Washington State Health Care Authority

Health Technology Assessment

Imaging for Rhinosinusitis

Final Evidence Report

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A Health Technology Assessment

Prepared for Washington State Healthcare Authority

FINAL REPORT

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List of Key Abbreviations

CRS, chronic rhinosinusitis

CT, computed tomography

(F)ESS, (functional) endoscopic sinus surgery

IFRS, invasive fungal rhinosinusitis

MRI, magnetic resonance imaging

NPV, negative predictive value

PPV, positive predictive value

RS, rhinosinusitis

SFB, sinus fungus ball

US, ultrasound

EXECUTIVE SUMMARY

The **EXECUTIVE SUMMARY** summarizes background information, the methods and search results for this report, findings with respect to the Key Questions, and payer policies and practice guidelines. The **EXECUTIVE SUMMARY** also includes conclusions and an assessment of the quality of the evidence for each Key Question. In general, references are not cited in the **EXECUTIVE SUMMARY**. The **EXECUTIVE SUMMARY** ends with an **Overall Summary and Discussion**. The **TECHNICAL REPORT** provides additional detail, with full citation, regarding background information, study results, and payer policies and guidelines, but does not include conclusions or quality assessment.

Summary of Clinical Background

Rhinosinusitis: Prevalence and Clinical Definition

Sinusitis is a condition that is characterized by inflammation of the lining of the paranasal sinuses. Because the nasal mucosa is simultaneously involved and because sinusitis rarely occurs without concurrent rhinitis (i.e., irritation and inflammation of the mucous membrane inside the nose), rhinosinusitis (RS) is now the preferred term for this condition. RS affects an estimated 35 million people per year in the United States and accounts for close to 16 million office visits per year. Chronic RS (CRS) is one of the top 20 reasons for office visits per year. Sinusitis is more common from early fall to early spring. RS can be caused by or associated with viral, bacterial, or fungal infection. Alternatively, RS can be due to allergy. Acute bacterial RS develops in 0.5% to 2% of adults and 6% to 13% of children with upper respiratory tract infections (URIs). The prevalence of RS is greater in women (20.3%) than in men (11.5%). The diagnosis of RS historically has been made based on symptom-based criteria. Symptomatic criteria for a presumptive diagnosis of bacterial RS include: (1) URI symptoms lasting > 10 days, (2) symptoms that worsen after an initial improvement, or (3) severe symptoms or high fever (≥ 39°C/102°F). Prominent symptoms of bacterial RS include nasal congestion, purulent rhinorrhea, facial-dental pain, postnasal drainage, headache, and cough.

Although there is some variability in the literature, duration of RS is characterized as acute when lasting less than 4 weeks, subacute when lasting 4 to 8 weeks, and chronic when lasting longer than 8 weeks. RS may be further classified according to the pathogenic organism (viral, bacterial, or fungal) and presence of associated factors (e.g., nasal polyposis, immunosuppression). Most RS episodes are caused by viral infection. Rarely, sinusitis is caused by fungi. Fungal RS can be seen in both immunocompetent and immunocompromised patients. Immunocompetent patients with CRS may develop a noninvasive form of fungal RS that may manifest as either a fungus ball or allergic fungal RS. Immunocompromised patients may develop an invasive fungal RS, which is a rapidly progressive disease. Prompt diagnosis and treatment is necessary in this patient population, as invasive fungal RS has a very high morbidity and mortality rate.

Predisposing Factors

Allergies, trauma, environmental factors, cystic fibrosis, anatomic abnormalities, recent dental work, or, as previously noted, an immunocompromised state may predispose individuals to bacterial RS. Nasal polyps, which can cause nasal obstruction, congestion, facial pressure, and diminished sense of smell, often accompany CRS. Polyposis may be the result of chronic inflammation of the nasal lining.

Objective Confirmation of RS

Objective confirmation of RS can be challenging due to symptomatic overlap with many other diseases or conditions (e.g., septal deviation, migraine disorders, atypical facial pain). Many studies have found that self-reported symptoms do not correlate well with extent of imaging abnormality (stage) in CRS.

Lab Testing

The gold standard for diagnosis of a bacterial infection of the sinuses involves aspiration of a mucosal specimen from the parasinuses and analysis of the microbiology of the specimen. However, the invasive and painful nature of the procedure and the time required to complete the process make sinus aspiration impractical for daily practice. Therefore, aspiration is not recommended prior to empiric treatment with antibiotics. Endoscopically guided culture of the middle meatus are considered reasonable alternatives to sinus puncture, but such a procedure is beyond the skills of a typical primary care physician. Accurate diagnosis of fungal RS also depends on histopathology, which includes surgical biopsy of the sinonasal tissue. Optimal objective diagnostic technologies for RS remain elusive.

