Tonsillectomy for Obstructive Sleep-Disordered Breathing or Recurrent Throat Infection in Children
Comparative Effectiveness Review
Number 183

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

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Preface

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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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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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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.

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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

<table>
<thead>
<tr>
<th>Category</th>
<th>Criteria</th>
</tr>
</thead>
</table>
| **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\textsuperscript{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.\textsuperscript{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.\textsuperscript{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.\textsuperscript{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). Nine 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 assess 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 reoperations overall 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)

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

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

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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 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>
<thead>
<tr>
<th>Intervention and Comparator</th>
<th>Number/Type of Studies (Total N Participants)</th>
<th>Key Outcome(s)</th>
<th>Strength of Evidence Grade</th>
<th>Findings</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tonsillectomy vs. no surgery in children with OSDB</td>
<td>Meta-analysis</td>
<td>Apnea Hypopnea Index</td>
<td>Low for greater improvement of Apnea Hypopnea Index with tonsillectomy compared with no surgery</td>
<td>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.</td>
</tr>
<tr>
<td></td>
<td>2 RCT (456)</td>
<td></td>
<td></td>
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<tr>
<td></td>
<td>1 Prospective cohort (38)</td>
<td></td>
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<td></td>
</tr>
<tr>
<td></td>
<td>2 Retrospective cohort (94)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>2 RCT (456)</td>
<td>Sleep-related quality of life</td>
<td>Moderate SOE for modest improvement in sleep-related quality of life after tonsillectomy vs. no surgery</td>
<td>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</td>
</tr>
<tr>
<td></td>
<td>1 Retrospective cohort (32)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>1 RCT (397)</td>
<td>Behavioral outcomes</td>
<td>Low SOE for improvements in negative behaviors after tonsillectomy vs. no surgery</td>
<td>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</td>
</tr>
<tr>
<td></td>
<td>1 Prospective cohort (38)</td>
<td>Cognitive changes (IQ)</td>
<td>Insufficient SOE</td>
<td>Insufficient evidence in one small study</td>
</tr>
<tr>
<td></td>
<td>1 RCT (397)</td>
<td>Executive function</td>
<td>Insufficient SOE</td>
<td>Differences in followup time and medium study limitations preclude conclusions</td>
</tr>
<tr>
<td></td>
<td>1 Prospective cohort (38)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>1 RCT (397)</td>
<td>Cardiometabolic outcomes</td>
<td>Insufficient SOE</td>
<td>Insufficient evidence in only one RCT</td>
</tr>
<tr>
<td></td>
<td>1 RCT (397)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tonsillectomy vs. CPAP in children with OSDB</td>
<td>1 RCT (73)</td>
<td>Apnea Hypopnea Index, sleep-related quality of life</td>
<td>Insufficient SOE</td>
<td>Insufficient evidence in small study</td>
</tr>
<tr>
<td>Tonsillectomy vs. CPAP or watchful waiting in children with OSDB and craniofacial abnormalities</td>
<td>1 RCT (73)</td>
<td>Apnea Hypopnea Index, sleep-related quality of life</td>
<td>Insufficient SOE</td>
<td>Insufficient evidence in small study</td>
</tr>
</tbody>
</table>
Table C. Summary of evidence in studies addressing effectiveness of tonsillectomy in children with OSDB, continued

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

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

<table>
<thead>
<tr>
<th>Intervention and Comparator</th>
<th>Number/Type of Studies (Total N Participants)</th>
<th>Key Outcome(s)</th>
<th>Strength of Evidence Grade</th>
<th>Findings</th>
</tr>
</thead>
</table>
| 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

<table>
<thead>
<tr>
<th>Intervention and Comparator</th>
<th>Number/Type of Studies (Total N Participants)</th>
<th>Key Outcome(s)</th>
<th>Strength of Evidence Grade</th>
<th>Findings</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total vs. partial cold dissection tonsillectomy</td>
<td>2 RCT (131)</td>
<td>Return to normal diet</td>
<td>Low SOE for faster return to normal diet after partial vs. total tonsillectomy</td>
<td>Children undergoing partial tonsillectomy returned to normal diet approximately 4 days sooner than children undergoing total tonsillectomy according to parent report</td>
</tr>
<tr>
<td></td>
<td>1 RCT (101)</td>
<td>Throat infection, OSDB persistence</td>
<td>Insufficient SOE</td>
<td>Insufficient data to assess effects on throat infections given single, small study</td>
</tr>
<tr>
<td>Partial vs. total coblation tonsillectomy</td>
<td>1 RCT (69)</td>
<td>Return to normal diet or activity</td>
<td>Insufficient SOE</td>
<td>Insufficient data to assess effects on return to normal diet or activity given single, small study</td>
</tr>
<tr>
<td>Partial vs. total electrocautery tonsillectomy</td>
<td>1 RCT (40)</td>
<td>Return to normal activity</td>
<td>Insufficient SOE</td>
<td>Insufficient data to assess effects on return to normal diet or activity given single, small study</td>
</tr>
<tr>
<td>Intervention and comparator</td>
<td>Number/Type of Studies (Total N Participants)</td>
<td>Key Outcome(s)</td>
<td>Strength of Evidence (SOE) Grade</td>
<td>Findings</td>
</tr>
<tr>
<td>----------------------------</td>
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</tr>
<tr>
<td>Total vs. partial tonsillectomy (mixed techniques)</td>
<td>6 RCT (620)</td>
<td>Return to normal diet or activity</td>
<td>Low SOE for more favorable return to normal diet and activity in children undergoing partial vs. total tonsillectomy</td>
<td>Children undergoing partial vs. total tonsillectomy had consistently more favorable outcomes but unit of measure varied across studies (e.g., mean days, N children)</td>
</tr>
<tr>
<td></td>
<td>3 RCT (214)</td>
<td>OSDB persistence</td>
<td>Low SOE for no difference in effects on long-term persistence of OSDB symptoms between partial and total tonsillectomy</td>
<td>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</td>
</tr>
<tr>
<td></td>
<td>2 RCT (159)</td>
<td>Quality of Life (≥12 months post-tonsillectomy)</td>
<td>Low SOE for no long-term differences in quality of life after partial vs. total tonsillectomy</td>
<td>Improvements from baseline in both groups in 2 small studies, but no significant group differences in quality of life in either study</td>
</tr>
<tr>
<td></td>
<td>2 RCT (159)</td>
<td>Behavioral Outcomes (≥12 months post-tonsillectomy)</td>
<td>Low SOE for no long-term differences in behavioral outcomes after partial vs. total tonsillectomy</td>
<td>Improvements from baseline in both groups on the Child Behavior Checklist in 2 small studies, but no significant group differences in either study</td>
</tr>
<tr>
<td></td>
<td>4 RCT (296)</td>
<td>Throat Infections (≥12 months post-tonsillectomy)</td>
<td>Low SOE for no effect on throat infections following partial vs. total tonsillectomy</td>
<td>More throat infections or sore throats following partial vs. total tonsillectomy in 3 of 4 RCTs but no significant group differences</td>
</tr>
<tr>
<td>Total coblation vs. total cold dissection tonsillectomy</td>
<td>6 RCT (276)</td>
<td>Return to normal activity</td>
<td>Low SOE for faster return with coblation</td>
<td>Coblation, compared with cold dissection, associated with moderately faster return to normal activity in 4 small studies</td>
</tr>
<tr>
<td></td>
<td>4 RCT (255)</td>
<td>Return to normal diet</td>
<td>Insufficient SOE</td>
<td>Insufficient data in small studies with medium limitations</td>
</tr>
<tr>
<td>Total electrocautery vs. total cold dissection tonsillectomy</td>
<td>3 RCT (254)</td>
<td>Return to normal diet</td>
<td>Low SOE for faster return with electrocautery</td>
<td>Electrocautery, compared with cold dissection, associated with faster return to normal diet in 2 studies and not significantly faster in a third</td>
</tr>
<tr>
<td>Other techniques for total tonsillectomy (laser, thermal welding, harmonic scalpel) vs. other technique</td>
<td>10 RCT (906)</td>
<td>Return to normal diet or activity</td>
<td>Insufficient SOE</td>
<td>Insufficient data in heterogenous, small studies evaluating different techniques and outcome measures</td>
</tr>
</tbody>
</table>
Table E. Summary of evidence in studies addressing effectiveness and harms of tonsillectomy techniques, continued

<table>
<thead>
<tr>
<th>Intervention and comparator</th>
<th>Number/Type of Studies (Total N Participants)</th>
<th>Key Outcome(s)</th>
<th>Strength of Evidence (SOE) Grade</th>
<th>Findings</th>
</tr>
</thead>
<tbody>
<tr>
<td>Partial tonsillectomy</td>
<td>Meta-analysis 16 RCT (1234)</td>
<td>PTH and PTH-associated utilization</td>
<td>High SOE for low frequency of PTH associated with partial tonsillectomy</td>
<td>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</td>
</tr>
<tr>
<td></td>
<td>3 RCT (221)</td>
<td>Readmissions/revisits for dehydration</td>
<td>Low SOE for low frequency of dehydration revisits/readmissions associated with partial tonsillectomy</td>
<td>5 readmissions reported across 3 study arms</td>
</tr>
<tr>
<td></td>
<td>3 RCT (221)</td>
<td>Readmissions for postoperative nausea and vomiting or pain</td>
<td>Insufficient SOE</td>
<td>Insufficient data in few studies</td>
</tr>
<tr>
<td>Total tonsillectomy</td>
<td>Meta-analysis 52 RCT (6293)</td>
<td>PTH and PTH-associated utilization</td>
<td>High SOE for low frequency associated with total tonsillectomy</td>
<td>Frequency of &lt;5% of PTH and PTH-associated utilization in both meta-analysis and unadjusted analyses associated with commonly used techniques</td>
</tr>
<tr>
<td></td>
<td>4 Non-RCT (478)</td>
<td>Readmissions for pain, postoperative nausea and vomiting, dehydration</td>
<td>Moderate SOE for low frequency of non-PTH readmissions/revisits associated with total tonsillectomy</td>
<td>In 37 study arms, overall frequency of non-PTH revisits/readmissions was below 2%</td>
</tr>
<tr>
<td></td>
<td>2 Cohort studies (350)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>17 RCT (2269)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>1 Prospective cohort (29)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>1 Retrospective cohort (145)</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

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

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

<table>
<thead>
<tr>
<th>Intervention and comparator</th>
<th>Number/Type of Studies (Total N Participants)</th>
<th>Key Outcome(s)</th>
<th>Strength of Evidence (SOE) Grade</th>
<th>Findings</th>
</tr>
</thead>
<tbody>
<tr>
<td>Perioperative antiemetics</td>
<td>5 RCT (964)</td>
<td>Need for rescue analgesic</td>
<td>Moderate SOE for no effect of antiemetics (5-HT receptor antagonists)</td>
<td>No significant group differences in 5 RCTs comparing 5-HT antagonists with other antiemetics, other 5-HT antagonists, or placebo</td>
</tr>
<tr>
<td></td>
<td>3 RCT (303)</td>
<td>Need for postoperative rescue antiemetic</td>
<td>Low SOE for reduced need for postoperative antiemetics with perioperative 5-HT antiemetics vs. placebo</td>
<td>Significantly less need for postoperative antiemetics in 3 small RCTs comparing 5-HT antagonists and placebo; imprecision precludes higher SOE</td>
</tr>
<tr>
<td>Postoperative prednisolone vs. Placebo</td>
<td>2 RCT (331)</td>
<td>Return to normal diet or activity in longer term (≥5 days)</td>
<td>Low SOE for no difference in effects of prednisolone vs. placebo on return to normal diet or activity</td>
<td>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</td>
</tr>
<tr>
<td></td>
<td>2 RCT (331)</td>
<td>PTH</td>
<td>Low SOE for no difference in PTH associated with steroids vs. placebo/no treatment</td>
<td>Numbers of PTH in steroid and placebo arms were similar in 2 studies (13 PTH in steroid arms vs. 15 in placebo/no treatment)</td>
</tr>
<tr>
<td>Postoperative NSAIDs</td>
<td>2 RCT (564)</td>
<td>PTH</td>
<td>Low SOE for low frequency of PTH</td>
<td>Unadjusted frequency of 0-6% in 3 studies; higher frequency associated with celecoxib</td>
</tr>
<tr>
<td></td>
<td>1 Non-RCT (115)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Postoperative analgesics (NSAIDs, non-NSAID analgesics)</td>
<td>2 RCT (157)</td>
<td>Return to normal diet or activity</td>
<td>Insufficient SOE</td>
<td>Outcomes defined differently in 2 small studies</td>
</tr>
<tr>
<td></td>
<td>3 RCT (500)</td>
<td>Need for rescue analgesics</td>
<td>Insufficient SOE</td>
<td>Studies compared different analgesics and different rescue medications</td>
</tr>
</tbody>
</table>

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 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.\textsuperscript{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.\textsuperscript{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 post-surgical 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.
References


Introduction

Background

Tonsillectomy or adenotonsillectomy (“tonsillectomy”) are commonly performed in the United States and 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 that rates of tonsillectomy varied almost 12-fold across adjacent counties in rural Vermont with similar populations.\(^5\) Variation in rates continues despite improved evidence and dissemination about indications.\(^1\)

Surgical Techniques

Table 1 categorizes common surgical techniques used for tonsillectomy. Choice of technique depends on patient factors including the surgical indication (e.g., recurrent infection, OSDB) and clinician practice patterns. All procedures are performed under general anesthesia. Hereafter, we use the term tonsillectomy to refer to removal of the tonsils alone, removal of tonsils and adenoids (adenotonsillectomy), and partial removal of the tonsils (tonsillotomy, partial tonsillectomy) using any surgical technique or approach.

<table>
<thead>
<tr>
<th>Surgical Technique or Tool</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cold dissection</td>
<td>Palatine tonsils dissected and removed from oropharynx using a scalpel, scissors or other nonpowered means.</td>
</tr>
<tr>
<td>Electrocautery</td>
<td>Palatine tonsils dissected and removed from oropharynx using electrocautery (i.e., monopolar cautery, bipolar cautery).</td>
</tr>
<tr>
<td>Harmonic scalpel</td>
<td>Palatine tonsils dissected and removed from oropharynx using ultrasonic energized instrumentation.</td>
</tr>
<tr>
<td>Microdebridement</td>
<td>Palatine tonsils removed from oropharynx using a microdebrider, which suctions tonsillar tissue into a rotary blade, which morselizes and removes tissue. All or part of the tonsil can be removed with this technique.</td>
</tr>
<tr>
<td>Laser ablation</td>
<td>Palatine tonsils removed from oropharynx with handheld laser.</td>
</tr>
<tr>
<td>Coblation</td>
<td>Palatine tonsils dissected and removed from oropharynx using low-temperature irrigation radio frequency energy device.</td>
</tr>
</tbody>
</table>

Indications for Tonsillectomy

Tonsillectomy has two primary indications: recurrent tonsillitis and obstructive sleep-disordered breathing (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 implicate etiologically 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 if the suspected pathogen represents normal bacterial flora for a particular child’s pharynx.
Despite evidence to the contrary, clinicians sometimes treat sore throat empirically with antibiotics without objective testing. Sore throat or pharyngitis may or may not have a tonsillar origin, and it is possible that many cases have alternative explanations. Nonetheless, many cases are termed “tonsillitis” without supportive documentation. Frequency of infections is a metric of severity used to determine eligibility for tonsillectomy. This criterion is fraught with complexity related to diagnostic variability and to incomplete and inconsistent medical documentation. Thus, heterogeneity in diagnostic accuracy, establishment of severity, and frequency of infections complicates treatment decisions regarding tonsillectomy and the performance of comparative effectiveness of its treatments.

Currently, the most common indication for tonsillectomy is OSDB (i.e., breathing difficulties during sleep including OSA, which has been defined as “a disorder in which a person frequently stops breathing during his or her sleep,” and may be diagnosed based on the frequency of cessation of airflow [apnea] or reduction in airflow with desaturation [hypopnea], 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 declines in quality of life and negative health consequences. It has been associated with a five-point decrease in intelligence quotient (IQ), hypersomnolence, emotional lability, decreased attention, small stature, enuresis, cardiopulmonary morbidity, and missed school. 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. Moreover, OSDB occurs at especially high rates in subsets of children with developmental disorders and craniofacial syndromes, including Down syndrome.

As in adults, the gold standard diagnostic test for OSA in children is polysomnography (PSG), which physiologically tests sleep architecture and efficiency. Treatment involves alleviating the inciting upper airway soft tissue obstruction or collapse. One method of primary treatment is continuous positive airway pressure (CPAP), which is a device worn over a child’s nose and/or mouth that delivers continuous high pressure flow to the lungs, acting as a pneumatic stent to maintain upper airway patency during sleep. CPAP compliance is highly variable in children. Therefore, other treatment approaches include weight loss in overweight children, orthodontic devices to expand the palate, and allergy or anti-inflammatory medications. However, since the most common culprit in children is tonsillar hypertrophy-related oropharyngeal obstruction, tonsillectomy is often used to establish an adequate airway.

Regardless of indication, age may affect tonsillectomy outcomes. In general, younger children tend to tolerate surgery better than older children and adults, but risk is increased with surgery in very young children (< 2 years) compared with older children. Tonsillectomy is not commonly performed in this very young age group. To date, little guidance regarding the comparative effectiveness of treating recurrent infection or OSDB in children less than 2 years of age exists. Furthermore, obesity may differentially affect OSDB, which may alter expectations and treatment efficacy and outcomes.

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., nonsteroidal anti-inflammatory drugs [NSAIDs] and other analgesics). A 2012 Cochrane review examining the effect of perioperative systemic antibiotics on post-tonsillectomy morbidity (pain, consumption of pain medications, secondary hemorrhage, fever, and return to normal diet) failed to find any clinically important impact of antibiotics in reducing pain, need for analgesia, or secondary post-tonsillectomy hemorrhage (PTH).23 However, this analysis combined adult and pediatric trials; thus, the applicability to children alone is not clear. Furthermore, this review included only randomized controlled trials (RCTs). The role of perioperative anti-inflammatory medications (e.g., NSAIDs) and systemic steroids have been addressed in prior meta-analyses and reviews, with consistent findings of low risk of PTH and reduced morbidity (pain, time to return to normal diet and activity) associated with perioperative dexamethasone in children,24-29 and less consistent findings regarding NSAIDs.30, 31 Two systematic reviews reported no significant risk of PTH with perioperative NSAID use31, 32 while one reported insufficient data to rule out risk.30 One review also noted an increased PTH risk with postoperative NSAIDs.31

Thus, 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 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 (primarily RCT) 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 of 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 (AAO-HNSF), 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 (KQ) 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.

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 obstructive sleep-disordered breathing (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 nonantibiotic—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 post-anesthesia care) pharmacologic agents intended to improve outcomes?

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

Table 2 outlines population, intervention, comparator, outcomes, timing, and setting (PICOTS) characteristics for each KQ.
<table>
<thead>
<tr>
<th>KQ</th>
<th>Population</th>
<th>Intervention</th>
<th>Comparators</th>
<th>Outcomes</th>
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</thead>
<tbody>
<tr>
<td>1</td>
<td>Children (3-18 years of age) with OSDB</td>
<td>Tonsillectomy</td>
<td>-Continuous positive airway pressure (CPAP) -Pharmacologic treatment including anti-inflammatory medications, decongestants, allergy medication, antihistamines, nasal steroids, leukotriene inhibitors</td>
<td>Sleep outcomes -Apnea Hypopnea Index (AHI) -Sleep quality measures (Obstructive Sleep Apnea-18 [OSA-18], Clinical Assessment Score-15 [CAS-15]) -Pediatric Sleep Questionnaire (PSQ) -Modified Epworth Sleepiness Scale -Desaturation nadir -OSDB persistence Cognitive or behavioral outcomes -Validated measures of attention, irritability, and memory Health outcomes -Growth velocity (height, BMI for age) -Cardiopulmonary issues -Self or caregiver-reported enuresis -Health care utilization (number of clinician visits) Harms -Re-admission or ER visit or ICU admission for postoperative pain, dehydration, PTH, or nausea and vomiting -Reoperation for primary or secondary PTH -Velopharyngeal insufficiency -30-day mortality -Harms of comparator agents reported in studies with comparison groups</td>
</tr>
<tr>
<td>1a</td>
<td>Children (3-18 years of age) with OSDB and neuromuscular or craniofacial abnormalities</td>
<td>Tonsillectomy</td>
<td>See comparators above (KQ1)</td>
<td>See outcomes above (KQ1)</td>
</tr>
<tr>
<td>1b</td>
<td>Children under age 3 with OSDB</td>
<td>Tonsillectomy</td>
<td>See comparators above (KQ1)</td>
<td>See outcomes above (KQ1) Length of stay</td>
</tr>
<tr>
<td>1c</td>
<td>Children (3-18 years of age) with OSDB and Down syndrome</td>
<td>Tonsillectomy</td>
<td>See comparators above (KQ1)</td>
<td>See outcomes above (KQ1) Length of stay</td>
</tr>
<tr>
<td>KQ</td>
<td>Population</td>
<td>Intervention</td>
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<tr>
<td>1d</td>
<td>Children (3-18 years of age) with OSDB who are overweight or obese</td>
<td>Tonsillectomy</td>
<td>-CPAP -Weight loss -Pharmacologic treatment including anti-inflammatory medications, decongestants, allergy medication, antihistamines, nasal steroids, leukotriene inhibitors</td>
<td>See outcomes above (KQ1)</td>
</tr>
<tr>
<td>2</td>
<td>Children (3-18 years) with recurrent throat infections</td>
<td>Tonsillectomy</td>
<td>-Antibiotics -Nonantibiotic pharmacologic treatments (e.g., anti-inflammatory agents, decongestants, antihistamines, leukotriene inhibitors, nasal or systemic steroids)</td>
<td>Throat infections -Number of throat infections/year -Severity of throat infections -Number of streptococcal infections/year Quality of life -Validated quality of life measures -Missed school or work for child or caregiver Other outcomes -Health care utilization (number of clinician visits, number of courses of antibiotics) Harms -ER visit or hospital or ICU admission for postoperative pain, PTH, dehydration, or nausea and vomiting -Reoperation for primary or secondary PTH -Velopharyngeal insufficiency -30-day mortality -Harms of comparator agents reported in studies with comparison groups</td>
</tr>
<tr>
<td>3</td>
<td>Children (3-18 years) undergoing tonsillectomy</td>
<td>Total tonsillectomy -Partial tonsillectomy</td>
<td>See sleep, cognitive or behavioral, and health outcomes (KQ1) and quality of life outcomes (KQ2)</td>
<td>Throat infections -Number of throat infections/year -Severity of throat infections -Number of streptococcal infections/year Other outcomes -Symptomatic tonsillar regrowth -Time to return to usual activity (diet, school) Harms See KQ1 Reoperation for complete tonsillectomy</td>
</tr>
<tr>
<td>KQ</td>
<td>Population</td>
<td>Intervention†</td>
<td>Comparators</td>
<td>Outcomes</td>
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<td>4</td>
<td>Children (3-18 years) undergoing tonsillectomy</td>
<td>Tonsillectomy</td>
<td>-Other technique for tonsillectomy</td>
<td>See sleep, cognitive or behavioral, and health outcomes (KQ1) and quality of life outcomes (KQ2)</td>
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<td>Throat infections</td>
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<td>-Number of throat infections/year</td>
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<td>-Severity of throat infections</td>
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<td>-Number of streptococcal infections/year</td>
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<td>Other outcomes</td>
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<td>-Time to return to usual activity (diet, school)</td>
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<td>Harms</td>
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<td>See KQ1</td>
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<tr>
<td>5</td>
<td>Children (3-18 years) undergoing tonsillectomy</td>
<td>Tonsillectomy plus adjunctive perioperative (i.e., preoperative, intraoperative, or immediate postoperative [post-anesthesia care] periods) pharmacologic agents</td>
<td>-Tonsillectomy without adjunctive perioperative pharmacologic agents (i.e., pharmacologic agents given to attempt to reduce postoperative morbidity including pain or nausea and vomiting)</td>
<td>-Pain management (need for rescue medications)</td>
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<td>-Time to return to usual activities (diet, school)</td>
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<td>-Health care utilization (number of clinician visits, number of courses of antibiotics)</td>
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<td>Harms</td>
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<td>-Harms of agent</td>
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<td>-Re-admission to hospital or ICU or ER visit for postoperative pain, PTH, dehydration, or nausea and vomiting</td>
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<td>-Reoperation for primary or secondary PTH</td>
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<td>-30-day mortality</td>
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<tr>
<td>6</td>
<td>Children (3-18 years) undergoing tonsillectomy and receiving pharmacologic agents for pain postoperatively (i.e., up to 10 days after discharge from post-anesthesia care)</td>
<td>Tonsillectomy plus postoperative pharmacologic agents for pain (e.g., NSAID, ketorolac)</td>
<td>-Tonsillectomy with other postoperative pharmacologic agents for pain</td>
<td>See outcomes and harms for KQ5</td>
</tr>
</tbody>
</table>

*Studies of any length or followup and in any setting, except for KQ6, which includes pharmacologic agents for pain given up to 10 days postsurgery.
**Includes breathing difficulties during sleep as operationalized in each study, including obstructive sleep apnea and upper airway resistance syndrome
†Tonsillectomy includes tonsillectomy, adenotonsillectomy, partial tonsillectomy
Abbreviations: AHI = Apnea Hypopnea Index; BMI = Body Mass Index; CAS-15 = Clinical Assessment Score-15; CPAP = Continuous Positive Airway Pressure; ER = Emergency Room; KQ = Key Question; NSAID = Nonsteroidal Anti-Inflammatory Drug; OSA-18 = Obstructive Sleep Apnea-18; OSDB = Obstructive Sleep-Disordered Breathing; PTH = Post-Tonsillectomy Hemorrhage
Analytic Framework

The analytic frameworks illustrate the population, interventions, and outcomes that guided the literature search and synthesis (Appendix A). The frameworks depict the key questions within the context of the population, intervention, comparator, outcomes, timing, and setting (PICOTS) parameters described in Table 2.

Organization of This Report

The Methods section describes the review processes. The Results section presents findings for each key question organized by intervention and outcome area where possible. We discuss harms reported in studies of surgical techniques in a separate section following discussion of effectiveness outcomes in each KQ, including a meta-analysis that provides expected frequency of PTH by surgical approach and by partial versus total tonsillectomy. Summary tables for each key question outline key outcomes.

The Discussion section of the report outlines the current state of the literature and challenges for future research in the field. We also provide a list of abbreviations and acronyms at the end of the report.

Uses of This Evidence Report

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, sleep medicine physicians, allergists, family physicians, anesthesiologists, infectious disease physicians, nurse practitioners, physician assistants, and nurses. 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.
Methods

In this chapter, we document the procedures that we used to produce a comparative effectiveness review (CER) on tonsillectomy in children with obstructive sleep-disordered breathing (OSDB) or recurrent throat infections. These procedures follow the methods outlined in the Agency for Healthcare Research and Quality (AHRQ) Effective Health Care Program Methods Guide for Effectiveness and Comparative Effectiveness Reviews.33

Topic Refinement and Review Protocol

The topic for this report was nominated by the American Academy of Otolaryngology-Head and Neck Surgery (AAO-HNSF) in a public process using the Effective Health Care website. Working from the nomination, we drafted the initial key questions (KQ) and analytic frameworks and refined them with input from key informants representing the fields of pediatrics, otolaryngology, anesthesiology, and sleep medicine. We also spoke with a caregiver representative. All members of the research team were required to submit information about potential conflicts of interest before initiation of the work. No members of the review team had any conflicts.

After review from AHRQ, the questions and framework were posted online for public comment. No changes to the questions or frameworks were recommended. We also developed population, interventions, outcomes, timing, and settings (PICOTS) criteria for intervention KQ.

We identified technical experts on the topic to provide assistance during the project. The Technical Expert Panel (TEP), representing the fields of pediatrics, otolaryngology, anesthesiology, infectious disease, and sleep medicine, contributed to the AHRQ’s broader goals of (1) creating and maintaining science partnerships as well as public-private partnerships and (2) meeting the needs of an array of potential users of its products. Thus, the TEP was both an additional resource and a sounding board during the project. The TEP included eight members serving as technical or clinical experts. To ensure robust, scientifically relevant work, TEP members participated in conference calls and discussions through e-mail to:

• Help to refine the analytic framework and KQ at the beginning of the project;
• Discuss inclusion/exclusion criteria; and
• Assist with determining key interventions and outcomes of interest.

The final protocol was posted to the AHRQ Effective Health Care web site and registered in the PROSPERO international register of systematic reviews (ID#: CRD42015025600).

Literature Search Strategy

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. A second librarian reviewed the search strategies.
We included only studies published in English as a review of non-English citations retrieved by our MEDLINE search identified few studies of relevance. Appendix B lists our search terms and strategies and the yield from each database.

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.

Gray Literature
AHRQ’s Scientific Resource Center notified companies that produce surgical instruments used for tonsillectomy or devices such as continuous positive airway pressure (CPAP) machines about the opportunity to provide Scientific Information Packets (SIPs) to inform the review. Because many manufacturers may produce medications used in the peri- or postoperative periods, a notice of the opportunity to submit scientific material to inform the review was posted in the Federal Register for 6 weeks.

We also searched ClinicalTrials.gov to assess reporting bias and to identify any study results that may not have been identified in our other database searches. We applied the inclusion criteria in Table 3 to studies identified via our gray literature searches.

Inclusion and Exclusion Criteria
Table 3 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 TEP, 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 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 whether including additional studies was warranted.34 We also included studies considered to have high risk of bias (as described below) in meta-analyses after sensitivity analyses showed no systematic effects on findings.

We limited our searches for comparative effectiveness questions to studies published in English and from January 1980 to June 2016 for studies of the effectiveness of tonsillectomy in children with OSDB or recurrent throat infections (KQs1-2). In consultation with the review nominator, we limited inclusion of studies relevant to KQs3-6 to those published between January 2000 and June 2016 as we identified a large literature base, including many randomized controlled trials (RCTs), addressing these questions.

We also excluded studies including both children and adults if the mean plus standard deviation age of participants was greater than 18 years and data were not reported separately for children (3-18 years of age for most KQs). We included comparative studies (studies including an intervention and a comparison group) evaluating the benefits or harms of tonsillectomy (tonsillectomy, adenotonsillectomy, and partial tonsillectomy conducted using any surgical technique such as cautery or cold dissection) compared with an inactive control or alternate intervention. We also included case series or database studies including at least 1,000 children undergoing tonsillectomy to address harms but not effectiveness. We selected the bound of 1,000 as a conservative value based on a preliminary review in which we identified numerous case series or database studies with 1,000 or more participants.
Table 3. Inclusion criteria for studies of tonsillectomy

<table>
<thead>
<tr>
<th>Category</th>
<th>Criteria</th>
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</table>
| 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 post-anesthesia 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 described in Table 2  
• 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 = Nonsteroidal Anti-Inflammatory Drug; OSDB = Obstructive Sleep-Disordered Breathing; RCT = Randomized Controlled Trial

**Study Selection**

Once we identified articles through the electronic database searches and hand-searching, we examined abstracts of articles to determine whether studies met our criteria. Two reviewers separately evaluated the abstracts of studies identified in our searches for KQs for inclusion or exclusion, using an Abstract Review Form (Appendix C). If one reviewer concluded that the article could be eligible for the review based on the abstract, we retained it. Following abstract review, two reviewers independently assessed the full text of each included study using a standardized form (Appendix C) that included questions stemming from our inclusion and exclusion criteria. We adjudicated disagreements through discussion between reviews or final adjudication by a senior reviewer.

We conducted all abstract and full text reviews using the DistillerSR online screening application (Evidence Partners Incorporated, Ottawa, Ontario). Appendix D includes a list of excluded studies and the reasons for exclusion. Data extracted for each study are available via the Systematic Review Data Repository (srdr.ahrq.gov).

**Data Extraction**

The staff members and clinical experts who conducted this review (including two otolaryngologists, one pediatrician, one pediatric pulmonology sleep medicine physician, one biostatistician, and three epidemiologists/systematic reviewers) jointly developed the data extraction forms for the KQs. We designed forms to provide sufficient information to enable
readers to understand the studies and to determine their quality; we gave particular emphasis to essential information related to the KQs. We used two templates to facilitate the extraction of data based on study type; one form was designed for case series or database studies that reported harms data and one was created to accommodate all types of comparative studies for effectiveness and harms data.

The team was trained to extract data by extracting several articles into the template and then reconvening as a group to discuss the utility of the template. We repeated this process through several iterations until we decided that the templates included the appropriate categories for gathering the information contained in the articles and for potential meta-analyses. Team data extractors shared the task of initially entering information into the evidence tables. A second team member also reviewed the articles and edited all initial entries for accuracy, completeness, and consistency. A senior reviewer reconciled disagreements concerning the information reported.

The full research team met regularly during the data extraction period and discussed issues related to the whole process. In addition to outcomes related to the effectiveness of tonsillectomy (e.g., changes in sleep parameters or quality of life), we extracted all data available on harms. Harms encompass the full range of specific negative effects, including the narrower definition of adverse events.

Data Synthesis

We summarized data for KQs qualitatively using summary tables when meta-analyses were not possible. We used a best evidence approach and focused on lower risk of bias studies when they provided sufficient data to address a KQ. We identified sufficient data to address studies comparing tonsillectomy with watchful waiting in children with OSDB. Studies used in this fixed effects meta-analysis included children with polysomnography-proven OSDB and reported the Apnea Hypopnea Index (AHI) at baseline and followup. We modeled the difference between followup and baseline scores as a Gaussian random variable.

We also meta-analyzed studies comparing the risk of post-tonsillectomy hemorrhage (PTH) with perioperative steroids compared with placebo. We used a zero-inflated binomial model to account for the relatively high number of studies with no PTH-related outcomes in the available data. We included study random effects to account for correlation among arms in the same study. Finally, we addressed PTH and 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 and the effect of partial compared with total tonsillectomy on the occurrence of PTH-related outcomes following surgery. We also conducted analyses to estimate the effects of including high risk of bias studies in our analyses. These analyses suggested no systematic effects of these studies; thus, we retained them in all three meta-analyses. Appendix E 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 the risk of bias of individual studies meeting eligibility criteria for our KQs. We used prespecified questions from Assessing the Risk of Bias of Individual Studies in Systematic Reviews of Health Care Interventions appropriate to each study design to assess risk of bias of randomized controlled
trials (RCT) and observational studies and a tool adapted from questions outlined in the McMaster McHarms tool to assess reporting of harms.36

Questions assessing risk of bias evaluate domains including selection bias, performance bias, attrition bias, detection bias, and reporting bias as well as methods for recruiting cohorts and controlling for confounding. The harms assessment tool addresses questions related to pre-specification and reporting of harms.

Risk of bias assessment of each study was conducted independently by two team members using the forms presented in Appendix C. Any discrepancies were adjudicated by the two team members or a senior investigator. Investigators did not rely on the study design as described by authors of individual papers; rather, the methods section of each paper was reviewed to determine which rating tool to employ. The results of these tools were then translated to “low,” “moderate,” and “high” risk of bias ratings as described below. Appendix F reports risk of bias scoring for each study.

We required that RCTs receive a positive rating (i.e., low risk of bias) on 12 of 13 of the questions used to assess each study to be considered to have low risk of bias. RCTs had to receive nine to eleven positive ratings to have moderate risk of bias, and studies with ≤ eight positive ratings were considered to have high risk of bias. We considered a rating of “unclear” for a question as a negative rating. We assessed the risk of bias for each major outcome of relevance reported but report an overall assessment unless the risk of bias varied by outcome.

We required that cohort studies receive positive ratings on at least 13 of the 14 questions used to assess each study to have low risk of bias for cohort studies and on nine to 12 questions to be considered to have moderate risk of bias for cohort studies. We considered studies that received positive ratings on ≤ eight questions to have high risk of bias. We required that studies assessed for harms reporting receive positive ratings on all four of the four questions used to assess each study to be considered to have low risk of bias. We considered studies receiving three positive ratings as moderate risk of bias and those with two or fewer positive ratings as high risk of bias.

**Strength of the Body of Evidence**

We applied explicit criteria for rating the overall strength of the evidence for each key intervention-outcome pair for which the overall risk of bias was not high. We rated the strength of the evidence for the outcomes of interest for our KQs (Table 2) and for clinically important harms. We used established concepts of the quantity of evidence (e.g., numbers of studies, aggregate ending-sample sizes), the quality of evidence (from the risk of bias ratings on individual articles), and the coherence or consistency of findings across similar and dissimilar studies and in relation to known or theoretically sound ideas of clinical knowledge.

The strength of evidence evaluation that we used is described in the Effective Health Care Program’s Methods Guide for Effectiveness and Comparative Effectiveness Reviews33 and in the updated strength of evidence guide.37 The latter emphasizes five major domains: study limitations (low, medium, high level of limitation), consistency (inconsistency not present, inconsistency present, unknown or not applicable), directness (direct, indirect), precision (precise, imprecise), and reporting bias (suspected, undetected). Study limitations are derived from the risk of bias assessment of the individual studies that addressed the KQs and specific outcome under consideration (see Appendix C for more information on strength of evidence domains). Each key outcome for each comparison of interest is given an overall evidence grade based on the ratings for the individual domains.
We graded the overall strength of evidence as outlined in Table 4. Two senior staff members independently graded the body of evidence; disagreements were resolved as needed through discussion or third-party adjudication. We recorded strength of evidence assessments in tables, summarizing results for each outcome. We did not consider case series and database studies in the assessment of strength of the evidence for harms.

Table 4. Strength of evidence grades and definitions

<table>
<thead>
<tr>
<th>Grade</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>High</td>
<td>We are very confident that the estimate of effect lies close to the true effect for this outcome. The body of evidence has few or no deficiencies. We believe that the findings are stable, i.e., another study would not change the conclusions.</td>
</tr>
<tr>
<td>Moderate</td>
<td>We are moderately confident that the estimate of effect lies close to the true effect for this outcome. The body of evidence has some deficiencies. We believe that the findings are likely to be stable, but some doubt remains.</td>
</tr>
<tr>
<td>Low</td>
<td>We have limited confidence that the estimate of effect lies close to the true effect for this outcome. The body of evidence has major or numerous deficiencies (or both). We believe that additional evidence is needed before concluding either that the findings are stable or that the estimate of effect is close to the true effect.</td>
</tr>
<tr>
<td>Insufficient</td>
<td>We have no evidence, we are unable to estimate an effect, or we have no confidence in the estimate of effect for this outcome. No evidence is available or the body of evidence has unacceptable deficiencies, precluding reaching a conclusion.</td>
</tr>
</tbody>
</table>

* Excerpted from Berkman et al., 2014

Applicability

We assessed the applicability of findings reported in the included literature addressing our KQs to the general population of children undergoing tonsillectomy; our approach involved 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 body mass index (BMI), Down syndrome, and craniofacial abnormalities. Applicability tables for each KQ are in Appendix G.

Peer Review and Public Commentary

Researchers and clinicians with expertise in tonsillectomy and individuals representing stakeholder and user communities provided external peer review of this report. The draft report was posted on the AHRQ Web site for 4 weeks to elicit public comment. We addressed all reviewer comments, revised the text as appropriate, and documented changes and revisions to the report in a disposition of comments report that will be made available 3 months after AHRQ posts the final review on the AHRQ Effective Health Care Web site.
Results

Results of Literature Searches for Key Questions

We identified 9608 nonduplicative titles or abstracts with potential relevance, with 1966 proceeding to full text review (Figure 1). We excluded 1725 studies at full text review. We included 218 unique studies (241 publications) in the review. These 218 studies included 165 comparative studies and 53 case series or database or registry studies providing data on harms only.

Figure 1. Disposition of studies identified for this review

†3 papers each reported 2 unique studies in each paper. Numbers next to each Key Question indicate number of unique studies addressing the question. Studies could address more than one Key Question.
*Numbers do not tally as studies could be excluded for multiple reasons.
Abbreviations: KQ = Key Question; n = Number.
Description of Included Studies

The 218 unique included studies (reported in multiple publications) comprised 141 randomized controlled trials (RCTs), 9, 38-192 12 nonrandomized trials, 6, 179, 193-202 seven prospective 203-209 and five retrospective cohort studies, 210-214 53 database or registry studies or case series with at least 1000 children (Table 5). 21, 215-276

We used database and registry studies and case series for harms data only. We considered 67 studies to have low risk of bias, 21, 39-41, 43, 49-54, 56, 57, 59, 70, 75, 76, 88-90, 93, 94, 97, 98, 105, 112, 113, 115, 118-120, 123, 125, 128, 131-136, 144, 146, 151, 155, 156, 163, 167-170, 217-222, 225, 226, 228, 229, 231, 233, 235, 236, 241, 247, 248, 250, 251, 258, 266-271 and 41 to have moderate risk, 6, 55, 61, 65, 67, 68, 73, 77, 81, 99-102, 104, 108, 129, 137, 143, 153, 162, 187-189, 193, 198, 199, 202, 204, 205, 208, 212, 237, 239, 243, 244, 264, 265, 278 and 41 to have high risk, 6, 56, 61, 65, 67, 68, 73, 77, 81, 99-102, 104, 108, 129, 137, 143, 153, 162, 187-189, 193, 198, 199, 202, 204, 205, 208, 212, 237, 239, 243, 244, 264, 265, 278

Studies were conducted globally (Table 5), with most conducted in the United States (n=56, including 4 unique studies published in 2 papers), 6, 9, 21, 47, 54, 66, 68, 70, 77, 85, 90, 92, 93, 95, 97-99, 107, 108, 110, 112, 114, 116, 120, 122, 124, 126, 130, 151, 171-178, 191, 201, 211-214, 223, 224, 227, 230, 232, 234, 238, 242, 245, 246, 249, 252, 253, 255-257, 259-263, 272-277 United Kingdom (n=22, including 2 unique studies reported in one paper), 56, 75, 102, 103, 123, 125, 131, 134, 179, 210, 217-219, 225, 226, 231, 238, 241, 243, 245, 259, 260, 262, 274 Turkey (n=19), 45, 48, 61, 65, 67, 73, 76, 80, 84, 101, 104-106, 113, 121, 139, 143, 194, 195 and Egypt (n=12), 6, 40, 42, 51, 52, 100, 119, 142, 152, 158, 159, 163, 196 Sixty-nine studies were conducted in developing or emerging nations (including, among others, Turkey, Egypt, Iran, Pakistan, Brazil, India, and China) according to United Nations classification. 39, 40, 42, 44-46, 48, 50-52, 55, 61-63, 65, 67, 71-73, 76, 79, 80, 84, 87, 91, 100, 101, 104-106, 109, 113, 117, 119, 121, 139-144, 146-149, 152, 154, 156-163, 188, 189, 194-196, 200, 202, 204-206, 208, 244, 246, 265, 280

Ages of children in studies ranged widely from less than 1 to over 18 (mean age ≤18 in all studies), and studies included a total of 1,845,683 children. Most studies did not specify an indication for tonsillectomy (n=89); 8, 9, 21, 41, 43, 48, 54, 57, 59-62, 65, 66, 68-70, 74, 78, 81-83, 89, 96, 99, 102, 104, 108, 110, 111, 116, 120, 130, 131, 134, 144, 145, 155, 162, 164-166, 169, 170, 182-184, 192, 194, 195, 209, 215, 217-219, 223, 224, 235-240, 249, 252, 253, 256, 258, 260, 263, 266, 267, 270, 273 and 42 specifically noted OSDB as the surgical indication; 38, 39, 42, 44-46, 48, 50-52, 55, 61-63, 65, 67, 71, 77, 84-86, 90, 95, 97, 98, 101, 107, 114, 124, 129, 139, 143, 151, 160, 171-178, 185-187, 189, 191, 193, 198, 201, 203-206, 208, 211, 212, 214, 220-222, 230, 264, 269 and 22 specifically noted recurrent throat infections as the indication. 6, 40, 45, 51, 52, 55, 56, 80, 91, 125, 142, 152, 163, 179-181, 196, 197, 200, 210, 213, 244
### Table 5. Overview of studies addressing tonsillectomy in children

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>RCTs (n=141)</th>
<th>Nonrandomized Trials (n=12)</th>
<th>Prospective Cohort Studies (n=7)</th>
<th>Retrospective Cohort Studies (n=5)</th>
<th>Case Series, or Registry Studies Reporting Harms (n=53)</th>
<th>Total Literature</th>
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<td><strong>Key Question</strong></td>
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<tr>
<td><strong>Total N participants</strong></td>
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<td>2875</td>
<td>518</td>
<td>14350</td>
<td>1810403</td>
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</table>

*One prospective cohort study addressed both KQ1 and KQ2.*  
This table includes the study only under KQ1.

KQ = Key Question; N = Number; OSDB = Obstructive Sleep-Disordered Breathing; RCT = Randomized Controlled Trial

### Gray Literature

We did not receive any materials from Federal Register notices. We sought reports of study protocols identified in ClinicalTrials.gov and other registers to assess for reporting bias but identified very few trials (n=8). Our gray literature searches did not contribute additional studies not identified in our database searches.

### Key Question 1. Effectiveness of Tonsillectomy Versus No Surgery for OSDB

**Key Points**

- In five studies of children with polysomnography (PSG) proven OSDB, respiratory parameters measured using the Apnea Hypopnea Index (AHI) improved more in children receiving tonsillectomy than those not undergoing surgery. In a meta-analysis of three studies, children who underwent tonsillectomy had a 4.8-point improvement in AHI scores compared with those who did not have surgery (95% credible interval: -6.5 to -
3.1). 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).

- For tonsillectomy compared with no surgery, we found greater improvement in AHI and negative behaviors with tonsillectomy vs. watchful waiting. Our confidence in these conclusions 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 intelligence quotient (IQ) (insufficient strength of evidence).
- We could not make conclusions about outcomes following tonsillectomy compared with continuous positive airway pressure (CPAP) and in studies assessing outcomes in subpopulations such as children with Down syndrome (KQ1a-d) (insufficient strength of evidence).

**Overview of the Literature**

We identified 13 unique studies (20 papers, 1180 participants) addressing tonsillectomy in children with OSDB (Table 6). One prospective cohort study included both children with OSDB and recurrent throat infection and did not report baseline data or outcomes by indication.209 Most studies were conducted in the United States (n=6),114, 171-176, 178, 191, 201, 211, 212, 214 two in Brazil,205, 281 two in Israel,204, 206 and one each in Ireland,209 Australia203 and India.44 Three studies were RCTs, including one multiple-publication study.44, 114, 171-178 Six were prospective203-206, 208, 209 and three were retrospective cohort studies.211, 212, 214 One study was a nonrandomized trial.201

Eleven studies compared tonsillectomy to watchful waiting (which could have included supportive treatment with medications such as nasal steroids) or no surgery.114, 171-178, 191, 201, 203-206, 208, 209, 211, 214 Two studies compared CPAP or oxygen with tonsillectomy.44, 212 Participant ages ranged from less than 2 years to 16 years across studies. Studies frequently reported change in AHI and cognitive or behavioral outcomes.

We considered eight studies to have moderate risk of bias44, 114, 171-178, 191, 201, 203-206, 211, 214 and five to have high risk of bias.204, 205, 208, 209, 212 Major sources of bias in these studies included the use of unblinded outcome assessors and unclear impact of concurrent interventions or variations in study execution. Given the relatively few studies addressing this question, we retained retrospective studies with low or moderate risk of bias as part of the evidence base. We retained high risk of bias studies in meta-analyses after sensitivity analyses reveal no significant effects on findings.
Table 6. Overview of studies addressing tonsillectomy in children with OSDB

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>RCTs</th>
<th>Nonrandomized Trial</th>
<th>Prospective Cohort Studies</th>
<th>Retrospective Cohort Studies</th>
<th>Total Literature</th>
</tr>
</thead>
<tbody>
<tr>
<td>Comparisons</td>
<td></td>
<td></td>
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<td></td>
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<tr>
<td>Watchful Waiting or No Surgery</td>
<td>2</td>
<td>1</td>
<td>6</td>
<td>2</td>
<td>11</td>
</tr>
<tr>
<td>CPAP</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>Effectiveness Outcomes</td>
<td></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Frequently Reported</td>
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<tr>
<td>AHI</td>
<td>3</td>
<td>0</td>
<td>2</td>
<td>3</td>
<td>8</td>
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<tr>
<td>Sleep-related Quality of Life (OSA-18, M-ESS, PSQ)</td>
<td>2</td>
<td>1</td>
<td>1*</td>
<td>1</td>
<td>5</td>
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<tr>
<td>Executive Function, Cognitive, or Behavioral Measure</td>
<td>1</td>
<td>0</td>
<td>2</td>
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<tr>
<td>Risk of Bias</td>
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</tr>
<tr>
<td>Total N participants</td>
<td>529</td>
<td>64</td>
<td>386</td>
<td>106</td>
<td>1085</td>
</tr>
</tbody>
</table>

AHI = Apnea–Hypopnea Index; CPAP = Continuous Positive Airway Pressure; M-ESS = Modified Epworth Sleepiness Scale; N = Number; OSA-18 = Obstructive Sleep Apnea-18; OSDB = Obstructive Sleep-Disordered Breathing; PSQ = Pediatric Sleep Questionnaire; RCT = Randomized Controlled Trial

*Reports the T14 Pediatric Throat Disorders Outcome Test

Detailed Analysis

Tonsillectomy Versus No Surgery or Watchful Waiting With Supportive Care

OSDB-Related Outcomes

Five studies (reported in multiple publications) of moderate risk of bias evaluated the improvement in AHI among children with PSG-proven OSDB. Two studies were RCTs, including the multi-publication Childhood Adenotonsillectomy Trial (CHAT);114, 171-178 one was a prospective203 and two were retrospective cohort studies,211, 214 All reported improvement in children after tonsillectomy compared with observation without intervention or with supportive/medical management (excluding CPAP). The watchful waiting groups also improved from baseline in three studies.114, 171-178, 191, 211 Differences in AHI between tonsillectomy and watchful waiting groups were statistically significant in three studies171-178, 191, 211 and not significant in two (Table 7).114, 203 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. Where reported, the respiratory disturbance index and oxygen saturation improved significantly after tonsillectomy.114, 172 Further, in a single, small low risk of bias study, tonsillectomy was associated with clinical benefit in symptoms of children with diagnoses of sleep apnea based on history, but with negative polysomnograms.114 This study is quite small, however, with fewer than 40 participants.

We combined three studies (the CHAT RCT, reported in multiple publications,171-178, 191 and
one prospective\textsuperscript{211} and retrospective\textsuperscript{204} study) reporting AHI outcomes in a fixed effects meta-
alysis. We estimated an effect size of -4.81 (95\% credible interval: -6.5 to -3.1), indicating a
reduction (improvement) in AHI of 4.81 points 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). Whether this degree of change is clinically
important to patients’ quality of life is not clear.

