Adenotonsillectomy or Watchful Waiting in Patients With Mild to Moderate Symptoms of Throat Infections or Adenotonsillar Hypertrophy

A Randomized Comparison of Costs and Effects

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Objective: To evaluate the cost-effectiveness of adenotonsillectomy compared with watchful waiting in Dutch children.

Design: Economic evaluation along with an open, randomized, controlled trial.

Setting: Multicenter, including 21 general and 3 university hospitals in the Netherlands.

Participants: Three hundred children aged 2 to 8 years were selected for adenotonsillectomy according to routine medical practice. Excluded were children who had frequent throat infections and those with suspected obstructive sleep apnea.

Main Outcome Measures: Incremental cost-effectiveness in terms of costs per episode of fever, throat infection, and upper respiratory tract infection avoided.

Results: Annual costs incurred in the adenotonsillectomy group were €803 (the average exchange rate for the US dollar in 2002 was $1.00=€1.1, except toward the end of 2002 when $0.95=€100) and €551 in the watchful waiting group (46% increase). During a median follow-up of 22 months, surgery compared with watchful waiting reduced the number of episodes of fever and throat infections by 0.21 per person-year (95% confidence interval, −0.12 to 0.54 and 0.06 to 0.36, respectively) and upper respiratory tract infections by 0.53 (95% confidence interval, 0.08 to 0.97) episodes. The incremental costs per episode avoided were €1136, €1187, and €465, respectively.

Conclusions: In children undergoing adenotonsillectomy because of mild to moderate symptoms of throat infections or adenotonsillar hypertrophy, surgery resulted in a significant increase in costs without realizing relevant clinical benefit. Subgroups of children in whom surgery would be cost-effective may be identified in further research.

Trial Registration: isrctn.org Identifier: ISRCTN04973569


In Western countries, tonsillectomy with or without adenoidectomy is among the most frequently performed surgical procedures in children. However, as may be inferred from the wide range of surgical incidences observed between countries, the indications and expected benefits are debated. In 1998, the Netherlands ranked high, with 115 adenotonsillectomies per 10,000 children compared with 65 per 10,000 children in England and 50 per 10,000 children in the United States. Preference for antibiotic therapy vs surgical management of upper respiratory tract infections may explain some of this variation. However, the lack of sound evidence about the balance between costs and effects of adenotonsillectomy compared with a conservative approach in children with mild to moderate symptoms of throat infections or adenotonsillar hypertrophy is also important. Historically, the reluctance of Dutch general practitioners to prescribe antibiotic therapy and the national notion that adenotonsillectomy may be considered minor surgery seems to have resulted in rather liberal indications for surgical intervention. Clearly, the considerable variation in practice may reflect either overtreatment or undertreatment, that is, suboptimal use of scarce health care resources. In the Netherlands, some 35% of children undergoing adenotonsillectomy have frequent throat infections (ie, ≥7 episodes in the previous year, ≥5 episodes in each of the previous 2 years, or ≥3 episodes in each of the previous 3 years) or...
obstructive sleep apnea. Conversely, the remaining 65% undergoing surgery have less frequent throat infections, milder symptoms of adenotonsillar hypertrophy, or other indications such as recurrent upper respiratory tract infections. Frequent throat infections and obstructive sleep apnea are generally recognized indications for tonsillectomy or adenotonsillectomy. However, in most children operated on in the Netherlands, the benefits are less clear. To resolve this issue, a randomized trial was conducted to compare the balance between costs and effects of adenotonsillectomy and watchful waiting in children with mild to moderate symptoms of throat infections, upper respiratory tract infections, or adenotonsillar hypertrophy.

METHODS

The design of the study has previously been reported. In brief, an open multicenter, randomized, controlled trial was conducted in 21 general hospitals and 3 university hospitals in the Netherlands between March 18, 2000, and February 28, 2003. Before enrollment, information about the indication to perform adenotonsillectomy was recorded for every child aged 2 to 8 years. The indications included recurrent throat infections (≥3) or other indications such as symptoms of obstruction or recurrent upper respiratory tract infections. Children with a history of frequent throat infections and those with a Brouillet obstructive upper respiratory tract infections. Children with a history of frequent throat infections or adenotonsillectomy or adentonsillar hypertrophy.

