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Update on evidence-based reviews with recommendations in adult chronic rhinosinusitis

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Chronic rhinosinusitis (CRS) has a significant impact not only on individuals who are afflicted but also on society as a whole. An increasing emphasis is being placed on incorporating the best available evidence into the care of patients, in association with an individual clinician’s expertise and the patient’s values. Recent evidence-based reviews with recommendations (EBRRs) have distilled our knowledge of CRS treatment options and have also pointed out continued gaps in this knowledge. This review synthesizes the findings of 8 EBRRs regarding CRS published in the International Forum of Allergy and Rhinology between 2011 and 2014. The recommendations in this review are based on the best available evidence and are meant to be incorporated into each patient’s individual care, along with the practitioner’s expertise and the individual patient’s values and expectations. It is hoped that the EBRRs, and the process that spawned them, can provide the foundation for future guidelines in the diagnosis and management of CRS.

Key Words: chronic rhinosinusitis; CRS; evidence-based review with recommendation; EBRR; evidence-based medicine; EBM


Executive summary

Chronic rhinosinusitis (CRS) has a significant impact not only on individuals who are afflicted but also on society as a whole. An increasing emphasis is being placed on incorporating the best available evidence into the care of patients, in association with an individual clinician’s expertise and the patient’s values. Recent evidence-based reviews with recommendations (EBRRs) have distilled our knowledge of CRS treatment options and have also pointed out continued gaps in this knowledge.

This review synthesizes the findings of 8 EBRRs regarding CRS published in the International Forum of Allergy and Rhinology between 2011 and 2014. These synthesized recommendations are summarized in Table 1. The authors used an online iterative process in evaluating and synthesizing these reviews. The process started with the development of an initial EBRR manuscript, which was then sequentially reviewed by additional authors, with special attention to the validity of the recommendations and the areas of knowledge gaps in current EBRRs. With each proposed revision, consensus of the prior authors was achieved before the input of the next author was sought.

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Potential conflict of interest: None provided.
### TABLE 1. Summary of recommendations synthesized from published EBRRs

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<td>Standard topical (spray) corticosteroids</td>
<td>Strong recommendation for routine cases of CRS.</td>
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<td>Nonstandard topical (off-label) corticosteroids</td>
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<tr>
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<td><strong>Strong recommendation</strong> for the use of oral steroids in the short-term management of CRSwNP. <strong>Recommendation</strong> for use in the perioperative period for CRSwNP.</td>
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<tr>
<td>Systemic corticosteroids—CRSsNP</td>
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</tr>
<tr>
<td>Systemic corticosteroids—AFRS</td>
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<td>Oral antibacterial therapy lasting less than 3 weeks (nonmacrolide therapy)</td>
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<td>Oral antifungals</td>
<td><strong>Recommendation against</strong> use for routine CRS cases.</td>
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<td>Topical antifungals</td>
<td><strong>Strong recommendation against</strong> use for routine CRS patients.</td>
</tr>
<tr>
<td>Distribution of topical therapies—effect of sinus surgery</td>
<td><strong>Recommendation</strong> for increased penetration of topical therapy. Surgery can be recommended on a case by case basis as the surgeon and patient deem necessary.</td>
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<tr>
<td>Distribution of topical therapies—effect of topical therapy delivery device</td>
<td><strong>Recommendation</strong> for use of disposable large volume devices for sinus delivery. <strong>Recommendation against</strong> low volume devices, such as simple nebulizers, drops and spray, which have limited sinus delivery. <strong>Option</strong> for low volume devices, such as drops or sprays, if large volume devices are not tolerated, but low volume devices must be used in optimal head position and even then sinus distribution is limited (see Head position).</td>
</tr>
<tr>
<td>Distribution of topical therapies—effect of head position</td>
<td><strong>Recommendation</strong> for HDF when using high-volume devices if patient will tolerate. HDF for low-volume device, but with limited sinus penetration. <strong>Recommendation</strong> for LHB or LHL position when using low-volume devices, which will only reliably distribute to the nasal cavity.</td>
</tr>
<tr>
<td>Distribution of topical therapies—</td>
<td><strong>Recommendation</strong> for use of high-volume delivery devices to achieve sinus delivery in patients with unfavorable nasal anatomy. <strong>Option</strong> for short-term (3–4 days or less) use of topical vasoconstrictor to improve nasal cavity delivery in cases of turbinate hypertrophy. <strong>Recommendation against</strong> long-term use of topical vasoconstrictor to improve nasal cavity delivery.</td>
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<tr>
<td><strong>Surgical therapy for CRS</strong></td>
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<td><strong>Recommendation</strong> for postoperative debridement.</td>
</tr>
<tr>
<td>Early postoperative care—systemic steroids</td>
<td>Option.</td>
</tr>
</tbody>
</table>
Diagnosis of CRS

No EBRRs dealing with the efficient diagnosis of CRS have yet been published and this topic would benefit from an EBRR.

Medical therapy for CRS

Allergy evaluation and management in CRS patients were found to have equivocal support in the literature and recommended as an option in CRS patients, both with polyps (CRSsNP) and without polyps (CRSwNP). Topical nasal steroid sprays were strongly recommended based on their efficacy and relatively low risk of harm. Nonstandard topical delivery of corticosteroids (eg, as a medicated irrigation) was recommended as an option, due mainly to the low level of evidence and poorly defined risks. Oral corticosteroids were recommended for the short-term management (up to 8–12 weeks’ duration) of CRSwNP and in the perioperative period, although risks were acknowledged. For CRSsNP, the risk-benefit ratio is less well known and oral corticosteroids were considered an option, with no evidence for or against their use in the perioperative period. For allergic fungal rhinosinusitis (AFRS), steroids were again found to be advantageous and were recommended overall and in the perioperative period.

Antimicrobials in CRS were extensively reviewed and found to have both advantages and disadvantages in CRS. Short-term oral antibiotic use (less than 3 weeks’ duration) was considered an option, while the authors recommended against the use of long-term oral antibiotics (greater than 3 weeks’ duration) in routine CRS cases. The exception to this recommendation was macrolide antibiotics, which have some evidence of efficacy with prolonged use. They were considered an option in the treatment of CRS. The evidence for efficacy of both intravenous and topical antibiotics was found to be lacking. With the significant risk of intravenous antibiotics and costs associated with both intravenous and topical antibiotics, the authors recommended against their use in routine CRS cases. Similarly, the weight of evidence was against the use of topical or oral antifungals for routine CRS cases and the authors recommended against their use as well.

Distribution of topical agents to the sinuses was found to be affected by a number of factors, including the type of device, head position, nasal anatomy, and sinus surgery. Based on the evidence in these areas, high-volume irrigations were recommended and were found to overcome variiances in nasal anatomy, such as septal deviation, and the effect of different head positions. Surgery appears to enhance the penetration of topical therapies into the sinuses.

Surgical therapy for CRS

The timing of surgery relative to medical therapy and patient symptoms, the appropriate extent of surgery, and the comparative efficacy of various techniques and tools are all areas that require additional evidence. Image-guided surgery (IGS) in sinus surgery has been studied much since its incorporation into surgery for CRS. The evidence is relatively low level and, with costs high, IGS was recommended as an option in surgery for CRS.