### Table 7. Key OSDB-related outcomes in studies comparing tonsillectomy with watchful waiting in
children with OSDB

<table>
<thead>
<tr>
<th>Author, Year</th>
<th>Study Type</th>
<th>Risk of Bias</th>
<th>Comparison Groups</th>
<th>Baseline AHI Scores (Mean\pmSD)</th>
<th>Followup AHI Scores (Mean\pmSD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Trosman 2016\textsuperscript{214} Retrospective Cohort Moderate ROB</td>
<td>G1: Tonsillectomy (18)</td>
<td>G1: 3.5 \pm 1.1</td>
<td>G1: 2.69 (1.48 to 3.9)</td>
<td>16-month followup (IQR)</td>
<td></td>
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<tr>
<td></td>
<td>G1a: Tonsillectomy – obese children (8)</td>
<td>G1a: 3.83</td>
<td>G1a: 3.08</td>
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<tr>
<td></td>
<td>G1b: Tonsillectomy – Syndromic children (6)</td>
<td>G1b: 3.09 \pm 1.1</td>
<td>G1b: 2.03</td>
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<td></td>
<td>G2: Watchful waiting with supportive care (44)</td>
<td>G2a: 3.2</td>
<td>G2: 5.18 (2.46 to 7.9)</td>
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<tr>
<td></td>
<td>G2a: Watchful waiting with supportive care, obese children (11)</td>
<td>G2b: 3.31</td>
<td>G2a: 3.4</td>
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<td></td>
<td>G2b: Watchful waiting with supportive care, Syndromic children (9)</td>
<td>G2b: 2.84</td>
<td>G2b: 2.84</td>
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<tr>
<td></td>
<td>Marcus 2014\textsuperscript{171-178, 191} RCT Moderate ROB</td>
<td>G1: Tonsillectomy (193)</td>
<td>Events/hour, median (IQR)</td>
<td>G1 vs G2: p=0.03</td>
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<tr>
<td></td>
<td>G2: Watchful Waiting with Supportive Care (208)</td>
<td>G1: 4.8 (2.7 to 8.8)</td>
<td>Events/hour, change from baseline to 7 months (IQR)</td>
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<td></td>
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<td>G2: 4.5 (2.5 to 8.9)</td>
<td>G1: -3.5 (-7.1 to -1.8)</td>
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<td></td>
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<td></td>
<td>G2: -1.6 (-3.7 to 0.5)</td>
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<td></td>
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<td>G1 vs. G2: p &lt; 0.001</td>
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<td><strong>Effect size: 0.57</strong></td>
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<td>Biggs 2014\textsuperscript{203} Prospective Cohort Moderate ROB</td>
<td>G1: Tonsillectomy or Nasal Steroids (12)</td>
<td>Events/hour</td>
<td>G1 vs. G2: p=NS</td>
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<td></td>
<td>G2: Watchful waiting with supportive care (27)</td>
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<td>Events/hour (4 year followup)</td>
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<td>G2: 1.0 \pm 1.2</td>
<td>G1: 1.8 \pm 5.2</td>
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<td>G2: 1.7 \pm 6.0</td>
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<td></td>
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<td></td>
<td>G1 vs. G2: p=NS</td>
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<tr>
<td></td>
<td>Burstein 2013\textsuperscript{211} Retrospective Cohort Moderate ROB</td>
<td>G1: Tonsillectomy (16)</td>
<td>G1: 14.4 (median)</td>
<td>G1 vs. G2, median change: p=0.04</td>
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<tr>
<td></td>
<td>G2: Watchful waiting with supportive care (16)</td>
<td>G2: 9.3 (median)</td>
<td>G1: 1.1 (median), median change=10.3</td>
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<td>G2: 3.7 (median), median change=6.5</td>
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<td></td>
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<td></td>
<td>G1 vs. G2, median change: p=0.04</td>
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<tr>
<td></td>
<td>Goldstein 2004\textsuperscript{114} RCT Moderate ROB</td>
<td>G1: PSG+ plus Tonsillectomy (21)</td>
<td>G1: 6.2 (median)</td>
<td>6-month followup</td>
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<tr>
<td></td>
<td>G2: PSG- plus Tonsillectomy (11)</td>
<td>G2: 0.5 (median)</td>
<td>G1: 0.9 (median)</td>
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<td></td>
<td>G3: PSG- plus Watchful Waiting (9)</td>
<td>G3: 0.6 (median)</td>
<td>G2: 0.4 (median)</td>
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<td></td>
<td></td>
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<td>G3: 0</td>
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<td></td>
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<td>G2 vs. G3: p=NS</td>
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</table>

\textsuperscript{Note: Followup periods differed in this study: mean 1.4 years in the tonsillectomy group and 2.0 years in the no surgery group, p=0.02\textsuperscript{211} IQR = Interquartile Range; n = Number; OSDB = Obstructive Sleep-Disordered Breathing; PSG = Polysomnography; NR = Not Reported; NS = Not Significant; RCT = Randomized Controlled Trial; ROB = Risk of Bias; SD = Standard Deviation}
Sleep-Related Quality of Life

Two RCTs, one nonrandomized trial, and one retrospective cohort (all rated as moderate risk of bias) assessed comparative effectiveness of tonsillectomy versus no surgery in the improvement of sleep quality (Table 8). Studies used several different parent-reported quality measures to assess sleep quality outcomes, limiting the ability to compare effectiveness directly across studies, although outcomes were consistently better in children receiving tonsillectomy.

One RCT and a retrospective cohort used the CAS-15 (Clinical Assessment Score), and both reported significant reduction in scores in the tonsillectomy compared with no tonsillectomy groups, indicating improvement in sleep quality following tonsillectomy. In the one study reporting baseline data, scores in the watchful waiting group improved from baseline to the 6-month followup (p=not reported [NR]). The CHAT RCT used the Modified Epworth Sleepiness Scale (M-ESS) and OSA-18 as a measure of quality of life; while control group scores improved over baseline scores (p=NR), children who had tonsillectomy had significantly greater improvements in sleep quality as measured on both scales (p values ≤ 0.01). This RCT also used the Pediatric Sleep Questionnaire Sleep-related Breathing Disorder scale (PSQ-SRBD), which showed significant improvements in sleep quality after tonsillectomy versus watchful waiting (p ≤ 0.01), and small improvements in the control group from baseline (p=NR). In a nonrandomized trial (moderate risk of bias), children with PSG-proven mild OSA self-allocated to tonsillectomy or observation. At a 4-month followup, quality of life assessed with the OSA-18 was significantly improved in children who had surgery (p=0.001) but not in the control group. Differences between groups, however, were not significant at the 8-month followup.

Finally, overall quality of life as measured by the Pediatric Quality of Life Inventory (PedsQL) improved significantly after tonsillectomy, compared with the untreated group in one RCT. Scores improved slightly in the control group from baseline (p=NR). Results for the benefit of tonsillectomy to improve sleep quality in children suffering from OSDB were positive across a number of outcomes and outcome domains. Many parents’ chief complaint in bringing their child with OSDB to medical attention related to impaired quality of life. Results were consistently positive for tonsillectomy relative to observation in short time frames, with limited data available in the longer term.
Table 8. Key sleep-related quality of life outcomes in studies comparing tonsillectomy and no surgery in children with OSDB

<table>
<thead>
<tr>
<th>Author, Year</th>
<th>Study Type</th>
<th>Risk of Bias</th>
<th>Comparison Groups (N)</th>
<th>Outcome Measure Baseline (Mean±SD)</th>
<th>Outcome Measure Followup (Mean±SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Volksy 2014</td>
<td>Nonrandomized trial</td>
<td>Moderate ROB</td>
<td>G1: Tonsillectomy (30) G2: Observation (34)</td>
<td>OSA-18 Total Score G1: 72.3 ± 20 G2: 58.5 ± 21.5</td>
<td>3 months followup OSA-18 Total Score G1: 33.9 ± 14.6 G2: 58.2 ± 24.5 G1 vs G2: p=0.0001</td>
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<td>8 months followup OSA-18 Total Score G1: 33.6 ± 8.6 G2: 45.1 ± 21.9 G1 vs G2: p=NS</td>
</tr>
<tr>
<td>Marcus 2014*</td>
<td>RCT</td>
<td>Moderate ROB</td>
<td>G1: Tonsillectomy (193) G2: Watchful waiting with supportive care (208)</td>
<td>OSA-18 Total Score G1: 53.1 ± 18.3 G2: 54.1 ± 18.8</td>
<td>OSAs-18 Total Score, change from baseline G1: -21 ±16.5 G2: -4.5 ± 19.3 G1 vs. G2: p≤0.01 Effect size: -0.93</td>
</tr>
<tr>
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<td>PSQ G1: 0.5 ± 0.2 G2: 0.5 ± 0.2</td>
<td>PSQ, change from baseline G1: -0.3 ± 0.2 G2: -0.0 ± 0.2 G1 vs. G2: p≤0.01 Effect size: -1.35</td>
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<td>M-ESS G1: 7.1 ± 4.7 G2: 7.5 ± 5.2</td>
<td>M-ESS, change from baseline G1: -2.01 ± 4.7 G2: 0.28 ± 4.1 G1 vs. G2: p &lt; 0.01 Effect size: -0.42</td>
</tr>
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<td>PedsQL G1: 77.3 ± 15.3 G2: 76.5 ± 15.7</td>
<td>PedsQL, change from baseline to 7 months G1: 5.9 ± 13.6 G2: 0.9 ± 13.3 G1 vs. G2: p≤0.001 Effect size: 0.37</td>
</tr>
</tbody>
</table>
Table 8. Key sleep-related quality of life outcomes in studies comparing tonsillectomy and no surgery in children with OSDB, continued

<table>
<thead>
<tr>
<th>Author, Year</th>
<th>Study Type</th>
<th>Risk of Bias</th>
<th>Comparison Groups (N)</th>
<th>Outcome Measure Baseline (Mean±SD)</th>
<th>Outcome Measure Followup (Mean±SD)</th>
</tr>
</thead>
</table>

Behavioral Outcomes

The CHAT RCT\textsuperscript{171-177} and one prospective\textsuperscript{203} and one retrospective cohort study\textsuperscript{211} addressed behavioral outcomes (Table 9). All studies had a moderate risk of bias and used different scales to assess outcomes, again limiting our ability to compare effectiveness directly across studies. Two studies used the Child Behavior Checklist (CBC) to measure internalizing (emotionally reactive, anxious/depressed, somatic complaints, withdrawn behavior) and externalizing (attention problems and aggressive behavior) behaviors. Total problem scores on the scale reflect the sum of these domains, and lower scores equate to fewer behavioral problems. In all studies reporting baseline data, scores on behavioral measures were not indicative of clinical concern.

Scores on the CBC improved from baseline in both groups in one cohort study, with no significant group differences.\textsuperscript{203} In the second study, scores were significantly better in the tonsillectomy compared with no tonsillectomy group at followup, but baseline measures were not reported.\textsuperscript{211}

CHAT investigators used the Conners’ rating scale to assess behavioral issues including emotional lability and reported improvements (i.e., lowering of scores) in both groups from baseline, with significantly greater improvements in the tonsillectomy arm compared with no tonsillectomy on both teacher and parent-reported scales.\textsuperscript{171-177} While children’s behaviors improved in these studies, the clinical significance of the improvement is not clear.
Table 9. Key OSDB-related behavioral outcomes in studies comparing tonsillectomy and no surgery in children with OSDB

<table>
<thead>
<tr>
<th>Author, Year</th>
<th>Study Type</th>
<th>Groups (N)</th>
<th>Risk of Bias</th>
<th>Comparison Groups (N)</th>
<th>Outcome Measure</th>
<th>Outcome Measure Followup (Mean±SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Marcus 2014</td>
<td>RCT</td>
<td>171</td>
<td>Moderate ROB</td>
<td>G1: Tonsillectomy (193) G2: Watchful waiting with supportive care (208)</td>
<td>Conners’ (CGI) caregiver G1: 52.5 ± 11.6 G2: 52.6 ± 11.7</td>
<td>Conners’ (CGI) caregiver, change from baseline to 7 months G1: -2.9 ± 9.9 G2: -0.2 ± 9.4 G1 vs. G2: p=0.01</td>
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<td></td>
<td>Conners’ (CGI) teacher G1: 56.4 ± 14.4 G2: 55.1 ± 12.8</td>
<td>Conners’ (CGI) teacher, change from baseline to 7 months G1: -4.9 ± 12.9 G2: -1.5 ± 10.7 G1 vs. G2: p=0.04</td>
</tr>
<tr>
<td>Burstein 2013</td>
<td>Retrospective Cohort</td>
<td>211</td>
<td>Moderate ROB</td>
<td>G1: Tonsillectomy (16) G2: Watchful waiting with supportive care (16)</td>
<td>CBC Total Problem G1: NR G2: NR</td>
<td>CBC Total Problem (1.66-1.97 years post-tonsillectomy) G1: 43.9 G2: 58.9 G1 vs. G2: p &lt; 0.001</td>
</tr>
</tbody>
</table>

CBC = Child Behavior Checklist; CGI = Connors Global Index; G = Group; N = Number; NA = Not Applicable; OSDB = Obstructive Sleep Disordered Breathing; RCT = Randomized Controlled Trial; ROB = Risk of Bias; SD = Standard Deviation

Executive Function

One RCT and one prospective cohort study used the Developmental NEuroPSYchological Assessment (NEPSY) to evaluate attention and the Behavior Rating Inventory of Executive Function (BRIEF) to assess behavioral regulation and meta-cognition (Table 10). In the RCT, scores on the NEPSY improved from baseline in both groups, but group differences were not significant. Global scores on the BRIEF improved significantly among treated children compared with untreated children when evaluated by caregivers. When BRIEF was completed by teachers in a single study, both groups improved, and differences between groups were not significant.
Table 10. Key OSDB-related executive function outcomes in studies comparing tonsillectomy and no surgery in children with OSDB

<table>
<thead>
<tr>
<th>Author, Year</th>
<th>Study Type</th>
<th>Risk of Bias</th>
<th>Comparison Groups (N)</th>
<th>Outcome Measure Baseline (Mean)</th>
<th>Outcome Measure Followup (Mean)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Marcus 2014</td>
<td>RCT</td>
<td>Moderate ROB</td>
<td>G1: Tonsillectomy (193) G2: Watchful waiting with supportive care (208)</td>
<td>NEPSY G1: 101.5 ± 15.9 G2: 101.1 ± 15</td>
<td>Change from baseline to 7 months NEPSY* G1: 7.1 ± 13.9 G2: 5.1 ± 13.4 G1 vs. G2: p=NS Effect size: 0.15</td>
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<tr>
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<td>BRIEF (GEC) caregiver G1: 50.1 ± 11.2 G2: 50.1 ± 11.5</td>
<td>BRIEF (GEC) caregiver G1: 57.2 ± 14.1 G2: 56.4 ± 11.7 Effect size: 0.28</td>
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<td>BRIEF (GEC) teacher G1: 50.1 ± 11.2 G2: 50.1 ± 11.5</td>
<td>BRIEF (GEC) teacher G1: 57.2 ± 14.1 G2: 56.4 ± 11.7 Effect size: 0.18</td>
</tr>
<tr>
<td>Biggs 2014</td>
<td>Prospective Cohort</td>
<td>Moderate ROB</td>
<td>G1: Tonsillectomy or Nasal Steroids (12) G2: Watchful waiting with supportive care (27)</td>
<td>BRIEF (GEC) caregiver G1: 62 ± 11 G2: 58 ± 11</td>
<td>BRIEF (GEC) caregiver (4 years post-tonsillectomy) G1: 58 ± 16 G2: 57 ± 12 G1 vs. G2: p &lt; 0.05</td>
</tr>
</tbody>
</table>

NEPSY = Neuropsychological Assessment; NS = Not Significant; OSDB = Obstructive Sleep-Disordered Breathing; RCT = Randomized Controlled Trial; ROB = Risk of Bias; SD = Standard Deviation

*NEPSY attention and executive function

**Cardiopulmonary and Physiologic Outcomes**

One RCT reported in multiple publications (moderate risk of bias) addressed outcomes including cardiometabolic measures. Evidence was insufficient to comment on physiologic parameters, with a single RCT reporting no change in cardiometabolic measures, including insulin, lipids, and C-reactive protein levels. Underweight children also showed a significant increase in weight and BMI in this RCT.

**Utilization and Other Outcomes**

Two cohort studies with moderate risk of bias assessed health care utilization, measured by number of clinician contacts or antibiotic prescriptions, or cognitive outcomes (Table 11). A single moderate risk of bias cohort study reported a 33 percent reduction in gross health care utilization, including a 60 percent reduction in hospital admissions over one year following tonsillectomy in children with PSG-proven OSDB, while admissions in the untreated group increased (p=NR).

One cohort study using the Weschler Abbreviated Scale of Intelligence reported a significant
improvement in performance IQ at 4-years post-tonsillectomy in children undergoing tonsillectomy, but both the tonsillectomy and no surgery groups had declines or no change in full scale IQ and verbal IQ over the same period.203

Table 11. Other outcomes in studies comparing tonsillectomy with watchful waiting in children with OSDB

<table>
<thead>
<tr>
<th>Author, Year Study Type Risk of Bias</th>
<th>Comparison Groups (N)</th>
<th>Outcome Measure Baseline (Mean)</th>
<th>Outcome Measure Followup (Mean)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tarasiuk 2004206 Prospective cohort Moderate ROB</td>
<td>G1: Tonsillectomy (130) G2: Watchful waiting with supportive care (90)</td>
<td>G1+G2: NR</td>
<td>Number of new admissions, mean±standard error/patient/year Year 1 G1: 0.15±0.04 G2: 0.08±0.03 Year 2 G1: 0.06±0.02 G2: 0.25±0.07</td>
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<td></td>
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<td>Number of emergency department visits, mean±standard error/patient/year Year 1 G1: 0.57±0.09 G2: 0.52±0.09 Year 2 G1: 0.35±0.05 G2: 0.37±0.10</td>
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<td></td>
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<td>Number of consultations, mean±standard error/patient/year Year 1 G1: 3.6±0.37 G2: 4.4±0.40 G1 vs. G2: p= NR Year 2 G1: 1.9±0.26 G2: 3.5±0.46 G1 vs. G2: p= NR</td>
</tr>
</tbody>
</table>

G = Group; IQ = Intelligence Quotient; N = Number; NA = Not Applicable; NS = Not significant; ROB = Risk of Bias; SD = Standard Deviation; WASI = Wechsler Abbreviated Scale of Intelligence

Tonsillectomy Versus CPAP

OSDB-Related and Sleep Outcomes

One RCT with moderate risk of bias addressed OSDB- and sleep-related outcomes in children with OSDB who received tonsillectomy compared with CPAP44 (Table 12). Children in the RCT
had concomitant Down syndrome or mucopolysaccharidoses (n=32). AHI scores improved from baseline in both groups, but group differences were not significant in this small study. More children in the tonsillectomy arm had resolution of OSDB (defined as AHI < 1, 91.8% vs. 86.1%, p=NR). The RCT also evaluated sleep outcomes using the ESS and OSA-18. Both groups improved on these measures from baseline with no significant group differences. Immediate improvement occurred on initiation with CPAP versus a gradual progression with tonsillectomy.

### Table 12. OSDB resolution and sleep outcomes in studies comparing tonsillectomy with CPAP

<table>
<thead>
<tr>
<th>Author, Year</th>
<th>Study Type</th>
<th>Risk of Bias</th>
<th>Comparison Groups (N)</th>
<th>Outcome Measure Baseline</th>
<th>Outcome Measure Followup</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sudarsan 2014</td>
<td>RCT</td>
<td>Moderate ROB</td>
<td>G1: Tonsillectomy (37) G2: CPAP (36)</td>
<td>AHI, mean±SD G1: 3.83 ± 1.36 G2: 3.46 ± 0.87</td>
<td>AHI, mean±SD G1: 1.06 ± 0.74 G2: 1.07 ± 0.57 G1 vs. G2: p=NS</td>
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<td>Sleep Outcomes OSA-18 Total Score, mean±SD G1:116.97 ± 2.25 G2: 116.87 ± 1.3</td>
<td>Resolution rate (resolution=AHI &lt; 1), (%) G1: 91.8 G2: 86.1 G1 vs. G2: p=NR</td>
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<td>ESS-C G1: 13.76 ± 1.32 G2: 14.44 ± 2.18</td>
<td>AHI &lt; 1, % G1+G2: 89</td>
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<tr>
<td></td>
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<td></td>
<td>Sleep Outcomes OSA-18 Total Score, mean±SD G1: 73.59 ± 4.14 G2: 75.02 ± 2.5 G1 vs. G2: p=NS</td>
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<td>ESS-C G1: 5.46 ± 1.35 G2: 7.86 ± 1.69 G1 vs. G2: p=NS</td>
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</tbody>
</table>

AHI = Apnea-Hypopnea Index; CI = Confidence Interval; CPAP = Continuous Positive Airway Pressure; ESS-C = Epworth Sleepiness Scale - Child; G = Group; M-ESS = Modified Epworth Sleepiness Scale; N = Number; NR = Not Reported; NS = Not Significant; OSDB = Obstructive Sleep Disordered Breathing; RCT = Randomized Controlled Trial; ROB = Risk of Bias; SD = Standard Deviation

**Key Question 1a. Effectiveness of Tonsillectomy for Children With OSDB and Neuromuscular or Craniofacial Abnormalities**

A single 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. Both groups showed improvement in AHI at 6-month followup, with maintenance at 12-month followup (no significant group differences). Within this study, three patients (8.1%) who underwent tonsillectomy had persistent symptoms of OSDB and five patients (13.8%) who initiated CPAP had persistent OSDB symptoms. Baseline mean AHI scores for children in this study were far higher than normative scores reported in studies of healthy patients. One retrospective cohort study that included 15 children with syndromic comorbidities (7 with Down syndrome, 1 with Pierre Robin Sequence and 1 with DiGeorge syndrome) reported no significant group differences in improvements in...
AHI in children with syndromic conditions.\textsuperscript{214}

**Key Question 1b. Effectiveness of Tonsillectomy for Children With OSDB Under 3 Years of Age**

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

**Key Question 1c. Effectiveness of Tonsillectomy for Children With OSDB and Down Syndrome**

One RCT and one retrospective cohort study (both with moderate risk of bias) specifically studied children with Down syndrome.\textsuperscript{44, 214} Data were reported along with children with mucopolysaccharidoses in the RCT and along with patients with various syndromic comorbidities in the cohort. These studies are discussed in detail above.

**Key Question 1d. Effectiveness of Tonsillectomy for Children With OSDB and Obesity**

One retrospective cohort study (moderate risk of bias) examining a mostly overweight/obese population with PSG-proven 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.\textsuperscript{211} 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.\textsuperscript{214}

**Key Question 2. Effectiveness of Tonsillectomy Versus No Surgery for Recurrent Throat Infection**

**Key Points**

- Overall, children undergoing tonsillectomy to improve number of throat infections, associated health care utilization, and days of work/school missed had improvements in these outcomes in the first postsurgical year vs. children not receiving surgery. These benefits did not persist over time. Data on long-term outcomes of children with recurrent sore throat who do not undergo tonsillectomy are limited.
- We have moderate confidence in the conclusion that, compared with no surgery, tonsillectomy reduces throat infections or streptococcal infections in the short term (≤12 months) (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)

**Overview of the Literature**

We identified ten unique studies addressing tonsillectomy specifically for recurrent throat infections (Table 13). As noted above, one study included both children with recurrent throat infection and OSDB. Four unique studies (3 RCTs and 1 nonrandomized trial) were reported in two papers, and one set of investigators reported RCT and nonrandomized trial results together in multiple papers. Another RCT was reported in multiple papers. Five studies were conducted in the United States, three in the United Kingdom, one in Ireland, and one in the Netherlands. Studies included five RCTs, two nonrandomized trials, and one prospective and two retrospective cohorts. Studies compared tonsillectomy to watchful waiting, which could have included medical treatment including antibiotics or other conventional medical management. Studies included a total of 15,754 participants (at time of randomization or the start of the study) ranging in age from 2 to 16 years. Outcomes reported in most studies included number of throat infections or streptococcal infections.

Four RCTs and one nonrandomized trial and two retrospective cohort studies had moderate risk of bias, and one RCT, one prospective cohort study, and one nonrandomized trial had high risk of bias. Major sources of bias in these studies included unclear concealment of study group allocation and unclear fidelity to the intervention protocol. Given the relatively few studies addressing this question, we retained retrospective studies as part of the evidence base.

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>RCTs</th>
<th>Nonrandomized Trials</th>
<th>Prospective Cohort Studies</th>
<th>Retrospective Cohort Studies</th>
<th>Total Literature</th>
</tr>
</thead>
<tbody>
<tr>
<td>Surgical Indication</td>
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<tr>
<td>Throat Infection</td>
<td>2</td>
<td>2</td>
<td>0</td>
<td>2</td>
<td>6</td>
</tr>
<tr>
<td>OSDB+Throat Infection</td>
<td>3</td>
<td>0</td>
<td>1</td>
<td>0</td>
<td>3</td>
</tr>
<tr>
<td>Effectiveness Outcomes Frequently Reported</td>
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<td></td>
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<tr>
<td>Number Throat Infections</td>
<td>5</td>
<td>2</td>
<td>0</td>
<td>1</td>
<td>8</td>
</tr>
<tr>
<td>Number Streptococcal Infections</td>
<td>3</td>
<td>1</td>
<td>0</td>
<td>1</td>
<td>5</td>
</tr>
<tr>
<td>Utilization (# clinician consultations or antibiotic prescriptions)</td>
<td>1</td>
<td>1</td>
<td>0</td>
<td>1</td>
<td>3</td>
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<tr>
<td>Missed School or Work</td>
<td>4</td>
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<td>Quality of life</td>
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<td>Risk of Bias</td>
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<tr>
<td>Moderate</td>
<td>4</td>
<td>1</td>
<td>0</td>
<td>2</td>
<td>7</td>
</tr>
<tr>
<td>High</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>0</td>
<td>2</td>
</tr>
<tr>
<td>Total N participants</td>
<td>944</td>
<td>557</td>
<td>71</td>
<td>14182</td>
<td>15754</td>
</tr>
</tbody>
</table>

N = number; OSDB = obstructive sleep-disordered breathing; RCT = randomized controlled trial
Detailed Analysis

Tonsillectomy Versus No Surgery/Watchful Waiting

Four RCTs \(^9, 164-166, 179-181\) (including 2 reported in one publication\(^9\) and 2 reported in multiple publications \(^{164-166, 179-181}\)), one nonrandomized trial \(^{179-181}\) and one retrospective cohort study \(^{213}\) included children with at least 3 throat infections in the 3 months to one year prior to surgery and reported on recurrent throat infections and clinician visits following surgery or no surgery (Tables 14-15). We considered four RCTs (including 2 published in one paper\(^9\)) to have moderate risk of bias. \(^9, 164, 166, 179-181, 277\) Another nonrandomized trial had moderate risk of bias. \(^{179-181}\) We considered one retrospective cohort study addressing these outcomes to have moderate risk of bias. \(^{213}\)

In all studies reporting baseline data, number of infections decreased from baseline in both groups, with significantly greater decreases in sore throat days and diagnosed Group A streptococcal throat infections in children who received tonsillectomy vs. no surgery/watchful waiting with supportive care in the short term ( < 12 months). As noted, in two papers in this section, investigators report multiple RCTs and/or nonrandomized trials conducted by the same team (but with unique populations) in single papers. In one such paper, both the RCT and nonrandomized trial \(^{179-181}\) reported that children in both studies who received tonsillectomy had fewer recorded days of sore throat in a symptom diary than children who had medical management. Using an intention-to-treat analysis for the RCT patients, the study found a decrease of 3.5 (95% CI: 1.8 to 5.2) sore throat episodes over the full 2-year study period for children who underwent tonsillectomy. The benefit was greatest in those quick to receive tonsillectomy after the onset of infections, with the relative benefit decreasing with longer times to intervention. Children who underwent tonsillectomy within 4 weeks of enrollment had an estimated 8.5 episodes of sore throat avoided, whereas children who waited longer times (up to 52 weeks) had 3.5 episodes of sore throats saved. Limitations of this study family include strong parental preference for surgery when the child had more severe symptoms, thus affecting the generalizability of the patients who were randomized. The study points out that the children who were ultimately randomized fell into the middle of the pack in terms of how much they were impacted by their symptoms. The study also had significant attrition in return of the symptom diaries over time and difficulty obtaining provider records for review.

In another paper reporting two unique RCTs, benefits of tonsillectomy or adenotonsillectomy were reported for children who experienced at least one sore throat. \(^{282}\) These studies had surgical and watchful waiting groups, and while the surgical groups had fewer visits for sore throat after surgery, the number of visits for sore throat in the watchful waiting groups was also low. The first year postsurgery, the tonsillectomy group had 1.74 (95% CI: 1.54 to 2.00) episodes of throat infection while the control group had 2.93 (95% CI: 2.69 to 3.22) episodes. Although statistically significant, it is unclear whether this difference is clinically meaningful. \(^{282}\)

In another RCT (moderate risk of bias) including children with mild symptoms of throat infection or hypertrophy (< 7 or more throat infections in prior year or 5 or more in prior 2 years or 3 or more in prior 3 years and Brouillette’s OSA score of less than 3.5—i.e., in no apnea or possible apnea range), children who received tonsillectomy had fewer throat infections (throat pain+fever) compared with those who had no surgery (0.56/person year vs. 0.77, \(p= \text{NR}\)). \(^{164-166}\) Of note, many children originally allocated to no surgery/watchful waiting (n=50 of 149) crossed over to the surgery arm.
One retrospective cohort found that children who did not undergo tonsillectomy were 3.1 times (95% CI: 2.1 to 4.6, \( p < 0.001 \)) more likely to test positive for Group A streptococcal (GAS) throat infection than their counterparts who underwent surgery.\(^{213}\) Children who did not have tonsillectomy also experienced GAS infection at a shorter time interval than the children without tonsils.

Two RCTs and one nonrandomized trial reported quality of life data, which were not markedly different between any of the study arms at any time point.\(^ {164, 179-181} \) Overall, comparative effectiveness assessment of tonsillectomy vs. no surgery to improve number of throat infections, associated health care utilization, and work/school absences shows a benefit in the first postsurgical year. These benefits did not persist over time. Quality of life improved in both groups (\( p=\text{NR} \)).

One retrospective cohort study included children who may have had fewer than three throat infections in the prior year.\(^ {210} \) The study reported a net reduction in the 3-year mean sore throat visits for children who underwent tonsillectomy compared with those who did not.\(^ {210} \) This reduction decreased over time with 2.46 fewer visits (95% CI: 2.29 to 2.63, \( p < 0.001 \)) in years 1-3 and 1.21 fewer visits (95% CI: 1.04 to 1.38, \( p < 0.001 \)) in years 4-6, or 0.61 sore throat visits per child per year (over the 6 year study period). This study focused on provider visits rather than sore throat episodes that did not generate a provider visit, or visits with multiple concerns, coded under another primary complaint.
Table 14. Key infection outcomes in studies comparing tonsillectomy and no surgery in children with recurrent throat infections

<table>
<thead>
<tr>
<th>Author, Year Study Type Risk of Bias</th>
<th>Comparison Groups (N)</th>
<th>Outcome Measure Baseline (Mean)</th>
<th>Outcome Measure Followup (Mean)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Lock 2010</strong> RCT Moderate ROB</td>
<td>G1: Tonsillectomy (119) G2: Watchful waiting with supportive care (112)</td>
<td><strong>Throat Infections</strong> N sore throats, 3 months prior to study entry, mean±SD G1: 3.09±2.08 G2: 3.34±2.63</td>
<td><strong>Throat Infections</strong> Sore throats/month, mean±SD Year 1 G1: 0.50±0.43 (n respondents=119) G2: 0.64±0.49 (n respondents=112) RR=0.70 (95% CI: 0.61 to 0.80), p &lt; 0.001</td>
</tr>
<tr>
<td></td>
<td></td>
<td><strong>Utilization</strong> # general practitioner consultations in 2 years prior to study entry, mean±SD G1+G2: 10.3±6.3</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td><strong>Utilization</strong> # consultations for sore throat in 2 years prior to study entry, mean±SD G1+G2: 6.0±3.7</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td><strong>Quality of Life</strong> N respondents G1: 111 G2: 108</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td><strong>PedSQL 4.0 Physical Health</strong> G1: 76.26±19.50 G2: 78.75±18.01</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td><strong>N respondents</strong> G1: 111 G2: 110</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td><strong>PedSQL 4.0 Psychosocial Health</strong> G1: 70.95±14.18 G2: 72.33±14.86</td>
<td></td>
</tr>
</tbody>
</table>
Table 14. Key infection outcomes in studies comparing tonsillectomy and no surgery in children with recurrent throat infections, continued

<table>
<thead>
<tr>
<th>Author, Year Study Type Risk of Bias</th>
<th>Comparison Groups (N)</th>
<th>Outcome Measure Baseline (Mean)</th>
<th>Outcome Measure Followup (Mean)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lock 2010\textsuperscript{179,181} RCT, continued</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Year 2</td>
</tr>
<tr>
<td></td>
<td></td>
<td># clinician consultations, mean±SD</td>
<td></td>
</tr>
<tr>
<td></td>
<td>G1: 2.84±2.90</td>
<td></td>
<td>G2: 3.40±3.20</td>
</tr>
<tr>
<td></td>
<td>G1: 0.89±1.44</td>
<td></td>
<td>G2: 1.33±1.56</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Quality of Life</td>
</tr>
<tr>
<td></td>
<td></td>
<td>12 months, N respondents</td>
<td></td>
</tr>
<tr>
<td></td>
<td>G1: 71</td>
<td>G2: 52</td>
<td></td>
</tr>
</tbody>
</table>

PedsQL 4.0 Physical Health
G1: 89.95±16.37 (adjusted effect size: 3.08 [95% CI: 3.11 to 9.27])
G2: 85.34±17.86

PedsQL 4.0 Psychosocial Health
G1: 83.81±15.31 (adjusted effect size: 2.43 [95% CI: -3.08 to 7.03])
G2: 79.97±17.49

24 months, N respondents
G1: 63
G2: 53

PedsQL 4.0 Physical Health
G1: 88.79±17.66 (adjusted effect size: 0.31 [95% CI: -5.74 to 6.37])
G2: 88.05±12.76

PedsQL 4.0 Psychosocial Health
G1: 84.30±15.02 (adjusted effect size: 0.39 [95% CI: -4.52 to 5.29])
G2: 83.897±12.95
Table 14. Key infection outcomes in studies comparing tonsillectomy and no surgery in children with recurrent throat infections, continued

<table>
<thead>
<tr>
<th>Author, Year Study Type Risk of Bias</th>
<th>Comparison Groups (N)</th>
<th>Outcome Measure Baseline (Mean)</th>
<th>Outcome Measure Followup (Mean)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lock 2010†</td>
<td>Nonrandomized trial Moderate ROB</td>
<td>G1: Tonsillectomy (349) G2: Watchful waiting with supportive care (67)</td>
<td><strong>Throat Infections</strong> N sore throat lasting &lt;2 weeks in 3 months prior to study entry, mean±SD G1: 3.6±2.5 G2: 2.7±1.6</td>
</tr>
<tr>
<td></td>
<td></td>
<td><strong>Utilization</strong> # general practitioner consultations in 2 years prior to study entry, mean±SD G1: 8.6±5.8 G2: 10.3±6.9 # consultations for sore throat in 2 years prior to study entry, mean±SD G1: 5.4±3.4 G2: 6.2±4.2</td>
<td><strong>Utilization</strong> Year 1 # clinician consultations, mean±SD G1: 3.69±3.33 G2: 3.16±3.14 # sore throat consultations, mean±SD G1: 1.86±2.23 G2: 1.63±1.98 Year 2 # clinician consultations, mean±SD G1: 2.71±3.51 G2: 3.12±3.10 # sore throat consultations, mean±SD G1: 0.78±1.31 G2: 1.45±2.07</td>
</tr>
</tbody>
</table>
Table 14. Key infection outcomes in studies comparing tonsillectomy and no surgery in children with recurrent throat infections, continued

<table>
<thead>
<tr>
<th>Author, Year Study Type Risk of Bias</th>
<th>Comparison Groups (N)</th>
<th>Outcome Measure Baseline (Mean)</th>
<th>Outcome Measure Followup (Mean)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Orvidas 2006</strong>&lt;sup&gt;113&lt;/sup&gt; Retrospective Cohort Moderate ROB</td>
<td>G1: Tonsillectomy (145) G2: Watchful waiting with supportive care (145)</td>
<td><strong>Throat Infections</strong> N with infection within one year prior to tonsillectomy/study entry, (%) G1: 141 (97.2) G2: 130 (89.7)</td>
<td><strong>Throat Infections</strong> Cumulative Incidence of Developing Group A Beta-hemolytic Streptococcal Throat Infection, % (95%CI) At 6 months G1: 13.2 (7.5 to 18.6) Number still at risk: 124 G2: 39.3 (30.8 to 46.8) Number still at risk: 87 At 1 year G1: 23.1 (15.9 to 29.7) Number still at risk: 107 G2: 58.5 (49.6 to 65.9) Number still at risk: 57 At 2 years G1: 38.5 (29.8 to 46) Number still at risk: 83 G2: 74.8 (66.4 to 81.1) Number still at risk: 34 At 3 years G1: 46.1 (37.1 to 53.9) Number still at risk: 65 G2: 82.2 (74.5 to 87.6) Number still at risk: 21 At 4 years G1: 51.9 (42.4 to 59.8) Number still at risk: 39 G2: 84.6 (76.7 to 89.8) Number still at risk: 12</td>
</tr>
<tr>
<td><strong>Van Staaij 2004</strong>&lt;sup&gt;104,106&lt;/sup&gt; RCT Moderate ROB</td>
<td>G1: Tonsillectomy (133) G2: Watchful waiting with supportive care (124)</td>
<td><strong>Throat Infections</strong> Throat infections in year prior to study, median (range) G1: 3 (0-6) G2: 3 (0-6)</td>
<td><strong>Throat Infections</strong> Episodes of throat infection/person year, n G1: 0.56 G2: 0.83 Difference: -0.21 (95% CI: -0.36 to -0.06) Incidence rate G1+G2: 0.73 (95% CI: 0.58 to 0.92) Quality of Life Data in figures only; study notes no clinically significant differences</td>
</tr>
<tr>
<td>Author, Year</td>
<td>Study Type</td>
<td>Risk of Bias</td>
<td>Comparison Groups (N)</td>
</tr>
<tr>
<td>--------------</td>
<td>------------</td>
<td>--------------</td>
<td>-----------------------</td>
</tr>
<tr>
<td>Paradise 2002 RCT A Moderate ROB</td>
<td>G1: Tonsillectomy (58 randomized, 52 received intervention) G2: Adenotonsillectomy (59 randomized, 50 received intervention) G3: Watchful waiting with supportive care (60 randomized, 60 received intervention)</td>
<td>Throat Infections</td>
<td>G1+G2: NR</td>
</tr>
<tr>
<td>Paradise 2002 RCT B Moderate ROB</td>
<td>G1: Adenotonsillectomy (73 randomized, 63 received intervention) G2: Watchful waiting with supportive care (78 randomized, 78 received intervention)</td>
<td>Throat Infections</td>
<td>G1+G2: NR</td>
</tr>
</tbody>
</table>
Table 14. Key infection outcomes in studies comparing tonsillectomy and no surgery in children with recurrent throat infections, continued

<table>
<thead>
<tr>
<th>Author, Year</th>
<th>Study Type</th>
<th>Risk of Bias</th>
<th>Comparison Groups (N)</th>
<th>Outcome Measure Baseline (Mean)</th>
<th>Outcome Measure Followup (Mean)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Koshy 2015</td>
<td>Retrospective Cohort</td>
<td>Moderate ROB</td>
<td>G1: Tonsillectomy and ≤3 acute throat infection consultations (450) G2: No tonsillectomy and ≤3 acute throat infection (13442)</td>
<td><strong>Utilization</strong> # throat infection consultations in 3 years prior to study index date, mean±SD G1: 1.3±1.1 G2: 0.4±0.8 G1 vs. G2: p &lt; 0.001</td>
<td><strong>Utilization</strong> # throat infection consultations 4-6 years post-index date, mean G1: 0.6 G2: 0.93 Mean difference in consultations, baseline to followup G1: −0.72 (95% CI: −0.88 to −0.56), p &lt; 0.001 G2: +0.49 (95% CI: 0.46 to 0.52), p &lt; 0.001</td>
</tr>
</tbody>
</table>

CI = Confidence Interval; G = Group; n = Number; NR = Not Reported; NS = Not Significant; PedsQL = Pediatric Quality of Life Questionnaire; ROB = Risk of Bias

Fewer days of missed school or work were associated with tonsillectomy in the short term, with differences diminishing over time in two RCTs\(^9\) while another RCT noted comparable school absences between groups\(^{164-166}\) (Table 15).

Table 15. Missed school or work outcomes reported in studies comparing tonsillectomy and no surgery in children with recurrent throat infections

<table>
<thead>
<tr>
<th>Author, Year</th>
<th>Study Type</th>
<th>Risk of Bias</th>
<th>Comparison Groups (N)</th>
<th>Sore Throat-Associated School Absences, Mean±SD Days/Year (Number Days/Year)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Van Staaij 2004(^{164-166}) RCT</td>
<td>G1: Tonsillectomy (133) G2: Watchful waiting with supportive care (124)</td>
<td>Difference in school absences G1 vs. G2: 0.09 (95% CI: -0.27 to 0.44)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Paradise 2002(^7) RCT A</td>
<td>G1: Tonsillectomy (58 randomized, 52 received intervention) G2: Adenotonsillectomy (59 randomized, 50 received intervention) G3: No surgery (60 randomized, 60 received intervention)</td>
<td>G1 vs. G3: p &lt; 0.05 Year 1: 3.3±4.0 (42) G2: 3.9±3.7 (44) G3: 5.3±4.7 (50) G1 vs. G3: p &lt; 0.05 Year 2: G1: 3.2±3.9 (39) G2: 2.4±3.2 (38) G3: 5.0±5.2 (44) G2 vs. G3: p &lt; 0.05 Year 3: G1: 2.5±3.2 (37) G2: 2.9±2.9 (29) G3: 3.7±3.2 (42) G2 vs. G3: p=NS</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Paradise 2002(^7) RCT B</td>
<td>G1: Tonsillectomy (73 randomized, 63 received intervention) G2: Watchful waiting with supportive care (78 randomized, 78 received intervention)</td>
<td>Year 1: G1: 3.5±4.2 (52) G2: 6.6±6.2 (58) G1 vs. G2: p &lt; 0.01 Year 2: G1: 3.2±4.1 (47) G2: 5.4±6.7 (56) G1 vs. G2: p=NS Year 3: G1: 2.6±3.4 (45) G2: 4.2±5.2 (55) G1 vs. G2: p=NS</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

G = Group; n = Number; NS = Not Significant; RCT = Randomized Controlled Trial; ROB = Risk of Bias
Key Question 3. Effectiveness of Partial Versus Total Tonsillectomy

Key Points

- Few studies compared the same surgical technique for partial or total tonsillectomy. In studies comparing partial and total cold dissection tonsillectomy, return to normal diet and activity was faster in children undergoing partial tonsillectomy. Our confidence in this conclusion is low (low strength of evidence).
- In studies comparing partial and total cold dissection tonsillectomy, we could not make conclusions about effects on throat infections or OSDB persistence (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.
- In studies comparing mixed techniques for partial or total tonsillectomy, 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).

Overview of the Literature

We identified 22 unique studies (20 RCTs, and 2 nonrandomized trials) addressing partial tonsillectomy compared with total tonsillectomy (Table 16). Most studies were conducted in Europe or North America. Four studies were conducted in Asia and one in Africa. Participants (n=2925) ranged in age from 1 to 18 years. 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 surgical removal (i.e., partial vs. total removal) and different surgical techniques (e.g., partial coblation vs. total electrocautery), it is not possible to determine whether effects are due to the technique or due to the extent of surgery. Thus, except for in those 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. We present results by partial vs. total cold dissection, partial vs. total coblation or electrocautery; and partial vs. total regardless of technique below.

Across studies, definitions of “partial” tonsillectomy varied or were not explicit. Five studies explicitly noted leaving anywhere from 10 to 70 percent of the tonsil intact, while others noted leaving a thin rim of tissue or removing the bulk of the tonsil, and yet others reported removing the obstructive or protruding portion of the tonsil only. Six studies did not describe the portion of tissue removed.
We considered five RCTs to have low risk of bias. Eleven RCTs had moderate risk of bias, and four RCTs and two nonrandomized trials had high risk of bias. Major sources of bias in these studies include unclear methods for randomization and unclear methods for concealment of treatment group allocation. We do not discuss high risk of bias studies in the detailed analyses below.

Table 16. Overview of studies comparing partial versus total tonsillectomy

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>RCTs</th>
<th>Nonrandomized Trials</th>
<th>Total Literature</th>
</tr>
</thead>
<tbody>
<tr>
<td>Comparisons</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total cold dissection vs. partial cold dissection</td>
<td>3</td>
<td>1</td>
<td>4</td>
</tr>
<tr>
<td>Total coblation vs. partial coblation</td>
<td>1</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Total electrocautery vs. partial electrocautery</td>
<td>1</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Partial vs. total</td>
<td>15</td>
<td>1</td>
<td>16</td>
</tr>
<tr>
<td>Surgical Indication</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>OSDB</td>
<td>17</td>
<td>2</td>
<td>19</td>
</tr>
<tr>
<td>OSDB+Throat Infection</td>
<td>2</td>
<td>0</td>
<td>2</td>
</tr>
<tr>
<td>Not specified</td>
<td>1</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Effectiveness Outcomes Frequently Reported</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Return to normal diet or activity</td>
<td>10</td>
<td>0</td>
<td>10</td>
</tr>
<tr>
<td>Number of throat infections</td>
<td>6</td>
<td>0</td>
<td>6</td>
</tr>
<tr>
<td>Tonsillar regrowth</td>
<td>5</td>
<td>1</td>
<td>6</td>
</tr>
<tr>
<td>Risk of Bias</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Low</td>
<td>5</td>
<td>0</td>
<td>5</td>
</tr>
<tr>
<td>Moderate</td>
<td>11</td>
<td>0</td>
<td>11</td>
</tr>
<tr>
<td>High</td>
<td>4</td>
<td>2</td>
<td>6</td>
</tr>
<tr>
<td>Total N participants</td>
<td>1709</td>
<td>1216</td>
<td>2925</td>
</tr>
</tbody>
</table>

n = Number; OSDB = Obstructive Sleep-Disordered Breathing; RCT = Randomized Controlled Trial

Detailed Analysis

Partial Cold Dissection Versus Total Cold Dissection Tonsillectomy

Three RCTs and one nonrandomized trial compared total and partial cold dissection and included 348 children in the partial tonsillectomy arms and 378 in the total tonsillectomy arms. Few of these studies reported the same outcomes (Table 17).

OSDB Persistence

In one RCT (low risk of bias) reporting on the persistence of OSDB, children in both arms had recurrence of snoring. Differences were not statistically significant.

Tonsillar Regrowth and Reoperation

Two RCTs (low and moderate risk of bias) addressed regrowth and/or revision surgery. In one RCT including 40 children with OSDB undergoing partial tonsillectomy and 41 undergoing total, no children had tonsillar regrowth (0 of 68 followed up) in the 2-year followup period. In a second study, 6 out of 43 children undergoing partial tonsillectomy and followed for 6 years had regrowth, in two cases requiring total tonsillectomy.
Growth

No studies provided baseline comparative data that could be used to assess the comparative effectiveness of surgery on growth outcomes.

Return to Normal Diet or Activity

Children in the partial tonsillectomy arm had significantly faster return to normal diet in the two RCTs (low and moderate risk of bias) addressing this outcome (p values< 0.001). 53, 86

Throat Infection

In one low risk of bias RCT with 6-year followup, no children (0/91) in either group had throat infections, although the study reports that five children in the partial tonsillectomy arm had at least one episode of tonsillitis/year in the followup period. 53 The study did not define throat infection or tonsillitis.

Table 17. Comparative effectiveness outcomes in studies addressing partial versus total cold dissection tonsillectomy

<table>
<thead>
<tr>
<th>Author, Year of Study</th>
<th>Design</th>
<th>Risk of Bias</th>
<th>Comparison</th>
<th>OSDB Persistence</th>
<th>Tonsillar Regrowth</th>
<th>Return to Normal Diet or Activity</th>
<th>Throat Infections</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chaidas 2013 53 RCT</td>
<td>Low ROB</td>
<td>Low ROB</td>
<td>G1: Partial cold tonsillectomy (50) G2: Total cold tonsillectomy (51)</td>
<td>Snoring (6- years post-tonsillectomy) G1: 13/43 (30.2) G2: 12/48 (25) G1 vs. G2: p=NS Episodic apnea (6- years post-tonsillectomy) G1: 2/43 (4.7) G2: 0 (0) G1 vs. G2: p=NS</td>
<td>Tonsillar regrowth, 6 years postsurgery, n (%) G1: 6/13 (46.2) G2: NA Tonsillar regrowth requiring revision surgery, n (%) G1: 2/13 (5) G2: 0</td>
<td>Time to return to normal diet, mean days ± SD G1: 3.8 ± 0.2 G2: 7.1 ± 0.3 G1 vs. G2: p &lt; 0.001</td>
<td>At least 1 episode of tonsillitis/year, 1-6 years post-tonsillectomy, n (%) G1: 5 (11.6) G2: 0 G1 vs. G2: p= NR Number throat infections/year, 1-6 years post-tonsillectomy, median (IQR) G1: 0 (0-1) G2: 0 (0-1) G1 vs. G2: p=NS</td>
</tr>
<tr>
<td>Korkmaz 2008 84 RCT</td>
<td>Moderate ROB</td>
<td>Moderate ROB</td>
<td>G1: Partial cold tonsillectomy (40) G2: Total cold tonsillectomy (41)</td>
<td>NR</td>
<td>Tonsillar regrowth within 2-years post-tonsillectomy, n G1+G2: 0/68</td>
<td>NR</td>
<td>NR</td>
</tr>
<tr>
<td>Skoulakis 2007 86 RCT</td>
<td>Moderate ROB</td>
<td>Moderate ROB</td>
<td>G1: Partial cold tonsillectomy (15) G2: Total cold tonsillectomy (15)</td>
<td>NR</td>
<td>NR</td>
<td>Time to return to normal diet G1: 4 days earlier than G2 G1 &lt; G2: p &lt; 0.001</td>
<td>NR</td>
</tr>
</tbody>
</table>

G = Group; N = Number; NA = Not Applicable; NR = Not Reported; NS = Not Significant; OSDB = Obstructive Sleep Disordered Breathing; RCT = Randomized Controlled Trial; ROB = Risk of Bias; SD = Standard Deviation
Partial Coblation or Electrocautery Versus Total Coblation or Electrocautery

Two small RCTs with low\(^90\) and moderate\(^85\) risk of bias addressed outcomes following partial vs. total coblation or electrocautery and reported only on return to usual diet or activity (Table 18). In the coblation study, children in the partial tonsillectomy arm consumed a significantly greater percentage of their normal diet and were engaged in a greater portion of their normal activity than were children in the total tonsillectomy arm at all time points assessed.\(^85\) In the one study comparing partial vs. total electrocautery tonsillectomy, differences in return to normal activity were not statistically significantly different between groups.\(^90\)

Table 18. Return to usual diet or activity in studies addressing partial versus total tonsillectomy with coblation or electrocautery

<table>
<thead>
<tr>
<th>Author, Year</th>
<th>Study Type</th>
<th>Risk of Bias</th>
<th>Comparison Groups (N)</th>
<th>Time to Return to Normal Diet or Activity, N (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chang 2008(^55) RCT</td>
<td>Moderate ROB</td>
<td>G1: Partial coblation tonsillectomy (34) G2: Total coblation tonsillectomy (35)</td>
<td>Mean % of normal diet resumed (POD1-2) G1: 56 G2: 42 G1 vs. G2: p = 0.05</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Mean % of normal diet resumed (POD5-6) G1: 73 G2: 48 G1 vs. G2: p &lt; 0.05</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Mean % of normal activity resumed (POD1-2) G1: 65 G2: 49 G1 vs. G2: p = 0.031</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Mean % of normal activity resumed (POD5-6) G1: 84 G2: 64 G1 vs. G2: p = 0.002</td>
<td></td>
</tr>
<tr>
<td>Park 2007(^&quot;) RCT</td>
<td>Low ROB</td>
<td>G1: Partial electrocautery tonsillectomy (19) G2: Total electrocautery tonsillectomy (21)</td>
<td>Time to return to normal activity G1 vs. G2: p = NS</td>
<td></td>
</tr>
</tbody>
</table>

G = Group; N = Number; NS = Not Significant; OSDB = Obstructive Sleep Disordered Breathing; POD = Postoperative Day; RCT = Randomized Controlled Trial; ROB = Risk of Bias; SD = Standard Deviation

Partial Tonsillectomy Versus Total Tonsillectomy With Mixed Surgical Approaches

Among the studies with low or moderate risk of bias addressing partial vs. total tonsillectomy without using the same surgical technique, eight (reported in multiple publications) addressed effectiveness outcomes\(^95, 97, 98, 107, 110, 139, 182-186\) and three reported only harms (addressed in Harms section).\(^71, 151, 158\) As with the studies outlined above, few studies addressed the same outcomes and because these studies differ in both extent of surgery and surgical technique, it is difficult to isolate the effect of partial tonsillectomy.
OSDB Persistence

Three RCTs (in multiple publications) addressed outcomes related to the persistence of OSDB (Table 19). In two studies with low and moderate risk of bias, 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 (12-24 months post-tonsillectomy. In the third RCT, no children in either group had snoring or apnea at 1 and 3 years postoperatively.

