JAMA Otolaryngology–Head & Neck Surgery | Original Investigation

# Effectiveness of Adenotonsillectomy vs Watchful Waiting in Young Children With Mild to Moderate Obstructive Sleep Apnea
## A Randomized Clinical Trial

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**IMPORTANCE** Adenotonsillectomy (ATE) is one of the most common surgical procedures to treat children with obstructive sleep apnea (OSA), but to our knowledge there are no randomized clinical trials confirming the benefit of surgery compared with watchful waiting in children between 2 and 4 years of age.

**OBJECTIVE** To determine whether ATE is more effective than watchful waiting for treating otherwise healthy children with mild to moderate OSA.

**DESIGN, SETTING, AND PARTICIPANTS** This randomized clinical trial was conducted from December 2014 to December 2017 at the Otorhinolaryngology Department of the Karolinska University Hospital, Stockholm, Sweden. A total of 60 children, 2 to 4 years of age, with an obstructive apnea–hypopnea index (OAHI) score of 2 or greater and less than 10, were randomized to ATE (n = 29) or watchful waiting (n = 31). A total of 53 participants (88%; ATE, n = 25; watchful waiting, n = 28) completed the study. Data were analyzed from August 2018 to December 2018.

**INTERVENTIONS** Adenotonsillectomy.

**MAIN OUTCOMES AND MEASURES** The primary outcome was the difference between the groups in mean OAHI score change. Secondary outcomes were other polysomnography parameters, score on the Obstructive Sleep Apnea–18 (OSA-18) questionnaire, and subgroup analyses. Polysomnography and the OSA-18 questionnaire were completed at baseline and after 6 months.

**RESULTS** Of the 60 included children, 34 (57%) were boys and the mean (SD) age at first polysomnography was 38 (9) months. Both groups had a decrease in mean OAHI score, and the difference in mean OAHI score change between the groups was small (−1.0; 95% CI, −2.4 to 0.5), in favor of ATE. However, there were large differences between the groups in favor of ATE regarding the OSA-18 questionnaire (eg, total OSA-18 score: −17; 95% CI, −24 to −10). Also, a subgroup analysis of 24 children with moderate OSA (OAHI ≥5 and <10) showed a meaningful difference in mean OAHI score change between the groups in favor of ATE (−3.1; 95% CI, −5.7 to −0.5). Of 28 children, 10 (36%) in the watchful waiting group received ATE after the follow-up, and 7 of these had moderate OSA at baseline.

**CONCLUSIONS AND RELEVANCE** This randomized clinical trial found only small differences between the groups regarding changes in OAHI, but further studies are needed. However, there were large improvements in quality of life after ATE. These results suggest that otherwise healthy children with mild OSA and mild effect on quality of life may benefit from watchful waiting, while children with moderate OSA should be considered for ATE.

**TRIAL REGISTRATION** ClinicalTrials.gov Identifier: NCT02315911

Invited Commentary

Supplemental content

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*JAMA Otolaryngol Head Neck Surg*. doi:10.1001/jamaoto.2020.0869
Published online May 28, 2020.

Pediatric obstructive sleep apnea (OSA) is a common disorder[1,2] and is recognized as a significant cause of morbidity in children.[3-6] Surgery is the primary treatment and adenotonsillectomy (ATE), removal of the tonsils and adenoid, is considered the first choice of treatment.[7-9] Although ATE compared with no treatment has been shown to have a good effect on respiratory sleep parameters, quality of life (QoL), and behavior, to our knowledge the effect in children between 2 and 4 years of age is still unknown.[10,11] This is an important issue to address, because ATE is one of the most common surgical procedures in children and there is a high prevalence of OSA in children younger than 5 years.[12]

According to some reports and studies, ATE is not always the first choice of treatment for otherwise healthy children with mild OSA.[13-15] Through studies and clinical experience, it has been demonstrated that children with less severe forms of OSA sometimes get better without surgical treatment. For instance, a large randomized clinical trial (RCT), the Childhood Adenotonsillectomy Trial (CHAT),[16] compared ATE with watchful waiting in 464 children with OSA. The children were between 5 and 9 years of age and had mild to moderate OSA. The authors reported that 46% in the group without treatment were normalized (defined as apnea-hypopnea index [AHI] of <2) at follow-up, compared with 79% in the ATE group. The group difference was significant, but there seemed to be a nonnegligible spontaneous improvement in some children without surgical treatment in terms of polysomnography (PSG) parameters. However, there is a poor correlation between QoL and PSG parameters in children,[17-20] and even though there were improvements in PSG parameters in the watchful waiting group, most of the children remained symptomatic, demonstrating persistent snoring and obstructive symptoms.[15] In addition to the treatment effect, there are also perioperative and postoperative risks to consider, such as pain, hemorrhage, and respiratory compromise.[21,22]

