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GUIDELINES

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OBJECTIVE: This guideline provides evidence-based recommendations on managing sinusitis, defined as symptomatic inflammation of the paranasal sinuses. Sinusitis affects 1 in 7 adults in the United States, resulting in about 31 million individuals diagnosed each year. Since sinusitis almost always involves the nasal cavity, the term *rhinosinusitis* is preferred. The guideline target patient is aged 18 years or older with uncomplicated rhinosinusitis, evaluated in any setting in which an adult with rhinosinusitis would be identified, monitored, or managed. This guideline is intended for all clinicians who are likely to diagnose and manage adults with sinusitis.

PURPOSE: The primary purpose of this guideline is to improve diagnostic accuracy for adult rhinosinusitis, reduce inappropriate antibiotic use, reduce inappropriate use of radiographic imaging, and promote appropriate use of ancillary tests that include nasal endoscopy, computed tomography, and testing for allergy and immune function. In creating this guideline the American Academy of Otolaryngology–Head and Neck Surgery Foundation selected a panel representing the fields of allergy, emergency medicine, family medicine, health insurance, immunology, infectious disease, internal medicine, medical informatics, nursing, otolaryngology–head and neck surgery, pulmonology, and radiology.

RESULTS: The panel made *strong recommendations* that 1) clinicians should distinguish presumed acute bacterial rhinosinusitis (ABRS) from acute rhinosinusitis caused by viral upper respiratory infections and noninfectious conditions, and a clinician should diagnose ABRS when (a) symptoms or signs of acute rhinosinusitis are present 10 days or more beyond the onset of upper respiratory symptoms, or (b) symptoms or signs of acute rhinosinusitis worsen within 10 days after an initial improvement (double worsening), and 2) the management of ABRS should include an assessment of pain, with analgesic treatment based on the severity of pain.

The panel made a *recommendation against* radiographic imaging for patients who meet diagnostic criteria for acute rhinosinusitis, unless a complication or alternative diagnosis is suspected.

The panel made *recommendations* that 1) if a decision is made to treat ABRS with an antibiotic agent, the clinician should prescribe amoxicillin as first-line therapy for most adults, 2) if the patient worsens or fails to improve with the initial management option by 7 days, the clinician should reassess the patient to confirm ABRS, exclude other causes of illness, and detect complications, 3) clinicians should distinguish chronic rhinosinusitis (CRS) and recurrent acute rhinosinusitis from isolated episodes of ABRS and other causes of sinonasal symptoms, 4) clinicians should assess the patient with CRS or recurrent acute rhinosinusitis for factors that modify management, such as allergic rhinitis, cystic fibrosis, immunocompromised state, ciliary dyskinesia, and anatomic variation, 5) the clinician should corroborate a diagnosis and/or investigate for underlying causes of CRS and recurrent acute rhinosinusitis, 6) the clinician should obtain computed tomography of the paranasal sinuses in diagnosing or evaluating a patient with CRS or recurrent acute rhinosinusitis, and 7) clinicians should educate/counsel patients with CRS or recurrent acute rhinosinusitis regarding control measures.

The panel offered as *options* that 1) clinicians may prescribe symptomatic relief in managing viral rhinosinusitis, 2) clinicians may prescribe symptomatic relief in managing ABRS, 3) observation without use of antibiotics is an option for selected adults with uncomplicated ABRS who have mild illness (mild pain and temperature $<38.3°C$ or 101°F) and assurance of follow-up, 4) the

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clinician may obtain nasal endoscopy in diagnosing or evaluating a patient with CRS or recurrent acute rhinosinusitis, and 5) the clinician may obtain testing for allergy and immune function in evaluating a patient with CRS or recurrent acute rhinosinusitis.

DISCLAIMER: This clinical practice guideline is not intended as a sole source of guidance for managing adults with rhinosinusitis. Rather, it is designed to assist clinicians by providing an evidence-based framework for decision-making strategies. It is not intended to replace clinical judgment or establish a protocol for all individuals with this condition, and may not provide the only appropriate approach to diagnosing and managing this problem.

Sinusitis affects 1 in 7 adults in the United States, resulting in 31 million individuals diagnosed each year.[1] The direct annual health-care cost of $5.8 billion stems mainly from ambulatory and emergency department services,[2] but also includes 500,000 surgical procedures performed on the paranasal sinuses.[3] More than 1 in 5 antibiotics prescribed in adults are for sinusitis, making it the fifth most common diagnosis for which an antibiotic is prescribed.[4] The indirect costs of sinusitis include 73 million days of restricted activity per year.[2] Despite the high prevalence and economic impact of sinusitis, considerable practice variations exist across and within the multiple disciplines involved in managing the condition.[5,6]

The target patient for the guideline is aged 18 years or older with a clinical diagnosis of uncomplicated rhinosinusitis:

- *Rhinosinusitis* is defined as symptomatic inflammation of the paranasal sinuses and nasal cavity. The term rhinosinusitis is preferred because sinusitis is almost always accompanied by inflammation of the contiguous nasal mucosa.[7-9] Therefore, *rhinosinusitis* is used in the remainder of the guideline.
- *Uncomplicated rhinosinusitis* is defined as rhinosinusitis without clinically evident extension of inflammation outside the paranasal sinuses and nasal cavity at the time of diagnosis (eg, no neurologic, ophthalmologic, or soft tissue involvement).

Rhinosinusitis may be further classified by duration as *acute* (less than 4 weeks), *subacute* (4-12 weeks), or *chronic* (more than 12 weeks, with or without acute exacerbations). Acute rhinosinusitis may be classified further by symptom pattern (see boldfaced statement #1 below) into *acute bacterial rhinosinusitis* (ABRS) or *viral rhinosinusitis* (VRS). When there are 4 or more acute episodes per year of ABRS, without persistent symptoms between episodes, the condition is termed *recurrent acute rhinosinusitis*.

Guideline statements regarding acute rhinosinusitis will focus on diagnosing presumed bacterial illness and using antibiotics appropriately. Guideline statements regarding chronic rhinosinusitis or recurrent acute rhinosinusitis will focus on appropriate use of diagnostic tests. The guideline panel made an explicit decision not to discuss management of subacute rhinosinusitis, because research evidence is lacking, and this designation arose as a filler term to describe the heterogeneous clinical entity between ABRS and chronic rhinosinusitis.

GUIDELINE PURPOSE

The primary purpose of this guideline is to improve diagnostic accuracy for adult rhinosinusitis, reduce inappropriate antibiotic use, reduce inappropriate use of radiographic imaging, and promote appropriate use of ancillary tests that include nasal endoscopy, computed tomography, and testing for allergy and immune function. Secondary goals include creating a guideline suitable for deriving a performance measure on rhinosinusitis and training participants in guideline methodology to facilitate future development efforts.

The guideline is intended for all clinicians who are likely to diagnose and manage adults with rhinosinusitis, and applies to any setting in which an adult with rhinosinusitis would be identified, monitored, or managed. This guideline, however, does not apply to patients under age 18 years or to patients of any age with complicated rhinosinusitis. No recommendations are made regarding surgery for rhinosinusitis.

The guideline will not consider management of the following clinical presentations, although differential diagnosis for these conditions and bacterial rhinosinusitis will be discussed: allergic rhinitis, eosinophilic nonallergic rhinitis, vasomotor rhinitis, invasive fungal rhinosinusitis, allergic fungal rhinosinusitis, vascular headaches, and migraines. Similarly, the guideline will not consider management of rhinosinusitis in patients with the following modifying factors, but will discuss their importance: cystic fibrosis, immotile cilia disorders, ciliary dyskinesia, immune deficiency, prior history of sinus surgery, and anatomic abnormalities (eg, deviated nasal septum).

Existing guidelines concerning rhinosinusitis tend to be broad literature reviews or consensus documents with limited cross-specialty input. Moreover, although some guidelines contain evidence rankings, the process used to link rankings with specific grades of recommendation is often unclear. Our goal was to create a multidisciplinary guideline with a limited set of focused recommendations based on a transparent and explicit process that considers levels of evidence, harm-benefit balance, and expert consensus to fill evidence gaps. Moreover, the guideline should have a well-defined focus based on aspects of management offering the greatest opportunity for quality improvement.

BURDEN OF RHINOSINUSITIS

Most acute rhinosinusitis begins when a viral upper respiratory infection (URI) extends into the paranasal sinuses, which may be followed by bacterial infection. About 20 million cases of ABRS occur annually in the United States,[4]

Table 1
Interventions considered in rhinosinusitis guideline development

Diagnosis	targeted history physical examination anterior rhinoscopy transillumination nasal endoscopy nasal swabs antral puncture culture of nasal cavity, middle meatus, or other site	imaging procedures blood tests: CBC, others allergy evaluation and testing immune function testing gastroesophageal reflux pulmonary function tests mucociliary dysfunction tests
Treatment	watchful waiting/observation education/information systemic antibiotics topical antibiotics oral/topical steroids systemic/topical decongestants antihistamines mucolytics	leukotriene modifiers nasal saline analgesics complementary and alternative medicine postural drainage/heat biopsy (excluded from guideline) sinus surgery (excluded from guideline)
Prevention	topical steroids immunotherapy nasal lavage smoking cessation hygiene	education pneumococcal vaccination influenza vaccination environmental controls

rendering it one of the most common conditions encountered by primary care clinicians. The importance of ABRS relates not only to prevalence, but to the potential for rare, but serious, sequelae that include meningitis, brain abscess, orbital cellulitis, and orbital abscess.[10-11]

ABRS has significant socioeconomic implications. The cost of initial antibiotic treatment failure in ABRS, including additional prescriptions, outpatient visits, tests, and procedures,[12] contributes to a substantial total rhinosinusitis-related health-care expenditure of more than $3.0 billion per year in the United States.[4] Aside from the direct treatment costs, decreased productivity and lost work days contribute to an even greater indirect health-care cost associated with this condition.

Chronic rhinosinusitis (CRS) is one of the most common chronic diseases, with prevalence as high as or higher than many other chronic conditions such as allergy and asthma. According to The National Health Interview Survey, CRS affects 14% to 16% of the U.S. population.[13-14] The period prevalence is approximately 2% per decade with peak at age 20 to 59 years.[15-16] CRS is more common in females[16-18] and is accompanied by nasal polyps in about 19% to 36% of patients.[19-20]

CRS has significant socioeconomic implications. In 2001 there were 18.3 million office visits for CRS, most of which resulted in prescription medications. Patients with CRS visit primary care clinicians twice as often as those without the disorder, and have five times as many prescriptions filled.[21] Extrapolation of these data yields an annual direct cost for CRS of $4.3 billion.[2] Patients with CRS have a substantial negative health impact due to their disease, which adversely affects mood, physical functioning, and social functioning.[22-23] Patients with CRS referred to otolaryngologists score significantly lower on measures of bodily pain and social functioning than do those with angina, back pain, congestive heart failure, and chronic obstructive pulmonary disease.[24]

The primary outcome considered in this guideline is resolution or change of the signs and symptoms associated with rhinosinusitis. Secondary outcomes include eradication of pathogens, recurrence of acute disease, and complications or adverse events. Other outcomes considered include cost, adherence to therapy, quality of life, return to work or activity, avoiding surgery, return physician visits, and effect on comorbid conditions (eg, allergy, asthma, gastroesophageal reflux). The high incidence and prevalence of rhinosinusitis and the diversity of interventions in practice (Table 1) make this an important condition for the use of an up-to-date, evidence-based practice guideline.

METHODS

General Methods and Literature Search

The guideline was developed using an explicit and transparent a priori protocol for creating actionable statements based on supporting evidence and the associated balance of benefit and harm.[25] The multidisciplinary guideline development panel was chosen to represent the fields of allergy, emergency medicine, family medicine, health insurance, immunology, infectious disease, internal medicine, medical informatics, nursing, otolaryngology–head and neck surgery, and radiology. Several group members

had significant prior experience in developing clinical practice guidelines.

Several literature searches were performed through November 30, 2006 by AAO-HNS staff. The initial MEDLINE search using "sinusitis OR rhinosinusitis" in any field, or "sinus* AND infect*" in the title or abstract, yielded 18,020 potential articles:

1) *Clinical practice guidelines* were identified by limiting the MEDLINE search to 28 articles using "guideline" as a publication type or title word. Search of the National Guideline Clearinghouse (www.guideline.gov) identified 59 guidelines with a topic of sinusitis or rhinosinusitis. After eliminating articles that did not have rhinosinusitis as the primary focus, 12 guidelines met quality criteria of being produced under the auspices of a medical association or organization and having an explicit method for ranking evidence and linking evidence to recommendations.
2) *Systematic reviews (meta-analyses)* were identified by limiting the MEDLINE search to 226 articles using a validated filter strategy for systematic reviews.[26] Search of the Cochrane Library identified 71 relevant titles. After eliminating articles that did not have rhinosinusitis as the primary focus, 18 systematic reviews met quality criteria of having explicit criteria for conducting the literature and selecting source articles for inclusion or exclusion.
3) *Randomized controlled trials* were identified by search of the Cochrane Controlled Trials Register, which identified 515 trials with "sinusitis" or "rhinosinusitis" as a title word.
4) *Original research studies* were identified by limiting the MEDLINE search to articles with a sinusitis (MeSH term) as a focus, published in English after 1991, not containing children age 12 years or younger and not having a publication type of case report. The resulting data set of 2039 articles yielded 348 related to diagnosis, 359 to treatment, 151 to etiology, and 24 to prognosis.

Results of all literature searches were distributed to guideline panel members at the first meeting. The materials included an evidence table of clinical practice guidelines, an evidence table of systematic reviews, full-text electronic versions of all articles in the evidence tables, and electronic listings with abstracts (if available) of the searches for randomized trials and original research. This material was supplemented, as needed, with targeted searches to address specific needs identified in writing the guideline.