Endoscopy

Endoscopy is sometimes used by otolaryngology specialists to provide objective confirmation of a clinical diagnosis of RS. The procedure provides a complete view of the nose and sinuses. Endoscopic findings that are considered consistent with a diagnosis of CRS are purulent mucus and edema at the middle meatus or ethmoid region or polyps. Endoscopy has high specificity for RS but low sensitivity. Practice guidelines recommend that either computed tomography (CT) or nasal endoscopy be considered if antibiotic treatment for RS is not effective, especially for recurrent RS or CRS, but they do not recommend endoscopy prior to empiric treatment.

A recent systematic review of the diagnostic accuracy of endoscopy for CRS reported positive predictive values (PPVs) of 65% to 84% at prevalences (according to CT as the reference standard) ranging from 40% to 56% and negative predictive values (NPVs) of 30% to 39%. Although the review authors described CT as the usual reference standard for assessing the accuracy of endoscopy, they recommended *against* follow-up CT in patients with *positive* endoscopy findings since CT cannot provide conclusive results. The review authors further expressed the opinion that a follow-up CT in patients with *negative* endoscopy findings should be reserved only for patients with a prolonged or complicated course of RS. (The use of follow-up CT after endoscopy only where endoscopy findings are negative was also assumed in the economic evaluations reviewed as evidence for Key Question #5 in the present report.)

Imaging

In the case of acute RS, current guidelines recommend against the use of imaging for differentiating uncomplicated ABRS from viral infection. Although nasal endoscopy is considered a standard means of corroborating an uncertain clinical diagnosis of RS, this technology is not widely available to primary care, allergy, and infectious disease care providers. Therefore, CT of the paranasal sinuses, with its widespread availability and ability to accurately depict sinus anatomy, is most commonly used to support a clinical diagnosis of *chronic* RS and the potential utility of antibiotic treatment. Approximately 20% to 36% of patients with symptoms of CRS have CT-confirmed disease. Depending on the accuracy of CT for diagnosing CRS, these prevalence estimates suggest that a large proportion of patients treated empirically might be taking antibiotics unnecessarily. Bacterial resistance is a concern when antibiotics are overused. Imaging may be particularly helpful in the diagnosis of fungal RS, and CT is considered an option.

Although MRI is limited in its ability to define bone anatomy, it may be useful for evaluating suspected fungal RS or complications of RS. The use of plain radiographs (x-ray) and ultrasound (US) for the diagnosis of RS has also been investigated. US has limited utility but might be useful in pregnant women in order to avoid radiation exposure or for determining amounts of retained sinus secretions. Standard radiographs are limited in the evaluation of the paranasal sinuses because they cannot localize the pathology well. In addition, although standard radiographs are nonspecific due to many false-positives, they have been found to be fairly sensitive in detecting maxillary sinusitis.

The purpose of imaging in refractory RS is primarily to identify anatomic abnormalities that might explain continued disease, or to investigate suspicion of serious problems such as fungal infection, threat to nearby structures, abscess, or tumor. These situations represent causes or sequelae of RS that might be addressed by surgery or biopsy. Sinus CT is considered mandatory for presurgical planning. (See ***Treatment of RS*** for a summary of systematic reviews of the effectiveness of surgery for RS.)

See **Appendix V** for details on the recommendations of professional associations regarding imaging for RS, and **PRACTICE GUIDELINES** in the **EXECUTIVE SUMMARY** for a synthesis of recommendations.

An analysis of data from the National Ambulatory Medical Care Survey (NAMCS) for the years 2005 through 2008 found that advanced radiographic imaging (CT, MRI, or positron emission tomography [PET]) for evaluation of CRS was much more common in otolaryngology practice than in primary care practice: 16.0% versus 1.9% (P<0.001). Use of plain radiographs occurred with similar frequency between otolaryngology and primary care practices: 4.0% versus 3.4%. The majority of office visits for CRS were in primary care practices.

Radiographic Staging

The most commonly used system for grading the severity of CRS according to imaging findings is the Lund-Mackay system. The system can be used with any form of imaging. The scale ranges from 0 (absence of any radiographic opacification of the sinuses) to 24 (all sinuses completely opacified). A

study of asymptomatic individuals from the general population found a mean Lund-Mackay score of 4.3 (95% CI, 3.5 to 4.1). Accordingly, a typical cutoff value for diagnosing the presence of RS is 4.

Safety of Imaging

Potential adverse effects associated with radiation exposure are an important factor to consider when utilizing imaging examinations. The American College of Radiology (ACR) provides a relative radiation level (RRL) for CT and MRI based on effective dose (i.e., the radiation dose quantity that is used to estimate population total radiation risk). Because children are at higher risk from exposure, the RRL dose estimate ranges for children are lower compared with those specified for adults. The primary risk associated with exposure to ionizing radiation is cancer. It is estimated that approximately 1 in 1000 individuals will develop cancer from an exposure of 10 millisieverts (mSv). Although the overall risk of cancer from a diagnostic imaging procedure involving ionizing radiation is small, it is not 0. Therefore, care should be taken to limit patient radiation exposure.

