's throat infection rate during the period preceding the surgery to the remaining portion of the 3-year follow-up period. To the children in surgical groups (including those who failed to undergo surgery) who were lost to follow-up, we applied a uniform zero event rate from the time of loss to the end of the 3-year follow-up period. And to the children in control groups who were lost to follow-up we applied the rates of control children who remained under surveillance. These analyses predictably gave to children in surgical groups mean throat infection rates that were generally lower than those shown in Table 2, and to control children, mean rates that were higher than those shown in Table 2. The largest resultant decrease in mean rate per year in children in the 3 surgical groups was 0.49 episode of all types combined, 0.13 counting episode, 0.05 streptococcal episode; and 0.02 moderate or severe episode. In children in the 2 control groups, the largest resultant increase was 0.71 episode of all types combined, 0.63 counting episode, 0.25 streptococcal episode, and 0.22 moderate or severe episode.

Nontrial Comparison Group

Fourteen children constituted the nontrial comparison group who met the eligibility criteria of our earlier trials, whose parents initially declined tonsillectomy, and whom we followed concurrently with the children in the present trials. Of these 14 children, 5 (36%) received tonsillectomy at parental request during their first follow-up year, a change in status that precluded analysis of their throat infection rates after the first follow-up year. Within that year, however, mean rates in the 14 children, compared with rates in control children in the 3-way trial and the 2-way trial, respectively, were as follows: for episodes of all types combined, 4.43 versus 2.78 and 3.60, (P values .003 and .15); for counting episodes, 3.43 versus 1.78 and 2.22, (P values $<.001$ and .01); for streptococcal episodes, 0.86 versus 0.81 and 0.84, (P values .88 and .94); and for moderate or severe episodes, 1.14 versus 0.24 and 0.43, (P values $<.001$ and .003).

Secondary Outcome Measures

Table 3 summarizes data concerning the 3 secondary outcome measures of throat-related illness. Results were generally more favorable in surgical than in control groups, although many of the surgical-versus-control differences were not statistically significant.

Complications and Untoward Reactions

Of the 203 children who underwent tonsillectomy or adenotonsillectomy, 16 (7.9%) had intraoperative or postoperative complications. One child developed anesthetic induction trismus and possible incipient malignant hyperthermia. Three children had intraoperative hemorrhage; 1 of these children underwent reexploration under anesthesia and ligation at the tonsillar site and was hospitalized for 8 days, 1 child received a posterior nasopharyngeal pack and was admitted to the intensive care unit for 48 hours, and 1 child was retained in hospital 1 additional day. Seven children developed hemorrhage 2 days to 2 weeks postoperatively; 5 of these children were readmitted to hospital for periods of 1 to 3 days, and 1 of the 5 received a transfusion of packed red blood cells because of a fall in hemoglobin concentration to 6.9 g/dL. The mean reported duration of postoperative sore throat was 6.3 days (range: 0–21 days). Four children in surgical groups and 3 children in control groups developed an erythematous rash while receiving an antimicrobial drug, in 2 of the instances prescribed for throat infection.

DISCUSSION

We undertook the present trials mainly to assess the efficacy of tonsillectomy in children who were

TABLE 3. Cervical Lymphadenopathy at Non-Throat-Infection Visits, Sore-Throat Days, and Sore-Throat-Associated School Absence, According to Trial, Whole Follow-up Year, and Treatment Group*

