Comparative Effectiveness Review

Number 183

Tonsillectomy for Obstructive Sleep-Disordered Breathing or Recurrent Throat Infection in Children

Prepared for:
Agency for Healthcare Research and Quality
U.S. Department of Health and Human Services
5600 Fishers Lane
Rockville, MD 20857
www.ahrq.gov

Contract No. 290-2015-00003-I

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AHRQ Publication No. 16(17)-EHC042-EF
December 2016

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None of the investigators have any affiliations or financial involvement that conflicts with the material presented in this report.

The information in this report is intended to help health care decisionmakers—patients and clinicians, health system leaders, and policymakers, among others—make well-informed decisions and thereby improve the quality of health care services. This report is not intended to be a substitute for the application of clinical judgment. Anyone who makes decisions concerning the provision of clinical care should consider this report in the same way as any medical reference and in conjunction with all other pertinent information, i.e., in the context of available resources and circumstances presented by individual patients.

This report may periodically be assessed for the currency of conclusions. If an assessment is done, the resulting surveillance report describing the methodology and findings will be found on the Effective Health Care Program Web site at www.effectivehealthcare.ahrq.gov. Search on the title of the report.

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Suggested citation: Francis DO, Chinnadurai S, Sathe NA, Morad A, Jordan AK, Krishnaswami S, Fonnesbeck C, McPheeters ML. Tonsillectomy for Obstructive Sleep-Disordered Breathing or Recurrent Throat Infection in Children. Comparative Effectiveness Review No. 183. (Prepared by the Vanderbilt Evidence-based Practice Center under Contract No. 290-2015-00003-I.) AHRQ Publication No. 16(17)-EHC042-EF. Rockville, MD: Agency for Healthcare Research and Quality. December 2016. www.effectivehealthcare.ahrq.gov/reports/final.cfm.

Preface

The Agency for Healthcare Research and Quality (AHRQ), through its Evidence-based Practice Centers (EPCs), sponsors the development of systematic reviews to assist public- and private-sector organizations in their efforts to improve the quality of health care in the United States. These reviews provide comprehensive, science-based information on common, costly medical conditions, and new health care technologies and strategies.

Systematic reviews are the building blocks underlying evidence-based practice; they focus attention on the strength and limits of evidence from research studies about the effectiveness and safety of a clinical intervention. In the context of developing recommendations for practice, systematic reviews can help clarify whether assertions about the value of the intervention are based on strong evidence from clinical studies. For more information about AHRQ EPC systematic reviews, see www.effectivehealthcare.ahrq.gov/reference/purpose.cfm.

AHRQ expects that these systematic reviews will be helpful to health plans, providers, purchasers, government programs, and the health care system as a whole. Transparency and stakeholder input are essential to the Effective Health Care Program. Please visit the Web site (www.effectivehealthcare.ahrq.gov) to see draft research questions and reports or to join an email list to learn about new program products and opportunities for input.

If you have comments on this systematic review, they may be sent by mail to the Task Order Officers named below at: Agency for Healthcare Research and Quality, 5600 Fishers Lane, Rockville, MD 20857, or by email to epc@ahrq.hhs.gov.

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Acknowledgments

The authors gratefully acknowledge the following individuals for their contributions to this project: Ms. Jessica Kimber was an invaluable resource for assistance with data extraction and checking, and helped to locate studies and track data. Ms. Katie Worley assisted with data extraction and developing tables, and Ms. Sanura Latham helped with data entry and extraction. Drs. Mamata Raj and Jeff Andrews assisted with screening studies and risk of bias assessment. We sincerely appreciate their dedicated work and the input of our Task Order Officers and Associate Editor, Key Informants, and Technical Experts.

Key Informants

In designing the study questions, the EPC consulted several Key Informants who represent the end-users of research. The EPC sought the Key Informant input on the priority areas for research and synthesis. Key Informants are not involved in the analysis of the evidence or the writing of the report. Therefore, in the end, study questions, design, methodological approaches, and/or conclusions do not necessarily represent the views of individual Key Informants.

Key Informants must disclose any financial conflicts of interest greater than $10,000 and any other relevant business or professional conflicts of interest. Because of their role as end-users, individuals with potential conflicts may be retained. The TOO and the EPC work to balance, manage, or mitigate any conflicts of interest.

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Technical Expert Panel

In designing the study questions and methodology at the outset of this report, the EPC consulted several technical and content experts. Broad expertise and perspectives were sought. Divergent and conflicted opinions are common and perceived as healthy scientific discourse that results in a thoughtful, relevant systematic review. Therefore, in the end, study questions, design, methodologic approaches, and/or conclusions do not necessarily represent the views of individual technical and content experts.

Technical Experts must disclose any financial conflicts of interest greater than $10,000 and any other relevant business or professional conflicts of interest. Because of their unique clinical or content expertise, individuals with potential conflicts may be retained. The TOO and the EPC work to balance, manage, or mitigate any potential conflicts of interest identified.

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Peer Reviewers

Prior to publication of the final evidence report, EPCs sought input from independent Peer Reviewers without financial conflicts of interest. However, the conclusions and synthesis of the scientific literature presented in this report do not necessarily represent the views of individual reviewers.

Peer Reviewers must disclose any financial conflicts of interest greater than $10,000 and any other relevant business or professional conflicts of interest. Because of their unique clinical or content expertise, individuals with potential nonfinancial conflicts may be retained. The TOO and the EPC work to balance, manage, or mitigate any potential nonfinancial conflicts of interest identified.

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Tonsillectomy for Obstructive Sleep-Disordered Breathing or Recurrent Throat Infection in Children

Structured Abstract

Objectives. To systematically review evidence addressing tonsillectomy in children with obstructive sleep-disordered breathing (OSDB) or recurrent throat infections.

Data sources. Multiple databases from January 1980 through June 2016.

Review methods. We included comparative studies of tonsillectomy, perioperative medications to improve outcomes, and postoperative medications for pain. We also included case series and database studies with ≥1,000 children to address harms. Two investigators independently screened studies and rated risk of bias. We extracted and summarized data qualitatively and quantitatively via Bayesian meta-analyses. We also assessed strength of the evidence (SOE).

Results. We identified 218 unique studies (141 randomized controlled trials [RCTs], 12 nonrandomized trials, 7 prospective and 5 retrospective cohort studies, and 53 database or registry studies or case series [67 low, 110 moderate, and 41 high risk of bias]). Populations; surgical approaches; anesthetic, analgesic, and antiemetic regimens varied across studies. For children with OSDB, most studies reported better sleep-related outcomes in those who had a tonsillectomy versus no surgery. For children with recurrent throat infections, tonsillectomy improved the number of infections, associated utilization (clinician visits), and work/school absences in the first postsurgical year. These benefits did not persist over time, however, and longer term outcomes are limited. Partial tonsillectomy was associated with faster return to normal diet or activity versus total tonsillectomy but also with a risk of tonsillar regrowth requiring reoperation. Commonly used "hot" techniques were generally associated with faster return to normal diet and activity than was cold dissection. In meta-analyses, frequency of post-tonsillectomy hemorrhage (PTH) was less than 4 percent, and frequency of bleeding-associated revisits or reoperations was less than 8 percent. Meta-analysis of nine RCTs reporting bleeding associated with perioperative dexamethasone compared with placebo did not indicate a significantly increased risk of bleeding with steroids, although confidence bounds were wide. Studies of perioperative medications were heterogeneous, but dexamethasone was consistently associated with less need for rescue analgesia than placebo. Preemptive perioperative 5-hydroxytryptamine (5-HT) antiemetics were associated with less need for postoperative antiemetics than placebo. Few studies of postoperative medications addressed the same agents or outcomes.

Conclusions. Tonsillectomy can produce short-term improvement in sleep outcomes compared with no surgery in children with OSDB (moderate SOE). In children with recurrent throat infections undergoing tonsillectomy, number of throat infections (moderate SOE) and associated health care utilization and work/school absences (low SOE) improved in the first postsurgical year. These benefits did not persist, and data on longer term results are lacking. Short-term improvements must be weighed against the risk of PTH (high SOE for low frequency of PTH). Surgical technique had little bearing on return to normal diet or activity (low SOE). Perioperative

dexamethasone and pre-emptive 5-HT receptor antagonist antiemetics reduced the need for additional analgesics or antiemetics (low SOE). Dexamethasone did not increase risk of PTH compared with placebo, but estimates had wide confidence bounds (low SOE). Little evidence addressed the use of postoperative medications for pain-related outcomes (insufficient SOE).

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Executive Summary

Introduction

Tonsillectomy or adenotonsillectomy ("tonsillectomy") represent more than 15 percent of all surgical procedures in children under the age of 15 years.[1, 2] The primary indication for tonsillectomy has shifted over the last 20 years from recurrent throat infections to obstructive sleep-disordered breathing (OSDB) and obstructive sleep apnea (OSA).[3, 4] Widely variable national and small area tonsillectomy rates are well-documented. In their seminal study, Wennberg and Gittlesohn found rates of tonsillectomy varied almost 12-fold across adjacent counties in rural Vermont with similar populations.[5] Variation in rates continue despite improved evidence and dissemination about indications.[1]

Indications for Tonsillectomy

Tonsillectomy has two primary indications: recurrent tonsillitis and OSDB recurrent or severe tonsillitis has been defined as seven or more episodes of sore throat in the preceding year OR five or more episodes in the each of the preceding 2 years OR 3 or more episodes in each of the preceding 3 years.[6] No gold standard diagnostic test exists to etiologically implicate or predictably attribute symptoms to tonsillitis. In fact, consensus is lacking on what symptoms attributable to tonsillitis are considered "disabling." Surrogates often used for tonsillitis include sore throat and pharyngitis. However, the degree to which either of these terms reflects true tonsillitis is not known. Bacterial pharyngitis can be diagnosed via rapid testing or culture. It is not possible, however, to determine whether the tonsil represents the infectious nidus or whether the suspected pathogen represents normal bacterial flora for a particular child's pharynx.

Currently, the most common indication for tonsillectomy is OSDB (i.e., breathing difficulties during sleep including OSA and upper airway resistance syndrome [UARS]). OSDB results from obstruction from or dynamic collapse due to upper airway soft tissue during sleep resulting in snoring, hypopnea, apnea, and restless sleep. Adenotonsillar hypertrophy can cause oropharyngeal crowding, thereby increasing the likelihood of symptomatic airway collapse during sleep. OSDB includes disorders ranging from simple snoring to OSA and can result in significant effects on quality of life and health consequences. It has been associated with a five-point decrease in IQ, hypersomnolence, emotional lability, decreased attention, small stature, enuresis, cardiopulmonary morbidity, and missed school.[7] Evidence of the relationship is reinforced by the effectiveness of OSDB treatment in improving behavior, attention, quality of life, neurocognitive functioning, enuresis, parasomnias, and restless sleep, and reversal of associated cardiovascular sequelae.[8, 9] Moreover, OSDB occurs at especially high rates in subsets of children with developmental disorders and craniofacial syndromes, including Down syndrome.