Some authors have suggested that the rationale for empiric medical therapy (EMT) and a postponement of CT scanning is no longer valid since CT scans deliver lower doses of radiation, are more readily available, and are less expensive than when current practices were established. Cone beam CT (CBCT) technologies provide high-spatial-resolution visualization of high-contrast structures in the head and neck areas at a significantly lower level of radiation than a conventional CT scanner.

Treatment of RS

The potential clinical utility of imaging in the evaluation of RS depends in part on whether treatments recommended on the basis of imaging findings are effective. The spontaneous cure for viral sinusitis is 98%. Four of the reviewed practice guidelines issued a recommendation or option that antibiotics should only be prescribed in patients with severe or worsening symptoms of acute RS who have failed decongestant therapy, or who have complications of RS. One guideline stated that concern has been raised about the overdiagnosis of RS and unnecessary treatment with antibiotics. In a discussion section, this guideline states that appropriate criteria for the prescription of antibiotics are RS symptoms lasting 10 to 14 days, or severe symptoms of acute sinus infection, including fever with purulent nasal discharge, facial pain or tenderness, and periorbital swelling. However, 1 guideline made a strong recommendation to initiate antibiotic treatment as soon as the clinical diagnosis of acute RS is made). Patients with acute RS, when treated with appropriate antibiotics, usually improve quickly. The relapse rate after successful treatment is less than 5%. Practice guidelines recommend that if the patient fails to improve within 3 to 14 days of initiation of the antibiotic, the clinician should change to a second-line antibiotic. Estimates of the rate of adverse events due to antibiotic use for patients with symptoms of CRS range from 1% to 10%. However, the appropriateness of antibiotics has not been well established for either acute or chronic RS (see discussion below).

Other possible treatments include antihistamines for allergic RS, decongestants, and oral and topical steroids. Adjunctive treatments include saline, mucolytics, and expectorants. Surgery for purposes of removing infected mucosal material or correcting a complication such as abscess or polyps is sometimes considered necessary for refractory RS. Surgery may also be considered in a patient who is

immunosuppressed and at greater risk of invasive infection. Functional endoscopic surgery (FESS) sometimes referred to simply as endoscopy surgery (ESS), is the current approach to sinus surgery and comprises a variety of techniques. Surgery is much less likely to be performed in children than in adults.

The following discussion of different forms of treatment for RS includes findings from several systematic reviews and meta-analyses. In the reviews that provided a description of how RS was diagnosed or confirmed, study protocols represented a mix of RS diagnosed clinically and RS diagnosed on the basis of imaging and/or endoscopy in addition to clinical assessment. Subgroup analyses of treatment effectiveness according to method of diagnostic confirmation are discussed as indirect evidence for **Key Question #2** in the **LITERATURE REVIEW**.

Antibiotics

Three systematic reviews of antibiotics for acute RS concluded that they are modestly effective in adults and children but that they should be used with caution. A review of antibiotics for acute RS found that 80% of adults in placebo groups improved within 2 weeks after administration of the placebo. There is no evidence that antibiotic therapy for recurrent RS should differ from that of sporadic acute RS. One systematic review assessed the use of macrolides for CRS, but no comprehensive review of antibiotics for CRS was identified. Antibiotics were not found to be effective for RS in patients with cystic fibrosis. As noted earlier, a large proportion of patients treated empirically might be taking antibiotics unnecessarily. Bacterial resistance is a concern when antibiotics are overused.

Steroids

Small bodies of evidence suggest that topical (intranasal) steroids may be effective for acute RS either as monotherapy or as adjunctive therapy combined with antibiotics, and that oral (systemic) steroids have modest benefit for acute RS only when used as adjunctive therapy. Topical steroids have been found to be effective for CRS with nasal polyps, but their benefit for CRS without nasal polyps is uncertain. Similarly, oral steroids may be more beneficial for CRS with polyps than for CRS without polyps, but data are sparse. Preliminary evidence suggests that topical steroids are effective for allergic rhinosinusitis. A large body of randomized controlled trials (RCTs) has shown that topical and oral steroids improve olfactory symptoms due to CRS with polyps.

Immunotherapy

A systematic review of adjunctive immunotherapy for allergic rhinitis in presence of CRS or acute fungal RS included 7 studies (3 prospective controlled studies, 2 cross-sectional analyses of the same study, 1 retrospective case series, and 1 retrospective chart review) in 353 atopic patients with CRS with nasal polyps, CRS without nasal polyps, or acute fungal RS. Generally, symptom scores improved compared with baseline or control patients.