In a series of conference calls, the working group defined the scope and objectives of the proposed guideline. During the 9 months devoted to guideline development ending in April 2007, the group met twice with interval electronic review and feedback on each guideline draft to ensure accuracy of content and consistency with standardized criteria for reporting clinical practice guidelines.[27]

The Guidelines Review Group of the Yale Center for Medical Informatics used GEM-COGS,[28] the guideline implementability appraisal and extractor software, to appraise adherence of the draft guideline to methodologic standards, to improve clarity of recommendations, and to predict potential obstacles to implementation. Panel members received summary appraisals in March 2007 and modified an advanced draft of the guideline.

The final draft practice guideline underwent extensive external peer review. Comments were compiled and reviewed by the group chairperson. The recommendations contained in the practice guideline are based on the best available published data through January 2007. Where data are lacking, a combination of clinical experience and expert consensus was used. A scheduled review process will occur at 5 years from publication or sooner if new compelling evidence warrants earlier consideration.

Classification of Evidence-based Statements

Guidelines are intended to reduce inappropriate variations in clinical care, to produce optimal health outcomes for patients, and to minimize harm. The evidence-based approach to guideline development requires that the evidence supporting a policy be identified, appraised, and summarized and that an explicit link between evidence and statements be defined. Evidence-based statements reflect both the *quality of evidence* and the *balance of benefit and harm* that is anticipated when the statement is followed. The definitions for evidence-based statements[29] are listed in Tables 2 and 3.

Guidelines are never intended to supersede professional judgment; rather, they may be viewed as a relative constraint on individual clinician discretion in a particular clinical circumstance. Less frequent variation in practice is expected for a strong recommendation than might be expected with a recommendation. Options offer the most opportunity for practice variability.[30] Clinicians should always act and decide in a way that they believe will best serve their patients' interests and needs, regardless of guideline recommendations. Guidelines represent the best judgment of a team of experienced clinicians and methodologists addressing the scientific evidence for a particular topic.[29]

Making recommendations about health practices involves value judgments on the desirability of various outcomes associated with management options. Values applied by the guideline panel sought to minimize harm, diminish unnecessary and inappropriate therapy, and reduce the unnecessary use of systemic antibiotics. A major goal of the committee was to be transparent and explicit about how values were applied and to document the process.

Table 2
Guideline definitions for evidence-based statements

Statement	Definition	Implication
Strong recommendation	A strong recommendation means the benefits of the recommended approach clearly exceed the harms (or that the harms clearly exceed the benefits in the case of a strong negative recommendation) and that the quality of the supporting evidence is excellent (Grade A or B)*. In some clearly identified circumstances, strong recommendations may be made based on lesser evidence when high-quality evidence is impossible to obtain and the anticipated benefits strongly outweigh the harms.	Clinicians should follow a strong recommendation unless a clear and compelling rationale for an alternative approach is present.
Recommendation	A recommendation means the benefits exceed the harms (or that the harms exceed the benefits in the case of a negative recommendation), but the quality of evidence is not as strong (Grade B or C)*. In some clearly identified circumstances, recommendations may be made based on lesser evidence when high-quality evidence is impossible to obtain and the anticipated benefits outweigh the harms.	Clinicians should also generally follow a recommendation but should remain alert to new information and sensitive to patient preferences.
Option	An option means that either the quality of evidence that exists is suspect (Grade D)* or that well-done studies (Grade A, B, or C)* show little clear advantage to one approach versus another.	Clinicians should be flexible in their decision making regarding appropriate practice, although they may set bounds on alternatives; patient preference should have a substantial influencing role.
No recommendation	No recommendation means there is both a lack of pertinent evidence (Grade D)* and an unclear balance between benefits and harms.	Clinicians should feel little constraint in their decision making and be alert to new published evidence that clarifies the balance of benefit versus harm; patient preference should have a substantial influencing role.

*See Table 3 for definition of evidence grades.

Financial Disclosure and Conflicts of Interest

The cost of developing this guideline, including travel expenses of all panel members, was covered in full by the AAO-HNS Foundation. Potential conflicts of interest for all panel members in the past 5 years were compiled and distributed before the first conference call. After review and discussion of these disclosures,[31] the panel concluded that individuals with potential conflicts could remain on the panel if they: 1) reminded the panel of potential conflicts before any related discussion, 2) recused themselves from a related discussion if asked by the panel, and 3) agreed not to discuss any aspect of the guideline with industry before publication. Lastly, panelists were reminded that conflicts of interest extend beyond financial relationships and may include personal experiences, how a participant earns a living, and the participant's previously established "stake" in an issue.[32]

RHINOSINUSITIS GUIDELINE EVIDENCE-BASED STATEMENTS

Each evidence-based statement is organized in a similar fashion: **evidence-based statement in boldface type**, *followed by an italicized statement on the strength of the recommendation*. Several paragraphs then discuss the evidence base supporting the statement, concluding with an "evidence profile" of aggregate evidence quality, benefit-harm assessment, and statement of costs. Lastly, there is an explicit statement of the value judgments, the role of patient preferences, and a repeat statement of the strength of the recommendation. An overview of evidence-based statements in the guideline and their interrelationship is shown in Table 4.

The role of patient preference in making decisions deserves further clarification. For some statements the evi-

Table 3
Evidence quality for grades of evidence

Grade	Evidence quality
A	Well-designed randomized controlled trials or diagnostic studies performed on a population similar to the guideline's target population
B	Randomized controlled trials or diagnostic studies with minor limitations; overwhelmingly consistent evidence from observational studies
C	Observational studies (case control and cohort design)
D	Expert opinion, case reports, reasoning from first principles (bench research or animal studies)
X	Exceptional situations where validating studies cannot be performed and there is a clear preponderance of benefit over harm

dence base demonstrates clear benefit, which would minimize the role of patient preference. If the evidence is weak or benefits are unclear, however, not all *informed* patients might opt to follow the suggestion. In these cases, the practice of *shared decision making*, where the management decision is made by a collaborative effort between the clinician and the informed patient, becomes more useful. Factors related to patient preference include (but are not limited to) absolute benefits (number needed to treat), adverse effects (number needed to harm), cost of drugs or tests, frequency and duration of treatment, and desire to take or avoid antibiotics. Comorbidity can also impact patient preferences by several mechanisms, including the potential for drug-drug interactions when planning therapy.

Statement 1a. Diagnosis of Acute Rhinosinusitis

Clinicians should distinguish presumed acute bacterial rhinosinusitis (ABRS) from acute rhinosinusitis caused by viral upper respiratory infections and noninfectious conditions. A clinician should diagnose ABRS when (a) symptoms or signs of acute rhinosinusitis are present 10 days or more beyond the onset of upper respiratory symptoms, or (b) symptoms or signs of acute rhinosinusitis worsen within 10 days after an initial improvement (double worsening). *Strong recommendation based*

Table 4
Outline of evidence-based statements

Clinical condition (*evidence-based statement number*)	Statement strength*
I. Presumed Viral Rhinosinusitis (VRS)	
a. Diagnosis (*Statement #1a*)	Strong recommendation
b. Radiographic imaging (*Statement #1b*)	Recommendation against
c. Symptomatic relief (*Statement #2*)	Option
II. Presumed Acute Bacterial Rhinosinusitis (ABRS)	
a. Diagnosis (*Statement #1a*)	Strong recommendation
b. Radiographic imaging (*Statement #1b*)	Recommendation against
c. Initial management	
i. Pain assessment (*Statement #3a*)	Strong recommendation
ii. Symptomatic relief (*Statement #3b*)	Option
iii. Watchful waiting (*Statement #4*)	Option
iv. Antibiotic selection (*Statement #5*)	Recommendation
d. Treatment failure (*Statement #6*)	Recommendation
III. Subacute Sinusitis (no statements)	
IV. Chronic Rhinosinusitis (CRS) and Recurrent Acute Rhinosinusitis	
a. Diagnosis (*Statement #7a*)	Recommendation
b. Modifying factors (*Statement #7b*)	Recommendation
c. Diagnostic testing (*Statement #8a*)	Recommendation
i. Nasal endoscopy (*Statement #8b*)	Option
ii. Radiographic imaging (*Statement #8c*)	Recommendation
iii. Testing for allergy and immune function (*Statement #8d*)	Option
d. Prevention (*Statement #9*)	Recommendation

*See Table 2 for definitions.

Table 5
Acute rhinosinusitis definitions

Term	Definition
Acute rhinosinusitis	Up to 4 weeks of *purulent nasal drainage* (anterior, posterior, or both) accompanied by *nasal obstruction, facial pain-pressure-fullness*, or both: • *Purulent nasal discharge* is cloudy or colored, in contrast to the clear secretions that typically accompany viral upper respiratory infection, and may be reported by the patient or observed on physical examination • *Nasal obstruction* may be reported by the patient as nasal obstruction, congestion, blockage, or stuffiness, or may be diagnosed by physical examination • *Facial pain-pressure-fullness* may involve the anterior face, periorbital region, or manifest with headache that is localized or diffuse
Viral rhinosinusitis (VRS)	Acute rhinosinusitis that is caused by, or is presumed to be caused by, viral infection. A clinician should diagnose VRS when: a. symptoms or signs of acute rhinosinusitis are present less than 10 days and the symptoms are not worsening
Acute bacterial rhinosinusitis (ABRS)	Acute rhinosinusitis that is caused by, or is presumed to be caused by, bacterial infection. A clinician should diagnose ABRS when: a. symptoms or signs of acute rhinosinusitis are present 10 days or more beyond the onset of upper respiratory symptoms, *or* b. symptoms or signs of acute rhinosinusitis worsen within 10 days after an initial improvement (double worsening)

on diagnostic studies with minor limitations and a preponderance of benefit over harm.

Cardinal Symptoms of Acute Rhinosinusitis

Acute rhinosinusitis is diagnosed as up to 4 weeks of purulent (not clear) nasal drainage accompanied by nasal obstruction, facial pain-pressure-fullness, or both (Table 5). When this symptom complex is present, the clinician should distinguish between viral rhinosinusitis (VRS) and presumed ABRS.[4,9,33,34] This distinction is based on illness pattern and duration (Table 5), because purulent nasal drainage as a sole criterion cannot distinguish between viral and bacterial infection.[35]

The rationale for selecting three cardinal symptoms is based on their high sensitivity and their relatively high specificity for ABRS, especially when considering the time interval of persistence for 10 days or longer.[36-38] Purulent nasal drainage predicts presence of bacteria on antral aspiration when reported as purulent rhinorrhea by the patient, when manifest as postnasal drip or purulent discharge in the posterior pharynx, or when observed in the nasal cavity or near the sinus ostium.[39,40] Purulent rhinorrhea also predicts radiographic evidence of ABRS.[41,42] Facial or dental pain also predicts ABRS,[38,40] but the location correlates poorly with the specific sinuses involved.[43] Lastly, patient complaints of nasal obstruction correlate with objective measures, such as rhinomanometry or nasal peak flow rate.[44]

Since the usual clinical dilemma is to differentiate ABRS from VRS, the specificity of ABRS symptoms has typically been studied in this context. The antecedent history of viral URI likely contributes to the specificity of these symptoms for ABRS, but the extent to which this is true has not been quantified. Similarly, although the differential diagnosis of isolated nasal obstruction or facial pain is broad (and beyond the scope of this guideline), the specificity for ABRS increases when coupled with concurrent purulent nasal discharge (Table 5). For example, migraine headaches, tension headaches, and dental abscess can mimic rhinosinusitis pain, but the absence of purulent nasal discharge excludes this diagnosis based on our definition.

Additional signs and symptoms of ABRS include fever, cough, fatigue (malaise), hyposomia, anosmia, maxillary dental pain, and ear fullness or pressure.[45] Although combinations of major and minor symptoms have been used to define sinusitis in early consensus reports,[45] more recent reports[9,44] have abandoned this system and instead focus on the three cardinal features outline above. There are no prospective trials, however, to validate this approach, which is based on expert opinion and extrapolation from studies that correlate prognostic factors with imaging results.

The initial diagnostic evaluation for acute rhinosinusitis should include measurement of vital signs and a physical examination of the head and neck. Particular attention should be paid to the presence or absence of the following: speech indicating "fullness of the sinuses"; swelling, erythema, or edema localized over the involved cheekbone or periorbital area; palpable cheek tenderness, or percussion

tenderness of the upper teeth; nasal or purulent drainage in the posterior pharynx; and signs of extrasinus involvement (orbital or facial cellulitis, orbital protrusion, abnormalities of eye movement, neck stiffness). However, of these physical findings, the only finding shown to have diagnostic value is that of purulence in the nasal cavity or posterior pharynx as discussed above.

Culture of secretions from the nasal cavity or nasopharynx has not been shown to differentiate ABRS from VRS, because nasal cultures correlate poorly with maxillary sinus cultures obtained by direct aspiration.[46] Endoscopically directed middle meatal cultures have better correlation, but a role in routine management of uncomplicated ABRS has not been established.[47]

Transition From Viral to Bacterial Infection

Only about 0.5% to 2.0% of VRS episodes are complicated by bacterial infection.[48] Although ABRS is often considered a transition from a preceding viral URI, bacterial infection can develop at any time during the course of illness. The concept of a transition, however, is useful for management decisions,[38] especially when considering the time course of VRS and which disease patterns are most likely to be associated with bacterial infection.