Because the CHAT study[16] did not include children younger than 5 years, the present Karolinska Adenotonsillectomy (KATE) RCT aimed to determine whether ATE is more effective than watchful waiting for treating mild to moderate OSA, by analyzing PSG data and scores from the QoL questionnaire Obstructive Sleep Apnea-18 (OSA-18), in otherwise healthy children 2 to 4 years of age. The hypothesis investigated was that ATE is superior for treating children with mild to moderate OSA compared with watchful waiting, as measured by the change in obstructive apnea-hypopnea index (OAHI) score after 6 months.

### Key Points

**Question** Is adenotonsillectomy (ATE) more effective than watchful waiting for treating otherwise healthy children, between 2 and 4 years of age, with mild to moderate obstructive sleep apnea (OSA)?

**Findings** In this randomized clinical trial including 60 children with OSA, there were only small differences between outcomes of ATE and watchful waiting, in favor of ATE, regarding changes in mean obstructive apnea-hypopnea index (OAHI), but there were large improvements in quality of life after ATE. Also, subgroup analyses showed that 11 children with moderate OSA who received ATE had a meaningful improvement in OAHI compared with 13 who received watchful waiting.

**Meaning** Children with moderate OSA should be considered for early ATE, while children with mild OSA and mild effect on quality of life may benefit from a period of watchful waiting.

## Methods

### Trial Design and Participants

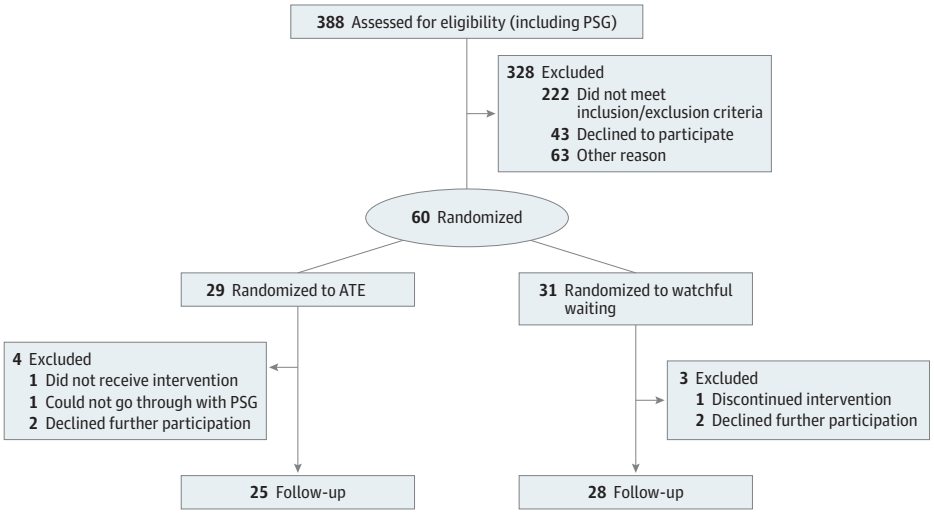
The current study was a single-center, prospective RCT with 2 parallel arms comparing ATE with watchful waiting. It was conducted at the Otorhinolaryngology Department at Karolinska University Hospital in Stockholm, Sweden, with study recruitment from December 2014 through December 2017. The Consolidated Standards of Reporting Trials (CONSORT) reporting guideline was followed. The trial protocol is presented in Supplement 1. All referred children with a history of habitual snoring, apneas, and/or restless sleep, with no obvious characteristics excluding them from study participation, were offered a PSG. Children were included in the study if they (1) completed the PSG, (2) were determined to be eligible by an otorhinolaryngologist, (3) met all inclusion criteria and were not otherwise excluded, (4) agreed to study participation, and (5) had written informed consent from their caregivers. The flow of participants is illustrated in **Figure 1**. Follow-up was planned 6 months after the first PSG for the watchful waiting group and 6 months after surgery for the ATE group. The PSG and questionnaires were completed at baseline and at the 6-month follow-up visit. This study was approved by the Swedish Regional Ethics Board in Stockholm, Sweden, and written, informed consent was obtained from participants' parents/guardians.