Ancillary Treatments

A systematic review of decongestants, antihistamines, and nasal irrigation for acute RS in children found no RCTs or quasi-RCTs that met inclusion criteria.

Surgery

Evidence collected by 4 recent systematic reviews failed to clearly demonstrate an advantage of endoscopic surgery over medical therapy in adults or children with CRS. The reviews did not provide detail on the specific surgical procedures performed. No systematic reviews of surgery for recurrent RS or for fungal RS were identified.

Policy Context

Radiological imaging for evaluation of RS, especially CRS, represents an area of substantial utilization in plans managed by the Washington HCA. Since imaging is insufficiently accurate to serve as the gold standard for diagnosis of RS, an understanding of its appropriate role is important. An evidence-based assessment of the accuracy of different imaging modalities for confirming or refining a diagnosis of RS and the impact on outcomes and cost is warranted to guide coverage policy.

Summary of Review Objectives and Methods

Review Objectives

Population: Adults and children diagnosed with or suspected of having chronic, acute, or recurrent rhinosinusitis (RS).

Interventions: Imaging technologies, including computed tomography (CT), magnetic resonance imaging (MRI), x-ray (plain radiography), and ultrasound (US).

Comparisons: Clinical diagnosis without imaging; another imaging modality.

Outcomes: Diagnostic performance (accuracy) in terms of sensitivity/specificity, positive predictive value (PPV)/negative predictive value (NPV), and positive/negative likelihood ratios; change in clinical management decisions or utilization; health outcomes such as improvement in symptoms, reduced incidence of episodes, improved quality of life (QOL), and prevention of disease-related complications; adverse events associated with imaging (e.g., radiation exposure); cost and cost-effectiveness.

Key Questions

1. What is the clinical performance (accuracy) of imaging technologies such as CT, MRI, x-ray, and US for evaluation of RS or related complications?
    1a. Does the clinical performance vary by imaging modality or technique?
2. What is the clinical utility of imaging for RS, i.e., what is the impact:
    2a. on clinical management decisions and utilization?
    2b. on health outcomes?

2c. according to different imaging modalities?

3. What are the safety issues associated with different forms of imaging technologies?
4. Does the diagnostic performance, impact on clinical management, impact on health outcomes, or incidence of adverse events vary by clinical history or patient characteristics (e.g., comorbidities, subtypes of RS)?
5. What are the cost and cost-effectiveness of imaging modalities in the diagnosis of sinusitis, including comparative costs and incremental cost-effectiveness when comparing modalities?

Analytic Framework

See **TECHNICAL REPORT, Review Objectives and Analytic Framework**.

Methods

See the **Methods** section of the **TECHNICAL REPORT**, **Appendix I**, and **Appendix II** for additional detail.

Search Strategy and Selection Criteria

Core databases, PubMed, and the websites of relevant specialty societies were searched for systematic reviews, meta-analyses, economic evaluations, and practice guidelines published in the last 10 years. Systematic reviews were selected if they reviewed studies considered eligible for answering the Key Questions or if they provided useful background information. No systematic reviews of direct evidence pertinent to the Key Questions were discovered. The PubMed (searched on October 24, 2014) and OVID-Embase (searched on November 7, 2014) databases were searched for primary studies and economic evaluations designed to answer the Key Questions. Update searches were conducted on January 14, 2015 and March 20, 2015.

Inclusion Criteria

- For Key Question #1 (accuracy):
  - Studies designed to assess clinical performance in terms of sensitivity and specificity or related measures in a population of patients with symptoms of RS.
  - Use of histopathology or mycology, skin prick, surgical findings, clinical follow-up, or intraoperative/postoperative outcomes as the reference standard.
  - For MRI, US, or x-ray as the index test, CT or endoscopy could be used as the reference standard. Although histopathology was the preferred reference standard for all imaging modalities, CT was considered an acceptable reference standard since, in practice, CT is considered the standard imaging choice for confirming or refining a diagnosis of RS. Using CT as the reference standard for alternative imaging modalities was thought to represent an indirect comparison with usual care.
  - For evaluation of the accuracy of CT, assessment of a global score or 1 or 2 features.
- For Key Question #2 (clinical utility):

- Randomized controlled trials (RCTs), nonrandomized trials, or observational studies comparing a group treated according to imaging results with a group treated without imaging, or comparing groups treated according to the results of different imaging modalities.

More detailed aspects of these criteria and the rationale for these criteria are presented in the **METHODS** section of the **TECHNICAL REPORT**.

Exclusion Criteria

- For Key Question #1:
  - Symptoms as the reference standard.
  - Accuracy measured only in terms of statistical association (e.g., correlation, chi-squared analysis of differences in prevalence).
  - Case-control studies in which the controls were "healthy controls," i.e., individuals who were not showing signs or symptoms of RS.
  - Use of imaging to describe or explore characteristics of RS or patients with RS and did not include a reference standard.
- For Key Question #2:
  - Case reports or case series.
- For any Key Question:
  - Use of imaging in inpatient settings (e.g., ventilator-induced sinusitis).
  - Non-English-language publication.