Postoperative care following sinus surgery was assessed and the following interventions were recommended: nasal saline irrigations, postoperative debridement, and topical nasal steroid sprays. Oral corticosteroids were considered an option, as were nonstandard topical corticosteroid delivery, antibiotics, and drug-eluting stents. Newer drug-eluting implants were not discussed. Topical decongestants were recommended against.

Future directions

While the EBRRs published to this point have explored a large number of important topics in CRS management, this review has also shown gaps in our collective knowledge of other areas of management and of evaluation as well. Possible topics for future EBRRs in CRS are the following:

- Cost-effective diagnosis
- Cost-effective evaluation of underlying conditions
- Etiologic factors
- Value of histopathologic assessment of sinus tissue
- Pediatric chronic rhinosinusitis
- Antibiotics in the management of acute exacerbations of CRS
- Other medical treatments (eg, aspirin desensitization, leukotriene modifiers, etc.)
• Optimal medical therapy to be employed prior to considering surgery
• Comparative efficacy of surgical instrumentation and techniques (eg, balloon dilation)
• Comparative efficacy of the extent of surgery
• Appropriate long-term sinus care.

The recommendations in this review are based on the best available evidence and are meant to be incorporated into each patient’s individual care, and along with the practitioner’s expertise and the individual patient’s values and expectations. They are not a “cookbook,” nor are they official guidelines sanctioned by any official bodies. Additionally, they are not static, but will always be subject to new evidence as it comes forward. It is hoped that the EBRRs, and the process that spawned them, can provide the foundation for future guidelines in the diagnosis and management of CRS.

Introduction
The societal and individual impact of CRS is significant and well documented. Decrements in quality of life (QOL) and work productivity are substantial and produce an extensive economic burden to society and the health systems required to alleviate the suffering associated with CRS.1–3 Over the last few decades, the pace of investigation into CRS has quickened and has led to a better understanding of many facets of this condition. Notwithstanding these significant advances in our understanding of CRS, it remains a condition, or more likely a group of conditions, with multiple potential etiologies and with many possible treatments. Prolonged inflammation of the nose and sinuses can manifest with different symptoms in different patients and may present differing physical manifestations as well (eg, the presence or absence of polyps). Despite a determined search, a single unifying pathophysiologic mechanism remains elusive. Without a clear cause (or at least a few clear causes), effective treatments that target specific underlying pathophysiologic mechanisms also remain unidentified. Physicians and others who treat CRS patients are thus left with a large number of treatment options that have arisen out of dogged efforts to alleviate the significant amount of suffering associated with this condition.

EBM has been defined as “the conscientious, explicit and judicious use of current best evidence in making decisions about the care of individual patients. The practice of evidence-based medicine means integrating individual clinical expertise with the best available external clinical evidence from systematic research.”4 To be clear, EBM is not a cookbook approach to all patients by all practitioners. Instead, EBM is a triad that incorporates the best available evidence into an individual practitioner’s clinical expertise combined with the individual patient’s values and desires. It is a method that maximizes the value of the care delivered, with value loosely defined as the ratio of outcome to cost. Clearly, a thorough understanding of the best available evidence is a key component in delivering maximum value through EBM.

In an effort to enhance the application of EBM to the treatment of CRS, Rudmik and Smith5 proposed a streamlined method for reviewing topics in CRS treatment and making recommendations based on the evidence. These EBRRs result from a less formal but sufficiently robust process of evaluating the current evidence on a particular topic. Following an initial review and development of recommendations, other experts in the topic sequentially review the EBRR until a broad consensus is reached. Since the development of this process in late 2011, 8 EBRRs have been published. The purpose of this article is to comprehensively review these documents, synthesize their recommendations, and point out additional areas that would benefit from additional EBRRs.

Methods
All published EBRRs regarding CRS were reviewed, following the method of Rudmik and Smith.5 The clinical topic selected was the current state of EBM as assessed by EBRRs in CRS. Potential authors were selected from a group of recognized experts in the field of CRS who were familiar with guideline development. Many had previously participated in development of EBRRs. Using an online iterative process, the initial review was sequentially reviewed by additional authors, with special attention to the validity of the recommendations and the areas of knowledge gaps in current EBRRs. Updates to the review were routed through the first author and the consensus of the prior authors was achieved before the input of the next author was sought. The identity of earlier authors was not revealed in order to minimize potential bias.

Results
Diagnosis of CRS
No EBRRs dealing with the efficient diagnosis of CRS have yet been published. Timing of referral to a specialist, role of nasal endoscopy, and impact of imaging are areas that would benefit from an EBRR.

Medical therapy for CRS
Allergy evaluation
In an effort to shed some light on the pathophysiology of CRS and 1 potential avenue of treatment, Wilson et al.6 examined the role of allergy in CRS with and without nasal polyps (CRSwNP, CRSSsNP). They reviewed 18 articles that dealt with the relationship between CRSwNP and allergy and found 10 articles supporting an association, 7 articles showing no association, and 1 article showing a possible association. The evidence for an association between CRSSsNP and allergy was similarly equivocal, with 4 articles demonstrating an association and 5 showing no association. The strength of the articles in these analyses did not vary significantly, leaving the authors to conclude that
evidence for a pathophysiologic association between allergy and CRS was mixed. No articles examined the role of allergy treatment in outcomes of CRSwNP or CRSsNP. The authors summarized their findings as follows:

- **Aggregate quality of evidence:** D (Expert opinion and reasoning from first principles and conflicting prevalence data).
- **Benefit:** Allergy evaluation and management are generally well tolerated. Management theoretically reduces triggers of CRS while modifying symptoms of allergic rhinitis, possibly impacting chronic rhinosinusitis.
- **Harm:** Mild local irritation associated with testing and immunotherapy, mild sedation seen with some antihistamine drugs; severe complications are rare.
- **Cost:** Moderate direct costs for testing and treatment; some therapies require significant patient time (eg, office-administered subcutaneous immunotherapy).
- **Benefits-Harm assessment:** Preponderance of benefit over harm.
- **Value Judgments:** None.
- **Recommendation:** Allergy testing and treatment are an option in CRSwNP and CRSsNP.