The following inclusion criteria were used: age 2 years or older and younger than 5 years; history or symptoms of habitual snoring, apneas, and/or restless sleep; mild to moderate OSA, defined as an OAHI score of 2 or more and less than 10 (mild OSA, OAHI ≥2 and <5; moderate OSA, OAHI ≥5 and <10); tonsil hypertrophy of 2 to 4 according to Brodsky[23] (scored according to occlusion of the oropharynx: 1, 0%-25%; 2, 26%-50%; 3, 51%-75%; and 4, 76%-100%); and parents with sufficient knowledge of Swedish to understand the written information and answer the questionnaires. The exclusion criteria were the presence of craniofacial abnormality, neuromuscular disease, chromosomal abnormality, previous adenotonsillar surgery, a bleeding disorder, and cardiopulmonary disease (eg, heart valve disease, cystic fibrosis, and asthma; mild infection-related asthma was not excluded).

### Sample Size and Power Analysis

The power analysis was based on results from a previous study.[16] It was calculated with an α level of .05 and 80% power. A difference of 2 in OAHI score change was used as a minimally clinically important difference between the groups, with a standard deviation of 2.5. This generated a study population of 26 children in each group. To compensate for limita-

Figure 1. Study Flowchart




ATE indicates adenotonsillectomy; PSG, polysomnography.

tions in the power analysis and for dropouts, a total of 60 children were included in the study.

## Polysomnography

Polysomnography measures sleep stages and respiratory functions using recordings of electroencephalography, electrooculography, electromyography, pulse, oronasal airflow, transcutaneous oxygen saturation, respiratory movements (abdomen and thorax), body position, and video and sound recordings. All PSGs were performed overnight in a sleep laboratory at the Otorhinolaryngology Department using Embla (Natus Medical Inc). All PSGs were scored manually by the same registered polysomnography technologist, according to the scoring rules of the American Academy of Sleep Medicine,[24] and the PSG scorer was blinded for treatment allocation.

## OSA-18

The OSA-18 questionnaire is validated for assessing QoL related to sleep-disordered breathing among children. It consists of 18 questions within the 5 domains of sleep disturbance, physical symptoms, emotional distress, daytime function, and caregivers' concerns. Each question is scored on a 7-point Likert scale and answers are summed to a total OSA-18 score ranging from 18 to 126 points, where higher scores indicate a worse QoL. Scores less than 60 suggest a mild impact on QoL, scores between 60 and 80 suggest a moderate impact, and scores greater than 80 suggest a severe impact.[25] The OSA-18 questionnaire also contains a global rating of QoL on a visual analog scale (VAS QoL) of 0 to 10 points. The total OSA-18 score, sleep disturbance score, and VAS QoL were decided to be of clinical importance and analyzed in the present study.

## Intervention

The children who participated were randomly assigned to either ATE or watchful waiting, and surgery was performed within approximately 3 months of the baseline PSG. The tonsils were removed by blunt extracapsular dissection, and the adenoid was removed with a ring knife or coblation.

## Outcomes

The primary outcome was the difference in OAHI score change at the 6-month follow-up between children who received ATE and children who were assigned to watchful waiting. Secondary outcomes analyzed were differences between the groups regarding changes in other PSG variables, including central AHI, rapid eye movement AHI, oxygen desaturation index (using the ≥3% desaturation criterion), respiratory distress index, mean oxygen saturation, lowest oxygen saturation level, sleep stages, total sleep time, wake after sleep onset, and sleep efficiency. Other outcomes were scores on the OSA-18 questionnaire and the differences between the groups in changes in total OSA-18 score, sleep disturbance score, and VAS QoL.

Subgroup analyses were performed regarding children with obesity (body mass index [BMI] $z$ score ≥1.67) and preoperative OSA severity (mild OSA, OAHI ≥2 and <5; moderate OSA, OAHI ≥5 and <10). Success rates at different scores of OAHI (<1, <2, and <5) at follow-up were also compared to evaluate the treatment effect. Baseline data were tested for ability to predict an OAHI score of 2 or greater and a total OSA-18 score of 60 or greater at follow-up. Also, the need for surgery because of residual OSA and postoperative complications, such as infection and readmission due to bleeding, were evaluated.

## Randomization and Blinding

The randomization was performed with 90 sealed envelopes, and the allocation ratio was 1:1 between ATE and watchful waiting. A total of 5 envelopes from each group were mixed together to create a block of 10. The envelopes were placed in folders containing study information and a consent form, and were opened together with the caregivers and children after they accepted study participation. The PSG scorer was blinded to treatment allocation.

## Statistical Analysis

The primary analysis was per protocol, but an intention-to-treat analysis was also performed as a sensitivity analysis regarding the primary outcome of changes in OAHI score.