More detailed aspects of these criteria and the rationale for these criteria are presented in the **METHODS** section of the **TECHNICAL REPORT**.

Quality Assessment

The process used by Hayes for assessing the quality of primary studies and bodies of evidence is in alignment with the methods recommended by the GRADE Working Group. Like the GRADE Working Group, Hayes uses the phrase *quality of evidence* to describe bodies of evidence in the same manner that other groups, such as the Agency for Healthcare Research and Quality (AHRQ), use the phrase *strength of evidence*. A tool created for internal use at Hayes was used to guide interpretation and critical appraisal of economic evaluations. The tool for economic evaluations was based on best practices as identified in the literature and addresses issues such as the reliability of effectiveness estimates, transparency of the report, quality of analysis (e.g., the inclusion of all relevant costs, benefits, and harms), generalizability/applicability, and conflicts of interest. The Rigor of Development domain of the Appraisal of Guidelines Research and Evaluation (AGREE) tool, along with a consideration of commercial funding and conflicts of interest among the guideline authors, was used to assess the quality of practice guidelines. See the **Methods** section of the **TECHNICAL REPORT** and **Appendix II** for details on quality assessment methods.

Summary of Search Results

A total of 21 studies were selected for detailed analysis as evidence pertaining to the Key Questions, and these 21 studies were analyzed in the literature review: 14 studies addressed the accuracy of diagnostic or prognostic imaging (Key Question #1), 3 studies assessed the clinical utility of diagnostic imaging (Key Question#2), and 4 studies addressed cost issues related to imaging (Key Question #5). No unique studies were identified that addressed Key Question #3 and Key Question #4. The accuracy studies addressed acute RS, chronic RS (CRS), or fungal RS. No studies specifically addressing imaging for cases of recurrent RS were identified. However, guidelines do not make different recommendations regarding imaging for recurrent acute RS and CRS.

See **Appendix III** for a list of the 64 studies that were excluded from analysis after full-text review.

Six relevant practice guidelines published in the last 10 years were identified.

Findings

Summary of Findings tables follow each Key Question. See **EXECUTIVE SUMMARY, Methods,** *Quality Assessment* and the corresponding section in the **TECHNICAL REPORT**, as well as **Appendix II**, for details regarding the assessment of bodies of evidence. See **Appendix IV** for full evidence tables.

Key Question #1

Key Question #1: What is the clinical performance (accuracy) of imaging technologies such as CT, MRI, x-ray, and US for evaluation of rhinosinusitis or related complications? #1a: Does the clinical performance vary by imaging modality or technique?

Fourteen (14) studies assessing the accuracy of imaging for diagnosis or prognosis in acute RS, CRS, or fungal RS were selected. No studies specifically addressing imaging for cases of recurrent RS were identified.

Acute RS (3 Studies)

See **Table 1** for a summary of findings.

Clinical Performance of Imaging for Acute RS (Key Question #1)

Three studies reported consistently good results for sensitivity, but mixed results for specificity of maxillary sinus radiographs in patients with clinical suspicion of acute RS. All 3 studies evaluated the use of plain radiographs as the index test assessed against CT scans as the reference standard. One study took place in an emergency department and 2 studies took place in a radiology department. Sample sizes ranged from 30 to 47 patients. Patient age ranged from 5 to 83 years, but mean age ranged from 37 to 52 years. Only 1 of the 3 studies specified symptoms that were required for suspicion of RS, which included nasal obstruction, postnasal drip, mucus or pus-like nasal discharge, and halitosis in the nasal cavity. In all 3 studies, radiographs and CT scans were obtained within 2 weeks of each other.

Three small studies that assessed *radiographs against CT* found that views of the maxillary sinuses had *moderate to moderately high sensitivity*, *very low to high specificity*, *very low to high PPV*, *and very low to moderately high NPV for detecting acute RS*. The evidence was considered to be of low quality because of the small quantity of data, unexplained inconsistency with respect to specificity, inconsistency with respect to PPV and NPV due possibly to variation in prevalence, and the studies' use of another imaging modality as the reference standard. The variable specificity is especially relevant to an assessment of the value of imaging for diagnosis of acute RS, given that one component of the rationale for imaging in patients with suspected RS is to avoid unnecessary use of antibiotics. A low risk of false-negative results (missed cases), i.e., high sensitivity, might be deemed as relatively less important than a low risk of false-positive results, i.e., high specificity, since acute RS is not typically a serious disorder and there are harms associated with antibiotics. Furthermore, according to a Cochrane Review of antibiotics for acute maxillary sinusitis, approximately 80% of clinical research patients who were *not* treated with antibiotics improved spontaneously within 2 weeks after administration of a placebo. Thus, high sensitivity is not as important as high specificity for diagnosis of acute RS. Similarly, a high PPV might be valued over high NPV for acute RS since a high PPV would indicate that most patients with positive imaging results would be true candidates for treatment. Although a low NPV would indicate that a high proportion of patients with negative imaging results might be candidates for treatment, the risks associated with missed treatment are relatively low.