FOLLOW-UP

During the study, parents kept a diary of upper respiratory tract symptoms in their child. Sore throat, pain or difficulty with swallowing, cough, rhinorrhea, earache, and otitis media were recorded. Furthermore, the child's temperature was measured daily with a validated infrared tympanic membrane thermometer. To prevent information bias, an inbuilt device stored the date and first temperature measurement for each day. Both diary and thermometer data were collected by study physicians (B.v.S. and J.v.d.A.) during scheduled follow-up visits at 3, 6, 12, 18, and 24 months.

OUTCOME MEASURES

The primary measure of clinical effectiveness used for the economic evaluation was the number of episodes of fever avoided per person-year. Fever was defined as a body temperature of 38.0°C or higher as measured by the infrared tympanic thermometer for at least 1 day. Fever was measured in number of episodes and days. An episode ended when a child was free from fever (body temperature <38.0°C) for at least 1 day. A new episode of fever was recorded after a fever-free interval of at least 7 days.

Secondary measures of clinical effectiveness were throat and upper respiratory tract infections. A throat infection was defined as sore throat, pain or difficulty with swallowing, or both as indicated in the diary, in combination with fever measured with the tympanic thermometer. An upper respiratory tract infection was defined as including 1 or more of the following symptoms: cough, earache, sore throat, rhinorrhea, or difficulty with swallowing, and otitis media with or without fever. Symptoms of sore throat and upper respiratory tract infections occurring immediately after adenotonsillectomy were included in the outcomes.

In parallel with the clinical study, annual costs in euros (€) were estimated at the patient level for 2002. (The average exchange rate for the US dollar in 2002 was $1.00=€1.1, except toward the end of 2002 when $0.95=€1.00.) Resource use such as over-the-counter drug use and outpatient visits were recorded in the diaries, as were out-of-pocket expenses such as babysitters and travel expenses. The study physician verified diary entries during the follow-up visits and recorded interventions such as adenoidectomy or placement of tympanostomy tubes. The scheduled visits by the research physician were excluded from the cost analyses.

Costs were estimated from a societal perspective and retrieved from available sources when possible. When unavailable, unit costs were estimated in a separate bottom-up costing study. The costs of adenotonsillectomy, adenoidectomy, and placement of tympanostomy tubes as well as those associated with surgical complications were calculated based on resource use and personnel input as estimated in 7 participating hospitals. The costs associated with surgical complications were similarly estimated.

Costs of medication, including antibiotics, were derived from the Dutch Formulary and increased with a pharmacist fee. Costs of diagnostic tests were derived from the Dutch Diagnostic Formulary and, when relevant, increased with a technician charge. Costs of over-the-counter drugs and alternative medicines were based on average retail prices. Costs of consultation of a general practitioner or medical specialist or of other procedures and hospitalizations were based on current Dutch guidelines for pharmacoeconomic evaluation or charges if no other estimates were available. Indirect costs to society associated with leave of absence were estimated using the friction cost method.

Incremental costs per episode of fever, throat infection, and upper respiratory tract infection avoided were calculated. Incremental cost-effectiveness ratios were calculated by dividing the estimated differences in yearly cost rates by the differences in effect rates, that is, episodes avoided per person-year. For all analyses, only a short time horizon was used and, therefore, no time preference or discount rate was considered. Uncertainty was addressed by means of bootstrapping. The original trial data were used to replicate the trial 1000 times using a random sampler with replacement. Subsequently, the incremental costs and effects were estimated and plotted for each replicate, yielding a cost-effectiveness plane.

STATISTICAL ANALYSIS

Calculations of group size were based on a clinically relevant reduction of 25% in episodes of fever and throat infections after adenotonsillectomy. Assuming a mean (±SD) baseline incidence of 4 (±2) fever episodes and 4 (±2) throat infections per year, and taking α = 0.05 (2-tailed) and a power of 0.80, at least 104 children were required in each arm of the trial.
greater than 3.5 is highly predictive of OSA; score between −1 and 3.5 indicates breathing indicated.

Between March 1, 2000, and August 31, 2002, 300 children were enrolled; 151 were allocated to adenotonsillectomy and 149 to watchful waiting. Baseline characteristics did not differ between the adenotonsillectomy and watchful-waiting groups; mean age of the children was 54 months and the median number of throat infections in the previous year was 3 episodes in both groups; mean age of the children enrolled; 151 were allocated to adenotonsillectomy during follow-up and 7 children allocated to the adenotonsillectomy group did not undergo the operation. Median follow-up was similar in both groups: 22.0 months (range, 0.4-27.1 months) in the adenotonsillectomy group and 22.4 months (range, 1.5-26.5 months) in the watchful-waiting group.