Key Decisional Dilemmas

Tonsillectomy is painful and is associated with odynophagia (painful swallowing) and dysphagia (difficulty swallowing) that can make it difficult to return to normal diet or stay hydrated, and can be associated with postoperative hemorrhage, nausea and vomiting. To help

minimize these concerns, clinicians may use perioperative antibiotics, steroids, antiemetics, and pain medications (e.g., non-steroidal anti-inflammatory drugs [NSAIDs] and other analgesics).

Clinicians and parents need to know three key things: 1) what is the likelihood that the surgery (compared with watchful waiting with supportive care) will improve clinical outcomes around recurrent throat infections and sleep disorders; 2) what is the risk that the child will experience a harm, primarily post-tonsillectomy hemorrhage (PTH), with the surgery; and 3) if surgery is indicated, what approach, in terms of both surgical technique and perioperative medical care, has been demonstrated to optimize effectiveness and minimize harms? We address these questions by reviewing the comparative data for effectiveness on a specific set of outcomes and also searching a broader set of studies for harms data in order to estimate the frequency of the most common and most severe harms, namely PTH, readmission, and reoperation. The results from this report will be widely applicable; however, lack of consistently reported modifier data (e.g., body mass index [BMI], surgical indications) may limit its generalizability to every child.

Scope and Key Questions

Scope and Uses of the Review

The current review addresses the comparative effectiveness and harms of tonsillectomy in children with the most common indications for the procedure, namely, OSDB and recurrent throat infections. We targeted the review on these two key indications in order to maximize its utility for a broad population while maintaining a scope of work feasible for the systematic review. The review, nominated by the American Academy of Otolaryngology - Head & Neck Surgery Foundation, addresses key decisional dilemmas identified by stakeholders and through our preliminary scan of the literature in a comprehensive manner. The review also includes Key Questions (KQs) to improve understanding of outcomes in subgroups such as very young children (1-2 years old), children with Down syndrome, and those who are overweight or obese.

We anticipate this report will be of primary value to organizations that develop guidelines for tonsillectomy, to clinicians who provide care for children with indications for tonsillectomy, and for families making treatment decisions. Children who are candidates for tonsillectomy may be treated by clinicians including pediatricians, otolaryngologists, family physicians, nurses, nurse-practitioners, and physician assistants. This report supplies practitioners and researchers up-to-date information about the current state of evidence, and assesses the quality of studies that aim to determine the outcomes and safety of tonsillectomy.

Key Questions

We developed KQs in consultation with Key Informants and the Task Order Officer. KQs were posted for review to the Agency for Healthcare Research and Quality Effective Health Care Web site. We note that OSDB includes breathing difficulties during sleep as operationalized in each study, including OSA and UARS. As noted, tonsillectomy includes tonsillectomy, partial tonsillectomy, and adenotonsillectomy. We also note that comparative effectiveness includes both the benefits and harms of interventions.

Questions were as follows:

KQ1. In children with OSDB, what is the comparative effectiveness of tonsillectomy compared with continuous positive airway pressure (CPAP) or watchful waiting with supportive care (including pharmacologic treatment) to improve sleep outcomes, cognitive or behavioral outcomes, and health outcomes?

KQ1a. In children with OSDB and neuromuscular or craniofacial abnormalities, what is the comparative effectiveness of tonsillectomy compared with CPAP or watchful waiting with supportive care (including pharmacologic treatment) to improve sleep outcomes, cognitive or behavioral outcomes, and health outcomes?

KQ1b. In children with OSDB under age 3 years, what is the comparative effectiveness of tonsillectomy compared with watchful waiting with supportive care (including pharmacologic treatment) to improve sleep outcomes, cognitive or behavioral outcomes, and health outcomes?

KQ1c. In children with OSDB and Down syndrome, what is the comparative effectiveness of tonsillectomy compared with CPAP or watchful waiting with supportive care (including pharmacologic treatment) to improve sleep outcomes, cognitive or behavioral outcomes, and health outcomes?

KQ1d. In children with OSDB who are overweight or obese, what is the comparative effectiveness of tonsillectomy compared with CPAP, weight loss, or watchful waiting with supportive care (including pharmacologic treatment) to improve sleep outcomes, cognitive or behavioral outcomes, and health outcomes?

KQ2. Among children with recurrent throat infections, what is the comparative effectiveness, including harms, of tonsillectomy compared with watchful waiting with supportive care (including pharmacologic—antibiotic or non-antibiotic—treatments) on the number and severity of throat infections, quality of life, and health care utilization?

KQ3. Do benefits and harms differ between partial tonsillectomy and total tonsillectomy?

KQ4. Do benefits and harms differ by surgical technique (e.g., cautery, coblation)?

KQ5. What are the benefits and harms of adjunctive perioperative (i.e., preoperative, intraoperative, or in postanesthesia care) pharmacologic agents intended to improve outcomes?

KQ6. What are the benefits and harms of postoperative (i.e., after discharge from postanesthesia care and up to 10 days postsurgery) pharmacologic agents intended to reduce pain-related outcomes?

Analytic Framework

The analytic frameworks illustrate the population, interventions, and outcomes that guided the literature search and synthesis (Appendix A of the main report). The frameworks depict the KQs within the context of population, intervention, comparator, outcomes, timing, and setting (PICOTS) parameters. In general, the figures illustrate how tonsillectomy may result in outcomes such as changes in sleep parameters, numbers of throat infections, quality of life, or health care utilization.

Methods

Literature Search Strategy

To ensure comprehensive retrieval of relevant studies of therapies for children undergoing tonsillectomy, we used three key databases: the MEDLINE® medical literature database via the PubMed® interface; EMBASE (Excerpta Medica Database), an international biomedical and pharmacological literature database via the Ovid® interface; and the Cochrane Library. Search strategies for KQs applied a combination of controlled vocabulary (Medical Subject Headings [MeSH] and Emtree headings) to focus specifically on tonsillectomy and harms of interventions. We restricted literature searches for KQs to studies published from January 1980 to June 2016 to reflect current techniques for tonsillectomy and perioperative or postoperative medications.

We carried out hand searches of the reference lists of recent systematic reviews or meta-analyses of studies addressing pediatric tonsillectomy. The investigative team also scanned the reference lists of studies included after the full-text review phase for additional studies that potentially could meet our inclusion criteria.

Inclusion and Exclusion Criteria

Table A lists the inclusion/exclusion criteria we used based on our understanding of the literature, key informant and public comment during the topic refinement phase, input from the Technical Expert Panel, and established principles of systematic review methods. We used a best evidence approach to determine final inclusion of studies. That is, if evidence from randomized studies or those with low risk of bias was insufficient to address a KQ or specific outcomes, we considered evidence from observational literature as well as factors related to the relevance of studies to determine if the inclusion of additional studies was warranted.[10]

Table A. Inclusion criteria for studies of tonsillectomy

Category	Criteria
Population	• Children with OSDB age 3-18 years, inclusive (KQ1) • Children with neuromuscular or craniofacial abnormalities and OSDB age 3-18 years, inclusive (KQ1a) • Children under age 3 years with OSDB (KQ1b) • Children with Down syndrome OSDB age 3-18 years, inclusive (KQ1c) • Children with obesity or overweight and OSDB age 3-18 years, inclusive (KQ1d) • Children with recurrent throat infection age 3-18 years, inclusive (KQ2) • Children with OSDB or recurrent throat infection undergoing tonsillectomy age 3-18 years, inclusive (KQ 4-6)
Intervention	• Tonsillectomy, adenotonsillectomy, or tonsillotomy (partial removal of tonsil) using any surgical approach (e.g., coblation, laser, cold dissection) (KQ 1-6) • Perioperative (preoperative, intraoperative, and immediate postoperative [postanesthesia care] periods) NSAIDs, steroids, or antiemetics (KQ5) • Any postoperative (discharge from postanesthesia care to up to 10 days postsurgery) agent for pain (KQ6)
Design	• Effectiveness outcomes: Comparative studies (RCTs, prospective or retrospective cohort studies with comparison groups, nonrandomized trials, case-control studies) (KQ1-6) • Harms: Comparative studies (RCTs, prospective or retrospective cohort studies with comparison groups, nonrandomized trials, case-control studies), database or registry studies (harms of tonsillectomy), case series with at least 1000 participants (harms of tonsillectomy)
Other	• Original research (KQ1-6) • Publication language: English (KQ1-6) • Publication year: January 1980-June 2016 (KQ1-2) or January 2000-June 2016 (KQ3-6) • Reports one or more of the outcomes of interest • Sufficiently detailed methods and results to enable data extraction (KQ1-6) • Reports outcome data by target population or intervention (KQ1-KQ6)

Abbreviations: KQ = Key Question; NSAID = non-steroidal anti-inflammatory drug; OSDB = obstructive sleep-disordered breathing; RCT = randomized controlled trial

Study Selection

Two reviewers independently assessed each abstract. If one reviewer concluded that the article could be eligible to address a KQ based on the abstract, we retained it for review of the full text. Two reviewers independently assessed the full text of each included study potentially addressing a KQ, with any disagreements adjudicated by a senior reviewer.

Data Extraction and Synthesis

We extracted data from included studies into templates that recorded study design, descriptions of the study population (for applicability), description of the interventions, and baseline and outcome data on constructs of interest. Data were initially extracted by one team member and reviewed for accuracy by a second. Extracted data for KQs are available in the Systematic Review Data Repository (srdr.ahrq.gov).

We summarized data for KQs qualitatively using summary tables where meta-analyses were not possible. We used a best evidence approach and focused on lower risk of bias studies where they provided sufficient data to address a KQ.[10]

We identified sufficient data to address PTH and PTH-related readmissions or clinician visits using quantitative meta-analysis methods. We implemented a mixed-effects, arm-based meta-analysis to assess the influence of different surgical procedures as well as the effect of partial compared with total tonsillectomy on the occurrence of PTH outcomes following surgery. We

also conducted analyses to estimate the effects of including high risk of bias studies in the analyses. These analyses suggested no systematic effects of these studies; thus, we retained them. Appendix E of the main report contains a full description of the meta-analytic methods.

Risk-of-Bias Assessment of Individual Studies

We used separate tools appropriate for specific study designs to assess quality of individual studies meeting eligibility criteria for our KQs. We used prespecified questions (Table 4 in *Assessing the Risk of Bias of Individual Studies in Systematic Reviews of Health Care Interventions*[11]) appropriate to each study design to assess risk of bias of randomized controlled trials (RCTs) and observational studies and a tool adapted from questions outlined in the McMaster McHarms tool to assess reporting of harms.[12]

Two team members independently assessed each included study, with discrepancies resolved through discussion to reach consensus and/or adjudication by a senior reviewer. We then translated these ratings into standards for low, moderate, or high risk of bias, as described in the full report. Risk-of-bias ratings for each study are in Appendix F of the full report.