In the first 3 to 4 days of illness VRS cannot be differentiated from an early-onset ABRS, and for that reason only patients with unusually severe presentations or extrasinus manifestations of infection are presumed to have a bacterial illness. Similarly, between 5 and 10 days persistent symptoms are consistent with VRS or may represent the beginning stages of ABRS. In this time period, however, a pattern of initial improvement followed by worsening ("double sickening") is consistent with ABRS.[9,41-42] Beyond 10 days, residual sinus mucosal thickness induced by the virus may persist, usually in the absence of active viral infection, but the probability of confirming a bacterial infection by sinus aspiration is about 60%.[49]

Gwaltney and colleagues[50] studied the time course of signs and symptoms of spontaneous rhinovirus infections (Fig 1). Typical symptoms peak at day 2 to 3 and wane thereafter, but may persist 14 days or longer. Antecedent viral infection can promote ABRS by obstructing sinus drainage during the nasal cycle,[51] promoting growth of bacterial pathogens that colonize the nose and nasopharynx (Gwaltney 1996),[48] and by depositing nasal bacteria into the sinuses during nose-blowing.

Fever is present in some patients with VRS in the first few days of illness (Fig 1) but does not predict bacterial infection as an isolated diagnostic criterion. Fever has a sensitivity and specificity of only about 50% for ABRS.[37,38,52] For this reason we did not include fever as a cardinal sign in diagnosing ABRS. Meltzer and co-workers,[9] however, defined a special circumstance of ABRS when purulent nasal discharge for 3 to 4 days was accompanied by high fever. In that document "high fever" was not defined, but the criterion only applied to severe disease with a shorter duration of illness.

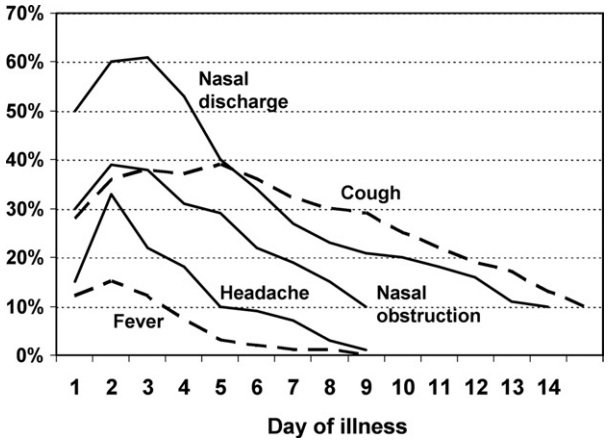

Figure 1 Symptom prevalence by day for rhinovirus illness (data from Gwaltney et al[50]).

Evidence Profile

- Aggregate evidence quality: Grade B, diagnostic studies with minor limitations regarding signs and symptoms associated with ABRS
- Benefit: decrease inappropriate use of antibiotics for nonbacterial illness; distinguish noninfectious conditions from rhinosinusitis
- Harm: risk of misclassifying bacterial rhinosinusitis as viral, or vice-versa
- Cost: not applicable
- Benefits-harm assessment: preponderance of benefit over harms
- Value judgments: importance of avoiding inappropriate antibiotic treatment of viral or nonbacterial illness; emphasis on clinical signs and symptoms for initial diagnosis; importance of avoiding unnecessary diagnostic tests
- Role of patient preferences: not applicable
- Policy level: strong recommendation

Statement 1b. Radiographic Imaging and Acute Rhinosinusitis

Clinicians should not obtain radiographic imaging for patients who meet diagnostic criteria for acute rhinosinusitis, unless a complication or alternative diagnosis is suspected. *Recommendation against based on diagnostic studies with minor limitations and a preponderance of benefit over harm.*

Supporting Text

Radiographic imaging of the paranasal sinuses is unnecessary for diagnosis in patients who already meet clinical diagnostic criteria (Table 5) for acute rhinosinusitis.[53-54] Imaging modalities for the paranasal sinuses include plain film radiography, computed tomography (CT), and magnetic resonance (MR) imaging. The utility of ultrasound for diagnosis is inconclusive[55] and will not be discussed further.

A meta-analysis of 6 studies showed that sinus radiography has moderate sensitivity (76%) and specificity (79%) compared with sinus puncture in diagnosing ABRS.[55] Sinus involvement is common in documented viral URIs,[56] making it impossible to distinguish ABRS from VRS based solely on imaging studies. Moreover, clinical criteria may have a comparable diagnostic accuracy to sinus radiography, and radiography is not cost effective regardless of baseline sinusitis prevalence.[55]

When a complication of acute rhinosinusitis or an alternative diagnosis is suspected, imaging studies may be obtained. Complications of ABRS include orbital, intracranial, or soft tissue involvement. Alternative diagnoses include malignancy and other noninfectious causes of facial pain. Radiographic imaging may also be obtained when the patient has modifying factors or comorbidities that predispose to complications, including diabetes, immune compromised state, or a past history of facial trauma or surgery.

Sinus plain film radiography series consists of three views: a lateral, Caldwell or posterior-anterior view (central ray angled 15 degrees), and Waters or occipito-mental view (orbitomeatal line angled 37 degrees to plane). A single Waters view may be adequate in some patients, especially if maxillary sinusitis is likely.[52] Radiographs should be obtained with the patient in the upright position to allow visualization of air-fluid levels. This three-view series allows for approximately 300 to 600 millirads skin dosage (100-200 per radiograph). Sinus opacification, air-fluid level, or marked or severe mucosal thickening is consistent with, but not diagnostic of, acute rhinosinusitis.

Prospective series looking at antral puncture results as the gold standard showed complete opacification, and air-fluid level, or both, on plain film radiography to have a sensitivity of 0.73 and specificity of 0.80 for acute rhinosinusitis.[57] Sensitivity and specificity for ethmoid and frontal sinusitis are lower on plain film radiography. The sphenoid sinus can be visualized with plain film radiography by including a base or submentovertex view.

CT imaging of the sinuses is an alternative choice that is preferred when a complication of acute rhinosinusitis is suspected. As with plain film radiography, imaging findings that correlate with sinusitis include opacification, air-fluid level, and moderate to severe mucosal thickening. An advantage of CT over plain film radiography is improved visualization of the paranasal sinuses (especially the ethmoid complex), frontal recess, soft tissue, orbital contents, and brain.

Limitations of CT imaging include increased cost and radiation dosage. Radiation dose is related to technique and may deliver over 10 times the dosage compared with plain film radiography. With careful choice of technical factors, however, CT dosage can be lowered to two times the dose of plain radiography. Other limitations of CT include lack of specificity for bacterial infection and a relative lack of correlation between localizing symptoms and sinus disease on CT.[56,58]

Complicated sinusitis, with suspected orbital, intracranial, or deep facial extension based on severe headache, proptosis, cranial nerve palsies, or facial swelling, should be evaluated with iodine contrast-enhanced CT or gadolinium-based MR imaging to identify extra-sinus extension or involvement.[59,60] Suspected complications of acute rhinosinusitis are the only indication for MR imaging in the setting of acute sinusitis.

Evidence Profile

- Aggregate evidence quality: Grade B, diagnostic studies with minor limitations
- Benefit: avoid unnecessary radiation exposure; avoid delays in diagnosis from obtaining and interpreting imaging studies
- Harm: delayed diagnosis of serious underlying condition
- Cost: savings by not performing routine radiologic imaging
- Benefits-harm assessment: preponderance of benefit over harm
- Value judgments: importance of avoiding unnecessary radiation and cost in diagnosing acute rhinosinusitis
- Role of patient preferences: minimal
- Patient exclusions: suspicion of complicated acute rhinosinusitis based on severe headache, proptosis, cranial nerve palsies, facial swelling, or other clinical findings
- Policy level: recommendation

Statement 2. Symptomatic Relief of Viral Rhinosinusitis (VRS)

Clinicians may prescribe symptomatic relief in managing VRS. *Option based on randomized trials with limitations and cohort studies with an unclear balance of benefit and harm that varies by patient.*

Supporting Text

VRS is a self-limited disease characterized by cough, sneezing, rhinorrhea, sore throat, and nasal congestion.[50] Antibiotics are not recommend for treating VRS because they are ineffective for viral illness and do not relieve symptoms directly.[61]

Sputum color should not be used to assess the need for antibiotic therapy, because color is related to presence of neutrophils, not bacteria. Since neutrophils often appear in the nasal discharge of patients with VRS,[35,62-64] sputum may be clear, cloudy, or colored. While there is always a small chance that an early ABRS will be misdiagnosed as a VRS, the indiscriminate use of antibiotics for all patients with acute rhinosinusitis is discouraged because of cost, adverse effects, allergic reactions, and potential drug-drug interactions.[54,65]

Management of VRS is primarily symptomatic, with an analgesic or antipyretic provided for pain or fever, respectively. Topical or systemic decongestants may offer additional symptomatic relief, but their ability to

prevent ABRS from developing is unproved. In theory, a decongestant (especially topical) can restore sinus ostial patency. The effect, however, is limited to the nasal cavity and does not extend to the paranasal sinuses.[66] Lack of symptomatic response to a topical decongestant has been proposed as an indicator of ABRS,[67] but this is also unproved.

The topical decongestants, most often the long-acting agent oxymetazoline hydrochloride, provide more symptom relief than oral decongestants because of increased potency. This benefit, however, is offset partly by the risk of developing a rebound nasal congestion after the topical decongestant is discontinued. For this reason, many clinicians limit use of a topical decongestant to only 3 days.

Systemic steroid therapy has not been shown effective for VRS, and weak evidence supports using topical nasal steroids.[68] Steroids could theoretically be beneficial by reducing the allergic response in patients with allergic rhinitis and by decreasing the swelling associated with rhinosinusitis. An advantage of the topical nasal steroids is that they are minimally absorbed and therefore have a low chance of systemic side effects. Short-term use of systemic steroids can produce behavioral changes, increased appetite, and weight gain.

Antihistamine therapy has been used to treat VRS because of a drying effect, but no studies have been published that assess the impact of antihistamines specifically on VRS outcomes. Adverse effects of antihistamines, especially first-generation H1-antagonists, include drowsiness, behavioral changes, and impaired mucus transport in the nose and sinuses because of drying.

Evidence Profile

- Aggregate evidence quality: Grade B and C, randomized controlled trials with limitations and cohort studies
- Benefit: reduction of symptoms; avoidance of unnecessary antibiotics
- Harm: adverse effects of decongestants, antihistamines, topical steroid sprays
- Cost: cost of medications
- Benefits-harm assessment: unclear balance of benefit and harm that varies by patient
- Value judgments: provide symptomatic relief, but avoid inappropriate use of antibiotics for viral illness
- Role of patient preferences: substantial role in selection and use of therapies for symptomatic relief
- Policy level: option

Statement 3a. Pain Assessment of Acute Bacterial Rhinosinusitis (ABRS)

The management of ABRS should include an assessment of pain. The clinician should recommend analgesic treatment based on the severity of pain. *Strong recommendation based on randomized controlled trials of general pain relief in non-ABRS populations with a preponderance of benefit over harm.*

Supporting Text

Pain relief is a major goal in managing ABRS, and is often the main reason that patients with this condition seek health care.[37,38] Ongoing assessment of the severity of discomfort is essential for proper management. Severity may be assessed using a faces pain scale[69] or a simple visual-analog scale,[44] or by asking the patient to qualitatively rate the discomfort as "mild" versus "moderate/severe."

Frequent use of analgesics is often necessary to permit patients to achieve comfort, rest, and resume normal activities. Adequate pain control requires knowing the dose, timing, routes of delivery, and possible adverse effects of an analgesic.[70,71] Mild to moderate pain usually responds to acetaminophen or nonsteroidal anti-inflammatory drugs given alone or in fixed combination with an opioid (eg, acetaminophen with codeine, oxycodone, or hydrocodone; ibuprofen with oxycodone).

Convenience, ease of use, and cost make orally administered analgesics the preferred route of administration whenever possible. When frequent dosing is required to maintain adequate pain relief, administering analgesics at fixed intervals rather than on a pro re nata (p.r.n.) basis may be more effective.

Evidence Profile

- Aggregate evidence quality: Grade B, randomized controlled trials demonstrating superiority of analgesics over placebo for general pain relief, but no trials specifically regarding patients with ABRS
- Benefit: pain reduction
- Harm: side effects of analgesic medications; potential for masking underlying illness or disease progression
- Costs: cost of analgesic medications
- Benefits-harm assessment: preponderance of benefit over harm
- Value judgments: pain relief is important
- Role of patient preferences: choice of analgesic
- Policy level: strong recommendation

Statement 3b. Symptomatic Relief of Acute Bacterial Rhinosinusitis (ABRS)

Clinicians may prescribe symptomatic relief in managing ABRS. *Option based on randomized trials with heterogeneous populations, diagnostic criteria, and outcome measures with a balance of benefit and harm.*

Supporting Text

Adjunctive treatments for rhinosinusitis that may aid in symptomatic relief include decongestants (alpha-adrenergic), corticosteroids, saline irrigation, and mucolytics. None of these products have been specifically approved by the Food and Drug Administration (FDA) for use in acute rhinosinusitis (as of February 2007), and few have data from controlled clinical studies supporting this use. Moreover, existing trials often include co-interventions and a hetero-

geneous population of patients with viral, recurrent bacterial, chronic, and allergic rhinosinusitis. Nonetheless, clinicians may wish to consider adjuvant therapy for ABRS on an individualized basis, and we therefore provide a brief overview of evidence in the remainder of this section.

Most clinical trials of topical corticosteroids for ABRS are industry supported and include studies of mometasone,[72-74] fluticasone,[75] flunisolide,[76] and beclomethasone. The best evidence comes from Meltzer and colleagues,[73] who showed significantly reduced mean symptom scores during days 2 to 15 of treatment for patients with nonsevere ABRS who received mometasone furoate nasal spray twice daily compared with patients who received amoxicillin or placebo. In another study,[75] patients with ABRS and a history of recurrent or chronic sinusitis benefited from adding fluticasone propionate nasal spray to cefuroxime axetil twice daily for 10 days, and xylometazoline hydrochloride for 3 days. In contrast with topical therapy, no controlled clinical trials of systemic glucocorticoids for treating ABRS have been published.