The measures of clinical effect were calculated as incidence rate difference per person-year with 95% confidence interval. Overall cost rates were compared between the randomized groups. When relevant, differences were calculated, inclusive of 95% confidence intervals, using bootstrap replications. All analyses, inclusive of the economic evaluation, were performed on the basis of intention to treat.

### RESULTS

#### PATIENTS

Between March 1, 2000, and August 31, 2002, 300 children were enrolled; 151 were allocated to adenotonsillectomy and 149 to watchful waiting. Baseline characteristics did not differ between the adenotonsillectomy and watchful-waiting groups; mean age of the children was 54 months and the median number of throat infections in the previous year was 3 episodes in both groups (Table 1). Overall, 43 children were lost to follow-up, 18 from the adenotonsillectomy group and 25 from the watchful-waiting group. Reasons were nonmedical in 36 children (parents moved to another town or considered participation too time-consuming), serious comorbidity in 1, or unknown in 6. In addition, 50 children allocated to the watchful-waiting group underwent adenotonsillectomy during follow-up and 7 children allocated to the adenotonsillectomy group did not undergo the operation. Median follow-up was similar in both groups: 22.0 months (range, 0.4-27.1 months) in the adenotonsillectomy group and 22.4 months (range, 1.5-26.5 months) in the watchful-waiting group.

#### COMPLICATIONS OF SURGERY

Of the 195 children (145 in the adenotonsillectomy group and 50 in the watchful-waiting group) who underwent adenotonsillectomy, 12 (6%) experienced surgery-related complications. Seven children had a primary hemorrhage, that is, occurring within 24 hours after intervention. Two of the 195 (1%) were managed surgically and 5 (3%) nonsurgically; 3 children (2%) were admitted for observation for 1 night. Five children (3%) had postoperative nausea, which was managed with antiemetic medication and intravenous fluid administration.

#### COSTS

A detailed overview of the most relevant cost estimates is given in Table 2. Overall, patients in the adenotonsillectomy group incurred €803 per person-year, on average, whereas patients in the watchful-waiting group incurred €1,100 per person-year, on average.

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### Abbreviations: ENT, ear, nose, and throat; OSA, obstructive sleep apnea.

### Table 1. Baseline Demographic and Clinical Characteristics in 300 Participants According to Treatment Allocation

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Adenotonsillectomy Group (n = 151)</th>
<th>Watchful-Waiting Group (n = 149)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male sex</td>
<td>81 (53.6)</td>
<td>66 (44.3)</td>
</tr>
<tr>
<td>Age, mean (SD), mo</td>
<td>54 (17.0)</td>
<td>54 (16.2)</td>
</tr>
<tr>
<td>Indication for surgery as indicated by local ENT surgeon</td>
<td>76 (50.3)</td>
<td>67 (45.0)</td>
</tr>
<tr>
<td>Recurrent throat infections</td>
<td>76 (50.3)</td>
<td>67 (45.0)</td>
</tr>
<tr>
<td>Other indications</td>
<td>73 (48.3)</td>
<td>82 (55.0)</td>
</tr>
<tr>
<td>Throat infections in previous year, mean (range), No.</td>
<td>3 (0 to 6)</td>
<td>3 (0 to 6)</td>
</tr>
<tr>
<td>Duration of throat infections, median (range), mo</td>
<td>13 (0 to 50)</td>
<td>12 (0 to 60)</td>
</tr>
<tr>
<td>Episodes of rhinorrhea or cough in previous year, median (range), No.</td>
<td>12 (0 to 24)</td>
<td>10 (0 to 24)</td>
</tr>
<tr>
<td>OSA score, median (range)</td>
<td>−1.7 (−3.83 to 2.55)</td>
<td>−1.7 (−3.83 to 2.56)</td>
</tr>
<tr>
<td>Previous ENT surgery</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Adenoidectomy</td>
<td>35 (23.2)</td>
<td>33 (22.1)</td>
</tr>
<tr>
<td>Placement of tympanostomy tubes</td>
<td>19 (12.6)</td>
<td>17 (11.4)</td>
</tr>
</tbody>
</table>

Abbreviations: ENT, ear, nose, and throat; OSA, obstructive sleep apnea.