Follow-up Year	Treatment Group	Cervical Lymphadenopathy Found at Non-Throat-Infection Visits		Sore-Throat Days†		Sore-Throat-Associated School Absence‡	
		3-Way Trial	2-Way Trial	3-Way Trial	2-Way Trial	3-Way Trial	2-Way Trial
		Percentage of Non-Throat-Infection Visits		mean ± SD (Number of Days per Year)		mean ± SD (Number of Days per Year)	
First	Tonsillectomy	2.1 (47)	—	20 ± 14 (48)	—	3.3 ± 4.0 (42)‖	—
	Adenotonsillectomy	1.6 (46)	2.6 (59)§	19 ± 15 (47)	23 ± 20 (60)	3.9 ± 3.7 (44)	3.5 ± 4.2 (52)¶
	Control	2.7 (54)	7.1 (67)	25 ± 21 (54)	24 ± 17 (68)	5.3 ± 4.7 (50)	6.6 ± 6.2 (58)
Second	Tonsillectomy	0.3 (41)§	—	12 ± 14 (43)¶	—	3.2 ± 3.9 (39)	—
	Adenotonsillectomy	1.6 (36)	1.1 (50)§	12 ± 14 (38)¶	13 ± 19 (50)‖	2.4 ± 3.2 (38)‖	3.2 ± 4.1 (47)
	Control	2.6 (47)	4.6 (62)	21 ± 16 (47)	20 ± 18 (60)	5.0 ± 5.2 (44)	5.4 ± 6.7 (56)
Third	Tonsillectomy	0.3 (36)	—	8 ± 11 (37)¶	—	2.5 ± 3.2 (37)	—
	Adenotonsillectomy	0.9 (28)	0.6 (44)§	9 ± 9 (30)¶	12 ± 13 (44)	2.9 ± 2.9 (29)	2.6 ± 3.4 (45)
	Control	1.3 (40)	4.3 (55)	19 ± 15 (41)	16 ± 17 (55)	3.7 ± 3.2 (42)	4.2 ± 5.2 (55)

* Numbers in parentheses denote numbers of children.
† Limited to children with at least 270 days of reportage in a follow-up year. Includes sore-throat days immediately after surgery. The number of days for each child for each follow-up year was standardized on the basis of 365 days.
‡ Limited to children 5 years of age or older with at least 130 days of reported school attendance or absence in a follow-up year. School absence immediately after surgery was excluded. The number of days for each child for each follow-up year was standardized on the basis of a 180-day school year.
§ $P \leq .01$ for the comparison with the corresponding control group mean value, with each child's value having been weighted by the child's number of visits.
‖ $P < .05$ for the comparison with the corresponding control group mean value.
¶ $P < .01$ for the comparison with the corresponding control group mean value.

less severely affected with recurrent throat infection than the children in our earlier trials,[3] but who had indications for tonsillectomy comparable to those in general use. A secondary goal was to determine whether, in such children who had no specific indications for adenoidectomy, the common practice nonetheless of adding adenoidectomy to tonsillectomy would offer additional benefit. To match circumstances in clinical practice, we constructed eligibility criteria for the trials that encompassed all types of episodes, weighted in ways that seemed clinically logical.

In the present trials, as in our earlier trials,[3] we found tonsillectomy to be effective in reducing the occurrence of throat infection. The results in the present trials were similar to those in our earlier randomized trial with 1 main exception: the rates of moderate or severe episodes of throat infection in the present trials among children in the control groups were considerably lower than corresponding rates in the earlier trial. Specifically, the mean numbers of moderate or severe episodes in control children in the earlier trial, based on the pragmatic (rather than intention-to-treat) analysis used, were 1.17, 1.03, and 0.45 in the first, second, and third follow-up years, respectively, whereas the corresponding values based on pragmatic analysis in the present 3-way trial were 0.22, 0.40, and 0.26, and in the present 2-way trial were 0.34, 0.38, and 0.16. (Note that most of these values for control children in the present trials differ slightly from the values shown in Table 2, which were derived from intention-to-treat analysis.) Another difference between the results of the present trials and those of the earlier trial concerns the proportion of nonthroat-infection visits at which cervical lymphadenopathy was found: among children in control groups in the present trials the proportions were much smaller than in control children in our earlier trial.

Finally, in the present 3-way trial, outcomes in children undergoing adenotonsillectomy were not more favorable than outcomes in children undergoing tonsillectomy only. The rate of intraoperative and postoperative complications in the present trials was substantial, but somewhat lower than rates found in children in our previous trials who underwent tonsillectomy.[3,18]

That the lesser illness experience of control children in the present trials, compared with that of control children in our earlier trial, was a consequence of lesser proneness to illness—as forecast by the less stringent eligibility criteria met by these children—rather than because of chance or extraneous or secular factors, is suggested by the substantially higher rates of throat infection experienced in their first follow-up year by the 14 children in the concurrently studied nontrial comparison group who met the more stringent criteria of our earlier trials.