Nasal saline irrigation, alone or in conjunction with other adjunctive measures, may improve quality of life, decrease symptoms, and decrease medication use for ABRS, particularly in patients with frequent sinusitis. Buffered hypertonic (3%-5%) saline irrigation showed a modest benefit for acute rhinosinusitis in 2 clinical trials.[77,78] Compared with isotonic saline, hypertonic saline may have a superior anti-inflammatory effect and better ability to thin mucus and transiently improve mucociliary clearance.[79-81] One randomized trial of patients with the common cold and acute rhinosinusitis, however, found no difference in outcomes for hypertonic saline, normal saline, or observation.[82]

Topical and systemic decongestants (sympathomimetics) have been used to treat nasal congestion associated with the common cold for many years.[83-87] There are no RCTs that specifically study the efficacy of decongestants for ABRS, but two small studies have shown that xylometazoline nasal spray reduces congestion of sinus and nasal mucosa on imaging studies[51,66] and is superior to a single orally administered dose of pseudoephedrine.[66] Another small, nonrandomized study showed improved outcomes when xylometazoline spray was added to antibiotics for ABRS.[77] Topical decongestants should not be used more than 3 consecutive days without a prolonged intervening drug-free period due to its propensity to cause rebound congestion (rhinitis medicamentosa).

Antihistamines have no role in the symptomatic relief of ABRS in nonatopic patients.[34,44,88] There are no studies that support their use in an infectious setting, and antihistamines may worsen congestion by drying the nasal mucosa. Conversely, one randomized trial in allergic patients with ABRS showed reduced sneezing and nasal congestion for loratadine vs placebo when used as an adjunct to antibiotics and oral corticosteroids.[89] Antihistamine therapy, therefore, can be considered in patients with ABRS whose symptoms support a significant allergic component. In this regard, newer second-generation H1-antagonists cause less sedation and fewer anticholinergic side effects than do older first-generation H1-antagonists.[90]

Guaifenesin is a water- and alcohol-soluble agent that is used as an expectorant to loosen phlegm and bronchial secretions associated with upper and lower airway infections complicated by tenacious mucus and congestion. There is currently insufficient evidence to support recommending guaifenesin as an adjunct in treating rhinosinusitis.

Evidence Profile

- Aggregate evidence quality: Grade B, randomized controlled trials with heterogeneous populations, diagnostic criteria, and outcomes measures; grade D for antihistamines (in nonatopic patients) and guaifenesin
- Benefit: symptom relief
- Harm: side effects of medications, which include local and systemic adverse reactions
- Costs: cost of medications
- Benefits-harm assessment: balance of benefit and harm
- Value judgments: provide symptomatic relief while minimizing adverse events and costs
- Role of patient preferences: substantial role for shared decision making
- Policy level: option

Statement 4. Watchful Waiting for Acute Bacterial Rhinosinusitis (ABRS)

Observation without use of antibiotics is an option for selected adults with uncomplicated ABRS who have mild illness (mild pain and temperature <38.3°C or 101°F) and assurance of follow-up. *Option based on double-blind randomized controlled trials with heterogeneity in diagnostic criteria and illness severity, and a relative balance of benefit and risk.*

Observation Option for Nonsevere ABRS

The observation option for ABRS refers to deferring antibiotic treatment of selected patients for up to 7 days after diagnosis and limiting management to symptomatic relief. Patients with *nonsevere illness* at presentation (mild pain and temperature <38.3°C or 101°F) are candidates for observation when follow-up is assured, and a system is in place that permits reevaluation if the illness persists or worsens. Antibiotics are started if the patient's condition fails to improve by 7 days or worsens at any time.

Observing nonsevere ABRS is consistent with other rhinosinusitis practice guidelines.[7,44,54] Conversely, patients with *severe illness* (moderate to severe pain or temperature ≥38.3°C or 101°F) are treated initially with oral antibiotics. Although illness severity is a primary determinant of suitability for observation, the clinician should also consider the patient's age, general health, cardiopulmonary status, and comorbid conditions as part of the decision-making process.

The rationale for observing ABRS is based upon a high percentage of spontaneous improvement when patients re-

Table 6
Double-blind randomized controlled trials of antibiotic vs placebo for acute rhinosinusitis*

Author year, country	Primary care	N	Age, y (male, %)	Diagnostic criteria	Illness duration, days	Antibiotic	Industry funding
Bucher[94] 2003, Switzerland	yes	252	≥18 (46)	clinical si/sx	4.5 median	amox/clav	yes
de Sutter[95] 2002, Belgium	yes	408	≥12 (45)	clinical si/sx	7.4 median	amox	ns
Ganança[96] 1973, Brazil	no	50	≥18 (60)	pos. nasal cx	ns	cyclacillin	ns
Hansen[97] 2000, Denmark	yes	139	≥18 (25)	algorithm†	6.0 median	pcn	no
Haye[98] 1998, Norway	yes	169	≥18 (26)	neg. imaging‡	10 to 30	azithro	ns
Kaiser[99] 2001, Switzerland	ns	269	≥18 (48)	clinical si/sx	4.0 median	azithro	ns
Lindbaek[100] 1996, Norway	yes	130	≥16 (35)	pos. imaging§	<30	pcn, amox	no
Lindbaek[101] 1998, Norway	yes	70	≥16 (39)	neg. imaging‡	≥7	pcn, amox	no
Meltzer[74] 2005, 14 countries	ns	981	≥12 (35)	clinical si/sx	7 to 28	amox	yes
Merenstein[102] 2005, USA	yes	135	≥18 (31)	clinical si/sx	11.2 median	amox	no
Stalman[103] 1997, Holland	yes	192	≥16 (34)	clinical si/sx	≥5	doxy	yes
van Buchem[104] 1997, Holland	yes	214	≥18 (37)	pos. imaging††	15.4 mean	amox	ns
Varonen[105] 2003, Finland	yes	150	≥18 (30)	clinical si/sx	>5d for 73%	pcn, doxy, amox	yes

amox, amoxicillin; *azithro*, azithromycin; *clav*, clavulanate; *cx*, culture; *doxy*, doxycycline; *neg*, negative; *ns*, not stated; *pcn*, penicillin V; *pos*, positive; *si/sx*, signs and symptoms.

*Data from Rosenfeld, Singer, and Jones.[93]
†Combined symptoms with C-reactive protein and erythrocyte sedimentation rate (68% positive predictive value).
‡Patients had clinical signs and symptoms of acute rhinosinusitis, but baseline radiograph/scan did not show complete opacity, air-fluid level, or mucosal thickening >5-6 mm.
§Baseline radiograph/scan showed fluid level or total opacification in any sinus.
††Baseline radiograph showed fluid level, opacity, and/or mucosal thickening >5mm.

ceive placebo in randomized controlled trials (RCTs), plus only a modest incremental benefit from antibiotic therapy. Three meta-analyses[33,91,92] comparing antibiotic vs placebo for acute rhinosinusitis show spontaneous improvement in 62% to 69% of patients after 7 to 14 days, spontaneous cure in 19% to 39%, and an absolute increase of 13% to 19% in favorable outcomes when antibiotics are used. These results, however, are limited by restricted subsets of included articles and failure to include several RCTs that were subsequently published.

Outcomes of Placebo vs Antibiotic

Systematic review[93] of MEDLINE and the Cochrane Trial Registry through January 2007 revealed 13 double-blind, placebo-controlled, randomized trials (Table 6)[74,94-105] of antibiotics for acute rhinosinusitis in adults (3 trials contained some older children). Diagnostic criteria and illness duration varied by study, with most including at least some patients with fewer than 10 days of symptoms. Four RCTs were excluded from further consideration because they were not double-blind,[106] excluded patients with sinusitis,[107] included only children,[108] or used a nonclinical outcome based on sinus irrigation.[109]

Meta-analysis results for the 13 RCTs in Table 6 are shown in Table 7.[93] Clinical outcomes are defined as "cured" (absence or near-absence of all presenting signs and symptoms of acute rhinosinusitis) or "improved" (partial or complete relief of presenting signs and symptoms). By 3 to 5 days after starting treatment less than one third of patients receiving placebo are cured or improved, and the impact of antibiotics on outcomes is not significant. By 7 to 12 days, however, 35% of patients are cured and 73% are improved (or cured), with an absolute increase in positive outcomes (rate difference, RD) of 14% to 15% when antibiotics are given (number needed to treat [NNT] of about 7 patients. By 14 to 15 days, however, the cure rate in the placebo group

Table 7
Meta-analysis of antibiotic vs placebo for acute rhinosinusitis*

Analysis performed outcome: studies combined (reference numbers)	N	Placebo (95% CI)†	Absolute RD (95% CI)‡	RR	P	Hetero-geneity§
Antibiotic efficacy, clinical cure						
1. Cured 3-5d: 97-98,100	397	0.08 (0.05, 0.14)	0.01 (−0.02, 0.05)	1.59	0.451	0
2. Cured 7-12d: 94-101,103	1607	0.35 (0.24, 0.48)	0.15 (0.04, 0.25)	1.28	0.007	80
3. Cured 14-15d: 74,94,102,104	1104	0.45 (0.23, 0.70)	0.04 (−0.02, 0.11)	1.09	0.214	27
Antibiotic efficacy, clinical improvement††						
4. Improved 3-5d: 98,100	258	0.30 (0.00, 0.99)	0.10 (−0.03, 0.24)	2.40	0.129	65
5. Improved 7-12d: 96,98,100-101,103	543	0.73 (0.56, 0.85)	0.14 (0.01, 0.28)	1.18	0.037	74
6. Improved 14-15d: 74,104-105	800	0.73 (0.67, 0.78)	0.07 (0.02, 0.13)	1.10	0.013	0
Adverse events						
7. Diarrhea: 74,95-96,98,100,102-103,105	1583	0.06 (0.03, 0.12)	0.05 (0.01, 0.09)	1.74	0.027	69
8. Any adverse event: 74,96-100,102-105	1853	0.14 (0.08, 0.24)	0.11 (0.05, 0.16)	1.83	0.001	55

CI, confidence interval; *P*, *P* value; *RD*, rate difference; *RR*, relative risk.

*Data from Rosenfeld, Singer, and Jones.[93]
†Estimated rate of spontaneous resolution based on random-effects meta-analysis of outcomes in placebo groups.
‡Absolute change in outcomes for antibiotic vs placebo groups, beyond the placebo rate (spontaneous resolution), based on random-effects meta-analysis (same as the absolute risk reduction, ARR, for treatment failure).
§Percentage of total variation across studies caused by heterogeneity (25% is low, 50% moderate, 75% high).
††Clinical improvement includes patients who were cured or improved.

is 45% and the impact of antibiotics becomes nonsignificant.

Adverse events occur more often with antibiotics than placebo (Table 7), with about one additional event for every 9 patients treated (number needed to harm, or NNH). Most adverse events are gastrointestinal, but other reported side effects include skin rash, vaginal discharge, headache, dizziness, and fatigue. A secondary analysis of adverse events in rhinosinusitis drug trials estimated that antibiotics resulted in 15 days (best case) to 89 days (worst case) of diarrhea, nausea/vomiting, or both per 100 treated patients, compared with only 8.5 days for placebo.[110] Since most placebo-controlled trials use amoxicillin, however, gastrointestinal side effects may be lower with other antibiotic classes. None of the trials assessed the impact of antibiotics on bacterial resistance, but the ability of oral antibiotic therapy to induce resistance by selective pressure on existing microflora is well documented.[111,112]

Only one suppurative complication of sinusitis was reported in the randomized trials in Table 6: a patient who initially received placebo was started on amoxicillin-clavulanate at day 14 and 7 days later developed a brain abscess.[94] This rate of one complication in more than 1100 patients receiving placebo, however, does not differ statistically from the null rate seen in the antibiotic treatment groups.

Applying Clinical Trial Results to Patient Care

Since nearly all placebo-controlled trials recruited subjects from a primary care setting, results may not apply to patients with more severe or persistent symptoms seen by specialists or emergency physicians. Several studies[74,99,100,103] excluded patients with "severe illness" defined most often as high fever (≥101°F/38.3°C) with severe facial/dental pain or a highly elevated C-reactive protein (>100 mg/L).[94] Common exclusion criteria in most studies were symptoms greater than 30 days, complicated sinusitis, immune deficiency, recent antibiotic treatment (2-4 weeks), chronic sinusitis or nasal polyps, prior sinus surgery, or coexisting bacterial illness (pneumonia, otitis media, or streptococcal pharyngitis).

Another factor to consider when applying meta-analysis results to patient care is variability (heterogeneity) among studies. Most analyses in Table 7 had moderate or high heterogeneity, likely related to how rhinosinusitis was diagnosed: studies with a more objective diagnosis tended to show greater antibiotic benefit. For improvement day 7 to 12 (analysis #5) the studies using positive imaging[100] or positive culture[96] showed larger antibiotic benefit, whereas no benefits were found in studies with negative imaging[98,101] or brief disease duration.[103] Similarly, for cure day 7 to 12 (analysis #2) studies with positive imaging,[100] positive culture,[96] or a validated algorithm[97] showed the largest benefits, whereas no benefits occurred with negative imaging[101] or relatively brief (median 4-7 days) illness duration.[94,95,99,103]

The treatment analyses in Table 7 describe success or failure for a given clinical outcome, which can potentially miss time-related events. As shown in Table 8, patients receiving antibiotic had improvement or resolution of their illness 4 to 8 days sooner in some studies than did those

Table 8
Time-related outcomes in double-blind, randomized controlled trials

Author year	Outcome definition	Placebo group, d	Antibiotic group, d	*P* value
de Sutter[95] 2002	Median pain duration	5	5	0.690
	Median illness duration	5	5	0.290
	Resolution of purulent rhinorrhea in ≥75%	14	9	0.007
Lindbaek[100] 1996	Median sinusitis duration (amoxicillin)	17	9	<0.001
Lindbaek[101] 1998	Median sinusitis duration (amoxicillin)	10	10	0.760
Merenstein[102] 2005	Median time to clinical improvement	11	8	0.039
Stalman[103] 1997	Median pain duration	5	4	0.250
Varonen[105] 2003	Mean illness duration	6	6	0.660

receiving placebo; however, this finding was not consistently observed. The largest time-related benefit from antibiotic therapy—reduced illness duration of 8 days—was seen in the only study[100] that relied upon positive imaging for sinusitis as a criterion for inclusion.