Table 1. Baseline Characteristics

| Parameter | No. (%) | |
|---|---|---|
| | ATE (n = 29) | Watchful waiting (n = 31) |
| Age at first PSG, mean (SD), mo | 39 (8) | 37 (11) |
| Sex | | |
| Male | 15 (52) | 19 (61) |
| Female | 14 (48) | 12 (39) |
| BMI *z* score, mean (SD) | 0.2 (1.4)[a] | 0.2 (1.1) |
| Tonsil size, median (IQR)[b] | 3 (3-3) | 3 (2-3) |
| OAHI, mean (SD), events/h of sleep | 4.9 (1.9) | 5.0 (2.2) |
| OSA severity[c] | | |
| Mild | 15 (52) | 16 (52) |
| Moderate | 14 (48) | 15 (48) |
| Total OSA-18 score, median (IQR)[d] | 59 (49-74) | 58.5 (48-69) |
| <60 | 14 (50) | 17 (57) |
| 60-80 | 10 (36) | 10 (33) |
| >80 | 4 (14) | 3 (10) |

Abbreviations: ATE, adenotonsillectomy; BMI, body mass index; IQR, interquartile range; OAHI, obstructive apnea-hypopnea index; OSA, obstructive sleep apnea; PSG, polysomnography.

[a] One missing value in the ATE group (n = 28).

[b] Tonsil size scored according to Brodsky[23] (scored according to occlusion [%] of the oropharynx: 1, 0%-25%; 2, 26%-50%; 3, 51%-75%; and 4, 76%-100%).

[c] Mild OSA, OAHI ≥2 and <5; moderate OSA, OAHI ≥5 and <10.

[d] One missing participant in each group.

Missing values were imputed by multiple imputation. The statistical inference was performed with effect sizes and 95% CIs.

The PSG variables were continuous data, and the results are given as the mean and SD or as the mean and 95% CI. Standardized effect sizes were calculated with the use of Cohen *d*, relating the magnitude of group difference to the SD, and may be interpreted as follows: small, more than 0.20 to 0.49; medium, 0.50 to 0.79; and large, 0.80 or more. The OSA-18 questionnaire consisted of ordinal data and the results are given as the median (interquartile range), the median (95% CI, which is given with the Hodges-Lehmann estimator), as well as a standardized effect size (Cohen *d*).

Univariate associations were tested using logistic regression models in order to find factors that could predict an OAHI score of 2 or greater and a total OSA-18 score of 60 or greater at follow-up. Variables that were considered predictive ($P < .05$) in the univariate analysis were included in a forward stepwise logistic multiple regression model. All data were analyzed with Stata, version 15 (StataCorp).

## Results

A total of 60 children were randomized to either ATE (n = 29) or watchful waiting (n = 31), and 53 children (88%) completed the study: 25 (86%) in the ATE group and 28 (90%) in the watchful waiting group. Of these children, 1 in the ATE group and 3 in the watchful waiting group had BMI *z* scores of 1.67 or greater. The groups were similar at baseline (**Table 1**).

### Primary Outcome

Both groups had a reduction in mean OAHI score at the follow-up in the per-protocol analysis. The ATE group had a mean OAHI score decrease of −2.9 (95% CI, −4.0 to −1.9; Cohen *d* = −1.14), the watchful waiting group had a mean decrease of −1.9 (95% CI, −3.0 to −0.9; Cohen *d* = −0.71), and the difference between the groups in mean change was small, −1.0 (95% CI, −2.4 to 0.5; Cohen *d* = −0.37) (**Table 2**). A total of 2 children in the ATE group had an increased OAHI score at follow-up compared with 4 in the watchful waiting group. Two children with moderate OSA in the watchful waiting group had developed severe OSA (defined as OAHI score ≥10) (**Figure 2**). The ITT analysis (n = 60) also showed a small difference between the groups in mean OAHI change (−1.0; 95% CI, −2.3 to 0.3; Cohen *d* = −0.38).

### Secondary Outcomes

There were no or small differences between the groups in other PSG variables, except for a medium difference in sleep stage 2 (Table 2). However, there was a medium difference between the groups already at baseline (−7.4; 95% CI, −14.3 to −0.5; Cohen *d* = −0.60).

Large improvements were observed in total OSA-18 score (−23.5; 95% CI, −31.5 to −15; Cohen *d* = −1.24) and sleep disturbance score, and medium improvements in VAS QoL, in the ATE group, but only small improvements were seen overall in the watchful waiting group. There was a large and clinically meaningful difference between the groups in favor of ATE in total OSA-18 score (Table 2). At follow-up, in the ATE group, all 23 children had a total OSA-18 score of less than 60. In the watchful waiting group, 20 of 26 (76%) had a score greater than 60, 5 (19%) had a score between 60 and 80, and 1 (4%) had a score over 80. A higher total OSA-18 score at baseline was the only significant factor that predicted a total OSA-18 score of 60 or more at follow-up after watchful waiting.