### Table 2. Resources Used and Cost Estimates for 2002

<table>
<thead>
<tr>
<th>Resources</th>
<th>Cost Estimate, €a</th>
<th>Source</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adenoidectomy</td>
<td>330.84</td>
<td>Cost study</td>
</tr>
<tr>
<td>Adenotonsillectomy plus myringotomy</td>
<td>365.93</td>
<td>Cost study</td>
</tr>
<tr>
<td>Adenotonsillectomy plus placement of tympanostomy tubes</td>
<td>683.56</td>
<td>Cost study</td>
</tr>
<tr>
<td>Adenotonsillectomy</td>
<td>361.32</td>
<td>Cost study</td>
</tr>
<tr>
<td>Adenotonsillectomy plus myringotomy</td>
<td>581.39</td>
<td>Cost study</td>
</tr>
<tr>
<td>Adenotonsillectomy plus placement of tympanostomy tubes</td>
<td>724.04</td>
<td>Cost study</td>
</tr>
<tr>
<td>Placement of tympanostomy tubes</td>
<td>362.72</td>
<td>Cost study</td>
</tr>
<tr>
<td>Repeat operation because of primary hemorrhage</td>
<td>1212.55</td>
<td>Cost study</td>
</tr>
<tr>
<td>Consultation with otorhinolaryngologist</td>
<td>45.09</td>
<td>Cost study</td>
</tr>
<tr>
<td>Consultation with otorhinolaryngologist</td>
<td>45.09</td>
<td>Guideline</td>
</tr>
<tr>
<td>Consultation with general practitioner</td>
<td>18.32</td>
<td>Guideline</td>
</tr>
<tr>
<td>Consultation with paramedical professional</td>
<td>20.04</td>
<td>Guideline</td>
</tr>
<tr>
<td>Leave of absence, per hour based on friction costs</td>
<td>21.66</td>
<td>Guideline</td>
</tr>
</tbody>
</table>

Abbreviation: Guideline, Dutch guidelines for pharmaco-economic research. The average exchange rate for the US dollar in 2002 was $1.00 equaled €1.1, except toward the end of 2002 when $0.95 equaled €1.00.
COST-EFFECTIVENESS

The balance between costs and effects, inclusive of uncertainty, was assessed by head-to-head comparison of costs and effects for the original trial data and for the 1000 bootstrap replicates of the trial. The incremental costs per episode of fever, throat infection, and upper respiratory tract infection avoided were €1136, €1187, and €465, respectively. The bootstrap replications yielded similar results.

Incremental costs (y-axis) and effects (x-axis) for the adenotonsillectomy strategy as compared with the watchful-waiting strategy of each of the replicates are shown in the Figure for episodes of fever, throat infections, and upper respiratory tract infections, respectively.

The Figure also shows the percentage of bootstrap estimates when adenotonsillectomy resulted in a lower disease episode rate than watchful waiting. For episodes of fever, 87% of the bootstrap replicates indicate an advantage of adenotonsillectomy over watchful waiting; for throat infections, 99%; and for upper respiratory tract infections, 93%.

COMMENT

In children selected to undergo adenotonsillectomy because of mild to moderate symptoms of throat infections or adenotonsillar hypertrophy, surgery, in comparison with watchful waiting, resulted in an overall increase in costs of 47%, that is, more than €250-cost increase per person-year. This increase was not counterbalanced by a clinically relevant reduction in the number of episodes of fever, throat infections, or upper respiratory tract infections. Although slightly better outcomes were observed with considerable certainty (85%-99%), the net effect in terms of discomfort as measured in days or episodes of disease avoided may be negligible. Effects in terms of quality of life and especially quality-adjusted life-years are not reported herein because the primary outcome indicated minor health effects. We previously reported a significant but clinically irrelevant short-term advantage in health-related quality of life for adenotonsillectomy over watchful waiting, and identical health-related quality of life at 24 months. Thus, if the difference in costs were balanced against a very small difference in quality-adjusted survival time, the incremental cost-effectiveness ratio would be less favorable.

Overall, the balance between costs and effects in this population seemed unfavorable for adenotonsillectomy, with incremental cost-effectiveness ratios in excess of €465 per disease episode averted. Note that this estimate includes societal costs such as parental leave of absence associated with their child’s illness. Had these costs been left out of the equation, the figures would be even somewhat less favorable. With time, the child’s immune system matures and the difference in adverse episodes disappears. Thus, the initial cost increment in the adenotonsillectomy group will never be counterbalanced by a continued positive health effect.