When considering the potential harms and benefit of antibiotic therapy for ABRS, the evidence suggests a relative balance for patients with nonsevere illness diagnosed in a primary care setting. The modest benefit of antibiotics for improving rates of clinical cure or improvement at 7 to 12 days (NNT of 7), and possibly reducing illness duration, is offset by more adverse events, the cost and inconvenience of therapy, gastrointestinal symptoms, and the potential for increased bacterial resistance. Moreover, most clinical improvement by 7 to 12 days reflects the natural history of rhinosinusitis, rather than antibiotic efficacy. Conversely, the evidence base for patients with severe illness is limited, and the increased risk of suppurative complications suggests a preponderance of benefit for antibiotic therapy.

In summary, the observation option for ABRS refers to deferring antibiotic treatment of selected patients for up to 7 days after diagnosis and limiting management to symptomatic relief. We recommend limiting observation of ABRS to patients with nonsevere illness at presentation, with assurance of follow-up so that antibiotics can be started if patients fail to improve by day 7 after diagnosis or have worsening at any time. Clinicians deciding whether or not to treat ABRS with antibiotics should also solicit and consider patient preference, and determine the relevance of existing evidence to their specific practice setting and patient population.

Evidence Profile

- Aggregate evidence quality: Grade B, randomized controlled trials with heterogeneity in diagnostic criteria and illness severity
- Benefit: increase in cure or improvement at 7 to 12 days (NNT 6), and improvement at 14 to 15 days (NNT 16); reduced illness duration in two studies
- Harm: adverse effects of specific antibiotics (NNH 9), especially gastrointestinal; societal impact of antibiotic therapy on bacterial resistance and transmission of resistant pathogens; potential disease progression in patients initially observed who do not return for follow-up
- Cost: antibiotics; potential need for follow-up visit if observation failure
- Benefits-harm assessment: relative balance of harm vs benefit for nonsevere ABRS, preponderance of benefit over harm for severe ABRS
- Value judgments: minimize drug-related adverse events and induced bacterial resistance
- Role of patient preferences: substantial role for shared decision-making
- Potential exceptions: include but are not limited to severe illness, complicated sinusitis, immune deficiency, prior sinus surgery, or coexisting bacterial illness; the clinician should also consider the patient's age, general health, cardiopulmonary status, and comorbid conditions when assessing suitability for observation
- Policy level: option

Statement 5. Choice of Antibiotic for Acute Bacterial Rhinosinusitis (ABRS)

If a decision is made to treat ABRS with an antibiotic agent, the clinician should prescribe amoxicillin as first-line therapy for most adults. *Recommendation based on randomized controlled trials with heterogeneity and noninferiority design with a preponderance of benefit over harm.*

Amoxicillin as First-line Therapy

The rationale for antibiotic therapy of ABRS is to eradicate bacterial infection from the sinuses, hasten resolution of symptoms, and enhance disease-specific quality of life. Antibiotic therapy should be efficacious, be cost-effective, and result in minimal side effects. Dozens of RCTs have assessed the comparative clinical efficacy of antibiotics in patients with ABRS,[92] with most trials either funded by pharmaceutical companies or conducted by authors associated with the pharmaceutical industry.[33]

No significant differences have been found in clinical outcomes for ABRS among different antibiotic agents. A systematic review[92] and two RCTs[113,114] of sinusitis pa-

Table 9
Clinical efficacy of amoxicillin vs placebo for initial, empiric treatment of acute rhinosinusitis*

	Cured at 10-15 days			Improved at 10-15 days†		
Author year	Amoxicillin n/N (%)	Placebo n/N (%)	Absolute RD (95% CI)‡	Amoxicillin n/N (%)	Placebo n/N (%)	Absolute RD (95% CI)‡
de Sutter[95] 2002	59/202 (29)	47/206 (23)	0.06 (−0.02, 0.15)	—	—	—
Lindbaek[100] 1996	20/45 (44)	5/44 (11)	0.33 (0.16, 0.50)	39/45 (87)	25/44 (57)	0.30 (0.12, 0.48)
Lindbaek[101] 1998	9/22 (41)	9/21 (43)	−0.02 (−0.31, 0.28)	17/22 (77)	14/21 (67)	0.11 (−0.16, 0.37)
Meltzer 2005[74]	54/251 (22)	56/252 (22)	−0.01 (−0.08, 0.07)	207/251 (82)	192/252 (76)	0.07 (0.00, 0.14)
Merenstein[102] 2005	32/67 (46)	25/68 (37)	0.11 (−0.06, 0.28)	—	—	—
van Buchem[104] 1997	68/108 (63)	53/106 (50)	0.13 (−0.01, 0.19)	87/108 (81)	78/106 (74)	0.07 (−0.04, 0.18)
Varonen[105] 2003	—	—	—	18/23 (78)	39/60 (65)	0.13 (−0.08, 0.34)
Combined§			0.10 (0.01, 0.19)			0.11 (0.03, 0.19)

CI, confidence interval; *RD*, absolute rate difference.

*Data from Rosenfeld, Singer, and Jones.[93]
†Includes patients who were cured or improved.
‡Absolute change in outcomes for amoxicillin vs placebo group, beyond the placebo rate (spontaneous resolution); the result is statistically significant if the 95% CI does not include zero.
§Combined absolute rate difference for the above studies based on random-effects meta-analysis.

tients with radiologic or bacteriologic confirmation found no significant difference in rates of clinical resolution for patients treated with amoxicillin or amoxicillin-clavulanate compared to cephalosporins or macrolides. Another review[33] found no differences in 11 comparative meta-analyses, but did find a small decrease in failure rates for amoxicillin-clavulanate vs cephalosporins (NNT 30).

The justification for amoxicillin as first-line therapy for most patients with ABRS relates to its safety, efficacy, low cost, and narrow microbiologic spectrum.[4,7,55,92,115,116] Amoxicillin increases rates of clinical cure or improvement compared with placebo (Table 9). Nearly all studies in Table 9 showed better outcomes with amoxicillin, but when assessed individually only one,[100] which based the diagnosis of ABRS on CT imaging, reached statistical significance. The combined effect, however, is significant based on the larger sample size.[93]

For penicillin-allergic patients, folate inhibitors (trimethoprim-sulfamethoxazole) are a cost-effective alternative to amoxicillin.[34,55,91,115,117] The macrolide class of antibiotics may also be used for patients with penicillin allergy.

Other Considerations

Most trials of ABRS administer antibiotic for 10 days. No significant differences have been noted, however, in resolution rates for ABRS with a 6- to 10-day course of antibiotics compared with a 3- to 5-day course (azithromycin, telithromycin, or cefuroxime) up to 3 weeks after treatment.[118-120] Another systematic review found no relation between antibiotic duration and outcome efficacy for 8 RCTs.[33] Conversely, shorter treatment courses of antibiotics are associated with fewer adverse effects.

Adverse events are common with antibiotic therapy, but the diverse reporting among studies precludes meaningful comparisons of rates across different antibiotic classes.[33] An average event rate of 15% to 40% is observed, with the most frequent complaints being nausea, vomiting, diarrhea, abdominal pain, headache, skin rash, and photosensitivity. Some women in each antibiotic class also experience vaginal moniliasis. The potential impact of antibiotics on bacterial resistance must also be considered. Adverse events rarely are of sufficient severity to cause a change in therapy.

The most common bacterial species isolated from the maxillary sinuses of patients with initial episodes of ABRS are *Streptococcus pneumoniae*, *Haemophilus influenzae*, and *Moraxella catarrhalis*,[4,34] the latter being more common in children. A review of sinus aspiration studies performed in adults with ABRS suggests that *S. pneumoniae* is isolated in approximately 20% to 43%, *H. influenzae* in 22% to 35%, and *M. catarrhalis* in 2% to 10% of aspirates.[49,121-123] Other bacterial isolates found in patients with ABRS include *Staphylococcus aureus* and anaerobes.

Local resistance patterns vary widely, but about 15% of *S. pneumoniae* has intermediate penicillin resistance and 25% is highly resistant.[4] When used in sufficient doses,

amoxicillin is effective against susceptible and intermediate resistant pneumococci. Amoxicillin is ineffective, however, against beta-lactamase–producing *M. catarrhalis* and *H. influenzae* (about 80% and 30% of isolates, respectively). The impact of amoxicillin resistance on clinical outcomes, however, will be reduced by the favorable natural history of acute rhinosinusitis observed when patients receive placebo in clinical trials (Table 9).

When selecting an antibiotic for ABRS it is also important to consider other factors that might modify the choice of initial antibiotic therapy:

1) Patients with penicillin allergy may receive a macrolide antibiotic or trimethoprim-sulfamethoxazole.
2) Recent use of prior antibiotics is a risk factor for the presence of antibiotic-resistant bacteria, and a different antibiotic should be selected if the patient has used antibiotics in the last 4 to 6 weeks. Guidelines from the Sinus and Allergy Partnership[4] recommend a fluoroquinolone or high-dose amoxicillin-clavulanate (4 grams/250 milligrams per day) for patients who have received antibiotics within the past 4 to 6 weeks.
3) Having a child in daycare in the household is a risk factor for penicillin-resistant *S. pneumoniae*, for which high-dose amoxicillin is an option.
4) There is no evidence to suggest difference in clinical outcomes associated with differing dose or duration schedules. However, adherence rates for antibiotics with once-daily dosing and a short duration of use are generally higher and assure a greater likelihood of completing the full course of treatment.

Patients started on antibiotic therapy for ABRS should be counseled on use of the medication, potential adverse effects, and the importance of adherence with dosing schedules. The out-of-pocket expense of antibiotics should be considered, because it could represent a potential barrier to having the prescription filled and used as directed. Information about the natural history of ABRS can aid patients in understanding symptomatology and defining realistic expectations concerning treatment. Measures such as hydration, analgesics, and other supportive therapies should be highlighted.

Evidence Profile

- Aggregate evidence quality: Grade B, randomized controlled trials with heterogeneity and noninferiority design
- Benefit: demonstrated superiority of amoxicillin over placebo, with clinical outcomes comparable to broader-spectrum antibiotics for initial therapy; potential reduced bacterial resistance by using a narrow-spectrum antibiotic as first-line therapy; cost-effectiveness of amoxicillin vs other antibiotic choices
- Harm: potential increased gastrointestinal adverse effects with amoxicillin compared to other antibiotics; adverse effects from penicillin allergy
- Cost: cost of antibiotics
- Benefits-harm assessment: preponderance of benefit over harm
- Value judgments: promote safe and cost-effective initial therapy
- Role of patient preferences: some role for shared decision-making
- Policy level: recommendation

Statement 6. Treatment Failure for Acute Bacterial Rhinosinusitis (ABRS)

If the patient worsens or fails to improve with the initial management option by 7 days after diagnosis, the clinician should reassess the patient to confirm ABRS, exclude other causes of illness, and detect complications. If ABRS is confirmed in the patient initially managed with observation, the clinician should begin antibiotic therapy. If the patient was initially managed with an antibiotic, the clinician should change the antibiotic. *Recommendation based on randomized controlled trials with limitations supporting a cut point of 7 days for lack of improvement and expert opinion and first principles for changing therapy with a preponderance of benefit over harm.*

Evaluating Treatment Failures of Presumed ABRS

If the patient worsens or fails to improve with the initial management option by 7 days after diagnosis, the clinician should reassess the patient to confirm ABRS, exclude other causes of illness, and detect complications.

Worsening is defined as progression of presenting signs or symptoms of ABRS or onset of new signs or symptoms.

Failure to improve is lack of reduction in presenting signs or symptoms of ABRS by 7 days after diagnosis, which would not apply if the patient had persistent, yet gradually improving, symptoms.

A clinical diagnosis of ABRS is confirmed when the patient's pattern of illness corresponds to the definition in Table 5.

The rationale for using a cut point of 7 days after initial diagnosis to assess treatment failure for ABRS is based on clinical outcomes in RCTs. Between 7 and 12 days after trial enrollment 73% of patients randomized to placebo have clinical improvement, rising to 85% when antibiotics are administered (Table 7). Defining treatment failure as a lack of clinical improvement within 7 days would therefore result in an acceptable percentage of poor outcomes. Conversely, rates of improvement at 3 to 5 days are only 30% for placebo with a nonsignificant rise to 41% for antibiotic (Table 7). A cut point of 5 days, therefore, would overdiagnose treatment failure. Similarly, using a stricter criterion of clinical cure (instead of improvement) would result in a failure rate of over 50% at 7 to 12 days.

Patients included in RCTs may not have identical risk factors or illness severity when compared to patients not included in (or excluded from) RCTs. Therefore, a 7-day cut

point for improvement may not apply to patients with severe illness, complicated sinusitis, immune deficiency, prior sinus surgery, or coexisting bacterial illness; the clinician should also consider the patient's age, general health, cardiopulmonary status, and comorbid conditions in determining an appropriate cut point for assessing treatment failure.

Patients who are treatment failures, especially those with a worsening pattern of illness, should be examined for complications of ABRS that include orbital or intracranial spread of infection. Suggestive findings on physical examination include proptosis, visual changes, severe headache, abnormal extraocular movements, changes in mental status, and periorbital inflammation, edema, or erythema. A severe headache may also indicate acute frontal or sphenoidal sinusitis, which can represent a medical emergency because of increased risk of intracranial complications.[124] Acute frontal sinusitis typically causes severe headache localized to the forehead over the orbits, with tenderness produced by pressure on the floor of the frontal sinus. Sphenoidal sinusitis typically causes a dull ache in the back of head, specifically over the occiput, with radiation to the frontal and retro-orbital regions.