Certain considerations regarding the study's findings deserve attention. First, as suggested by the sensitivity analyses described earlier, the receipt of surgery by some of the control children and the loss to follow-up of some of the children in each of the treatment groups may have resulted in an underestimation, by the trials' results, of the true effect of surgery on the occurrence of episodes of throat infection. Nonetheless, even under the extreme assumptions used in the sensitivity analyses—ie, "best-case" scenario for children in surgical groups and "worst-case" scenario for control children—the resultant differences in throat infection rates, in comparison with the rates found in the intention-to-treat analyses, were small. Most notably was this so in regard to the rates of moderate or severe episodes. It

is also the case that the control children who underwent surgery generally did so because they were continuing to have episodes of throat infection. Thus, they were coming to meet the eligibility criteria of our earlier trials and thereby, in our view, would become reasonable candidates for surgery.

Second, one might speculate that if the trials' close monitoring and prompt application of treatment were in themselves beneficial, children in the control groups may have benefited disproportionately, because those treated surgically had less illness and therefore less need for care. If that were the case, the effectiveness of surgery in nonresearch settings might be greater than indicated by our findings. On the other hand, if the trials' close monitoring resulted mainly in better identification of mild episodes of throat infection, such episodes would have been identified more often among children in the control groups than among children in the surgical groups, in which case the relative effectiveness of surgery in nonresearch settings might appear less than was indicated by our findings. In either case, it seems unlikely that the differences would be substantial.

How should our findings be applied? All of the children we studied met criteria that were more stringent than the criterion in the current official guidelines for tonsillectomy or adenotonsillectomy cited earlier. Nonetheless, the degree of benefit conferred by either operation in these children was modest, and appears not justify the inherent risks,[19] morbidity, and cost of the operations. Accordingly, we conclude that, under ordinary circumstances, neither eligibility criteria such as those we used for the present trials nor the criterion for surgery in the above-cited official guidelines are sufficiently stringent for use in clinical practice. Rather, the more stringent criteria of our earlier trials, as described earlier and summarized in the Appendix, would seem more suitable—but with the proviso, as discussed previously,[3] that application of even those more stringent criteria should be tempered by awareness of the substantial possibility of spontaneous improvement and by the need for individualized decision-making.

ACKNOWLEDGMENTS

This work was supported by grant HD 07403 from the National Institute of Child Health and Human Development. Inpatient charges and professional fees to subjects' parents who lacked insurance coverage were waived by the Children's Hospital of Pittsburgh and the Departments of Anesthesiology and Otolaryngology.

We are indebted to the many Children's Hospital of Pittsburgh house officers and Pittsburgh-area practitioners who referred patients for the study; a complete listing would exceed space limitations. We are especially grateful to James G. Hawkins, MD, Abdul Hameed Mahsoob, MD (deceased), Maribel McKelvy, MD, Howard A. Mermelstein, MD (deceased), Bernard I. Michaels, MD, William R. Nichols, MD, K. Gopalkrishna Pai, MD, H. Richard Paul, MD, and Harvey M. Rubin, MD, who also made their office facilities and patient files available.

Kenneth D. Rogers, MD (deceased), and Floyd H. Taylor, ScD, assisted with study design, planning, and data analysis. Sylvan F. Stool, MD, served as otolaryngological consultant and supervisor. The following people also assisted in the conduct of this study: Julie Hughes, Carol Saez-Henry, Ida H. Smith, and Kimberly A. Zoelle (follow-up interviewers); Ruth Z. Bachman, RN, BS, Kathleen M. DiGaudio, RN, PhD, Connie R. Dudek, RN, and Edwarda O. Lee, RN, MA, (nurse practitioners); Omar Ali, MD, Bruce Bedingfield, DO, Steven D. Blatt, MD, Paul V. Catalana, MD, Han-Pu Chao, MD, Cindy Feidt Gavula, MD, S. Nasrin Ghorbanian, MD, Lynne M. Haverkos, MD, Ingrid Y. Henar, MD, Alejandro Hoberman, MD, Dena Hofkosh, MD, David M. Keller, MD, Christine B. Koerner, MD, Arthur J. Kovel, MD, James M. Lewis, MD, Ellen M. Mandel, MD, Susan L. Martini, MD, Joan M. Mavrinac, MD, MPH, Denise M. Medwick, DO, Patricia S. Miller, MD, Karuna T. Ratanabanangkoon, MD, Mildred Kinghorn Romberger, MD, Bruce W. Rosenthal, MD, Alison C. Selbst, MD, Madeline Simasek, MD, Carol F. Truitt, MD, and Jacob Urkin, MD (pediatricians); Margaretha L. Casselbrant, MD, Margaret A. Kenna, MD, James S. Reilly, MD, and John S. Supance, MD (otolaryngologists); Sheryl M. Neely, RN, BSN (allergy nurse); Lionel W. Young, MD, (radiologic consultant); Gilbert A. Friday, MD and Bruce S. Rabin, MD (immunologic consultants); Sharon Caputo (deceased), Charlotte M. Heller, Lori L. McLaughlin, Robert H. Schwarzbach, MSIS, Stephen T. Sefcik, BS, and Hsiao-Lan Wei, MS (data processing); Jennifer Dietrich, Deirdre Glenn, Sybilla M. Hagan (deceased), Carolyn M. Harman, Paul S. Kramer, MHA, Judy Z. Lincoff, and Clyde G. Smith, MS (administration).