**Treatment for allergic rhinitis**

While the exact pathophysiologic role of allergy in CRS remains unclear, there is significant symptom overlap. Treatment of allergy when it coexists with CRS will likely enhance patient outcome by mitigating the allergic contribution to the symptoms that are common to both allergic rhinitis and CRS. To that end, Purkey et al.7 exhaustively reviewed the evidence on subcutaneous immunotherapy (SCIT) for allergic rhinitis (AR). Building upon the Cochrane Review of Allergen Injection Immunotherapy for Seasonal Allergic Rhinitis published in 2007,8 they examined the literature published between 2006 and 2011. The authors assessed the literature on both seasonal and perennial allergic rhinitis and included only those studies graded as Level 1 evidence, yielding 12 articles for consideration. Primary outcome measurements were mostly symptoms scores, medications scores, or a combination of symptom and medication scores. Additional endpoints included the Rhinoconjunctivitis Quality of Life Questionnaire (RQLQ), immunoglobulin assays, challenge tests, and adverse events. This EBRR found the studies examined showed uniform efficacy of SCIT in reducing symptoms and/or medication use in patients being treated for seasonal or perennial AR. Moreover, they found SCIT to be safe, with only 0.13% to 0.2% of conventional dosing injections producing a systemic reaction. The authors summarized their findings as follows:

- **Aggregate quality of evidence:** A (Level 1b: 12 studies).
- **Benefit:** Improvement in symptom and/or medication scores and validated quality of life measures. Associated changes in surrogate markers of immunologic protection.
- **Harm:** Local and systemic reactions (rare but with significant morbidity/mortality if they occur).
- **Cost:** Moderate in both monetary cost and time commitment.
- **Benefits-harm assessment:** Preponderance of benefit over harm in appropriately selected patients.
- **Value judgments:** None.
- **Recommendation level:** Recommend subcutaneous immunotherapy for patient with seasonal or perennial allergic rhinitis not responsive to conservative medical therapy and whose symptoms significantly affect QOL.

Sublingual immunotherapy (SLIT) has emerged as a popular treatment and a number of publications have examined its efficacy and safety, including a number of systematic analyses.

**Corticosteroids**

While the exact etiology (or etiologies) of CRS remains unknown, it is well accepted to be an inflammatory condition of the nose and paranasal sinuses. To that end, corticosteroid therapy has been a mainstay of treatment for many years. Two EBRRs have examined the role of corticosteroids in the treatment of CRS, with Rudmik et al.9 examining topical therapy and Poetker et al.10 exploring systemic therapy.

**Standard topical (spray) corticosteroids.** Rudmik et al.9 identified 5 meta-analyses that examined the efficacy and safety of standard topical nasal corticosteroid sprays in both CRSwNP and CRSsNP. All were graded as 1a in quality and 4 of the 5 demonstrated significant improvements in symptoms and endoscopic appearance. Overall, the authors concluded the following:

- **Aggregate quality of evidence:** A (Level 1a: 5 studies).
- **Benefit:** Improved symptoms and endoscopic appearance. Reduced polyp size.
- **Harm:** Headache. Epistaxis. Cough.
- **Cost:** Low to moderate (range, $0.61/day to $4.80/day); depends on preparation.
- **Benefits-harm assessment:** Preponderance of benefit over harm.
- **Value judgments:** The authors recognize that other topical therapy options may be required when an adequate trial of standard metered-dose topical nasal steroid spray has failed to improve clinical outcomes.
- **Recommendation level:** Strong recommendation for routine cases of CRS.

**Nonstandard topical corticosteroids.** Rudmik et al.9 also reviewed evidence regarding nonstandard or “off-label” applications of topical corticosteroids, such as high-volume irrigations, nebulized preparations, and low-volume drops.
They found a much less robust body of evidence, with 6 studies examining these nonstandard therapies. Only 1 was a randomized control trial (Level 1b) while the other 5 were Level 4 studies. Safety related to the potential for unwanted systemic absorption was addressed in several studies, with no evidence to substantiate this concern. The authors acknowledged the potential advantages of these nonstandard delivery methods but at the same time called for more robust data to guide medical decision-making. They summarized their findings as follows:

- **Aggregate quality of evidence:** C (Level 1b: 1 study; Level 4: 5 studies).
- **Benefit:** Potentially reduce risk of ostial stenosis postoperatively. May reduce systemic steroid rescue episodes. Potential alternative to systemic steroids.
- **Harm:** Known risks of steroids; unknown absorption.
- **Cost:** Moderate to high (range, $4.19 to $10.51), depends on preparation and dosing schedule.
- **Benefits-harm assessment:** Equal balance of benefit to harm.
- **Recommendation level:** Option in cases of CRS.

**Systemic corticosteroids—CRSwNP.** An EBRR by Poetker et al.¹⁰ thoroughly explored the efficacy and safety of oral corticosteroids for both CRSwNP and CRSsNP. Sixteen studies examined oral corticosteroids in the management of CRSwNP, ranging from Level 2 to Level 4 in quality. The studies employed varying dosages and durations of therapy and evaluated both subjective and objective outcomes. All of the studies showed improvements in the majority of measurements examined, at least in the short term (8–12 weeks). Longer-term efficacy was not thoroughly examined and, while no substantial adverse events were noted, most of the studies contained relatively small sample sizes and were limited in duration. Known but rare adverse events of oral corticosteroids would likely become evident with larger, longer-duration studies.

The authors also examined the use of oral corticosteroids in the perioperative management of CRSwNP. They found 3 studies that showed improvements in surgical field visualization but no effect on total blood loss. One study examined the postoperative use of oral corticosteroids and found improvement in subjective olfaction at 2 weeks postoperatively. Otherwise, there was no difference in symptoms compared to placebo. The EBRR summarized the use of oral corticosteroids in CRSwNP as follows:

- **Summary for oral steroid use in the medical management of CRSwNP**
  - Aggregate quality of evidence: A (Level 2: 5 studies; Level 3: 2 studies; Level 4: 11 studies).
  - **Benefit:** Significant short-term improvements in subjective and objective measures in CRSwNP patients. Duration of improvement may last 8 to 12 weeks in conjunction with topical nasal steroid use.
  - **Harm:** More gastrointestinal (GI) symptoms in steroid group, no severe reactions reported. Other known risks of steroids. **Cost:** Low.
  - **Benefits-harm assessment:** Preponderance of benefit vs harm in small, short-term follow-up.
  - **Value judgments:** Significant improvements in subjective and objective measures based on high quality data, low risk, and low cost.
  - **Recommendation level:** Strong recommendation.
  - **Intervention:** Strong recommendation for the use of oral steroids in the short-term management of CRSwNP.

**Systemic corticosteroids—CRSsNP.** For patients with CRSsNP, the data were substantially less robust. Poetker et al.¹⁰ examined 4 studies, all of which were Level 4 in quality. All 4 studies included corticosteroids with other treatments; there were no studies that examined oral corticosteroids as sole modalities of therapy. Moreover, there were variable dosing regimens and durations of therapy for the corticosteroid treatments. With the potential risk associated with systemic corticosteroid therapy, higher-quality evidence in CRSsNP is clearly needed. As with CRSwNP, studies were sought that evaluated the use of oral corticosteroids perioperatively. None were found, pointing out the need for study in this area. Overall, this EBRR summarized its findings as follows:

- **Summary for oral steroid use in the perioperative period for CRSwNP**
  - Aggregate quality of evidence: B (Level 2: 2 studies; Level 3: 1 study).
  - **Benefit:** Improves surgical visualization, may decrease operative time.
  - **Harm:** Known risks of steroids.
  - **Cost:** Low.
  - **Benefits-harm assessment:** Benefit over harm.
  - **Value judgments:** Improved visualization during surgery and improved postoperative course.
  - **Recommendation level:** Recommend.
  - **Intervention:** Consider use of oral steroids in the perioperative management of CRSwNP.