Table 19. OSDB persistence reported in studies comparing partial and total tonsillectomy

<table>
<thead>
<tr>
<th>Study, Year</th>
<th>Study Design</th>
<th>Risk of Bias</th>
<th>Comparison Groups (N)</th>
<th>OSDB Persistence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ericsson 2009</td>
<td>RCT</td>
<td>Moderate ROB</td>
<td>G1: Partial tonsillectomy-coblation (35) G2: Total tonsillectomy-cold dissection (32)</td>
<td>Persistence of snoring 6-months post-tonsillectomy Greater number of children in G1 vs. G2 had snoring, p &lt; 0.05 24-months post-tonsillectomy G1 vs. G2: p=NS</td>
</tr>
<tr>
<td>Hultcrantz 2004</td>
<td>RCT</td>
<td>Moderate ROB</td>
<td>G1: Partial tonsillectomy-coblation (49) G2: Total tonsillectomy-cold dissection (43)</td>
<td>Persistence of snoring 12-months and 3-years post-tonsillectomy No difference in frequency or loudness of snoring between groups Presence of apnea, 1-3 years post-tonsillectomy G1: 0 G2: 0</td>
</tr>
</tbody>
</table>

G = Group; N = Number; NR = Not Reported; NS = Not Significant; OSDB = Obstructive Sleep Disordered Breathing; RCT = Randomized Controlled Trial; ROB = Risk of Bias; SD = Standard Deviation

Tonsillar Regrowth

Two RCTs (moderate risk of bias) reported low rates of tonsillar regrowth after partial tonsillectomy (Table 20). Out of an estimated 126 children providing followup data, three (2.4%) reported regrowth and had total tonsillectomy.

Table 20. Tonsillar regrowth or reoperation after partial tonsillectomy

<table>
<thead>
<tr>
<th>Study, Year</th>
<th>Study Design</th>
<th>Risk of Bias</th>
<th>Comparison Groups (N)</th>
<th>Tonsillar Regrowth</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hultcrantz 2004</td>
<td>RCT</td>
<td>Moderate ROB</td>
<td>G1: Partial tonsillectomy-coblation (49) G2: Total tonsillectomy- Cold dissection (43)</td>
<td>Total tonsillectomy for OSDB-symptom persistence, n G1: 1 (denominator not clear, 91 children in both groups assessed at 1 year) G2: NA</td>
</tr>
</tbody>
</table>

G = Group; N = Number; NA = Not Applicable; OSDB = Obstructive Sleep Disordered Breathing; RCT = Randomized Controlled Trial; ROB = Risk of Bias; SD = Standard Deviation
Return to Normal Diet or Activity

Six RCTs (four with moderate and two with low risk of bias) addressed time to return to normal diet or activity (Table 21). Studies were typically small (< 100 children) with short term followup and used a variety of methods for assessing these outcomes (e.g., mean days, mean percentage, number of children). In all six studies addressing return to normal diet, children in the partial tonsillectomy arms had more favorable outcomes compared with those receiving total tonsillectomy. Two studies reported that children undergoing partial surgeries either consumed a significantly greater proportion of their normal diet \(^{107}\) or returned to normal diet in fewer days \(^{97}\) than did children in total tonsillectomy arms. Four RCTs reported faster return in the partial tonsillectomy groups or greater numbers of children consuming a normal diet after partial compared with total tonsillectomy, but differences were not statistically significant \(^{98,185,186}\) or significance was not assessed. \(^{95,110}\)

Five RCTs (2 low and 3 moderate risk of bias) addressed return to normal activity. \(^{97,98,107,110,185,186}\) As with diet, in all studies children undergoing partial tonsillectomy had a faster return to normal activity or engaged in a greater percentage of normal activity than did children who had total tonsillectomy. Differences were statistically significant in two RCTs \(^{98,107}\)

<table>
<thead>
<tr>
<th>Author, Year</th>
<th>Study Type</th>
<th>Risk of Bias</th>
<th>Comparison Groups (N)</th>
<th>Time to Return to Normal Diet or Activity, N (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chang 2005 (^{107})</td>
<td>RCT</td>
<td>Moderate ROB</td>
<td>G1: Partial tonsillectomy-coblation (52) G2: Total tonsillectomy- electrocautery (49)</td>
<td>Mean % of normal diet resumed (POD1-2) G1: 49 G2: 30 G1 vs. G2: p &lt; 0.005 Mean % of normal diet resumed (POD5-6) G1: 74 G2: 42 G1 vs. G2: p &lt; 0.005 Mean % of normal activity resumed (POD1-2) G1: 53 G2: 42 G1 vs. G2: p = NS Mean % of normal activity resumed (POD5-6) G1: 82 G2: 56 G1 vs. G2: p &lt; 0.005</td>
</tr>
</tbody>
</table>
### Table 21. Return to normal diet or activity in studies comparing partial and total tonsillectomy, continued

<table>
<thead>
<tr>
<th>Author, Year Study Type Risk of Bias</th>
<th>Comparison Groups (N)</th>
<th>Time to Return to Normal Diet or Activity, N (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Coticchia 2006²³ RCT Moderate ROB</td>
<td>G1: Partial tonsillectomy-coblation (13) G2: Total tonsillectomy-cold (10)</td>
<td>N children resuming normal diet by POD7, (%) G1: 11 (85) G2: 0 (0) G1 vs. G2: p = NR</td>
</tr>
<tr>
<td>Sobol 2006²⁷ RCT Low ROB</td>
<td>G1: Partial tonsillectomy-microdebrider (36) G2: Total tonsillectomy-electrocautery (38)</td>
<td>Time to return to normal diet, mean days ± SD G1: 2.7 ± 2.3 G2: 4.4 ± 3.4 G1 vs. G2: p = 0.04 Time to return to normal activity, mean days ± SD G1: 2.4 ± 1.8 G2: 3.8 ± 3 G1 vs. G2: p = NS</td>
</tr>
<tr>
<td>Derkay 2006²⁸ RCT Low ROB</td>
<td>G1: Partial tonsillectomy-microdebrider (150) G2: Total tonsillectomy-electrocautery (150)</td>
<td>Time to return to normal diet, median days (Q1 – Q3) G1: 3 (1.5-6) G2: 3.5 (1.5-6.5) G1 vs. G2: p = NS Time to return to normal activity, median days (Q1 – Q3) G1: 2.5 (1-5) G2: 4 (2.5-6.5) G1 vs. G2: p &lt; 0.01</td>
</tr>
<tr>
<td>Ericsson 2009¹⁸³, ¹⁸⁶ RCT Moderate ROB</td>
<td>G1: Partial tonsillectomy-coblation (35) G2: Total tonsillectomy-cold dissection (32)</td>
<td>Time to return to normal diet G1: 4 days earlier than G2 G1 vs. G2: p=NS Time to return to normal activity G1: 3 days earlier than G2 G1 vs. G2: p=NS</td>
</tr>
</tbody>
</table>

G = Group; N = Number; NR = Not Reported; NS = Not Significant; POD = Postoperative Day; OSDB = Obstructive Sleep Disordered Breathing; Q=quartile; RCT = Randomized Controlled Trial; ROB = Risk of Bias; SD = Standard Deviation

### Throat Infections

Four RCTs (multiple publications, all moderate risk of bias) addressed recurrent throat infections (Table 22).¹¹⁰, ¹³⁹, ¹⁸²-¹⁸⁶ One study included children with OSDB (hypertrophy causing obstruction) as the primary indication for surgery,²⁸⁵ while the others included children with both OSDB and recurrent throat infections. Two studies explicitly reported on baseline or previous throat infections (number of episodes/year),¹¹⁰, ¹⁸²-¹⁸⁴ and one explicitly excluded children with >3 streptococcal throat infections in the 2 years prior to surgery.¹³⁹ One study reported that 21 percent of all children had had ≤ one episode of tonsillitis before the 3 months prior to surgery.¹⁸⁵, ¹⁸⁶ In three of the four studies, children in the partial tonsillectomy arm had more throat infections than did those in the total tonsillectomy arms, though differences were not statistically significant in three studies.¹¹⁰, ¹⁸²-¹⁸⁶ In two studies, children experienced fewer infections compared with baseline rates,¹⁸²-¹⁸⁶ but other studies did not comment on changes from baseline.
<table>
<thead>
<tr>
<th>Study, Year</th>
<th>Study Design</th>
<th>Risk of Bias</th>
<th>Comparison Groups (N)</th>
<th>Throat Infections</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ericsson 2009</td>
<td>RCT</td>
<td>Moderate ROB</td>
<td>G1: Partial tonsillectomy- coblation (35) G2: Total tonsillectomy- cold dissection (32)</td>
<td>Sore throats requiring antibiotics, 6-months post-tonsillectomy, n</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>G1: 4 G2: 2 G1 vs. G2: p=NS</td>
<td>Sore throats requiring antibiotics, 24-months post-tonsillectomy, n</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>G1: 8 G2: 1 G1 vs. G2: p= NR</td>
<td></td>
</tr>
<tr>
<td>Hultcrantz 2004</td>
<td>RCT</td>
<td>Moderate ROB</td>
<td>G1: Partial tonsillectomy-coblation (49) G2: Total tonsillectomy-cold dissection (43)</td>
<td>Sore throats requiring antibiotics, 12-months post-tonsillectomy, n</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>G1: 6 G2: 4 G1 vs. G2: p=NS</td>
<td>Sore throats requiring antibiotics, 1-3 years post-tonsillectomy, n</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>G1: 6 G2: 5 G1 vs. G2: p=NS</td>
<td></td>
</tr>
<tr>
<td>Beriat 2013</td>
<td>RCT</td>
<td>Moderate ROB</td>
<td>G1: Partial tonsillectomy- microdebrider (37) G2: Total tonsillectomy- cold dissection (45)</td>
<td>Recurrent throat infection (within 12-months post-tonsillectomy), n</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>G1: 2 G2: 0 G1 vs. G2: p= NR</td>
<td></td>
</tr>
<tr>
<td>Chan 2004</td>
<td>RCT</td>
<td>Moderate ROB</td>
<td>G1: Partial tonsillectomy- coblation (27) G2: Total tonsillectomy- electrocautery (28)</td>
<td>Incidence of sore throat or antibiotic use (3 and 12 months post-tonsillectomy)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>G1 vs. G2: p=NS</td>
</tr>
</tbody>
</table>

G = Group; N = Number; NR = Not Reported; NS = Not Significant; OSDB = Obstructive Sleep Disordered Breathing; RCT = Randomized Controlled Trial; ROB = Risk of Bias; SD = Standard Deviation

**Quality of Life**

Three RCTs (1 low and 2 moderate risk of bias) assessed quality of life using different scales and at different time points (Table 23). In one study with assessment at 1-month postsurgery, changes in physical suffering, sleep disturbances, speech issues, or caregiver concerns did not differ significantly between groups, but decreases in emotional distress and in activity limitations were greater in the partial tonsillectomy arm than in the total tonsillectomy arm. In two additional studies (one using the OSA-18, which uses a 7-point scale to assess frequency of symptoms from 1 [none of the time] to 7 [all of the time] and also assesses disease-specific quality of life) and one using the Glasgow Children’s Benefit Inventory [GCBI]), changes in quality of life were not significantly different between groups, and both groups improved from baseline. In one study more than 30 percent of children in both arms had large improvements in disease-specific quality of life at 6 months and 2 years postsurgery, but group differences were not significant.
### Table 23. Quality of life following partial or total tonsillectomy

<table>
<thead>
<tr>
<th>Study, Year</th>
<th>Study Design</th>
<th>Risk of Bias</th>
<th>Comparison Groups (N)</th>
<th>Baseline Outcome Measure, Mean±SD</th>
<th>Followup Outcome Measure, Mean±SD</th>
</tr>
</thead>
</table>
| Derkay 2006<sup>183</sup> RCT Low ROB | G1: Partial tonsillectomy-microdebrider (150)  
G2: Total tonsillectomy-electrocautery (150) | NR | Baseline to postoperative changes in physical suffering, sleep disturbance, speech or swallowing problems, and caregiver concerns, 1 month post-tonsillectomy  
G1 vs. G2: p=NS  
Decrease in emotional distress  
G1>G2: p < 0.01  
Decrease in activity limitation  
G1>G2: p < 0.01 |
| Ericsson 2009<sup>185, 186</sup> RCT Moderate ROB | G1: Partial tonsillectomy-coblation (35)  
G2: Total tonsillectomy-cold dissection (32) | OSA-18 (Total), Mean±SD  
G1: 3.5±1.0  
G2: 3.4±1.0 | OSA-18 (Total)  
Change score 6-months post-tonsillectomy  
G1: 1.8±1.2  
G2: 1.8±1.0  
G1 vs. G2: p=NS  
Change score 24-months post-tonsillectomy  
G1: 1.8±1.2  
G2: 1.9±1.4  
G1 vs. G2: p=NS  
Disease-specific quality of life data in figures only |
| Hultcrantz 2004<sup>183, 184</sup> RCT Moderate ROB | G1: Partial tonsillectomy-coblation (49)  
G2: Total tonsillectomy-cold dissection (43) | Glasgow Children’s Benefit Inventory G1+G2: NR | Glasgow Children’s Benefit Inventory, %  
33 months post-tonsillectomy  
Overall QoL-Much better  
G1: 61  
G2: 79  
Overall QoL-A little better  
G1: 35  
G2: 18  
Overall QoL-No change  
G1: 5  
G2: 3  
G1 vs. G2: all p=NS |

G = Group; IQR = Interquartile Range; N = Number; NR = Not Reported; NS = Not Significant; OSA-18 = Obstructive Sleep Apnea - 18; OSDB = Obstructive Sleep Disordered Breathing; QoL = Quality of Life; RCT = Randomized Controlled Trial; ROB = Risk of Bias; SD = Standard Deviation.

### Behavioral Outcomes

Two RCTs with moderate risk of bias reported changes in behavior using the Child Behavior Checklist (CBC) (Table 24).<sup>182-186</sup> Both groups improved from baseline overall and in each domain assessed (internalization, externalization), with no significant differences between groups in the short or longer (≥12 months) term. One study also assessed behavior changes with the GCBI and reported no significant differences between groups.<sup>182-184</sup>
<table>
<thead>
<tr>
<th>Study, Year</th>
<th>Study Design</th>
<th>Risk of Bias</th>
<th>Comparison Groups (N)</th>
<th>Baseline Outcome Measure, Mean±SD</th>
<th>Followup Outcome Measure, Mean±SD</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Hultcrantz 2004</strong>&lt;sup&gt;182-184&lt;/sup&gt;</td>
<td>RCT</td>
<td>Moderate ROB</td>
<td>G1: Partial tonsillectomy-coblation (49) G2: Total tonsillectomy-cold dissection (43)</td>
<td>Child Behavior Checklist, Total Score G1: 21.3±17.4 G2: 17.3±12.8 G1 vs. G2: p &lt; 0.001</td>
<td>Child Behavior Checklist, Total Score 12-months post-tonsillectomy No differences in degree of improvement between groups Glasgow Children’s Benefit Inventory, % 33 months post-tonsillectomy Behavior-Much better G1: 19 G2: 10 Behavior-A little better G1: 19 G2: 15 Behavior-No change G1: 62 G2: 74 G1 vs. G2: all p=NS</td>
</tr>
</tbody>
</table>

G = Group; N = Number; NS = Not Significant; OSDB = Obstructive Sleep Disordered Breathing; RCT = Randomized Controlled Trial; ROB = Risk of Bias; SD = Standard Deviation

**Other Outcomes**

Two RCTs with moderate risk of bias also addressed enuresis.<sup>182-186</sup> One study reported a second partial tonsillectomy in a child with pre-existing enuresis and encopresis temporarily improved by the index partial tonsillectomy; encopresis did not improve after the second surgery.<sup>185, 186</sup> Another reported that 7 children undergoing total tonsillectomy and 3 undergoing partial had baseline enuresis, which improved in nine children (treatment group not specified) postoperatively.<sup>182-184</sup>

**Key Question 4. Effectiveness of Surgical Techniques**

**Key Points**

- Few studies reported effectiveness outcomes. In those that did, commonly used “hot” techniques such as coblation and electrocautery were generally associated with faster return to normal diet or activity compared with cold dissection (roughly 1 to 3 days). We found a
faster return to diet with coblation or electrocautery tonsillectomy compared with cold dissection and have low confidence in these conclusions (low strength of evidence).

- 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 could not make conclusions about effects associated with other techniques (insufficient strength of evidence).

Overview of the Literature

We identified 59 unique studies (reported in 61 publications) comparing surgical techniques for tonsillectomy (Table 25). Most (n=54) studies were RCTs; 43, 48, 56, 58, 61, 63-70, 74, 75, 77, 79-83, 87, 89, 91, 93, 96, 99, 100, 102-104, 108, 111, 116, 120, 123-125, 127, 130, 131, 134, 141, 143-145, 152-154, 160, 163, 167-170, 192, 195-197, 200, 207 four were nonrandomized trials, 195-197, 200 and one was a prospective cohort study. 207 Twenty-two studies were conducted in Europe. Nineteen studies were conducted in Asia (including Turkey), 48, 61, 63-65, 67, 79-81, 87, 91, 104, 141, 143, 144, 153, 154, 195, 200 and 12 in North America (11 in the United States). 56, 68, 70, 77, 93, 99, 108, 116, 120, 124, 127, 130 Four studies were conducted in Egypt, 100, 152, 163, 196 and one in New Zealand 96 and Brazil. 160 Study participants (n=6984) ranged in age from 6 months to 41 years (mean age in study under 18 years). Studies compared multiple techniques including coblation, cold dissection, electrocautery, laser, harmonic scalpel, and thermal welding, and the majority of studies reported only harms data. Twenty-one studies reported effectiveness data, chiefly time to return to normal diet or activity. 66, 75, 80, 83, 89, 91, 93, 103, 111, 116, 124, 127, 130, 131, 134, 144, 152, 163, 169, 170, 195, 197

We considered 16 studies to have low risk of bias, 43, 56, 69, 70, 75, 89, 93, 120, 123, 125, 131, 134, 144, 163, 167-170 30 to have moderate risk, 48, 58, 63, 64, 66, 74, 79, 80, 82, 83, 87, 91, 96, 103, 111, 116, 124, 127, 130, 141, 145, 152, 154, 160, 192, 195-197, 200, 207 and 13 to have high risk. 61, 65, 67, 68, 77, 81, 99, 100, 102, 104, 108, 143, 153 Major sources of bias in these studies included unclear methods for randomization, for accounting for potential confounding or modifying variables, and for handling imbalances between study groups. We do not discuss high risk of bias studies in the detailed analyses below.

Table 25. Overview of studies comparing surgical techniques for tonsillectomy

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>RCTs</th>
<th>Nonrandomized Trials</th>
<th>Prospective Cohort Studies</th>
<th>Total Literature</th>
</tr>
</thead>
<tbody>
<tr>
<td>Comparisons</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Coblation vs. Cold Techniques</td>
<td>6</td>
<td>1</td>
<td>0</td>
<td>7</td>
</tr>
<tr>
<td>Coblation vs. Electrocautery</td>
<td>7</td>
<td>0</td>
<td>0</td>
<td>7</td>
</tr>
<tr>
<td>Coblation vs. Laser</td>
<td>2</td>
<td>0</td>
<td>0</td>
<td>2</td>
</tr>
<tr>
<td>Cold Techniques vs. Electrocautery</td>
<td>11</td>
<td>2</td>
<td>1</td>
<td>14</td>
</tr>
<tr>
<td>Cold Techniques vs. Harmonic Scalpel</td>
<td>4</td>
<td>0</td>
<td>0</td>
<td>4</td>
</tr>
<tr>
<td>Cold Techniques vs. Laser</td>
<td>2</td>
<td>0</td>
<td>0</td>
<td>2</td>
</tr>
<tr>
<td>Cold Techniques vs. Thermal Welding</td>
<td>3</td>
<td>0</td>
<td>0</td>
<td>3</td>
</tr>
<tr>
<td>Electrocautery vs. Electrocautery</td>
<td>1</td>
<td>1</td>
<td>0</td>
<td>2</td>
</tr>
</tbody>
</table>
Electrocautery vs. Harmonic Scalpel

| Other          | 13 | 0 | 0 | 13 |

Study Characteristics

| Allocates Intervention by Tonsil | 8  | 2 | 0 | 10 |
| Assesses Total Tonsillectomy    | 51 | 4 | 1 | 56 |
| Assesses Partial Tonsillectomy  | 3  | 0 | 0 | 3  |

Surgical Indication

| Throat Infection | 6  | 3 | 0 | 9  |
| OSDB             | 7  | 0 | 0 | 7  |
| OSDB+Throat Infection | 28 | 1 | 0 | 29 |
| Not specified    | 13 | 0 | 1 | 14 |

Effectiveness Outcomes Frequently Reported

| Time to Return to Normal Diet | 14 | 1 | 0 | 15 |
| Time to Return to Normal Activity | 6  | 1 | 0 | 7  |

Risk of Bias

| Low  | 16 | 1 | 1 | 18 |
| Moderate | 25 | 3 | 0 | 28 |
| High | 13 | 0 | 0 | 13 |

Total N participants | 6446 | 478 | 60 | 6984 |

*Includes comparisons of 3 techniques:44, 55, 82, 99, 163 cold techniques vs. other cold techniques56 or molecular resonance;83, 192 electrocautery vs. laser111 or molecular resonance,64 or unspecified tonsillectomy;144 coblation vs. molecular resonance;74 and laser vs. other lasers.58

N = number; OSDB = obstructive sleep-disordered breathing; RCT = randomized controlled trial

Detailed Analysis

As noted, most studies reported harms data (see Harms of Tonsillectomy section below). Nineteen studies (17 RCTs and 2 nonrandomized trials)—eight with low75, 89, 93, 131, 134, 144, 163, 169, and 11 with moderate risk of bias66, 80, 91, 103, 111, 116, 124, 127, 130, 152, 197—reported on return to normal diet or activity—the only usable effectiveness outcomes reported.

Findings By Surgical Comparison

Coblation Versus Cold Dissection Tonsillectomy

Five RCTs (4 low89, 93, 144, 169, 170 and 1 moderate75 risk of bias) and one nonrandomized trial with moderate risk of bias197 compared coblation and cold dissection tonsillectomy (Table 26). Across these small, short-term studies, coblation tonsillectomy was generally associated with faster return to normal diet or activity. Four studies reported on return to normal diet, with mixed results. In two low risk of bias studies, children receiving coblation tonsillectomy returned to normal diet sooner (roughly 2-3 days) than those undergoing cold dissection;89, 144 in two other studies (one low, one moderate risk of bias), differences were not significant between groups.75, 93 Return to normal activity occurred significantly earlier after coblation in three low risk of bias studies.89, 144, 169, 170 In one moderate risk of bias nonrandomized study, children undergoing coblation tonsillectomy had fewer post-procedure school absences than those receiving cold dissection (mean 5.3 vs. 8.9 days, p<0.001).197

Table 26. Return to normal diet and activity in studies comparing coblation and cold dissection tonsillectomy

<table>
<thead>
<tr>
<th>Author, Year Study Type Risk of Bias</th>
<th>Comparison Groups (N)</th>
<th>Return to Normal Diet or Activity</th>
</tr>
</thead>
</table>

50
Electrocautery Versus Cold Dissection Tonsillectomy

Electrocautery was generally associated with more favorable results in three small RCTs addressing this comparison (one with low risk of bias and two with moderate risk of bias) (Table 27). Electrocautery was superior to cold dissection in a faster return to normal diet in two studies and 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.

Table 27. Return to normal diet and activity in studies comparing electrocautery and cold dissection tonsillectomy

<table>
<thead>
<tr>
<th>Author, Year</th>
<th>Study Type</th>
<th>Risk of Bias</th>
<th>Comparison Groups (N)</th>
<th>Return to Normal Diet or Activity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nunez 2000</td>
<td>RCT</td>
<td>Low ROB</td>
<td>G1: Electrocautery tonsillectomy (24) G2: Cold dissection tonsillectomy (26)</td>
<td>Time to return to normal diet, median days (95% CI) G1: 7.5 (5-8) G2: 5 (3-7) G1 vs. G2: p &lt; 0.05</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Time to return to normal activity, median days (95% CI) G1: 7 (5-8)</td>
</tr>
<tr>
<td>Mitic 2007</td>
<td>RCT</td>
<td>Low ROB</td>
<td>G1: Coblation tonsillectomy (20) G2: Cold dissection tonsillectomy (20)</td>
<td>Expected postoperative day to achieve normal diet G1: 6.80 G2: 8.93 G1 vs. G2: p&lt;0.001</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Expected postoperative day to achieve normal activity G1: 6.62 G2: 8.45 G1 vs. G2: p&lt;0.001</td>
</tr>
<tr>
<td>Parker 2000</td>
<td>RCT</td>
<td>Moderate ROB</td>
<td>G1: Coblation tonsillectomy (35) G2: Cold dissection tonsillectomy (35)</td>
<td>Return to normal diet, days Data reported only in figures G1 vs. G2: p=NS</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Time to return to normal activity, mean days (range) G1: 2 (1-7) G2: 4 (1-9) G1 vs. G2: p &lt; 0.001</td>
</tr>
<tr>
<td>Roje 2009</td>
<td>RCT</td>
<td>Low ROB</td>
<td>G1: Coblation tonsillectomy (50) G2: Cold dissection tonsillectomy (50)</td>
<td>Time to return to normal activity, mean days ± SD G1: 7.63 ± 1.16 G2: 11.7 ± 1.68 G1 vs. G2: p &lt; 0.0001</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Time to return to normal diet, mean days ± SD G1: 6.27 ± 1.07 G2: 9.25 ± 1.3 G1 vs. G2: p &lt; 0.0001</td>
</tr>
<tr>
<td>Di Rienzo Businco 2008</td>
<td>Nonrandomized trial</td>
<td>Moderate ROB</td>
<td>G1: Coblation tonsillectomy (21) G2: Cold dissection tonsillectomy (21)</td>
<td>Days absent from school post-procedure, mean±SD G1: 5.3 ± 1.7 G2: 8.9 ± 1.5 G1 vs. G2: p&lt;0.001</td>
</tr>
<tr>
<td>Shapiro 2007</td>
<td>RCT</td>
<td>Low ROB</td>
<td>G1: Coblation tonsillectomy (23) G2: Cold dissection tonsillectomy (23)</td>
<td>Time to return to normal diet, mean days G1: 4 G2: 3 G1 vs. G2: p = NS</td>
</tr>
</tbody>
</table>

G=group; N=number; NS=not significant; ROB=risk of bias
Coblation Versus Electrocautery Tonsillectomy

Four RCTs with moderate risk of bias compared coblation and electrocautery tonsillectomy with mixed results (Table 28).66, 116, 124, 131 Children who underwent coblation returned to normal diet more quickly than those who underwent electrocautery tonsillectomy in two studies,66, 131 but return did not differ significantly between groups in two others.116, 124 Children who underwent coblation also returned to normal activity roughly two days more quickly than those who underwent electrocautery in two studies.116, 124

<table>
<thead>
<tr>
<th>Study</th>
<th>Group 1</th>
<th>Group 2</th>
<th>Outcome Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hesham 20099</td>
<td>G1: Electrocautery tonsillectomy (71)</td>
<td>G2: Cold dissection tonsillectomy (69)</td>
<td>Mean % of normal diet resumed (POD1), mean ± SD</td>
</tr>
<tr>
<td></td>
<td>G1: 54.67 ± 13.69</td>
<td>G2: 48.53 ± 21.54</td>
<td>G1 vs. G2: p &lt; 0.05</td>
</tr>
<tr>
<td></td>
<td>Mean % of normal diet resumed (POD7), mean ± SD</td>
<td></td>
<td>G1: 84 ± 19</td>
</tr>
<tr>
<td></td>
<td>G2: 91.3 ± 14.17</td>
<td>G1 vs. G2: p &lt; 0.05</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Mean % of normal activity resumed (POD1), mean ± SD</td>
<td></td>
<td>G1: 73.33 ± 19.68</td>
</tr>
<tr>
<td></td>
<td>G2: 78.13 ± 16.9</td>
<td>G1 vs. G2: p=NS</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Mean % of normal activity resumed (POD7), mean ± SD</td>
<td></td>
<td>G1: 92.67 ± 14.92</td>
</tr>
<tr>
<td></td>
<td>G2: 96 ± 7.17</td>
<td>G1 vs. G2: p=NS</td>
<td></td>
</tr>
<tr>
<td>Young 2001127</td>
<td>G1: Electrocautery tonsillectomy (26)</td>
<td>G2: Cold dissection tonsillectomy (31)</td>
<td>Time to return to normal diet and activity</td>
</tr>
<tr>
<td></td>
<td>G1 vs. G2: p=NS</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

G=group; N=number; NS=not significant; POD=postoperative day; ROB=risk of bias
<table>
<thead>
<tr>
<th>Author, Year</th>
<th>Study Type</th>
<th>Risk of Bias</th>
<th>Comparison Groups (N)</th>
<th>Return to Normal Diet or Activity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Temple 2001</td>
<td>RCT</td>
<td>Low ROB</td>
<td>G1: Coblation tonsillectomy (18) G2: Electrocautery tonsillectomy (20)</td>
<td><strong>Time to return to normal diet, mean days</strong>&lt;br&gt; G1: 2.4&lt;br&gt; G2: 7.6&lt;br&gt; G1 vs. G2: p &lt; 0.0001</td>
</tr>
<tr>
<td>Parker 2011</td>
<td>RCT</td>
<td>Moderate ROB</td>
<td>G1: Coblation tonsillectomy (40) G2: Electrocautery tonsillectomy (40)</td>
<td><strong>Time to return to normal diet, mean days</strong>&lt;br&gt; G1: 5.2&lt;br&gt; G2: 6.2&lt;br&gt; G1 vs. G2: p=0.04</td>
</tr>
<tr>
<td>Stoker 2004</td>
<td>RCT</td>
<td>Moderate ROB</td>
<td>G1: Coblation tonsillectomy (44) G2: Electrocautery tonsillectomy (45)</td>
<td><strong>Time to return to normal diet, mean days ± SD</strong>&lt;br&gt; G1: 4.6 ± 2.1&lt;br&gt; G2: 5.2 ± 2&lt;br&gt; G1 vs. G2: p = NS&lt;br&gt; <strong>Time to return to normal activity, mean days ± SD</strong>&lt;br&gt; G1: 7.4 ± 1.9&lt;br&gt; G2: 6.7 ± 1.8&lt;br&gt; G1 vs. G2: p = NS</td>
</tr>
<tr>
<td>Shah 2002</td>
<td>RCT</td>
<td>Moderate ROB</td>
<td>G1: Coblation tonsillectomy (17) G2: Electrocautery tonsillectomy (17)</td>
<td><strong>Time to return to normal diet for &gt;50% of participants</strong>&lt;br&gt; G1: within 7 days postoperatively&lt;br&gt; G2: &gt;10 days postoperatively&lt;br&gt; G1 vs. G2: p=NS&lt;br&gt; <strong>Time to return to normal activity for &gt;50% of participants</strong>&lt;br&gt; G1: 8 days postoperatively&lt;br&gt; G2: 10 days postoperatively&lt;br&gt; G1 vs. G2: p=NS&lt;br&gt; <strong>Parental return to work</strong>&lt;br&gt; G1 vs. G2: p=NS</td>
</tr>
</tbody>
</table>

G=group; N=number; NR=not reported; NS=not significant; POD=postoperative day; ROB=risk of bias

### Harmonic Scalpel Versus Other Tonsillectomy Techniques

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 (Table 29). Studies compared different measures of return to normal diet or activity, thus limiting our ability to draw conclusions about differences in effectiveness. In the most recent RCT, children who had harmonic scalpel tonsillectomy returned to school after surgery in a median of 6 days compared with 8 who had coblation (p=NR). Another RCT comparing harmonic scalpel and cold dissection reported “dietary intake scores” ranging from zero to 3, with a score of zero indicating fluids only and a score of 3 indicating fluids plus normal diet. Children in the harmonic scalpel group had better dietary scores at each postoperative measurement (days 1, 3, 5, 7, 9), but scores in both groups declined over time. A final RCT reported the number of children who returned to normal diet and activity. Significantly more children in the harmonic scalpel group resumed their normal diet or activity compared with children undergoing electrocautery at postoperative day 1 and day 3.
Table 29. Return to normal diet and activity in studies comparing harmonic scalpel and other techniques for tonsillectomy

<table>
<thead>
<tr>
<th>Author, Year</th>
<th>Study Type</th>
<th>Risk of Bias</th>
<th>Comparison Groups (N)</th>
<th>Return to Normal Diet or Activity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Salama 2012</td>
<td>RCT</td>
<td>Moderate ROB</td>
<td>G1: Harmonic scalpel tonsillectomy (75) G2: Coblation tonsillectomy (75)</td>
<td>Days to return to school post-tonsillectomy, median G1: 6 G2: 8</td>
</tr>
<tr>
<td>Oko 2005</td>
<td>RCT</td>
<td>Moderate ROB</td>
<td>G1: Harmonic scalpel tonsillectomy (45) G2: Cold dissection (48)</td>
<td>Dietary intake scores, median (range) POD1 G1: 1 (0-1) G2: 0 (0-1) G1 vs. G2: p&lt;0.0001</td>
</tr>
<tr>
<td>Walker 2001</td>
<td>RCT</td>
<td>Moderate ROB</td>
<td>G1: Harmonic scalpel tonsillectomy (97) G2: Electrocautery tonsillectomy (75)</td>
<td>N returned to normal diet by POD1 G1: 43 (44.3) G2: 17 (22.7) G1 vs. G2: p = 0.004</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>N returned to normal diet by POD3 G1: 72 (74.2) G2: 35 (46.7) G1 vs. G2: p = 0.001</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>N returned to normal activity by POD1 G1: 27 (27.8) G2: 9 (12) G1 vs. G2: p = 0.011</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>N returned to normal activity by POD3 G1: 48 (49.5) G2: 17 (22.7) G1 vs. G2: p = 0.001</td>
</tr>
</tbody>
</table>

G=group; N=number; NR=not reported; POD=postoperative day; ROB=risk of bias

Laser Versus Coblation and/or Cold Dissection Tonsillectomy

Only two small RCTs addressed laser and did not provide sufficient data to draw conclusions about effectiveness compared with more standard techniques (Table 30). Two RCTs with low\textsuperscript{163} and moderate\textsuperscript{91} risk of bias comparing either potassium titanyl phosphate (KTP) laser or diode laser tonsillectomy to coblation and/or cold dissection reported no significant group differences in time to return to normal diet.
Table 30. Return to normal diet and activity in studies comparing laser and coblation and/or cold dissection for tonsillectomy

<table>
<thead>
<tr>
<th>Author, Year</th>
<th>Study Type</th>
<th>Risk of Bias</th>
<th>Comparison Groups (N)</th>
<th>Return to Normal Diet or Activity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Elabdawey 2015&lt;sup&gt;105&lt;/sup&gt;</td>
<td>RCT</td>
<td>Low ROB</td>
<td>G1: Coblation tonsillectomy (40) G2: Cold dissection tonsillectomy (40) G3: Diode laser tonsillectomy (40)</td>
<td>Time to return to normal diet or activity G1 vs. G2 vs. G3: p = NS</td>
</tr>
<tr>
<td>Hegazy 2008&lt;sup&gt;101&lt;/sup&gt;</td>
<td>RCT</td>
<td>Moderate ROB</td>
<td>G1: Laser tonsillectomy (40) G2: Coblation tonsillectomy (40)</td>
<td>Time to return to normal diet or activity G1 vs. G2: p = NS</td>
</tr>
</tbody>
</table>

G = group; N = number; NS = not significant; ROB = risk of bias

Thermal Welding Versus Cold Dissection and/or Electrocautery Tonsillectomy

Two studies compared thermal welding tonsillectomy (a newer tonsillectomy technique which uses heated forceps to cut and cauterize tissue) and either cold dissection<sup>80</sup> or cold dissection and electrocautery (Table 31).<sup>195</sup> Studies reported different measures, which limits our ability to draw conclusions. The RCT comparing thermal welding and cold dissection (moderate risk of bias) reported no differences in return to normal activity (mean of 5 days post-tonsillectomy).<sup>80</sup> Time to return to normal diet was lowest in the cold dissection group followed by thermal welding (p<0.001) followed by the electrocautery arm in the nonrandomized trial.<sup>195</sup>

Table 31. Return to normal diet and activity in studies comparing thermal welding and other techniques for tonsillectomy

<table>
<thead>
<tr>
<th>Author, Year</th>
<th>Study Type</th>
<th>Risk of Bias</th>
<th>Comparison Groups (N)</th>
<th>Return to Normal Diet or Activity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ozkiris 2012&lt;sup&gt;193&lt;/sup&gt;</td>
<td>Nonrandomized trial</td>
<td>Moderate ROB</td>
<td>G1: Thermal welding tonsillectomy (104) G2: Cold dissection tonsillectomy (99) G3: Electrocautery tonsillectomy (102)</td>
<td>Time to return to normal diet, mean days ± SD (range) G1: 7.3 ± 0.7 (7-9) G2: 7 ± 1.5 (6-9) G3: 9.3 ± 1.7 (9-11) G1 vs. G2: p &lt; 0.001 Other p values = NR</td>
</tr>
<tr>
<td>Sezen 2008&lt;sup&gt;80&lt;/sup&gt;</td>
<td>RCT</td>
<td>Moderate ROB</td>
<td>G1: Thermal welding tonsillectomy (25) G2: Cold dissection tonsillectomy (25)</td>
<td>Time to return to normal activity, mean days G1+G2: 5 G1 vs. G2: p = NS</td>
</tr>
</tbody>
</table>

G = group; N = number, NR = not reported; NS = not significant; ROB = risk of bias
Harms of Tonsillectomy

Key Points

- We found a low frequency of post-tonsillectomy hemorrhage (PTH) and utilization harms across surgical techniques and have confidence in these findings (high strength of evidence).
- 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. Overall, estimates of PTH and utilization harms associated with tonsillectomy were below 8 percent.
- The pooled frequency (without adjustment) of PTH was below 5 percent overall (4.2% for total tonsillectomy; 1.5% for partial tonsillectomy) in comparative studies.
- 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 nonbleeding 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).
- Overall unadjusted frequencies of revisits for pain, dehydration, or PONV were below 5 percent.
- Other harms were disparate and generally not clinically significant. No comparative studies reported deaths.
- The frequency of harms in case series and database or registry studies was consistent with that in comparative studies. At least four deaths were reported in case series including 1,778,342 children.

Overview of the Literature

In order to account fully for potential harms of tonsillectomy, primarily PTH, readmission and reoperation, we compiled all comparative studies and examined rates of harms by arm, then reviewed case series and database studies, which were 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 (low or moderate risk of bias) and comment on their consistency. Finally, we conducted a Bayesian meta-analysis to estimate predicted primary PTH, secondary PTH, reoperation and readmission by partial and total tonsillectomy, and by surgical approach.

Comparative Study Arms Reporting PTH or Other Harms Data

One-hundred and one comparative studies of low or moderate risk of bias reported harms data.

Most studies (n=85) reported PTH-related outcomes including number of PTH, which may have been reported as primary (generally defined as occurring within 24 hours of surgery), secondary (generally defined as occurring more than 24 hours postoperatively), or at an undefined or unspecified time.9, 38, 40, 41, 43-45, 47, 48, 53, 54, 56-60, 63, 64, 66, 69, 71, 74, 75, 78-80, 82, 84-87, 89-91, 93, 95, 96, 98, 103, 105, 106, 108, 110-112, 115-117, 119, 120, 123-125, 127, 130, 131, 134, 138, 139, 141, 144, 145, 148, 150-153, 158, 160, 161, 163-178, 182-186, 192, 194-197, 199, 200, 207, 212, 213, 286

Other frequently reported harms in comparative studies (n=32) included revisits or readmissions for postoperative pain, dehydration, or PONV.39, 43, 52, 66, 69, 74, 85, 93, 98, 103, 107, 111, 112, 114, 116, 119, 121-125, 130, 134, 139, 148, 154, 164-166, 171-178, 185, 186, 207, 212, 213, 287

We present detailed harms tables in Appendix H. The tables in this appendix report pooled frequency of harms without adjustment, typically presented by technique (e.g., coblation, cold dissection), extent of surgery (partial or total tonsillectomy), and indication (OSDB, throat infection, mixed [OSDB and throat infection], or unspecified) where possible. We included studies with low or moderate risk of bias in our unadjusted estimates.

Studies Reporting Harms Combined in Meta-Analysis


As noted, in sensitivity analyses, high risk of bias studies did not affect findings, so we included them in final analyses.

Case Series and Database Studies Reporting Harms
In addition, we captured PTH reported in case series and database analyses to determine whether the frequency supported findings in the comparative literature and to assess harms in larger study populations. We identified 53 unique database or registry studies or case series with ≥ 1000 children (reported in 63 papers) addressing PTH or other harms including readmissions or revisits for dehydration or nausea.21, 215-276 Twenty-three studies were conducted in North America,21, 215, 223, 224, 227, 228, 232-237, 239, 247, 248, 256, 257, 261, 266-268, 270-273 and three in Australia or New Zealand.240, 242, 275 Twenty-two were conducted five in Asia,230, 244, 246, 249, 265 and 27 as moderate.
We considered seven studies to have a high risk of bias and do not present them in the detailed analysis. Studies included a total of 1,808,568 children, with numbers of participants ranging from 1,109 to over 500,000 across studies. Most studies (n=36) reported generally on PTH or other sequelae of tonsillectomy without specifying surgical technique. Twelve studies reported PTH or other harms by surgical technique or instrument, three reported specifically on PTH related to dexamethasone or nonsteroidal anti-inflammatory drug (NSAID) use, and four reported PTH by surgical indication and technique. One reported readmission data by comorbidity, and one reported specifically on reoperation following partial or total tonsillectomy. PTH was reported in nearly all studies. Eleven studies reported on readmission for non-PTH indications. Twelve studies reported mortality or other harms. Appendix H provides more details on harms reported in each study and tables of unadjusted pooled frequency of PTH and other harms reported in studies with low or moderate risk of bias.

Detailed Analysis

Unadjusted PTH-Related Outcomes in Comparative Studies Addressing Tonsillectomy

Total Tonsillectomy

One-hundred and four study arms reported postoperative PTH after total tonsillectomy. The 6299 children across studies who were treated with total tonsillectomy experienced 265 episodes (4.2%) of PTH (Table 32). Among these episodes, 33 were primary (typically occurring within 24 hours of tonsillectomy), 166 were secondary (occurring more than 24 hours post-tonsillectomy), and for 66, timing was not specified. Sixty-eight children required reoperation to control PTH (2.2%), and 80 had nonoperative revisits or readmissions for PTH (3.0%). Children who underwent 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=3.2 percent. The frequency of revisits and reoperations overall was typically less than 6 percent. Tables in Appendix H outline rates associated with each technique in each study arm.
Table 32. Unadjusted PTH-related outcomes in study arms evaluating total tonsillectomy

<table>
<thead>
<tr>
<th>Technique (N arms)</th>
<th>Total N</th>
<th>Total PTH (%)</th>
<th>Total Primary PTH (%)</th>
<th>Total Secondary PTH (%)</th>
<th>Total Unspecified PTH (%)</th>
<th>Total Nonoperative Revisits/Readmissions for PTH (%)</th>
<th>Total Reoperations for PTH (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>All arms (105)</td>
<td>6299</td>
<td>265 (4.2)</td>
<td>33 (1.3)</td>
<td>166 (4.8)</td>
<td>66 (2.7)</td>
<td>80 (3)</td>
<td>68 (2.2)</td>
</tr>
<tr>
<td>Electrocautery (29)</td>
<td>1668</td>
<td>82 (4.9)</td>
<td>5 (0.37)</td>
<td>62 (3.7)</td>
<td>15 (2.3)</td>
<td>36 (5)</td>
<td>21 (2.6)</td>
</tr>
<tr>
<td>Cold dissection (34)</td>
<td>1904</td>
<td>72 (3.8)</td>
<td>6 (0.54)</td>
<td>49 (4.2)</td>
<td>17 (2.7)</td>
<td>9 (1.6)</td>
<td>19 (2.3)</td>
</tr>
<tr>
<td>Coblation (19)</td>
<td>728</td>
<td>23 (3.2)</td>
<td>3 (2.1)</td>
<td>7 (2.4)</td>
<td>12 (2.7)</td>
<td>2 (1.1)</td>
<td>4 (2.5)</td>
</tr>
<tr>
<td>Unspecified/other technique (5)</td>
<td>748</td>
<td>25 (3.3)</td>
<td>9 (3.1)</td>
<td>NR</td>
<td>16 (3.5)</td>
<td>8 (2)</td>
<td>10 (2.3)</td>
</tr>
<tr>
<td>Molecular resonance (5)</td>
<td>466</td>
<td>4 (0.9)</td>
<td>0 (0)</td>
<td>4 (1.22)</td>
<td>0 (0)</td>
<td>1 (0.23)</td>
<td>1 (0.31)</td>
</tr>
<tr>
<td>Harmonic scalpel (5)</td>
<td>397</td>
<td>45 (11.3)</td>
<td>1 (0.63)</td>
<td>38 (11.3)</td>
<td>6 (9.8)</td>
<td>15 (5.5)</td>
<td>9 (2.8)</td>
</tr>
<tr>
<td>Thermal welding (4)</td>
<td>199</td>
<td>5 (2.5)</td>
<td>0 (0)</td>
<td>5 (2.6)</td>
<td>0 (0)</td>
<td>NR</td>
<td>1 (0.96)</td>
</tr>
<tr>
<td>Laser (4)</td>
<td>189</td>
<td>10 (5.3)</td>
<td>9 (11.4)</td>
<td>1 (0.91)</td>
<td>NR</td>
<td>9 (11.4)</td>
<td>3 (2.8)</td>
</tr>
</tbody>
</table>

Note: Percentages for primary and secondary PTH, readmissions/revisits, and reoperations reflect the number of each instance of bleeding or reencounter divided by the total number of patients in the studies reporting such data, and not in the total number of participants across all studies in a given row.

Partial Tonsillectomy

Total PTH did not exceed 5 percent among the 18 study arms contributing data to assess bleeding after partial tonsillectomy (Table 33). PTH was highest after coblation tonsillectomy (4.2%). No PTH was associated with laser approaches, but few studies assessed this modality.

Table 33. Unadjusted PTH-related outcomes in study arms evaluating partial tonsillectomy

<table>
<thead>
<tr>
<th>Technique (n arms)</th>
<th>Total N</th>
<th>Total PTH (%)</th>
<th>Total Primary PTH (%)</th>
<th>Total Secondary PTH (%)</th>
<th>Total Undefined PTH (%)</th>
<th>Total Nonoperative Revisits/Readmissions for PTH (%)</th>
<th>Total Reoperations for PTH (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>All arms (18)</td>
<td>599</td>
<td>8 (1.5)</td>
<td>0 (0)</td>
<td>2 (1.6)</td>
<td>6 (1.4)</td>
<td>5 (1.8)</td>
<td>1 (0.64)</td>
</tr>
<tr>
<td>Microdebrider (5)</td>
<td>252</td>
<td>3 (1.2)</td>
<td>NR</td>
<td>NR</td>
<td>3 (1.2)</td>
<td>3 (1.5)</td>
<td>NR</td>
</tr>
<tr>
<td>Coblation (6)</td>
<td>169</td>
<td>4 (4.2)</td>
<td>0 (0)</td>
<td>2 (6.3)</td>
<td>2 (2.2)</td>
<td>2 (2.8)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Cold dissection (4)</td>
<td>124</td>
<td>1 (0.81)</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td>1 (1.4)</td>
<td>NR</td>
<td>1 (1.1)</td>
</tr>
<tr>
<td>Laser (3)</td>
<td>54</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
</tr>
</tbody>
</table>

Note: Percentages for primary and secondary PTH, readmissions/revisits, and reoperations reflect the number of each instance of bleeding or reencounter divided by the total number of patients in the studies reporting such data, and not in the total number of participants across all studies in a given row.

PTH by Indication

Across all techniques and types of tonsillectomy (partial or total), the overall occurrence of PTH after surgery was lowest in children with OSDB (Table 34).
### Table 34. Unadjusted PTH-related outcomes by indication in study arms evaluating total or partial tonsillectomy

<table>
<thead>
<tr>
<th>Indication (N arms)</th>
<th>Total N</th>
<th>Total PTH (%)</th>
<th>Total Primary PTH (%)</th>
<th>Total Secondary PTH (%)</th>
<th>Total Undefined PTH (%)</th>
<th>Total Nonoperative Revisits/Readmissions for PTH (%)</th>
<th>Total Reoperations for PTH (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>OSDB (28)</td>
<td>1219</td>
<td>22 (1.9)</td>
<td>11 (2.1)</td>
<td>9 (1.4)</td>
<td>8 (1.4)</td>
<td>3 (0.85)</td>
<td></td>
</tr>
<tr>
<td>Throat infection</td>
<td>1764</td>
<td>88 (5.0)</td>
<td>64 (6.2)</td>
<td>12 (2.3)</td>
<td>29 (3.4)</td>
<td>10 (1.6)</td>
<td></td>
</tr>
</tbody>
</table>

**Note:** Percentages for primary and secondary PTH, readmissions/revisits, and reoperations reflect the number of each instance of bleeding or reencounter divided by the total number of patients in the studies reporting such data, and not in the total number of participants across all studies in a given row.