Managing ABRS Initial Treatment Failures

If the diagnosis of ABRS is confirmed and the treatment failure involves a patient managed initially with observation, the clinician should begin treatment with amoxicillin as discussed in the preceding section. For penicillin-allergic patients, folate inhibitors (trimethoprim-sulfamethoxazole) or a macrolide antibiotic may be used.

If treatment failure is observed following 7 days of antibiotic therapy, a nonbacterial cause or infection with drug-resistant bacteria should be considered and should prompt a switch to alternate antibiotic therapy and reevaluation of the patient. When a change in antibiotic therapy is made, the clinician should consider the limitations in coverage of the initial agent.[4]

Very few studies have investigated the microbiology of treatment failure in ABRS; however, those that cultured sinus material identified a large percentage of bacteria with reduced susceptibility to the original antibiotic.[125-128] For example, in patients receiving amoxicillin, it is common to identify a beta-lactamase–producing *H. influenzae* or *M. catarrhalis*. Recovery of *S. pneumoniae* with reduced susceptibility to beta-lactams, macrolides, tetracyclines, and trimethoprim-sulfamethoxazole is also common, and has been strongly correlated with previous antibiotic therapy.

Optimal antibiotic therapy in patients with ABRS treatment failure has not been studied, but the choice of antibiotic should be based on adequate coverage of anticipated bacteria. This decision should consider the prior antibiotic used, anticipated susceptibility of bacterial pathogens, and the ability of antibiotics to produce adequate exposure at the site of infection. As discussed above, beta-lactam–, macrolide-, tetracycline-, and trimethoprim-sulfamethoxazole–resistant *S. pneumoniae* and beta-lactamase–producing *H. influenzae* and *M. catarrhalis* are more common following previous antibiotic exposure.[129-133]

Predicting the likelihood of adequate antibiotic coverage for resistant organisms is addressed by studies of pharmacokinetics, in vitro susceptibility testing, and minimum inhibitory concentration.[134-137] Experimental and clinical studies suggest a relationship between treatment outcomes and pharmacodynamic concepts, but involve extrapolations from acute otitis media and community-acquired pneumoniae. Optimal therapy of multidrug-resistant *S. pneumoniae* and beta-lactamase–producing *H. influenzae* and *M. catarrhalis* would include high-dose amoxicillin-clavulanate (4 g per day amoxicillin equivalent) or a respiratory fluoroquinolone (levofloxacin, moxifloxacin, gemifloxacin). These agents would also cover less common pathogens, such as *S. aureus* and anaerobic bacteria. Conversely, cephalosporins and macrolides are predicted to offer inadequate coverage for *S. pneumoniae* or *H. influenzae*. Patients with penicillin allergy could receive a fluoroquinolone.

Evidence Profile

- Aggregate evidence quality: Grade B, randomized controlled trials with limitations supporting a cut point of 7 days for lack of improvement; Grade D, expert opinion and first principles for changing therapy
- Benefit: prevent complications, detect misdiagnosis, institute effective therapy
- Harm: delay of up to 7 days in changing therapy if patient fails to improve
- Cost: medication cost
- Benefits-harm assessment: preponderance of benefit over harm
- Value judgments: avoid excessive classification as treatment failures because of a premature time point for assessing outcomes; emphasize importance of worsening illness in definition of treatment failure
- Role of patient preferences: limited
- Potential exceptions: include but are not limited to severe illness, complicated sinusitis, immune deficiency, prior sinus surgery, or coexisting bacterial illness; the clinician should also consider the patient's age, general health, cardiopulmonary status, and comorbid conditions in determining an appropriate cut point for assessing treatment failure
- Policy level: recommendation

Statement 7a. Diagnosis of Chronic Rhinosinusitis or Recurrent Acute Rhinosinusitis

Clinicians should distinguish chronic rhinosinusitis and recurrent acute rhinosinusitis from isolated episodes of acute bacterial rhinosinusitis and other causes of sinonasal symptoms. *Recommendation based on cohort and observational studies with a preponderance of benefit over harm.*

Table 10
Chronic and recurrent rhinosinusitis definitions

Term	Definition
Chronic rhinosinusitis (CRS)	Twelve (12) weeks or longer of two or more of the following signs and symptoms: • mucopurulent drainage (anterior, posterior, or both) • nasal obstruction (congestion), • facial pain-pressure-fullness, or • decreased sense of smell AND inflammation is documented by one or more of the following findings: • purulent (not clear) mucus or edema in the middle meatus or ethmoid region, • polyps in nasal cavity or the middle meatus, and/or • radiographic imaging showing inflammation of the paranasal sinuses
Recurrent acute rhinosinusitis	Four (4) or more episodes per year of ABRS without signs or symptoms of rhinosinusitis between episodes: • each episode of ABRS should meet diagnostic criteria in Table 5

Definitions

Chronic rhinosinusitis (CRS) and recurrent acute rhinosinusitis are temporal- and frequency-based patterns of illness (Table 10) that are distinct from isolated episodes of ABRS.[9,45,138] In both diagnoses, the clinical presentation, disease impact, subsequent diagnostic evaluation, and therapy differ significantly from ABRS. Furthermore, because of the chronicity and variety of symptoms that accompany CRS and recurrent acute rhinosinusitis, these should be distinguished from other causes of symptoms that are commonly associated with sinonasal disorders.

Chronic Rhinosinusitis

Symptoms of CRS vary in severity and prevalence. Nasal obstruction is most common (81%-95%), followed by facial congestion-pressure-fullness (70%-85%), discolored nasal discharge (51%-83%), and hyposmia (61%-69%).[139-140] The presence of two or more signs or symptoms persisting beyond 12 weeks is highly sensitive for diagnosing CRS, but symptom-based criteria alone are relatively nonspecific.[19,58,141-142] *Consequently, diagnosing CRS requires that inflammation be documented in addition to persistent symptoms*.[19,138,143] Rarely, CRS may be suspected based primarily on objective findings (eg, nasal polyps or CT imaging) when other conditions have been excluded.

CRS has a substantial negative health impact with respect to mood, bodily pain, energy level, physical functioning, and social functioning in addition to local sinonasal symptoms.[22-24] In some domains of general health, medically resistant chronic sinusitis is substantially more debilitating than angina, congestive heart failure, chronic obstructive pulmonary disease, and chronic back pain or sciatica.[24] CRS impacts both patients and the health-care system, requiring repeated physician office visits, prescription medications, over-the-counter medications, and surgical therapy.

Distinguishing CRS from conditions with similar symptoms is difficult but important. Using CT imaging as the criterion standard, the true prevalence of CRS in patients referred for evaluation of potential CRS based on patients' reported symptoms ranges from 65% to 80%.[19] This prevalence may be lower in primary care settings. CRS may be accompanied by headache, fever, cough, halitosis, fatigue, dental pain, and other nonspecific signs or symptoms. Therefore, the differential diagnosis of CRS includes allergic rhinitis, nonallergic rhinitis, vasomotor rhinitis, eosinophilic nonallergic rhinitis, nasal septal deformity, and nonrhinogenic causes of facial pain. The latter include neurologic disorders, such as vascular headaches, migraine, trigeminal neuralgia, and other facial pain syndromes.[144-146]

Other forms of sinusitis not directly within the scope of this guideline may produce symptoms compatible with CRS. These entities include allergic fungal rhinosinusitis and invasive fungal rhinosinusitis.[147] In the appropriate clinical setting, such as the immunocompromised state or obvious evidence of facial deformity adjacent to the paranasal sinuses, patients with more aggressive forms of sinusitis should be appropriately diagnosed with the aid of nasal endoscopy, imaging studies, or both.

Recurrent Acute Rhinosinusitis

Recurrent acute rhinosinusitis is diagnosed when 4 or more episodes of ABRS occur per year, without signs or symptoms of rhinosinusitis between episodes.[45] Although recognized as a distinct form of rhinosinusitis, only a few cohort studies have documented the characteristics and clinical impact of recurrent acute rhinosinusitis. The frequency cutoff for a minimum number of episodes to be considered for the diagnosis of recurrent acute rhinosinusitis has varied in literature ranging from 2 episodes to 4 episodes per year.[148-149] Recent consensus from a multidisciplinary panel has reaffirmed a minimum cutoff of 4 or more episodes per year of ABRS.[138]

RCTs for preventing the common cold indicate that the average adult has 1.4 to 2.3 episodes per year.[150,151] Although select individuals may be more likely to develop ABRS after a URI than others,[56,148] the average adult would be expected to have less than one ABRS episode annually.

Considering the difficulties in distinguishing ABRS from viral illness, adopting a cutoff closer to the natural frequency of the common cold (ie, 2.0 infections per year) would result in unnecessary diagnostic overlap. Thus, establishing a minimum cutoff frequency of 4 infections per year should reduce the chance that patients with frequent URIs are misdiagnosed as recurrent acute rhinosinusitis.

The proper diagnosis of recurrent acute rhinosinusitis requires that each episode meet the criteria for ABRS (Table 4). Confirming a true bacterial episode of rhinosinusitis is difficult, but highly desirable, for substantiating an underlying diagnosis of recurrent acute rhinosinusitis. In such cases, examination of the patient during an episode of ABRS (among the 4 episodes occurring per year) may be necessary to corroborate the diagnosis.[149] Examination of the middle meatus for purulence in the decongested state may strongly suggest ABRS and allows endoscopically guided culture.[152] Polyps in the nasal cavity may suggest an underlying diagnosis of acute exacerbations of CRS rather than recurrent acute rhinosinusitis. CT imaging during acute rhinosinusitis is not recommended because it cannot distinguish ABRS from VRS.[56]

Recurrent acute rhinosinusitis should be distinguished from isolated ABRS because of a greater disease burden, diagnostic approach, and approach to management. The symptom burden of recurrent acute rhinosinusitis is similar to CRS, but antibiotic utilization is higher.[149] Patients with both conditions may benefit from nasal culture or imaging studies. For recurrent acute rhinosinusitis, however, culture is most useful during an acute episode and imaging is most useful between episodes to identify anatomical changes that may predispose to recurrent disease. An allergy-immunology evaluation may be considered to detect coexisting allergic rhinitis or an underlying immunologic deficiency. Last, surgical intervention is not appropriate for uncomplicated ABRS but may have a role in managing CRS and recurrent acute rhinosinusitis.[153]

Evidence Profile

- Aggregate evidence quality: Grade C, cohort and observational studies
- Benefit: distinguish conditions that might benefit from additional diagnostic evaluation and management from isolated cased of ABRS
- Harm: potential misclassification of illness because of overlapping symptomatology with other illnesses
- Cost: none
- Benefits-harm assessment: preponderance of benefit over harm
- Value judgments: importance of accurate diagnosis
- Role of patient preferences: not applicable
- Policy level: recommendation

Statement 7b. Modifying Factors

Clinicians should assess the patient with chronic rhinosinusitis or recurrent acute rhinosinusitis for factors that modify management, such as allergic rhinitis, cystic fibrosis, immunocompromised state, ciliary dyskinesia, and anatomic variation. *Recommendation based on observational studies with a preponderance of benefit over harm.*

Supporting Text

In contrast to ABRS, CRS and recurrent acute rhinosinusitis have potential predisposing factors that may contribute to illness persistence, recurrence, or both.[45] Allergic rhinitis,[154] cystic fibrosis,[155] immunocompromised state,[156] ciliary dyskinesia,[157] and anatomic variation are some factors that have been investigated in this regard. Ideally, early identification of factors contributing to the recurrence or persistence of rhinosinusitis could play a crucial role in selecting the most appropriate treatment for individual patients.