Strength of the Body of Evidence

Two senior investigators graded the strength of the evidence (SOE) for key intervention/outcome pairs using methods based on the *Methods Guide for Effectiveness and Comparative Effectiveness Reviews*.[13] We assessed the domains of study limitations (low, medium, high level of limitation), consistency (inconsistency not present, inconsistency present, unknown), directness (direct, indirect), precision (precise, imprecise), and reporting bias (detected, unsuspected). The full team reviewed the final strength of evidence designations. The possible grades were:

- High: High confidence that the evidence reflects the true effect. Further research is unlikely to change estimates.
- Moderate: Moderate confidence that the evidence reflects the true effect. Further research may change our confidence in the estimate of effect and may change the estimate.
- Low: Low confidence that the evidence reflects the true effect. Further research is likely to change confidence in the estimate of effect and is also likely to change the estimate.
- Insufficient: Evidence is either unavailable or does not permit a conclusion.[14]

Applicability

We assessed the applicability of findings reported in the included literature addressing KQs to the general population of children who are candidates for tonsillectomy because of OSDB or recurrent throat infection by determining the population, intervention, comparator, and setting in each study and developing an overview of these elements for each intervention category. We anticipated that areas in which applicability would be especially important to describe would include the indication for tonsillectomy, age at treatment, surgical technique, and population characteristics such as BMI, Down syndrome, or craniofacial abnormalities. Applicability tables for each intervention are in Appendix G of the full report.

Results

We identified 9608 nonduplicative titles or abstracts with potential relevance, with 1966 proceeding to full text review. We excluded 1725 studies at full text review. We included 218 unique studies (241 publications) in the review (see main report for all references). These 218 studies (reported in multiple publications) included 165 comparative studies (comprising 141 RCTs, 12 nonrandomized trials, seven prospective and five retrospective cohort studies) and 53 database or registry studies or case series with at least 1000 children. We used database and registry studies and case series for harms data only. We considered 67 studies to have low risk of bias, 110 to have moderate risk, and 41 to have high risk. We did not retain high risk of bias studies as part of the evidence for any KQ, except for in meta-analyses after sensitivity analyses showed that they had no systematic effects on outcomes.

KQ1. Effectiveness of Tonsillectomy Versus No Surgery for OSDB

We identified 13 unique studies addressing tonsillectomy in children with OSDB. Three RCTs, one nonrandomized trial, and four cohort studies had moderate risk of bias. Five cohort studies had high risk. Given the relatively few studies addressing this question, we retained retrospective studies as part of the evidence base.

Two RCTs, two prospective, and two retrospective cohort studies (all with moderate risk of bias) all reported improvement in the Apnea Hypopnea Index (AHI) in children after tonsillectomy compared with watchful waiting (without intervention or with supportive/medical management, excluding CPAP). Differences in AHI between tonsillectomy and watchful waiting groups were statistically significant in three studies and not significant in two. This benefit was consistent across age ranges (1-18 years), though data were most frequently available on children ages 4 to 12. Benefits seemed durable, with followup ranging from 6 months to 4 years. The watchful waiting groups also improved from baseline in three studies and worsened in two cohort studies.

We combined three studies reporting AHI outcomes in a fixed effects meta-analysis. We found a mean effect size of -4.81 (95% credible interval: -6.5 to -3.1), indicating an approximately 5-point improvement in obstructive symptoms in children receiving tonsillectomy compared with those not undergoing surgery. The clinical significance of this improvement is likely influenced by baseline disease severity and may be most obvious in children with mild or moderate OSDB (i.e., AHI scores of 1 to 10). Two RCTs, one nonrandomized trial, and one retrospective cohort (all with moderate risk of bias) used several different parent-reported quality measures to assess sleep quality outcomes, limiting the ability to compare effectiveness directly across studies, although better outcomes were consistently associated with tonsillectomy. In one RCT and one prospective and one retrospective cohort study (moderate risk of bias) evaluating behavioral outcomes (emotional lability, attention, aggression) again using different measures, outcomes were consistently better among children receiving tonsillectomy; in all studies reporting baseline data, scores on behavioral measures were not indicative of clinical concern. While children's behaviors improved in these studies, the clinical significance and magnitude of the improvement is not clear. Executive function measures did not differ among children receiving tonsillectomy or no surgery in one RCT and one prospective cohort study, both with moderate risk of bias. In studies reporting baseline scores, sleep quality and behavioral outcomes for children in the no surgery groups also moderately improved from baseline, with greater improvement in children who had tonsillectomy. Studies rarely reported other outcomes (e.g.,

utilization, cognitive outcomes).

One moderate risk of bias RCT compared tonsillectomy and CPAP. Children had concomitant Down syndrome or mucopolysaccharidoses. Children receiving tonsillectomy had improved AHI scores compared with children receiving CPAP, but group differences were not significant in this small study.

KQ1a. Effectiveness of Tonsillectomy for Children With OSDB and Neuromuscular or Craniofacial Abnormalities

One RCT (moderate risk of bias) compared the efficacy of tonsillectomy to immediate initiation of CPAP in children with Down syndrome and mucopolysaccharidoses who were diagnosed with obstructive sleep apnea by polysomnogram. As discussed above, both groups showed improvement in AHI at 6-month followup, with maintenance at 12-month followup (no significant group differences). One retrospective cohort study including 15 children with syndromic comorbidities reported no significant group differences in improvements in AHI in children with syndromic conditions.

KQ1b. Effectiveness of Tonsillectomy for Children With OSDB Under 3 Years of Age

Although several studies included children under 3, these data were not extractable from the aggregate data of the entire study population. We did not identify studies explicitly addressing this question.

KQ1c. Effectiveness of Tonsillectomy for Children With OSDB and Down Syndrome

As noted, few studies specifically reported analyses of children with Down syndrome. These studies are discussed in detail under KQ1a.

KQ1d. Effectiveness of Tonsillectomy for Children With OSDB and Obesity

One retrospective cohort study, including a mostly overweight/obese population with OSDB, reported a significant improvement in AHI in children who received tonsillectomy compared with those who did not; however, data were insufficient to suggest effect modification by obesity/overweight status in this single, small study. In another retrospective cohort including children with mild OSA, analysis of subgroups of obese children and those with syndromic comorbidities showed no significant benefit between groups in these populations.

KQ2. Effectiveness of Tonsillectomy Versus No Surgery for Recurrent Throat Infection

We identified ten unique studies addressing tonsillectomy specifically for recurrent throat infections. Four RCTs, one nonrandomized trial, and two retrospective cohort studies had moderate risk of bias, and one RCT and one prospective cohort study and nonrandomized trial had high risk of bias. Given the relatively few studies addressing this question, we retained retrospective studies as part of the evidence base. In all studies reporting baseline data, the

number of subsequent infections decreased from baseline in both groups, with significantly greater decreases in children who received tonsillectomy vs. no surgery/watchful waiting with supportive care in the short term (< 12 months).

Children who received tonsillectomy missed fewer days of school in the short-term compared to the non-surgery control group but differences diminished over time in two moderate risk of bias RCTs; no difference in school absences between groups was reported from a third moderate risk of bias trial. Three studies (two RCTs and one nonrandomized trial, all with moderate risk of bias) collected quality of life data, which were not markedly different between any of the study arms at the 24-month time point. Overall, comparative effectiveness assessment of tonsillectomy vs. no surgery to improve number of throat infections, associated health care utilization, and days of work/school missed shows a benefit in the first postsurgical year; benefits did not persist over time, and quality of life improved in both groups.

KQ3. Effectiveness of Partial Versus Total Tonsillectomy

We identified 22 unique studies (20 RCTs—5 with low, 11 with moderate, and 4 with high risk of bias—and 2 nonrandomized trials with high risk of bias) addressing partial tonsillectomy compared with total tonsillectomy. In addition to comparing partial with total tonsil removal, most studies (n=16) also compared surgical techniques including microdebrider, laser, coblation, and electrocautery partial tonsillectomy and cold dissection, coblation, and electrocautery total tonsillectomy. In studies comparing both extent of surgery and surgical techniques (e.g., partial coblation vs. total electrocautery), it is not possible to determine whether effects can be attributed to the technique or to the amount of tissue removed. Thus, except for studies that compared partial or total removal of the tonsils using the same technique (e.g., partial cold dissection vs. total cold dissection), we considered the comparison of interest broadly as partial vs. total tonsil removal. Studies defined "partial" tonsillectomy in varied ways or not explicitly.

Few studies reported the same outcomes, and few reported significant differences in any outcome between partial or total tonsil removal. Two RCTs (low and moderate risk of bias) that compare total and partial cold dissection found that children receiving partial tonsillectomy had significantly faster return to normal diet (~4 days earlier). Two small RCTs with low and moderate risk of bias addressed outcomes following partial vs. total coblation or electrocautery and reported only on return to usual diet or activity. In the coblation study, children in the partial tonsillectomy arm consumed a significantly greater percentage of normal diet and were engaged in a greater portion of normal activity than were children in the total tonsillectomy arm at all time points assessed. In the study of electrocautery tonsillectomy, differences in return to normal activity were not statistically significantly different between groups.

Eight studies with low or moderate risk of bias addressed partial vs. total tonsillectomy using different surgical techniques. In two studies, obstructive symptoms including snoring worsened in the short term in the partial tonsillectomy arm compared with total tonsillectomy, but differences between groups were not significant at longer-term followup (12 to 24 months) post-tonsillectomy. In a third RCT, no children in either group had snoring or apnea at 1 and 3 years postoperatively. In all six studies addressing return to normal diet, children receiving partial tonsillectomy had more favorable outcomes compared with those receiving total tonsillectomy; studies reported different measures to assess this outcome. As with diet, in five RCTs children undergoing partial tonsillectomy had a more favorable return to normal activity (roughly 1 to 4 days faster) than did children who had total tonsillectomy in (significant differences in two). In three of the four studies addressing throat infection, children who had partial tonsillectomy had

more throat infections (1 to 7 more infections, depending on time period) than did those in the total tonsillectomy arms, though differences were not statistically significant in three studies. Three studies addressed quality of life or behavioral outcomes with no significant group differences. Across all studies, 10 of an estimated 166 children (6%) had tonsillar regrowth after partial tonsillectomy. Of these, five ultimately underwent completion of total tonsillectomy as a revision surgery.

KQ4. Effectiveness of Surgical Techniques

We identified 59 unique studies (54 RCTs, 4 nonrandomized trials, and 1 prospective cohort study) comparing surgical techniques for tonsillectomy. Eighteen studies had low risk of bias, 28 had moderate risk, and 13 had high risk. Most studies reported harms data (see Harms of Tonsillectomy section below). Nineteen studies (17 RCTs and 2 nonrandomized trials)—eight with low and 11 with moderate risk of bias—reported on return to normal diet or activity, the only usable effectiveness outcomes reported. Five RCTs and one nonrandomized trial compared coblation and cold dissection tonsillectomy. Across these small, short-term studies, coblation tonsillectomy was generally associated with faster return to normal diet or activity (roughly 1 to 4 days). Four studies reported on return to normal diet, with faster return associated with coblation in two studies and no significant group differences in two studies. Return to normal activity occurred significantly earlier after coblation in three low risk of bias studies.