N = Number; PTH = Post-Tonsillectomy Hemorrhage

---

**Revisits for Pain, Dehydration, or PONV Following Tonsillectomy Reported in Comparative Studies**

Revisits for pain, dehydration, or PONV typically occurred in less than 10 percent of children (Table 35). Eight studies reported zero revisits for non-PTH indications associated with interventions studied. Two studies reported that more than 10 percent of children had revisits or readmissions (see Appendix H for full details). One RCT comparing KTP laser and cold dissection total tonsillectomy as day-stay procedures reported 25 total admissions for pain (13 for cold dissection and 12 in laser) and 29 for vomiting (16 in cold dissection arm and 13 in laser) on the day of surgery. In another RCT comparing electrocautery and coblation tonsillectomy, revisits comprised both return visits and phone calls to the provider; thus, numbers are higher than those reported in other studies.
Table 35. Unadjusted revisits for pain, dehydration, or PONV reported after tonsillectomy in arms of comparative studies

<table>
<thead>
<tr>
<th>Technique (N arms)</th>
<th>Total Arm N</th>
<th>Pain Revisits/Readmissions, n (%)</th>
<th>Dehydration Revisits/Readmissions, n (%)</th>
<th>PONV Revisits/Readmissions, n (%)</th>
<th>Other Revisits/Readmissions, n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>All arms (37)</td>
<td>2969</td>
<td>45 (1.5)</td>
<td>39 (1.6)</td>
<td>45 (1.5)</td>
<td>3 (0.09)</td>
</tr>
<tr>
<td>Electrocautery-total (12)</td>
<td>883</td>
<td>12 (7.3)</td>
<td>20 (2.3)</td>
<td>7 (5.1)</td>
<td>NR</td>
</tr>
<tr>
<td>Cold dissection-total (9)</td>
<td>622</td>
<td>14 (5.4)</td>
<td>1 (0.21)</td>
<td>16 (10.5)</td>
<td>NR</td>
</tr>
<tr>
<td>Unspecified tonsillectomy (4)</td>
<td>529</td>
<td>NR</td>
<td>9 (2.4)</td>
<td>5 (0.85)</td>
<td>NR</td>
</tr>
<tr>
<td>Molecular resonance-total (2)</td>
<td>362</td>
<td>NR</td>
<td>0</td>
<td>NR</td>
<td>NR</td>
</tr>
<tr>
<td>Harmonic scalpel-total (2)</td>
<td>216</td>
<td>NR</td>
<td>2 (1.3)</td>
<td>NR</td>
<td>3 (4.9)</td>
</tr>
<tr>
<td>Coblation-total (5)</td>
<td>198</td>
<td>6 (8.8)</td>
<td>7 (3.5)</td>
<td>4 (9.8)</td>
<td>NR</td>
</tr>
<tr>
<td>Laser-total (3)</td>
<td>159</td>
<td>13 (10.1)</td>
<td>0</td>
<td>13 (16.5)</td>
<td>NR</td>
</tr>
<tr>
<td>Microdebrider-partial (2)</td>
<td>187</td>
<td>0</td>
<td>5 (2.5)</td>
<td>NR</td>
<td>NR</td>
</tr>
<tr>
<td>Coblation-partial (1)</td>
<td>34</td>
<td>NR</td>
<td>0</td>
<td>NR</td>
<td>NR</td>
</tr>
</tbody>
</table>

Note: Percents for readmissions/revisits reflect the number of each reencounter divided by the total number of patients in the studies reporting such data, and not in the total number of participants across all studies in a given row.
N = Number, NR = Not Reported; PONV = Postoperative Nausea and Vomiting

Other Harms Following Tonsillectomy Reported in Comparative Studies

Twenty-three studies also reported other non-PTH harms of surgical procedures.6, 9, 43, 44, 54, 58, 69, 70, 85, 107, 111, 112, 114, 120, 124, 125, 130, 145, 158, 196, 207, 213, 287 Harms were largely minor and included burns or unspecified breathing complications (Table 36), and two studies including children with OSDB reported velopharyngeal insufficiency (VPI).85, 124 One study noted that VPI resolved within two months,85 and the other did not comment on resolution or severity.124 Eight studies explicitly reported that no non-PTH harms occurred (not shown in table);78, 70, 107, 120, 125, 145, 158, 207 Seven studies (15 arms) explicitly reported that no deaths occurred,43, 54, 69, 74, 111, 130, 213, and two studies reported that no cases of VPI occurred.107, 125
Table 36. Other harms reported in studies of surgical techniques compared with medical treatment or other surgical techniques

<table>
<thead>
<tr>
<th>Nonbleeding Harms of Surgical Techniques</th>
<th>Number of Studies (# Participants With Harm/Total Participants)</th>
<th>Reported Occurrence Across Studies</th>
</tr>
</thead>
<tbody>
<tr>
<td>Electrocautery total tonsillectomy</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Thermal burns in oral mucosa and tongue or other burns 196</td>
<td>1 (14/91)</td>
<td>15%</td>
</tr>
<tr>
<td>Burn to thigh from improper grounding of electrocautery unit –hospitalized 3 days 114</td>
<td>1 (1/21)</td>
<td>4.7%</td>
</tr>
<tr>
<td>Coblation total tonsillectomy</td>
<td></td>
<td></td>
</tr>
<tr>
<td>VPI 185,124</td>
<td>2 (2/52)</td>
<td>2.8%-5.8%</td>
</tr>
<tr>
<td>Airway obstruction 124</td>
<td>1 (2/34)</td>
<td>5.9%</td>
</tr>
<tr>
<td>Cold dissection partial tonsillectomy</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Breathing complications 196</td>
<td>1 (1/243)</td>
<td>0.4%</td>
</tr>
<tr>
<td>Other complications 198</td>
<td>1 (0/243)</td>
<td>0%</td>
</tr>
<tr>
<td>Cold dissection total tonsillectomy</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lip burn from cautery 112</td>
<td>1 (1/57)</td>
<td>1.7%</td>
</tr>
<tr>
<td>Breathing complications 198</td>
<td>1 (2/780)</td>
<td>0.2%</td>
</tr>
<tr>
<td>Other (unspecified) complications 198</td>
<td>1 (1/780)</td>
<td>0.1%</td>
</tr>
<tr>
<td>CPAP</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rash from mask 14</td>
<td>1 (1/36)</td>
<td>2.7%</td>
</tr>
<tr>
<td>Total tonsillectomy (not specified)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Complications from GABHS infection or medical treatment of infection (drug reaction, peritonsillar abscess, scarlet fever) 113</td>
<td>1 (16/145)</td>
<td>5.7%</td>
</tr>
<tr>
<td>Erythematous rash from penicillin for throat infection 6</td>
<td>1 (1/96)</td>
<td>1%</td>
</tr>
<tr>
<td>Erythematous rash while receiving antimicrobial drug 9</td>
<td>2 (4/190)</td>
<td>2.1%</td>
</tr>
</tbody>
</table>

Note: 4 children in a no tonsillectomy arm also experienced erythematous rash while receiving penicillin in studies described in one publication, and three children in nonsurgical arms in another publication reporting 2 studies developed an antibiotic-associated erythematous rash. The table notes one study reporting these outcomes as the publications combined data from each of the 2 studies reported in each paper and did not present harms data by study.

CPAP = Continuous Positive Airway Pressure

Meta-Analysis Results

Harms Associated With Total Tonsillectomy

Frequency of primary PTH associated with total tonsillectomy in the meta-analysis was below 4 percent and with overlapping confidence bounds (Table 37). Electrocautery and harmonic scalpel were associated with the highest frequency of secondary PTH (occurring >24 hours postprocedure), with estimates of 4.2 to 4.3 percent and wide 95% Bayesian credible intervals (BCI). Readmission ranged from 0.2 percent to 6 percent. Although laser tonsillectomy was associated with the highest estimated readmissions, the confidence bounds were very wide.
Table 37. PTH and PTH-associated readmissions or revisits after total tonsillectomy: percent (95% BCI)

<table>
<thead>
<tr>
<th>Technique</th>
<th>Primary PTH</th>
<th>Secondary PTH</th>
<th>Nonoperative Revisit or Readmission</th>
<th>Reoperation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cold</td>
<td>0.7 (0.1 to 1.5)</td>
<td>3.3 (1.9 to 5.5)</td>
<td>2.7 (0.7 to 4.9)</td>
<td>1.3 (0.5 to 2.1)</td>
</tr>
<tr>
<td>Electrocautery</td>
<td>0.6 (0 to 1.5)</td>
<td>4.2 (2.4 to 6.5)</td>
<td>2.9 (0.7 to 5.3)</td>
<td>1.2 (0.5 to 1.9)</td>
</tr>
<tr>
<td>Coblation</td>
<td>1.1 (0 to 3.0)</td>
<td>2.3 (0.7 to 4.4)</td>
<td>1.4 (0.1 to 3.3)</td>
<td>1.2 (0.3 to 2.4)</td>
</tr>
<tr>
<td>Harmonic Scalpel</td>
<td>1.0 (0 to 3.3)</td>
<td>4.3 (1.8 to 7)</td>
<td>1.5 (0.2 to 3.1)</td>
<td>3.9 (1.6 to 6.9)</td>
</tr>
<tr>
<td>Laser</td>
<td>2.2 (1.0 to 5.8)</td>
<td>1.2 (0 to 3.4)</td>
<td>5.7 (0.7 to 12.6)</td>
<td>5.2 (0.2 to 13.7)</td>
</tr>
<tr>
<td>Molecular Resonance</td>
<td>0.6 (0 to 2.5)</td>
<td>1.1 (0.2 to 2.4)</td>
<td>0.2 (0.0 to 0.6)</td>
<td>0.2 (0.0 to 0.5)</td>
</tr>
<tr>
<td>Thermal Welding</td>
<td>0.5 (0 to 2.1)</td>
<td>3.6 (0.5 to 7.5)</td>
<td>2.7 (0 to 12.7)</td>
<td>0.8 (0 to 2.4)</td>
</tr>
</tbody>
</table>

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

Harms Associated With Partial Tonsillectomy

Primary PTH associated with partial tonsillectomy was predicted to be below 4 percent regardless of technique, and secondary bleeding at or below 3 percent. Data on readmissions and reoperations were sparse; thus confidence bounds are very wide, and it is difficult to predict PTH and PTH-related outcomes with any certainty (Table 38).

Table 38. PTH and PTH-associated readmissions or revisits after partial tonsillectomy: percent (95% BCI)

<table>
<thead>
<tr>
<th>Technique</th>
<th>Primary PTH</th>
<th>Secondary PTH</th>
<th>Nonoperative Revisit or Readmission</th>
<th>Reoperation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cold</td>
<td>1.5 (0 to 4.7)</td>
<td>2.3 (1 to 5.9)</td>
<td>3.7 (0.1 to 10.3)</td>
<td>0.5 (0 to 1.3)</td>
</tr>
<tr>
<td>Electrocautery</td>
<td>1.5 (0 to 5.3)</td>
<td>3 (0.2 to 8)</td>
<td>4 (0.2 to 12.3)</td>
<td>0.4 (0 to 1.2)</td>
</tr>
<tr>
<td>Coblation</td>
<td>1.5 (0.1 to 4.2)</td>
<td>1.4 (1 to 3.5)</td>
<td>1.4 (0.1 to 3.1)</td>
<td>0.4 (0 to 1.1)</td>
</tr>
<tr>
<td>Harmonic Scalpel</td>
<td>2.2 (0 to 8.3)</td>
<td>3 (1 to 7.9)</td>
<td>2.1 (0 to 6.3)</td>
<td>1.4 (0 to 3.9)</td>
</tr>
<tr>
<td>Laser</td>
<td>3.9 (0 to 12.9)</td>
<td>0.7 (0 to 2.4)</td>
<td>7.3 (0.2 to 20.7)</td>
<td>1.8 (0 to 5.4)</td>
</tr>
<tr>
<td>Molecular Resonance</td>
<td>1.4 (0 to 6)</td>
<td>0.8 (0 to 2.3)</td>
<td>0.3 (0 to 1)</td>
<td>0.1 (0 to 2)</td>
</tr>
<tr>
<td>Thermal Welding</td>
<td>1 (0 to 4.5)</td>
<td>2.6 (0 to 7.7)</td>
<td>3.4 (0 to 17)</td>
<td>0.3 (0 to 1)</td>
</tr>
</tbody>
</table>

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

Case Series and Database Analyses

Overall, 2.1 percent of children in case series experienced a PTH episode (Appendix H). Few children in these studies required readmission or reoperation for PTH (0.41% to 0.72%). Few cases of revisits for pain, dehydration, or PONV (ranging from 1% to 11%) were reported in the 11 studies providing data. At least four deaths were reported across four case series or database studies reporting mortality. In one study, a 10-year old child with muscular dystrophy and other comorbidities died from suspected ventricular fibrillation one month after tonsillectomy; investigators did not consider the death related to
surgery. In another, a 42-month old child with recurrent PTH died from bleeding-related shock after he was discharged 6 days post-tonsillectomy.252,253,290 Another database study reported two deaths (out of 36,221 tonsillectomies, 0.006%) but did not report cause of death.247 Finally, another database study did not report exact numbers or cause of death but compared tonsillectomy complications occurring in different hospital types (teaching or nonteaching children’s hospitals, nonteaching hospitals).370 In each hospital type ≤10 deaths occurred, but the study does not report specific numbers.

Other harms reported in these studies were disparate and typically not clinically significant (Appendix H). One registry specifically examined the rate of reoperation following partial vs. total tonsillectomy and reported a greater risk of reoperation after partial tonsillectomy (hazard ratio=7.16, 95% CI: 5.52 to 9.13).569 Seventy-five of 11,741 (0.6%) children who underwent total tonsillectomy required reoperation compared with 609 of 15,794 who underwent partial (3.9%, p<0.0001). The most common indication for reoperation after either type of tonsillectomy was upper airway obstruction (80% of cases). Three studies reported respiratory-related harms (Appendix H). In one database study, 383 out of 40,591 children had respiratory failure requiring mechanical ventilation (0.94%).270 In another database study evaluating outcomes in 21,434 obese or non-obese children undergoing tonsillectomy, 5 percent of obese children had major respiratory complications (pulmonary insufficiency, respiratory failure) compared with 3 percent of non-obese children.228 One case series including 1735 children reported postoperative desaturation, pulmonary edema, or lung collapse in 13 children (0.75%).238

**Key Question 5. Effectiveness of Perioperative Medications To Improve Outcomes**

**Key Points**

- 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 low frequency of PTH and 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).
- 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 return to normal diet or activity or non-PTH-related readmissions or revisits (insufficient strength of evidence).
• 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-hydroxytryptamine (5-HT) perioperative antiemetics on postoperative analgesia requirements. We have moderate confidence in this conclusion (moderate strength of evidence).

Overview of the Literature
Forty-nine studies (48 RCTs and one nonrandomized trial) involving 5817 children ranging in age from less than 1 to 18 years addressed perioperative medications (NSAIDs, steroids, antiemetics, alone or in combination) for improving post-tonsillectomy outcomes (Table 39). Studies were primarily conducted in Asia (including China, India, Turkey, and Japan). Six studies were conducted in Europe, and six in North America (United States). Six studies were conducted in Africa, and one in Australia.

Twenty-three studies had low risk of bias; 21 had moderate; and five had high. Major sources of bias in these studies included unclear methods for randomization and for concealment of study group allocation. We do not discuss high risk of bias studies in the detailed analyses below.

Outcomes reported varied among studies: PTH, use of rescue medications, and use of rescue antiemetics were most frequently reported.
Table 39. Overview of studies addressing perioperative pharmacologic agents to improve outcomes

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>NSAIDs</th>
<th>Steroids</th>
<th>Antiemetics</th>
<th>Multi-agent Therapy</th>
<th>Total Literature</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Study design</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>RCT</td>
<td>14</td>
<td>18</td>
<td>6</td>
<td>10</td>
<td>48</td>
</tr>
<tr>
<td>Nonrandomized trial</td>
<td>0</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td><strong>Surgical Indication</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Throat Infection</td>
<td>2</td>
<td>0</td>
<td>0</td>
<td>2</td>
<td>4</td>
</tr>
<tr>
<td>OSDB +Throat Infection</td>
<td>0</td>
<td>6</td>
<td>0</td>
<td>1</td>
<td>7</td>
</tr>
<tr>
<td>Unspecified</td>
<td>11</td>
<td>12</td>
<td>5</td>
<td>10</td>
<td>38</td>
</tr>
<tr>
<td><strong>Key Effectiveness Outcomes Reported</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rescue analgesics</td>
<td>7</td>
<td>12</td>
<td>1</td>
<td>11</td>
<td>31</td>
</tr>
<tr>
<td>Rescue antiemetics</td>
<td>1</td>
<td>12</td>
<td>2</td>
<td>7</td>
<td>22</td>
</tr>
<tr>
<td>Time to return to normal diet/activity</td>
<td>2</td>
<td>2</td>
<td>0</td>
<td>3</td>
<td>7</td>
</tr>
<tr>
<td><strong>Risk of Bias</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Low</td>
<td>3</td>
<td>8</td>
<td>5</td>
<td>7</td>
<td>23</td>
</tr>
<tr>
<td>Moderate</td>
<td>9</td>
<td>6</td>
<td>0</td>
<td>6</td>
<td>21</td>
</tr>
<tr>
<td>High</td>
<td>1</td>
<td>4</td>
<td>0</td>
<td>0</td>
<td>5</td>
</tr>
<tr>
<td><strong>Total N participants</strong></td>
<td>1103</td>
<td>2368</td>
<td>1040</td>
<td>1306</td>
<td>5817</td>
</tr>
</tbody>
</table>

*Combination of drug classes. NSAIDs = nonsteroidal anti-inflammatory drugs; OSDB = obstructive sleep-disordered breathing; RCT = randomized controlled trial

**Detailed Analysis**

Most studies addressed the outcomes of time to return to 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. We discuss findings by agent and key outcome below. Appendix H includes a detailed table of findings for each study.

**NSAIDs**

**Return to Normal Diet and Activity**

In two RCTs with moderate risk of bias comparing diclofenac suppository with or without other analgesics (acetaminophen plus tramadol) to lidocaine\textsuperscript{72} or placebo,\textsuperscript{126} time to resume normal activity or diet did not differ significantly between groups.
Need for Rescue Analgesics

**Diclofenac**

**Analgesics.** Two low risk of bias RCTs evaluated perioperative diclofenac. Two RCTs compared diclofenac suppository to placebo. In both, consumption of opioids was significantly lower in diclofenac groups. Another study comparing oral gabapentin, diclofenac suppository, and placebo found the mean 24h opioid consumption was equivalent in gabapentin and diclofenac groups but significantly less than placebo.

Other trials were not placebo-controlled and used a variety of comparative treatments. One that compared 2 percent viscous lidocaine post-tonsillectomy vs. diclofenac suppository reported no difference in analgesic need during the immediate 2 postoperative hours. Another study comparing diclofenac suppository vs. intravenous pethidine found fewer children in the diclofenac arm required analgesia medication and used a significantly lower mean paracetamol dose in the first 24 postoperative hours. A third trial compared triple analgesic regimen (diclofenac suppository, IV paracetamol, and IV tramadol) vs. placebo and reported that, in the immediate 4-6 postoperative period, no child in study group used rescue analgesia compared with 70 percent and 45 percent of controls who required rescue analgesia in the PACU and on the day surgery ward, respectively.

**Antiemetics.** A single moderate risk of bias study that evaluated effectiveness of peritonsillar bupivacaine infiltration vs. diclofenac suppository reported no difference in antiemetic rescue use between arms.

**Ibuprofen**

**Analgesics.** Three moderate risk of bias RCTs compared the effect of perioperative ibuprofen treatment vs. multiple different comparators and assessed postoperative analgesic requirements. Two evaluated IV ibuprofen, while one used ibuprofen syrup. One trial comparing IV paracetamol alone, IV paracetamol + mefenamic acid, and IV paracetamol + ibuprofen reported that over the 24 hour followup period, the ibuprofen group used significantly less postoperative analgesia than paracetamol alone. A second trial compared single dose IV ibuprofen vs. placebo and assessed opioid use in the PACU. In intent to treat analysis, percentage of opioid use did not differ between groups, mean number of rescue opioid doses, or mean dose. Another trial compared ibuprofen syrup (administered 1 hour pre-operatively) + peritonsillar infiltrated epinephrine vs. infiltrated lidocaine with epinephrine and reported no differences in mean paracetamol dose between arms.

**Ketoprofen**

**Analgesics.** Two low risk of bias RCTs evaluated the post-tonsillectomy analgesic use among patients treated with ketoprofen vs. placebo. Study results differed. In one trial, no difference was observed in mean dose or proportion of patients receiving analgesia between those treated with IV ketoprofen at induction, IV ketoprofen after surgery, or placebo. Another RCT compared ketoprofen, tramadol, and placebo and reported that patient-controlled analgesia requests were significantly lower in the ketoprofen group. No difference was observed in 24 hour total opioid use.
Lornoxicam

**Analgesics.** A single moderate risk of bias RCT comparing IV lornoxicam, infiltrated lornoxicam, and placebo, reported rescue diclofenac consumption during first 24 hours was significantly lower in the IV group compared with either infiltration or placebo group (p<0.000). No difference was observed between infiltration and placebo groups.

Ketorolac

**Analgesics.** A single moderate risk of bias trial compared IV ketorolac vs. fentanyl and reported that fewer children in the ketorolac arm required rescue analgesia than in fentanyl arm (8% [n=2] vs. 28% [n=9]) in the immediate postoperative period in PACU. No overall difference in use of rescue medications was observed the first 24-hours postoperatively.

Steroids

**Return to Normal Diet and Activity**

Two low risk of bias RCTs assessed whether steroids affected time to return to normal diet post-tonsillectomy. One comparing IV dexamethasone vs. placebo found that those treated with steroids were ingesting a significantly higher percentage of their normal diet than those in the placebo group on postoperative day (POD) one. A second trial comparing tropisetron and tropisetron + dexamethasone found no difference in the percentage of children returning to normal diet on POD one or five.

A single low risk of bias RCT compared time to normal activity between children treated with IV dexamethasone vs. no steroid (both groups had peritonsillar infiltration of ropivacaine + clonidine) and found a nonsignificant longer time to resume normal activity in the steroid group.

**Need for Rescue Medications**

**Dose Escalation Trials**

**Analgesics.** Four low- and moderate-risk of bias RCTs evaluated the efficacy of escalating doses of dexamethasone on post-tonsillectomy analgesia requirements. Doses studied varied by trial, ranging from 0.05 to 1 mg/kg. Three of four trials of dexamethasone at escalating doses, or escalating doses and placebo, or doses of dexamethasone compared with ondansetron or placebo, showed no differences in postoperative analgesic requirements by dose.

In contrast, one placebo controlled dose-escalation trial showed that children who received dexamethasone required significantly less ibuprofen during 24 hour followup. Higher doses of dexamethasone did not significantly alter ibuprofen requirements.

**Antiemetics.** Two dexamethasone dose escalation trials assessed the postoperative need for antiemetic rescue. Both studies showed significantly reduced use in groups treated with dexamethasone vs. placebo. One compared dexamethasone 0.05, 0.15, or 0.5 mg/kg vs. placebo after induction of anesthesia and found the need for rescue antiemetic to be significantly less in all steroid arms at 24 hour followup. A second study comparing IV dexamethasone at 0.15 mg/kg, 0.5 mg/kg vs. placebo reported that the use of alizapride was significantly lower in the steroid groups than placebo. In contrast, the use of tropisetron did not differ between arms.
IV Dexamethasone Versus Placebo

Analgesics. Eight trials compared outcomes among children treated with IV dexamethasone vs. placebo.\textsuperscript{50, 105, 109, 119, 126, 146-148} This included four low risk of bias studies. Time of followup varied from assessment of PACU or surgical ward analgesic use,\textsuperscript{50, 105, 119, 126, 146} to 24 hours postoperatively,\textsuperscript{109, 147, 148} to 3 postoperative days.\textsuperscript{126} The majority of studies found steroid treatment significantly reduced postoperative analgesic requirements vs. placebo or other agents such as ropivacaine.\textsuperscript{50, 109, 146-148} However, in three studies, no differences between those treated with dexamethasone or placebo were observed.\textsuperscript{105, 109, 126}

Antiemetics. Two of five placebo-controlled studies showed reduced antiemetic use in children treated with dexamethasone.\textsuperscript{105, 109, 119, 126, 146} One trial comparing IV dexamethasone vs. placebo reported significantly lower 24 hour antiemetic requirement in the dexamethasone arm.\textsuperscript{146} Another trial that compared IV dexamethasone and placebo found no difference in antiemetic use in the PACU, but did show significantly reduced 24 hour and overall antiemetic rescue use in steroid arm.\textsuperscript{119}

In contrast, three trials demonstrated no difference in need for antiemetic rescue between dexamethasone and placebo. For example, one trial found no difference in PACU or day surgical ward use of rescue metoclopramide or ondansetron between groups.\textsuperscript{105} A second trial comparing IV dexamethasone vs. placebo (both groups receiving peritonsillar infiltration of ropivacaine + clonidine) found no group differences in antiemetic rescue use in the first 4 hours postoperatively.\textsuperscript{126} A third trial found no statistical difference in PACU need for rescue antiemetic.\textsuperscript{109}

Dexamethasone Versus Other Comparators

Analgesics. Four RCTs including one low and three moderate risk of bias studies compared postoperative analgesic requirements between IV dexamethasone and other comparators. One found no difference in PACU or 24 hour followup doses of morphine or paracetamol between those treated with a single dose of IV dexamethasone vs. IV methylprednisolone.\textsuperscript{59} Another trial that compared IV dexamethasone vs. oral gabapentin, vs. the combination for 18 hours post-tonsillectomy found that the combined treatment group had fewer rescue medication (pethidine) requirements.\textsuperscript{42} Intravenous dexamethasone was compared with IV acetaminophen in another trial that observed no difference in meperidine usage during 24 hour followup. A fourth trial compared IV dexamethasone vs. IV ketamine vs. the combination vs. placebo and found the combined therapy group had no 24-hour postoperative analgesia requirements. Both the steroid and ketamine alone groups had lower analgesia needs than placebo.\textsuperscript{62}

Antiemetics. One trial comparing IV dexamethasone vs. IV methylprednisolone observed no difference in percentage of patients receiving antiemetic medications in the PACU.\textsuperscript{59} Another study assessed effectiveness of IV dexamethasone + infiltrated ropivacaine vs. ropivacaine alone showed a significantly reduced rate of antiemetic use in the dexamethasone arm.\textsuperscript{50} Another RCT compared IV dexamethasone vs. ketamine vs. the combination, vs. placebo showed that all treatment groups had significantly lower antiemetic use (ondansetron) than placebo.\textsuperscript{62}
IV Versus Infiltrated Dexamethasone

Analgesics. Two low-risk of bias RCTs evaluated the efficacy of IV versus peritonsillar infiltrated dexamethasone with or without concomitant levobupivacaine among children undergoing tonsillectomy.39, 51 Both RCTs found infiltrated dexamethasone reduced postoperative analgesic requirements significantly.

Antiemetics. A single RCT compared IV vs. infiltrated dexamethasone vs. placebo and found use of postoperative rescue anti-emetic medications was significantly lower in both steroid groups compared with placebo.39 Investigators observed no differences between dexamethasone groups.

Infiltrated Dexamethasone Versus Placebo

Analgesics. One moderate risk of bias trial compared dexamethasone infiltration, 0.25-percent levobupivacaine with epinephrine infiltration, and saline placebo.45 The total doses of rescue analgesia were significantly fewer for dexamethasone than other groups at all time points during the first postoperative week.

Antiemetics

Need for Rescue Medications

Analgesics. Five RCTs (four low risk of bias88, 118, 132, 133 and one moderate122) evaluated the effect of perioperative antiemetic use on post-tonsillectomy analgesic requirements. All studies evaluated 5-HT receptor antagonists including ramosetron,118, 135 granisetron,132, 133 ondansetron,88, 122 and dolasetron.122 Antiemetic medications did not have any effect on pain control in any trial.

Two compared different 5-HT antagonists. In one trial, children were randomized to IV granisetron vs. ramosetron at the end of surgery and demonstrated no difference in analgesics administered 24 hour postoperatively.133 Another compared IV ondansetron vs. dolasetron, vs. placebo and found opioid use in the PACU did not differ between arms.

Two compared 5-HT antagonists to antiemetic from other classes including droperidol,132 metoclopramide.88, 132 In one trial that assessed the effectiveness of IV granisetron vs. droperidol vs. metoclopramide found no difference in analgesic use during 24 hour postoperatively.132 Another RCT compared ondansetron vs. metoclopramide and also reported no difference in opioid use in the first 24 hours.88

One dose-escalating trial of ramosetron evaluated IV placebo vs. IV ramosetron at 3, 6, or 12 microgram/kg immediately after end of surgery.118 It found no difference in 24 hour post-tonsillectomy analgesia use between groups.

Postoperative antiemetics. Three studies including two low118, 136 and one moderate122 risk of bias RCTs assessed the effect of pre-emptive antiemetic use in reducing need for postoperative antiemetic rescue. Pre-emptive use of 5-HT receptor antagonists reduced the need for immediate postoperative anti-emetic use compared with placebo.

One study that compared IV tropisetron vs. placebo found significantly reduced 24 hour need for postoperative rescue-antiemetic use in the tropisetron arm (tropisetron 1/35, placebo 12/36, p<0.01). A second trial assessed preoperative IV ondansetron vs. dolasetron vs. placebo with each group pretreated with dexamethasone.122 Both 5-HT receptor antagonists had significantly
less antiemetic rescue needs in PACU than placebo (ondansetron 4%, dolasetron 6%, placebo 22%, p<0.05). No child in any arm required antiemetic rescue in the 48 hours post-PACU. However, the overall antiemetic rescue requirement was significantly less overall for 5-HT receptor antagonists (ondansetron 4%, dolasetron 8%, placebo 24%, p<0.05). A third trial compared placebo vs. escalating ramosetron doses (3, 6, or 12 μg/kg). Requirement for antiemetic rescue in first 24 hours were 30 percent for placebo, 25 percent for 3 μg/kg (p=NS), while none required rescue in higher dose ramosetron arms. Similarly, during 24-48 hour followup, 25 percent of placebo and 25 percent of the 3 μg/kg-ramosetron arm required rescue antiemetic, while none in higher dose arms needed it.

Harms Associated With Perioperative Medications

PTH

Seventeen studies provided data on PTH associated with perioperative medications for pain. PTH frequency overall ranged from 0 percent to 8.9 percent, with higher PTH frequency reported in patients who received anesthetics and steroids than those in other perioperative medications.

NSAIDs. Few studies of NSAIDs (6 studies, 7 treatment arms) reported PTH (6 PTH in 277 treated children, 2.6%). 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. Dexamethasone was the most commonly used steroid (9/10 studies). The tenth study used methylprednisolone. Three steroid studies explicitly noted no PTH, and three did not explicitly note number of bleeds but reported that no children receiving steroids had revisits or reoperation for PTH. Another study did not explicitly note number of bleeds but reported that one child in the placebo and one in the steroid arm required reoperation.

In one study comparing dexamethasone with placebo, 17 children in the steroid arm and 13 in the placebo arm had PTH (p=NR). Revisits and reoperations differed significantly between groups, with more revisits occurring in the placebo arm (3.2% vs. 1.9%, p<0.001) but more reoperations for hemostasis in the steroid arm (1.9% vs. 0.6%, p=0.002). In another RCT comparing 3 doses of dexamethasone (0.05, 0.15, or 0.5 mg/kg) with placebo, dexamethasone decreased the incidence of PONV but increased the risk of PTH. In total 22 children experienced 26 PTH episodes, which included any PTH, with or without evidence at clinical examination (placebo, n=2, dexamethasone 0.05 mg, n=6, dexamethasone 0.15 mg, n=2, and dexamethasone 0.5 mg, n=12, p=.003). The highest dose of dexamethasone was associated with the greatest PTH risk (adjusted RR compared with placebo=6.80; 95% CI: 1.77 to 16.5, p=0.05). Eight children, all receiving steroids, required reoperation for hemostasis. In a third study comparing dexamethasone with placebo, two children in each arm had PTH requiring readmission but not reoperation for hemostasis.

We combined nine studies comparing dexamethasone with placebo in a random effects meta-analysis to assess effects on risk of PTH. These studies comprised eight RCTs with low, moderate, and high risk of bias and one nonrandomized trial with high risk of bias. We retained high risk of bias studies as an analysis indicated no systematic effects on the

71
model. To account for the relatively high number of zero cases of PTH in the data, we used a zero-inflated binomial model. Sixteen percent of studies had no PTH; among the 84 percent that did, the odds of primary, secondary, and undefined (either primary or secondary) PTH and PTH-associated reoperation or readmission were each nominally $\geq 1$, with wide 95% credible intervals (Table 40). Pooling the outcomes did not systematically affect the estimates. These wide intervals prohibit firm conclusions about the effects of dexamethasone on PTH. Table 41 lists the unadjusted frequency of PTH in these studies.

Table 40. Odds estimates in meta-analysis of PTH risk associated with perioperative dexamethasone compared with placebo

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Odds Ratio</th>
<th>95% Credible Interval</th>
</tr>
</thead>
<tbody>
<tr>
<td>Primary PTH</td>
<td>1.9</td>
<td>0.03 to 6</td>
</tr>
<tr>
<td>Secondary PTH</td>
<td>1.3</td>
<td>0.04 to 3.3</td>
</tr>
<tr>
<td>Undefined PTH</td>
<td>2.1</td>
<td>0.9 to 3.7</td>
</tr>
<tr>
<td>PTH-associated revisit or readmission</td>
<td>1.0</td>
<td>0.1 to 2.2</td>
</tr>
<tr>
<td>PTH-associated reoperation</td>
<td>3.1</td>
<td>0.3 to 7.8</td>
</tr>
</tbody>
</table>

Other medications. Among arms addressing anesthetics (reported in two studies$^{45, 161}$), four cases of PTH occurred with bupivacaine in one study,$^{161}$ and none with levobupivacaine.$^{45}$ No PTH was reported with non-NSAID analgesics (propacetamol, fentanyl) in the two studies addressing these agents.$^{117, 150}$

Table 41. Unadjusted PTH-related outcomes in study arms evaluating perioperative medications for pain

<table>
<thead>
<tr>
<th>Drug Class (n arms)</th>
<th>Total N</th>
<th>Total PTH (%)</th>
<th>Total Primary PTH (%)</th>
<th>Total Secondary PTH (%)</th>
<th>Total Other/ Undefined PTH (%)</th>
<th>Total Non-operative Readmission or Revisit for PTH (%)</th>
<th>Total Re-operation for PTH (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>All arms</td>
<td>1839</td>
<td>69 (3.8)</td>
<td>4 (0.7)</td>
<td>3 (0.66)</td>
<td>61 (4.3)</td>
<td>13 (1.4)</td>
<td>14 (1.2)</td>
</tr>
<tr>
<td>Steroids (14)</td>
<td>811</td>
<td>38 (4.7)</td>
<td>2 (0.61)</td>
<td>0 (0)</td>
<td>36 (5.3)</td>
<td>4 (0.84)</td>
<td>11 (1.8)</td>
</tr>
<tr>
<td>Placebo (12)</td>
<td>672</td>
<td>21 (3.3)</td>
<td>2 (0.89)</td>
<td>3 (1.8)</td>
<td>16 (3.6)</td>
<td>9 (2.1)</td>
<td>2 (0.43)</td>
</tr>
<tr>
<td>NSAIDs (7)</td>
<td>227</td>
<td>6 (2.6)</td>
<td>NR</td>
<td>NR</td>
<td>5 (2.96)</td>
<td>0 (0)</td>
<td>1 (0.93)</td>
</tr>
<tr>
<td>Anesthetics (2)</td>
<td>45</td>
<td>4 (8.9)</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td>4 (8.9)</td>
<td>0 (0)</td>
<td>NR</td>
</tr>
<tr>
<td>Non-NSAID Analgesics (3)</td>
<td>84</td>
<td>0 (0)</td>
<td>NR</td>
<td>0 (0)</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
</tr>
</tbody>
</table>

Note: Percentages for primary and secondary PTH, readmissions/revisits, and reoperations reflect the number of each instance of bleeding or reencounter divided by the total number of patients in the studies reporting such data, and not in the total number of participants across all studies in a given row.

Concordance With Case Series and Database Studies

Four case series or database studies reported PTH associated with perioperative medications.$^{230, 234-236, 271}$ One study evaluated differences in PTH requiring reoperation among children ($\leq$ age 15) who had (n=1680) and had not (n=30254) received perioperative steroids (intravenous dexamethasone or hydrocortisone).$^{230}$ Most children had obstructive symptoms (over 65% in each arm), and 20 children in the steroid arm (1.2%) and 140 control children (0.5) had PTH requiring reoperation ($p<0.001$). Steroid use was associated with an increased rate of reoperation in children but not in adults in this study (OR for children=2.50, 95% CI: 1.47 to 4.23, $p=0.001$). Age was also noted as a risk factor in children (OR=1.10, 95% CI: 1.04 to 1.17,
p<0.001) but the direction of effect was not clearly reported. Female children were also less likely to require reoperation than male (OR=0.73, 95%CI: 0.54 to 1.00, p=0.05).230

Another study evaluating adherence to 2011 AAO-HNSF guideline recommendations related to perioperative dexamethasone and antibiotic use also reported PTH associated with these medications.234 Out of all 15950 children (1-18 years of age) included in analyses, 432 experienced PTH (2.7%). PTH occurred in 92 of 7432 children in the pre-guideline era (1.2%) and in 229 of 8518 children after guidelines were issued (2.7%). Differences between physicians or hospitals that did or did not use these medications perioperatively, either before or after the publication of guidelines, were not significant.

Another study assessed how well hospitals adhered to evidence-based process measures including use of perioperative dexamethasone and antibiotics using data from the Pediatric Health Information System database and reported a significantly greater risk of PTH-associated revisits in children who received dexamethasone (3.11%, 95% CI: 2.99% to 3.23%) compared with those who did not (2.71%, 95% CI: 2.50% to 2.91%; standardized difference=0.40%, 95% CI: 0.13% to 0.67%, p=0.003). A final case series evaluated PTH after tonsillectomy with perioperative ibuprofen and reported 98 readmissions for PTH among 2697 children (3.6%).271 Fifty-eight children (2.2%) required reoperation for hemostasis.

**Non-PTH Revisits**

Few studies evaluating perioperative agents reported any revisits for non-PTH indications39, 52, 112, 119, 121, 148 (Table 42); in 8 of 11 study arms, no revisits or readmissions occurred. Higher, though still low, frequency of revisits typically occurred with combination agents such as dexamethasone plus antiemetics122 or in placebo arms.112, 122, 148 In one study that compared perioperative IV dexamethasone with placebo, four children in the placebo arm (11%) were readmitted for dysphagia and throat pain compared with none in the dexamethasone arm (p=NR).148

Table 42. Unadjusted revisits or readmissions for pain, dehydration, and PONV reported in comparative study arms addressing perioperative agents

<table>
<thead>
<tr>
<th>Drug Class (N arms)</th>
<th>Total Arm N</th>
<th>N Pain Revisits/Readmissions (%)</th>
<th>N Dehydration Revisits/Readmissions (%)</th>
<th>N PONV Revisits/Readmissions (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>All arms (11)</td>
<td>542</td>
<td>4 (1.1)</td>
<td>1 (0.33)</td>
<td>1 (0.26)</td>
</tr>
<tr>
<td>Steroids (5)</td>
<td>279</td>
<td>0</td>
<td>1 (1.6)</td>
<td>0</td>
</tr>
<tr>
<td>NSAIDs (1)</td>
<td>20</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Anesthetic (1)</td>
<td>80</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Placebo (4)</td>
<td>163</td>
<td>4 (6.9)</td>
<td>0</td>
<td>1 (1.4)</td>
</tr>
</tbody>
</table>

Note: Percentages for readmissions/revisits reflect the number of each instance of reencounter divided by the total number of patients in the studies reporting such data, and not in the total number of participants across all studies in a given row.

N = number; NSAID = nonsteroidal anti-inflammatory drug; PONV = postoperative nausea and vomiting

**Key Question 6. Effectiveness of Postoperative Medications To Reduce Pain-Related Outcomes After Tonsillectomy**

**Key Points**
- Few studies of postoperative medications addressed the same intervention and outcomes, limiting our ability to make conclusions about this body of literature.
- 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).
- In studies of postoperative steroids, we found no difference in effects on bleeding between steroids and placebo or no treatment. Our confidence in this conclusion is low (low strength of evidence).

**Overview of the Literature**

Of 13 studies addressing postoperative medications for pain-related outcomes identified, 11 were RCTs, and two were nonrandomized trials (Table 43). Study country of origin included New Zealand, Canada, Denmark, Serbia, Egypt, Pakistan, Jordan, and South Korea. Studies included a total of 2660 children ranging in age from 1 to 18 years.

Studies assessed three categories of postoperative medications: analgesics (n=9), steroids (n=2), and antibiotics (n=2). Specific analgesics considered included nonsteroidal anti-inflammatory drugs (NSAID), acetaminophen, morphine, benzylamine oral rinse plus ibuprofen, and metamizole. Two studies evaluated oral prednisolone and two evaluated the effect of amoxicillin + clavulanic acid (one comparing it to cefaclor) on postoperative outcomes.

Indication for tonsillectomy varied among studies. Most included a combination of patients with recurrent infection and OSDB (n=4). One study enrolled children with recurrent tonsillitis, and several studies did not specify tonsillectomy indication(s) (n=8). All but three trials had low or moderate risk of bias, and were included in further analyses. Major sources of bias in these studies included use of unblinded outcome assessors and unclear methods for concealment of study group allocation.
Table 43. Overview of studies addressing postoperative medications for pain-related outcomes

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>RCTs</th>
<th>Nonrandomized Trials</th>
<th>Total Literature</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Comparisons</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Acetaminophen vs. Non-NSAID Analgesic or Acetaminophen</td>
<td>4</td>
<td>0</td>
<td>4</td>
</tr>
<tr>
<td>Acetaminophen vs. NSAID</td>
<td>2</td>
<td>1</td>
<td>3</td>
</tr>
<tr>
<td>Steroid vs. Placebo or No Steroid</td>
<td>2</td>
<td>0</td>
<td>2</td>
</tr>
<tr>
<td>NSAID vs. Placebo</td>
<td>1</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Other*</td>
<td>2</td>
<td>1</td>
<td>3</td>
</tr>
<tr>
<td><strong>Surgical Indication</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Throat Infection</td>
<td>1</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>OSDB + Throat Infection</td>
<td>3</td>
<td>1</td>
<td>4</td>
</tr>
<tr>
<td>Unspecified</td>
<td>7</td>
<td>1</td>
<td>8</td>
</tr>
<tr>
<td><strong>Effectiveness Outcomes Frequently Reported</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rescue analgesic use</td>
<td>5</td>
<td>1</td>
<td>6</td>
</tr>
<tr>
<td>Time to return to normal diet/activity</td>
<td>5</td>
<td>1</td>
<td>6</td>
</tr>
<tr>
<td>Quality of life</td>
<td>1</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td><strong>Risk of Bias</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Low</td>
<td>4</td>
<td>0</td>
<td>4</td>
</tr>
<tr>
<td>Moderate</td>
<td>5</td>
<td>1</td>
<td>6</td>
</tr>
<tr>
<td>High</td>
<td>2</td>
<td>1</td>
<td>3</td>
</tr>
<tr>
<td><strong>Total N participants</strong></td>
<td>2200</td>
<td>440</td>
<td>2660</td>
</tr>
</tbody>
</table>

*Antibiotic vs. no antibiotic or antibiotic vs. antibiotic vs. placebo or benzydamine oral rise vs. other oral rinse

N = Number; NSAID = Nonsteroidal Anti-Inflammatory Drug; OSDB = Obstructive Sleep-Disordered Breathing; RCT = Randomized Controlled Trial

**Detailed Analysis**

Only four studies evaluating postoperative analgesic medications provided effectiveness outcomes, which included need for rescue medication and return to normal diet. Four studies reported postoperative PTH or harms outcomes, but no effectiveness data.

**Analgesics**

**Pain-Related Outcomes**

Studies investigating the need for postoperative rescue medication after tonsillectomy considered different treatment comparisons. One RCT (moderate risk of bias) randomized 282 children to celecoxib given preoperatively (6mg/kg) and twice daily (3mg/kg) postoperatively for 5 doses or placebo. Children who received celecoxib had lower mean consumption of acetaminophen on postoperative days (POD) 0-2 (celecoxib 78 vs. placebo 97 mg/kg, p=0.03), but no difference in mean morphine consumption (celecoxib 0.56 vs. placebo 0.70 mg/kg, p=NS).

Another low risk of bias trial randomized 152 children who underwent tonsillectomy to acetaminophen + ibuprofen, acetaminophen alone, or ibuprofen alone (60mg per 5 mL suspension) for postoperative pain control. Groups did not differ in the use of rescue analgesia in the recovery room, but after discharge from the recovery room during postoperative days 0-2, fewer patients required rescue analgesia (i.e., acetaminophen + ibuprofen) in the combination group than in the other arms (0% combined, 16% acetaminophen, 15% ibuprofen). A third study (moderate risk of bias) compared postoperative treatment with acetaminophen or diclofenac...
(dose NR) to be administered every 8 hours or as needed for pain.\textsuperscript{159} Mean analgesic use did not differ between groups in the first 24 hours. All trials assessing analgesia outcomes had short-term followup ranging from 24 to 48 hours postoperatively and assessed a heterogeneous group of medications. Available data are conflicting as to whether postoperative use of NSAIDs (celecoxib, ibuprofen, diclofenac) decreases rescue pain medication requirement in the first 24-48 hours among children post-tonsillectomy. Longer-term effectiveness of these medications cannot be gleaned from currently available data (Table 44).

Table 44. Need for rescue medications reported in studies of postoperative medications

<table>
<thead>
<tr>
<th>Author, Year</th>
<th>Study Type</th>
<th>Risk of Bias</th>
<th>Comparison Groups (N)</th>
<th>Need for Rescue Medications</th>
</tr>
</thead>
<tbody>
<tr>
<td>Merry 2013\textsuperscript{39}</td>
<td>RCT</td>
<td>Low ROB</td>
<td>G1: Acetaminophen 120 mg+ ibuprofen 60 mg/5mL suspension (52) G2: Acetaminophen 120 mg/5 mL suspension (49) G3: Ibuprofen 60 mg/5 mL suspension (51)</td>
<td>\textbf{N requiring rescue analgesia, (%)} In PACU G1: 1 (2) G2: 1 (2) G3: 1 (2) Post-PACU discharge G1: 0 G2: 8 (16) G3: 8 (15)</td>
</tr>
<tr>
<td>Monem 2005\textsuperscript{49}</td>
<td>RCT</td>
<td>Moderate ROB</td>
<td>G1: Acetaminophen (32) G2: Diclofenac (34)</td>
<td>\textbf{N requiring additional analgesia, (%)} G1: 3 (9) G2: 2 (6) No significant group differences in total analgesic use in first postoperative day or in at-home antiemetic use</td>
</tr>
<tr>
<td>Murto 2015\textsuperscript{59}</td>
<td>RCT</td>
<td>Moderate ROB</td>
<td>G1: Celecoxib (141) G2: Placebo (141)</td>
<td>\textbf{Analgesic consumption} \begin{itemize} \item No group differences in opioid consumption in PACU \item No group differences in cumulative co-analgesic consumption in postoperative days 0-7 \item No group differences in N morphine-free patients \end{itemize} \textbf{Postoperative day 0-2 acetaminophen consumption, mean} G1: 78 mg/kg\textsuperscript{-1} (95% CI: 68 to 89) G2: 97 mg/kg\textsuperscript{-1} (95% CI: 85 to 109) G1 vs. G2: p=0.03 \textbf{Postoperative day 0-2 morphine consumption} G1: 0.56 mg/kg\textsuperscript{-1} (95% CI: 0.47 to 0.65) G2: 0.70 mg/kg\textsuperscript{-1} (95% CI: 0.59 to 0.81) G1 vs. G2: p=NS</td>
</tr>
</tbody>
</table>

CI=Confidence Interval; G=Group; kg = Kilogram; mg = Milligram; N=Number; NR=Not Reported; NS=Not Significant; PACU=Post-Anesthesia Care Unit; RCT=Randomized Controlled Trial; ROB=Risk of Bias

Return to Normal Diet

Return to normal diet was evaluated and defined differently in two studies (Table 45). In one RCT with low risk of bias, 91 children (1-10 years of age) with OSDB with or without recurrent tonsillitis undergoing tonsillectomy were randomized to postoperative acetaminophen + ibuprofen or acetaminophen + morphine.\textsuperscript{155} Both groups used pain medications for a mean of 4 postoperative days (ibuprofen 4.64 vs. morphine 4.04 days). No difference was observed in days to return to preoperative diet between arms (morphine 7.31 vs. ibuprofen 7.17 days, p=0.89).
Another moderate risk of bias trial randomized children undergoing tonsillectomy to postoperative acetaminophen or diclofenac.\(^{159}\) Children in the acetaminophen group had faster return to normal oral intake compared with those getting diclofenac, and this reached significance on the first 5 postoperative days. Altogether, current data do not consistently indicate a differential return to preoperative/normal diet among children treated with NSAIDs (i.e., ibuprofen, diclofenac), morphine, or acetaminophen.

### Table 45. Return to normal diet or activity in studies of postoperative medications

<table>
<thead>
<tr>
<th>Author, Year</th>
<th>Study Type</th>
<th>Groups (N)</th>
<th>Risk of Bias</th>
<th>Comparison Groups</th>
<th>Time to Return to Normal Diet/Activity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Watanabe 2015(^{159})</td>
<td>RCT</td>
<td>Low ROB</td>
<td>G1: Acetaminophen + morphine (46) G2: Acetaminophen + ibuprofen (38)</td>
<td></td>
<td>N days to return to preoperative diet, mean±SD G1: 7.31±3.82 G2: 7.17±5.23 G1 vs. G2: p=NS</td>
</tr>
<tr>
<td>Monem 2005(^{159})</td>
<td>RCT</td>
<td>Moderate ROB</td>
<td>G1: Acetaminophen (32) G2: Diclofenac (34)</td>
<td></td>
<td>Significantly greater percent of normal diet consumed in G1 vs. G2, p &lt; 0.05</td>
</tr>
</tbody>
</table>

G = Group; NR = Not Reported; NS = Not Significant; RCT = Randomized Controlled Trial; ROB = Risk of Bias; SD = Standard Deviation

### Steroids

#### Return to Normal Diet

Two RCTs evaluated the effectiveness of postoperative prednisolone in children undergoing tonsillectomy (Table 46).\(^{41,60}\) In one trial (low risk of bias) 138 children (≥4 years of age) undergoing elective tonsillectomy for tonsillitis or hypertrophy were randomized to oral prednisolone (0.25 mg/kg/day) for seven postoperative days or no prednisolone.\(^{41}\) No difference in type of diet (i.e., none, fluid, soft, normal) was seen between arms on POD 1 (p=0.30); however, significantly more children had normal diet (46% vs. 25%, p < 0.001) and a higher activity level in the prednisolone arm on postoperative day 7 (p=0.004). No difference between groups in either diet or activity was present on postoperative day 14. Although not reported specifically for children, outcomes did differ based on tonsillectomy indication. In a stratified post hoc analysis, those undergoing tonsillectomy for OSDB were significantly more likely to have normal diet and improved activity by postoperative day 7 if treated postoperatively with prednisolone compared with controls. These associations were not observed in patients whose indication was recurrent tonsillitis.