A total of 11 children in the ATE group had moderate OSA (mean [SD] OAHI score 6.5 [1.2]) at baseline, and 13 in the watchful waiting group had moderate OSA (mean [SD] OAHI score 7.1 [1.1]). Subgroup analyses in these children with moderate OSA showed a meaningful group difference in mean OAHI score change (−3.1; 95% CI, −5.7 to −0.5; Cohen *d* = −1.00), in favor of ATE. The difference between the groups for children with mild OSA was 0.7 (95% CI, −0.5 to 1.9; Cohen *d* = 0.42). Also, subgroup analyses for children with different preoperative BMI *z* scores did not change the differences between the groups in OAHI score change (eg, group difference for children without obesity: −0.8; 95% CI, −2.3 to 0.8; Cohen *d* = −0.29).

There were differences in favor of ATE in success rate at different levels of OAHI (<1, <2, and <5) (**Table 3**). There were no factors that predicted an OAHI score of 2 or more at follow-up after ATE, and a high OAHI score at baseline was the only factor that predicted an OAHI score of 2 or more after watchful waiting.

In the watchful waiting group, 10 of 28 children (36%) received ATE after the follow-up because of persistent symptoms and/or residual OSA according to PSG. Of these children, 7 (70%) had moderate OSA at baseline, and 2 (20%) had an OAHI score of 2 or more at the postoperative follow-up. One

Table 2. Polysomnography, Obstructive Sleep Apnea–18 (OSA-18), and Visual Analog Scale Quality of Life (VAS QoL) Results From Baseline to Follow-up

| | ATE | | | | Watchful waiting | | | | Group differences | |
|---|---|---|---|---|---|---|---|---|---|---|
| Parameter[a] | No. of patients | Baseline | Mean change at follow-up (95% CI) | Effect size[b] | No. of patients | Baseline | Mean change at follow-up (95% CI) | Effect size[b] | Mean difference in change (95% CI) | Effect size[b] |
| OAHI | 25 | 4.8 (1.9) | −2.9 (−4.0 to −1.9) | −1.14 | 28 | 5.1 (2.2) | −1.9 (−3.0 to −0.9) | −0.71 | −1.0 (−2.4 to 0.5) | −0.37 |
| Central AHI | 24 | 1.7 (1.6) | −0.5 (−1.2 to 0.3) | −0.26 | 25 | 2.1 (2.2) | −0.5 (−1.2 to 0.2) | −0.32 | 0.1 −0.9 to 1.1) | 0.03 |
| $ODI_{3\%}$ | 25 | 3.0 (2.5) | −0.4 (−1.3 to 0.5) | −0.20 | 27 | 3.7 (2.6) | −1.0 (−1.9 to −0.1) | −0.44 | 0.5 (−0.7 to 1.7) | 0.24 |
| Mean Sat $O_2$, % | 25 | 97.2 (1.0) | −0.3 (−0.7 to 0.1) | −0.31 | 27 | 97.0 (0.7) | −0.2 (−0.4 to 0.1) | −0.29 | −0.1 (−0.6 to 0.3) | −0.16 |
| Nadir $O_2$, % | 24 | 89.6 (3.7) | 0.2 (−1.7 to 2.0) | 0.04 | 27 | 88.0 (5.5) | −0.1 (−3.2 to 3.0) | −0.01 | 0.2 (−3.4 to 3.9) | 0.04 |
| Sleep efficiency, % | 25 | 91.7 (5.9) | 2.0 (−1.4 to 5.4) | 0.24 | 26 | 93.6 (6.0) | 0.1 (−3.7 to 3.9) | 0.01 | 1.9 (−3.1 to 6.9) | 0.22 |
| Sleep stage, %[c] | | | | | | | | | | |
| 1 | 25 | 1.7 (1.9) | −0.3 (−1.4 to 0.7) | −0.13 | 26 | 2.1 (2.2) | −1.1 (−2.1 to −0.1) | −0.43 | −0.7 (−0.7 to 2.2) | 0.30 |
| 2 | 25 | 23.4 (12.4) | 1.6 (−3.7 to 6.9) | 0.12 | 26 | 30.7 (12.5) | −7.1 (−14.1 to −0.1) | −0.13 | 8.7 (0.1 to 17.4) | 0.57 |
| 3-4 | 25 | 56.9 (14.2) | 0.0 (−6.5 to 6.6) | 0.00 | 26 | 49.0 (14.3) | 7.3 (−0.1 to 14.6) | 0.40 | −7.2 (−16.9 to 2.4) | −0.42 |
| REM | 25 | 18.0 (5.5) | −1.3 (−4.2 to 1.6) | −0.19 | 26 | 18.1 (5.0) | 1.0 (−1.2 to 3.1) | 0.18 | −2.3 (−5.8 to 1.2) | −0.37 |
| Total OSA-18 score | 23 | 57 (48 to 74) | −23.5 (−31.5 to −15) | −1.24 | 26 | 56.5 (48 to 70) | −4.5 (−12 to 1.5) | −0.36 | −17.0 (−24 to −10) | −0.97 |
| Sleep disturbance score | 23 | 15 (11 to 18) | −7.0 (−8.5 to −4.5) | −1.39 | 26 | 15.0 (12.0 to 16.0) | −0.5 (−2.5 to 1.0) | −0.13 | −6.0 (−9.0 to −4.0) | −1.23 |
| VAS QoL | 24 | 6.5 (5 to 9) | 1.5 (0.5 to 3.0) | 0.72 | 24 | 7.0 (4.5 to 8.5) | 0.5 (−0.5 to 2.0) | 0.25 | 1.0 (0 to 2.0) | 0.40 |