Electrocautery was generally associated with more favorable results in three small RCTs comparing it with cold dissection. Two studies reported more favorable results associated with electrocautery, whereas results did not differ in the third. Return to activity was significantly faster in the electrocautery arm in one study, but no different in two others.

Four RCTs with moderate risk of bias compared coblation and electrocautery tonsillectomy with mixed results. Children undergoing coblation returned to normal diet more quickly than children undergoing electrocautery tonsillectomy in two studies, but recovery time did not differ significantly between groups in two other trials. Children undergoing coblation also returned to normal activity roughly 2 days more quickly than those receiving electrocautery in two studies.

Three RCTs with moderate risk of bias evaluated tonsillectomy with a harmonic scalpel (which uses ultrasonic frequency to cut and cauterize tissue) compared with electrocautery, coblation, or cold dissection. Studies compared different measures of recovery, thus limiting our ability to draw conclusions about differences in effectiveness, though patients treated with harmonic scalpel recovered more quickly in all studies. Only two small RCTs addressed laser tonsillectomy or thermal welding tonsillectomy and did not provide sufficient data to draw conclusions about effectiveness compared with more standard techniques.

Harms of Tonsillectomy

To account fully for potential harms of tonsillectomy, primarily PTH and readmission and reoperation, we compiled all comparative studies and examined frequency of harms by arm, then reviewed additional case series and database studies not included in the effectiveness analysis. We considered PTH to comprise any report of post-tonsillectomy bleeding, including the entire range of bleeding as reported in each study, from bloody sputum to frank bleeding requiring readmission or reoperation. We did not assess harms separately by indication because there is no reason to expect that they would differ; therefore, we do not separate them into the KQ1 through KQ4 results sections but combine surgical harms here.

We present the data obtained from comparative studies that had low or moderate risk of bias followed by that of the case series and database studies and comment on their consistency. Finally, we conducted a Bayesian meta-analysis to estimate predicted frequency of primary PTH, secondary PTH, reoperation and readmission by partial and total tonsillectomy, and by surgical approach.

Unadjusted frequency of harms reported in comparative studies. One-hundred and four comparative studies of low or moderate risk of bias reported harms data. The 6299 children across studies who were treated with total tonsillectomy experienced 265 episodes (4.2%) of PTH. Sixty-eight children required reoperation to control PTH (2.2%), and 80 had nonoperative revisits or readmissions for PTH (3.0%) Children undergoing tonsillectomy with harmonic scalpel had the highest frequency of PTH (11.3%), although few children underwent this procedure (n=397). Few children also had laser tonsillectomy (n=189), with 5.3 percent experiencing PTH. Frequencies were similar among techniques that are more commonly used: cold dissection=3.8 percent; electrocautery=4.9 percent; and coblation=3.3 percent. Frequency of revisits and reoperations overall were typically less than 6 percent. Frequency of revisits or readmissions for postoperative nausea and vomiting, pain, or dehydration ranged from 0 to 17 percent across techniques used for total tonsillectomy; laser tonsillectomy was associated with the highest frequencies.

PTH did not exceed 5 percent among the 18 study arms contributing data to asses bleeding in partial tonsillectomy. The frequency was highest for coblation partial tonsillectomy (4.2%). No PTH was associated with laser approaches, but few studies assessed this modality. Frequency of readmissions/revisits or reoperation were 1.8 percent and 0.64 percent across all types of techniques. Only three studies of partial tonsillectomy reported revisits for pain, dehydration, or postoperative nausea and vomiting. No children required readmission for dehydration in a single coblation study while 2.5 percent of children in studies of microdebrider had revisits for dehydration. No children in these microdebrider studies had revisits for pain.

Other harms reported in studies of total or partial tonsillectomy were largely minor and included burns or unspecified breathing complications. No comparative study reported deaths.

Meta-analysis of PTH-related data. Seventy studies evaluating partial or total tonsillectomy contributed data to the meta-analysis (63 RCTs, 6 nonrandomized trials, and 1 prospective cohort study). Twenty-two studies had low risk of bias; 36 had moderate risk; and 12 had high risk. In sensitivity analyses, high risk of bias studies did not affect findings, so we included them in final analyses (Table B). Frequency of primary PTH associated with total tonsillectomy in the meta-analyses were consistently at or below 5 percent and with overlapping confidence bounds. Electrocautery and harmonic scalpel were associated with the highest frequencies of secondary PTH (occurring >24 hours postprocedure), with estimates of 4.2 to 4.3 percent and wide 95% Bayesian credible intervals. Frequency of readmission related to PTH ranged from 0.2 percent to 6 percent. Although laser tonsillectomy was associated with the highest estimated risk of readmission, the confidence bounds were very wide. Primary PTH associated with partial tonsillectomy was predicted to be below 4 percent regardless of technique, and secondary PTH below 3 percent. Data on PTH-related readmissions and reoperations were sparse; thus confidence bounds are wide, and it is difficult to predict frequency with any certainty.

Table B. Frequency of PTH and PTH-associated readmissions or revisits after tonsillectomy: percent (95% BCI)

	Technique	Primary PTH	Secondary PTH	Nonoperative Readmission	Reoperation
Total Tonsillectomy	Cold	0.7 (0.1 to 1.5)	3.3 (1.9 to 5.3)	2.7 (0.7 to 4.9)	1.3 (0.5 to 2.1)
	Electrocautery	0.6 (0 to 1.5)	4.2 (2.4 to 6.5)	2.9 (0.7 to 5.3)	1.2 (0.5 to 1.9)
	Coblation	1.1 (0 to 3.0)	2.3 (0.7 to 4.4)	1.4 (0.1 to 3.3)	1.2 (0.3 to 2.4)
	Harmonic Scalpel	1.0 (0 to 3.3)	4.3 (1.8 to 7)	1.5 (0.2 to 3.1)	3.9 (1.6 to 6.9)
	Laser	2.2 (1.0 to 5.8)	1.2 (0 to 3.4)	5.7 (0.7 to 12.6)	5.2 (0.2 to 13.7)
	Molecular Resonance	0.6 (0 to 2.5)	1.1 (0.2 to 2.4)	0.2 (0 to 0.6)	0.2 (0 to 0.5)
	Thermal Welding	0.5 (0 to 2.1)	3.6 (0.5 to 7.5)	2.7 (0 to 12.7)	0.8 (0 to 2.4)
Partial Tonsillectomy	Cold	1.5 (0 to 4.7)	2.3 (1 to 5.9)	3.7 (0.1 to 10.3)	0.5 (0 to 1.3)
	Electrocautery	1.5 (0 to 5.3)	3 (0.2 to 8)	4 (0.2 to 12.3)	0.4 (0 to 1.2)
	Coblation	1.5 (0.1 to 4.2)	1.4 (1 to 3.5)	1.4 (0.1 to 3.1)	0.4 (0 to 1.1)
	Harmonic Scalpel	2.2 (0 to 8.3)	3 (1 to 7.9)	2.1 (0 to 6.3)	1.4 (0 to 3.9)
	Laser	3.9 (0 to 12.9)	0.7 (0 to 2.4)	7.3 (0.2 to 20.7)	1.8 (0 to 5.4)
	Molecular Resonance	1.4 (0 to 6)	0.8 (0 to 2.3)	0.3 (0 to 1)	0.1 (0 to 2)
	Thermal Welding	1 (0 to 4.5)	2.6 (0 to 7.7)	3.4 (0 to 17)	0.3 (0 to 1)

BCI = Bayesian credible interval; PTH = post-tonsillectomy hemorrhage

Unadjusted frequency of harms in case series and database studies. Fifty-three studies addressed harms (19 low risk of bias, 27 moderate, and 7 high [not included in analyses]). Overall, 2.1 percent of children in case series experienced a PTH episode. Few children required readmission or reoperation for PTH (0.41% to 0.72%). Few cases of revisits for pain, dehydration, or postoperative nausea and vomiting (frequency ranging from 1% to 7%) were reported in the 11 studies reporting these data.

At least four deaths were reported across four case series or database studies reporting mortality. Deaths, when cause was reported, were attributed to continued bleeding and suspected ventricular fibrillation. One study compared tonsillectomy complications occurring in different hospital types (teaching or non-teaching children's hospitals, nonteaching hospitals); in each hospital type ≤10 deaths occurred, but the study did not report specific numbers. Another study reported two deaths (out of 36,221 tonsillectomies, 0.006%) but did not report cause of death. Other harms reported in these studies were disparate and typically not clinically significant.

KQ5. Effectiveness of Perioperative Medications To Improve Outcomes

Forty-nine studies (48 RCTs—23 low, 21 moderate, and 4 high risk of bias—and one nonrandomized trial with high risk of bias) evaluated the use of perioperative NSAIDs, steroids, or antiemetics. Most studies reported on time to resume normal diet or activity or need for

rescue medications, which we defined as the need for additional or higher doses of pain medications or antiemetics beyond those given as part of the standard surgical protocol. Doses, routes of administration, combinations of agents, and comparators differed across studies. Followup was limited to <7 days postprocedure, with most studies reporting outcomes in the immediate postoperative period (postanaesthesia care unit and up to 24 hours).

NSAIDs. Fourteen RCTs evaluated NSAIDs. In two studies of diclofenac, postoperative consumption of opioids was significantly lower in diclofenac groups compared with placebo, but analgesics typically did not differ between groups in three trials comparing diclofenac and other analgesics or diclofenac in combination with other agents and placebo. Analgesic needs typically did not differ by group in three studies comparing perioperative ibuprofen (with or without other agents) and placebo or other analgesics. In two studies comparing ketoprofen and including a placebo arm, results were mixed, with significantly lower analgesic needs associated with ketoprofen in one and no group differences in another. Lornoxicam and ketorolac, each addressed in a single study, both reported no differences in analgesic use between these agents and comparators (placebo, fentanyl).

A single moderate risk of bias study evaluating effectiveness of peritonsillar bupivacaine infiltration vs. diclofenac suppository reported no difference in antiemetic rescue use between arms. In two RCTs comparing diclofenac with or without other analgesics to lidocaine or placebo, time to normal activity or diet did not differ significantly between groups.

Six studies of NSAIDs reported six episodes of PTH in 277 treated children (2.2%). Three cases of PTH were associated with diclofenac, two with ibuprofen, and one with ketorolac. Two studies (one of ketorolac and one of lornoxicam) reported no cases of PTH.