A second trial (low risk of bias) randomized 215 children to a 5-day postoperative course of prednisolone (0.5 mg/kg up to 20 mg/day) or placebo.\(^{60}\) Time to return to preoperative diet or activity did not differ between groups (p values > 0.2). Overall, data from these studies provide inconsistent evidence that postoperative treatment with oral prednisolone decreases time to return to preoperative/normal diet or activity level.
Table 46. Time to return to normal diet or activity in studies addressing postoperative steroids

<table>
<thead>
<tr>
<th>Author, Year</th>
<th>Study Type</th>
<th>Risk of Bias</th>
<th>Comparison Groups (N)</th>
<th>Time to Return to Normal Diet/Activity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Park 2015</td>
<td>RCT</td>
<td>Low ROB</td>
<td>G1: Prednisolone 0.25 mg/kg/day (69) G2: No prednisolone (69)</td>
<td>Normal diet at day 14 postoperative, N (%) G1: 64 (93) G2: 65 (94) G1 vs. G2: p=NS</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Normal activity at day 14, N (%)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>G1: 69 (100) G2: 66 (96) G1 vs. G2: p=NS</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Time to normal activity G1 vs. G2: p=NS</td>
</tr>
</tbody>
</table>

G=group; NR=not reported; NS=not significant; RCT=randomized controlled trial; ROB=risk of bias

Harms Associated With Postoperative Medications

PTH

Six studies of low or moderate risk of bias addressed postoperative medications for pain and reported PTH-related outcomes.\(^{38, 41, 60, 115, 138, 194}\) PTH occurred in less than 10 percent of children overall (Table 47). In steroid studies 8.1 percent of children had PTH overall, but numbers of PTH in steroid and placebo arms in the two studies addressing that comparison were similar (n\(^{PTH}\) in steroid arms=13, n\(^{placebo/no treatment arms}\)=15).\(^{41, 60}\) Frequency of PTH in studies comparing NSAIDs (celecoxib, ibuprofen) to placebo or other medications were also similar (n\(^{PTH}\) in NSAID arms=14, n\(^{comparison arms}\)=16).\(^{38, 194}\) Frequency of PTH were similar among studies of non-NSAID analgesics (2%-4%).\(^{115, 138, 194}\) One NSAID study did not specify adverse effects assessed but noted that no events occurred in children receiving either diclofenac or placebo.\(^{190}\)

Table 47. Unadjusted PTH-related outcomes in study arms evaluating postoperative medications for pain

<table>
<thead>
<tr>
<th>Drug Class (n arms)</th>
<th>Total N</th>
<th>Total PTH (%)</th>
<th>Total Primary PTH (%)</th>
<th>Total Secondary PTH (%)</th>
<th>Total Other/Undefined PTH (%)</th>
<th>Total Nonoperative Readmission or Revisit for PTH (%)</th>
<th>Total Reoperation for PTH (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>All arms (13)</td>
<td>2063</td>
<td>97 (4.7)</td>
<td>12 (1.4)</td>
<td>15 (1.8)</td>
<td>70 (5.7)</td>
<td>18 (3.8)</td>
<td>17 (1.2)</td>
</tr>
<tr>
<td>Non-NSAID analgesics (4)</td>
<td>772</td>
<td>23 (3.0)</td>
<td>7 (1.7)</td>
<td>2 (0.49)</td>
<td>14 (3.9)</td>
<td>NR</td>
<td>3 (0.47)</td>
</tr>
<tr>
<td>NSAIDs (3)</td>
<td>679</td>
<td>32 (4.7)</td>
<td>5 (1.2)</td>
<td>13 (3.1)</td>
<td>14 (5.5)</td>
<td>8 (5.7)</td>
<td>12 (1.8)</td>
</tr>
<tr>
<td>No treatment/Placebo (3)</td>
<td>312</td>
<td>23 (7.4)</td>
<td>NR</td>
<td>NR</td>
<td>23 (7.4)</td>
<td>9 (3.7)</td>
<td>2 (1.4)</td>
</tr>
<tr>
<td>Steroids (2)</td>
<td>160</td>
<td>13 (8.1)</td>
<td>NR</td>
<td>NR</td>
<td>13 (8.1)</td>
<td>1 (1.1)</td>
<td>NR</td>
</tr>
<tr>
<td>Other (1)</td>
<td>140</td>
<td>6 (4.3)</td>
<td>NR</td>
<td>NR</td>
<td>6 (4.3)</td>
<td>NR</td>
<td>NR</td>
</tr>
</tbody>
</table>

Note: Percentages for primary and secondary PTH, readmissions/revisits, and reoperations reflect the number of each instance of bleeding or reencounter divided by the total number of patients in the studies reporting such data, and not in the total number of participants across all studies in a given row.

N = Number; NR = Not Reported; NSAID = Nonsteroidal Anti-Inflammatory Drug; PTH = Post-Tonsillectomy Hemorrhage
Discussion

State of the Literature

We identified 218 unique studies addressing the benefits and harms of tonsillectomy (which we consider to encompass tonsillectomy, adenotonsillectomy, partial tonsillectomy or tonsillotomy). These unique studies (reported in multiple publications) comprised 141 randomized controlled trials (RCTs), 12 nonrandomized trials, seven prospective and five retrospective cohort studies, and 53 database or registry studies or case series including at 1000 children. Key Questions (KQs) addressed in this review assessed the likelihood that tonsillectomy will improve clinical outcomes around throat infections and sleep disorders; the risk of harm associated with tonsillectomy, primarily post-tonsillectomy hemorrhage (PTH); and whether different approaches to tonsillectomy (e.g., partial vs. total tonsil removal, surgical technique such as coblation or laser) optimize effectiveness and minimize harms. We addressed these questions by reviewing the comparative (primarily RCT) data for effectiveness on a specific set of outcomes, then by searching a broader set of studies (case series and database or registry studies including at least 1000 children) for harms data in order to estimate the frequency of the most common and most severe harms (PTH, readmission, and reoperation). While we attempted to stratify on key covariates, including body mass index (BMI), documentation of throat infections, and surgical indication, such data were rarely available.

The literature on tonsillectomy in children for obstructive sleep-disordered breathing (OSDB) or recurrent throat infection is heterogeneous in terms of populations, interventions, comparators, and outcomes. Most studies included children with widely varying ages (e.g., 2 to 14 years), unspecified or mixed (both OSDB and throat infections) indications for surgery, and varying degrees of severity. Few studies stratified on potential confounding factors such as degree of tonsillar hypertrophy.

Anesthetic, analgesic, and anti-emetic regimens varied across studies, as did surgical techniques and perioperative and postoperative agents or combinations of agents assessed. Comparison groups included placebo, observation, historical control groups, and other active interventions. While studies typically addressed similar effectiveness outcomes including changes in respiratory or sleep parameters (e.g., Apnea Hypopnea Index [AHI], sleep-related quality of life), number and severity of throat infections, return to normal diet and activity, need for rescue analgesia or antiemetics postoperatively, and behavioral outcomes, measures used to evaluate the outcomes varied. Although a large number of studies reported PTH, definitions of “bleeding” varied and ranged from episodes of blood-tinged sputum to profuse bleeding requiring reoperation for hemostasis. Outcome measures were also frequently caregiver- or child-reported pain or bleeding diaries.

Summary of Key Findings and Strength of the Evidence

KQ1. Effectiveness of Tonsillectomy for OSDB

Key Findings

Relative to no intervention, most studies reported better sleep-related outcomes in children who had a tonsillectomy, but improvements were modest overall. In five studies that included children whose OSDB was confirmed with polysomnography (PSG), AHI scores improved more
in children receiving tonsillectomy than in those with no surgery (significant group differences in 3 studies). Meta-analysis of three studies showed a 4.8-point decline (improvement) in AHI in children who underwent tonsillectomy compared with no surgery. Sleep-related quality of life and 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. Children in the studies typically did not have behavioral scores indicative of clinical concern at baseline. Changes in executive function were not significantly different between groups.

We did not find tonsillectomy to be superior to continuous positive airway pressure (CPAP) in the one RCT addressing this comparison, which included children with significant comorbidities.

**Strength of the Evidence**

For tonsillectomy compared with no surgery, we found greater improvement in AHI and negative behaviors with tonsillectomy vs. watchful waiting. Our confidence in these conclusions 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 more confidence in this conclusion (moderate strength of evidence). We could not make conclusions about effects on executive function and other outcomes including cognitive changes (insufficient strength of evidence). Table 48 outlines strength of evidence findings for this KQ. 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) given the few studies addressing CPAP or these populations (insufficient strength of evidence).
Table 48. Strength of evidence for effectiveness of tonsillectomy versus watchful waiting/no treatment for OSDB

<table>
<thead>
<tr>
<th>Intervention/Outcome</th>
<th>Study Design</th>
<th>Risk of Bias and Number of Studies (N Total)</th>
<th>Study Limitations</th>
<th>Consistency</th>
<th>Directness</th>
<th>Precision</th>
<th>Reporting Bias</th>
<th>Strength of Evidence Grade</th>
<th>Finding</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Tonsillectomy vs. No Tonsillectomy</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
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</tr>
<tr>
<td><strong>AHI</strong></td>
<td>Meta-analysis</td>
<td></td>
<td>Medium</td>
<td>Inconsistent</td>
<td>Indirect</td>
<td>Precise</td>
<td>Undetected</td>
<td>Low SOE for greater improvement of AHI with tonsillectomy compared with no surgery</td>
<td>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.</td>
</tr>
<tr>
<td></td>
<td>RCT: 2 moderate (^{114, 172}) (N=456)</td>
<td></td>
<td></td>
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<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td></td>
<td>Prospective Cohort: 1 moderate (^{203}) (N=38)</td>
<td></td>
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<td></td>
<td></td>
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<tr>
<td></td>
<td>Retrospective Cohort: 2 moderate (^{211, 214}) (N=94)</td>
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<tr>
<td><strong>Sleep-related Quality of Life</strong></td>
<td></td>
<td></td>
<td>Medium</td>
<td>Consistent</td>
<td>Direct</td>
<td>Precise</td>
<td>Undetected</td>
<td>Moderate SOE for improvement in sleep-related quality of life after tonsillectomy vs. no surgery</td>
<td>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</td>
</tr>
<tr>
<td></td>
<td>RCT: 2 moderate (^{114, 172}) (N=456)</td>
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<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Retrospective Cohort: 1 moderate (^{211}) (N=32)</td>
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<td></td>
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<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Behavioral Outcomes</strong></td>
<td></td>
<td></td>
<td>Medium</td>
<td>Inconsistent</td>
<td>Direct</td>
<td>Imprecise</td>
<td>Not suspected</td>
<td>Low SOE for improvements in negative behaviors after tonsillectomy vs. no surgery</td>
<td>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</td>
</tr>
<tr>
<td></td>
<td>RCT: 1 moderate (^{172}) (N=397)</td>
<td></td>
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<tr>
<td></td>
<td>Prospective Cohort: 1 moderate (^{203}) (N=38)</td>
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</tr>
<tr>
<td></td>
<td>Retrospective Cohort: 1 moderate (^{211}) (N=32)</td>
<td></td>
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</tr>
</tbody>
</table>

AHI = apnea-hypopnea index; OSDB = obstructive-sleep disordered breathing; RCT = randomized controlled trial; SOE = strength of the evidence
KQ1a-d. Effectiveness of Tonsillectomy for Subpopulations of Children With OSDB

Key Findings
While studies may have included some children with craniofacial abnormalities, only a single, small RCT compared the efficacy of tonsillectomy to immediate initiation of CPAP in children with OSDB and concurrent Down syndrome or mucopolysaccharidoses. Both groups showed improvement in AHI at 6-month followup, with no significant group differences in AHI at 12 months. Another study reported no significant group differences in outcomes in analyses of children with syndromic comorbidities receiving tonsillectomy or watchful waiting.

Several studies included children who were overweight or obese; however, only 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. In another including children with mild OSA, analysis of subgroups of obese children showed no significant differences in outcomes between groups in these populations.

While several studies included children less than 3 years of age, these data were not extractable from the aggregate study population data. We did not identify studies explicitly addressing this question.

Strength of the Evidence
Strength of the evidence is insufficient to assess effects on outcomes in subpopulations of children with OSDB (children with neuromuscular or craniofacial abnormalities, those under 3 years of age, those with Down syndrome, or those with obesity).

KQ2. Effectiveness of Tonsillectomy for Recurrent Throat Infection

Key Findings
Although studies assessed frequency of infections and a number of utilization measures, such as missed school in the short term, longer-term results were rarely reported, and 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 very rarely was bacterial infection confirmed.

Overall, children undergoing tonsillectomy to improve number of throat infections, associated health care utilization (clinician visits), and days of work/school missed had improvements in these outcomes in the first postsurgical year compared with children not receiving surgery. These benefits diminished over time, however, and data on the longer-term outcomes are limited.

Strength of the 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). We have moderate confidence that compared with no surgery, tonsillectomy reduced throat infections or streptococcal infections in the short term (<12 months) (moderate strength of evidence). In the longer term (>12 months) we found no difference between groups in reduction
in streptococcal infections (low strength of evidence). We found no significant differences between groups in missed school/work or quality of life in the long term (>12 months) and have low confidence in these conclusions (low strength of evidence). Table 49 outlines strength of evidence ratings.

We could not make a conclusion about long term (>12 months) effects on throat infections (insufficient strength of evidence) as few studies reported longer-term data, and those that did had high attrition rates. 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 49. Strength of evidence for effectiveness of tonsillectomy versus watchful waiting/no treatment for recurrent throat infections

<table>
<thead>
<tr>
<th>Intervention/Outcome</th>
<th>Study Design</th>
<th>Risk of Bias and Number of Studies (N Total)</th>
<th>Study Limitations</th>
<th>Consistency</th>
<th>Directness</th>
<th>Precision</th>
<th>Reporting Bias</th>
<th>Strength of Evidence Grade</th>
<th>Findings</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tonsillectomy vs. No tonsillectomy in children with at least 3 episodes of sore throat in year prior to study</td>
<td>RCT: 4 moderate (N=761)</td>
<td>Medium Consistent Direct Precise Undetected</td>
<td>Moderate SOE for reduction in throat infection after tonsillectomy vs. no treatment in short-term (12 months) Fewer throat infections in tonsillectomy arms in short-term</td>
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<tr>
<td>Throat Infection</td>
<td>Non-RCT: 1 moderate (N=303)</td>
<td>Retrospective Cohort: 1 moderate (N=290)</td>
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</tbody>
</table>
Table 49. Strength of evidence for effectiveness of tonsillectomy vs. watchful waiting/no treatment for recurrent throat infections, continued

<table>
<thead>
<tr>
<th>Intervention/Outcome</th>
<th>Study Limitations</th>
<th>Consistency</th>
<th>Directness</th>
<th>Precision</th>
<th>Reporting Bias</th>
<th>Strength of Evidence Grade</th>
<th>Findings</th>
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</thead>
<tbody>
<tr>
<td><strong>Tonsillectomy vs. No tonsillectomy in children with at least 3 episodes of sore throat in year prior to study</strong></td>
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<td></td>
<td>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</td>
</tr>
<tr>
<td><strong>Streptococcal Infection (≤ 12 months post-tonsillectomy)</strong></td>
<td><strong>Medium</strong></td>
<td><strong>Consistent</strong></td>
<td><strong>Direct</strong></td>
<td><strong>Precise</strong></td>
<td>Undetected</td>
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<tr>
<td>RCT: 2 moderate⁹ (N=273)</td>
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<td></td>
<td>Fewer streptococcal infections in tonsillectomy arms in short-term</td>
</tr>
<tr>
<td>Retrospective Cohort: 1 moderate²¹³ (N=290)</td>
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<tr>
<td><strong>Streptococcal Infection (2-3 years post tonsillectomy)</strong></td>
<td><strong>Medium</strong></td>
<td><strong>Inconsistent</strong></td>
<td><strong>Direct</strong></td>
<td><strong>Imprecise</strong></td>
<td>Undetected</td>
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<tr>
<td>RCT: 2 moderate⁹ (N=203)</td>
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<tr>
<td>Retrospective Cohort: 1 moderate²¹³ (N=290)</td>
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<tr>
<td><strong>Utilization (clinician contacts)</strong></td>
<td><strong>Medium</strong></td>
<td><strong>Consistent</strong></td>
<td><strong>Direct</strong></td>
<td><strong>Precise</strong></td>
<td>Undetected</td>
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<tr>
<td>RCT: 1 moderate¹⁷⁹ (N=231)</td>
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<td>Fewer consultations in tonsillectomy arms vs. no surgery, but high loss to followup and differences in outcome assessment</td>
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<tr>
<td>Non-RCT: 1 moderate¹⁷⁹ (N=303)</td>
<td></td>
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</tbody>
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### Table 49. Strength of evidence for effectiveness of tonsillectomy vs. watchful waiting/no treatment for recurrent throat infections, continued

<table>
<thead>
<tr>
<th>Intervention/Outcome</th>
<th>Study Design</th>
<th>Risk of Bias and Number of Studies (N Total)</th>
<th>Study Limitations</th>
<th>Consistency</th>
<th>Directness</th>
<th>Precision</th>
<th>Reporting Bias</th>
<th>Strength of Evidence Grade</th>
<th>Findings</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tonsillectomy vs. No tonsillectomy in children with at least 3 episodes of sore throat in year prior to study</td>
<td>RCT: 3 moderate&lt;sup&gt;9, 164&lt;/sup&gt; (N=503)</td>
<td>Medium</td>
<td>Inconsistent</td>
<td>Direct</td>
<td>Im-precise</td>
<td>Undetected</td>
<td>Low SOE for improvements in missed school after tonsillectomy vs. no surgery in short term (&lt; 12 months)</td>
<td>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</td>
<td></td>
</tr>
<tr>
<td>Missed school/work (&lt; 12 months post tonsillectomy)</td>
<td>RCT: 3 moderate&lt;sup&gt;9, 164&lt;/sup&gt; (N=245)</td>
<td>Medium</td>
<td>Consistent</td>
<td>Direct</td>
<td>Im-precise</td>
<td>Undetected</td>
<td>Low SOE for no difference in effects between in longer term (&gt;12 months)</td>
<td>No significant differences between groups in all studies at longer-term followup; SOE is low given medium study limitations and relatively low number of participants</td>
<td></td>
</tr>
<tr>
<td>Missed school/work (&gt; 12 months post tonsillectomy)</td>
<td>RCT: 3 moderate&lt;sup&gt;9, 164&lt;/sup&gt; (N=245)</td>
<td>Medium</td>
<td>Consistent</td>
<td>Direct</td>
<td>Im-precise</td>
<td>Undetected</td>
<td>Low SOE for no difference in longer term (&gt;12 months) quality of life</td>
<td>Modest improvements in quality of life in both groups in all studies; SOE is low given high attrition in studies</td>
<td></td>
</tr>
<tr>
<td>Quality of Life (&gt; 12 months)</td>
<td>RCT: 2 moderate&lt;sup&gt;164, 179&lt;/sup&gt; (N=373)</td>
<td>Non-RCT: 1 moderate&lt;sup&gt;179&lt;/sup&gt; (N=123)</td>
<td>Medium</td>
<td>Consistent</td>
<td>Direct</td>
<td>Im-precise</td>
<td>Undetected</td>
<td>Low SOE for no difference in longer term (&gt;12 months) quality of life</td>
<td>Modest improvements in quality of life in both groups in all studies; SOE is low given high attrition in studies</td>
</tr>
</tbody>
</table>

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

**KQ3. Effectiveness of Partial Versus Total Tonsillectomy**

**Key Findings**

Few studies compared partial and total tonsillectomy using the same surgical technique.<sup>53, 84, 86, 90</sup> In studies comparing cold dissection or coblation for partial or total tonsillectomy, return to
normal diet or activity were faster in children undergoing partial removal. 53, 84-86 Differences in time to return to normal activity were not significant in a study comparing partial and total electrocautery. 90

In studies evaluating partial vs. total tonsillectomy using differing surgical techniques, differences between partial and total tonsillectomy were generally not significant for outcomes related to OSDB persistence, quality of life, or behavior (although it is not possible to be certain that effects are due to the surgical technique rather than the extent of surgery). 71, 95, 97, 98, 107, 110, 139, 151, 158, 182-186

In six studies, children in the partial tonsillectomy arms had faster return to diet and normal activity compared with those in total tonsillectomy groups; however, these effects may be due to confounding by indication as surgical indication varied across studies. Across all studies, 10 out of an estimated 166 children (6%) had tonsillar regrowth after partial tonsillectomy, 5 of whom ultimately underwent revision surgery. Data from these studies do not allow firm conclusions about the benefits or harms of one technique over another or about the comparative benefit of partial vs. total removal; however, neither surgical technique or extent of surgery appear to have a marked effect on outcomes.

**Strength of the Evidence**

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 assess effects on throat infections, OSDB persistence, or return to normal activity in these studies (insufficient SOE).

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 SOE).

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. In studies comparing mixed techniques for partial or total tonsillectomy, 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 50 outlines strength of evidence findings.
### Table 50. Strength of evidence for effectiveness of total tonsillectomy versus partial tonsillectomy

<table>
<thead>
<tr>
<th>Intervention/Outcome</th>
<th>Study Design</th>
<th>Risk of Bias and Number of Studies (N Total)</th>
<th>Study Limitations</th>
<th>Consistency</th>
<th>Directness</th>
<th>Precision</th>
<th>Reporting Bias</th>
<th>Strength of Evidence Grade</th>
<th>Findings</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Total vs. partial cold dissection tonsillectomy</strong></td>
<td></td>
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<td></td>
<td><strong>Low SOE for faster return to normal diet after partial vs. total tonsillectomy</strong></td>
</tr>
<tr>
<td>Return to Normal Diet</td>
<td>RCT: 1 low, 1 moderate</td>
<td>86 (N=131)</td>
<td>Medium</td>
<td>Consistent</td>
<td>Direct</td>
<td>Imprecise</td>
<td>Undetected</td>
<td></td>
<td>Children undergoing partial tonsillectomy returned to normal diet approximately 4 days sooner than children undergoing total tonsillectomy according to parent report</td>
</tr>
<tr>
<td><strong>Total vs. Partial tonsillectomy (mixed techniques)</strong></td>
<td></td>
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<td></td>
<td></td>
<td></td>
<td><strong>Low SOE for more favorable return to normal diet and activity in children undergoing partial vs. total tonsillectomy</strong></td>
</tr>
<tr>
<td>Return to Normal Diet or Activity</td>
<td>RCT: 2 low, 4 moderate</td>
<td>97, 98, 95, 107, 110, 185, 186 (N=620)</td>
<td>Medium</td>
<td>Consistent</td>
<td>Direct</td>
<td>Imprecise</td>
<td>Undetected</td>
<td></td>
<td>Children undergoing partial vs. total tonsillectomy had consistently favorable outcomes but unit of measure varied across studies (e.g., mean days, N children)</td>
</tr>
<tr>
<td>Intervention/Outcome</td>
<td>Study Design</td>
<td>Risk of Bias and Number of Studies (N Total)</td>
<td>Study Limitations</td>
<td>Consistency</td>
<td>Directness</td>
<td>Precision</td>
<td>Reporting Bias</td>
<td>Strength of Evidence Grade</td>
<td>Findings</td>
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<tr>
<td>Total vs. Partial Tonsillectomy (mixed techniques)</td>
<td>OSDB Persistence (≥12 months post-tonsillectomy)</td>
<td>RCT: 3 moderate(^{110, 182-186}) (N=214)</td>
<td>Medium</td>
<td>Consistent</td>
<td>Direct</td>
<td>Imprecise</td>
<td>Undetected</td>
<td>Low SOE for no difference in effects on long-term persistence of OSDB symptoms between partial and total tonsillectomy</td>
<td>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</td>
</tr>
<tr>
<td>Quality of Life (≥12 months post-tonsillectomy)</td>
<td>RCT: 2 moderate(^{182-186}) (N=159)</td>
<td>Medium</td>
<td>Consistent</td>
<td>Direct</td>
<td>Imprecise</td>
<td>Undetected</td>
<td>Low SOE for no long-term differences in quality of life after partial vs. total tonsillectomy</td>
<td>Improvements from baseline in both groups in 2 small studies, but no significant group differences in quality of life in either study</td>
<td></td>
</tr>
<tr>
<td>Behavioral Outcomes (≥12 months post-tonsillectomy)</td>
<td>RCT: 2 moderate(^{182-186}) (N=159)</td>
<td>Medium</td>
<td>Consistent</td>
<td>Direct</td>
<td>Imprecise</td>
<td>Undetected</td>
<td>Low SOE for no long-term differences in behavioral outcomes after partial vs. total tonsillectomy</td>
<td>Improvements from baseline in both groups on the Child Behavior Checklist in 2 small studies, but no significant group differences in either study</td>
<td></td>
</tr>
<tr>
<td>Throat Infections (≥12 months post-tonsillectomy)</td>
<td>RCT: 1 low(^{185, 186}), 3 moderate(^{110, 139, 182-184}) (N=296)</td>
<td>Medium</td>
<td>Inconsistent</td>
<td>Direct</td>
<td>Imprecise</td>
<td>Undetected</td>
<td>Low SOE for no effect on throat infections following partial vs. total tonsillectomy</td>
<td>More throat infections or sore throats following partial vs. total tonsillectomy in 3 of 4 RCTs but no significant group differences</td>
<td></td>
</tr>
</tbody>
</table>

\(^{110}\) = number; OSDB = obstructive sleep-disordered breathing; RCT = randomized controlled trial; SOE = strength of the evidence
**KQ4. Effectiveness of Surgical Techniques for Tonsillectomy**

**Key Findings**

Few studies addressing this question reported effectiveness data. Nineteen studies reported resumption of normal activity and/or diet. Commonly used “hot” techniques were generally associated with faster return to normal diet or activity than was cold dissection (roughly 1 to 4 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.

**Strength of the Evidence**

We found a faster return to diet with coblation or electrocautery tonsillectomy compared with cold dissection and have low confidence in these conclusions (low strength of evidence) (Table 51). We could not make conclusions about effects associated with other techniques including laser, thermal welding, and harmonic scalpel (insufficient strength of evidence) on these outcomes given that studies were typically small and evaluated different measures (e.g., dietary intake score, number of children consuming normal diet, parental return to work).

<table>
<thead>
<tr>
<th>Intervention/Outcome</th>
<th>Study Design</th>
<th>Risk of Bias and Number of Studies (N Total)</th>
<th>Study Limitations</th>
<th>Consistency</th>
<th>Directness</th>
<th>Precision</th>
<th>Reporting Bias</th>
<th>Strength of Evidence Grade Findings</th>
</tr>
</thead>
<tbody>
<tr>
<td>Coblation vs. Cold dissection tonsillectomy</td>
<td>RCT: 3 low [109, 144, 169, 170] [4] moderate [197] (N=276)</td>
<td>Low Consistent Direct Imprecise Undetected</td>
<td>Low SOE for faster return with coblation</td>
<td>Coblation, compared with cold dissection, associated with moderately faster return to normal activity in 4 small studies</td>
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<tr>
<td>Return to normal activity</td>
<td>Electrocautery vs. cold dissection tonsillectomy</td>
<td>Medium Inconsistent Direct Imprecise Undetected</td>
<td>Low SOE for faster return with electrocautery</td>
<td>Electrocautery associated with faster return to normal diet in 2 studies and not significantly faster in a third</td>
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</table>

N = number; RCT = randomized controlled trial; SOE = strength of the evidence
Harms of Surgical Techniques

Key Findings

We included harms data reported in comparative studies and case series and database and registry studies to address this KQ; however, we considered only data from meta-analyses and comparative studies in our assessment of the strength of the evidence. Overall, estimates of PTH and utilization harms associated with tonsillectomy are less than 5 percent. 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 also 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 (PONV) were less than 2 percent. Other harms were disparate and generally not clinically significant (e.g., thermal burn from a cautery apparatus). No comparative studies reported deaths. Frequency of PTH in case series and database or registry studies generally aligned with that in comparative studies. At least four deaths were reported across case series or database studies (low or moderate risk of bias) including 1,778,342 children.

Strength of the Evidence

We found a low frequency of PTH and PTH-related utilization across surgical techniques and have confidence in these findings (high strength of evidence). We found a low frequency of visits or readmission for dehydration associated with partial tonsillectomy. Our confidence in this conclusion is low given the few studies reporting these outcomes (low strength of evidence). We have greater confidence in a low frequency of nonbleeding readmissions/revisits associated with total tonsillectomy (moderate strength of evidence). We could not draw conclusions about effects on admissions or revisits for pain or PONV associated with partial tonsillectomy given the few comparative studies addressing the outcome (insufficient strength of evidence). Table 52 outlines strength of evidence.
### Table 52. Strength of evidence for harms associated with surgical techniques for tonsillectomy

<table>
<thead>
<tr>
<th>Intervention/Outcome</th>
<th>Study Design</th>
<th>Risk of Bias and Number of Studies (N Total)</th>
<th>Study Limitations</th>
<th>Consistency</th>
<th>Directness</th>
<th>Precision</th>
<th>Reporting Bias</th>
<th>Strength of Evidence Grade Findings</th>
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</thead>
<tbody>
<tr>
<td>Partial tonsillectomy</td>
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<tr>
<td>PTH and PTH-associated utilization</td>
<td>Meta-analysis</td>
<td>RCT: 5 low, 53, 90, 98, 151, 167, 168, 186</td>
<td>11 (N=1234)</td>
<td>Medium</td>
<td>Consistent</td>
<td>Direct</td>
<td>Precise</td>
<td>Undetected</td>
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<td></td>
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<td>moderate 58, 71, 84-86, 95, 110, 139, 158, 182-186</td>
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<td>High SOE for low frequency of PTH associated with partial tonsillectomy</td>
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<td>Frequency did not exceed 4% for total PTH; fewer data available to assess associated utilization, but frequency is likely low given the low frequency of PTH</td>
</tr>
<tr>
<td>Readmissions /revisits for dehydration</td>
<td>Meta-analysis</td>
<td>RCT: 1 low, 98 2 moderate 85, 139</td>
<td>2 (N=221)</td>
<td>Medium</td>
<td>Consistent</td>
<td>Direct</td>
<td>Imprecise</td>
<td>Undetected</td>
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<td></td>
<td>Low SOE for low frequency of dehydration revisits/readmissions associated with partial tonsillectomy</td>
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<td>5 readmissions reported across 3 study arms</td>
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<td>Total tonsillectomy</td>
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<td></td>
<td>High SOE for low frequency of PTH associated with total tonsillectomy</td>
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<td>Frequency of &lt;5% of PTH and PTH-associated utilization in both meta-analysis and unadjusted analyses associated with commonly used techniques</td>
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</table>
Table 52. Strength of evidence for harms associated with surgical techniques for tonsillectomy, continued

<table>
<thead>
<tr>
<th>Intervention/Outcome</th>
<th>Study Design</th>
<th>Risk of Bias and Number of Studies (N Total)</th>
<th>Study Limitations</th>
<th>Consistency</th>
<th>Directness</th>
<th>Precision</th>
<th>Reporting Bias</th>
<th>Strength of Evidence Grade Findings</th>
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<tbody>
<tr>
<td>Total tonsillectomy</td>
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<tr>
<td>Readmissions for pain, PONV, dehydration</td>
<td>RCT: 9 low, 42, 43, 66, 69, 93, 103, 114, 123, 125, 134, 48 moderate 110, 111, 116, 124, 130, 154, 164</td>
<td>(N=2269)</td>
<td>Medium</td>
<td>Consistent</td>
<td>Direct</td>
<td>Precise</td>
<td>Undetect ed</td>
<td>Moderate SOE for low frequency of non-PTH readmissions/revisits associated with total tonsillectomy</td>
</tr>
<tr>
<td></td>
<td>Prospective cohort: 1 moderate 207</td>
<td>(N=29)</td>
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<td></td>
<td>In 37 study arms, overall frequency of nonbleeding revisits/readmissions was below 2%; SOE is moderate given smaller sample size</td>
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<td></td>
<td>Retrospective cohort: 1 moderate 213</td>
<td>(N=145)</td>
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</table>

N = number; PTH = post-tonsillectomy hemorrhage; RCT = randomized controlled trial; SOE = strength of the evidence

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

Key Findings

A variety of medications have been the focus of research including different steroids (dexamethasone, prednisolone); nonsteroidal anti-inflammatory drugs (NSAIDs) including diclofenac, ibuprofen, ketoprofen, lornoxicam, and ketorolac; and antiemetics (ramosetron, granisetron, dolasetron, ondansetron) Studies 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.

NSAIDs. Studies comparing NSAIDs with placebo reported reduced need for analgesia (significant group differences in 4 of 5 studies). Results in trials comparing NSAIDs vs. other agents were not consistent in terms of effects on need for additional analgesia. A single study found no effect of NSAIDS on reducing anti-emetic use. NSAIDs were not associated with a faster return to normal diet or activity. Few studies reported PTH.
**Steroids.** Most placebo-controlled steroid trials (5/8) found that perioperative intravenous dexamethasone administration reduced the need for analgesics immediately after surgery (postanesthesia care unit [PACU] and up to 24 hours postoperatively), but no longer-term results were reported. The two studies reported that peritonsillar infiltration of dexamethasone also reduced immediate postoperative analgesic requirements (PACU, surgical day ward) compared with placebo. Five RCTs found perioperative steroid administration decreased postoperative anti-emetic use in the immediate postoperative period (PACU and up to 24 hours postoperatively). While most studies reported reductions in analgesic or anti-emetic use associated with perioperative steroids, roughly half of studies addressing each outcome reported no group differences. Steroids had little effect on return to normal diet in two RCTs.

**Antiemetics.** Data were consistent in terms of antiemetic medications. All five trials of 5-hydroxytryptamine (5-HT) receptor antagonists found their administration to have no effect on postoperative analgesic requirements. Three trials consistently reported reduced postoperative antiemetic requirements in patients treated with intraoperative 5-HT receptor antagonists.

**Strength of the Evidence**

We considered the strength of the evidence for studies with placebo comparison in most cases given the heterogeneity of agents and comparators ( ). We considered the drug class (instead of individual agent such as diclofenac) in assessing strength of evidence for NSAIDs and antiemetics. 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 low frequency of PTH (< 6%) and 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 return to 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.** 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).

need for postoperative antiemetics given the small number of children evaluated in these studies.

<table>
<thead>
<tr>
<th>Intervention/Outcome</th>
<th>Study Design</th>
<th>Risk of Bias and Number of Studies (N Total)</th>
<th>Study Limitations</th>
<th>Consistency</th>
<th>Directness</th>
<th>Precision</th>
<th>Reporting Bias</th>
<th>Strength of Evidence Grade Findings</th>
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<tbody>
<tr>
<td><strong>NSAID vs. Placebo</strong></td>
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<tr>
<td>Need for rescue analgesic</td>
<td>RCT: 3 low, 94, 128, 136, 2 moderate121, 142 (N=345)</td>
<td>Medium Inconsistent Direct Imprecise Undetected</td>
<td>Low SOE for reduced need for rescue analgesia with NSAIDs vs. placebo</td>
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<td>Significantly less need in 4 small studies, no group differences in a 5th study</td>
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<td>Return to Normal diet and activity</td>
<td>RCT: 2 moderate 72, 126 (N=180)</td>
<td>Medium Consistent Direct Imprecise Undetected</td>
<td>Low SOE for no difference in return to normal diet or activity with NSAIDs vs. placebo</td>
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<td>No significant group differences in 2 small studies with medium study limitations</td>
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<tr>
<td>PTH and PTH-related revists/readmissions</td>
<td>RCT: 1 low, 40, 5 moderate 47, 106, 117, 150, 161 (N=277)</td>
<td>Medium Consistent Direct Imprecise Undetected</td>
<td>Low SOE for low frequency of PTH or PTH-related revists/readmissions associated with perioperative dexamethasone</td>
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<td>Frequency of PTH or associated utilization &lt;3% (unadjusted analyses) in 277 children receiving NSAIDs</td>
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<tr>
<td>Intervention/Outcome</td>
<td>Study Design</td>
<td>Risk of Bias and Number of Studies (N Total)</td>
<td>Study Limitations</td>
<td>Consistency</td>
<td>Directness</td>
<td>Precision</td>
<td>Reporting Bias</td>
<td>Strength of Evidence Grade Findings</td>
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<tr>
<td>Need for rescue analgesic</td>
<td>RCT: 4 low, 50, 105, 119, 146, 6 moderate 45, 78, 109, 126, 147, 148 (N=979)</td>
<td>Medium</td>
<td>Inconsistent</td>
<td>Direct</td>
<td>Precise</td>
<td>Undetected</td>
<td>Low SOE for reduction in analgesic need with dexamethasone vs. placebo</td>
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<tr>
<td><strong>Need for rescue anti-emetic</strong></td>
<td>RCT: 4 low, 37, 105, 119, 146, 4 moderate 62, 78, 109, 126 (N=812)</td>
<td>Medium</td>
<td>Inconsistent</td>
<td>Direct</td>
<td>Precise</td>
<td>Undetected</td>
<td>Low SOE for reduction in anti-emetic need with dexamethasone vs. placebo</td>
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<tr>
<td><strong>PTH</strong></td>
<td>Meta analysis</td>
<td>Medium</td>
<td>Consistent</td>
<td>Direct</td>
<td>Imprecise</td>
<td>Undetected</td>
<td>Low SOE for no increased risk of PTH with dexamethasone compared with placebo</td>
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*ODS*
Table 53. Strength of the evidence for studies addressing perioperative medications, continued

<table>
<thead>
<tr>
<th>Intervention/Outcome</th>
<th>Study Design</th>
<th>Risk of Bias and Number of Studies (N Total)</th>
<th>Study Limitations</th>
<th>Consistency</th>
<th>Directness</th>
<th>Precision</th>
<th>Reporting Bias</th>
<th>Strength of Evidence Grade</th>
<th>Findings</th>
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<tbody>
<tr>
<td><strong>Dexamethasone</strong></td>
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<td></td>
<td>Moderate SOE for low frequency of PTH or PTH-related revisits/readmissions associated with perioperative dexamethasone</td>
<td>Frequency of PTH or associated utilization &lt;6% (unadjusted analyses) in 811 children receiving steroids</td>
</tr>
<tr>
<td>PTH and PTH-related revisits/readmissions</td>
<td>RCT: 6 low, 34, 57, 59, 105, 112, 119, moderate 45, 78, 148 (N=811)</td>
<td>Medium</td>
<td>Consistent</td>
<td>Direct</td>
<td>Precise</td>
<td>Undetected</td>
<td></td>
<td>Moderate SOE for no effect of antiemetics (5-hydroxytryptamine [5-HT] receptor antagonists)</td>
<td>No significant group differences in 5 RCTs comparing 5-HT antagonists with other antiemetics, other 5-HT antagonists, or placebo</td>
</tr>
<tr>
<td><strong>5-HT Antiemetics vs. Placebo or Other Comparators</strong></td>
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<td></td>
<td>Low SOE for reduced need for postoperative antiemetics with perioperative 5-HT antiemetics vs. placebo</td>
<td>Significantly less need for postoperative antiemetics in 3 small RCTs comparing 5-HT antagonists and placebo; imprecision precludes higher SOE</td>
</tr>
<tr>
<td>Need for rescue analgesic</td>
<td>RCT: 4 low, 108, 118, 132, 133, moderate 122 (N=964)</td>
<td>Low</td>
<td>Consistent</td>
<td>Direct</td>
<td>Precise</td>
<td>Undetected</td>
<td></td>
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<tr>
<td>Need for postoperative rescue antiemetic</td>
<td>RCT: 2 low, 118, 136, 1 moderate 122 (N=303)</td>
<td>Low</td>
<td>Consistent</td>
<td>Direct</td>
<td>Imprecise</td>
<td>Undetected</td>
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5-HT = 5-hydroxytryptamine; N = number; PTH = post-tonsillectomy hemorrhage; RCT = randomized controlled trial; SOE = strength of the evidence

KQ6. Effectiveness of Postoperative Medications for Pain After Tonsillectomy

Key Findings
Drugs assessed in studies addressing this question included steroids (prednisolone), NSAIDs (diclofenac, ibuprofen, celecoxib, aspirin), non-NSAID analgesics (acetaminophen) and
antibiotics (amoxicillin). Few studies addressed the same interventions and comparisons, and studies typically reported on need for rescue pain medication, PTH, and return to normal diet or activity as outcomes. Data on the effect of NSAIDS on 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. \(^{41, 60}\)

PTH frequency overall was less than 10 percent. The frequency of PTH in steroid and placebo arms in the two studies addressing that comparison were similar. \(^{41, 60}\) In studies comparing NSAIDs (celecoxib, ibuprofen) and non-NSAID analgesics to placebo or other medications, occurrences of PTH were also similar. \(^{38, 49, 137, 138, 155, 159, 194}\)

### Strength of the Evidence

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 54 outlines these findings.

**Table 54. Strength of evidence for effectiveness of postoperative medications for pain-related outcomes**

<table>
<thead>
<tr>
<th>Intervention/Outcome</th>
<th>Study Design</th>
<th>Risk of Bias and Number of Studies (N Total)</th>
<th>Study Limitations</th>
<th>Consistency</th>
<th>Directness</th>
<th>Precision</th>
<th>Reporting Bias</th>
<th>Strength of Evidence Grade</th>
<th>Findings</th>
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</thead>
<tbody>
<tr>
<td>Prednisolone vs. Placebo</td>
<td>RCT: 1 low, (^{31}) 1 moderate (^{60}) (N=331)</td>
<td>Medium</td>
<td>Consistent</td>
<td>Direct</td>
<td>Imprecise</td>
<td>Undetected</td>
<td>Low SOE for no difference in effects of prednisolone vs. placebo on return to normal diet or activity</td>
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<td>Return to Normal Diet or activity in longer term (≥5 days)</td>
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<tr>
<td>PTH</td>
<td>RCT: 1 low, (^{31}) 1 moderate (^{60}) (N=331)</td>
<td>Medium</td>
<td>Consistent</td>
<td>Direct</td>
<td>Imprecise</td>
<td>Undetected</td>
<td>Low SOE for no difference in PTH associated with steroids vs. placebo/no treatment</td>
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<td>Numbers of PTH in steroid and placebo arms were similar in 2 studies (13 PTH in steroid arms vs. 15 in placebo/no treatment)</td>
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Table 54. Strength of evidence for effectiveness of postoperative medications for pain-related outcomes, continued

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<th>Intervention/Outcome</th>
<th>Study Design</th>
<th>Risk of Bias and Number of Studies (N Total)</th>
<th>Study Limitations</th>
<th>Consistency</th>
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<th>Reporting Bias</th>
<th>Strength of Evidence Grade</th>
<th>Findings</th>
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<td>Study Limitations</td>
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<td>NSAIDs</td>
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<td>RCT: 2</td>
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<td>moderate</td>
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<td>Low SOE for a low frequency of PTH</td>
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<td>(N=564)</td>
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<td>Unadjusted frequency ranged from 0-6% across agents; higher frequency associated with celecoxib; SOE is low given small sample size</td>
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<td>Non-RCT: 1</td>
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<td>(N=115)</td>
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Findings in Relation to What Is Already Known

We identified 23 recent (2011-present) systematic reviews or meta-analyses assessing tonsillectomy. Most reviews or meta-analyses (n=9) addressed perioperative medications and PTH risk or other morbidity: three addressed NSAIDs five addressed dexamethasone; and one addressed antibiotics. Two reviews addressed tonsillectomy for recurrent tonsillitis; seven addressed tonsillectomy for OSDB (including one comparing partial and total tonsillectomy in children with OSDB and two comparing outcomes among children with or without OSA or with obesity) and five addressed partial vs. total tonsillectomy or specific surgical techniques.

Across reviews, investigators commented on methodologic limitations such as lack of blinding and limited allocation concealment; heterogeneity of techniques and indications for tonsillectomy; use of subjective outcome measures; short-term followup; small sample sizes; and generally low to moderate quality studies. Appendix I includes an overview of findings of all reviews. Findings in prior reviews and meta-analyses generally aligned with our findings in the current report. Reviews of tonsillectomy specifically in children with OSDB or tonsillitis reported modest benefits in obstructive symptoms or sore throat reduction, typically in the short-term, for tonsillectomy compared with no surgery. Reviews comparing partial and total tonsillectomy reported few differences between techniques: partial tonsillectomy was generally associated with faster return to normal diet and activity and less PTH, but changes in resolution of OSDB symptoms or recurrent throat infections were not significantly different between approaches. Reviews comparing surgical techniques (e.g., coblation, electrocautery) similarly reported few significant differences among techniques. Reviews of perioperative steroids consistently reported no significant association with PTH in children, though one review reported greater need for reintervention when PTH occurred. Reviews of perioperative NSAIDs and PTH risk were less consistent, with two reporting no increased risk in children and one
noting insufficient data to rule out risk. One review of antibiotics reported no evidence for a consistent effect of antibiotics on pain, PTH, or need for pain medications. Finally, in one review assessing weight gain in a general population of normal and overweight children undergoing tonsillectomy, participants gained more weight than expected postoperatively.

**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 addressing this comparison (2 studies reported in one paper) 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 AHI or other PSG 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 infection. 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 includes applicability tables for each KQ.
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 for either 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. Data on specific approaches to tonsillectomy (either partial versus total or by surgical technique) offer 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 5 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.310-312

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 subject was insufficient to inform guidance on whether any perioperative medications affect time to normal diet or activity. Low strength of evidence suggested that a single dose of IV dexamethasone intraoperatively reduces analgesic requirement in the PACU 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 preemptive 5-HT receptor antagonists given intra-operatively do reduce the need for rescue antiemetics post-tonsillectomy.

Limitations of the Comparative Effectiveness Review Process

We included studies published in English only. We scanned a random sample of 100 non-English abstracts retrieved by our MEDLINE search (25 selected from each decade 1980 to 2015). Most studies appeared to be case series, narrative reviews, imaging or basic science studies, or studies dealing with malignant lesions. Only two studies appeared to meet inclusion criteria; thus, given the high percentage of ineligible items in this scan (98%), we concluded that excluding non-English studies would 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 adenoïdectomy alone or studies comparing tonsillectomy with adenoïdectomy 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 clinical outcome data, focusing instead on intermediate outcomes and harms. In addition, few studies addressed questions about the need for tonsillectomy compared with a nonsurgical 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 special populations at particular risk.

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 outcomes, and behavioral outcomes 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 on apparent effectiveness is unknown.

A particular problem in the literature is a lack of full characterization of the patient population, particularly about 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 opinions 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 severity or 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 as we did not identify many comparative studies with low or
moderate risk of bias; 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.

**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 describe population factors that may predict resolution.¹⁷⁵, ³¹³, ³¹⁴ 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 key 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;²⁵¹, ³¹⁵-³¹⁷ 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 emerge, as they continuously have over the past few decades, high quality research will continue to 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 gaps in data surrounding treatment of 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 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 surgery, 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 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.
References


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36. McMaster Evidence Based Practice Centre., McMaster Quality Assessment Scale of Harms (McHarm) for primary studies. Hamilton ON: McMaster University; 2008.


87. Bolton CM, Myles PS, Carlin JB, et al. Randomized, double-blind study comparing the efficacy of moderate-dose metoclopramide and ondansetron for the


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134. Nunez DA, Provan J, Crawford M. Postoperative tonsillectomy pain in pediatric patients: electrocautery (hot) vs cold dissection and snare tonsillectomy--a


## Acronyms and Abbreviations

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<tr>
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<th>Description</th>
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<td>AAO-HNSF</td>
<td>American Academy Of Otolaryngology - Head &amp; Neck Surgery Foundation</td>
</tr>
<tr>
<td>AHI</td>
<td>Apnea Hypopnea Index</td>
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<tr>
<td>AHRQ</td>
<td>Agency For Healthcare Research And Quality</td>
</tr>
<tr>
<td>BCI</td>
<td>Bayesian Credible Intervals</td>
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<tr>
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<tr>
<td>BRIEF</td>
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</tr>
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<td>CAS-15</td>
<td>Clinical Assessment Score-15</td>
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<td>CGI</td>
<td>Connors Global Index</td>
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<td>Childhood Adenotonsillectomy Trial</td>
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<td>CI</td>
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<td>CPAP</td>
<td>Continuous Positive Airway Pressure</td>
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<td>Group A Strep</td>
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<tr>
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<td>PACU</td>
<td>Post-Anesthesia Care Unit</td>
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<td>PFAPA</td>
<td>Periodic Fever, Aphthous Stomatitis, Pharyngitis, Cervical Adenitis</td>
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<td>PICOTS</td>
<td>Population, Intervention, Comparator, Outcomes, Timing, And Setting</td>
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<td>PTH</td>
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<td>UARS</td>
<td>Upper Airway Resistance Syndrome</td>
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<td>WASI</td>
<td>Wechsler Abbreviated Scale Of Intelligence</td>
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Appendix A. Analytic Frameworks

Figure A-1. Analytic framework for Key Question 1

Abbreviations: CPAP = Continuous Positive Airway Pressure; KQ = Key Question; OSDB = Obstructive Sleep-Disordered Breathing

*Includes breathing difficulties during sleep as operationalized in each study, including obstructive sleep apnea and upper airway resistance syndrome
†Includes tonsillectomy, adenotonsillectomy, or partial tonsillectomy performed using any method or approach (e.g., coblation, cold dissection, laser)

Figure A-2. Analytic framework for Key Question 1a

Abbreviations: CPAP = Continuous Positive Airway Pressure; KQ = Key Question; OSDB = Obstructive Sleep-Disordered Breathing

*Includes breathing difficulties during sleep as operationalized in each study, including obstructive sleep apnea and upper airway resistance syndrome
†Includes tonsillectomy, adenotonsillectomy, partial tonsillectomy performed using any method or approach (e.g., coblation, cold dissection, laser)
Figure A-3. Analytic framework for Key Question 1b

Abbreviations: CPAP = Continuous Positive Airway Pressure; KQ = Key Question; OSDB = Obstructive Sleep-Disordered Breathing

*Includes breathing difficulties during sleep as operationalized in each study, including obstructive sleep apnea and upper airway resistance syndrome
†Includes tonsillectomy, adenotonsillectomy, partial tonsillectomy performed using any method or approach (e.g., coblation, cold dissection, laser)

Figure A-4. Analytic framework for Key Question 1c

Abbreviations: CPAP = Continuous Positive Airway Pressure; KQ = Key Question; OSDB = Obstructive Sleep-Disordered Breathing

*Includes breathing difficulties during sleep as operationalized in each study, including obstructive sleep apnea and upper airway resistance syndrome
†Includes tonsillectomy, adenotonsillectomy, partial tonsillectomy performed using any method or approach (e.g., coblation, cold dissection, laser)
Figure A-5. Analytic framework for Key Question 1d

 Abbreviations: CPAP = Continuous Positive Airway Pressure; KQ = Key Question; OSDB = Obstructive Sleep-Disordered Breathing

*Includes breathing difficulties during sleep as operationalized in each study, including obstructive sleep apnea and upper airway resistance syndrome
†Includes tonsillectomy, adenotonsillectomy, partial tonsillectomy performed using any method or approach (e.g., coblation, cold dissection, laser)

Figure A-6. Analytic framework for Key Question 2

Abbreviations: KQ = Key Question; QoL = Quality of Life

†Includes tonsillectomy, adenotonsillectomy, partial tonsillectomy performed using any method or approach (e.g., coblation, cold dissection, laser)
Figure A-7. Analytic framework for Key Question 3

Children (3-18 years old) with OSDB or recurrent throat infections

(KQ 3)

Total or partial tonsillectomy

Outcomes
-Sleep, cognitive or behavioral, health, quality of life, and other outcomes (see Table 1 for full details)

Harms
See Table 1

Abbreviations: KQ = Key Question; OSDB = Obstructive Sleep-Disordered Breathing

*Includes breathing difficulties during sleep as operationalized in each study, including obstructive sleep apnea and upper airway resistance syndrome
†Includes tonsillectomy or adenotonsillectomy.

Figure A-8. Analytic framework for Key Question 4

Children (3-18 years old) with OSDB or recurrent throat infections

(KQ 4)

Tonsillectomy* via varied techniques

Outcomes
-Sleep, cognitive or behavioral, health, quality of life, and other outcomes (see Table 1 for full details)

Harms
See Table 1

Abbreviations: KQ = Key Question; OSDB = Obstructive Sleep-Disordered Breathing

*Includes breathing difficulties during sleep as operationalized in each study, including obstructive sleep apnea and upper airway resistance syndrome
†Includes tonsillectomy or adenotonsillectomy.
Figure A-9. Analytic framework for Key Question 5

Children (3-18 years old) with OSDB* or recurrent throat infections undergoing tonsillectomy†

Adjunctive perioperative pharmacologic agents

(KQ 5)

Outcomes
- Pain management
- Time to return to usual activities
- Health care utilization

Harms
See Table 1

Abbreviations: KQ = Key Question; OSDB = Obstructive Sleep-Disordered Breathing

*Includes breathing difficulties during sleep as operationalized in each study, including obstructive sleep apnea and upper airway resistance syndrome
†Includes tonsillectomy, adenotonsillectomy, partial tonsillectomy performed using any method or approach (e.g., coblation, cold dissection, laser).