Abbreviations: AHI, apnea–hypopnea index; ATE, adenotonsillectomy; OAHI, obstructive apnea–hypopnea index; $ODI_{3\%}$, oxygen desaturation index; Mean Sat $O_2$, mean oxygen saturation; Nadir $O_2$, oxygen saturation nadir; REM, rapid eye movement.

[a] Polysomnography data are expressed as mean (SD); OSA-18 scores and VAS QoL are expressed as median (interquartile range).

[b] Effect sizes were calculated with the use of Cohen *d*, relating the magnitude of group difference to the SD, and may be interpreted as follows: small, more than 0.20 to 0.49; medium, 0.50 to 0.79; and large, 0.80 or more.

[c] Percentage of total sleep time.

patient in the ATE group was readmitted due to postoperative bleeding, but no other complications were seen.

## Discussion

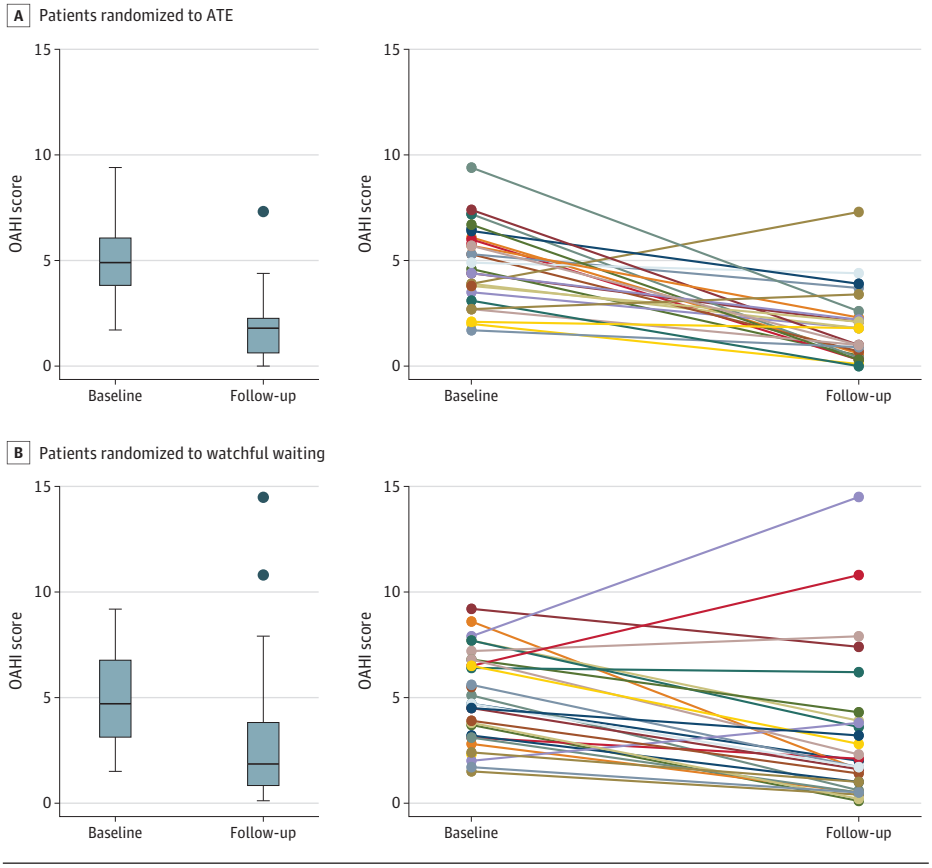
The effect of ATE in children between 2 and 4 years of age has been unknown, and to our knowledge this is the first RCT comparing ATE with watchful waiting in otherwise healthy children, 2 to 4 years of age, with mild to moderate OSA. There were only small differences between ATE and watchful waiting regarding change in mean OAHI score, but there were large and meaningful improvements in QoL in favor of ATE. Also, subgroup analyses showed that children with moderate OSA who received ATE had a meaningful improvement in mean OAHI score change compared with watchful waiting. These findings suggest, in accordance with earlier recommendations from the European Respiratory Society,[14] that otherwise healthy children with moderate OSA benefit from ATE, whereas watchful waiting could be an alternative for otherwise healthy children with mild OSA.