Steroids. Eighteen RCTs and one nonrandomized trial evaluated steroids. Three of four trials of dexamethasone at escalating doses, or comparing escalating doses with placebo, or doses of dexamethasone compared with ondansetron or placebo showed no differences in postoperative analgesic requirements by dose. In one placebo controlled trial children who received dexamethasone required significantly less analgesia. Five of eight studies comparing intravenous (IV) dexamethasone and placebo found steroid treatment reduced postoperative analgesic requirements significantly. In four RCTs comparing IV dexamethasone and either IV methylprednisolone, oral gabapentin, IV acetaminophen, or IV ketamine, results varied. Two studies reported less use of analgesia associated with dexamethasone arms; one reported no differences between dexamethasone and methylprednisolone; and one reported no differences between dexamethasone and acetaminophen. Two studies comparing IV and infiltrated dexamethasone both found infiltrated dexamethasone reduced postoperative analgesic requirements significantly. Another study comparing dexamethasone infiltration, levobupivacaine infiltration, and placebo reported lower analgesic use in the dexamethasone arm compared with the other groups.

Two dose-escalation trials reported significantly reduced antiemetic use in groups treated with dexamethasone vs. placebo, and two of five RCTS comparing IV dexamethasone and placebo reported significantly reduced antiemetic use in children treated with dexamethasone. Other studies reported lower use of antiemetics associated with dexamethasone vs. analgesic infiltration; no differences noted comparing dexamethasone and methylprednisolone; and less need for antiemetics with combination dexamethasone and ketamine or dexamethasone alone than placebo. A single RCT comparing IV vs. infiltrated dexamethasone vs. placebo reported

significantly lower rescue antiemetic use in both steroid groups compared with placebo and no differences between active groups.

Two RCTs assessed whether steroids affected time to return to normal diet with favorable effects associated with steroids in one and no group differences in another. In one RCT, time to normal activity was improved in children treated with IV dexamethasone vs. no steroid.

Ten studies reported PTH or PTH-associated utilization (9 study arms addressing dexamethasone and one addressing methylprednisolone). Three steroid studies explicitly noted no PTH. In a meta-analysis of studies comparing dexamethasone and placebo, PTH and PTH-associated reoperation or readmission were each nominally ≥ 1, with wide 95% credible intervals. The wide intervals prohibit firm conclusions about the effects of dexamethasone on PTH. The overall frequency of PTH associated with steroids was 4.7 percent, with frequencies of revisits/readmissions or reoperation for hemostasis below 2 percent. Few studies evaluating perioperative agents reported any revisits for non-PTH indications.

Antiemetics. Six RCTs evaluated the effect of perioperative antiemetic use on post-tonsillectomy analgesic requirements. All studies evaluated 5-hydroxytryptamine (5-HT) receptor antagonists including ramosetron, granisetron, ondansetron, and dolasetron. Antiemetic medications did not have any effect on pain control in any trial. Pre-emptive use of 5-HT receptor antagonists reduced the need for immediate postoperative antiemetic use compared with placebo in three RCTs.

KQ6. Effectiveness of Postoperative Medications To Reduce Pain-Related Outcomes After Tonsillectomy

Thirteen studies addressed postoperative medications for pain-related outcomes including 12 RCTs and 1 nonrandomized trial (4 studies with low, 6 with moderate, and 3 with high risk of bias). Study drugs included steroids (prednisolone), NSAIDs (diclofenac, ibuprofen, celecoxib, aspirin), non-NSAID analgesics (acetaminophen) and antibiotics (amoxicillin). Four trials reported effectiveness outcomes. In the trials comparing analgesics (celecoxib, acetaminophen with or without ibuprofen, ibuprofen, diclofenac), the need for rescue medications typically did not differ among study groups; all trials assessing analgesia outcomes had short-term followup (24 to 48 hours postoperatively). Time to return to normal diet was significantly better for children receiving acetaminophen compared with diclofenac reported in one study, but no time differences were noted for children receiving acetaminophen with morphine or with ibuprofen in another study. Two studies of steroids reported no differences in return to normal diet and activity associated with steroid vs. no steroid over longer-term followup (≥5 days).

Discussion

Key Findings and Strength of Evidence

KQ1. Effectiveness of Tonsillectomy Versus No Surgery for OSDB

Relative to no intervention, most studies reported better sleep-related outcomes in children who had a tonsillectomy. In five studies that included children whose OSDB was confirmed with polysomnography, AHI scores were more improved in children receiving tonsillectomy than in those with no surgery (significant group differences in 3 studies). Meta-analysis of three studies

showed a 5-point improvement in AHI in children who underwent tonsillectomy compared with no surgery. Sleep-related quality of life and reduction in negative behaviors (e.g., anxiety, emotional lability) also improved more among children who had tonsillectomy, but the clinical significance of these changes is not clear. Changes in executive function were not significantly different. We did not find tonsillectomy to be superior to CPAP in the one RCT addressing this comparison, which included children with significant comorbidities.

Our confidence in these conclusions of greater improvement in AHI and negative behaviors with tonsillectomy vs. watchful waiting is low (low strength of evidence). We also found consistently greater improvement in sleep-related quality of life with tonsillectomy vs. watchful waiting and have greater confidence in this conclusion (moderate strength of evidence). We could not make conclusions about effects on executive function or IQ (insufficient strength of evidence). We could not make conclusions about outcomes following tonsillectomy compared with CPAP and in studies assessing outcomes in sub-populations such as children with Down syndrome (KQ1a-d) (insufficient strength of evidence).

KQ1a-d. Effectiveness of Tonsillectomy for Subpopulations of Children With OSDB

While studies may have included some children with craniofacial abnormalities, only a single, small RCT compared tonsillectomy with immediate initiation of CPAP in children with OSDB and concurrent Down syndrome or mucopolysaccharidoses and reported no significant group differences in AHI at 12 months. Another study reported no significant group differences in outcomes in analyses of a subset of children with syndromic comorbidities receiving tonsillectomy or watchful waiting. Two retrospective cohorts specifically evaluated overweight/obese populations with OSDB. One reported a significant decrease in AHI in children who received tonsillectomy compared with those who did not. The other study including children with mild OSA reported no significant differences in subgroup analysis of obese children. Similarly, while several studies included some children less than 3 years old, these data were not extractable from the aggregate study population data. We did not identify studies explicitly addressing this question.

We could not make conclusions about outcomes following tonsillectomy compared with CPAP and in studies assessing outcomes in sub-populations such as children with Down syndrome (insufficient strength of evidence). Table C outlines these findings.

Table C. Summary of evidence in studies addressing effectiveness of tonsillectomy in children with OSDB

Intervention and Comparator	Number/Type of Studies (Total N Participants)	Key Outcome(s)	Strength of Evidence Grade	Findings
Tonsillectomy vs. no surgery in children with OSDB	Meta-analysis 2 RCT (456) 1 Prospective cohort (38) 2 Retrospective cohort (94)	Apnea Hypopnea Index	Low for greater improvement of Apnea Hypopnea Index with tonsillectomy compared with no surgery	Significant improvement in tonsillectomy vs. no surgery groups in 1 RCT and 2 retrospective cohort studies; no significant group differences in 1 RCT and 1 prospective cohort. In 3 studies, children in control arms improved from baseline. 4.8-point improvement in AHI in tonsillectomy arms in meta-analysis.
	2 RCT (456) 1 Retrospective cohort (32)	Sleep-related quality of life	Moderate SOE for modest improvement in sleep-related quality of life after tonsillectomy vs. no surgery	Significant improvements in tonsillectomy vs. no tonsillectomy groups on measures of sleep-related quality of life in 2 RCTs and 1 cohort study in the short term
	1 RCT (397) 1 Prospective cohort (38) 1 Retrospective cohort (32)	Behavioral outcomes	Low SOE for improvements in negative behaviors after tonsillectomy vs. no surgery	Significant improvements in tonsillectomy vs. no surgery in 1 RCT and 1 retrospective cohort; no significant differences in 1 prospective cohort; differences in measurement time frames across studies (7 months-4 years) and unclear clinical significance of changes
	1 Prospective cohort (38)	Cognitive changes (IQ)	Insufficient SOE	Insufficient evidence in one small study
	1 RCT (397) 1 Prospective cohort (38)	Executive function	Insufficient SOE	Differences in followup time and medium study limitations preclude conclusions
	1 RCT (397)	Cardiometabolic outcomes	Insufficient SOE	Insufficient evidence in only one RCT
Tonsillectomy vs. CPAP in children with OSDB	1 RCT (73)	Apnea Hypopnea Index, sleep-related quality of life	Insufficient SOE	Insufficient evidence in small study
Tonsillectomy vs. CPAP or watchful waiting in children with OSDB and craniofacial abnormalities	1 RCT (73)	Apnea Hypopnea Index, sleep-related quality of life	Insufficient SOE	Insufficient evidence in small study

Table C. Summary of evidence in studies addressing effectiveness of tonsillectomy in children with OSDB, continued

Intervention and comparator	Number/Type of Studies (Total N Participants)	Key Outcome(s)	Strength of Evidence (SOE) Grade	Findings
Tonsillectomy vs. CPAP or watchful waiting in children with OSDB & DS	1 RCT (73)	Apnea Hypopnea Index, sleep-related quality of life	Insufficient SOE	Insufficient evidence in small study
Tonsillectomy vs. no surgery in children with OSDB and obesity	1 Retrospective cohort (33)	Apnea Hypopnea Index	Insufficient SOE	Insufficient evidence in small study

CPAP = continuous positive airway pressure; DS = Down syndrome; Non-RCT = nonrandomized trial; OSDB = obstructive sleep-disordered breathing; SOE = strength of the evidence; RCT = randomized controlled trial

KQ2. Effectiveness of Tonsillectomy for Recurrent Throat Infection

Although studies assessed numbers of infections and several utilization measures, such as missed school in the short term, longer term results were rarely reported; studies that did report longer-term results suffered from high attrition and incomplete data. In addition, "throat infection" was not defined consistently across studies and rarely was bacterial infection confirmed. Overall, children undergoing tonsillectomy to improve number of throat infections, associated health care utilization (clinician visits or contacts), and days of work/school missed had improvements in these outcomes in the first postsurgical year compared with children not receiving surgery. These benefits did not persist over time, however, and data on the longer-term outcomes are limited. Quality of life outcomes improved regardless of surgery.

We have moderate confidence in the conclusion that tonsillectomy reduces throat infections or streptococcal infections in the short term (≤12 months) compared with no surgery (moderate strength of evidence). Compared with no surgery, tonsillectomy reduced utilization (clinician contacts), and missed school/work in the short term. We have low confidence in this conclusion (low strength of evidence). In the longer term (>12 months) we found no difference between groups in reduction in streptococcal infections. We have low confidence in this conclusion (low strength of evidence). We found no differences between groups in missed school/work or quality of life in the long term (>12 months) and have low confidence in this conclusion (low strength of evidence). We could not make a conclusion about effects of tonsillectomy on throat infections in the long term (>12 months) (insufficient strength of evidence). Only one study included children with less than 3 episodes of throat infection in the year prior to surgery; we could not make conclusions about outcomes (utilization) reported in this single study (insufficient strength of evidence). Table D outlines strength of evidence findings.