Allergic rhinitis is more often associated with CRS and recurrent acute rhinosinusitis than isolated ABRS.[158-160] Furukawa and colleagues[161] found that patients with allergic rhinitis documented during enrollment in two antibiotic studies experienced more frequent rhinosinusitis episodes than those without allergies. More recently, patients followed within a health-care system with the diagnosis of recurrent acute rhinosinusitis or CRS had a 57% prevalence of a positive in vitro or skin allergy test.[162] Similar findings have been reported by other investigators.[159,163] Data supporting a link between allergy and CRS or recurrent acute rhinosinusitis have been criticized, however, because of investigator bias and retrospective design.[44]

Edema caused by allergic rhinitis may obstruct the paranasal sinuses,[164] and this concept is supported by a higher prevalence of mucoperiosteal disease on CT imaging in patients with allergies compared to others without.[158,165] Further, a hyperresponsive state associated with allergic rhinitis may increase susceptibility to inflammation within the nose and paranasal sinuses, thereby predisposing to rhinosinusitis.[166] Signs of hyperresponsiveness in rhinosinusitis-prone patients with allergic rhinitis, as compared to patients without recurrent illness, are manifest as differences in cytokine concentrations, lysozyme, and other measures of cellular inflammation.[167-171]

The association between *cystic fibrosis* and CRS is well recognized,[172] with a 43% prevalence of nasal polyps in afflicted patients.[173] Symptoms of CRS are reported by 36% of obligate carriers of a cystic fibrosis gene mutation,[174] compared with a background prevalence of CRS estimated between 13% and 14%.[13,175] The most common mutation identified in a subgroup of this study population was ΔF508, which was present in 72% of the study group regardless of CRS presence or absence.[174] The association of cystic fibrosis mutation and CRS has been assessed in different fashions and within different populations, sometimes yielding conflicting results. In Finland, where the reported incidence of mutation carriage is about 1:80, only 1:127 patients with CRS screened for ΔF508 and 394delTT revealed the presence of a cystic fibrosis mutation.[176]

Table 11
Diagnostic tests for chronic rhinosinusitis and recurrent acute rhinosinusitis

	Nasal endoscopy	Radiographic imaging	Allergy and immune testing
Chronic rhinosinusitis	Evaluate inflammatory mucosal disease, obstructions, and masses; obtain middle meatal cultures	Evaluate inflammatory disease and anatomic obstruction	Detect allergies and immunodeficient states
Recurrent acute rhinosinusitis	Confirm purulent discharge for diagnosis; evaluate obstructions and obtain middle meatal cultures	Evaluate anatomic obstruction	Detect allergies and immunodeficient states

Several *immunodeficient states* have been documented in patients with CRS or recurrent acute rhinosinusitis,[177-179] supporting the role of immunological testing when evaluating patients with refractory or recurrent disease.[178] Common immunodeficiencies identified have included decreases in serum IgA, IgG and its subclasses, and abnormalities in markers of T-lymphocyte function.[178,179] Further, correcting the underlying immune deficiency can result in clinical improvement of CRS.[177]

Ciliary dyskinesia may account for the decreased mucociliary clearance observed in CRS.[180-183] The normal mucociliary transit time (MTT) of 10 to 14 minutes increases significantly when CRS is present.[182] Increased MTT has been identified in a growing number of patients with human immunodeficiency virus and has been implicated in this population's increased risk of recurrent rhinosinusitis.[183] Not all studies, however, support the role of decreased mucociliary function in the pathogenesis of CRS. Ciliary beat frequency in mucosa from the nose and paranasal sinuses of patients with CRS showed no difference compared to normal controls, and frequency was increased in specimens recovered from patients with nasal polyposis.[181]

Early research on the pathogenesis of CRS and recurrent acute rhinosinusitis focused on *anatomic abnormalities*,[184-187] which could obstruct the paranasal sinuses and trigger infection.[188,189] Based upon this assumption, descriptions of anatomic relationships, variances, associations with adjacent anatomic regions, and the importance of accurate radiographic data upon surgical planning and intervention have populated the literature.[190-195] Nonetheless, evidence is lacking regarding a causal relationship between anatomic abnormalities and chronic or recurrent disease. Some indirect support for this concept, however, is offered by studies that show improvement in objective measures of CRS status after surgical correction of obstruction and anatomic abnormalities.[196-197]

Evidence Profile

- Aggregate evidence quality: Grade C, observational studies
- Benefit: identify modifying factors that would alter management of CRS or recurrent acute rhinosinusitis; identify conditions that require therapy independent of rhinosinusitis
- Harm: identifying and treating incidental findings or subclinical conditions that might not require independent therapy; morbidity related to specific tests
- Cost: variable based on testing ordered
- Benefits-harm assessment: preponderance of benefit over harm
- Value judgments: consensus that identifying and managing modifying factors will improve outcomes
- Role of patient preferences: limited
- Policy level: recommendation

Statement 8a. Diagnostic Testing

The clinician should corroborate a diagnosis and/or investigate for underlying causes of chronic rhinosinusitis and recurrent acute rhinosinusitis. *Recommendation based on observational studies with a preponderance of benefit over harm.*

Supporting Text

The clinician should corroborate a diagnosis of CRS or recurrent acute rhinosinusitis to avoid mistaking these entities for neoplastic disorders, other causes of headaches or facial pain, anatomic abnormalities that obstruct the nasal cavity, and underlying systemic disease that may predispose to recurrent infection. Diagnostic tests that may be used to corroborate a diagnosis or investigate for underlying causes of CRS and recurrent acute rhinosinusitis include nasal endoscopy, radiographic imaging, and allergy and immune testing. The utility of each investigation based on disease type is summarized in Table 11.

Nasal Endoscopy: Endoscopic evaluation is generally an office procedure utilized to evaluate the inflammatory status of the sinonasal mucosa, and to assess nasal masses or lesions that are noted on physical examination.[198] In addition, middle meatal cultures may be obtained under endoscopic guidance to direct antibiotic choice.[47,152] Endoscopic findings can be divided into inflammatory, neoplastic, and anatomic. Scoring systems to quantify inflammatory disease have been utilized and endoscopy scores have been shown to correlate with CT scores.[199,200]

Radiographic Evaluation: CT is considered the gold standard for radiographic evaluation of the paranasal sinuses and enables an understanding of the patency of the intercommunicating passages of the sinuses and how inflammatory disease, anatomic variation, or both infringe on the patency of these channels.[201] CT can quantify the extent of inflammatory disease based upon opacification of the paranasal sinuses;[198] however, patient symptoms and quality of life do not necessarily correlate with the extent of disease seen on CT.[19,20,141]

Allergy and Immunology Evaluation: Evidence supports the association of allergy and rhinosinusitis in adults.[159,202-206] Most patients with extensive sinus disease, quantified by CT, have demonstrated evidence of allergy,[165,207] and about twice as many patients with allergic rhinitis, compared with normal subjects, have abnormal CT scans (67% vs 33%).[208] Identification of allergies, however, does not imply they are the only cause of sinusitis, and other factors should be considered.

An immunodeficient state should be suspected in patients with CRS or recurrent acute rhinosinusitis when other causes have been excluded,[209] especially when rhinosinusitis is associated with otitis media, bronchitis, bronchiectasis, or pneumonia. Similarly, patients with persistent recurrent purulent infections despite surgical intervention should have immune testing. The test battery might include measurement of quantitative serum IgG, IgA, and IgM levels and assessment of specific antibody responses to protein and polysaccharide antigens, such as tetanus toxoid or pneumococcal polysaccharide vaccine.[34]

Evidence Profile

- Aggregate evidence quality: Grade C, observational studies
- Benefit: corroborate diagnosis and identify underlying causes that may require management independent of rhinosinusitis for symptom relief
- Harm: relates to the specific test or procedure
- Cost: relates to the specific test or procedure
- Benefits-harm assessment: preponderance of benefit over harm
- Value judgments: identifying and managing underlying conditions will improve outcomes
- Role of patient preferences: limited
- Policy level: recommendation

Statement 8b. Nasal Endoscopy

The clinician may obtain nasal endoscopy in diagnosing or evaluating a patient with chronic rhinosinusitis or recurrent acute rhinosinusitis. *Option based on expert opinion and a preponderance of benefit over harm.*

Supporting Text

A diagnosis of CRS requires documentation of inflammation by examination (anterior rhinoscopy or nasal endoscopy) or radiographic imaging, in addition to persistent signs and symptoms (Table 10). Findings on examination that support a diagnosis of CRS include purulent (not clear) mucus or edema in the middle meatus or ethmoid region, or polyps in the nasal cavity or middle meatus.[9,44,138]

Patients with CRS or recurrent acute rhinosinusitis may manifest findings in the nasal cavity, nasopharynx, or paranasal sinuses that assist in diagnosis, require targeted management, or both. Examples include abnormalities directly related to CRS or recurrent acute rhinosinusitis, such as nasal polyps, purulent nasal discharge, and septal deviation. Alternative findings that may suggest a more complicated or different disease process include neoplasms, soft tissue masses, foreign objects, tissue necrosis, and findings consistent with autoimmune or granulomatous disease.

CRS or recurrent acute rhinosinusitis implies persistent disease that is unlikely to resolve without intervention tailored to the etiology. To diagnose and monitor these entities, evaluations that go beyond anterior rhinoscopy should be obtained.[34,45,124] Anterior rhinoscopy allows visualization of the anterior one-third of the nasal cavity with direct illumination and a speculum or other instrument to dilate the nasal vestibule. In contrast, nasal endoscopy also allows visualization of the posterior nasal cavity, nasopharynx, and, in some instances, the sinus drainage pathways in the middle meatus and superior meatus. Thus, nasal endoscopy allows identification of posterior septal deviation, and polyps or secretions in the posterior nasal cavity, within the middle meatus, or in the sphenoethmoidal recess. Further, nasal endoscopy allows directed aspiration of abnormal secretions for analysis and culture.

Nasal endoscopy involves placement of an endoscope inside the nose to capture images of the nasal cavity and sinus openings that are otherwise not visible by simple inspection of the nasal cavity with a nasal speculum and illumination.[200] Nasal endoscopy can be performed with a flexible or rigid endoscope, typically after a topical decongestant and anesthetic are applied to the nasal mucosa. Nasal endoscopy allows visualization of the nasal cavity; inferior turbinate, inferior meatus, and nasopharynx; sphenoethmoidal recess and sphenoidal ostium behind the middle and supreme turbinate; and middle meatus, including the uncinate process, hiatus semilunaris, maxillary ostia, nasofrontal recess, and anterior ethmoidal bulla.

Nasal endoscopy has potential risks. Hemorrhage secondary to mucosal trauma and pain during inspection and middle meatal culture may be experienced, although the latter is brief and usually tolerable. In patients with a history of bleeding diathesis, or patients who are anti-coagulated, nasal endoscopy should be approached with care. Adverse reactions to topical anesthetic and decongestant agents may occur. Without proper infection control precautions, cross-contamination and disease transmission among patients may occur. Last, nasal biopsy can rarely result in life-threatening hemorrhage, pain, or possible central nervous system and ocular injury; as such, general anesthesia with airway pro-

tection should be considered for pathology requiring nasal biopsies.[210]

Evidence Profile

- Aggregate evidence quality: Grade D, expert opinion
- Benefit: confirm diagnosis of CRS; detect structural abnormalities, masses, lesions; perform biopsy or culture
- Harm: adverse effects from topical decongestants, anesthetics, or both; discomfort; hemorrhage; trauma
- Cost: procedural cost
- Benefits-harm assessment: preponderance of benefit over harm
- Value judgments: importance of a detailed, complete intranasal examination
- Role of patient preferences: limited
- Policy level: option

Statement 8c. Radiographic Imaging

The clinician should obtain computed tomography (CT) of the paranasal sinuses in diagnosing or evaluating a patient with chronic rhinosinusitis or recurrent acute rhinosinusitis. *Recommendation based on diagnostic and observational studies and a preponderance of benefit over harm.*

Supporting Text

A diagnosis of CRS requires documentation of inflammation by examination (anterior rhinoscopy or nasal endoscopy) or radiographic imaging, in addition to persistent signs and symptoms (Table 10). CT imaging without intravenous contrast can be used to establish the presence of inflammation in the paranasal sinuses.[9,44,138] CT imaging findings also correlate with the presence or absence of CRS in patients with suggestive clinical symptoms.[139,211]

CT imaging without intravenous contrast plays a significant role in evaluating patients diagnosed with CRS or recurrent acute rhinosinusitis. Although CT findings do not necessarily correlate with symptom severity, they offer an objective method for monitoring recurrent or chronic disease.[58,212] Mucosal abnormalities, sinus ostial obstruction, anatomic variants, and sinonasal polyposis are best displayed on CT. The appearance of the mucosa, however, is nonspecific, and mucosal thickening should be interpreted in the context of clinical examination, nasal endoscopy, or both.[213]

An important role of CT imaging in this patient population is to exclude aggressive infections or neoplastic disease that might mimic CRS or recurrent acute rhinosinusitis. Osseous destruction, extra-sinus extension of the disease process, and local invasion suggest malignancy. If any such findings are noted, magnetic resonance (MR) imaging should be performed to differentiate benign obstructed secretions from tumor, and to assess for intracranial spread.[60]

CT of the paranasal sinuses should be obtained when endoscopic sinus surgery is considered or planned in patients with CRS or recurrent acute rhinosinusitis.[214] In addition to demonstrating abnormal mucosa and opacified sinuses, the study will provide the anatomic detail necessary to guide the surgery.[60,193] Anatomic variants that might predispose to sinus obstruction and inflammation are well displayed on CT and include septal deviation, concha bullosa, Haller cells, hypoplasia of the maxillary sinus, and narrowing or obstruction of the osteomeatal complex.

CT imaging of the paranasal sinuses had traditionally involved direct axial and coronal images to adequately visualize the osteomeatal complex. Multidetector CT is a newer technology that offers advantages over single detector imaging of the paranasal sinuses, because the patient is scanned once and all other planes (eg, coronal, sagittal) are reconstructed from the original data set. Multidetector CT imaging may reduce total radiation dose to the patient.

Evidence Profile

- Aggregate evidence quality: Grade C, diagnostic and observational studies
- Benefit: confirm diagnosis of CRS; detect structural abnormalities, masses, lesions
- Harm: radiation exposure
- Cost: procedural cost
- Benefits-harm assessment: preponderance of benefit over harm
- Value judgments: minimize radiation exposure and avoid unnecessary intravenous contrast
- Role of patient preferences: limited
- Policy level: recommendation

Statement 8d. Testing for Allergy and Immune Function

The clinician may obtain testing for allergy and immune function in evaluating a patient with chronic rhinosinusitis or recurrent acute rhinosinusitis. *Option based on observational studies with an unclear balance of benefit vs harm.*

Supporting Text

The prevalence of allergic rhinitis is 40% to 84% in adults with CRS[159,202] and 25% to 31% in young adults with acute maxillary sinusitis.[204,215] Extensive sinus disease, as quantified by sinus CT imaging, is associated with allergy in 78% of patients and asthma in 71%.[165,207] In addition, patients with both allergy and CRS are more symptomatic than nonallergic patients with similar CT findings.[158,216] About twice as many patients with allergic rhinitis, compared with normal subjects, have abnormal CT scans.[208] In one study of 200 patients with CRS more than half had allergic rhinitis, which was considered the most important underlying cause of sinusitis.[206]

Allergy testing should be considered in patients with CRS or recurrent acute rhinosinusitis. If allergy testing is

positive, and appears clinically relevant based on individual assessment, management may include environmental control measures, pharmacologic therapy, or immunotherapy as an immunomodulating approach. Although recommended,[34,44] limited data exist to support improvements in CRS or recurrent acute rhinosinusitis from allergen avoidance, immunotherapy, or both, in the allergic patient with sinusitis.