**Systemic corticosteroids—CRSsNP.** For patients with CRSsNP, they did not find enough evidence to recommend the use of oral corticosteroids. However, given the potential benefit and the lack of severe side effects, further study is warranted.

- **Summary for oral steroid use in CRSsNP**
  - Aggregate quality of evidence: C (Level 4: 4 studies).
  - **Benefit:** Subjective improvement in patient symptoms associated with CRS, objective improvement in imaging. May avoid need for surgery in some.
• Harm: No specific reports, but potential risks of steroids are well known. Optimum duration and dosage are not known.
• Cost: Low.
• Benefits-harm assessment: Perceived balance of benefit to harm.
• Value judgments: Significant improvement in patient symptoms is important.
• Recommendation level: Optional.
• Intervention: The use of oral steroid in CRS without polyposis is optional. Patients with more severe disease may have a more favorable benefit-to-harm ratio than patients with mild disease.

Summary for oral steroid use in the perioperative period for CRSsNP

• Aggregate quality of evidence: N/A; there is a significant gap in evidence for this topic.
• Recommendation level: No recommendation.

Systemic corticosteroids—AFRS. Poetker et al.10 also examined the role of oral corticosteroids in the treatment of AFRS. While a number of retrospective reports were found to address this issue, only 4 studies met strict criteria for diagnosis of AFRS and were thus included. Overall, the findings were similar to those of the CRSwNP analysis, with the data supporting the use of oral corticosteroids in AFRS. While the dosing in AFRS was similar to that used in CRSwNP, the duration was longer and the risks of such prolonged use become more of an issue in AFRS. Inasmuch as oral corticosteroids are frequently used as an adjunct in the perioperative period, this use was separately evaluated in this EBRR:

Summary for oral steroid use in AFRS

• Aggregate quality of evidence: B (Level 2: 1 study; Level 4: 3 studies).
• Benefit: Improvement in subjective and objective measures and decreased markers of inflammation.
• Harm: Known risks of steroids.
• Cost: Low.
• Benefits-harm assessment: Benefit over harm in short term.
• Value judgments: High-dose, long courses of steroids showed improvement in symptoms with relatively low adverse events; given the difficulty in treating AFRS, this course is very reasonable.
• Recommendation level: Recommend.
• Intervention: Consider the use of oral steroids in the management of AFRS.

Summary for oral steroid use in the perioperative period for AFRS

• Aggregate quality of evidence: B (Level 2: 1 study; Level 4: 1 studies).
• Benefit: Improvement in endoscopic findings intraoperatively, as well as delayed recurrence of disease following surgical treatment.
• Harm: Known risks of steroids.
• Cost: Low.
• Benefits-harm assessment: Benefit over harm, particularly after surgical debridement of fungal debris.
• Value judgments: Improvement in control of disease postoperatively with moderate adverse events.
• Recommendation level: Recommend.
• Intervention: Consider the use of oral steroids in the perioperative management of AFRS.

Antimicrobials

Persistent infection has been traditionally thought to be a source of inflammation in CRS. While this concept has more recently come under increasing scrutiny, antimicrobials continue to play a large role in the treatment of CRS.11 Different from the use of antimicrobials for acute exacerbations of CRS, especially when culture-driven, many practitioners appear to use of antimicrobials to diminish longstanding inflammation in CRS, and especially as an essential component of medical therapy prior to considering surgery. Despite this widespread practice, Soler et al.12 noted a paucity of evidence-based recommendations for the use of antimicrobials in CRS. Their EBRR resulted from examination of the use of systemic and topical antibacterials and antifungal medications in CRS by an American Rhinologic Society ad hoc committee. The EBRR investigated 8 different methods for using antimicrobials in CRS.

Oral antibacterial therapy lasting less than 3 weeks (non-macrolide therapy). Six studies examined this issue and, despite some being randomized controlled trials (RCTs), most did not include a placebo arm, making the effect of therapy difficult to assess. Soler et al.12 found the evidence supporting oral nonmacrolide antibacterial use surprisingly weak given how commonly they are used in the treatment of CRS. Given the potential side effects and costs associated with this therapy, their aggregate recommendation was to use antibacterials as an option in treating CRS:

• Aggregate quality of evidence: B (Level 1b: 4 studies; Level 4: 2 studies).
• Benefit: Reduction in visible polyp size and patient reported postnasal drainage. Potential for overall clinical improvement in uncontrolled studies.
• Cost: Variable (low to high).
• Benefits-harm assessment: Balance of benefit vs harm.
• Value judgments: Modest reduction in some symptoms vs side effects and cost.
• Recommendation level: Option.
Orlandi et al.

Orlandi et al. examined nonmacrolide oral antibacterial use lasting more than 3 weeks and found no clear benefit. Again, balancing the risks and costs of this approach with the limited evidence of benefit, the authors recommended against the use of antibacterials for more than 3 weeks for routine cases of CRS:

- **Aggregate quality of evidence:** N/A (single study).
- **Benefit:** No clear benefit demonstrated for prolonged course.
- **Harm:** GI upset. Potential for *Clostridium difficile* colitis. Anaphylaxis. Bacterial resistance. Rash.
- **Cost:** Variable (low to high).
- **Benefits-harm assessment:** Preponderance of harm over benefit: known risk of medication side effects, quantifiable costs, and potential for bacterial resistance vs unproven benefit of prolonged course.
- **Value judgments:** None.
- **Recommendation level:** Recommend against a prolonged (>3 week) course of oral antibacterial antibiotics (except for macrolide class) for routine CRS cases.

**Macrolide antibiotics.** Because of their anti-inflammatory properties as well as other effects beyond bactericide, macrolides have been relatively well-studied in CRS. Soler et al. found 17 studies evaluating them in CRS, with 2 randomized, placebo-controlled trials, 1 retrospective case-control study, and 14 prospective observational studies. Specific medications and dosages varied and duration of therapy ranged from 2 weeks to 12 months. Outcome measures included validated questionnaires, radiology, endoscopy, as well as other measures. The EBRR found abundant Level 4 evidence supporting the use of macrolide antibiotics in CRS, with 1 RCT also demonstrating modest improvements. In weighing the benefits and potential risks and costs, the EBRR summarized the evidence as follows:

- **Aggregate quality of evidence:** B (Level 1b: 2 studies; Level 3b: 1 study; Level 4: 14 studies).
- **Benefit:** Improved patient symptoms and endoscopy findings vs placebo in 1 controlled study. Uncontrolled studies showed additional improvements in imaging findings, characteristics of nasal mucus, and reduction of inflammatory mediators in mucus.
- **Harm:** GI upset. Rash. Taste disturbance. Hand numbness. All graded as mild to moderate and none required discontinuation of the medication. Potential liver function abnormalities. Theoretical risk of antibiotic resistance but none confirmed in the studies.
- **Cost:** Moderate to high. Treatment duration ranged from 2 weeks to 12 months. Most treated for at least 3 months.
- **Benefits-harm assessment:** Balance of benefit vs harm.
- **Value judgments:** Consistent benefit shown in multiple observational studies and 1 controlled study vs cost and minimal side effects. No evidence for superiority of any individual macrolides.
- **Recommendation level:** Option.