Table D. Summary of evidence in studies addressing effectiveness of tonsillectomy in children with recurrent throat infections

Intervention and Comparator	Number/Type of Studies (Total N Participants)	Key Outcome(s)	Strength of Evidence Grade	Findings
Tonsillectomy vs. no surgery in children with ≥ 3 throat infections in year prior to study	4 RCT (761) 1 Non-RCT (303) 1 Retrospective cohort (290)	Throat infection	Moderate SOE for modest reduction in throat infection after tonsillectomy vs. no treatment in short-term (12 months)	Fewer throat infections in tonsillectomy arms in short-term
	3 RCT (260) 1 Non-RCT (138)	Throat infection	Insufficient SOE for reduction following tonsillectomy vs. no surgery over longer term (>12 months)	Insufficient data based on lack of long-term data and high attrition rates in studies
	2 RCT (273) 1 Retrospective cohort (290)	Streptococcal infection	Moderate SOE for reduction in streptococcal infection after tonsillectomy vs. no tonsillectomy in short term (≤12 months)	Fewer streptococcal infections in tonsillectomy arms in short-term
	2 RCT (203) 1 Retrospective cohort (290)	Streptococcal infection	Low SOE for no difference in reduction in streptococcal infection after tonsillectomy vs.no surgery over longer term (2-3 years)	Similar proportion of infections in retrospective cohort and significantly more infections in nonsurgical groups in 2 RCTs
	1 Retrospective cohort (290)	Streptococcal infection	Insufficient SOE for no difference in effects after 4 years of followup	Insufficient evidence in one study
	1 RCT (231) 1 Non-RCT (303)	Utilization (clinician visits or contacts)	Low SOE for reduction in clinician visits or contacts after tonsillectomy vs. no surgery in short term (<12 months)	Fewer consultations in tonsillectomy arms vs. no surgery, but high loss to followup and differences in outcome assessment
	2 RCT (373) 1 Non-RCT (123)	Quality of life	Low SOE for no difference in quality of life after tonsillectomy vs. no tonsillectomy	Improvements in quality of life in both groups; high attrition in both studies
	3 RCT (503)	Missed school or work	Low SOE for greater improvements in missed school after tonsillectomy vs. no surgery in short term (≤ 12 months)	Significantly fewer missed days in tonsillectomy arms vs. no surgery in 2 RCTs with medium study limitations at 12 month followup; no differences in third RCT
	3 RCT (245)	Missed school or work	Low SOE for no difference in effects between in longer term (>12 months)	No significant differences between groups in all studies at longer-term followup; medium study limitations
Tonsillectomy vs. no surgery in children with < 3 throat infections in year prior to study	1 Retrospective cohort (13892)	Utilization	Insufficient SOE	Insufficient evidence in one study with medium limitations

Non-RCT = nonrandomized trial; RCT = randomized controlled trial; SOE = strength of the evidence

KQ3. Effectiveness of Partial Versus Total Tonsillectomy

Twenty-two studies compared partial to total tonsillectomy, but few compared partial and total using the same surgical technique. Three studies compared partial with total cold dissection and reported no differences other than a faster return to normal diet for partial tonsillectomy. Among those comparing partial and total coblation or partial and total electrocautery, return to normal diet and activity were more favorable in children undergoing partial coblation tonsillectomy compared with total. Group differences were not statistically significant in the electrocautery study.

Most studies evaluated partial vs. total tonsillectomy using differing surgical techniques. Our comparison of interest was "partial vs. total," although we cannot be certain that effects can confidently be attributed to the surgical technique rather than the amount of tissue removed. Differences between partial and total tonsillectomy were generally not significant for outcomes related to OSDB persistence, quality of life, or behavior in these studies.

In six studies, children in the partial tonsillectomy arms had faster resumption of normal diet and normal activity compared with those in the total tonsillectomy groups; however, these effects may be due to confounding by indication as surgical indication varied across studies. Across all studies, 10 of an estimated 166 children (6%) had tonsillar regrowth after partial tonsillectomy.

In studies comparing partial and total cold dissection tonsillectomy, return to normal diet was faster in children undergoing partial tonsillectomy. Our confidence in this conclusion is low (low strength of evidence). We could not make conclusions about effects on return to normal activity, throat infections, or OSDB persistence in these studies (insufficient strength of evidence). In studies comparing either partial and total coblation tonsillectomy or partial and total electrocautery tonsillectomy, we could not make conclusions about effects on return to normal diet or activity (insufficient strength of evidence).

In studies comparing mixed techniques for partial or total tonsillectomy, return to normal diet and activity was more favorable in children undergoing partial versus total tonsillectomy. Our confidence in this conclusion is low (low strength of evidence). These effects may be due to confounding by indication as indication varied across studies. We found no difference in effects on long-term (>12 months) persistence of OSDB symptoms, quality of life, behavioral outcomes, or throat infections between partial and total tonsillectomy. Our confidence in these conclusions is low (low strength of evidence). Table E outlines findings.

KQ4. Effectiveness of Surgical Techniques for Tonsillectomy

Only 19 studies identified for this KQ reported return to normal activity and/or diet outcomes. Commonly used "hot" techniques such as coblation and electrocautery were generally associated with faster return to normal diet or activity than was cold dissection (roughly 1 to 3 days). Few studies, typically addressing different measures and using different comparison techniques, addressed newer techniques such as thermal welding, laser, or harmonic scalpel, thus limiting our ability to draw conclusions about these approaches.

We found a speedier return to regular diet with coblation or electrocautery tonsillectomy compared with cold dissection and have low confidence in these conclusions (low strength of evidence). We could not make conclusions about effects associated with other techniques (insufficient strength of evidence). Table E outlines these findings.

Harms of Surgical Techniques

In meta-analyses, the frequency of primary and secondary PTH associated with total and partial tonsillectomy was below 4 percent for any technique and with overlapping confidence bounds. Pooled frequencies (without adjustment) of PTH were less than 5 percent overall (4.2% for total tonsillectomy; 1.5% for partial tonsillectomy) in comparative studies. Unadjusted frequencies of revisits for pain, dehydration, or postoperative nausea and vomiting were less than 5 percent overall. Other harms were disparate and generally not clinically significant (e.g., thermal burn from a cautery apparatus). No comparative studies reported deaths. The frequency of harms in case series and database or registry studies generally aligned with that in comparative studies. At least four deaths were reported in case series including 1,778,342 children.

We found a low frequency of PTH and utilization harms across surgical techniques and have confidence in these findings (high strength of evidence) (Table E). We found a low frequency of revisits or readmission for dehydration associated with partial tonsillectomy. Our confidence in this conclusion is low (low strength of evidence). We have greater confidence in a low frequency of non-bleeding readmissions/revisits associated with total tonsillectomy (moderate strength of evidence). We could not draw conclusions about effects on admissions or revisits for pain or postoperative nausea and vomiting (PONV) associated with partial tonsillectomy given the few comparative studies addressing the outcome (insufficient strength of evidence).

Table E. Summary of evidence in studies addressing effectiveness and harms of tonsillectomy techniques

Intervention and Comparator	Number/Type of Studies (Total N Participants)	Key Outcome(s)	Strength of Evidence Grade	Findings
Total vs. partial cold dissection tonsillectomy	2 RCT (131)	Return to normal diet	Low SOE for faster return to normal diet after partial vs. total tonsillectomy	Children undergoing partial tonsillectomy returned to normal diet approximately 4 days sooner than children undergoing total tonsillectomy according to parent report
	1 RCT (101)	Throat infection, OSDB persistence	Insufficient SOE	Insufficient data to assess effects on throat infections given single, small study
Partial vs. total coblation tonsillectomy	1 RCT (69)	Return to normal diet or activity	Insufficient SOE	Insufficient data to assess effects on return to normal diet or activity given single, small study
Partial vs. total electrocautery tonsillectomy	1 RCT (40)	Return to normal activity	Insufficient SOE	Insufficient data to assess effects on return to normal diet or activity given single, small study

Table E. Summary of evidence in studies addressing effectiveness and harms of tonsillectomy techniques, continued

Intervention and comparator	Number/Type of Studies (Total N Participants)	Key Outcome(s)	Strength of Evidence (SOE) Grade	Findings
Total vs. partial tonsillectomy (mixed techniques)	6 RCT (620)	Return to normal diet or activity	Low SOE for more favorable return to normal diet and activity in children undergoing partial vs. total tonsillectomy	Children undergoing partial vs. total tonsillectomy had consistently more favorable outcomes but unit of measure varied across studies (e.g., mean days, N children)
	3 RCT (214)	OSDB persistence	Low SOE for no difference in effects on long-term persistence of OSDB symptoms between partial and total tonsillectomy	More children undergoing partial vs. total tonsillectomy had short-term snoring or obstructive symptoms in 2 studies but no group differences in longer term in any study
	2 RCT (159)	Quality of Life (≥12 months post-tonsillectomy)	Low SOE for no long-term differences in quality of life after partial vs. total tonsillectomy	Improvements from baseline in both groups in 2 small studies, but no significant group differences in quality of life in either study
	2 RCT (159)	Behavioral Outcomes (≥12 months post-tonsillectomy)	Low SOE for no long-term differences in behavioral outcomes after partial vs. total tonsillectomy	Improvements from baseline in both groups on the Child Behavior Checklist in 2 small studies, but no significant group differences in either study
	4 RCT (296)	Throat Infections (≥12 months post-tonsillectomy)	Low SOE for no effect on throat infections following partial vs. total tonsillectomy	More throat infections or sore throats following partial vs. total tonsillectomy in 3 of 4 RCTs but no significant group differences
Total coblation vs. total cold dissection tonsillectomy	6 RCT (276)	Return to normal activity	Low SOE for faster return with coblation	Coblation, compared with cold dissection, associated with moderately faster return to normal activity in 4 small studies
	4 RCT (255)	Return to normal diet	Insufficient SOE	Insufficient data in small studies with medium limitations
Total electrocautery vs. total cold dissection tonsillectomy	3 RCT (254)	Return to normal diet	Low SOE for faster return with electrocautery	Electrocautery, compared with cold dissection, associated with faster return to normal diet in 2 studies and not significantly faster in a third
Other techniques for total tonsillectomy (laser, thermal welding, harmonic scalpel) vs. other technique	10 RCT (906) 1 Non-RCT (305)	Return to normal diet or activity	Insufficient SOE	Insufficient data in heterogenous, small studies evaluating different techniques and outcome measures

Table E. Summary of evidence in studies addressing effectiveness and harms of tonsillectomy techniques, continued