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APPENDIX. Number, Type, and Documentation of Previous Episodes of Throat Infection in Relation to Eligibility for the Earlier Trials[3] and the Present Trials

Age, Years	Required History of Episodes*	Required Documentation of Episodes
Earlier trials[3]		
3 to 15	≥7 counting episodes in past 1 y, or ≥5 counting episodes in each of past 2 y, or ≥3 counting episodes in each of past 3 y	Each episode and its qualifying features substantiated by concurrent notation in a clinical record or At least 2 counting episodes observed by a study-team clinician within the expected time frame†
Present trials		
	Less Stringent Criteria Regarding Number and Type of Episodes	
3 to 6	5 or 6 qualifying units‡ in past 1 y, including at least 2 counting episodes§ or 4 qualifying units in each of past 2 y, including at least 2 counting episodes in each y§	For at least 2 qualifying units in past 1 y, notation in a clinical record indicating a clinical diagnosis of throat infection or For 1 qualifying unit in past 1 y, notation in a clinical record indicating a clinical diagnosis of throat infection; and also 1 qualifying unit observed by a study-team clinician within the expected time frame‖
7 to 15	4 to 6 qualifying units in past 1 y, including at least 1 counting episode§ or 3 qualifying units in each of past 2 y, including at least 1 counting episode in each y§	or At least 2 qualifying units observed by a study-team clinician within the expected time frame‖
	Less Stringent Criteria Regarding Documentation of Episodes	
3 to 15	≥7 counting episodes in past 1 y, or ≥5 counting episodes in each of past 2 y, or ≥3 counting episodes in each of past 3 y	Previous episodes must have been wholly or in part undocumented. If all previous episodes were undocumented, 1 qualifying unit observed by a study-team clinician within 4 months after initial evaluation. If previous episodes were partially documented, notation in a clinical record indicating the occurrence of 1 qualifying unit within the 3-mo period preceding initial evaluation provided that the number of undocumented counting episodes was >7 in the past 1 y or >5 in each of the past 2 y or >3 in each of the past 3 y

* Previous episodes of throat infection were classified on the basis of information obtained from parents or from medical records. "Counting" episodes were those characterized by 1 or more of the following features: oral temperature of at least 38.3°C; cervical lymphadenopathy (enlarged [>2 cm] or tender cervical lymph nodes); tonsillar or pharyngeal exudate; or a positive culture for Group A beta-hemolytic streptococcus. "Intermediate" episodes were those without any features of counting episodes, but with oral temperature estimated or recorded above 37.0°C but below 38.3°C. "Minor" episodes were those with a complaint of sore throat, but without any features of counting episodes or apparent fever.

† For example, if there had been a history of 5 episodes in each of the 2 preceding years, 2 episodes would have had to be observed within 2/5 year, ie, 146 days.

‡ A qualifying unit consisted of 1 counting episode, or 2 intermediate episodes, or 3 minor episodes, or 1 intermediate and 2 minor episodes.

§ The specified number of qualifying units could be exceeded only if the excess consisted only of intermediate or minor episodes.

‖ For example, if there had been a history of 4 episodes in 1 year, 2 qualifying units would have to have been observed within 6 months.

Tonsillectomy and Adenotonsillectomy for Recurrent Throat Infection in Moderately Affected Children

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Pediatrics 2002;110;7-15
DOI: 10.1542/peds.110.1.7