**Intravenous antibacterials.** Two relatively lower-quality (Level 4) studies examined this method of therapy for CRS and, while they showed some efficacy, they also demonstrated substantial adverse events. Overall, Soler et al. recommended against this therapy for routine cases of CRS:

- **Aggregate quality of evidence:** C (Level 4: 2 studies).
- **Benefit:** Potential for improvement in patient-reported symptoms in uncontrolled studies.
- **Cost:** High.
- **Benefits-harm assessment:** Preponderance of harm over benefit.
- **Value judgments:** Clear risk of harmful side effects and high cost vs modest benefits reported in uncontrolled studies.
- **Recommendation level:** Recommend against use of intravenous antibiotics for uncomplicated CRS cases.

**Topical antibacterials.** In their EBRR of topical therapies for CRS, Rudmik et al. examined 3 RCTs and a systematic review of topical antibacterials. Soler et al. additionally included 5 studies ranging from observational cohorts to retrospective case series in their EBRR on antimicrobials. All 3 RCTs failed to show a significant clinical benefit, although all were small and none provided the intrinsic power of the study to show a clinically relevant difference between groups. The majority of published studies either showed no adverse events from treatment or failed to report these data. Rudmik et al. separated their recommendations, based on the evidence, into those involving nebulizer and spray delivery and those involving other delivery methods, such as irrigations. They recommended against nebulizers and spray delivery as questionably effective but costly and with potential risk. No recommendation was made regarding other delivery methods. Soler et al.’s findings involved all delivery methods and recommended against their use in routine cases of CRS. Their summaries are synthesized below:

- **Aggregate quality of evidence:** B (Level 1b: 2 studies; Level 2b: 1 study; Level 2c: 2 studies; Level 3a: 1 study; Level 4: 4 studies).
- **Benefit:** Potential for improvement in patient-reported symptoms, endoscopic appearance, and QOL in uncontrolled studies. Controlled clinical trials failed to show a benefit; however, it is unclear whether studies were adequately powered.
- **Harm:** Increased congestion was seen with nebulized tobramycin. Nebulized forms of some antibiotics can cause bronchospasm. Topically applied antibiotics have been detected systemically in serum, and potential systemic adverse effects (ototoxicity or nephrotoxicity) with
topical aminoglycosides must be considered. Bioavailability of most antibiotics and ideal dosing regimens remain unknown. Topical regimens can be time consuming for patients, depending on frequency and route of administration. Risk of bacterial resistance must be considered.

- Cost: Moderate to high.
- Benefits-harm assessment: Potential for harm over benefit.
- Value judgments: Clinical benefit seen only in uncontrolled observational studies vs monetary expense, time commitment, and unknown safety profile.
- Recommendation level: Recommendation against use of topical antibiotics for routine CRS cases.

**Oral antifungals.** Soler et al.’s EBRR examined 3 studies concerning the use of antifungal antibiotics in CRS. One double-blind RCT with placebo and 2 retrospective studies showed differing outcomes. The RCT showed no difference in computed tomography (CT) scores, QOL, and patient and physician evaluations. The 2 unblinded observational studies showed improvement in some patients. Adverse events, such as elevation in liver function studies, were seen in about one-quarter of patients. Due to the lack of clear benefit and the significant potential harm and cost of therapy, this EBRR recommended against oral antifungal therapy for routine CRS cases:

- Aggregate quality of evidence: B (Level 1b: 1 study; Level 4: 1 study).
- Benefit: Potential for overall clinical improvement in uncontrolled studies not seen in the single RCT.
- Harm: Elevated liver function studies.
- Cost: Moderate to high.
- Benefits-harm assessment: Preponderance of harm over benefit.
- Value judgments: Low-level evidence showing clinical improvement vs risk of liver dysfunction and considerable costs.
- Recommendation level: Recommendation against use of oral antifungal antibiotics for routine CRS cases.

**Topical antifungals.** As with topical antibacterials, topical antifungal therapy has been addressed by 2 EBRRs, with identical findings and recommendations. Eight Level 1b RCTs involving placebos, 1 non–placebo-controlled RCT, and 4 observational studies have examined the use of topical antifungal therapy in CRS. Most of the studies examined topical amphotericin B, either as a spray or as an irrigation and with varying dosages. One study involved fluconazole nasal spray. Symptom, radiologic, and endoscopic improvement were assessed by the studies. Overall, both EBRRs found that the abundance of evidence failed to show a clinical benefit from any of the topical antifungal treatments.

- Aggregate quality of evidence: A (Level 1a, 1 study; Level 1b: 9 studies; Level 4: 4 studies).
- Benefit: No consistent benefit shown in clinical symptoms, endoscopy, or CT scans compared to placebo controls.
- Cost: Moderate to high.
- Benefits-harm assessment: Preponderance of harm over benefit.
- Value judgments: No demonstrable benefit over placebo in multiple RCTs vs side effects and cost.
- Recommendation level: Strong recommendation against the use of topical antifungals for routine CRS patients.

**Topical alternative therapies**

Rudmik et al.’s EBRR also examined nontraditional topical therapies that have been suggested for CRS, baby shampoo surfactant, manuka honey, and xylitol. Their report on these 3 promising therapies was unable to generate evidence tables or recommendations in light of the relative paucity of evidence for their efficacy.

**Distribution of topical therapies**

EBRRs performed by Rudmik et al.9 and Soler et al.12 demonstrated that some topical therapies may be beneficial in the treatment of CRS. An EBRR completed by Thomas et al.13 examined how the distribution of these therapies are affected by nasal anatomy, device, head position, and previous surgery. Thirty-two studies published between 1987 and 2011 examining topical medication distribution in the nose and sinuses were included.

**Effect of sinus surgery.** Eight studies examined the effect of sinus surgery on the distribution of topical medications in the nose and sinuses. Much of the evidence was obtained through staged dissection of cadaver heads (Level 4) although 1 case-control study was also included (Level 3b). Surgical interventions ranged from sinus ostium dilation to modified Lothrop frontal sinus surgery and medial maxillectomy. Unoperated sinuses appeared to receive little topical therapy, with more extensive procedures resulting in increasing distribution in general. Exceptions to this finding were seen with maxillary sinus ostial dilation, perhaps due to uncinate process deflection, and in nebulization, where poor distribution was seen regardless of surgical state. Thomas et al.13 recommended sinus surgery as an effective method to increase topical therapy distribution in appropriate patients:

- Aggregate quality of evidence: C (Level 3b: 1 study, Level 4: 7 studies).
- Benefit. Standard sinus surgery increases distribution of topical therapies to all sinuses, but has no impact upon nasal cavity delivery.
- Harm. Surgery is associated with potential complications and recovery.
- Cost. Significant, with direct costs of procedure, postoperative debridement, and medical costs in 2008 of

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Benefits-harm assessment. Preponderance of benefit over harm when more aggressive local topical therapies to the sinuses are needed and systemic therapy carries significant risk.

Value judgments. Patients and surgeons must decide if topical sinus therapies are needed and balance the risks and costs of surgery with ongoing systemic therapies.

Recommendation level. Recommendation for: penetration of topical therapy is better in post-ESS patients.