Intervention and comparator	Number/Type of Studies (Total N Participants)	Key Outcome(s)	Strength of Evidence (SOE) Grade	Findings
Partial tonsillectomy	Meta-analysis 16 RCT (1234)	PTH and PTH-associated utilization	High SOE for low frequency of PTH associated with partial tonsillectomy	Frequency did not exceed 4% for PTH; fewer data available to assess associated utilization, but rates are likely low given the low frequency of PTH
	3 RCT (221)	Readmissions/ revisits for dehydration	Low SOE for low frequency of dehydration revisits/readmissions associated with partial tonsillectomy	5 readmissions reported across 3 study arms
	3 RCT (221)	Readmissions for postoperative nausea and vomiting or pain	Insufficient SOE	Insufficient data in few studies
Total tonsillectomy	Meta-analysis 52 RCT (6293) 4 Non-RCT (478) 2 Cohort studies (350)	PTH and PTH-associated utilization	High SOE for low frequency associated with total tonsillectomy	Frequency of <5% of PTH and PTH-associated utilization in both meta-analysis and unadjusted analyses associated with commonly used techniques
	17 RCT (2269) 1 Prospective cohort (29) 1 Retrospective cohort (145)	Readmissions for pain, postoperative nausea and vomiting, dehydration	Moderate SOE for low frequency of non-PTH readmissions/revisits associated with total tonsillectomy	In 37 study arms, overall frequency of non-PTH revisits/readmissions was below 2%

Non-RCT = nonrandomized trial; OSDB = obstructive sleep-disordered breathing; PTH = post-tonsillectomy hemorrhage; RCT = randomized controlled trial; SOE = strength of the evidence

KQ5. Effectiveness of Adjunctive Perioperative Medications To Improve Outcomes After Tonsillectomy

Studies addressing this KQ were heterogeneous, addressing multiple agents, combinations of agents, routes of administration and dosage, timing of agents, and rescue medications provided. This heterogeneity limits our ability to draw conclusions about perioperative medications. We considered the strength of the evidence for the subset of studies with placebo comparisons. We considered the drug class (instead of individual agent such as diclofenac) in assessing strength of evidence for NSAIDs and antiemetics (Table F). All steroid studies addressed dexamethasone.

NSAIDs. We found a reduced need for analgesia with NSAIDs compared with placebo. Our confidence in this conclusion is low (low strength of evidence). We found no difference in effects on return to normal diet or activity with perioperative NSAIDs compared with placebo. Our confidence in this conclusion is low (low strength of evidence). We found a frequency of PTH of less than 6% and low associated utilization with perioperative NSAIDs. Our confidence

in this conclusion is low (low strength of evidence). We could not make conclusions about non-PTH related readmissions or revisits following NSAID use as few studies addressed these outcomes (insufficient strength of evidence).

Steroids. We found a reduced need for analgesics or antiemetics associated with steroids (IV or infiltrated dexamethasone) compared with placebo. Our confidence in this conclusion is low (low strength of evidence). Studies of steroids reported few cases of PTH and PTH-related utilization. We have moderate confidence that steroids are associated with a low frequency of PTH (moderate strength of evidence).

Meta-analysis of nine studies comparing steroids and placebo did not indicate a significantly increased risk of PTH with steroids vs. placebo; confidence bounds were wide for all estimates, and we have low confidence in this conclusion (low strength of evidence). We could not make conclusions about the effects of steroids on time to resume normal diet or activity, as the two small studies addressing the outcome reported inconsistent results, or on non-PTH-related readmissions or revisits as few studies reported these outcomes (insufficient strength of evidence).

Antiemetics. Data were consistent in terms of antiemetic medications. We found a reduced need for postoperative antiemetics in studies of perioperative antiemetics; our confidence in this conclusion is low (low strength of evidence). We found no effect of 5-HT perioperative antiemetics on postoperative analgesia requirements. We have moderate confidence in this conclusion (moderate strength of evidence).

KQ6. Effectiveness of Postoperative Medications for Pain After Tonsillectomy

Few studies addressed the same interventions and comparisons, and studies typically reported on need for rescue pain medication, PTH, and time to resume normal diet or activity as outcomes. Data on the effects of NSAIDs on need for rescue pain medication in the first 24 to 48 hours after surgery are conflicting, and no long-term data are available. Two studies compared prednisolone and placebo and found no effect on return to normal diet or activity.

PTH frequency overall was less than 10 percent. PTH in steroid and placebo arms in the two studies addressing that comparison were similar. The frequency of PTH in studies comparing NSAIDs (celecoxib, ibuprofen) and non-NSAID analgesics to placebo or other medications was also similar. In three study arms reporting use of NSAIDs, PTH occurred in 4.7 percent of children (n=32/679).

In studies of postoperative NSAIDs, we found a low frequency of PTH. Our confidence in this estimate is low (low strength of evidence). We could not make conclusions about the effects of postoperative analgesics on need for rescue medications; return to normal diet or activity; or PTH (insufficient strength of evidence).

In studies of postoperative steroids, we found no difference in effects on return to normal diet or activity between steroids and placebo. Our confidence in this conclusion is low (low strength of evidence). We also found no difference in effects on bleeding between postoperative steroids and placebo or no treatment. Our confidence in this conclusion is low (low strength of evidence). Table F outlines these findings.

Table F. Summary of evidence in studies addressing effectiveness and harms of perioperative or postoperative medications

Intervention and Comparator	Number/Type of Studies (Total N Participants)	Key Outcome(s)	Strength of Evidence Grade	Findings
Perioperative NSAID vs. Placebo	2 RCT (180)	Return to normal diet and activity	Low SOE for no difference in return to normal diet or activity with NSAIDs vs. placebo	No significant group differences in 2 small studies with medium study limitations
	5 RCT (345)	Need for analgesics	Low SOE for reduced need for rescue analgesia with NSAIDs vs. placebo	Significantly less need in 4 small studies, no group differences in a 5th study
Perioperative NSAIDs	6 RCT (277)	PTH and PTH related admissions or revisits	Low SOE for low frequency of PTH or PTH-related revisits/readmissions associated with perioperative dexamethasone	Frequency of PTH or associated utilization <3% (unadjusted analyses) in 277 children receiving NSAIDs
	1 RCT (20)	Non-PTH readmissions or revisits	Insufficient SOE	Insufficient data in one small study
Perioperative dexamethasone vs. Placebo	10 RCT (979)	Need for rescue analgesic	Low SOE for reduction in analgesic need with dexamethasone vs. placebo	Significantly less need for analgesics after dexamethasone (IV or infiltration) vs. placebo in 7 small studies; no significant differences in 3 studies; inconsistency precludes higher SOE
	8 RCT (812)	Need for rescue antiemetic	Low SOE for reduction in antiemetic need with dexamethasone vs. placebo	Significantly less need for antiemetics after dexamethasone vs. placebo in 5 small studies; no significant differences in 3 studies; inconsistency precludes higher SOE
	2 RCT (354)	Return to normal diet or activity	Insufficient SOE	Insufficient data in 2 studies
	Meta-analysis	PTH and PTH-related revisits or reoperations	Low SOE for no increased risk of PTH with dexamethasone compared with placebo	Odds ratios ≥1 with wide credible intervals. SOE is low given imprecision of estimates
Perioperative dexamethasone	9 RCT (811)	PTH and PTH-related readmissions or revisits	Moderate SOE for low frequency of PTH or PTH-related revisits/readmissions associated with perioperative dexamethasone	Frequency of PTH or associated utilization <5% in 811 children receiving steroids
	4 RCT (279)	Non-PTH readmissions or revisits	Insufficient SOE	Few studies reported outcome

Table F. Summary of evidence in studies addressing effectiveness and harms of perioperative or postoperative medications, continued

Intervention and comparator	Number/Type of Studies (Total N Participants)	Key Outcome(s)	Strength of Evidence (SOE) Grade	Findings
Perioperative antiemetics	5 RCT (964)	Need for rescue analgesic	Moderate SOE for no effect of antiemetics (5-HT receptor antagonists)	No significant group differences in 5 RCTs comparing 5-HT antagonists with other antiemetics, other 5-HT antagonists, or placebo
	3 RCT (303)	Need for postoperative rescue antiemetic	Low SOE for reduced need for postoperative antiemetics with perioperative 5-HT antiemetics vs. placebo	Significantly less need for postoperative antiemetics in 3 small RCTs comparing 5-HT antagonists and placebo; imprecision precludes higher SOE
Postoperative prednisolone vs. Placebo	2 RCT (331)	Return to normal diet or activity in longer term (≥5 days)	Low SOE for no difference in effects of prednisolone vs. placebo on return to normal diet or activity	Number of children consuming normal diet or engaging in normal activity did not differ at 14 days post-tonsillectomy in one study; time to return to normal diet or activity did not differ in second small RCT
	2 RCT (331)	PTH	Low SOE for no difference in PTH associated with steroids vs. placebo/no treatment	Numbers of PTH in steroid and placebo arms were similar in 2 studies (13 PTH in steroid arms vs. 15 in placebo/no treatment)
Postoperative NSAIDs	2 RCT (564) 1 Non-RCT (115)	PTH	Low SOE for low frequency of PTH	Unadjusted frequency of 0-6% in 3 studies; higher frequency associated with celecoxib
Postoperative analgesics (NSAIDs, non-NSAID analgesics)	2 RCT (157)	Return to normal diet or activity	Insufficient SOE	Outcomes defined differently in 2 small studies
	3 RCT (500)	Need for rescue analgesics	Insufficient SOE	Studies compared different analgesics and different rescue medications

5-HT = 5- hydroxytryptamine; non-RCT = nonrandomized trial; NSAID = non-steroidal anti-inflammatory drug; PTH = post-tonsillectomy hemorrhage; RCT = randomized controlled trial; SOE = strength of the evidence

Applicability

Studies included in this review typically did not describe severity of indications of tonsillectomy and comorbidities for populations adequately, which makes applicability difficult to assess. As would be expected, studies addressing KQ1 (tonsillectomy in children with OSDB) and KQ2 (tonsillectomy in children with recurrent throat infection) specified surgical indication and generally provided greater characterization of study participants. Baseline severity of OSDB or throat infection varied across these studies as did definitions of "cure" or resolution of symptoms. Of note, the largest U.S.-based RCT addressing tonsillectomy vs. no surgery for children with OSDB included a majority African-American and majority overweight or obese population as did two additional studies addressing this comparison. Two other studies

addressing this comparison included a majority of children with Down syndrome or mucopolysaccharidoses or children under 2 years of age. RCTs addressing tonsillectomy vs. no surgery for recurrent throat infection explicitly included children with mild to moderate baseline symptoms, and definitions of "throat infection" varied across studies. Two larger studies that addressed this comparison included majority white populations.