Allergy skin tests are the preferred method for detecting IgE-mediated sensitivity. For most allergens, in vitro allergen-specific immunoassays detect IgE-specific antibody in the serum of most, but not all, patients who respond clinically to those allergens. The sensitivity of immunoassay compared with prick or puncture skin tests ranges from 50% to 90%, with an average of 70% to 75% for most studies.[217] A direct correlation for clinical disease cannot be assumed by evidence provided from skin testing or in vitro allergen-specific immunoassays unless results are interpreted by a qualified physician based on history and physical examination obtained on face-to-face contact with the patient.

Immunodeficiency should be considered in patients with CRS or recurrent acute rhinosinusitis, particularly when aggressive management has failed[178] or the patient has persistent purulent infection. One study of recurrent acute rhinosinusitis that was refractory to therapy found only 8 (3%) of 245 patients to have hypogammaglobulinemia, impaired pneumococcal vaccine responses, or both (May 1999). Another study of 79 patients with sinusitis diagnosed radiographically and refractory to medical and surgical therapy revealed 10% of patients to have common variable immunodeficiency and 6% to have IgA deficiency.[178] Sinusitis is a recurrent or chronic problem in 30% to 68% of patients with HIV infection.[218]

The most common primary immunodeficiency disorders associated with recurrent acute rhinosinusitis as a clinical feature are humoral immunodeficiencies, such as selective IgA deficiency, common variable immunodeficiency, and hypogammaglobulinemia. Patients may also have comorbid infections that include bronchitis, bronchiectasis, or recurrent otitis media. The connection of IgG subclass deficiency to recurrent or chronic sinusitis is controversial, and the clinical significance of abnormal IgG subclass levels in patients with recurrent infections is unclear.

Laboratory studies in patients with CRS or recurrent acute rhinosinusitis may include quantitative immunoglobulin measurements (IgG, IgA, and IgM), preimmunization and postimmunization specific antibody responses to tetanus toxoid and pneumococcal vaccine, and measurement of T cell number and function (delayed hypersensitivity skin tests and flow cytometric enumeration of T cells).

Evidence Profile

- Aggregate evidence quality: Grade C, observational studies
- Benefit: identify allergies or immunodeficient states that are potential modifying factors for CRS or recurrent acute rhinosinusitis
- Harm: procedural discomfort; instituting therapy based on test results with limited evidence of efficacy for CRS or recurrent acute rhinosinusitis; very rare chance of anaphylactic reactions during allergy testing
- Cost: procedural and laboratory cost
- Benefits-harm assessment: unclear balance of benefit vs harm
- Value judgments: need to balance detecting allergy in a population with high prevalence vs limited evidence showing benefits of allergy management on rhinosinusitis outcomes
- Role of patient preferences: role for shared decision making
- Policy level: option

Statement #9: Prevention

Clinicians should educate/counsel patients with chronic rhinosinusitis or recurrent acute rhinosinusitis regarding control measures. *Recommendation based on randomized controlled trials and epidemiologic studies with limitations and a preponderance of benefit over harm.*

Supporting Text

Primary prevention, by definition, reduces the risk of an initial rhinosinusitis episode. Patients with CRS or recurrent acute rhinosinusitis cannot prevent disease onset, but can engage in practices that may reduce the risk of developing VRS, which often precedes ABRS. Patients can minimize their exposure to pathogens by practicing good hand hygiene, especially when in contact with ill individuals. Washing hands with soap or using an alcohol-based hand rub is one of the most effective strategies for reducing the risk of developing VRS.[219]

Clinicians should counsel patients that smoking increases the risk of sinusitis. Secondary data analyses from the Third National Health and Nutrition Examination Survey, 1988-1994 examined the question if tobacco use or exposure to second-hand smoke was associated with an increased prevalence of sinusitis or sinus problems.[220] Based on survey data from more than 20,000 adults in the U.S. population, the prevalence of acute, recurrent, and chronic sinusitis is increased in cigarette smokers. Exposure to second-hand smoke was not found to increase the risk of sinusitis.

Secondary prevention minimizes symptoms and exacerbations of CRS and recurrent acute rhinosinusitis when symptoms are initially detected. Saline nasal irrigation is recommended for secondary prevention and after sinus surgery.[34,44,221] Benefits of nasal irrigation are improved mucociliary function, decreased nasal mucosal edema, and mechanical rinsing of infectious debris and allergens, each of which could improve nasal function, although the exact mechanism of action is not clearly understood.[222] Limited

evidence suggests that saline nasal irrigations relieve sinonasal symptoms and may reduce reliance on other medications.[223]

Several RCTs report improved nasal symptoms with isotonic or hypertonic saline solutions, with slightly greater benefits when hypertonic saline is used.[222,224,225] Mucociliary clearance times improve after irrigation, especially for buffered hypertonic saline.[80] All studies determined the efficacy of nasal irrigations in relieving sinonasal symptoms over brief follow-up periods of 4 to 6 weeks, and did not evaluate long-term or preventative benefits of saline nasal irrigations in CRS or recurrent acute rhinosinusitis. Metered nasal spray, nebulization, nasal douching, and bulb syringe irrigation have been shown to relieve symptoms in patients with CRS.[226-228]

Saline irrigation may be efficacious for secondary prevention of rhinosinusitis. In one unblinded RCT, daily hypertonic saline nasal irrigation improved disease-specific quality of life, requiring treatment of 2 patients (NNT) for a 10% improvement in survey scores after 6 months.[78] The definition of sinusitis, however, was ambiguous, and nearly all subjects were from a primary care setting. Adherence to therapy was 87%, but side effects included nasal irritation, nosebleeds, nasal burning, tearing, headaches, and nasal drainage. In an uncontrolled follow-up study,[229,230] a subset of patients reported reduced sinus symptoms and sinusitis-related medication use for an additional 12 months.

There are no studies to support superiority of a specific saline preparation (eg, hypertonic vs normal saline) for nasal irrigation. Patient education on nasal irrigations is most effective when instruction includes patient participation to achieve proficiency in performing this technique. Clinicians should work with patients to develop strategies that facilitate incorporating saline nasal irrigations as part of routine sinus care while minimizing side effects.

Secondary prevention also involves treatment of underlying conditions that may be associated with rhinosinusitis. A systematic review of the evidence linking gastroesophageal reflux (GERD) and sinusitis found weak evidence, consisting primarily of observational studies.[231] Although research in this area is quite limited, a pilot study demonstrated that treatment of GERD with a proton pump inhibitor may prevent CRS.[232]

Since CRS and recurrent acute rhinosinusitis have periods of symptom exacerbation, clinicians and patients should work together in developing treatment strategies that can minimize symptoms, promote recovery, and prevent recurrences. Including a multi-instructional approach that combines information with demonstration to educate patients on nasal irrigation (videotapes, illustrated booklets, interactive CD-ROM) may also help. Finally, incorporating individual preferences into a prevention regimen to improve adherence and minimize adverse effects is desirable.

Evidence Profile

- Aggregate evidence quality: Grade B, randomized controlled trials and epidemiologic studies with limitations
- Benefit: reduce symptoms and prevent exacerbations
- Harm: local irritation from saline irrigation
- Cost: minimal
- Benefits-harm assessment: preponderance of benefit over harm
- Value judgments: importance of prevention in managing patients with CRS or recurrent acute rhinosinusitis
- Role of patient preferences: substantial opportunities for shared decision making
- Policy level: recommendation

IMPLEMENTATION CONSIDERATIONS

The complete guideline is published as a supplement to *Otolaryngology–Head and Neck Surgery* to facilitate reference and distribution. The guideline will be presented to AAO-HNSF members as a miniseminar at the annual meeting following publication. Existing brochures and publications by the AAO-HNSF will be updated to reflect the guideline recommendations.

An anticipated barrier to the diagnosis of rhinosinusitis is the differentiation of VRS from ABRS in a busy clinical setting. This may be assisted by a laminated teaching card or visual aid summarizing diagnostic criteria and the time course of VRS. When diagnosed with VRS, patients may pressure clinicians for antibiotics, in addition to symptomatic therapy, especially when nasal discharge is colored or purulent. Existing educational material from the Centers for Disease Control (CDC) Get Smart Campaign can be used by clinicians to help clarify misconceptions about viral illness and nasal discharge.[233]

Anticipated barriers to using the "observation option" for ABRS are reluctance of patients and clinicians to consider observing a presumed bacterial illness, and misinterpretation by clinicians and lay press of the statement regarding observation of ABRS as a "recommendation" instead of an "option." These barriers can be overcome with educational pamphlets and information sheets that outline the favorable natural history of nonsevere ABRS, the moderate incremental benefit of antibiotics on clinical outcomes, and the potential adverse effects of orally administered antibiotics (including induced bacterial resistance).

Some patients and clinicians might object to amoxicillin as first-line therapy for ABRS, based on assumptions that newer, more expensive alternatives "must be" more effective. Most favorable clinical outcomes for nonsevere ABRS, however, result from natural history, not antibiotics, and randomized trials of comparative efficacy do not support superiority of any single agent for initial empiric therapy. Pamphlets may help in dispelling myths about comparative efficacy.

Barriers may also be anticipated concerning guideline statements for CRS and recurrent acute rhinosinusitis. The diagnostic criteria for these entities are unfamiliar to many clinicians, who might benefit from a summary card or teaching aid that lists these criteria along with those for ABRS and VRS. Performance of nasal endoscopy, allergy evaluation, and immunologic assessment, when appropriate, may be hindered by access to equipment and by procedural cost. Last, successfully achieving smoking cessation in patients with CRS or recurrent acute rhinosinusitis will require patient cooperation and clinician access to education materials and support services.

RESEARCH NEEDS

Research needs are as follows:

1) Define the natural history and management of subacute rhinosinusitis.
2) Determine the validity of diagnosing ABRS by patient history without confirmatory physical examination.
3) Refine and validate diagnostic criteria for VRS and ABRS.
4) Assess the validity of diagnosing ABRS before 10 days based on persistent fever plus concurrent purulent nasal discharge.
5) Determine whether a diagnostic algorithm tool would change physician behavior in terms of antibiotic prescription practices.
6) Assess the value of viral screening methods in the routine management of patients with suspected ABRS.
7) Conduct clinical trials to determine the efficacy of an "observation option" for nonsevere ABRS, by randomizing patients to immediate vs delayed antibiotics and assessing clinical outcomes.
8) Standardize the definition of "severe" illness in patients diagnosed with ABRS.
9) Conduct randomized controlled trials with superiority design that emphasize time to improvement/resolution, not just binary outcomes at fixed time points.
10) Perform RCTs of antibiotic vs placebo for ABRS in settings other than primary care, including emergency rooms and specialist offices.
11) Evaluate the role of analgesic therapy in managing rhinosinusitis and the comparative efficacy of different drug classes.
12) Assess the benefits of symptomatic therapy for VRS in properly conducted RCTs.
13) Assess the benefits of symptomatic therapy for ABRS in properly conducted RCTs.
14) Determine optimum salinity, pH, and regimen for administering nasal saline irrigation.
15) Devise strategies or treatment regimens to avoid the rebound effect of topical nasal decongestants.
16) Determine the comparative clinical efficacy of antibiotics for culture-proven ABRS using RCTs with standardized, uniform definitions of clinical disease, severity, and clinical outcomes.
17) Conduct RCTs to determine the benefits of efficacy of adjuvant therapy (nasal steroids, antihistamines, decongestants) in combination with antibiotics.
18) Acquire more evidence of which patients with ABRS are most suited for short-course antibiotic regimens.
19) Perform RCTs examining antibiotic efficacy among patient subpopulations; efficacy of fluoroquinolones relative to other antibiotics.
20) Include quality-of-life measures as study outcomes in RCTs.
21) Further assess the diagnosis of CRS and recurrent acute rhinosinusitis in primary care settings, rather than specialty clinic settings such as allergy and/or otolaryngology practices, because of biased disease prevalence.
22) Conduct investigations to further characterize the role of fungi in the etiology of inflammation of the paranasal sinuses.
23) Conduct investigations to determine the underlying cause of the inflammation that characterizes CRS and to determine the value of individualizing therapy based on this information.
24) Perform clinical trials to address outcomes of allergy management in patients with CRS or recurrent acute rhinosinusitis.
25) Perform clinical trials to address outcomes of detecting and managing immunodeficient states in patients with CRS or recurrent acute rhinosinusitis.
26) Validate nasal endoscopy scoring systems.
27) Assess the impact of intravenous immune globulin (IVIG) on CRS or recurrent acute rhinosinusitis in patients with humoral immune deficiency.
28) Conduct longitudinal studies with comparable control groups to evaluate long-term benefits of adjunctive therapies in the secondary prevention of CRS and recurrent acute rhinosinusitis.
29) Perform quantitative studies evaluating the impact of healthy lifestyle changes such as smoking cessation, dietary modification, and exercise on CRS.
30) Conduct RCTs of saline nasal irrigations as short-term vs long-term treatment for recurrent acute and chronic rhinosinusitis.

DISCLAIMER

As medical knowledge expands and technology advances, clinical indicators and guidelines are promoted as conditional and provisional proposals of what is recommended under specific conditions, but they are not absolute. Guidelines are not mandates and do not and should not purport to be a legal standard of care. The responsible physician, in light of all the circumstances presented by the individual patient, must determine the appropriate treatment. Adherence to these guidelines will not ensure successful patient

outcomes in every situation. The American Academy of Otolaryngology–Head and Neck Surgery (AAO-HNS), Inc. emphasizes that these clinical guidelines should not be deemed inclusive of all proper treatment decisions or methods of care, or exclusive of other treatment decisions or methods of care reasonably directed to obtaining the same results.

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