Figure A-10. Analytic framework for Key Question 6

Children (3-18 years old) with OSDB* or recurrent throat infections undergoing tonsillectomy†

Postoperative pharmacologic agents for pain

(KQ 6)

Outcomes
- Pain management
- Time to return to usual activities
- Health care utilization

Harms
See Table 1

Abbreviations: KQ = Key Question; OSDB = Obstructive Sleep-Disordered Breathing

*Includes breathing difficulties during sleep as operationalized in each study, including obstructive sleep apnea and upper airway resistance syndrome
†Includes tonsillectomy, adenotonsillectomy, partial tonsillectomy performed using any method or approach (e.g., coblation, cold dissection, laser).
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<th>KQ</th>
<th>Population</th>
<th>Intervention</th>
<th>Comparators</th>
<th>Outcomes</th>
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<td>1</td>
<td><strong>Children (3-18 years of age) with OSDB</strong></td>
<td>Tonsillectomy</td>
<td>-Continuous positive airway pressure (CPAP) -Pharmacologic treatment including anti-inflammatory medications, decongestants, allergy medication, antihistamines, nasal steroids, leukotriene inhibitors</td>
<td>Sleep outcomes -Apnea Hypopnea Index (AHI) -Sleep quality measures (Obstructive Sleep Apnea-18 [OSA-18], Clinical Assessment Score-15 [CAS-15]) -Pediatric Sleep Questionnaire (PSQ) -Modified Epworth Sleepiness Scale -Desaturation nadir -OSDB persistence Cognitive or behavioral outcomes -Validated measures of attention, irritability, and memory Health outcomes -Growth velocity (height, BMI for age) -Cardiopulmonary issues -Self or caregiver-reported enuresis -Health care utilization (number of clinician visits) Harms -Re-admission or ER visit or ICU admission for postoperative pain, dehydration, bleeding, or nausea and vomiting -Reoperation for primary or secondary bleeding -Velopharyngeal insufficiency -30-day mortality -Harms of comparator agents reported in studies with comparison groups</td>
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<td>1a</td>
<td><strong>Children (3-18 years of age) with OSDB and neuromuscular or craniofacial abnormalities</strong></td>
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<td>Length of stay</td>
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<td><strong>Children (3-18 years of age) with OSDB who are overweight or obese</strong></td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>antihistamines, nasal steroids, leukotriene inhibitors</td>
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</table>
| 2  | Children (3-18 years) with recurrent throat infections | Tonsillectomy | -Antibiotics  
-Nonantibiotic pharmacologic treatments (e.g., anti-inflammatory agents, decongestants, antihistamines, leukotriene inhibitors, nasal or systemic steroids) | Throat infections  
-Number of throat infections/year  
-Severity of throat infections  
-Number of streptococcal infections/year  

Quality of life  
-Validated quality of life measures  
-Missed school or work for child or caregiver  

Other outcomes  
-Health care utilization (number of clinician visits, number of courses of antibiotics)  

Harms  
-ER visit or hospital or ICU admission for postoperative pain, bleeding, dehydration, or nausea and vomiting  
-Reoperation for primary or secondary bleeding  
-Velopharyngeal insufficiency  
-30-day mortality  
-Harms of comparator agents reported in studies with comparison groups |
| 3  | Children (3-18 years) undergoing tonsillectomy | Total tonsillectomy | -Partial tonsillectomy | See sleep, cognitive or behavioral, and health outcomes (KQ1) and quality of life outcomes (KQ2)  
Throat infections  
-Number of throat infections/year  
-Severity of throat infections  
-Number of streptococcal infections/year  

Other outcomes  
-Symptomatic tonsillar regrowth  
-Time to return to usual activity (diet, school)  

Harms  
See KQ1  
Reoperation for complete tonsillectomy |
| 4  | Children (3-18 years) undergoing tonsillectomy | Tonsillectomy | -Other technique for tonsillectomy | See sleep, cognitive or behavioral, and health outcomes (KQ1) and quality of life outcomes (KQ2)  
Throat infections  
-Number of throat infections/year  
-Severity of throat infections  
-Number of streptococcal infections/year  

Other outcomes |
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<th>KQ</th>
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<th>Comparators</th>
<th>Outcomes</th>
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<td>5</td>
<td>Children (3-18 years) undergoing tonsillectomy</td>
<td>Tonsillectomy plus adjunctive perioperative (i.e., preoperative, intraoperative, or immediate postoperative [post-anesthesia care] periods) pharmacologic agents</td>
<td>-Tonsillectomy without adjunctive perioperative pharmacologic agents (i.e., pharmacologic agents given to attempt to reduce postoperative morbidity including pain or nausea and vomiting)</td>
<td>-Time to return to usual activity (diet, school)</td>
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<td>Harms</td>
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<td>See KQ1</td>
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<td>Children (3-18 years) undergoing tonsillectomy and receiving pharmacologic agents for pain postoperatively (i.e., up to 10 days after discharge from post-anesthesia care)</td>
<td>Tonsillectomy plus postoperative pharmacologic agents for pain (e.g., NSAID, ketorolac)</td>
<td>-Tonsillectomy with other postoperative pharmacologic agents for pain</td>
<td>-Pain management (need for or # of rescue medications)</td>
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<td>-Time to return to usual activities (diet, school)</td>
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<td>-Health care utilization (number of clinician visits, number of courses of antibiotics)</td>
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<td></td>
<td>Harms</td>
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<td>-Harms of agent</td>
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<td>-Re-admission to hospital or ICU or ER visit for postoperative pain, bleeding, dehydration, or nausea and vomiting</td>
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<td>-Reoperation for primary or secondary bleeding</td>
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<td></td>
<td></td>
<td>-30-day mortality</td>
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Studies of any length or follow-up and in any setting, except for KQ6, which includes pharmacologic agents for pain given up to 10 days post-surgery.

†Includes breathing difficulties during sleep as operationalized in each study, including obstructive sleep apnea and upper airway resistance syndrome

‡Tonsillectomy includes tonsillectomy, adenotonsillectomy, partial tonsillectomy

Abbreviations: AHI = Apnea Hypopnea Index; BMI = Body Mass Index; CAS-15 = Clinical Assessment Score-15; CPAP = Continuous Positive Airway Pressure; ER = Emergency Room; KQ = Key Question; NSAID = Non-steroidal Anti-Inflammatory Drug; OSA-18 = Obstructive Sleep Apnea-18; OSDB = Obstructive Sleep-Disordered Breathing
# Appendix B. Search Strategies

## Table B-1. Preliminary PubMed search strategy (July 2015)

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<td>9. #8 AND eng [la]</td>
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Key: [la] language; [mh] medical subject heading; [pt] publication type.

## Table B-2. EMBASE search (August 2015)

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<td>1. tonsillectomy/ or palatine tonsillectomy/ or tonsillectomy.mp.</td>
<td>11409</td>
</tr>
<tr>
<td>2. adenotonsillectomy.mp. or adentonsillectomy/</td>
<td>2843</td>
</tr>
<tr>
<td>3. 1 or 2</td>
<td>13036</td>
</tr>
<tr>
<td>4. Limit 3 to English, 1980-current, non-medline journals</td>
<td>613</td>
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</table>

## Table B-3. Cochrane Trials Register

<table>
<thead>
<tr>
<th>Search terms</th>
<th>Search results</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Tonsillectomy or adentonsillectomy</td>
<td>1860</td>
</tr>
<tr>
<td>2. 1980-2015</td>
<td>1789</td>
</tr>
</tbody>
</table>
Appendix C. Information for Screening, Risk of Bias Assessment, and Strength of the Evidence

Tonsillectomy Abstract Review Form

1. Paper addresses one or more of the following in children (check all that apply):
   □ Benefits or harms of tonsillectomy (total or partial tonsillectomy or adenotonsillectomy) for obstructive sleep disordered breathing or throat infection (KQ1-2)
   □ Benefits/harms of undergoing tonsillectomy or not undergoing tonsillectomy after a given number of throat infections (KQ2a)
   □ Benefits or harms of different tonsillectomy techniques (coblation, cautery, etc.) or surgical types (partial, total) (KQ3-4)
   □ Benefits or harms of adjunctive perioperative pharmacologic treatments (steroids, analgesics, etc.) used with tonsillectomy (KQ5)
   □ Benefits or harms of postoperative pharmacologic agents for pain following tonsillectomy (KQ6)
   □ Cannot determine
   □ None of the above

2. Paper is original research?
   □ Yes □ No □ Cannot Determine

3. Study includes children ≤ 18 years of age?
   □ Yes □ No □ Cannot Determine

4. Record the total N children/total population (e.g., 70/100):
   ______________________

5. Study is a:
   □ Comparative study (i.e., has a treatment and comparison group. Includes case-control studies)
   □ Controlled pre-post study
   □ Case series or database/registry study with at least 1000 participants addressing harms
   □ Narrative review or SER/MA
   □ Other (please indicate design)
   □ Cannot determine

6. If excluded, retain for review of references/background?
   □ Yes □ No

7. If excluded, retain for potential data source for former KQ2a (threshold # throat infections/untreated throat infection)
   □ Yes □ No

Comments:
Tonsillectomy Full Text Review Form

1. Is the study original research (does not include systematic reviews or meta-analyses) ADRESSING TONSILLECTOMY?
   □ Yes  □ No

2. Does the study address tonsillectomy in children with OSDB or recurrent throat infection?
   □ OSDB
   □ Throat infection
   □ Not specified
   □ None of the above

3. Is the overall mean or median age of participants ≤ 18 years OR are at least 80% of participants ≤ 18 years of age OR are data for children (0-18 years) presented separately?
   □ Yes  □ No

3a. List total N: ______________________

4. Is this a comparative study (includes a treatment and a comparison group) OR database/registry study or case series with at least 1000 eligible participants reporting harms data?
   □ Yes  □ No

5. Does the study provide data related to at least one of the following of interest for the current review?
   □ Benefits or harms of tonsillectomy (total or partial tonsillectomy or adenotonsillectomy) for obstructive sleep-disordered breathing or throat infection (KQ1-2)
   □ Benefits or harms of different tonsillectomy techniques (coblation, cautery, etc.) or surgical types (partial, total) (KQ3-4)
   □ Benefits or harms of adjunctive perioperative pharmacologic treatments (steroids, analgesics, etc.) used with tonsillectomy (KQ5)
   □ Benefits or harms of postoperative pharmacologic agents for pain following tonsillectomy (KQ6)
   □ None of the above

6. Does the study provide outcome data on subpopulation of interest (children under age 3; Down syndrome; obesity or overweight; craniofacial or neuromuscular abnormalities)?
   □ Yes  □ No

7. Does the study provide data to address threshold number of throat infections (Among children with recurrent throat infections, what are the harms of not intervening at different clinical thresholds based on numbers of infections and severity)?
   □ Yes  □ No

C-2
8. Does the study provide data to address criteria for admission (i.e., which children should be admitted postoperatively and where (ICU, observation, etc.))?  
□ Yes  □ No

9. If excluded, retain this paper for review of references or background?  
□ Yes  □ No

10. Comments:  
______________________________________________________________________________  

                                                            

C-3
<table>
<thead>
<tr>
<th>Question</th>
<th>Yes</th>
<th>No</th>
<th>Unclear</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. List harms reported:</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2. Were the harms pre-defined using standardized or precise definitions?</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pre-defined indicates that the harms that were expected are explicitly defined prior to the collection of these expected events. For example, if bleeding is listed as a harmful event, the criteria by which they determine the bleeding (i.e. body location, type, or amount of blood loss that counts as an event, etc) should be specified. Standardized classification of harms can be derived from any of the following: 1) reference to standard terminology or classifications of harms from a recognized external organization(s)(such as government regulatory or health agencies. Examples of standardized terminology for harms includes, WHO-ART, MEDra, HTA report on the Measurement and Monitoring of Surgical Adverse Events) 2) previously explicitly defined classifications of harms in the literature, or 3) based on pre-specified clinical criteria, or 4) pre-specified laboratory test (may not need to have a specific cut-off level specified in all cases) <strong>In some instances only some of the harms identified in a study will be precisely defined. In this case, there must be some judgement if the nature of the harms not pre-defined.</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3. Are all pre-specified harms reported?</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>4. Did the author(s) use STANDARD scale(s) or checklist(s) for harms collection? <strong>Standard</strong> scales or checklists are those that have at least one of the following: -Established reliability and validity (specified in the text); -Are very widely used within the discipline (may have to check the reference list for the scale) <strong>In the instance where the methods indicate that a NEW scale or checklist was developed for the study specifically, the author(s) must</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
explicitly specify the CONTENT of the new scale or checklist in sufficient detail (for example, the body systems evaluated, or the specific tests or questions included.)

| 5. Are the statistical methods used to assess the main harm or adverse event outcomes adequate? |   |   |   |

Good= 4-5 “yes”; Fair=3 “yes” out of 5; Poor=2 “yes” or less
## Risk of Bias Assessment for Observational Studies

RefID: __________________  Reviewer:____________________

<table>
<thead>
<tr>
<th>QUESTION</th>
<th>Yes</th>
<th>No, differs</th>
<th>Cannot determine</th>
<th>Not applicable</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Please list observational study design</td>
<td>Prospective cohort</td>
<td>Non-randomized trial</td>
<td>Other prospective comparative</td>
<td>Case-control</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>No, criteria vary</td>
<td>Cannot determine</td>
</tr>
<tr>
<td>2. Were the inclusion/exclusion criteria the same across the comparison groups of the study?</td>
<td>Yes</td>
<td>Partially: some, but not all</td>
<td>No, criteria vary</td>
<td>Cannot determine</td>
</tr>
<tr>
<td>3. Is the strategy for recruiting participants into the study the same across groups?</td>
<td>Yes</td>
<td>No, differs</td>
<td>Cannot determine</td>
<td>Not applicable</td>
</tr>
<tr>
<td>4. Is the selection of the comparison group appropriate, after taking into account feasibility and ethical considerations?</td>
<td>Yes, appropriate</td>
<td>No, inappropriate</td>
<td>Cannot determine or no description of the derivation of the comparison group</td>
<td>Not applicable</td>
</tr>
<tr>
<td>5. Does the study account for important variations in the execution of the study from the proposed protocol?</td>
<td>Yes, accounts for variations</td>
<td>Partially, fails to account</td>
<td>No, does not account</td>
<td>Cannot determine</td>
</tr>
<tr>
<td>6. Was the outcome assessor blinded to the intervention or exposure status of participants?</td>
<td>Yes, blinded</td>
<td>No, not blinded</td>
<td>Not applicable: assessor cannot be blinded</td>
<td></td>
</tr>
</tbody>
</table>

C-6
<table>
<thead>
<tr>
<th>Question</th>
<th>Yes, valid and reliable measure used</th>
<th>No, valid and reliable measure not used</th>
<th>Cannot determine or measurement approach not reported</th>
</tr>
</thead>
<tbody>
<tr>
<td>7. Were valid and reliable measures, implemented consistently across all study participants, used to assess inclusion/exclusion criteria?</td>
<td>Yes, valid and reliable measure used</td>
<td>No, valid and reliable measure not used</td>
<td>Cannot determine or measurement approach not reported</td>
</tr>
<tr>
<td>8. Were valid and reliable measures, implemented consistently across all study participants, used to assess intervention/exposure outcomes and participant health benefits?</td>
<td>Yes, valid and reliable measure used for all outcomes of interest</td>
<td>Partially, valid and reliable measures used for some outcomes of interest</td>
<td>No, valid and reliable measure not used</td>
</tr>
<tr>
<td>9. Were valid and reliable measures, implemented consistently across all study participants used to assess confounding?</td>
<td>Yes, valid and reliable measure used</td>
<td>No, valid and reliable measure not used</td>
<td>Cannot determine or measurement approach not reported</td>
</tr>
<tr>
<td>10. Any attempt to balance the allocation between the groups or match groups (e.g., through stratification, matching, propensity scores)?</td>
<td>Yes, or study accounts for imbalance between groups through a post hoc approach such as multivariate analysis</td>
<td>No or cannot determine</td>
<td>Not applicable: study does not include a comparison group (case series or one study group)</td>
</tr>
<tr>
<td>11. Were important confounding variables taken into account in the design or analysis (e.g., through matching, stratification, interaction terms, multivariate analysis, or other statistical adjustment such as instrumental variables)?</td>
<td>Yes, accounted for or none identified</td>
<td>Partially; some variables taken into account or adjustment achieved to some extent</td>
<td>No, not taken into account</td>
</tr>
<tr>
<td>12. Are all important primary outcomes reported in the results?</td>
<td>Yes, all important outcome(s) reported</td>
<td>No, important outcome(s) are missing</td>
<td>Cannot determine</td>
</tr>
<tr>
<td>13. Was the length of follow-up the same across study groups?</td>
<td>Yes, same length of follow-up or remedied through analysis</td>
<td>No, different length of follow-up</td>
<td>Not applicable: cross-sectional or only one group followed over time</td>
</tr>
<tr>
<td>---</td>
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</tr>
<tr>
<td>14. In cases of high loss to follow-up (or differential loss to follow-up), was the impact assessed (e.g., through sensitivity analysis or other adjustment method)?</td>
<td>Yes, impact assessed</td>
<td>No, impact not assessed</td>
<td>Cannot determine</td>
</tr>
</tbody>
</table>
## Risk of Bias for RCTs Form

**Reviewer Initials: _____ Ref ID: __________**

<table>
<thead>
<tr>
<th>Risk of Bias</th>
<th>Criterion</th>
<th>Yes</th>
<th>No</th>
<th>Unclear</th>
<th>COMMENTS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Selection bias</td>
<td>Was the allocation sequence generated adequately (e.g., random number table, computer-generated randomization)?</td>
<td></td>
<td></td>
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</tr>
<tr>
<td></td>
<td>Was the allocation of treatment adequately concealed (e.g., pharmacy-controlled randomization or use of sequentially numbered sealed envelopes)?</td>
<td></td>
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<tr>
<td></td>
<td>Were participants analyzed within the groups they were originally assigned to?</td>
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<tr>
<td></td>
<td>Does the design or analysis control account for important confounding and modifying variables through matching, stratification, multivariable analysis, or other approaches?</td>
<td></td>
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</tr>
<tr>
<td>Performance bias</td>
<td>Did researchers rule out any impact from a concurrent intervention or an unintended exposure that might bias results? (Look for differences in anesthesia regimen, additional analgesics or medications at the time of anesthesia.)</td>
<td></td>
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<tr>
<td></td>
<td>Did the study maintain fidelity to the intervention protocol? (Consider differences in effects from crossover of pts—how much power was diminished; this is especially important to consider if there are no differences in effects.)</td>
<td></td>
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<td></td>
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</tr>
<tr>
<td>Attrition bias</td>
<td>If attrition (overall or differential nonresponse, dropout, loss to follow-up, or exclusion of participants) was a concern, were missing data handled appropriately (e.g., intention-to-treat analysis and imputation)?</td>
<td></td>
<td></td>
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<td></td>
</tr>
<tr>
<td>Detection bias</td>
<td>Was the length of follow-up different between the groups?</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Were the outcome assessors blinded to the intervention or exposure status of participants? (For bleeding, if only a subjective assessment was reported, we would expect to see something about method of follow-up in a lower RoB study.)</td>
<td></td>
<td></td>
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</tr>
<tr>
<td></td>
<td>Were interventions/exposures assessed/defined using clearly defined measures, implemented consistently across all study participants?</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Were outcomes assessed using valid and reliable measures, implemented consistently across all study participants?</td>
<td></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Reporting bias</td>
<td>Were the potential outcomes prespecified by the researchers?</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Are all prespecified outcomes reported?</td>
<td></td>
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<td></td>
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</table>
## Strength of the Evidence Domains

**Table C-1. Domains used to assess strength of evidence**

<table>
<thead>
<tr>
<th>Domain</th>
<th>Explanation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Study Limitations</td>
<td>Degree to which included studies for a given outcome have a high likelihood of adequate protection against bias (i.e., good internal validity), assessed through study design and study conduct.</td>
</tr>
</tbody>
</table>
| Consistency     | Degree to which included studies find either the same direction or similar magnitude of effect. Assessed through two main elements:  
  - Direction of effect: Effect sizes have the same sign (that is, are on the same side of no effect or a minimally important difference).  
  - Magnitude of effect: The range of effect sizes is similar.                                                                                                                                                                                                                                                                                     |
| Directness      | Extent to which evidence links interventions directly to a health outcome of specific importance for the review, and for comparative studies, whether the comparisons are based on head-to-head studies. Evidence may be indirect in several situations such as:  
  - Outcome being graded is considered intermediate in a review that is focused on clinical health outcomes (such as morbidity, mortality).  
  - Data do not come from head-to-head comparisons but rather from two or more bodies of evidence to compare.  
  - Data are available only for proxy respondents instead of directly from patients for situations in which patients are capable of self-reporting and self-report is more reliable.                                                                                                                                 |
| Precision       | Degree of certainty surrounding an effect estimate with respect to a given outcome, based on the sufficiency of sample size and number of events. A body of evidence will generally be imprecise if the optimal information size (OIS) is not met. OIS refers to the minimum number of patients (and events when assessing dichotomous outcomes) needed for an evidence base to be considered adequately powered.                                                                                                    |
| Reporting bias  | Degree of selective publishing or reporting of research findings based on the favorability of direction or magnitude of effect.                                                                                                                                                                                                                                                                                  |

## Appendix D. Excluded Studies

### Reasons for Exclusion

<table>
<thead>
<tr>
<th></th>
<th>Reason for Exclusion</th>
<th>Study Details</th>
</tr>
</thead>
</table>


395. Young JR. A comparative study of benzydamine hydrochloride 0.15% w.v. ('Difflam' pump spray) and placebo as analgesics following tonsillectomy. J Int Med Res. 1985;13(4):245-7. PMID: 3899773. X-1


423. Maw AR. Adenoidectomy and Adenotonsillectomy for Otitis Media with Effusion in Children: A Prospective Randomized Controlled Study. 1986 PMID: CN-00849155.X-1


D-29


805. Wyatt HV. Incubation of poliomyelitis as calculated from the time of entry into the central nervous system via the peripheral nerve pathways. Rev Infect Dis. 1990 May-Jun;12(3):547-56. PMID: 2163095.X-1


<table>
<thead>
<tr>
<th>ID</th>
<th>Title</th>
<th>Authors</th>
<th>Journal</th>
<th>Volume Issue Page</th>
<th>PMID</th>
</tr>
</thead>
</table>


D-63


D-64


D-70


D-73


D-83


D-86


D-88


D-93


1573. Rolling C, Treton D, Beckmann P, et al. JAK3 associates with the human interleukin 4 receptor and is tyrosine phosphorylated following receptor triggering. Oncogene. 1995 May 4;10(9):1757-61. PMID: 7538655.X-1


1846. Vaudaux BP, Cherpillod J, Dayer P. Concentrations of azithromycin in tonsilar and/or adenoid tissue from paediatric patients. J Antimicrob Chemother. 1996 Jun;37 Suppl C:45-51. PMID: 8818845. X-1


D-119


D-121


D-133


2277. Treatment strategy for IgA nephropathy depends on the risk of disease progression. Drugs and Therapy Perspectives. 1999 18 Jan;13(1):5-8. PMID: 1999028584.X-1


D-139


D-140


D-142


D-144


D-161


D-169


D-187


D-203


3330. Fagnani F, German-Fattal M. Antibiotic
prescribing patterns of French GPs for upper
respiratory tract infections: impact of
fusafungine on rates of prescription of systemic
PMID: 14719988.X-1

3331. Fechner FP, Kieff D. Cervical emphysema
complicating tonsillectomy with argon beam
coagulation. Laryngoscope. 2003
May;113(5):920-1. doi: 10.1097/00005537-
200305000-00027. PMID: 12792334.X-1

3332. Felder-Puig R, Maksys A, Noestlinger C, et
al. Using a children's book to prepare children
and parents for elective ENT surgery: results of a
randomized clinical trial. Int J Pediatr
Otorhinolaryngol. 2003 Jan;67(1):35-41. PMID:
12560148. X-1

3333. Fink W, Zimpfer A, Ugurel S. Mucosal
metastases in malignant melanoma. Onkologie.
2003 Jun;26(3):249-51. doi: 71620. PMID:
12845209.X-1

3334. Flanary VA. Long-term effect of
adenotonsillectomy on quality of life in pediatric
patients. Laryngoscope. 2003 Oct;113(10):1639-
44. PMID: 14520088.X-5

3335. Flickinger JC, Kondziolka D, Maizt AH, et
al. Gamma knife radiosurgery of imaging-
diagnosed intracranial meningioma. Int J Radiat
PMID: 12788188.X-1

3336. Fregosi RF, Quan SF, Kaemingk KL, et al.
Sleep-disordered breathing, pharyngeal size and
soft tissue anatomy in children. J Appl Physiol
PMID: 12897029.X-1

3337. Friedman BC, Hendele-Amotai A,
Kozminsky E, et al. Adenotonsillctomy
improves neurocognitive function in children
with obstructive sleep apnea syndrome. Sleep.
X-5

Radiofrequency tonsil reduction: safety,
morbidity, and efficacy. Laryngoscope. 2003
May;113(5):882-7. doi: 10.1097/00005537-
200305000-00020. PMID: 12792327. X-5

Telithromycin (HMR 3647) achieves high and
sustained concentrations in tonsils of patients
undergoing tonsillectomy. Int J Antimicrob
Agents. 2003 May;21(5):441-5. PMID:
12727077.X-1

3340. Gessler EM, Bondy PC. Respiratory
complications following tonsillectomy/UPPP: is
step-down monitoring necessary? Ear Nose
Throat J. 2003 Aug;82(8):626-32. PMID:
14503103.X-1

Value-based approach to power-assisted
Jul;112(7):606-10. PMID: 12903680.X-1

3342. Gnanalingham KK, Lafuente J, Thompson
D, et al. The natural history of ventriculomegaly
and tonsillar herniation in children with posterior
fossa tumours--an MRI study. Pediatr
PMID: 14512688.X-1

3343. Graham SM, Nerad JA. Orbital
complications in endoscopic sinus surgery using
powered instrumentation. Laryngoscope. 2003
May;113(5):874-8. doi: 10.1097/00005537-
200305000-00018. PMID: 12792325.X-1

Obstructive sleep apnea syndrome due to
adenotonsillar hypertrophy in infants. Int J
Pediatr Otorhinolaryngol. 2003 Oct;67(10):1055-
60. PMID: 14550958.X-1, X-5


3479. Rosefsky JB. Tonsillectomies and adenotonsillectomies--will the debate never be over? Pediatrics. 2003;112(1 Pt 1):205; author reply PMID: CN-00558898.


3617. Dsida R, Cote CJ. Nonsteroidal antiinflammatory drugs and hemorrhage following tonsillectomy: do we have the data? Anesthesiology. 2004 Mar;100(3):749-51; author reply 51-2. PMID: 15109002. X-2


3668. Hotta O. Use of corticosteroids, other immunosuppressive therapies, and tonsillectomy in the treatment of IgA nephropathy. Semin Nephrol. 2004 May;24(3):244-55. PMID: 15156529. X-1


zoster virus transfer to skin by T Cells and 
 modulation of viral replication by epidermal cell 
 PMID: 15452178.X-1

3687. Kubba H, Swan IR, Gatehouse S. The 
Glasgow Children's Benefit Inventory: a new 
instrument for assessing health-related benefit 
2004 Dec;113(12):980-6. PMID: 15633901. X-1, X-5

3688. Kumar TV, Kuriakose S. Ultrasonographic 
evaluation of effectiveness of circumoral muscle 
exercises in adenotonsillectomized children. J 
PMID: 15554404.X-1

3689. Kumar VV, Kumar NV, Isaacson G. 
Superstition and post-tonsillectomy hemorrhage. 
Laryngoscope. 2004 Nov;114(11):2031-3. doi: 
10.1097/01.mlg.0000147942.82626.1c. PMID: 
15510037.X-1

Prominent clonal B-cell populations identified 
by flow cytometry in histologically reactive 
lymphoid proliferations. Am J Clin Pathol. 2004 
Apr;121(4):464-72. doi: 10.1309/4ej8-t3r2-erkq- 
61wh. PMID: 15080297.X-1

3691. Lake AP, Khater M. Effects of postoperative 
nonsteroidal antiinflammatory drugs on bleeding 
risk after tonsillectomy. Anesthesiology. 2004 
Mar;100(3):748-9; author reply 51-2. PMID: 
15109001. X-2

3692. Langton Hewer SC, Langton Hewer CD, 
with mild symptoms: watchful waiting may deny 
children opportunity for development. Bmj. 2004 
Oct 30;329(7473):1045; author reply doi: 
10.1136/bmj.329.7473.1045. PMID: 15514365. 
X-2

Surgical advances in tonsillectomy: report of a 
roundtable discussion. Ear Nose Throat J. 2004 
Aug;83(8 Suppl 3):4-13; quiz 4-5. PMID: 
15485055.X-1

3694. Lee MS, Montague ML, Hussain SS. Post-
tonsillectomy hemorrhage: cold versus hot 
Dec;131(6):833-6. doi: 10.1016/j.otohns.2004.08.008. PMID: 
15577776. X-1

3695. Leighton S, Drake AF. Airway 
considerations in craniofacial patients. Oral 
Maxillofac Surg Clin North Am. 2004 
18088754. X-2

3696. Lemos P. Ambulatory surgery in Portugal: 
2004 May;10(4):179-80. doi: 
PMID: 2004175166.X-1

3697. Leontidou A, Papadopoulou K, Vlachtsis K, 
et al. Child's cardiac tumour unmasked during 
tonsillectomy. Eur J Anaesthesiol. 2004 
Mar;21(3):246-9. PMID: 15055906.X-1

3698. Li AM, Chan DF, Fok TF, et al. Childhood 
obstructive sleep apnoea: an update. Hong Kong 
15591600.X-1, X-5

3699. Li HY, Wang PC, Hsu CY, et al. Same-stage 
palatopharyngeal and hypopharyngeal surgery 
for severe obstructive sleep apnea. Acta 
Otolaryngol. 2004 Sep;124(7):820-6. doi: 
10.1080/00016480410018034. PMID: 
15370567.X-1

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Appendix E. Methods for Meta-Analyses

Key Question 1

To assess whether treatment of children suffering from obstructive sleep-disordered breathing (OSDB) with tonsillectomy results in improved outcomes compared with continuous positive airway pressure (CPAP), or watchful waiting with supportive care (including pharmacologic treatment), we constructed a simple meta-analysis using the change in apnea hypopnea index (AHI) as a measure of treatment efficacy. Because there were only three studies included in the final dataset, we fit a fixed effects model for the treatment effect. The expected arm response was modeled as:

\[ \theta_i = \mu + \delta I(t_i) \]

where \( I \) is the indicator function, \( t_i \) is a dummy variable that equals one for a treatment arm and zero for a control arm.

The response variable \( d_i \) is the difference between the outcome and baseline for arm \( i \), and is hypothesized to have the sampling distribution:

\[ d_i \sim N(\theta_i, s_i) \]

where \( s_i \) is assumed to be the empirical standard error of the difference between the sample means of the outcome and baseline response variables:

\[ s_i = \sqrt{s_i(o)^2 + s_i(b)^2} \]

where \( s_i(o) \) and \( s_i(b) \) are the standard errors of the outcome and baseline responses, respectively, and \( n_i(o) \) and \( n_i(b) \) are the sample sizes for the outcome and baseline responses, respectively.

The effectiveness of the treatment was assessed by examining the estimate of \( \delta \) and its associated 95% credible interval.

Key Questions 3 and 4 (Harms)

We implemented a mixed-effects, arm-based meta-analysis to assess the influence of different surgical procedures as well as the effect of partial vs. total removal procedures on the occurrence of bleeding outcomes following tonsillectomy. The occurrence of bleeding events in most studies are reported as counts, and can therefore be modeled as a binomial response, with inference derived from estimates of the probability of a bleeding event.

\[ x_{ki} \sim \text{Binomial}(n_i, \pi_{ki}) \]

where \( \pi_{ki} \) is the probability of a bleeding event for intervention \( k \) for study \( i \). This probability is modeled hierarchically as a logit-linear model with treatment effects and a study-specific random effect as follows:

\[ \text{logit}(p_{ki}) = \theta_k + \beta I(\text{partial}_k) + \alpha I(\text{high RoB}_i) + \epsilon_i \]
here, $\theta_k$ is a surgery-specific mean and $\beta$ the effect of a partial removal when partial$_k$ is true, while $\epsilon_i$ and $\alpha_i$ are a study random effect and a high risk of bias effect, respectively, that correspond to study $i$.

Logit-linear model parameters were given zero-mean normal priors with $\sigma = 5$, which correspond to diffuse information when transformed to the inverse-logit scale. The study random effect was assumed normally distributed with an unknown standard deviation that was estimated from data, with a broad half-Cauchy prior distribution.

This model was fit to each of four bleeding outcome data: re-operation bleeding, re-admission bleeding, primary bleeding, and secondary bleeding.

**Key Question 5**

To assess the effectiveness of perioperative steroids on post-operative bleeding rates associated with tonsillectomy, we employed a Bayesian mixed-effects binomial meta-analytic model. We assumed bleeding type-specific baseline rates of bleeding, as well as bleeding type-specific intervention effects, and a fixed effect for dose. Additionally, we included study random effects to account for correlation among arms in the same study.

$$\logit(p_{ijk}) = \theta_k + \alpha_i x_i^{(dose)} + \delta_k x_i^{(treat)} + \epsilon_i$$

However, the model above showed substantial lack of fit due to the prevalence of zeros in the bleeding counts. There appeared to be a mixture of outcomes, one of which never results in bleeding, and the other which may (according to the binomial model). Thus, we expanded the model to account for the zero-inflated data. Hence the distribution of the observed bleeding cases becomes:

$$y_i \sim \begin{cases} 
0, \text{with probability } (1 - \psi) \\
\text{Binomial}(n_i, p_{ijk}), \text{with probability } \psi 
\end{cases}$$

In other words, some study arms had no chance of post-operative bleeding, with probability $1 - \psi$, while the remainder experienced bleeding with probability $p_{ijk}$.

Logit-linear model parameters were given zero-mean normal priors with $\sigma = 5$, which correspond to diffuse information when transformed to the inverse-logit scale. Random effects were assumed normally distributed with an unknown standard deviation that was estimated from data, with a broad half-Cauchy prior distribution.

**Model Fitting**

All models were fit using the No U-turn Sampler (Hoffman and Gelman 2014), a self-tuning, gradient-based Markov chain Monte Carlo (MCMC) algorithm. Models were checked for convergence using the Gelman-Rubin statistic (Gelman and Rubin 1992) and for goodness of fit using posterior predictive checks (Gelman et al. 2013). None of the final models showed evidence for lack of convergence or fit using these criteria.
References


## Appendix F. Risk of Bias Ratings

### Table F-1. Risk of bias assessment for randomized controlled trials

| Author Year   | Allocation Sequence Generated Adequately | Allocation Treatment Adequately Concealed | Participants Analyzed in Groups Originally Assigned | Design Account for Confounding | Rule Out Impact from Concurrent Interventions or Unintended Exposure | Fidelity Maintained to Intervention Protocol | If Attrition, Were Missing Data Handled Appropriately | Difference in Length of Follow-up Between Groups | Outcome Assessors Blinded | Interventions/Exposures Assessed Clearly | Outcomes Assessed Clearly | Potential Outcomes Prespecified | All Prespecified Outcomes Reported | Risk of Bias Rating |
|---------------|------------------------------------------|-------------------------------------------|-----------------------------------------------------|-------------------------------|---------------------------------------------------------------|---------------------------------------------|---------------------------------------------------|-----------------------------------------------|-----------------------------------------------|--------------------------------------------|----------------------------|------------------------------------------|------------------------------------------|----------------------|-------------------|
| Kordeluk 2016 | Unclear                                   | Unclear                                   | Yes                                                 | Yes                           | Unclear                                                        | No                                          | Yes or NA                                        | No                                            | Yes                                           | Yes or NA                                  | Yes                                         | Yes                                      | Yes                                      | High                 |
| Murto 2015    | Yes                                      | Yes                                       | Yes                                                 | No                            | Yes                                                           | Yes or NA                                  | Yes                                              | Yes                                           | Yes                                           | Yes or NA                                  | Yes                                         | Yes                                      | Yes                                      | Moderate             |
| Gao 2015      | Yes                                      | Yes                                       | Yes                                                 | Yes                           | Yes                                                           | Yes or NA                                  | Yes or NA                                        | Yes                                           | Yes                                           | Yes or NA                                  | Yes                                         | Yes                                      | Yes                                      | Low                  |
| Abdel-Ghaffar 2015 | Yes                                      | Yes                                       | Yes                                                 | Yes                           | Yes                                                           | Yes or NA                                  | Yes                                              | Yes                                           | Yes                                           | Yes or NA                                  | Yes                                         | Yes                                      | Yes                                      | Low                  |
| Park 2015     | Yes                                      | Unclear                                   | Yes                                                 | Yes                           | Yes                                                           | Yes or NA                                  | Yes                                              | Yes                                           | Yes                                           | Yes or NA                                  | Yes                                         | Yes                                      | Yes                                      | Low                  |
| Kelly 2015    | Yes                                      | Yes                                       | Yes                                                 | Yes                           | Yes                                                           | Yes or NA                                  | Yes                                              | Yes                                           | Yes                                           | Yes or NA                                  | Yes                                         | Yes                                      | Yes                                      | Low                  |

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<th>Valid and Reliable Measures Used to Assess Outcomes</th>
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Table F-3. Risk of bias assessment for studies reporting harms

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<th>Were all pre-specified harms reported?</th>
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<th>Were the statistical methods used to assess the main harm or adverse event outcomes adequate?</th>
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<td>Author, Year</td>
<td>Were the harms predefined using standardized or precise definitions?</td>
<td>Were all pre-specified harms reported?</td>
<td>Did the author(s) use STANDARD scale(s) or checklist(s) for harms collection?</td>
<td>Were the statistical methods used to assess the main harm or adverse event outcomes adequate?</td>
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References


94. Kim MS, Cote CJ, Cristoloveanu C, et al. There is no dose-escalation response to dexamethasone (0.0625-1.0 mg/kg) in
pediatric tonsillectomy or adenotonsillectomy patients for preventing vomiting, reducing pain, shortening time to first liquid intake, or the incidence of voice change. Anesth Analg 2007 May;104(5):1052-8, tables of contents. PMID: 17456652.


126. Stoker KE, Don DM, Kang DR, et al. Pediatric total tonsillectomy using coblation compared to conventional electrosurgery: a


## Appendix G. Applicability of Findings

### Table G-1. Tonsillectomy vs. no surgery/watchful waiting for children with OSDB

<table>
<thead>
<tr>
<th>Domain</th>
<th>Description of applicability of evidence</th>
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<tbody>
<tr>
<td>Population</td>
<td>Studies included children ages less than 2 to 16 years. In most studies children had PSG-proven OSDB. Three studies—including the largest RCT—had majority African-American populations. One study included children with Down Syndrome or mucopolysaccharidosis and another included children under 24 months.</td>
</tr>
<tr>
<td>Intervention</td>
<td>Tonsillectomy or tonsillectomy with adenoidectomy</td>
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<tr>
<td>Comparators</td>
<td>Comparators included watchful waiting or medical management.</td>
</tr>
<tr>
<td>Outcomes</td>
<td>Studies outcomes included changes in AHI, sleep-related quality of life, and behavioral and cognitive outcomes. Data were collected from PSG, direct interviews/assessments, provider records, and quality of life surveys. Outcomes were collected at various time points with followup times ranging from 5 months to 4 years. Most studies reported outcomes at 5-7 months.</td>
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<tr>
<td>Setting</td>
<td>Studies were conducted in the United States (6), Brazil (2), Israel (2), Australia (1), Ireland (1), and India (1). Patients were typically selected from otolaryngology clinics or their information was collected from a database.</td>
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PSG = Polysomnography; OSDB = Obstructive Sleep Disordered Breathing; RCT = Randomized Controlled Trial

### Table G-2. Tonsillectomy vs. no surgery/watchful waiting for children with recurrent throat infections

<table>
<thead>
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<th>Domain</th>
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<td>Population</td>
<td>Studies included children ages 3-16 with differing requirements for inclusion based on number of sore throat episodes from mildly impacted children with a minimum of one sore throat episode in the previous year to more severely impacted children with more than 7 sore throat episodes in the previous year. One study based inclusion on three or more documented episodes of Group A Strep throat infections. Studies typically did not report race/ethnicity or BMI. Four RCTs or non-randomized trials included majority Caucasian populations.</td>
</tr>
<tr>
<td>Intervention</td>
<td>Tonsillectomy or tonsillectomy with adenoidectomy</td>
</tr>
<tr>
<td>Comparators</td>
<td>Comparators included watchful waiting or medical management.</td>
</tr>
<tr>
<td>Outcomes</td>
<td>Study outcomes included number of sore throat days, healthcare visits, missed school or work, quality of life. Data were collected from patient diaries, direct interviews, provider records and quality of life surveys. Outcomes were collected at various time points with most studies offering a time point of one year post procedure and at least one additional study year. One study reported data 6-years post-procedure and had the longest duration.</td>
</tr>
<tr>
<td>Setting</td>
<td>Studies were conducted in the United States, Netherlands, Ireland, and the United Kingdom and patients were selected from otolaryngology or primary care clinics or their information was collected from a database.</td>
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BMI = Body Mass Index; RCT = Randomized Controlled Trial
### Table G-3. Partial vs. total tonsillectomy

<table>
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<th>Domain</th>
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<td><strong>Population</strong></td>
<td>Studies included children ages less than 2 to 17 years. Most studies (19) included children with OSDB (typically based on clinical diagnosis vs. PSG). Neither race/ethnicity nor BMI were typically reported.</td>
</tr>
<tr>
<td><strong>Intervention</strong></td>
<td>Partial or total tonsillectomy/adenotonsillectomy. “Partial” tonsillectomy was variously defined (ranging from 10-70% removal or removal of protruding tissue only or removal of all but a thin rim of tissue) or not described across studies.</td>
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<tr>
<td><strong>Comparators</strong></td>
<td>Comparators included surgical technique (e.g., coblation, electrocautery) and partial or total removal of tonsils.</td>
</tr>
<tr>
<td><strong>Outcomes</strong></td>
<td>Outcomes included persistence of OSDB, return to normal diet or activity, recurrent throat infection, tonsillar regrowth, quality of life, postoperative bleeding, and behavioral outcomes. Outcomes were reported in multiple ways (means, %, days, N, etc.). Studies collected data from patient diaries, direct interviews/assessments, provider records, and quality of life or other outcome surveys. Outcomes were collected at various time points with followup times ranging from 5-7 days post-procedure to 6 years.</td>
</tr>
<tr>
<td><strong>Setting</strong></td>
<td>Studies were conducted in the United States (8), Greece (3), Sweden (2), Turkey (2), Brazil (2), Lebanon (1), Israel (1), Egypt (1), France (1), and Thailand (1). Patients were typically selected from otolaryngology clinics.</td>
</tr>
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</table>

BMI = Body Mass Index; N = Number; PSG = Polysomnography; OSDB = Obstructive Sleep Disordered Breathing

### Table G-4. Techniques for tonsillectomy

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<tr>
<th>Domain</th>
<th>Description of applicability of evidence</th>
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<tbody>
<tr>
<td><strong>Population</strong></td>
<td>Studies included individuals ages less than 2 to 41 years (mean age in all studies &lt;18 years). Most studies (28) included children with OSDB (typically based on clinical diagnosis vs. PSG) and recurrent throat infection (typically not defined). Studies typically did not report race/ethnicity or BMI.</td>
</tr>
<tr>
<td><strong>Intervention</strong></td>
<td>Partial or total tonsillectomy/adenotonsillectomy using various surgical techniques.</td>
</tr>
<tr>
<td><strong>Comparators</strong></td>
<td>Comparators included other surgical techniques (e.g., coblation, electrocautery).</td>
</tr>
<tr>
<td><strong>Outcomes</strong></td>
<td>Outcomes included return to normal diet or activity and postoperative bleeding and were reported in multiple ways (days, %, n children, etc.). Studies collected data from patient diaries and direct interviews/assessments. Outcomes were collected at various time points with followup times ranging from 9 days post-procedure to 12 months. Most studies had short-term (&lt; 6 months) followup.</td>
</tr>
<tr>
<td><strong>Setting</strong></td>
<td>Studies were conducted in the United States (8), Greece (3), Sweden (2), Turkey (2), Brazil (2), Egypt (1), France (1), and Thailand (1). Patients were typically selected from otolaryngology clinics.</td>
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</table>

BMI = Body Mass Index; N = Number; PSG = Polysomnography; OSDB = Obstructive Sleep Disordered Breathing
### Table G-5. Perioperative medications

<table>
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<tr>
<th>Domain</th>
<th>Description of applicability of evidence</th>
</tr>
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<tbody>
<tr>
<td>Population</td>
<td>Studies included individuals from 1-18 years of age. Most studies (38) did not specify indications for tonsillectomy. Six studies included children with mixed indications, and five studies included children with recurrent throat infection (typically not defined). Studies typically did not report race/ethnicity and BMI.</td>
</tr>
<tr>
<td>Intervention</td>
<td>NSAIDs, anti-emetics, or steroids (different doses and/or routes or combinations of these agents or these agents plus a non-NSAID analgesic or anesthetic) given perioperatively during tonsillectomy. Doses and routes of administration of intervention and comparator agents and of rescue medications varied widely.</td>
</tr>
<tr>
<td>Comparators</td>
<td>Comparators included other agents or no agent/placebo.</td>
</tr>
<tr>
<td>Outcomes</td>
<td>Outcomes included return to normal diet or activity, need for rescue medications, and postoperative bleeding. Studies reported outcomes in multiple ways (days, %, n children, mean dose, etc.). Data were collected from patient diaries and direct interviews/assessments. Most studies had short-term followup (24 hours post-op to ≤ 5 months).</td>
</tr>
<tr>
<td>Setting</td>
<td>Most studies (32) were conducted in less developed countries; 17 were conducted in the US, European countries, Japan, South Korea, or Australia. Studies typically recruited patients from otolaryngology or pediatric clinics.</td>
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</table>

BMI = Body Mass Index; N = Number; NSAID = Nonsteroidal Anti-Inflammatory Drug

### Table G-6. Postoperative medications

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<th>Domain</th>
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<tbody>
<tr>
<td>Population</td>
<td>Studies included children between 1 and 18 years of age. Most studies did not specify the indication for tonsillectomy (8). Four studies included children who had either OSDB or recurrent throat infection as surgical indications, and one included only children with throat infection. Neither race/ethnicity nor BMI were typically reported. One study included primarily Asian children.</td>
</tr>
<tr>
<td>Intervention</td>
<td>Postoperative medications for pain following tonsillectomy (typically via unspecified techniques). Agents included steroids, NSAIDs, non-NSAID analgesics, and antibiotics, individually or in combination.</td>
</tr>
<tr>
<td>Comparators</td>
<td>Other agents or no agent/placebo.</td>
</tr>
<tr>
<td>Outcomes</td>
<td>Studies reported primarily on need for rescue medications, bleeding, and time to return to normal diet or activity. Outcomes were primarily reported using diaries or questionnaires, and studies typically had short-term followup (3-16 days post-procedure. One study had 5-month followup.</td>
</tr>
<tr>
<td>Setting</td>
<td>Studies were conducted in Denmark (3), New Zealand (2), Canada (2) Jordan (1), Serbia (1), Korea (1), Egypt (1), Pakistan (1), and Turkey (1). Patients were recruited primarily from otolaryngology clinics or pediatric surgery units.</td>
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NSAID = Nonsteroidal Anti-Inflammatory Drug; OSDB = Obstructive Sleep Disordered Breathing
References

### Appendix H. Detailed Tables of Findings

#### Bleeding-Related Harms in Comparative Studies Addressing Tonsillectomy

**Table H-1. Postoperative hemorrhage reported in comparative study arms addressing total tonsillectomy**

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<tr>
<th>Technique</th>
<th>Indication Author, Year</th>
<th>Total Arm N</th>
<th>Total PTH</th>
<th>Primary PTH n (%)</th>
<th>Secondary PTH n (%)</th>
<th>Other/Undefined PTH n (%)</th>
<th>Nonoperative Revisit or Readmission for PTH n (%)</th>
<th>Reoperation for PTH n (%)</th>
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<td>NR</td>
<td>2 (1.4)</td>
</tr>
<tr>
<td>Van Staaij 2004**</td>
<td></td>
<td>194</td>
<td>7</td>
<td>7 (4)</td>
<td>NR</td>
<td>NR</td>
<td>3 (2)</td>
<td>2 (1)</td>
</tr>
<tr>
<td><strong>Unspecified</strong></td>
<td></td>
<td>97</td>
<td>6</td>
<td>NR</td>
<td>NR</td>
<td>6 (6.2)</td>
<td>NR</td>
<td>6 (6.2)</td>
</tr>
<tr>
<td>Al-Shehri 2012**</td>
<td></td>
<td>100</td>
<td>2</td>
<td>2 (2)</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
</tr>
<tr>
<td>Bukhari 2007**</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Electrocautery and cold dissection (left or right tonsil)</strong></td>
<td></td>
<td>6299</td>
<td>265</td>
<td>33 (1.3)</td>
<td>166 (4.8)</td>
<td>66 (2.7)</td>
<td>80 (3.0)</td>
<td>66 (2.2)</td>
</tr>
<tr>
<td><strong>Cold dissection (34)</strong></td>
<td></td>
<td>1668</td>
<td>82</td>
<td>4.9</td>
<td>50 (0.99)</td>
<td>62 (6.3)</td>
<td>15 (2.3)</td>
<td>36 (5)</td>
</tr>
<tr>
<td><strong>Harmonic scalpel (5)</strong></td>
<td></td>
<td>1904</td>
<td>72</td>
<td>3.8</td>
<td>60 (0.54)</td>
<td>49 (4)</td>
<td>17 (2.7)</td>
<td>9 (1.6)</td>
</tr>
<tr>
<td><strong>Unspecified/ other technique (5)</strong></td>
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<td>397</td>
<td>45</td>
<td>11.3</td>
<td>1 (0.63)</td>
<td>38 (1.3)</td>
<td>6 (9.8)</td>
<td>15 (5.5)</td>
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<td><strong>Coblation (19)</strong></td>
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<td>748</td>
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<td>9 (3.1)</td>
<td>NR</td>
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<td>8 (2.0)</td>
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<tr>
<td><strong>Laser (4)</strong></td>
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<td>189</td>
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<td>5.3</td>
<td>9 (1.4)</td>
<td>1 (0.91)</td>
<td>NR</td>
<td>9 (1.4)</td>
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<tr>
<td><strong>Thermal welding (4)</strong></td>
<td></td>
<td>199</td>
<td>5</td>
<td>2.5</td>
<td>0 (0)</td>
<td>5 (2.96)</td>
<td>0 (0)</td>
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<td>0.86</td>
<td>0 (0)</td>
<td>4 (1.22)</td>
<td>0 (0)</td>
<td>1 (0.23)</td>
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N=Number; NR=Not Reported; OSDB=Obstructive Sleep Disordered Breathing; PTH=Post-Tonsillectomy Hemorrhage
Table H-2. Postoperative hemorrhage reported in comparative study arms addressing partial tonsillectomy