Studies addressing surgical approaches and peri- or post- operative medications typically did not specify surgical indications or included both children with OSDB or recurrent throat infections without stratifying analyses. Roughly one-third of studies were conducted in less developed countries in which surgical techniques and procedures may differ from those used in the United States. Regardless of the country in which studies were performed, anesthetic approaches, analgesic agents and dosing, surgical expertise, and surgical and hemostatic techniques (including definitions of "partial tonsillectomy") varied widely across studies. Studies reporting weight or BMI typically did not address whether children were under- or over- weight for age at baseline, and few studies reported baseline comorbidities such as asthma or Down syndrome; thus assessing applicability to these sub-populations is challenging. Most studies used subjective outcome measures or relied on caregiver- or child-completed diaries to assess longer-term outcomes. Objective measures such as the Apnea Hypopnea Index or other polysomnography parameters may not accurately reflect effects on the totality of symptoms associated with OSDB (e.g., behavioral issues, sleepiness, overall quality of life). We also included only studies addressing tonsillectomy for the two most common indications for the surgery: OSDB and recurrent throat infection; thus, individuals seeking information about tonsillectomy for Periodic Fever, Aphthous Stomatitis, Pharyngitis, Cervical Adenitis (PFAPA) or other indications will not find applicable studies in the current review.

Despite these limitations to generalizability, findings reported here are likely widely applicable given the heterogeneous population of children without comorbidities who undergo tonsillectomy for OSDB or recurrent throat infections. Applicability of findings to children with Down syndrome, craniofacial abnormalities, obesity, or under age 2 is limited. Although studies included some children with these comorbidities or in the younger age range, few provided explicit analyses of these subgroups. Appendix G of the full report includes applicability tables for each KQ.

Limitations of the Comparative Effectiveness Review Process

We included studies published in English only; as few non-English studies would have met criteria based on our scan of a random sample of these studies, we believe their exclusion does not introduce significant bias into the review. We also included only studies of perioperative NSAID, steroids, and antiemetics to address KQ5. Although this focus means that some medications are not included in this review, the drug classes addressed in the review comprise key agents frequently used in the perioperative period. We also did not include studies addressing adenoidectomy alone or studies comparing tonsillectomy with adenoidectomy as the choice of procedure is likely driven by the indication for surgery; thus, comparing these approaches would not be appropriate. Given heterogeneity in anesthetic regimens, surgical techniques, postoperative analgesia and medications, and patient populations themselves, we were limited in our ability to stratify findings or identify potential subgroups that may respond more favorably to tonsillectomy or to supportive care.

Limitations of the Evidence Base

A relatively large number of studies have been published on tonsillectomy, including for OSDB and throat infections, but risk of bias is mixed, with fewer studies (31%) having low risk of bias than moderate or high risk. Furthermore, most available studies provided little to no long-term clinical outcome data, focusing instead on intermediate outcomes and harms. In addition, few studies addressed questions about the need for tonsillectomy compared with a non-surgical treatment. Patient populations were generally poorly characterized, and little information was available on first-line treatment attempts before surgery. Very few studies focused on high risk or other special populations.

Particularly in studies intended to assess effects of tonsillectomy on throat infections, parents of severely affected children were noted to refuse randomization and cross over to surgery at high rates. Long-term effects are limited in the literature base, particularly regarding outcomes that include growth and development, sleep quality, and behavior for children with OSDB. Exploration of demographics of patient populations more likely to be refractory to initial management strategies is also limited. It appears clear that throat infections decline in children over time regardless of treatment group, but with high loss to followup, the relative contribution of this decline to apparent effectiveness is unknown.

A particular problem in the literature is a lack of full characterization of the patient population, particularly the clinically documented severity of both sleep-disordered breathing and throat infections. Understanding of "obstructive sleep-disordered breathing" varied from study to study as did degree of hypertrophy and number and severity of throat infections or sore throats. In the context of general lay expectations of the benefit of tonsillectomy, and common opinion that tonsillectomy is a "minor" surgery, patients undergoing tonsillectomy may vary widely in the severity of their clinical states. Among those studies focused on throat infection that did characterize patients, most had low numbers of reported infections, and few reported culture-confirmed bacterial infections.

Of particular importance for this surgical topic is a complete assessment of potential harms, particularly frequency of PTH, including PTH that leads to further intervention. However, the degree, number of repeat episodes, and timing of PTH were rarely defined or measured; thus outcomes can be broadly defined only in terms of primary versus secondary PTH, readmissions, and reoperations, where reported. Our estimates include PTH as reported in eligible studies, which could have ranged from parent-reported bleeding that did not require a clinician visit to PTH requiring surgical hemostasis.

Few studies of postoperative medications for pain met our inclusion criteria; thus, evidence in the current review is inadequate to draw firm conclusions about PTH associated with postoperative NSAIDs. In attempting to assess partial versus total tonsillectomy we note that partial tonsillectomy was rarely precisely specified. These studies also most often used different techniques for the partial and total tonsillectomy, thus introducing confounding that cannot be disentangled.

Implications for Clinical and Policy Decisionmaking

This review provides evidence for decisionmaking in the care of children who are potential candidates for tonsillectomy. Despite the large body of literature, most evidence addresses effects in the short term. The literature reports short-term improvements in obstructive symptoms and throat infections following tonsillectomy compared with no surgery. Evidence about long-

term benefits of tonsillectomy either for OSDB or throat infection is limited. Thus, individual decisionmaking needs to balance needs for relief of illness-related outcomes (including missing school and work) with the risks associated with surgery. Caregivers and providers may wish to consider the potential benefits and drawbacks of attempting to manage children's illnesses for a period of time to see if they outgrow the propensity for infection and may be able to avoid surgery. That said, shared decisionmaking rests in the hands of families and their clinicians, and decisions should be made on an individual basis. Harms are rare and generally minor, and clinicians have information from this review with which to counsel their patients and families.

In cases where families are considering surgery or CPAP for OSDB, comparative evidence is currently inconclusive to inform decisionmaking. Families with children in special subgroups, including those with Down syndrome, similarly cannot rely solely on currently available scientific evidence for their decision as few studies address these populations explicitly. Benefits of specific approaches to tonsillectomy (either partial versus total or by surgical technique) provide little clear guidance for clinicians. Some evidence suggests that partial removal may speed time to return to normal diet or activity relative to total removal; however, we found a roughly 6 percent rate of regrowth with partial tonsillectomy.

PTH typically occurred in less than 4 percent of children across all surgical techniques, and no clear evidence exists for a superior approach. Familiarity with a technique and surgical skill may both have a role in driving outcomes, as has been demonstrated in other fields.[15-17]

Decisional dilemmas still exist regarding the perioperative use of medications and whether they speed postoperative return to normal diet and activity and reduce the need for post-tonsillectomy analgesia and rescue anti-emetic use. Clinical care would be improved by optimizing perioperative use of medication to improve outcomes. The literature base on this topic was insufficient to provide guidance on whether any perioperative medications affect time to resume normal diet or activity. Low strength of evidence suggested that a single dose of IV dexamethasone intraoperatively reduces analgesic requirement in the postanesthesia care unit and up to 24 hours postoperatively. Evidence is mixed as to whether dexamethasone reduces the need for postoperative rescue antiemetics. In contrast, clinicians can have some confidence that pre-emptive 5-HT receptor antagonists given intra-operatively do reduce the need for rescue antiemetics post-tonsillectomy.

Research Gaps and Areas for Future Research

Tonsillectomy is heavily researched, with far more data available to assess safety than efficacy. Despite substantial research, the literature is largely silent on the natural history of OSDB or throat infections that would provide a basis for the need for tonsillectomy in the long term. Many young patients may outgrow the need for intervention, but more data are needed to describe the potential to outgrow these indications to parents and to discern population factors that may predict resolution.[18-20] Indeed, in many studies, outcomes for children in nonsurgical groups also improved, though improvements were generally greater in children receiving tonsillectomy. Long-term data are needed in order to enable caregivers to weigh the benefits of surgery versus the reality of managing their child's condition as they wait for it to resolve; obtaining longer-term data, however, is difficult, as evidenced by the high rate of attrition in most studies with more than 6 months followup included in this review.

Future studies should take more care to characterize patient populations completely—including severity of OSDB or throat infections—such that applicability can be much more specifically described and potential candidates for surgery or watchful waiting identified. Indeed

the literature lacks a consistent, consensus definition of infection; defining infection consistently is critical for promoting synthesis of research in the area. Tonsillitis or "sore throat" may also include cases of entities such as PFAPA; clear characterization of children in studies is necessary for understanding effects on subpopulations.

Similarly, studies also typically did not clearly characterize severity of PTH, and many did not clearly specify timing or number of repeat episodes. Severity of bleeding or repeat episodes may be more predictive of serious morbidity than simple frequency; however, our ability to assess this association was limited. Improved characterization could allow analyses to inform our understanding of factors that may contribute to revisits or readmissions and outcomes such as mortality.

As new technologies for tonsillectomy continue to emerge, as they continuously have over the past few decades, high quality research will be needed to evaluate these technologies, in terms of both efficacy and safety. As we learn more about the deleterious effects of sleep apnea and detection rates increase, more refined and specific treatment algorithms will be in demand. Related to this issue, more data are needed on the use of CPAP in children as an initial modality; such data should address compliance and duration of use.

Future research should also address the current lack of data regarding treatment in special populations including very young children and children with comorbidities such as obesity and neuromuscular disease. Further, concerns about perioperative and postoperative management persist, including over-narcotization and potential respiratory suppression. Better data regarding optimal medication regimens are essential, both in terms of symptomatic relief and minimizing iatrogenic harm.

Measures commonly used to assess objective improvements in obstructed breathing, such as the AHI, are not patient-centered and may not reflect subjective reports of improvements or worsening of outcomes experienced by patients. Future research exploring the alignment of the AHI with patient-reported outcomes such as quality of life would help to gauge effects of tonsillectomy more precisely. Additionally, standardized measures of sleep outcomes are lacking.

Finally, relatively little data exist regarding predictable factors contributing to recurrence of symptoms of failure of OSDB and throat infections following tonsillectomy for primary management. A better understanding of these factors would allow for more specific patient selection.

Conclusions

Tonsillectomy can produce short-term improvement in sleep outcomes and reduction in throat infections compared with no surgery in children with OSDB or recurrent throat infections. Relative to no intervention, most studies reported better sleep-related outcomes in children with OSDB who had a tonsillectomy, but longer term data on durability of outcomes are limited. Children undergoing tonsillectomy to improve number of throat infections, associated health care utilization (clinician visits), and work/school absences had improvements in these outcomes in the first postsurgical year compared with children not receiving surgery. These benefits did not persist over time, and data on longer-term results are lacking. This short-term improvement must be weighed against a roughly 4 percent frequency of PTH. Surgical technique had little bearing on either time to return to normal diet or activity or PTH frequency. Perioperative dexamethasone improved pain and pre-emptive 5-HT receptor antagonist antiemetics reduced antiemetic use in the immediate postoperative period. Dexamethasone did not increase risk of

PTH compared with placebo, but estimates had wide confidence bounds. Little evidence addressed the use of postoperative medications for pain-related outcomes.

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