To our knowledge, this is the first elaborate economic evaluation along with a randomized clinical trial on adenotonsillectomy in children, yielding informa-
tion readily applicable in policy decisions. However, to fully appreciate the results of our study, certain aspects must be discussed in more detail.

Children selected for adenotonsillectomy because of frequent throat infections or obstructive sleep apnea were excluded from this trial because these indications are not disputed. Generalization of our results, therefore, may be limited to children with milder symptoms. For children with frequent throat infections, no data on cost-effectiveness of surgical interventions are available as yet. In children with obstructive sleep apnea syndrome, adenotonsillectomy reduces health care use.\(^7\) Owing to variable inclusion criteria, outcome parameters, duration of follow-up, and other study characteristics, quite different results may be anticipated. However, the effects of adenotonsillectomy were not that much more favorable in the subgroups of children with more severe symptoms. Overall, results of all previous trials show that about 1 or 2 episodes per year may be avoided with adenotonsillectomy.\(^7\) It would seem that in as much as the initial costs associated with an operation are similar, the likelihood of attaining an acceptable incremental cost-effectiveness ratio is questionable. Accordingly, cost-effectiveness studies in this field seem to be indicated as well.

Another issue that requires further elaboration is that 50 children (34%) crossed over from the watchful-waiting group to the surgery group during follow-up. Inappropriate handling of these data could have led to bias; that is, per protocol analyses, either excluding children who changed treatment group or analyzing children on the basis of the time spent in any treatment arm might have resulted in underestimation or overestimation of the treatment effect. To prevent such bias, and considering our intention to compare strategies as observed in daily practice rather than to perform a strictly controlled comparison of adenotonsillectomy vs watchful waiting, we performed an intention-to-treat analysis. During follow-up, subsequent episodes of disease in children enrolled in the watchful-waiting arm apparently urged a considerable percentage of parents and physicians to decide on surgery. This may be a consequence of the Dutch setting, in which parents and physicians apparently had positive expectations about the benefits of adenotonsillectomy. Scrutiny of the baseline characteristics revealed that initially all children, that is, those who crossed over to the other treatment arm and those who did not, were similar. Also, note that a crossover added to the costs but also may have had an effect on the net effects because surgery is associated with discomfort as well. Overall, we believe that a possible minor short-term effect on perceived quality of life is irrelevant in the perspective of identical longer-term outcomes.

For episodes of fever, however, there were no differences because, in terms of less bias-prone parameters and outcome parameters, there were no differences between children who crossed over and those who did not. Thus, our results stand as they are.

A final point about the generalizability of our results is related to the adenotonsillectomy technique generally used in the Netherlands, that is, the Sluder guillotine technique.\(^19\) We noted that, in this trial population, 4% of the patients had a primary hemorrhage, of whom 1% were returned to the operating room. This may seem fairly high compared with some other series. The technique is usually combined with inhalation anesthesia with sevoflurane administered through a face mask and does not require endotracheal intubation. This combination of surgical technique and anesthetic takes only about 15 minutes from entry to the operating room to transfer to the recovery room. Almost all procedures are performed in an outpatient setting. This has considerable consequences for the costs of the procedure. Compared with other Western countries, our cost estimates may be low; the incremental cost-effectiveness ratios based on Dutch cost estimates seem too favorable. In other settings, the cost-effectiveness would be further offset by more costly procedures.

In most Dutch children undergoing adenotonsillectomy because of mild to moderate tonsillar disorders, surgery resulted in a significant increase in costs without realizing relevant clinical benefit. Additional research is needed to identify subgroups of children in whom surgery might be cost effective.

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Author Contributions: Dr Buskens had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis. Study concept and design: Buskens, van Staaij, van den Akker, Hoes, and Schilder. Acquisition of data: van Staaij and van den Akker. Analysis and interpretation of data: Buskens, van Staaij, Hoes, and Schilder. Drafting of the manuscript: Buskens, van Staaij, and van den Akker. Critical revision of the manuscript for important intellectual content: Buskens, van Staaij, Hoes, and Schilder. Statistical analysis: Buskens and van Staaij. Obtained funding: Buskens, Hoes, and Schilder. Administrative, technical, and material support: van Staaij and van den Akker. Study supervision: Buskens, Hoes, and Schilder.

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