<table>
<thead>
<tr>
<th>Technique</th>
<th>Indication</th>
<th>Total Arm N</th>
<th>Total PTH</th>
<th>Primary PTH n (%)</th>
<th>Secondary PTH n (%)</th>
<th>Other/ Undefined PTH n (%)</th>
<th>Nonoperative Revisit or Readmission for PTH n (%)</th>
<th>Reoperation for PTH n (%)</th>
</tr>
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<tbody>
<tr>
<td>Coblation</td>
<td>OSDB</td>
<td>32</td>
<td>2</td>
<td>0</td>
<td>2 (6)</td>
<td>NR</td>
<td>2 (6)</td>
<td>0 (0)</td>
</tr>
<tr>
<td></td>
<td>Ericsson 2009(^{22, 23})</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Chang 2008(^{8})</td>
<td>34</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>Coticchia 2006(^{49})</td>
<td>13</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>0</td>
<td>NR</td>
</tr>
<tr>
<td>Throat infection</td>
<td>Stelter 2012(^{73, 1437})</td>
<td>14</td>
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<td>NR</td>
<td>0</td>
<td>NR</td>
<td>NR</td>
</tr>
<tr>
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<td>49</td>
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<td>NR</td>
<td>NR</td>
<td>2 (4)</td>
<td>NR</td>
<td>NR</td>
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<td>Chan 2004(^{38})</td>
<td>27</td>
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<td>0</td>
<td>0</td>
<td>NR</td>
<td>NR</td>
</tr>
<tr>
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<td>OSDB</td>
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<td>0</td>
<td>NR</td>
<td>NR</td>
<td>0</td>
<td>NR</td>
<td>NR</td>
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<td>Skoulakis 2007(^{26})</td>
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<td>Chaidas 2013(^{21})</td>
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<td>0</td>
<td>0</td>
<td>NR</td>
<td>NR</td>
<td>0</td>
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<tr>
<td></td>
<td>Korkmaz 2008(^{34})</td>
<td>40</td>
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<td>NR</td>
<td>NR</td>
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<td>NR</td>
<td>1 (3)</td>
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<td>19</td>
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<td>NR</td>
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<td>NR</td>
<td>NR</td>
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<td>0</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
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<tr>
<td></td>
<td>Havel 2012(^{74}) (diode laser)</td>
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<td></td>
<td></td>
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<tr>
<td></td>
<td>Havel 2012(^{74}) (CO(_2) laser)</td>
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<td>0</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
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<tr>
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<td>Stelter 2010(^{71, 75})</td>
<td>12</td>
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<td>NR</td>
<td>NR</td>
<td>0</td>
<td>NR</td>
<td>NR</td>
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<td>Microdebrider</td>
<td>OSDB</td>
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<td>0</td>
<td>NR</td>
<td>NR</td>
<td>0</td>
<td>NR</td>
<td>NR</td>
</tr>
<tr>
<td></td>
<td>Lister 2006(^{56})</td>
<td></td>
<td></td>
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</tr>
<tr>
<td></td>
<td>Beriat 2013(^{28})</td>
<td>37</td>
<td>0</td>
<td>NR</td>
<td>NR</td>
<td>0</td>
<td>0</td>
<td>NR</td>
</tr>
<tr>
<td>Mixed</td>
<td>Gabr</td>
<td>20</td>
<td>0</td>
<td>NR</td>
<td>NR</td>
<td>0</td>
<td>NR</td>
<td>NR</td>
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<td>Technique</td>
<td>Indication Author, Year</td>
<td>Total Arm N</td>
<td>Total PTH</td>
<td>Primary PTH n (%)</td>
<td>Secondary PTH n (%)</td>
<td>Other/ Undefined PTH n (%)</td>
<td>Nonoperative Revisit or Readmission for PTH n (%)</td>
<td>Reoperation for PTH n (%)</td>
</tr>
<tr>
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<td>--------------------------</td>
<td>-------------</td>
<td>-----------</td>
<td>-------------------</td>
<td>---------------------</td>
<td>--------------------------</td>
<td>-----------------------------------------------</td>
<td>----------------------------</td>
</tr>
<tr>
<td>2014&lt;sup&gt;11&lt;/sup&gt;</td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Unspecified</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pruegsanusak 2010&lt;sup&gt;48&lt;/sup&gt;</td>
<td>20</td>
<td>1</td>
<td>NR</td>
<td>NR</td>
<td>1 (5)</td>
<td>1 (5)</td>
<td>NR</td>
<td></td>
</tr>
<tr>
<td>Derkay 2006&lt;sup&gt;56&lt;/sup&gt;</td>
<td>150</td>
<td>2</td>
<td>NR</td>
<td>NR</td>
<td>2 (1.3)</td>
<td>2 (1.3)</td>
<td>NR</td>
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</tr>
<tr>
<td>Totals (N arms)</td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>All arms (18)</td>
<td>599</td>
<td>8 (1.5)</td>
<td>0 (0)</td>
<td>2 (1.6)</td>
<td>6 (1.4)</td>
<td>5 (1.8)</td>
<td>1 (0.64)</td>
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<tr>
<td>Coblation (6)</td>
<td>169</td>
<td>4 (4.2)</td>
<td>0 (0)</td>
<td>2 (6.3)</td>
<td>2 (2.2)</td>
<td>2 (2.8)</td>
<td>0 (0)</td>
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<tr>
<td>Microdebrider (5)</td>
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<td>3 (1.2)</td>
<td>NR</td>
<td>NR</td>
<td>3 (1.2)</td>
<td>3 (1.45)</td>
<td>NR</td>
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</tr>
<tr>
<td>Cold dissection (4)</td>
<td>124</td>
<td>1 (0.81)</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td>1 (1.4)</td>
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</tr>
<tr>
<td>Laser (3)</td>
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<td>0 (0)</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td>NR</td>
<td>NR</td>
<td></td>
</tr>
</tbody>
</table>

N=Number; NR=Not Reported; OSDB=Obstructive Sleep Disordered Breathing; PTH=Post-Tonsillectomy Hemorrhage
## Non-Bleeding Harms

### Table H-3. Revisits for pain or dehydration reported after partial tonsillectomy in arms of comparative studies

<table>
<thead>
<tr>
<th>Technique for Partial Tonsillectomy</th>
<th>Author, Year Indication</th>
<th>Total Arm N</th>
<th>Pain Revisits/Readmissions, n (%)</th>
<th>Dehydration Revisits/Readmissions, n (%)</th>
<th>PONV Revisits/Readmissions, n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Microdebrider OSDB</td>
<td>Derkay 2006&lt;sup&gt;36&lt;/sup&gt;</td>
<td>150</td>
<td>NR</td>
<td>5 (3.3)</td>
<td>NR</td>
</tr>
<tr>
<td></td>
<td>Beriat 2013&lt;sup&gt;24&lt;/sup&gt;</td>
<td>37</td>
<td>0</td>
<td>0 (0)</td>
<td>NR</td>
</tr>
<tr>
<td>Coblation</td>
<td>Chang 2008&lt;sup&gt;7&lt;/sup&gt;</td>
<td>34</td>
<td>NR</td>
<td>0 (0)</td>
<td>NR</td>
</tr>
<tr>
<td><strong>Totals</strong></td>
<td></td>
<td><strong>187</strong></td>
<td></td>
<td><strong>5 (3.3)</strong></td>
<td><strong>NR</strong></td>
</tr>
</tbody>
</table>

|               | Microdebrider (2) | 187         |                              |                                        |                                |
|               | Coblation (1)     | 34          | 0                             | 5 (3.3)                                 | NR                             |

N=Number; NR=Not Reported; PONV=Post-Operative Nausea Vomiting

### Table H-4. Revisits for pain, dehydration, PONV reported after total tonsillectomy in arms of comparative studies

<table>
<thead>
<tr>
<th>Technique for Total Tonsillectomy</th>
<th>Author, Year Indication</th>
<th>Total Arm N</th>
<th>Pain Revisits/Readmissions, n (%)</th>
<th>Dehydration Revisits/Readmissions, n (%)</th>
<th>PONV Revisits/Readmissions, n (%)</th>
<th>Other Revisits/Readmissions, n (%)</th>
</tr>
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<td>NR</td>
<td>13 (16.4)</td>
<td>NR</td>
</tr>
<tr>
<td></td>
<td>Kothari 2002&lt;sup&gt;44&lt;/sup&gt;</td>
<td>79</td>
<td>12 (15.1)</td>
<td>NR</td>
<td>13 (16.4)</td>
<td>NR</td>
</tr>
<tr>
<td></td>
<td>Matin 2012&lt;sup&gt;16&lt;/sup&gt;</td>
<td>50</td>
<td>1 (2)</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
</tr>
<tr>
<td></td>
<td>D’Eredita 2004&lt;sup&gt;33&lt;/sup&gt;</td>
<td>30</td>
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<td>NR</td>
<td>NR</td>
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<tr>
<td>Electrocautery OSDB</td>
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<td>150</td>
<td>NR</td>
<td>4 (2.6)</td>
<td>NR</td>
<td>NR</td>
</tr>
<tr>
<td></td>
<td>Derkay 2006&lt;sup&gt;36&lt;/sup&gt;</td>
<td>150</td>
<td>NR</td>
<td>4 (2.6)</td>
<td>NR</td>
<td>NR</td>
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<tr>
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<td>Chang 2005&lt;sup&gt;7&lt;/sup&gt;</td>
<td>49</td>
<td>0 (0)</td>
<td>1 (2)</td>
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<td>NR</td>
</tr>
<tr>
<td>Throat Infection</td>
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<td>161</td>
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<td>4 (2.5)</td>
<td>NR</td>
<td>NR</td>
</tr>
<tr>
<td></td>
<td>Walker 2001&lt;sup&gt;34&lt;/sup&gt;</td>
<td>161</td>
<td>NR</td>
<td>4 (2.5)</td>
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<td>D’Eredita 2014&lt;sup&gt;34&lt;/sup&gt;</td>
<td>279</td>
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<tr>
<td></td>
<td>Stoker 2004&lt;sup&gt;16&lt;/sup&gt;</td>
<td>45</td>
<td>Post-op calls/visits to doctor 11 (24.4)</td>
<td>Post-op calls/visits to doctor 7 (15.5)</td>
<td>Post-op calls/visits to doctor 7 (15.5)</td>
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<tr>
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<td>Parker 2011&lt;sup&gt;19&lt;/sup&gt;</td>
<td>40</td>
<td>NR</td>
<td>1 (2.5)</td>
<td>NR</td>
<td>NR</td>
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<tr>
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<td>D’Eredita 2010&lt;sup&gt;15&lt;/sup&gt;</td>
<td>32</td>
<td>NR</td>
<td>2 (6.2)</td>
<td>NR</td>
<td>NR</td>
</tr>
<tr>
<td>Technique for Total Tonsillectomy</td>
<td>Author, Year Indication</td>
<td>Total Arm N</td>
<td>Pain Revisits/Readmissions, n (%)</td>
<td>Dehydration Revisits/Readmissions, n (%)</td>
<td>PONV Revisits/Readmissions, n (%)</td>
<td>Other Revisits/Readmissions, n (%)</td>
</tr>
<tr>
<td>----------------------------------</td>
<td>-------------------------</td>
<td>-------------</td>
<td>-----------------------------------</td>
<td>----------------------------------------</td>
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<td>-----------------------------------</td>
</tr>
<tr>
<td>Cold dissection</td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>OSDB</td>
<td></td>
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<td></td>
<td></td>
<td></td>
</tr>
<tr>
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<td>0 (0)</td>
<td>0</td>
<td>NR</td>
<td>NR</td>
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<td>Throat infection</td>
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<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>D’Eredita 2014</td>
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<td>16 (22.2)</td>
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<td>Nunez 2000</td>
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<td>Shah 2002</td>
<td>17</td>
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<td>Post-op calls/visits to doctor 4 (9)</td>
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<td>Technique for Total Tonsillectomy</td>
<td>Author, Year Indication</td>
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<td>Pain Revisits/Readmissions, n (%)</td>
<td>Dehydration Revisits/Readmissions, n (%)</td>
<td>PONV Revisits/Readmissions, n (%)</td>
<td>Other Revisits/Readmissions, n (%)</td>
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<td>NR</td>
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<td>Molecular resonance</td>
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<td>Van Staaaj et al. 2004&lt;sup&gt;10-11&lt;/sup&gt;</td>
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<td>Orvidas 2006&lt;sup&gt;6&lt;/sup&gt;</td>
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<td>Totals</td>
<td>(N arms)</td>
<td></td>
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<td>39 (1.6)</td>
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<td>Cold dissection-total (9)</td>
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<td>Molecular resonance-total (2)</td>
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<td>Harmonic scalpel-total (2)</td>
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<td>NR</td>
<td>3 (4.9)</td>
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<tr>
<td>Coblation-total (5)</td>
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<td>6 (8.8)</td>
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<td>Laser-total (3)</td>
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<td>Microdebrider-total (2)</td>
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<td>Coblation-partial (1)</td>
<td>34</td>
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N=Number; NR=Not Reported; PONV=Post-Operative Nausea Vomiting
### Bleeding-Related Harms in Case Series, Database, and Registry Studies

#### Table H-5. Post-tonsillectomy hemorrhage rates reported across all studies

<table>
<thead>
<tr>
<th>Author, Year RoB</th>
<th>Age Range, Years Surgical Indication Data Source Description</th>
<th>Total N</th>
<th>Total PTH</th>
<th>Primary PTH, n (%)</th>
<th>Secondary PTH, n (%)</th>
<th>Unspecified PTH, n (%)</th>
<th>Nonoperative revisit or readmission for PTH, n (%)</th>
<th>Reoperation for PTH, n (%)</th>
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<tbody>
<tr>
<td><strong>Database Studies</strong></td>
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<td>Edmonson 2015&lt;sup&gt;79&lt;/sup&gt; Low</td>
<td>0-24 Mixed CA hospital discharge database-return visits within 30 days postop</td>
<td>30092</td>
<td>1331</td>
<td>NR</td>
<td>NR</td>
<td>1331 (3.8)</td>
<td>1331 (3.8)</td>
<td>NR</td>
</tr>
<tr>
<td>Bhattacharya 2015&lt;sup&gt;80, 81&lt;/sup&gt; Low</td>
<td>&lt;18 years (mean=7.5 years) Unspecified CA, IA, FL, NY ER and ambulatory surgery and ER databases-return visits within 14 days postop</td>
<td>79520</td>
<td>1652</td>
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<td>NR</td>
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<td>1652 (2.1)</td>
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<tr>
<td>Duval 2015&lt;sup&gt;82&lt;/sup&gt; Low</td>
<td>1-18 Unspecified Hospital system database-return visits within 21 days postop</td>
<td>39906</td>
<td>935</td>
<td>NR</td>
<td>NR</td>
<td>935 (2.3)</td>
<td>NR</td>
<td>463 (1.2)</td>
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<tr>
<td>Padia 2015&lt;sup&gt;83&lt;/sup&gt; Moderate</td>
<td>1-18 Unspecified Hospital system database-return visits within 21 days post-same-day tonsillectomy</td>
<td>15953</td>
<td>1187</td>
<td>NR</td>
<td>NR</td>
<td>1187 (7.4)</td>
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<tr>
<td>Mahant 2014&lt;sup&gt;84, 85&lt;/sup&gt; Low</td>
<td>1-18 Mixed</td>
<td>139715</td>
<td>4182</td>
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<td>NR</td>
<td>4182 (3)</td>
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<tr>
<td>Author, Year RoB</td>
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<td>Total N</td>
<td>Total PTH</td>
<td>Primary PTH, n (%)</td>
<td>Secondary PTH, n (%)</td>
<td>Unspecified PTH, n (%)</td>
<td>Nonoperative revisit or readmission for PTH, n (%)</td>
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<td><em>Suzuki 2014</em></td>
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<td>31934</td>
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<td>NR</td>
<td>NR</td>
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<td><em>Tomkinson 2012</em></td>
<td>&lt;12 years Low Mixed Wales Surgical Instrument Surveillance Programme Database-5 years</td>
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<td>38 (0.9)</td>
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<td><em>Tomkinson 2005</em></td>
<td>12 years Low Unspecified Patient Episode Database for Wales-return visits within 28 days post-tonsillectomy</td>
<td>6730</td>
<td>225</td>
<td>53 (0.79)</td>
<td>172 (3)</td>
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<td>153 (2.3)</td>
<td>41 (0.61)</td>
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<td><em>Clark 2004</em></td>
<td>0-14 Low Unspecified Hospital Episode Statistics for England-4 years</td>
<td>131577</td>
<td>500</td>
<td>NR</td>
<td>NR</td>
<td>500 (0.38)</td>
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<td>500 (0.38)</td>
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<tr>
<td>Kshirsagar 2016</td>
<td>1-17 years Low Mixed California Ambulatory Surgery Data records-6 years</td>
<td>138998</td>
<td>156</td>
<td>NR</td>
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<td>156 (0.1)</td>
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<td>NR</td>
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<td><em>Harounian 2016</em></td>
<td>1-17 years Low Unspecified California Ambulatory Surgery Data records-6 years</td>
<td>305860</td>
<td>8518</td>
<td>NR</td>
<td>NR</td>
<td>8518 (2.8)</td>
<td>500 (0.16)</td>
<td>2480 (0.81)</td>
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<td>Author, Year RoB</td>
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<td>Total PTH</td>
<td>Primary PTH, n (%)</td>
<td>Secondary PTH, n (%)</td>
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<td>Reoperation for PTH, n (%)</td>
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<td>0-18 Low Mixed</td>
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<td>Secondary PTH, n (%)</td>
<td>Unspecified PTH, n (%)</td>
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<td>Jones 2007&lt;sup&gt;101&lt;/sup&gt; Moderate</td>
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<td>Children's Hospital, Boston, MA patient records- 4 years</td>
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<td>4850</td>
<td>209</td>
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<td>163 (3; 95% CI: 2.8% to 3.9%)</td>
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<td>84</td>
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<td>Windfuhr 2001&lt;sup&gt;104-106&lt;/sup&gt; Moderate</td>
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<td>Single institution chart</td>
<td>2567</td>
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<td>Total PTH</td>
<td>Primary PTH, n (%)</td>
<td>Secondary PTH, n (%)</td>
<td>Unspecified PTH, n (%)</td>
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<td>Liu 2001&lt;sup&gt;107&lt;/sup&gt; Moderate</td>
<td>2.5 months-20 years</td>
<td>Unspecified</td>
<td>Single institution chart review of 1 year</td>
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<td>9 (0.63)</td>
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<td>Kang 1994&lt;sup&gt;108&lt;/sup&gt; Moderate</td>
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<td>Unspecified</td>
<td>In-patient and out-patient clinic records from the Children's Hospital of Buffalo- 4 years</td>
<td>1061</td>
<td>64</td>
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<td>0 (0)</td>
<td>NR</td>
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<td>Lannigan 1993&lt;sup&gt;109&lt;/sup&gt; Moderate</td>
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<td>Unspecified</td>
<td>Single institution chart review of 4 years</td>
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<td>Yardley 1992&lt;sup&gt;110&lt;/sup&gt; Moderate</td>
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<td>Unspecified</td>
<td>Two South Yorkshire hospitals- 3 years</td>
<td>2091</td>
<td>11</td>
<td>NR</td>
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<td>11 (0.52)</td>
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<tr>
<td>Colclasure 1990&lt;sup&gt;111&lt;/sup&gt; Moderate</td>
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<td>Unspecified</td>
<td>Single institution chart review of 8 years</td>
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<td>36</td>
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<td>29 (1.4)</td>
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<td>Chowdhury 1988&lt;sup&gt;112&lt;/sup&gt; Moderate</td>
<td>&quot;Pediatric&quot; (under 4 -over 12)</td>
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<td>171</td>
<td>90 (1.3)</td>
<td>81 (1.2)</td>
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<tr>
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<td>Age Range, Years Surgical Indication Data Source Description</td>
<td>Total N</td>
<td>Total PTH</td>
<td>Primary PTH, n (%)</td>
<td>Secondary PTH, n (%)</td>
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<td>Nonoperative revisit or readmission for PTH, n (%)</td>
<td>Reoperation for PTH, n (%)</td>
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<td>Total PTH</td>
<td>Primary PTH, n (%)</td>
<td>Secondary PTH, n (%)</td>
<td>Unspecified PTH, n (%)</td>
<td>Nonoperative revisit or readmission for PTH, n (%)</td>
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<td>128</td>
<td>23661</td>
<td>1005 (1.2)</td>
<td>1586 (2.1)</td>
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<td>Totals</td>
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<td>23661</td>
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<td>1750</td>
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<td>155 (1.4)</td>
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Note: primary typically defined as within 24 hours postoperatively and secondary as greater than 24 hours.
*Defined primary as during the initial admission and secondary as PTH requiring admission up to 28 days postoperatively.
CI=Confidence Interval; N=Number; NR=Not Reported; OSDB=Obstructive Sleep Disordered Breathing; PTH=Post-Tonsillectomy Hemorrhage
Table H-6. PTH rates reported by technique in case series, database, or registry studies

<table>
<thead>
<tr>
<th>Surgical Technique</th>
<th>Author, Year RoB</th>
<th>Total N</th>
<th>Total PTH</th>
<th>Primary PTH, n (%)</th>
<th>Secondary PTH, n (%)</th>
<th>Unspecified PTH, n (%)</th>
<th>Non-operative revisit or readmission, n (%)</th>
<th>Reoperation, n (%)</th>
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<td>Electrocautery (total tonsillectomy)</td>
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<td>1500</td>
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<td>NR</td>
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<td>Kim 2010 Moderate</td>
<td>1109</td>
<td>33</td>
<td>0</td>
<td>33 (3)</td>
<td>NR</td>
<td>3 (0.27)</td>
<td>2 (0.18)</td>
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<td>Lowe 2007 Low</td>
<td>6161</td>
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<td>NR</td>
<td>NR</td>
<td>204 (3.3)</td>
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<td>Liu 2001 Moderate</td>
<td>1438</td>
<td>134 (evaluations for PTH in 112 children)</td>
<td>9 (0.63)</td>
<td>125 (9)</td>
<td>NR</td>
<td>60 (4.2)</td>
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<td>172 (3)</td>
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<td>3945</td>
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<td>118 (3)</td>
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<td>Windfuhr 2001 Moderate</td>
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<td>14 (0.54)</td>
<td>NR</td>
<td>NR</td>
<td>41 (1.6)</td>
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<tr>
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<td>Carmody 1982 Moderate</td>
<td>3380</td>
<td>54</td>
<td>30 (0.8)</td>
<td>24 (0.7)</td>
<td>NR</td>
<td>NR</td>
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<td>5 (0.3)</td>
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<td>Chowdhury 1988</td>
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<td>NR</td>
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<td>82 (4)</td>
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<td>97 (3.6)</td>
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<td>Primary PTH, n (%)</td>
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<td>Non-operative revisit or readmission, n (%)</td>
<td>Reoperation, n (%)</td>
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<td>Reoperation, n (%)</td>
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<td>Reoperation, n (%)</td>
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*Study notes that most total tonsillectomies were performed using cold dissection. Non-operative revisits may have included reoperations.
N=Number; NR=Not Reported; PTH=Post-Tonsillectomy Hemorrhage
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<th>Secondary PTH, n (%)</th>
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<th>Reoperation, n (%)</th>
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*The authors of this study reported bleeding rates on children with recurrent throat infection and OSDB in further publications.
N=Number; NR=Not Reported; OSDB=Obstructive Sleep Disordered Breathing; PTH=Post-Tonsillectomy Hemorrhage
# Other Harms

Table H-8. Revisits for pain, nausea, or dehydration reported in case series, database, or registry studies

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<th>Technique</th>
<th>Indication Author, Year</th>
<th>Total Arm N</th>
<th>Pain Revisits/Readmissions, n (%)</th>
<th>Dehydration Revisits/Readmissions, n (%)</th>
<th>PONV Revisits/Readmissions, n (%)</th>
<th>Mixed/Other Revisits/Readmissions, n (%)</th>
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<tr>
<td>Unspecified Tonsillectomy</td>
<td>Elinder 2016[22,123]</td>
<td>18,712</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>Unplanned contact of health care provider 2,180 (11.6)</td>
</tr>
<tr>
<td></td>
<td>Mahant 2014[84,85]</td>
<td>139,715</td>
<td>1060 (0.8)</td>
<td>Revisit for dehydration and vomiting 3,011(2.2)</td>
<td>NR</td>
<td>NR</td>
</tr>
<tr>
<td></td>
<td>Edmonson 2015[19]</td>
<td>35,085</td>
<td>Acute post-op pain 354 (6.9)</td>
<td>311 (7.6)</td>
<td>PONV 118 (0.37)</td>
<td>NR</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Throat pain 224 (4.2)</td>
<td></td>
<td>Vomiting alone 106 (0.3)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Mills 2004[16]</td>
<td>4,853</td>
<td>NR</td>
<td>NR</td>
<td>Vomiting requiring admission overnight 107 (2.7)</td>
<td>Rehydration or analgesia 24 (0.5)</td>
</tr>
<tr>
<td></td>
<td>Achar 2015[84]</td>
<td>3,527</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>ER visit for pain relief, poor oral intake, fever, and NV 346 (9.8)</td>
</tr>
<tr>
<td>Not Specified</td>
<td>Mahadevan 2016[177]</td>
<td>5,400</td>
<td>74 (1.37)</td>
<td>4 (0.07)</td>
<td>32 (0.59)</td>
<td>Fever or Drug Reaction 2 (.03)</td>
</tr>
<tr>
<td></td>
<td>Bhattacharyya 2014[180]</td>
<td>79,520</td>
<td>1,180 (1.5)</td>
<td>NR</td>
<td>7503 (1.4)</td>
<td>Fever/ NV/ Dehydration 1,765 (2.2)</td>
</tr>
<tr>
<td></td>
<td>Duval 2015[12]</td>
<td>39,906</td>
<td>NR</td>
<td>898 (2.3)</td>
<td>NR</td>
<td>NR</td>
</tr>
<tr>
<td></td>
<td>Colclasure 1990[131]</td>
<td>2,011</td>
<td>NR</td>
<td>2 (0.05) [Not specific to]</td>
<td>NR</td>
<td>NR</td>
</tr>
<tr>
<td>Technique</td>
<td>Indication Author, Year</td>
<td>Total Arm N</td>
<td>Pain Revisits/Readmissions, n (%)</td>
<td>Dehydration Revisits/Readmissions, n (%)</td>
<td>PONV Revisits/Readmissions, n (%)</td>
<td>Mixed/Other Revisits/Readmissions, n (%)</td>
</tr>
<tr>
<td>-----------</td>
<td>-------------------------</td>
<td>-------------</td>
<td>----------------------------------</td>
<td>------------------------------------------</td>
<td>----------------------------------</td>
<td>----------------------------------------</td>
</tr>
<tr>
<td>Granell 2004&lt;sup&gt;10&lt;/sup&gt;</td>
<td>1,243</td>
<td>NR</td>
<td>Poor oral intake 2 (0.2)</td>
<td>NR</td>
<td>NR</td>
<td></td>
</tr>
<tr>
<td><strong>Totals</strong> (N studies)</td>
<td><strong>All (11)</strong></td>
<td><strong>331890</strong></td>
<td><strong>2668 (0.11)</strong></td>
<td><strong>4257 (1.9)</strong></td>
<td><strong>7760 (6.2)</strong></td>
<td><strong>4317 (3.8)</strong></td>
</tr>
<tr>
<td>Coblation total tonsillectomy (1)</td>
<td>1,918</td>
<td>NR</td>
<td>29 (1.5)</td>
<td>NR</td>
<td>NR</td>
<td></td>
</tr>
<tr>
<td>Unspecified tonsillectomy (10)</td>
<td>329972</td>
<td>2668 (0.11)</td>
<td>4228 (1.9)</td>
<td>7760 (6.2)</td>
<td>4317 (3.8)</td>
<td></td>
</tr>
</tbody>
</table>

ER=Emergency Room; N=Number; NR=Not Reported; NV= Nausea and Vomiting; PONV=Postoperative Nausea and Vomiting

**Table H-9. Other harms reported in case series and database studies**

<table>
<thead>
<tr>
<th>Author</th>
<th>Study Design</th>
<th>Indication</th>
<th>Intervention</th>
<th>Total Arm N</th>
<th>Harms of Intervention N (%)</th>
<th>Mortality N (%)</th>
<th>VPI N (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Odhagen 2016&lt;sup&gt;11&lt;/sup&gt; Registry Low</td>
<td>OSDB, Throat Infection</td>
<td>Total or partial tonsillectomy (unspecified)</td>
<td>Total: 11741 Partial: 15794</td>
<td>Total tonsillectomy Total reoperations 75 (0.6)</td>
<td>Reoperation for airway obstruction 49 (66.2)</td>
<td>Reoperation for Infection 11 (14.9)</td>
<td>Reoperation for Other cause 14 (18.9)</td>
</tr>
<tr>
<td>Author</td>
<td>Study Design</td>
<td>Indication</td>
<td>Intervention</td>
<td>Total Arm N</td>
<td>Harms of Intervention N (%)</td>
<td>Mortality N (%)</td>
<td>VPI N (%)</td>
</tr>
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<td>--------------</td>
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</tr>
<tr>
<td>Mahadevan 2016</td>
<td>Case Series</td>
<td>Not Specified</td>
<td>Tonsillectomy (unspecified)</td>
<td>5,400</td>
<td>501 (82.3)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Moderate</td>
<td></td>
<td></td>
<td></td>
<td>Reoperation for Infection 73 (12)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Reoperation for Other cause 35 (5.7)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Raol 2016</td>
<td>Database</td>
<td>Not Specified</td>
<td>Tonsillectomy (unspecified)</td>
<td>40,591</td>
<td>383 (0.94)</td>
<td>383 (0.94)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Low</td>
<td></td>
<td></td>
<td></td>
<td>Respiratory failure</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Children’s Teaching Hospital (n=10,220) ≤10 (0.09)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Non- Children’s Teaching Hospital (n=20,176) ≤10 (0.04)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Nonteaching Hospital (n=8,235) ≤10 (0.12)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lavin 2015</td>
<td>Database</td>
<td>OSDB</td>
<td>Tonsillectomy (unspecified)</td>
<td>21,434</td>
<td>146 (16.2)</td>
<td>146 (16.2)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Low</td>
<td></td>
<td></td>
<td></td>
<td>Obese T&amp;A patients respiratory complications</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>45 (5.04)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Non-obese T&amp;A patients respiratory</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>0 (0)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

NR: Not reported
<table>
<thead>
<tr>
<th>Author</th>
<th>Study Design</th>
<th>Indication</th>
<th>Intervention</th>
<th>Total Arm N</th>
<th>Harms of Intervention N (%)</th>
<th>Mortality N (%)</th>
<th>VPI N (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Shay 2015&lt;sup&gt;11&lt;/sup&gt;</td>
<td>Case Series Low</td>
<td>Not Specified</td>
<td>Tonsillectomy (unspecified)</td>
<td>36,221</td>
<td>Non-obese T&amp;A major respiratory complications (pulmonary insufficiency or respiratory failure) 1984 (9.7)</td>
<td>2(0.005)</td>
<td>NR</td>
</tr>
<tr>
<td>Walner 2012&lt;sup&gt;13&lt;/sup&gt;</td>
<td>Database/Registry Moderate</td>
<td>OSDB, Throat Infection</td>
<td>Coblation total tonsillectomy</td>
<td>1,918</td>
<td>Postoperative desaturation or pulmonary edema or lung collapse 13 (0.75)</td>
<td>0(0)</td>
<td>NR</td>
</tr>
<tr>
<td>Tweedie 2012&lt;sup&gt;131&lt;/sup&gt;</td>
<td>Case Series Moderate</td>
<td>OSDB, Throat Infection</td>
<td>Tonsillectomy (unspecified)</td>
<td>1,735</td>
<td>Postoperative aspiration 2 (0.12) Malignany hyperpyrexia 1 (0.06)</td>
<td>0(0)</td>
<td>NR</td>
</tr>
<tr>
<td>Sarny 2011&lt;sup&gt;125, 126&lt;/sup&gt;</td>
<td>Database/Registry Low</td>
<td>Not Specified</td>
<td>Tonsillectomy (unspecified)</td>
<td>9,405</td>
<td></td>
<td>0(0)</td>
<td>NR</td>
</tr>
<tr>
<td>Bhattacharyya 2010&lt;sup&gt;134&lt;/sup&gt;</td>
<td>Database/Registry Moderate</td>
<td>Not Specified</td>
<td>Tonsillectomy (unspecified)</td>
<td>535,949</td>
<td>Airway obstruction NR (0.04)</td>
<td>NR</td>
<td>NR</td>
</tr>
<tr>
<td>Jones 2007&lt;sup&gt;101&lt;/sup&gt;</td>
<td>Case Series Moderate</td>
<td>OSDB, Throat Infection</td>
<td>Tonsillectomy, (unspecified)</td>
<td>2,554</td>
<td></td>
<td>NR</td>
<td>NR</td>
</tr>
<tr>
<td>Granell 2004&lt;sup&gt;103&lt;/sup&gt;</td>
<td>Case Series Moderate</td>
<td>OSDB, Throat Infection</td>
<td>Tonsillectomy (unspecified)</td>
<td>1,243</td>
<td></td>
<td>0(0)</td>
<td>NR</td>
</tr>
</tbody>
</table>
### Studies of Perioperative or Postoperative Medications

#### Bleeding-Related Harms

**Table H-10. Bleeding-related outcomes in comparative study arms evaluating perioperative medications**

<table>
<thead>
<tr>
<th>Drug class</th>
<th>Indication Author, Year</th>
<th>Intervention</th>
<th>Total Arm N</th>
<th>Total PTH</th>
<th>Primary PTH n (%)</th>
<th>Secondary PTH n (%)</th>
<th>Undefined PTH n (%)</th>
<th>Nonoperative Readmission or Revisit for PTH n (%)</th>
<th>Reoperation for PTH n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Steroid</td>
<td>Mixed</td>
<td>Dexamethasone, 0.5 mg/kg (injection)</td>
<td>154</td>
<td>17</td>
<td>2 (1)</td>
<td>NR</td>
<td>15 (9.7)</td>
<td>3 (1.9)</td>
<td>3 (1.9)</td>
</tr>
<tr>
<td></td>
<td>Gallagher 2012</td>
<td>Dexamethasone, 0.5 mg/kg (IV)</td>
<td>52</td>
<td>12</td>
<td>NR</td>
<td>NR</td>
<td>12 (24)</td>
<td>NR</td>
<td>4 (8)</td>
</tr>
<tr>
<td></td>
<td>Czarnetzki 2008</td>
<td>Dexamethasone, 0.05 mg/kg (IV)</td>
<td>53</td>
<td>6</td>
<td>NR</td>
<td>NR</td>
<td>6 (11)</td>
<td>NR</td>
<td>3 (6)</td>
</tr>
<tr>
<td></td>
<td>Czarnetzki 2008</td>
<td>Dexamethasone, 0.15 mg/kg (IV)</td>
<td>54</td>
<td>2</td>
<td>0</td>
<td>0</td>
<td>2 (4)</td>
<td>NR</td>
<td>1 (2)</td>
</tr>
<tr>
<td>Drug class</td>
<td>Indication Author, Year</td>
<td>Intervention</td>
<td>Total Arm N</td>
<td>Total PTH</td>
<td>Primary PTH n (%)</td>
<td>Secondary PTH n (%)</td>
<td>Undefined PTH n (%)</td>
<td>Nonoperative Readmission or Revisit for PTH n (%)</td>
<td>Reoperation for PTH n (%)</td>
</tr>
<tr>
<td>------------</td>
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<td>-----------------------------------------------</td>
<td>------------------------</td>
</tr>
<tr>
<td>Hanasono 2004•&lt;sup&gt;138&lt;/sup&gt;</td>
<td>Cold tonsillectomy+ dexamethasone, 1 mg/kg (IV)</td>
<td>44</td>
<td>1</td>
<td>NR</td>
<td>NR</td>
<td>1 (2.3)</td>
<td>1 (2)</td>
<td>NR</td>
<td></td>
</tr>
<tr>
<td>Aysenur 2014•&lt;sup&gt;139&lt;/sup&gt;</td>
<td>Dexamethasone sodium phosphate, 1 mg/kg (infiltration)</td>
<td>20</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Hermans 2012•&lt;sup&gt;140&lt;/sup&gt;</td>
<td>Dexamethasone, 0.15 mg/kg (IV)</td>
<td>46</td>
<td>0</td>
<td>NR</td>
<td>NR</td>
<td>0</td>
<td>NR</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Hermans 2012•&lt;sup&gt;140&lt;/sup&gt;</td>
<td>Dexamethasone, 0.5 mg/kg (IV)</td>
<td>44</td>
<td>0</td>
<td>NR</td>
<td>NR</td>
<td>0</td>
<td>NR</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Aouad 2012•&lt;sup&gt;141&lt;/sup&gt;</td>
<td>Methylprednisolone, 2.5 mg/kg (IV)</td>
<td>78</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Aouad 2012•&lt;sup&gt;141&lt;/sup&gt;</td>
<td>Dexamethasone, 0.5 mg/kg (IV)</td>
<td>75</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Hanasono 2004•&lt;sup&gt;138&lt;/sup&gt;</td>
<td>Hot tonsillectomy+ dexamethasone, 1 mg/kg (IV)</td>
<td>62</td>
<td>0</td>
<td>NR</td>
<td>NR</td>
<td>0</td>
<td>0</td>
<td>NR</td>
<td></td>
</tr>
<tr>
<td>Elhakim 2003&lt;sup&gt;•142&lt;/sup&gt;</td>
<td>Dexamethasone, 0.5 mg/kg (IV)</td>
<td>55</td>
<td>0</td>
<td>NR</td>
<td>0</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td></td>
</tr>
<tr>
<td>Alajmi 2008&lt;sup&gt;•143&lt;/sup&gt;</td>
<td>Dexamethasone, 1mg/kg (IV)</td>
<td>42</td>
<td>0</td>
<td>NR</td>
<td>0</td>
<td>NR</td>
<td>0</td>
<td>NR</td>
<td></td>
</tr>
<tr>
<td>Kaan 2006&lt;sup&gt;•144&lt;/sup&gt;</td>
<td>Dexamethasone</td>
<td>32</td>
<td>0</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Unspecified</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>NSAIDs</td>
<td>Throat infection</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Abdel-Ghaffar 2015&lt;sup&gt;•145&lt;/sup&gt;</td>
<td>Lornoxicam in one tonsil , 8 mg (infiltration)</td>
<td>34</td>
<td>0</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>0</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Unspecified</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Solanki 2012&lt;sup&gt;•146&lt;/sup&gt;</td>
<td>Diclofenac, 2 mg/kg (rectal)</td>
<td>25</td>
<td>3</td>
<td>NR</td>
<td>NR</td>
<td>3 (12)</td>
<td>NR</td>
<td>NR</td>
<td></td>
</tr>
<tr>
<td>Moss 2014&lt;sup&gt;•147&lt;/sup&gt;</td>
<td>Ibuprofen, 10 mg/kg (IV)</td>
<td>73</td>
<td>2</td>
<td>NR</td>
<td>NR</td>
<td>2 (3)</td>
<td>0</td>
<td>1 (1.4)</td>
<td></td>
</tr>
<tr>
<td>Lee 2009&lt;sup&gt;•48&lt;/sup&gt;</td>
<td>Ketorolac, preoperative, 1 mg/kg (IV)</td>
<td>24</td>
<td>1</td>
<td>NR</td>
<td>NR</td>
<td>1 (4)</td>
<td>NR</td>
<td>NR</td>
<td></td>
</tr>
<tr>
<td>Keidan 2004&lt;sup&gt;•149&lt;/sup&gt;</td>
<td>Ketoroloc, 1 mg/kg •&lt;sup&gt;1&lt;/sup&gt; (IV)</td>
<td>25</td>
<td>0</td>
<td>NR</td>
<td>NR</td>
<td>0</td>
<td>NR</td>
<td>NR</td>
<td></td>
</tr>
<tr>
<td>Lee 2009&lt;sup&gt;•48&lt;/sup&gt;</td>
<td>Ketorolac, perioperative, 1</td>
<td>26</td>
<td>0</td>
<td>NR</td>
<td>NR</td>
<td>0</td>
<td>NR</td>
<td>NR</td>
<td></td>
</tr>
<tr>
<td>Drug class</td>
<td>Indication</td>
<td>Intervention</td>
<td>Total Arm N</td>
<td>Total PTH</td>
<td>Primary PTH n (%)</td>
<td>Secondary PTH n (%)</td>
<td>Undefined PTH n (%)</td>
<td>Nonoperative Readmission or Revisit for PTH n (%)</td>
<td>Reoperation for PTH n (%)</td>
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<td>--------------------------</td>
</tr>
<tr>
<td>Non-NSAID Analgesics</td>
<td>Unspecified</td>
<td>Kedek 2005</td>
<td>Ibuprofen, 10 mg/kg (oral)</td>
<td>20</td>
<td>0</td>
<td>NR</td>
<td>NR</td>
<td>0</td>
<td>NR</td>
</tr>
<tr>
<td></td>
<td>Lee 2009&lt;sup&gt;46&lt;/sup&gt;</td>
<td>Propacetamol, perioperative, 30 mg/kg (IV)</td>
<td>26</td>
<td>0</td>
<td>NR</td>
<td>NR</td>
<td>0</td>
<td>NR</td>
<td>NR</td>
</tr>
<tr>
<td></td>
<td>Keidan 2004&lt;sup&gt;49&lt;/sup&gt;</td>
<td>Fentanyl, 2 μg/kg&lt;sup&gt;-1&lt;/sup&gt; (IV)</td>
<td>32</td>
<td>0</td>
<td>NR</td>
<td>NR</td>
<td>0</td>
<td>NR</td>
<td>NR</td>
</tr>
<tr>
<td></td>
<td>Lee 2009&lt;sup&gt;46&lt;/sup&gt;</td>
<td>Propacetamol, preoperative, 30 mg/kg (IV)</td>
<td>26</td>
<td>0</td>
<td>NR</td>
<td>NR</td>
<td>0</td>
<td>NR</td>
<td>NR</td>
</tr>
<tr>
<td>Anesthetic</td>
<td>Mixed</td>
<td>Aysenur 2014&lt;sup&gt;39&lt;/sup&gt;</td>
<td>Levobupivacaine with epinephrine, ND (infiltration)</td>
<td>20</td>
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<td>0</td>
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</tr>
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<td></td>
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<td>Safavi 2012&lt;sup&gt;48&lt;/sup&gt;</td>
<td>Bupivacaine (0.25%), 5 mL (infiltration)</td>
<td>25</td>
<td>4</td>
<td>NR</td>
<td>NR</td>
<td>4 (16)</td>
<td>NR</td>
</tr>
<tr>
<td>Placebo</td>
<td>Throat infection</td>
<td>Abdel-Ghaffar 2015&lt;sup&gt;45&lt;/sup&gt;</td>
<td>peritonsillar saline in other tonsil (infiltration)</td>
<td>34</td>
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<td>NR</td>
<td>NR</td>
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<td></td>
<td>Abdel-Ghaffar 2015&lt;sup&gt;45&lt;/sup&gt;</td>
<td>bilateral peritonsillar saline (infiltration)</td>
<td>68</td>
<td>0</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>Mixed</td>
<td>Gallagher 2012&lt;sup&gt;36&lt;/sup&gt;</td>
<td>placebo (saline), 0.5 mg/kg (injection)</td>
<td>151</td>
<td>13</td>
<td>2 (1)</td>
<td>NR</td>
<td>11 (7.3)</td>
<td>5 (3.2)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Czarnetzki 2008&lt;sup&gt;37&lt;/sup&gt;</td>
<td>Placebo (saline), NR (IV)</td>
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<td>NR</td>
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<td>NR</td>
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<td>Hermans 2012&lt;sup&gt;48&lt;/sup&gt;</td>
<td>Placebo (saline), 0.5 mL/kg (IV)</td>
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<td></td>
<td>Hanasono 2004&lt;sup&gt;38&lt;/sup&gt;</td>
<td>Cold tonsillectomy+placebo, 1 mg/kg (IV)</td>
<td>57</td>
<td>1</td>
<td>NR</td>
<td>NR</td>
<td>1 (1.8)</td>
<td>1 (1.8)</td>
</tr>
<tr>
<td>Drug class</td>
<td>Indication Author, Year</td>
<td>Intervention</td>
<td>Total Arm N</td>
<td>Total PTH</td>
<td>Primary PTH n (%)</td>
<td>Secondary PTH n (%)</td>
<td>Undefined PTH n (%)</td>
<td>Nonoperative Readmission or Revisit for PTH n (%)</td>
<td>Reoperation for PTH n (%)</td>
</tr>
<tr>
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<td>-------------</td>
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<td>-------------------</td>
<td>---------------------</td>
<td>---------------------</td>
<td>-----------------------------------------------</td>
<td>------------------------</td>
</tr>
<tr>
<td>Aysenur 2014(^{39})</td>
<td>Saline, ND (infiltration)</td>
<td>20</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>NR</td>
<td>0</td>
<td>0</td>
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<td>Hanasono 2004(^{38})</td>
<td>Hot tonsillectomy+placebo, 1 mg/kg (IV)</td>
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<td>NR</td>
<td>NR</td>
<td>0</td>
<td>0</td>
<td>NR</td>
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<td></td>
<td></td>
<td></td>
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<tr>
<td>Alajmi 2008(^{43})</td>
<td>Placebo, 5 mL (IV)</td>
<td>38</td>
<td>3</td>
<td>NR</td>
<td>3 (7.9)</td>
<td>NR</td>
<td>3 (7.9)</td>
<td>NR</td>
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<tr>
<td>Moss 2014(^{27})</td>
<td>Placebo (normal saline), 10 mg/kg (IV)</td>
<td>65</td>
<td>1</td>
<td>NR</td>
<td>NR</td>
<td>1 (2)</td>
<td>NR</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Elhakim 2003(^{42})</td>
<td>Placebo (saline), 0.5 mg/kg (IV)</td>
<td>55</td>
<td>0</td>
<td>NR</td>
<td>0</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
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<tr>
<td>Kaan 2006(^{144})</td>
<td>Placebo (saline), 0.5 mg/kg (IV)</td>
<td>30</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>0</td>
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<tr>
<td><strong>Totals (N arms)</strong></td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>All arms</td>
<td>NA</td>
<td>1839</td>
<td>69 (3.8)</td>
<td>4 (0.7)</td>
<td>3 (0.66)</td>
<td>51 (5.9)</td>
<td>13 (1.4)</td>
<td>14 (1.2)</td>
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<tr>
<td>Steroids (14)</td>
<td>NA</td>
<td>811</td>
<td>38 (4.7)</td>
<td>2 (0.61)</td>
<td>0 (0)</td>
<td>38 (7.1)</td>
<td>4 (0.48)</td>
<td>11 (1.8)</td>
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<tr>
<td>Placebo (12)</td>
<td>NA</td>
<td>672</td>
<td>21 (3.3)</td>
<td>2 (0.89)</td>
<td>3 (1.8)</td>
<td>16 (3.6)</td>
<td>9 (2.1)</td>
<td>2 (0.43)</td>
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<tr>
<td>NSAIDs (7)</td>
<td>NA</td>
<td>227</td>
<td>6 (2.6)</td>
<td>NR</td>
<td>NR</td>
<td>5 (2.96)</td>
<td>0 (0)</td>
<td>1 (0.93)</td>
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</tr>
<tr>
<td>Anesthetics (2)</td>
<td>NA</td>
<td>45</td>
<td>4 (8.9)</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td>4 (8.9)</td>
<td>0 (0)</td>
<td>0 (0)</td>
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<tr>
<td>Non-NSAID Analgesics (3)</td>
<td>NA</td>
<td>84</td>
<td>0 (0)</td>
<td>NR</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td>NR</td>
<td>NR</td>
<td></td>
</tr>
</tbody>
</table>