Evidence of the *clinical performance of any imaging modality other than radiographs for diagnosis* in patients with acute RS is insufficient due to the lack of studies.

Differential Clinical Performance by Imaging Modality for Acute RS (Key Question #1a)

Evidence regarding the *relative clinical performance of different imaging modalities for the same application* is insufficient due to the lack of studies evaluating different modalities against the same reference standard.

Table 1. Summary of Findings, Key Questions #1 and #1a: Acute RS

Key: CT, computed tomography; NPV, negative predictive value; NS, nonsignificant; PICO, population-intervention-comparator-outcome; PPV, positive predictive value

Number, Size, and Quality of Studies	Quality of Evidence	Direction of Findings	Key Study Results
KQ #1. Clinical Performance of Radiographs for Diagnosis			
3 studies (n=119) Burke 1994 (cohort, good) Aaløkken 2003 (cross-sectional, fair) Chiu 2010	**OVERALL: LOW** **Study quality:** Fair-Good **Quantity and precision:** Few studies, small sample sizes **Consistency:** Unexplained inconsistency for specificity and NPV **Applicability to PICO:** ✓	X-ray has moderate to moderately high sensitivity, and very low to high specificity	***Burke 1994 (n=30):*** *Diagnostic accuracy for all sinuses (Radiologist 1, Radiologist 2) (%, 95% CI):* Sensitivity: 57% (34%-78%), 62% (38%-82%) Specificity: 88% (47%-100%), 88% (47%-100%) PPV: 92%, 93% NPV: 44%, 47% *Diagnostic accuracy for maxillary sinuses (Radiologist 1, Radiologist 2) (%, 95% CI):* Sensitivity: 70% (35%-93%), 70% (35%-93%) Specificity: 100% (93%-100%), 100% (93%-100%)

Number, Size, and Quality of Studies	Quality of Evidence	Direction of Findings	Key Study Results
(cohort, fair)	**Reference standard:** CT rather than histopathology **Publication Bias:** Unknown		PPV:* 14%, 14% NPV:* 62%, 62% ***Aaløkken 2003 (n=47):*** *Diagnostic accuracy for maxillary sinuses (94 sinuses) (%, 95% CI):* Sensitivity: 80% (65%-90%) Specificity: 92% (80%-98%) PPV:* 90% NPV:* 83% See **Appendix IVb** for data from other individual sinuses. ***Chiu 2010 (n=42):*** *Diagnostic accuracy for all sinuses (%, 95% CI):* Sensitivity: 93% Specificity: Could not be calculated** PPV:* 100% NPV: Could not be calculated** *Diagnostic accuracy for maxillary sinuses (%, 95% CI):**** Sensitivity: 89% Specificity: 43% PPV:* 89% NPV:* 43%
KQ #1. Clinical Performance of Any Modality Other Than Radiographs for Diagnosis: *Insufficient (no studies)*			
KQ #1a. Variation in Clinical Performance by Imaging Modality: *Insufficient (no studies)*			

*Values calculated with data from the study article.

**Value could not be calculated due to divide by 0 error (i.e., there were no patients negative for RS).

***It is coincidental that values of sensitivity and PPV, and specificity and NPV were identical in this study.

CRS (5 Studies)

See **Table 2** for a summary of findings.

Clinical Performance of Imaging for CRS (Key Question #1)

Five studies reported mixed results with respect to the clinical performance of imaging in patients with suspected CRS. The studies evaluated different imaging modalities for different purposes. Three studies assessed the diagnostic performance of radiographs using CT as the reference standard. One study assessed the diagnostic performance of US using CT as the reference standard. One study assessed the use of CT for predicting perioperative complications or revisions following sinonasal surgery. Four studies took place in a Department of Otolaryngology, 1 study took place in multiple head and neck surgery hospitals, and 1 study took place in a Department of Diagnostic Imaging following referral from an otolaryngologist. Sample sizes ranged from 40 to 1840 patients. Patient age ranged from 6 to 88 years, but mean or median age ranged from 37 to 59 years. Only 1 of the 5 studies specified symptoms that were required for suspicion of RS, which included pain in the paranasal sinus, recurrent mucopurulent rhinorrhea, and nasal congestion lasting at least 3 months. Another study noted that patients must have experienced symptoms for at least 3 months; however, the symptoms were not specified.