Although the results only showed a small difference in mean OAHI score change between the groups according to Cohen *d* effect size, the minimal clinically important difference of 2 was within the confidence intervals. This suggests that a meaningful difference between the groups cannot be ruled out and further studies with larger samples are needed to confirm the result.

In meta-analyses[8,26] the results after ATE are generally better, with a success rate (defined as AHI <1) of 51% to 60% compared with 36% in the present study. An unexpected low treatment effect of ATE in the present study could be a possible explanation for the small difference between the groups, but to compare this study with meta-analyses is difficult, because they include a variety of nonrandomized studies. However, the results after ATE in the present study are similar to the results in a large RCT (CHAT) by Marcus et al.[16] In the CHAT trial,[16] 194 children between 5 and 9 years of age, with mild to moderate OSA, received ATE. The preoperative median OAHI score of 4.8, the median OAHI score change of −3.5, and the medium effect size are all comparable with the results in the present study, but the effect size was smaller.

Some children improve spontaneously, but the natural history of OSA is not well known. Previous studies have shown, for instance, that baseline OAHI score, waist circumference, tonsil size, and sex might predict the outcome.[15,27] In the present study, as well as in the CHAT trial,[16] baseline OAHI score was a predictor for residual OSA (OAHI ≥2) after watchful waiting. The improvement in mean OAHI score after watchful waiting may also have other explanations, such as wider airways due to growth, night-to-night variability, and regression to the mean.

Figure 2. Obstructive Apnea-Hypopnea Index (OAHI) Scores for the Adenotonsillectomy (ATE) Group and the Watchful Waiting Group




Box plots and line graphs illustrate the OAHI scores for ATE (A) and watchful waiting (B) at baseline and follow-up. Boxes include the median and interquartile range. Whiskers are within the 1.5 interquartile range, and circles are outliers.

Table 3. Success Rate at Different Levels of Obstructive Apnea-Hypopnea Index (OAHI) Score at Follow-up

| OAHI score | Patients, No. (%) | | Difference (95% CI) |
|---|---|---|---|
| | ATE (n = 25) | Watchful waiting (n = 28) | |
| <1 | 9 (36) | 7 (25) | 11 (−14 to 36) |
| <2 | 15 (60) | 14 (50) | 10 (−17 to 37) |
| <5 | 24 (96) | 23 (82) | 14 (−2 to 30) |

Abbreviation: ATE, adenotonsillectomy.

The difference of OAHI score change between the groups in the present study might also be explained by the fact that children with mild OSA do not respond as well to ATE as children with moderate OSA, or they might have a higher degree of spontaneous improvement. In the subgroup analysis, there was a meaningful difference in mean OAHI score change, in favor of ATE, for children with moderate OSA (n = 24).The subgroup analyses should be interpreted with caution, but similar results were seen in the CHAT study.[16] Also, in the present study, as many as 70% of the children in the watchful waiting group who received ATE after the follow-up had moderate OSA at baseline.

There was a difference in percentage of sleep stage 2 (8.7; 95% CI, 0.1 to 17.4) between the groups, which might be explained by an uneven distribution at baseline regarding this parameter. There were no differences in other PSG variables, which further supports the finding that ATE is not more effective than watchful waiting regarding objective PSG outcomes in children with mild to moderate OSA.

A minimal clinically important difference in total OSA-18 score change was not defined before the start of the study. However, when using a difference of 10, which has also been used by Mitchell et al,[28] there was a large and meaningful difference in QoL after ATE compared with watchful waiting. The large improvement in QoL after ATE is consistent with results in other RCTs.[17,29,30] Even though QoL is recognized as an important health outcome measure, success after ATE is most often focused on normalization of PSG parameters. However, previous studies have not shown a strong correlation between changes in PSG outcomes and changes in QoL.[17-20] Also, Volsky et al[31] showed that even mild OSA can be strongly associated with QoL in children. Hence, to solely focus on PSG parameters may miss improvements in QoL that are important to children and families, and therefore, pediatric OSA outcomes should include more than just PSG parameters.