\(N=\)Number; NR=Not Reported; NSAID=Nonsteroidal Anti-Inflammatory Drug; PTH=Post-Tonsillectomy Hemorrhage
<table>
<thead>
<tr>
<th>Drug class</th>
<th>Indication Author, Year</th>
<th>Intervention</th>
<th>Total Arm N</th>
<th>Total PTH, n</th>
<th>Primary PTH n (%)</th>
<th>Secondary PTH n (%)</th>
<th>Other/ Undefined PTH n (%)</th>
<th>Nonoperative Readmission or Revisit for PTH n (%)</th>
<th>Reoperation for PTH n (%)</th>
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<tbody>
<tr>
<td><strong>NSAIDs</strong></td>
<td>Throat infection</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stage</td>
<td>1988&lt;sup&gt;131&lt;/sup&gt;</td>
<td>Acetylsalicylic acid (Oral, dose not specified)</td>
<td>423</td>
<td>18</td>
<td>5 (1.2)</td>
<td>13 (3.1)</td>
<td>NR</td>
<td>NR</td>
<td>8 (2)</td>
</tr>
<tr>
<td><strong>Mixed</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ozkiris</td>
<td>2012&lt;sup&gt;132&lt;/sup&gt;</td>
<td>Ibuprofen, 30 mg/kg/day (Oral)</td>
<td>115</td>
<td>6</td>
<td>NR</td>
<td>NR</td>
<td>6 (5.21)</td>
<td>NR</td>
<td>1 (1)</td>
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<tr>
<td><strong>Unspecified</strong></td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Murto</td>
<td>2015&lt;sup&gt;133&lt;/sup&gt;</td>
<td>Celecoxib, 6 mg/kg preoperative and 3 mg/kg post-op (Oral)</td>
<td>141</td>
<td>8</td>
<td>NR</td>
<td>NR</td>
<td>8 (5.7)</td>
<td>8 (5.7)</td>
<td>3 (2.1)</td>
</tr>
<tr>
<td><strong>Non-NSAID analgesics</strong></td>
<td>Throat infection</td>
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<td></td>
<td></td>
<td></td>
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<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stage</td>
<td>1988&lt;sup&gt;131&lt;/sup&gt;</td>
<td>Acetaminophen (Oral)</td>
<td>409</td>
<td>9</td>
<td>7 (1.7)</td>
<td>2 (0.49)</td>
<td>NR</td>
<td>NR</td>
<td>3 (1)</td>
</tr>
<tr>
<td><strong>Mixed</strong></td>
<td></td>
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<tr>
<td>Ozkiris</td>
<td>2012&lt;sup&gt;132&lt;/sup&gt;</td>
<td>Metamizole sodium, 0.4 mg/kg/day (Oral)</td>
<td>115</td>
<td>4</td>
<td>NR</td>
<td>NR</td>
<td>4 (3.47)</td>
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<td>0</td>
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<td>Ozkiris</td>
<td>2012&lt;sup&gt;132&lt;/sup&gt;</td>
<td>Acetaminophen, 40 mg/kg/day (Oral)</td>
<td>110</td>
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<td>NR</td>
<td>NR</td>
<td>4 (3.63)</td>
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</tr>
<tr>
<td>Lalicevic et al. 2004&lt;sup&gt;134&lt;/sup&gt;</td>
<td>Benzydamine hydrochloride oral rinse, 20 mg/kg (Oral)</td>
<td>138</td>
<td>6</td>
<td>NR</td>
<td>NR</td>
<td>6 (4.3)</td>
<td>NR</td>
<td>NR</td>
<td></td>
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<tr>
<td><strong>Steroids</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Park</td>
<td>2015&lt;sup&gt;135&lt;/sup&gt;</td>
<td>Prednisolone, 0.25 mg/kg/day (Oral)</td>
<td>69</td>
<td>2</td>
<td>NR</td>
<td>NR</td>
<td>2 (2.5)</td>
<td>NR</td>
<td>NR</td>
</tr>
<tr>
<td>Macassey</td>
<td></td>
<td>Prednisolone</td>
<td>91</td>
<td>11</td>
<td>NR</td>
<td>NR</td>
<td>11 (12)</td>
<td>1 (1)</td>
<td>NR</td>
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<tr>
<td>Drug class</td>
<td>Indication</td>
<td>Author, Year</td>
<td>Intervention</td>
<td>Total Arm N</td>
<td>Total PTH, n</td>
<td>Primary PTH n (%)</td>
<td>Secondary PTH n (%)</td>
<td>Other/Undefined PTH n (%)</td>
<td>Nonoperative Readmission or Revisit for PTH n (%)</td>
</tr>
<tr>
<td>------------</td>
<td>------------</td>
<td>--------------</td>
<td>--------------</td>
<td>-------------</td>
<td>--------------</td>
<td>------------------</td>
<td>-------------------</td>
<td>------------------------</td>
<td>---------------------------------</td>
</tr>
<tr>
<td>Other</td>
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<td></td>
<td></td>
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</tr>
<tr>
<td></td>
<td>Lalicevic 2004&lt;sup&gt;134&lt;/sup&gt;</td>
<td>Salvia officinalis oral rinse, 20 mg/kg (Oral)</td>
<td>140</td>
<td>6</td>
<td>NR</td>
<td>NR</td>
<td>6 (4.3)</td>
<td>NR</td>
<td>NR</td>
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<tr>
<td>No treatment/Placebo</td>
<td>Throat infection</td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td></td>
<td>Macassey 2012&lt;sup&gt;156&lt;/sup&gt;</td>
<td>Placebo syrup, 0.5 mg/kg (Oral)</td>
<td>102</td>
<td>13</td>
<td>NR</td>
<td>NR</td>
<td>13 (12)</td>
<td>1 (1)</td>
<td>NR</td>
</tr>
<tr>
<td></td>
<td>Park 2015&lt;sup&gt;155&lt;/sup&gt;</td>
<td>No Prednisolone</td>
<td>69</td>
<td>2</td>
<td>NR</td>
<td>NR</td>
<td>2 (2.5)</td>
<td>NR</td>
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<td></td>
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<td></td>
<td></td>
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<td></td>
<td>Murto 2015&lt;sup&gt;153&lt;/sup&gt;</td>
<td>Placebo</td>
<td>141</td>
<td>8</td>
<td>NR</td>
<td>NR</td>
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<td>2 (1.4)</td>
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<td>Totals</td>
<td>(N arms)</td>
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<td>All arms (13)</td>
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<td>2063</td>
<td>97</td>
<td>NA</td>
<td>12 (1.4)</td>
<td>15 (1.8)</td>
<td>70 (5.7)</td>
<td>18 (3.8)</td>
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<td>NSAIDs (3)</td>
<td>NA</td>
<td>679</td>
<td>32</td>
<td>5 (1.2)</td>
<td>13 (3.1)</td>
<td>14 (5.5)</td>
<td>8 (5.7)</td>
<td>12 (1.8)</td>
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<td>Non-NSAID analgesics (4)</td>
<td>NA</td>
<td>772</td>
<td>23</td>
<td>7 (1.7)</td>
<td>2 (0.49)</td>
<td>14 (3.9)</td>
<td>NR</td>
<td>3 (0.47)</td>
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<td>NR</td>
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<td>13 (8.1)</td>
<td>1 (1.1)</td>
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<td>Other (1)</td>
<td>NA</td>
<td>140</td>
<td>6</td>
<td>NA</td>
<td>NR</td>
<td>NR</td>
<td>6 (4.3)</td>
<td>NR</td>
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<td>No treatment/Placebo (3)</td>
<td>NA</td>
<td>312</td>
<td>23</td>
<td>NA</td>
<td>NR</td>
<td>NR</td>
<td>23 (7.4)</td>
<td>9 (3.7)</td>
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</tbody>
</table>

N=Number; NR=Not Reported; NSAID=Nonsteroidal Anti-Inflammatory Drug; PTH=Post-Tonsillectomy Hemorrhage
### Table H-12. Revisits or readmissions for pain, dehydration, and PONV reported in comparative study arms addressing perioperative agents

<table>
<thead>
<tr>
<th>Drug Class</th>
<th>Author</th>
<th>Perioperative Agent</th>
<th>Total Arm N</th>
<th>N Pain Revisits, (%)</th>
<th>N Dehydration Revisits, (%)</th>
<th>N PONV Revisits, (%)</th>
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<tbody>
<tr>
<td>Steroids</td>
<td>Gao^{37}</td>
<td>Dexamethasone (IV)</td>
<td>78</td>
<td>0 (0)</td>
<td>NR</td>
<td>0</td>
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<tr>
<td>Steroids</td>
<td>Gao^{157}</td>
<td>Dexamethasone (infiltration)</td>
<td>78</td>
<td>0 (0)</td>
<td>NR</td>
<td>0</td>
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<tr>
<td>Steroids</td>
<td>Hanasono^{38}</td>
<td>Dexamethasone</td>
<td>61</td>
<td>NR</td>
<td>1 (1.6)</td>
<td>NR</td>
</tr>
<tr>
<td>Steroids</td>
<td>Alajmi^{145}</td>
<td>Dexamethasone</td>
<td>42</td>
<td>0 (0)</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Steroids</td>
<td>Elhakim^{142}</td>
<td>Dexamethasone</td>
<td>20</td>
<td>0 (0)</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>NSAIDs</td>
<td>Oztekin^{38}</td>
<td>Diclofenac</td>
<td>20</td>
<td>0 (0)</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>EAnesthetic</td>
<td>El-Fattah^{139}</td>
<td>Propofol</td>
<td>80</td>
<td>0 (0)</td>
<td>0</td>
<td>0</td>
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<tr>
<td>Placebo/no agent</td>
<td>Hanasono^{38}</td>
<td>Placebo</td>
<td>56</td>
<td>NR</td>
<td>0</td>
<td>NR</td>
</tr>
<tr>
<td>Placebo/no agent</td>
<td>Sukhani^{160}</td>
<td>Placebo</td>
<td>49</td>
<td>NR</td>
<td>NR</td>
<td>ER or hospital admit for vomiting and poor oral intake 1 (2)</td>
</tr>
<tr>
<td>Placebo/no agent</td>
<td>Alajmi^{145}</td>
<td>Placebo</td>
<td>38</td>
<td>Readmitted for throat pain/dysphagia 4 (10.5)</td>
<td>NR</td>
<td>NR</td>
</tr>
<tr>
<td>Placebo/no agent</td>
<td>Oztekin^{38}</td>
<td>No perioperative agent</td>
<td>20</td>
<td>0 (0)</td>
<td>0</td>
<td>0</td>
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<tr>
<td><strong>Totals</strong></td>
<td><strong>(N arms)</strong></td>
<td><strong>(N arms)</strong></td>
<td>542</td>
<td>4 (1.1)</td>
<td>1 (0.33)</td>
<td>1 (0.26)</td>
</tr>
</tbody>
</table>

*Indication for surgery in these arms was throat infection; indication not specified in all other arms

N=Number; NR=Not Reported; NSAID=Nonsteroidal Anti-Inflammatory Drug
## Rescue Medications

**Table H-13. Need for rescue analgesics and anti-emetics reported in studies addressing perioperative medications**

<table>
<thead>
<tr>
<th>Author, Year</th>
<th>Study Design</th>
<th>Age range</th>
<th>Intervention</th>
<th>Surgical Technique</th>
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<th>Rescue Analgesic Needed, N (%) or mean ± SD</th>
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<tr>
<td>Gao 2015³⁷</td>
<td>RCT</td>
<td>5-10 low</td>
<td>G1: Intravenous dexamethasone, 0.5mg/kg (IV) (78) G2: Local infiltration dexamethasone, 0.5mg/kg (infiltration) (78) G3: Control (no dexamethasone) (79)</td>
<td>sharp dissection technique with cautery hemostasis</td>
<td>mCHEOPS score &gt; 4 assessed by anesthesiologist Vomiting &gt; 2 times in 2 minutes</td>
<td>From PACU to 24 hrs post-op</td>
<td>Doses of IV fentanyl needed, mean(μg) ± SD G1: 14.2 ± 12 G2: 9.4 ± 6.8 G3: 23.1 ± 17.5 Number of patients needing 2nd injection of fentanyl, G1: 9/44 (20.5) G2: 0/32 (0) G3: 17/60 (28.3)</td>
<td>Doses of IV metoclopramide, mean ± SD G1: 1.9 ± 0.5 G2: 2.3 ± 0.9 G3: 4.1 ± 1.2</td>
<td>G1 vs. G3, p &lt; 0.01 G2 vs. G3, p &lt; 0.01 G1 vs. G2, p = 0.002 G1 vs. G3, p = NR G2 vs. G3, p = NR G1 vs. G2, p = NR G1 vs. G3, p &lt; 0.001 G2 vs. G3, p &lt; 0.001 G1 vs. G2, p &lt; 0.001</td>
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<tr>
<td>Aysenur 2014³⁹</td>
<td>RCT</td>
<td>3-14 moderate</td>
<td>G1: Dexamethasone sodium phosphate, 1 mg/kg (infiltration) (20) G2: Levobupivacaine with epinephrine (infiltration) (20) G3: Saline</td>
<td>A standard dissection and snare technique</td>
<td>Upon Request NA</td>
<td>POD0</td>
<td>Number of analgesic interventions needed (paracetamol suspension) – POD0, G1: 2.5±0.5 G2: 2.8±0.3 G3: 3.5±0.5</td>
<td>Number of analgesic interventions needed (paracetamol)</td>
<td>G1 vs. G2, p&lt;0.05 G1 vs. G3, p&lt;0.05 G2 vs. G3, p &lt;0.05 G1 vs. G2, p&lt;0.05 G1 vs. G3, p&lt;0.05</td>
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<td>(infiltration) (20)</td>
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<td>Number of analgesic interventions needed (paracetamol suspension) – POD1, G1: 2±0.3 G2: 2.6±0.5 G3: 3.3±0.4</td>
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<td>G2 vs G3, p = ns</td>
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<td>Number of analgesic interventions needed (paracetamol suspension) – POD2, G1: 1.9±0.3 G2: 2.5±0.5 G3: 3.2±0.4</td>
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<td>G1 vs. G2, p&lt;0.05 G1 vs. G3, p&lt;0.05 G2 vs G3, p &lt; 0.05</td>
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<td>Number of analgesic interventions needed (paracetamol suspension) – POD3, G1: 1.9±0.3 G2: 2.4±0.6 G3: 3.1±0.3</td>
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<td>G1 vs. G2, p&lt;0.05 G1 vs. G3, p&lt;0.05 G2 vs G3, p &lt; 0.05</td>
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<td>Number of analgesic interventions needed (paracetamol suspension) – POD7, G1: 1.4±0.6 G2: 2.2±0.4 G3: 2.6±0.4</td>
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<td>G1 vs. G2, p&lt;0.05 G1 vs. G3, p&lt;0.05 G2 vs G3, p &lt; 0.05</td>
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<td>Faiz 2013&lt;sup&gt;161&lt;/sup&gt;</td>
<td>RCT</td>
<td>4-13</td>
<td>moderate</td>
<td>G1: Dexamethasone, 0.1 mg/kg (IV) (42)</td>
<td>G2: Acetaminophen, 15 mg/kg (IV) (42)</td>
<td>Unspecified tonsillectomy</td>
<td>Objective pain score ≥5</td>
<td>Appearance of vomiting</td>
<td>post-op (Ward)</td>
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<tr>
<td>Hermans 2012&lt;sup&gt;140&lt;/sup&gt;</td>
<td>RCT</td>
<td>2-18</td>
<td>low</td>
<td>G1: Dexamethasone, 0.15 mg/kg (IV) (46)</td>
<td>G2: Dexamethasone, 0.5 mg/kg (IV) (44)</td>
<td>G3: Placebo (saline), 0.5 mL/kg (IV) (44)</td>
<td>Cold dissection</td>
<td>CHEOPS score &gt;7 or VAS score ≥3</td>
<td>Vomiting and/or retching without expulsion of gastric content</td>
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<tr>
<td>Aouad 2012&lt;sup&gt;164&lt;/sup&gt;</td>
<td>RCT</td>
<td>2-12</td>
<td>low</td>
<td>G1: Methylprednisolone, 2.5 mg/kg (IV) (78)</td>
<td>G2: Dexamethasone, 0.5 mg/kg (IV) (75)</td>
<td>Electrocautery</td>
<td>Wong-Baker faces pain score &gt;6</td>
<td>Upon request</td>
<td>From PACU to 24 hrs post-op</td>
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<td>Khani 2009</td>
<td>RCT</td>
<td>4-12</td>
<td>G1: Dexamethasone, 0.5 mg/kg (IV) (33)</td>
<td>G1: Dexamethasone, 0.5 mg/kg (IV) (33)</td>
<td>G2: Placebo (saline), 0.5 mg/kg (IV) (33)</td>
<td>Recurrent vomiting &gt;2 episodes less than 5 minutes apart</td>
<td>From PACU to 24 hrs post-op</td>
<td>G1: 2 (0-4) G2: 3 (1-4)</td>
<td>N needing IV ondansetron (mg), (%) G1: 1 (1) G2: 2 (3)</td>
</tr>
<tr>
<td>Alajmi 2008</td>
<td>RCT</td>
<td>5-18</td>
<td>G1: Dexamethasone, 1mg/kg (IV) (42)</td>
<td>G1: Dexamethasone, 1mg/kg (IV) (42)</td>
<td>G2: Placebo, 5 mL (IV) (38)</td>
<td>When patient complained of pain</td>
<td>PACU to 24 hrs post-op</td>
<td>Patients needing IV morphine (µg), G1: 5 (15.1) G2: 16 (48.4)</td>
<td>Patients needing IV metoclopramide (mg), G1: 6 (18.1) G2: 17 (51.5)</td>
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<tr>
<td>Czarnetzki 2008</td>
<td>RCT</td>
<td>2-17</td>
<td>G1: Dexamethasone, 0.05 mg/kg (IV) (53)</td>
<td>G1: Dexamethasone, 0.05 mg/kg (IV) (53)</td>
<td>G2: Dexamethasone, 0.15 mg/kg (IV) (54)</td>
<td>Total tonsillectomy with dissection (cold dissection, hot dissection, or combination)</td>
<td>PACU</td>
<td>VAS pain score ≥ 3, CHEOPS pain score ≥8, revised Faces Pain Scale ≥3</td>
<td>N needing IV morphine (mg) in PACU, (%) G1: 42 (78) G2: 36 (79) G3: 37 (67) G4: 42 (78)</td>
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<th>Author, Year</th>
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<tr>
<td>Kim 2007**</td>
<td>RCT</td>
<td>2-7</td>
<td>Dexamethasone, 0.5 mg/kg (IV) (52) G4: Placebo (saline) (IV) (54)</td>
<td>Electrocautery</td>
<td>Objective pain score ≥6 for 2 consecutive 5 minute intervals or if the patients articulated that their throat hurt</td>
<td>Within 24 hrs post-op</td>
<td>G3: 20 (38) G4: 35 (65) N needing IV ondansetron (µg), (%) G1: 4 (8) G2: 3 (5.6) G3: 2 (4) G4: 11 (20)</td>
<td>G1 vs. G2 vs. G3 vs. G4, p = 0.04</td>
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<tr>
<td>Kaan 2006**</td>
<td>RCT</td>
<td>4-12 low</td>
<td>G1: Dexamethasone, 0.0625 mg/kg (IV) (24) G2: Dexamethasone, 0.125 mg/kg (IV) (25) G3: Dexamethasone, 0.25 mg/kg (IV) (23) G4: Dexamethasone, 0.5 mg/kg (IV) (25) G5: Dexamethasone, 1 mg/kg (IV) (24)</td>
<td>Cold dissection</td>
<td>“Faces” scale pain score &gt;3 Retching or vomiting more than once in 3</td>
<td>PACU 0-24 hours post-op</td>
<td>Need for IV morphine (mg) (up to 24 hrs), G1: NR G2: NR G3: NR G4: NR G5: NR</td>
<td>G1 vs. G2 vs. G3 vs. G4 vs. G5, p &gt; 0.05</td>
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<td>Samarkandi 2004&lt;sup&gt;134&lt;/sup&gt; 2-12 moderate</td>
<td>(IV) (30)</td>
<td>Electrocautery</td>
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<td>minutes If vomiting was not under control in 20 minutes, ondansetron was given</td>
<td>3 hrs post-op</td>
<td>G1: 6 (19) G2: 4 (13) <strong>N needing oral paracetamol (mg, 3 hrs), (%)</strong> G1: 11 (34) G2: 17 (57)</td>
<td>G1 vs G2, p = NR</td>
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<td>4 hrs post-op</td>
<td>G1: 12 (38) G2: 7 (23) <strong>N needing oral paracetamol (mg, 4 hrs), (%)</strong> G1: 3 (9) G2: 2 (7)</td>
<td>G1 vs G2, p = NR</td>
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<td>5 hrs post-op</td>
<td>G1: 3 (9) G2: 2 (7) <strong>N needing oral paracetamol (mg, 5 hrs), (%)</strong> G1: 0 (0) G2: 0 (0)</td>
<td>G1 vs G2, p = NR</td>
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<td>1-8 hrs post-op</td>
<td>G1: 10 (37) G2: 17 (54.8) <strong>N needing IV ondansetron (mg), (%)</strong> G1: 6 (19) G2: 10 (33)</td>
<td>G1 vs G2, p = NR</td>
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<td>1-8 hrs post-op</td>
<td>G1: 10 (37) G2: 17 (54.8) <strong>N needing IV metoclopramide (mg), (%)</strong> G1: 6 (19) G2: 10 (33)</td>
<td>G1 vs G2, p = NR</td>
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<td>Need for analgesia, G1 vs G2, p = 0.275</td>
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<td>Elhakim 200342 RCT 4-11 low</td>
<td>G1: Dexamethasone, 0.5 mg/kg (IV) (55) G2: Placebo (saline), 0.5 mg/kg (IV) (55)</td>
<td>Electrocautery</td>
<td>CHEOPS pain score &gt;7 or children who were crying during two consecutive five-minute observation periods until the child was comfortable More than two episodes of vomiting (repeatedly one to two minute period)</td>
<td>PACU to 24 hrs post-op</td>
<td>G1: 17 (63) G2: 14 (45.1) N needing IV metoclopramide (mg), (%) G1: 7 (24.1) G2: 15 (48.4)</td>
<td>G1 vs G2, p =0.09</td>
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<tr>
<td>NSAID</td>
<td>G1: Ibuprofen, 10 mg/kg (IV) (73) G2: Placebo (normal saline), 10 mg/kg (IV) (65)</td>
<td>Electrocautery</td>
<td>VAS pain score rating &gt;30 mm</td>
<td>PACU</td>
<td>Doses of IV fentanyl needed, mean(µg) ± SD G1: 1.6±1.3 G2: 1.9±1.06</td>
<td>G1 vs. G2, p = 0.021</td>
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<td>Moss 201447 RCT 6-17 moderate</td>
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<td>NA</td>
<td>PACU</td>
<td>N needing IV fentanyl (µg), (%) G1: 61 (84)</td>
<td>G1 vs. G2, p = 0.068</td>
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<td>Abdel-Ghaffar 2012&lt;sup&gt;65&lt;/sup&gt;</td>
<td>RCT</td>
<td>G1: IV lornoxicam, 8 mg (20)</td>
<td>Unspecified tonsillectomy</td>
<td>VRS pain score ≥2</td>
<td>24-28 hrs post-op</td>
<td>G2: 61 (94) N needing more than 1 dose of IV fentanyl (µg), (%): G1: 31 (42) G2: 40 (62)</td>
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<td>G1 vs. G2, p=0.028</td>
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<tr>
<td>Solanki 2012&lt;sup&gt;146&lt;/sup&gt;</td>
<td>RCT</td>
<td>G1: Diclofenac, 2mg/kg (rectal) (25)</td>
<td>Unspecified tonsillectomy</td>
<td>NA</td>
<td>Within 24 hrs post-op</td>
<td>Doses of injection diclofenac needed, mean(mg) ± SD G1: 44.73 ± 9.31 G2: 69.8 ± 38.71 G3: 87.8 ± 24.4 N needing 3 rescue doses of injection diclofenac (%): G1: 0 (0) G2: 9 (45) G3: 12 (60)</td>
<td></td>
<td>G1 vs. G3, p &lt; 0.000 G2 vs. G3, p = NS G1 vs. G2, p &lt; 0.009 G1 vs. G3: p=0.000 G2 vs G3: NS G1 vs. G2: p=0.01</td>
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<tr>
<td>Yegane Moghaddam 2012&lt;sup&gt;66&lt;/sup&gt;</td>
<td>RCT</td>
<td>G1: Diclofenac, 1.0 mg/kg (rectal) (30)</td>
<td>Unspecified tonsillectomy</td>
<td>Pain felt in recovery room or ward and VAS pain score &gt;4</td>
<td>PACU and Ward</td>
<td>Doses of injection meperidine, mean(mg) ± SD G1: 16.66 ± 8.95 G2: 14.16 ± 6.97 G3: 33.4 ± 13.97</td>
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<td>G1 vs. G3, p = 0.59 G2 vs. G3, p = 0.004 G1 vs. G3, p = 0.001 G1 vs. G2, p=0.59</td>
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<tr>
<td>Rhendra 2010&lt;sup&gt;167&lt;/sup&gt;</td>
<td>RCT</td>
<td>G1: Sodium diclofenac, 1 mg/kg (rectal) (65)</td>
<td>Cold dissection</td>
<td>Patient complained of intolerable pain and VAS score (0-100 mm) assessment (unspecified)</td>
<td>0.5 hrs post-op</td>
<td>Doses of IV pethidine needed 0.5 hrs post-op, mean(units) ± SD G1: 0.16 ± 0.13 G2: 0 ± 0</td>
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<td>G1 vs. G2, p = 0.301 G1 vs. G2, p = 0.023</td>
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<tr>
<td>Antila 2006</td>
<td>RCT</td>
<td>mg/kg (topical) (65)</td>
<td>NA</td>
<td>needed 2 hrs post-op, mean(units) ± SD</td>
<td>12 hrs post-op</td>
<td>G1: 0.11 ± 0.32</td>
<td>G2: 0.02 ± 0.12</td>
<td>G1 vs. G2, p = 0.061</td>
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<td>Doses of IV pethidine needed 12 hrs post-op, mean(units) ± SD</td>
<td>24 hrs post-op</td>
<td>G1: 0.46 ± 0.59</td>
<td>G2: 0.65 ± 0.59</td>
<td>G1 vs. G2, p = 0.068</td>
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<td>G1 vs. G2, p = 0.061</td>
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<td>Bhattacharya</td>
<td>RCT</td>
<td>G1: ketoprofen, 2 mg/kg (IV) (15) G2: tramadol, 1 mg/kg (IV) (15) G3: placebo (saline), (IV) (15)</td>
<td>Standard adenotonsillectomy</td>
<td>On patient demand</td>
<td>0 to 24 hrs post-op</td>
<td>N needing fentanyl mean ±SD, G1: 5.5 ± 5 G2: 7.6 ± 7.1 G3: 9.4 ± 10</td>
<td>G1 vs. G2, p = 0.035 G1 vs G3, p = 0.049 G2 vs G3, p=NR</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2005</td>
<td>8-12</td>
<td></td>
<td></td>
<td>NA</td>
<td></td>
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<tr>
<td></td>
<td>moderate</td>
<td>G1: Diclofenac, 2 mg/kg (rectal) (25) G2: Pethidine, 0.5 mg/kg (IV) (25)</td>
<td>Unspecified tonsillectomy or adenoidectomy</td>
<td>VAS score &gt; 40 mm or on patient demand</td>
<td></td>
<td>Doses of oral paracetamol needed, mean(mg) ± SD G1: 350 ± 0.2 G2: 500 ± 0.5</td>
<td>G1 vs G2, p &lt;0.05 G1 vs G2: p=NR</td>
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<td></td>
<td>Ward (1 hr post-op to following morning)</td>
<td></td>
<td>N needing 2nd dose of rescue oral paracetamol (mg) (%) G1: 5 (20) G2: 6 (24)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Kedek 2005</td>
<td>5-12</td>
<td>G1: Ibuprofen syrup, 10 mg/kg (20) G2: Lidocaine infiltration, 0.5%, 10 mg/kg (20)</td>
<td>Unspecified adenotonsillectomy</td>
<td>VAS score &gt;4</td>
<td>1 hrs post-op – 6 hrs post-op</td>
<td>Doses of syrup paracetamol needed, mean(mg doses) ± SD G1: 4.1 ± 1.41 G2: 3.8 ± 1.15</td>
<td>G1 vs G2, p = ns</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Author, Year</td>
<td>Study Design</td>
<td>Age range</td>
<td>Intervention</td>
<td>Surgical Technique</td>
<td>Criteria for using rescue analgesia/rescue anti-emetics</td>
<td>Assessment Timepoint</td>
<td>Rescue Analgesic Needed, N (%) or mean ± SD</td>
<td>Rescue Anti-emetic Needed, N (%) or mean ± SD</td>
<td>Group Differences</td>
</tr>
<tr>
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</tr>
<tr>
<td>Oztekin 2002</td>
<td>RCT</td>
<td>5-14</td>
<td>G1: Diclofenac, 1 mg/kg (rectal) (20) G2: No Rx (20)</td>
<td>Unspecified tonsillectomy with or without adenoidectomy</td>
<td>Children had any throat pain (unspecified)</td>
<td>PACU</td>
<td>G1: 130.33 ± 11.26 G2: 169.92 ± 9.22</td>
<td></td>
<td>G1 vs. G2, p = 0.012</td>
</tr>
<tr>
<td></td>
<td></td>
<td>moderate</td>
<td></td>
<td></td>
<td>NA</td>
<td>WARD</td>
<td>G1: 50.80 ± 11.38 G2: 87.77 ± 10.55</td>
<td></td>
<td>G1 vs. G2, p = 0.021</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>(PACU+WARD)</td>
<td></td>
<td>G1: 181.13 ± 19.15 G2: 257.68 ± 16.04</td>
<td></td>
<td>G1 vs. G2, p = 0.009</td>
</tr>
</tbody>
</table>

**Anti-emetics**

<table>
<thead>
<tr>
<th>Author, Year</th>
<th>Study Design</th>
<th>Age range</th>
<th>Intervention</th>
<th>Surgical Technique</th>
<th>Criteria for using rescue analgesia/rescue anti-emetics</th>
<th>Assessment Timepoint</th>
<th>Rescue Analgesic Needed, N (%) or mean ± SD</th>
<th>Rescue Anti-emetic Needed, N (%) or mean ± SD</th>
<th>Group Differences</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bolton 2007</td>
<td>RCT</td>
<td>6 mos-12 years</td>
<td>G1: Odansetron, 0.1 mg/kg (injection) (273) G2: Metoclopramide, 0.5 mg/kg (injection) (284)</td>
<td>Unspecified tonsillectomy with or without adenoidectomy</td>
<td>Post-op every four hours (P.R.N.)</td>
<td>post-op (unspecified)</td>
<td>G1: 1.4 ± 1.5 G2: 1.7 ± 1.7</td>
<td></td>
<td>G1 vs G2, p = NR</td>
</tr>
<tr>
<td>Fuji 2003</td>
<td>RCT</td>
<td>4-10</td>
<td>G1: Ramosetron, 3 µg/kg (IV) (20) G2: Ramosetron, 6 µg/kg (IV) (20) G3: Ramosetron, 12 µg/kg (IV) (20) G4: Placebo, NR</td>
<td>Unspecified tonsillectomy with or without adenoidectomy</td>
<td>NA</td>
<td>PACU-48 hrs post-op</td>
<td>N needing IV metoclopramide (mg), (%)</td>
<td></td>
<td>G1 vs. G4, p = ns G2,G3 vs. G4, p=0.024</td>
</tr>
<tr>
<td></td>
<td></td>
<td>low</td>
<td></td>
<td></td>
<td>Retching and/or vomiting ≥2 episodes within 48 hours</td>
<td></td>
<td>G1: 5 (25) G2: 0 (0) G3: 0 (0) G4: 5 (25)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Author, Year</td>
<td>Study Design</td>
<td>Age range</td>
<td>Intervention</td>
<td>Surgical Technique</td>
<td>Criteria for using</td>
<td>Assessment</td>
<td>Rescue Analgesic</td>
<td>Rescue Anti-emetic</td>
<td>Group Differences</td>
</tr>
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</tr>
<tr>
<td>Holt 2000</td>
<td>RCT</td>
<td>2-14</td>
<td>G1: Tropisetron, 0.2 mg/kg – 5 mg/kg (IV) (35)</td>
<td>Unspecified tonsillectomy or adenotonsillectomy</td>
<td>NA</td>
<td>PACU-24 hrs post-op</td>
<td>Patients needing IV metoclopramide (mg), G1: 1 (3) G2: 12 (33)</td>
<td>G1 vs G2, p &lt;0.01</td>
<td></td>
</tr>
<tr>
<td></td>
<td>low</td>
<td></td>
<td>G2: Placebo (IV) (36)</td>
<td>Vomiting &gt;2 times and clinician discretion</td>
<td></td>
<td></td>
<td></td>
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</tr>
</tbody>
</table>

G = Group; hrs= Hours; IV = Intravenous; kg = Kilograms; mCHEOPS = modified Eastern Ontario Children’s Hospital Pain Scale; mg = Milligrams; N= Number; NA = Not Applicable; NR = Not Reported; NS = Not Significant; PACU = Post-Anesthesia Care Unit; POD = Post-Op Day; PRN = As Needed (“pro re nata”); RCT = Randomized Controlled Trial; SD = Standard Deviation; µg = Micrograms; VAS = Visual Analog Scale; VRS = Visual Rating Scale

Table H-14. Time to return to normal activity associated with perioperative medications

<table>
<thead>
<tr>
<th>Author, Year</th>
<th>Age</th>
<th>Study Design</th>
<th>RoB</th>
<th>Drug Class</th>
<th>Intervention</th>
<th>Time to return to normal activity, n/N (%) or mean ± SD (n)</th>
<th>Outcome measure (e.g., mean days)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Giannoni et al. (2002)</td>
<td>3-15</td>
<td>RCT</td>
<td>moderate</td>
<td>Perioperative steroid + analgesics</td>
<td>Dexamethasone and ropivacaine + clonidine, 1.0 mg/kg (IV) and 0.15 mL/kg + 1 ug/kg</td>
<td>Time to return to normal activity, 7.74 ± 2.49 (25)</td>
<td>Mean days</td>
</tr>
<tr>
<td>Giannoni et al. (2002)</td>
<td>3-15</td>
<td>RCT</td>
<td>moderate</td>
<td>Placebo + analgesics</td>
<td>Placebo (saline) and ropivacaine + clonidine, 0.25 mL/kg (IV) and 0.15 mL/kg + 1 ug/kg</td>
<td>Time to return to normal activity, 6.38 ± 2.24 (25)</td>
<td>Mean days</td>
</tr>
</tbody>
</table>

IV = intravenous; RCT = Randomized Controlled Trial; µg = Micrograms

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References


59. Chang H, Hah JH. Comparison of post-tonsillectomy pain with two different types of bipolar forceps: low temperature quantum molecular resonance device versus high temperature conventional


74. Havel M, Sroka R, Englert E, et al. Intraindividual comparison of 1,470 nm diode laser versus carbon dioxide laser for tonsillotomy:
a prospective, randomized, double blind, controlled feasibility trial.


163. Kim MS, Cote CJ, Cristoloveanu C, et al. There is no dose-escalation response to dexamethasone (0.0625-1.0 mg/kg) in pediatric tonsillectomy or adenotonsillectomy patients for preventing vomiting, reducing pain, shortening time to first liquid intake, or the incidence of voice change. Anesth Analg. 2007 May;104(5):1052-8, tables of contents. doi: 10.1213/01.ane.0000263276.52287.3b. PMID: 17456652.


## Appendix I. Summary of Existing Systematic Reviews

### Table I-1. Existing reviews of surgical interventions for OSDB/SDB (7 reviews)

<table>
<thead>
<tr>
<th>Author, Year</th>
<th>Intervention Category</th>
<th>Inclusion Criteria</th>
<th>Outcome(s)</th>
<th># Included Studies</th>
<th>Key Findings</th>
</tr>
</thead>
<tbody>
<tr>
<td>Song et al. 2016¹</td>
<td>Tonsillectomy or Adenotonsillectomy (T&amp;A); OSA in children</td>
<td>• Children &lt;18 years&lt;br&gt;• Prospective studies&lt;br&gt;• Literature search database inception to 2015&lt;br&gt;• Included studies published 1996 to 2014</td>
<td>• Neurocognitive function&lt;br&gt;• AHI</td>
<td>19 studies with 898 children</td>
<td>• There was a reduction in AHI after T&amp;A in children with SDB across studies&lt;br&gt;• Improvement in neurocognitive function and IQ after T&amp;A&lt;br&gt;• Decreased effectiveness of T&amp;A in older children suggests a threshold age when neurocognitive deficits become irreversible</td>
</tr>
<tr>
<td>De Luca Canto et al. 2015²</td>
<td>Adenotonsillectomy (AT); OSA in children</td>
<td>• Children 0 to 18 years&lt;br&gt;• Clinical studies with postop evaluation within 3 weeks after AT&lt;br&gt;• Literature search up to 2015&lt;br&gt;• Included studies published 1987 to 2015</td>
<td>• Postop complications that required intervention including respiratory, hemorrhage, pain, NV, refusal to drink, inadequate oral intake, dehydration, fever, dysphagia, cardiac</td>
<td>23 studies with 13537 children</td>
<td>• Most frequent postop complication was respiratory compromise at 9.4% followed by secondary hemorrhage at 2.6% and primary hemorrhage at 2.4%&lt;br&gt;• Children with OSA have 5 times more respiratory complications after AT than children without OSA (across only 4 studies with 9394 children)&lt;br&gt;• Bleeding is more likely to occur among children without OSA compared to children with OSA (across only 4 studies with 9394 children)</td>
</tr>
<tr>
<td>Lee et al. 2015³</td>
<td>Adenotonsillectomy (T&amp;A); OSA in obese and non-obese children</td>
<td>• Children &lt;18 years&lt;br&gt;• Obese and non-obese children with OSA&lt;br&gt;• RCTs, retrospective observational case series, NRCTs&lt;br&gt;• Literature search published up to 2014&lt;br&gt;• Included studies 1994 to 2014</td>
<td>• PSG parameters&lt;br&gt;• Residual OSA postop</td>
<td>51 studies with 3413 children</td>
<td>• Residual OSA remained in ~1/2 the children especially those with severe OSA and obesity after T&amp;A&lt;br&gt;• Postop improvements in non-obese exceeded obese children&lt;br&gt;• Postop T&amp;A saw increased sleep efficiency, slow wave sleep, oxygen saturation, spontaneous arousals</td>
</tr>
<tr>
<td>Author, Year</td>
<td>Intervention Category</td>
<td>Inclusion Criteria</td>
<td>Outcome(s)</td>
<td># Included Studies</td>
<td>Key Findings</td>
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</tbody>
</table>
| Van et al. 2015<sup>1</sup> | Adenotonsillectomy (T&A); OSA in children | • Children 0 to 14 years  
• Children with OSA  
• RCTs, observational  
• Literature search 1995 to 2014  
• Included studies published | • BMI  
• Weight percentiles | 6 studies with 729 children | • Postop T&A saw decreased REM and non-REM AHI, number and severity of respiratory events, and total arousals  
• T&A postop saw a prominent decrease in AHI by 12.4 events/hr  
• Evidence for significant weight gain in short term following T&A in children with OSA regardless of initial weight status |
| Venekamp et al. 2015<sup>5</sup> | Tonsillectomy or adenoidectomy; OSDB in children | • Children 2 to 16 years with OSDB  
• RCTs  
• Literature search from database inception to 2015  
• Included studies published 2004 to 2014 | Primary  
• Disease-specific quality of life  
• Adverse events, complications and morbidity  
• Intraoperative and postoperative bleeding  
• Postoperative infection, dehydration, and pain  
Secondary  
• Generic quality of life  
• Respiratory events  
• Cardiovascular complications  
• Neurocognitive performance, attention, behavior, school performance, absence from school and weight changes | 3 studies with 562 children | • Only 3 included studies  
• Disease-specific QoL mean scores were lower (better or fewer symptoms) at 7 months after adenotonsillectomy compared to watchful waiting in one study (CHAT Trial)  
• Mean OSAS QoL at 12 months did not differ significantly between adenotonsillectomy vs. CPAP(Sudarsan Trial)  
• Mean ESS score did not differ at 6 months, but was lower in adenotonsillectomy group at 12 months in one study (Sudarsan Trial)  
• 15 children (3%) had a serious adverse event (CHAT Trial) |
<p>| Walton et al. | Intracapsular | • Children &lt;16 years | Postop pain | 16 studies with | Secondary hemorrhage rate |</p>
<table>
<thead>
<tr>
<th>Author, Year</th>
<th>Intervention Category</th>
<th>Inclusion Criteria</th>
<th>Outcome(s)</th>
<th># Included Studies</th>
<th>Key Findings</th>
</tr>
</thead>
</table>
| 2015⁶       | tonsillectomy or Total tonsillectomy; SDB in children | • Children with SDB  
• RCTs  
• Included studies published 1999 to 2010 | • Analgesic use  
• Recovery time  
• Diet  
• Bleeding rate  
• Infection  
• Regrowth rate requiring further surgical intervention | 1312 participants  
(699 in the partial tonsillectomy group and 635 in the TT group) | and number of days until pain free were superior in the IT group than the TT group  
• Formal meta-analysis was not conducted due to lack of raw data reporting within individual studies |
| Wang et al. 2015⁷ | Tonsillectomy or Tonsillotomy; SDB in children | • Children birth to 18 years  
• Sleep disordered breathing  
• Studies compared tonsillectomy and tonsillectomy directly  
• Prospective studies  
• Literature search up to 2014  
• Included studies published 1999 to 2014 | • Operation time, secondary postop bleeding, pain-free days, PSG outcomes, QoL, immune function, rate of SBD recurrence | 10 studies with 1029 children | Tonsillectomy had lower hemorrhage rate, shorter operation time, and more pain-free days over tonsillectomy  
• No significant difference in QoL, Postop immune function, and resolving obstructive symptoms |

AHI= Apnea Hypopnea Index ; BMI=Body Mass Index; CPAP=Continuous Positive Airway Pressure; OSA=Obstructive Sleep Apnea; OSAS= Obstructive Sleep Apnea Syndrome ; PSG=Polysomnography; QoL=Quality of Life; RCT=Randomized Controlled Trials; SDB=Sleep Disordered Breathing; TT=Total Tonsillectomy
<table>
<thead>
<tr>
<th>Author, Year</th>
<th>Intervention Category</th>
<th>Inclusion Criteria</th>
<th>Outcome(s)</th>
<th># Included Studies</th>
<th>Key Findings</th>
</tr>
</thead>
</table>
| Burton et al. 2014<sup>8</sup> | Tonsillectomy or adenotonsillectomy; Chronic/recurrent acute tonsillitis | • Children and adults with diagnosed recurrent acute tonsillitis or chronic tonsillitis  
• RCTs  
• Literature search up to 2014  
• Included studies with children published 1984 to 2010 | Primary  
• Number/severity of episodes of tonsillitis/sore throat  
• Number of days with sore throat  
• Morbidity/mortality of surgery (include complications and no. days with postop pain from surgery)  
Secondary  
• Consumption of antibiotics, analgesics  
• Absence/time off work/school  
• QoL | 5 studies with 987 children only; 3 studies with 196 adults only | • Demonstrated moderate reduction in number of episodes of sore throat during first year postop |
| Georgalas et al. 2014<sup>9</sup> | Tonsillectomy; Acute recurrent or Chronic throat infections | • RCTs, Published systematic reviews of RCTs  
• Literature search 1966 to 2014  
• Included SRs published 2001 to 2010 | • Episodes of tonsillitis or sore throat  
• Time off school or work  
• Surgery: bleeding (intraoperative and postop)  
• Surgery: postop pain (includes analgesia use) | 15 studies/SRs | • Findings that tonsillectomy is more beneficial in children with severe symptoms, and only modestly beneficial for children with low incidence of tonsillitis  
• Diathermy is associated with reduced rates of primary bleeding, but increased rates of secondary bleeding |

RCT=Randomized Controlled Trials; SR=Systematic Review
<table>
<thead>
<tr>
<th>Author, Year</th>
<th>Intervention Category</th>
<th>Inclusion Criteria</th>
<th>Outcome(s)</th>
<th># Included Studies</th>
<th>Key Findings</th>
</tr>
</thead>
</table>
| Acevedo et al. 2012<sup>10</sup> | Tonsillotomy or Tonsillectomy | • Children and adults  
• RCTs, Observational  
• Literature search 2010 to 2011  
• Included studies published 1999 to 2010 | Primary  
• Postop bleeding rate  
• Rate of dehydration requiring medical care  
Secondary  
• Days of analgesic use  
• Days to return to normal diet  
• Est. intraoperative blood loss | 39 studies with 14707 children and adults | • Tonsillotomy had lower postop bleeding rate, postop dehydration rate requiring medical care, reduced days of analgesic use, and reduced days to return to normal diet  
• No clinically significant difference in intraoperative blood loss  
• Subgroup analysis suggests that coblation technique confers more of an advantage than microdebrider for postop complications  
• Data not sufficient to assess tonsil regrowth rates |
| Jeyakumar et al. 2011<sup>11</sup> | Adenotonsillectomy (T&A) or Tonsillectomy | • Children 0 to 10 years  
• Children of normal weight or overweight  
• Prospective studies  
• Literature search 1970 to 2009  
• Included studies published 1988 to 2009 | • Postop BMI vs. control group BMI  
• % of weight gain greater than expected postop  
• Change in weight pre-op to postop | 9 studies with 795 children | • A large number of normal weight and overweight children gained a greater than expected amount of weight after T&A |
| Alexiou et al. 2011<sup>12</sup> | Tonsillectomy (Vessel Sealing Systems (VSS) (e.g., LigaSure Vessel Sealing System, Thermal Welding System,BiClamp)) or Harmonic Scalpel or Coblation (e.g., Cold Steel (CS), Electrocautery Dissection (EC)) | • Children and Adults  
• RCTs  
• Literature search database inception to 2010  
• Included studies published 2001 to 2011 | • Operative time  
• Intraoperative and Postop bleeding (primary and secondary)  
• Postop pain | 33 studies with 3139 patients (11 studies with children only; 8 studies with adults only; 14 studies with mixed population) | • VSS group postop bleeding was significantly less than Conventional techniques in 792 patients  
• Postop pain was significantly less on the 1<sup>st</sup> and 7<sup>th</sup> days in the VSS group in 740 patients  
• No difference in outcomes between Coblation and CS/EC groups  
• Included studies with weak evidence maintaining a lower threshold for inclusion in meta analysis |
| Mösges et al. 2011<sup>13</sup> | Tonsillectomy (Coblation) | • Children and Adults  
• RCTs, prospective studies | • Postop hemorrhage (primary and secondary) | 24 studies with 796 patients (461 | • Postop hemorrhage rate for children is 2.9% |
<table>
<thead>
<tr>
<th>Author, Year</th>
<th>Intervention Category</th>
<th>Inclusion Criteria</th>
<th>Outcome(s)</th>
<th># Included Studies</th>
<th>Key Findings</th>
</tr>
</thead>
</table>
| Bellis et al. 2014<sup>15</sup> | Dexamethasone (Tonsillectomy) | • Children up to 18 years  
• RCTs and quasi-RCTs  
• During perioperative period (24 hrs prior, during procedure, or 24 hrs postop)  
• Included studies published 1991-2012 | Hemorrhage rate | 61 studies with 13933 children | • No significant increase in risk of post-tonsillectomy hemorrhage  
• Clinical heterogeneity was noted across studies  
• Inadequate evidence due to majority of studies not designed to investigate post-tonsillectomy hemorrhage with use of dexamethasone  
• Overall ROB was high or unclear for all RCTs |
| Plante et al. 2012<sup>16</sup> | Dexamethasone or Prednisolone (Tonsillectomy) | • Adults and children  
• RCTs  
• Literature search 1947 to 2011  
• Included studies published | Primary  
• Incidence of postop bleeding  
Secondary  
• Incidence of admission for | 29 studies with 2674 patients (19 studies with children only, 6 studies with adults only, 4 studies) | • Administration of steroids did not increase the incidence of bleeding postop  
• The incidence of admission due to bleeding did not increase in steroid group compared to |

Table I-4. Existing reviews of perioperative medications (9 reviews)

CS=Cold Steel, EC=Electrocautery Dissection, RCT=Randomized Controlled Trials; T&A= Adenotonsillectomy, VAS=Visual Analog Scale, VSS= Vessel Sealing Systems
<table>
<thead>
<tr>
<th>Author, Year</th>
<th>Intervention Category</th>
<th>Inclusion Criteria</th>
<th>Outcome(s)</th>
<th># Included Studies</th>
<th>Key Findings</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>1991 to 2011</td>
<td>bleeding episodes</td>
<td>included mixed population)</td>
<td>control group</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>• Operative interventions for bleeding episodes</td>
<td></td>
<td>The incidence for operative re-intervention for bleeding was significantly increased in the steroid group compared to control group; with a significant increase of re-interventions in children (8 studies) but not in adults (4 studies)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>• Red blood cell transfusion</td>
<td></td>
<td>No dose effect was observed</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>• Mortality</td>
<td></td>
<td>Dexamethasone was used in 28 studies and Prednisolone used in 1 study</td>
</tr>
<tr>
<td>Shargorodsky et al. 2012</td>
<td>Dexamethasone (Tonsillectomy or Adenotonsillectomy)</td>
<td>• Children ≤18 years</td>
<td>Primary and secondary hemorrhage</td>
<td>12 studies with 1180 children</td>
<td>No significant association between dexamethasone at any dose and bleeding compared to placebo</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• RCTs</td>
<td></td>
<td></td>
<td>No significant association between increasing dosage and bleeding</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Dexamethasone administration preop or intraoperatively</td>
<td></td>
<td></td>
<td>Doses on 0.4 to 0.6 mg/kg showed significantly increased odds of bleeding compared to placebo</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Literature search from 1990 to 2010</td>
<td></td>
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</tr>
<tr>
<td></td>
<td></td>
<td>• Included studies published 1991 to 2009</td>
<td></td>
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<tr>
<td>Geva et al. 2011</td>
<td>Dexamethasone (Tonsillectomy)</td>
<td>• Children and Adults</td>
<td>Intraoperative and postop bleeding</td>
<td>14 studies with 1429 children and adults (11 studies with 1166 children only, 3 studies with 263 adults only)</td>
<td>No significant increase in postop bleeding between patients receiving dexamethasone and control patients across mixed population</td>
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<td></td>
<td></td>
<td>• RCTs</td>
<td>Bleeding requiring reoperation</td>
<td></td>
<td>Younger patients receiving dexamethasone resulted in a statistically nonsignificant decrease in the risk of postoperative bleeding</td>
</tr>
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<td></td>
<td></td>
<td>• Literature search up to 2009</td>
<td></td>
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<td>• Included studies published 1991 to 2008</td>
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<tr>
<td>Steward et al. 2011</td>
<td>Dexamethasone (Tonsillectomy)</td>
<td>• Children 9 months to 18 years</td>
<td>Number of children experiencing emesis during 24 hrs postop</td>
<td>19 studies with 1756 children</td>
<td>ROB in included studies was not formally assessed</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• RCTs</td>
<td>Number of children return to soft/solid diet by day 1 postop</td>
<td></td>
<td>Statistically significant reduction in emesis during the 1st 24 hrs postop compared to placebo group</td>
</tr>
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<td></td>
<td></td>
<td>• Literature search up to 2010</td>
<td>Pain at 24 hrs</td>
<td></td>
<td>Statistically significant increase</td>
</tr>
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<td></td>
<td></td>
<td>• Included studies published 1991 to 2009</td>
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<td>Author, Year</td>
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<td>Inclusion Criteria</td>
<td>Outcome(s)</td>
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<td>Key Findings</td>
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| Chan et al. 2014<sup>20</sup> | Ketorolac (NSAID) (Tonsillectomy) | • Children and Adults  
• RCTs, retrospective case-control studies  
• Literature search from 1970 to 2013  
• Included studies published 1995 to 2004 | • Postop hemorrhage  
• Measured by VAS | 10 studies with (7 studies with children only, 2 studies with mixed population, 1 study adults only) | • Children under 18 are not at statistically significantly increased risk for postop hemorrhage with ketorolac use  
• Statistically significant improvement in postop pain compared to placebo using VAS as measurement |
| Lewis et al. 2013<sup>21</sup> | NSAIDs (Tonsillectomy or Adenotonsillectomy) | • Children up to and including 16 years  
• RCTs  
• Literature search from database inception to 2012  
• Included studies published 1995 to 2011 | • Bleeding  
• Postop complications | 15 studies with 1101 children | • Use of NSAIDs was associated with a non-significant increase in the risk of bleeding requiring surgical intervention  
• NSAIDs did not significantly alter the number of perioperative bleeds requiring non-surgical intervention  
• NSAIDs benefit a reduction of vomiting  
• Insufficient evidence to exclude an increased risk of bleeding when NSAIDs are used |
| Riggin et al. 2013<sup>22</sup> | NSAIDs (Tonsillectomy) | • Children and adults who underwent tonsillectomy  
• RCTs  
• Literature search from database inception to 2012  
• Included studies published 1984 to 2012 | • Postop hemorrhage  
• Secondary hemorrhage  
• Bleeding requiring readmission, reoperation, or tranexamic acid | 36 studies with 1747 children and 1446 adults | • No increased risk of bleeding in those using NSAIDs after tonsillectomy  
• Use of NSAIDs in children was not associated with increased risk of general bleeding, most severe bleeding, secondary hemorrhage, readmission or need of reoperation due to bleeding  
• In pediatrics population, overall odds ratio of bleeding was lower than general population (including adults) and not... |
<table>
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</tr>
</thead>
</table>
| Dhiwakar et al. 2012<sup>3</sup> | Antibiotics (Tonsillectomy or Adenotonsillectomy) | • Children and adults undergoing tonsillectomy or adenotonsillectomy  
• RCTs  
• Antibiotic administration 48 hrs pre-op, intraoperatively, postop  
• Literature search from database inception to 2012  
• Included studies published 1986 to 2008 | • Pain  
• Consumption of analgesia  
• Secondary hemorrhage  
• Fever  
• Time to resume normal diet/activities  
• Adverse events (e.g., rash, anaphylaxis, candidiasis, diarrhea) | 10 studies with 1035 children and adults | • No evidence to support clinically important impact of antibiotics in reducing pain, need for analgesia, and secondary hemorrhage rates  
• No significant reduction in pain with antibiotics  
• Mostly not shown to be effective in reducing need for analgesics  
• Not associated with reduction in significant secondary hemorrhage rates  
• Antibiotics reduced the proportion of patients with fever |

AHI=Apnea-Hypopnea Index, AT=Adenotonsillectomy, CPAP=Continuous positive airway pressure, CS=Cold Steel, EC=Electrocautery Dissection, ESS=Epworth Sleepiness Scale, NSAIDs=Non-steroidal anti-inflammatory drugs, OSDB=Obstructive sleep-disordered breathing, QoL=Quality of life, RCTs=Randomized controlled trials, ROB=Risk of bias, RR=Pooled Relative Risk, SBD=Sleep disordered breathing, T&A=Adenotonsillectomy, VAS=Visual Analog Scale, VSS=Vessel Sealing Systems

**References**