Intervention. Penetration of topical therapy is better in post-ESS patients. This is best done with large volume devices. Surgery can be recommended on a case-by-case basis as the surgeon and patient deem necessary.

Effect of topical therapy delivery devices. This EBRR found that the devices play an important role in the differing distribution of topical medications within the sinuses. Delivery devices were divided into low-volume (eg, spray, drops, atomizers, nebulizers) and high-volume (eg, squeeze bottles, neti pots, bulb syringes). Twenty-one of the 34 studies contained information regarding delivery-device efficacy, although no single paper compared all possible devices. Low-volume devices did not appear to reliably penetrate the sinuses, although delivery into the nasal cavity was demonstrated. Overall, high-volume devices were found to maximize delivery into the sinuses:

- Aggregate quality of evidence. C (Level 3b: 2 studies; Level 4: 18 studies).
- Benefit. High-volume (>50 mL) irrigation improves both sinus and nasal cavity distribution, which may be important for mechanical cleaning/lavage and potential drug delivery.
- Harm. High-volume devices can result in Eustachian tube dysfunction and local irritation up to 23% of patients. However, these are often mild and compliance is high. Low-volume devices (drops, sprays, and simple nebulizers) are reasonable nasal cavity treatments, but do not reliably reach the sinuses and may result in unnecessary expense without demonstrable clinical benefit.
- Cost. Varies depending upon device (range, $9.97 to $149.00). Simple disposable devices, such as neti pots, squeeze bottles, and droppers have relatively low cost in comparison to powered devices such as nebulizers or pulsed irrigators.
- Benefits-harm assessment. Preponderance of benefit over harm of using low-cost, high-volume devices. There is potential harm in using low-volume devices that do not reliably reach the sinus cavities due to needless cost and lack of appropriately treating the patient.

- Value judgments. None.
- Recommendation level. Recommend for: use of disposable high-volume devices for sinus delivery. Recommend against: low-volume devices, such as simple nebulizers, drops, and sprays, which have limited sinus delivery. Option for: low-volume devices, such as drops or sprays, if high-volume devices are not tolerated, but low-volume devices must be used in optimal head position and even then sinus distribution is limited (see Effect of head position).
- Intervention. If effective paranasal sinus distribution is desired, use high-volume devices.

Effect of head position. Thomas et al. found 10 studies that evaluated the impact of head position on topical delivery and separated their analysis for delivery to the paranasal sinuses and delivery to the nasal cavity. The head down and forward (HDF) position appeared to be optimal regardless of device for topical delivery into the sinuses. The HDF position was effective for sinus delivery in postoperative patients but was associated with more discomfort than other positions. Distribution of large volumes does not appear to be affected by head position, inasmuch as the volume is likely sufficiently large to fill the nasal cavity. In postoperative patients, filling the nasal cavity with high-volume delivery appears to deliver agents into the widely-open sinuses. For nasal cavity delivery with low-volume devices, the lying head back (LHB) and lateral head low (LHL) positions appeared most effective. Summarizing the data, the EBRR recommended the following:

- Aggregate quality of evidence. C (Level 3b: 1 study; Level 4: 9 studies).
- Benefit. Sinus delivery is not seen in the unoperated patient regardless of head position; however, in the postoperative cavity, sinus delivery is improved with HDF position regardless of device, although head position has less impact when high-volume devices are used. Head position has the greatest impact when using low-volume devices. Nasal cavity delivery of low-volume devices is optimal in LHL or LHB positions.
- Harm. The HDF position was found to be the most uncomfortable and may not be needed for effective sinus delivery if using high-volume devices. When using low-volume devices, use of ineffective head position will impair even the limited nasal cavity distribution.
- Cost. Minimal cost in choosing optimal head position for effective delivery.
- Benefits-harm assessment. Preponderance of benefit over harm.
- Value judgments. For effective nasal delivery with low-volume devices, proper head position is critical.
- Recommendation level. Recommendation for #1: HDF when using high-volume devices if patient will tolerate. HDF for low-volume device, but with limited sinus penetration.
Recommendation for #2: LHB or LHL position when using low-volume devices, which will only reliably distribute to the nasal cavity.

Intervention. Only prescribe low-volume devices with concurrent education on the proper position in which to administer them.

Effect of nasal anatomy. Nasal cavity anatomy and nasal congestion was seen to impact distribution of topical therapies. Five studies examined this effect, although only 1 addressed sinus delivery. In balancing the potential benefits and harms of altering nasal anatomy and/or using longstanding decongestants to improve topical medication delivery, the EBRR found data supporting this practice lacking. It therefore recommended high-volume delivery to overcome these effects:

- Aggregate quality of evidence. C (Level 3b: 1 study; Level 4: 4 studies).
- Benefit. High-volume irrigations are able to overcome anatomic variations in the nasal cavity and achieve sinus delivery. Nasal cavity delivery with low-volume devices can be overcome with pharmacologic decongestion or LHL position. The impact of surgical correction of unfavorable nasal cavity anatomy upon delivery to the paranasal sinuses has not been studied.
- Harm. Achieving better delivery by using high-volume devices to overcome unfavorable nasal anatomy may be associated with side effects. Use of the LHL position to improve nasal cavity delivery of low-volume devices carries little harm. The impact of chronic topical vasoconstrictors upon nasal cavity delivery to the middle turbinate/middle meatus is not proven and may result in rhinitis medicamentosa.
- Cost. Optimal head position with low-volume devices or high-volume delivery devices to overcome unfavorable nasal cavity anatomy are low. Nasal surgery cost.
- Benefits-harm assessment. Proven benefit in using high-volume devices; optimal head position with low-volume devices has little harm.
- Value judgments. Chronic topical vasoconstrictor use or nasal surgery, in the absence of airflow obstruction, is unproven and carries the risk for harm and cost.
- Intervention. Educate patients with unfavorable nasal cavity anatomy regarding optimal delivery position/device depending upon the desired site of topical delivery.

Surgical therapy for CRS

Rhinologic literature over the last 30 years is rich with descriptions of surgical therapies, with some outcome data for individual methods. Current evidence indicates that standard ESS provides clinically significant QOL improvements for CRS patients that have failed medical therapy. Different approaches, devices, and techniques have been described in an effort to reduce the significant morbidity associated with CRS. Comparative efficacy is largely lacking, however, with knowledge gaps in extent of surgery, optimal ostial size, resection vs dilation, hemostasis methods, and postoperative packing. These and other areas would be well served by additional evidence and, where appropriate, a review of the available evidence with recommendations.

Two recent EBRRs have examined surgically-related topics. Ramakrishnan et al. examined the role of image guidance in ESS, specifically addressing the ability of this technology to prevent complications and to improve outcomes. Rudmik et al. reviewed the evidence pertaining to a number of postoperative therapies following sinus surgery in order to provide recommendations for the most beneficial treatment strategy.