More outcomes regarding symptoms and behavior in young children, in addition to objective PSG parameters, as well as long-term results, would be of value in future research. In the present study, the follow-up period was only 6 months and long-term outcomes are still unknown, but an additional follow-up is planned after 3 years. Also, there are studies

regarding medical treatment (eg, anti-inflammatory drugs, such as intranasal steroids and montelukast) of nonsevere OSA that have shown improvements in both PSG parameters as well as QoL,[32-34] but further studies are needed to confirm their efficacy and long-term results.

To summarize, the results of the present study suggest that otherwise healthy children, 2 to 4 years of age, with mild OSA and mild effect on QoL may benefit from a period of watchful waiting, while children with moderate OSA should be considered for early ATE.

### Strengths and Limitations

There were a number of strengths to this study. It was an RCT with a low dropout rate (12%), it used PSG, the PSG scorer was blinded for treatment allocation, and it studied children between 2 and 4 years of age. Although OSA is a common disorder in this age, to our knowledge there are no previous RCTs confirming the benefit of surgery, and this study was needed.[10,11]

There were also several limitations to this study. It had a small study sample (n = 60), and it included only otherwise healthy children, making the generalizability limited and therefore not applicable to children with comorbidities or severe OSA. There were only 4 children with obesity who completed the study, and therefore it was not possible to evaluate the effect in patients with obesity. However, excluding these patients did not affect the primary result. Also, QoL is a subjective measure, and the children and caregivers were not blinded to treatment allocation. Therefore, there is a possibility that larger improvements in QoL after ATE could be explained by a surgical placebo effect. Even so, it is important to not only focus on PSG parameters; additional outcomes measuring symptoms and behavior would have been of value to this study. Furthermore, the choice to combine children with mild and moderate OSA might be considered arbitrary, but it was done to compare the results with those of the CHAT study.[16] Also, it is difficult to separate children with mild and moderate OSA, based on the clinical presentation, and PSG is seldom used in clinical practice.

## Conclusions

In this RCT there were small differences between ATE and watchful waiting in favor of ATE regarding changes in mean OAHI scores in otherwise healthy children without obesity who have mild to moderate OSA. However, children undergoing ATE had greater improvements in QoL, and ATE was more effective in children with moderate OSA regarding change in mean OAHI score. These results suggest that otherwise healthy children with moderate OSA benefit from early ATE and that watchful waiting could be an alternative for mild OSA. Nonetheless, QoL should also be taken into consideration when deciding to perform surgery. Furthermore, the results should be interpreted with caution, and future studies with larger samples are needed to confirm these results.


### ARTICLE INFORMATION

**Accepted for Publication:** March 29, 2020.

**Published Online:** May 28, 2020. doi:10.1001/jamaoto.2020.0869

**Author Contributions:** Dr Fehrm 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.
*Concept and design:* Fehrm, Nerfeldt, Friberg.
*Acquisition, analysis, or interpretation of data:* All authors.
*Drafting of the manuscript:* Fehrm.
*Critical revision of the manuscript for important intellectual content:* All authors.
*Statistical analysis:* Fehrm, Browaldh, Friberg.
*Obtained funding:* Fehrm, Friberg.
*Administrative, technical, or material support:* Fehrm, Nerfeldt, Friberg.
*Supervision:* Nerfeldt, Browaldh, Friberg.

**Conflict of interest Disclosures:** Dr Fehrm reported grants from the Samaritan Foundation for Pediatric Research, from the ACTA Oto-Laryngologica Foundation, and from the Stockholm City Council during the conduct of the study. No other disclosures were reported.

**Funding/Support:** This study was supported by grants from the Stockholm County Council (ALF project), the ACTA Oto-Laryngologica Foundation, and the Samaritan Foundation for Pediatric Research.

**Role of the Funder/Sponsor:** The funders had no role in the design and conduct of the study; collection, management, analysis, and interpretation of the data; preparation, review, or approval of the manuscript; and decision to submit the manuscript for publication.

**Data Sharing Statement:** See Supplement 2.

**Additional Contributions:** We thank our colleagues at the Otorhinolaryngology Department, Karolinska University Hospital, for recruiting and operating on the study patients; Anne-Charlotte Hessén-Söderman, MD, PhD, for operating and performing follow-up on study patients; statistician Johan Bring, PhD, for providing statistical advice; polysomnographic technologist Therese Murphy for interpreting the polysomnography results; and nurse Carina Hedenström and other personnel for assisting in the sleep laboratory. They received no extra compensation beyond normal salary.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