No studies evaluated the clinical performance of *CT for diagnosis of CRS*; thus, the evidence for this application of CT is insufficient. One large fair-quality study found that *CT was not useful in predicting complications and the need for revision surgery* following sinonasal surgery. The evidence was considered to be of low quality because of study quality, the lack of overall clinical performance calculations, and the availability of only a single study.

Three small studies that assessed *radiographs* against CT found that views of the maxillary sinuses had *moderate to moderately high overall accuracy*, *moderate to high PPV*, *and low to moderately high NPV for detecting CRS*. The evidence was considered to be of low quality because of the small quantity of data, inconsistency with respect to specificity and NPV, and the studies' use of another imaging modality of unknown accuracy as the reference standard.

One very small study found that *US has low overall accuracy, PPV, and NPV for detecting CRS* when CT scans were used as the reference standard. The evidence was considered to be of very low quality because of the quantity of data and the studies' use of another imaging modality of unknown accuracy as the reference standard.

Evidence of the clinical performance of *any imaging modality other than CT for prognosis of surgical outcomes* in patients with CRS is insufficient due to the lack of studies.

Indirect Evidence Regarding the Clinical Performance of CT for CRS

Since no studies meeting inclusion criteria were identified for assessing the accuracy of CT in the evaluation of CRS, and since CT is the standard imaging modality for evaluation of CRS, other evidence that might shed light on the potential clinical performance of CT was considered. The following discussion reviews several studies that measured the association between CT results and other objective measures but that were excluded because they did not report data that could be used to compute sensitivity and specificity.

Association Between CT Scores and Histopathology:

Two studies investigated the relationship between the Lund-Mackay score on preoperative CT scans and the results of histopathological analysis of specimens obtained during surgery in adults undergoing endoscopic sinus surgery (ESS) for CRS. In both studies, CRS was defined as persistence of symptoms for more than 3 months despite maximal medical therapy, which included at least 2 trials of antibiotics in 1 study. CT scanning had been used as part of the process for diagnosing RS, but the CT criteria were not reported.

In the first study (79 patients), the authors found that the severity of CRS, as measured by the Lund-Mackay scale for CT scans, increased as the extent of infection increased (Pearson's correlation coefficient r=0.3984). In the second study (115 patients), CT and pathology scores were positively correlated (linear regression coefficient, 3.28; P<0.001). The authors also analyzed the relationship between symptom score and pathology score and observed small, negative regression coefficients, but all coefficients were statistically nonsignificant.

Although neither set of authors commented on the implication of their findings for the use of CT in diagnosing CRS, the study findings suggest the possibility that CT would add information to symptom assessment and improve the accuracy of CRS diagnoses. This conclusion is supported by the positive and statistically significant association between CT scores and severity of inflammation according to pathology. Additionally, 1 study found no statistically significant association between symptoms and pathology, which speaks to the inadequacy of symptom-based diagnoses. However, neither study performed an analysis that would allow an assessment of the magnitude of the discriminatory power of CT. In other words, the sensitivity and specificity of CT for diagnosing CRS remains unknown.

Association Between Changes on CT and Outcome of Treatment:

Five studies evaluated whether disease severity, as measured by CT scan, was associated with better treatment outcome. One study compared change in CT severity score (stage) with improvement according to multiple outcome measures after treatment with triamcinolone, and reported a statistically significant, positive relationship between CT change and scores for 2 of 5 endoscopic features, 4 of 8 symptoms, and 4 of 8 disease-specific QOL measures. In other words, a greater reduction in CT severity score was associated with generally better outcomes from antibiotic treatment. Four other studies compared pretreatment CT stage with outcomes of surgical or medical treatment and reported mixed findings. Sample sizes ranged from 57 to 202, with the larger studies failing to find a relationship.

The authors of studies that detected significant associations concluded that their findings support the use of CT scoring to evaluate the effect of medical therapy, or that CT scanning has a potential role in predicting treatment outcomes. However, the inconsistent findings across all 5 studies preclude a conclusion about the potential of pretreatment CT scanning as a predictive tool. The studies varied considerably in terms of type of treatment; duration of follow-up; scale used for CT scoring; outcome measurement scale; whether change in CT score or simply pretreatment score was evaluated; whether CT score was compared with percent change in symptoms, absolute change in symptoms, or final symptom score; and the type of statistical test used to measure an association. The volume of data is too small to allow an assessment of the variation in findings according to differences in study methods.

Differential Clinical Performance by Imaging Modality for CRS (Key Question #1a)

Evidence regarding the *relative clinical performance of different imaging modalities for the same application* is insufficient due to the lack of studies evaluating different modalities against the same reference standard.