IGS in ESS

IGS has evolved to become a common adjunct to ESS but has been challenged as having little evidence to support it. Ramakrishnan et al. addressed this topic in a recent EBRR, acknowledging the relative paucity of evidence and delineating the significant barriers to overcoming this gap. Six studies were included in their analysis of complications associated with ESS; 4 were retrospective and 2 were prospective nonrandomized studies. The available evidence mostly showed nonsignificant trends and also showed some conflicting results. Due to the low incidence of complications associated with ESS, most studies were significantly underpowered to show a clinical difference. With regard to complications, the EBRR found IGS to be a valuable option:

- Aggregate quality of evidence: C (Level 2b: 2 studies, Level 4: 4 studies).
- Benefit: Potential for fewer surgical complications, particularly severe complications; provides additional anatomic information, particularly for cases in which anatomy can be significantly obscured.
- Harm: Local skin irritation, potential for poor IGS registration/calibration/accuracy; potential for more extensive surgery than otherwise necessary.
- Cost: Disposable supplies, equipment costs, possible extra operating room (OR) time.
- Benefits-Harm assessment: Preponderance of benefit over harm.
- Value judgments: IGS can provide critical information, particularly in the setting of altered anatomy or severe disease; avoiding major complications is essential; ideal studies are neither practical nor feasible.
- Policy level: Option.
Of note, a more recent analysis of the same literature using a meta-analysis has concluded that IGS, within selected populations, is associated with a lower risk of major and total complication compared to non-IG sinus surgery.\textsuperscript{18}

Ramakrishnan et al.\textsuperscript{16} also looked at surgical outcome following ESS associated with IGS. Five studies were examined, with 2 again being prospective nonrandomized studies and 3 being retrospective reviews. One prospective study showed improved QOL in the IGS group while 1 showed no difference. The 3 retrospective studies also demonstrated conflicting results. The EBRR again found a preponderance of benefit over harm, seeing IGS as a valuable option in selected ESS cases:

- Aggregate quality of evidence: C (Level 2b: 2 studies, Level 4: 3 studies).
- Benefit: More complete surgery with IGS; potential for improved surgical outcomes, including less need for revision surgery.
- Harm: Local skin irritation, potential for poor IGS registration/calibration/accuracy; potential for more extensive surgery than otherwise necessary.
- Cost: Disposable supplies, equipment costs, possible extra OR time.
- Benefits-Harm assessment: Preponderance of benefit over harm.
- Value judgments: Improving outcomes and decreasing need for revision surgery is highly desired.
- Policy level: Option.

**Early postoperative care following ESS**

Rudnik et al.\textsuperscript{17} assayed the data on 7 different treatments that may be used following ESS: saline irrigations, sinus cavity debridements, systemic steroids, topical steroids, oral antibiotics, topical decongestants, and drug-eluting spacers/stents. They reviewed the evidence and provided recommendations based on this evidence for each of the 7 postoperative treatment strategies.

**Nasal saline irrigation.** Six studies examined the efficacy of high-volume nasal saline irrigation in the early postoperative period. All were RCTs and at least single-blinded. Outcomes assessed by these studies included patient symptoms, amount of crusting, endoscopic appearance, histology, and mucociliary clearance. The EBRR recommended the routine use of saline irrigations postoperatively as follows:

- Aggregate quality of evidence: B (Level 1b: 2 studies; Level 2b: 4 studies).
- Benefit: Generally well tolerated. Improved early postoperative symptoms and endoscopic appearance.
- Harm: Local irritation, nasal burning, headaches, ear pain (predominantly with hypertonic solutions).
- Cost: Minimal; patient time for application.
- Benefits-Harm assessment: Preponderance of benefit over harm.
- Value Judgments: None.
- Policy level: Recommendation for use of nasal saline irrigations.
- Intervention: Begin daily normal saline irrigations between 24 and 48 hours after ESS.

**Postoperative debridement.** The EBRR found 4 RCTs evaluating postoperative debride ment’s effects on clinical outcomes. Three studies were Level 1b and demonstrated significant benefit on symptoms and endoscopic appearance. An unblinded Level 2b pilot study that was underpowered and did not use a standardized endoscopic grading system showed no difference. These studies demonstrated heterogeneity in the frequency and timing of debridements. Overall, debridement was found to be beneficial and was recommended by the EBRR. Future studies will be necessary to determine the optimal frequency, duration, extent, and timing of debridements.

- Aggregate quality evidence: B (Level 1b: 3 studies; Level 2b: 1 study).
- Benefit: Improved postoperative symptoms and endoscopic appearance. Minimizes risk of synechiae and middle turbinate lateralization.
- Cost: It is a surgical procedure (in-office) and has associated costs.
- Benefits-Harm assessment: Preponderance of benefit over harm.
- Value Judgments: Relating the surgeon’s assessment of healing into the clinical need for debridement.
- Policy level: Recommendation for postoperative debridement.
- Intervention: Perform sinus cavity debridement after ESS.

**Postoperative systemic steroids.** The EBRR identified 1 study addressing systemic steroids specifically in the immediate postoperative period. This Level 1b RCT with placebo found no difference in symptoms in the CRSwNP patients treated with perioperative steroids but did find an improved endoscopic appearance in this group, compared to patients treated with placebo. As addressed by Poetker et al.’s\textsuperscript{10} EBRR on oral corticosteroid treatment overall, the potential benefit of this treatment must be assessed in light of the potential harms as well, making this therapy an option in appropriate patients:

- Aggregate quality of evidence: N/A (Level 1b: 1 study).
- Benefit: Improvement in endoscopic appearance compared to placebo.
- Cost: Minimal.
• Benefits-Harm assessment: Relative balance of benefit and harm.
• Value Judgments: Difficult to develop a postoperative recommendation based on 1 study where the clinical benefit was limited to endoscopic appearance.
• Recommendation level: Option.

Topical corticosteroids. Similar to the findings in topical therapies overall, topical corticosteroids were found to be a helpful adjunct in the early postoperative period. The use of topical corticosteroid sprays immediately postoperatively was found to be supported by 4 Level 1b studies, although the optimal timing for starting this therapy postoperatively has not been well defined. This postoperative care EBRR recommended topical nasal steroid sprays be initiated following ESS:

• Aggregate quality of evidence: A (Level 1b: 4 studies).
• Benefit: Improved symptoms and endoscopic appearance. Lengthen time to polyp recurrence.
• Cost: Moderate; depends on preparation.
• Benefits-Harm assessment: Preponderance of benefit over harm.
• Value Judgments: None.
• Recommendation level: Recommendation for standard nasal steroid spray.
• Intervention: Begin standard topical nasal steroid spray after ESS.

The use of nonstandard delivery mechanisms for corticosteroids postoperatively was also examined in this EBRR. Examples include steroid-containing irritations, drops, or nebulizers. A single Level 3b study addressed this topic, although the subjects of the study were patients with severe inflammatory disease who were felt to be at risk for ostial stenosis and further surgery. Further, since no comparison group was used, the relative efficacy of nonstandard corticosteroid delivery in the immediate postoperative period is difficult to assess. This EBRR found this therapy to be an option in selected cases, the same conclusion as that of the EBRR examining nonstandard corticosteroid delivery in CRS overall:

• Aggregate quality of evidence: N/A (Level 3b: 1 study).
• Benefit: Potentially reduce risk of ostial stenosis. May reduce systemic steroid rescue episodes. Potential alternative to course of systemic steroids.
• Harm: Poorly defined risks. Potential adrenal suppression, ocular absorption, wound healing, and other systemic steroid effects.
• Cost: Minimal to moderate, depends on preparation.
• Benefits-Harm assessment: Equal balance of benefit to harm.
• Value Judgments: Lack of data regarding systemic absorption is concerning but the only other option in many cases is a systemic steroid.

• Recommendation level: Option in patients with severe mucosal inflammatory disease.

Postoperative antibiotics. Rudmik et al. found 3 studies examining the use of antibacterial antibiotics in the immediate period following ESS. An RCT examining a 2-day course showed no effect. Another RCT examining a longer course (3 weeks) also showed no effect at 3 weeks, although another double-blind RCT with placebo demonstrated 2 weeks of antibiotics led to improved patient symptoms at 5 days and improved endoscopic appearance at 12 days. In light of the disparate evidence on this topic, this EBRR found antibiotics to be an option in the early postoperative period:

• Aggregate evidence: B (Level 1b: 2 studies; Level 2b: 1 study).
• Benefit: Improved early postoperative symptoms and endoscopic appearance. Reduced sinonasal crusting.
• Cost: Generally Moderate to high.
• Value Judgments: Reducing early postoperative symptoms is important; active bacterial infection may trigger inflammation postoperatively.
• Recommendation level: Option in routine endoscopic sinus surgery.

Topical decongestants. Only 1 study has examined the effect of topical decongestants. They were used 4 times a day routinely in the early postoperative period and were found to be harmful. This EBRR thus recommended against their routine use, with the caveat that this recommendation does not relate to the management of postoperative epistaxis, where their use may be potentially beneficial:

• Aggregate evidence: N/A (Level 2b: 1 study).
• Benefit: Potential for reduced mucosal swelling and reduced bleeding.
• Cost: Minimal; over the counter medication.
• Benefits-Harm assessment: Preponderance of harm over benefit.
• Value Judgments: Increased pain and risk of rhinitis medicamentosa is concerning despite only one study evaluating this intervention.
• Recommendation level: Recommendation against.

Drug eluting spacers/stents. This EBRR lastly examined the role of these newer technologies in the early period following ESS. Three studies involving non–U.S. Food and Drug Administration (FDA)-approved stents or steroid-soaked ethmoid cavity packing materials were examined, with 2 being RCTs. All 3 showed benefit in the form of better symptom scores, reduced nasal polyp rate, and improved...
overall endoscopic scores, both early and up to 6 months postoperatively. These potential benefits are balanced by the potential for systemic and ocular absorption and the variable cost of these materials. Moreover, the studies reviewed in this EBRR had rather small sample sizes. This EBRR, therefore, recommended this treatment as an option in the early postoperative period.

- Aggregate evidence: B (Level 1b: 1 study; Level 2b: 1 study; Level 3b: 1 study).
- Benefit: Improved endoscopic appearance. Reduced polyp recurrence.
- Cost: Variable depending on the stent/spacer selected and medication utilized.
- Benefits-Harm assessment: Relative balance of benefit and harm.
- Value Judgments: Standard topical steroids have a proven role in postoperative management but nonstandard topical steroids require further study. Although some trials have been conducted, sample sizes are small and data is considered insufficient to extrapolate to larger populations, particularly with respect to safety concerns.
- Recommendation level: Option.

Following the publication of this EBRR on drug eluting spacers and stents in 2011, additional RCTs have been published using FDA-approved corticosteroid-eluting implants. The results of these RCTs have been partially summarized in a recent meta-analysis,\(^1\) yielding Level 1a evidence in support of their effectiveness. This technology offers the potential to create a local drug-delivery platform for an array of therapeutic agents in the future. It is anticipated that this topic will be the subject of an updated EBRR in the near future.

**Discussion**

Since their development by Rudmik and Smith,\(^5\) EBRRs have proven to be an effective method for comprehensively yet rapidly evaluating published evidence on a particular topic. Furthermore, these reviews have allowed for generation of useful evidence-based recommendations while at the same time pointing out deficiencies in the available evidence. Such publications are a crucial part of the triad of EBM, combined with the individual practitioner’s clinical expertise and the individual patient’s values and desires.

The rapid online iterative process used in the EBRR development ensures timeliness of the review and also facilitates updating the EBRR as additional evidence becomes available. It is assumed that the senior authors responsible for the production of these EBRRs will ensure their timely updating as needed.

The EBRR process, though robust, does have some limitations. First, no EBRR is a substitute for the individual practitioner’s clinical judgment and expertise, nor are they to be universally applied to all patients. CRS is a heterogeneous condition and has been best described as a syndrome rather than a single disease. Indeed, the classification of CRS into CRSwNP, CRSsNP, AFRS, and other entities such as aspirin-exacerbated respiratory disease (AERD) underscores the heterogeneity of this condition. While the EBRRs provide valuable guidance to the clinician practicing EBM, as noted, they are only 1 part of the application of EBM to an individual clinical situation.

Another limitation of the EBRRs is the evidence on which they are based. Evidence is constantly changing so EBRRs should not be interpreted as being “carved in stone,” but are dynamic, because the process is also dynamic. In addition, many recommendations are limited to options not because extensive data shows equivocal efficacy or safety, but because the evidence itself is scarce. Lack of evidence for clinical efficacy should not be confused with evidence for lack of clinical efficacy. In those circumstances where a treatment is recommended as an option, it may be entirely viable and indicated for an individual clinical situation.

Last, the EBRRs are not clinical guidelines sanctioned by the societies for which the *International Forum of Allergy and Rhinology* is the official publication. These societies, the American Academy of Otolaryngic Allergy, the American Rhinologic Society, and the International Rhinologic Society, may in the future choose to sanctioned the EBRRs or use them as the basis for a clinical guideline on CRS. While the development of the EBRR is meant to ensure these authors are a diverse representation of experts on the EBRR subjects, without such sanctioning however, the EBRRs remain the findings and opinions of their authors alone.

While the EBRRs published to this point have explored a large number of important topics in CRS management, this review has also shown gaps in our collective knowledge of other areas of management and evaluation. Possible topics for future EBRRs in CRS are:

- Cost-effective diagnosis
- Cost-effective evaluation of underlying conditions
- Etiologic factors
- Value of histopathologic assessment of sinus tissue
- Pediatric chronic rhinosinusitis
- Antibiotics in the management of acute exacerbations of CRS
- Other medical treatments (e.g., aspirin desensitization, leukotriene modifiers, etc.)
- Optimal medical therapy to be employed prior to considering surgery
- Comparative efficacy of surgical instrumentation and techniques (e.g., balloon dilation)
- Comparative efficacy of the extent of surgery
- Appropriate long-term sinus care.

**Conclusion**

EBRRs have individually and, as can be seen from this review, collectively enhanced the knowledge base for the
treatment of CRS. They form an effective template for additional reviews that will further enhance the use of EBM in the treatment of CRS. They also provide direction for future research efforts. Additionally, they may form a useful foundation for the development of evidence-based guidelines for the management of CRS.

References