Table 2. Summary of Findings, Key Questions #1 and #1a: CRS

Key: CRS, chronic rhinosinusitis; CT, computed tomography; NPV, negative predictive value; NS, nonsignificant; OR, odds ratio; PICO, population-intervention-comparator-outcome; PPV, positive predictive value; pt(s), patient(s); SD, standard deviation; US, ultrasound

Number, Size, and Quality of Studies	Quality of Evidence	Direction of Findings	Key Study Results (statistically significant results bolded)
KQ #1. Clinical Performance of CT for Diagnosis: *Insufficient (no studies)*			
KQ #1. Clinical Performance of CT for Prognosis of Surgical Outcomes			
1 fair-quality study (n=1840) Hopkins 2007 (multicenter prospective cohort study)	**OVERALL: LOW** **Study quality:** Fair **Quantity and precision:** Single study **Consistency:** Unknown **Applicability to PICO:** ✓ **Reference standard:** ✓ **Publication Bias:** Unknown	General discriminatory power but not obvious cutoff value	*Prognostic accuracy (adjusted OR for 1-point increase in Lund-Mackey score, 95% CI):* Occurrence of complication (corrected for extent of surgery): **1.09 (1.06-1.13), *P*=0.001** Revision surgery w/in 12 mos: 1.006 (0.96-1.05), NS Revision surgery w/in 36 mos: **1.03 (1.001-1.06), *P*=0.046** Authors found no evidence of a threshold Lund-Mackey score below which pts are not offered surgery; 2.1% had a score of 0-4.
KQ #1. Clinical Performance of X-ray Assessed Against CT for Diagnosis			
3 studies (n=217) Konen 2000 Timmenga 2002 (cross-sectional, good) Kasapoğlu 2009 (cohort, fair)	**OVERALL: LOW** **Study quality:** Fair-Good **Quantity and precision:** Few studies, small sample sizes **Consistency:** Inconsistency for specificity and NPV **Applicability to PICO:** ✓ **Reference standard:** Another imaging modality (CT) **Publication Bias:** Unknown	X-ray has moderate to moderately high overall accuracy	***Konen 2000 (n=134):*** *Maxillary sinuses (weighted mean±SD):* Accuracy: 78.6±1.9 Sensitivity: 67.7±8.4 Specificity: 87.6±4.7 PPV: 82.5±4.5 NPV: 76.9±4.1 *Frontal sinuses (weighted mean±SD):* Accuracy: 78.5±4.9 Sensitivity: 14.6±16.3 Specificity: 94.5±9.3 PPV: 49.2±18.0 NPV: 81.7±2.6 ***Timmenga 2002 (n=40):*** *Investigator 1, Investigator 2:* Overall accuracy: 77%, 81% Sensitivity: 95.0%, 83.3% Specificity: 53.0%, 69.2% PPV: 73.1%, 83.3% NPV: 88.9%, 68.6% ***Kasapoğlu 2009 (n=43):*** *Maxillary, frontal, ethmoid, sphenoid:* Overall accuracy: 87.2%, 87.2%, 69.8%, 70.9% Sensitivity: 86.9% , 57.4%, 66.2%, 54.5% Specificity: 88%, 92.3%, 86.7%, 81.1% PPV: 94.6%, 90%, 95.9%, 64.3% NPV: 73.3%, 64.3%, 35.1%, 74.1%
KQ #1. Clinical Performance of US Assessed Against CT for Diagnosis			
1 study (n=40) Vento 1999 (cohort study,	**OVERALL: VERY LOW** **Study quality:** Fair **Quantity and precision:** Very sparse data	US has low accuracy	*Diagnostic for fluid level (Investigator 1, Investigator 2):* Overall accuracy: 68%, 59% Sensitivity: 30%, 28% Specificity: 81%, 69%

Number, Size, and Quality of Studies	Quality of Evidence	Direction of Findings	Key Study Results (statistically significant results bolded)
fair)	**Consistency:** Unknown **Applicability to PICO:** ✓ **Reference standard:** Another imaging modality (CT) **Publication Bias:** Unknown		PPV: 35%, 23% NPV: 77%, 74% *Diagnostic accuracy for mucosal thickening (Investigator 1, Investigator 2):* Overall accuracy: 44%, 54% Sensitivity: 40%, 50% Specificity: 48% 58% PPV: 44%, 55% NPV: 44%, 53%
KQ #1. Clinical Performance of Any Modality Other Than CT for Prognosis of Surgical Outcomes: *Insufficient (no studies)*			
KQ #1a. Variation in Clinical Performance by Imaging Modality: *Insufficient (lack of appropriate studies)*			

Fungal RS (6 Studies)

See **Table 3** for a summary of findings.

Clinical Performance of Imaging for Fungal RS (Key Question #1)

Six studies evaluated the use of CT as the index test assessed against histopathology as the reference standard. In addition to CT, 1 study also assessed the use of MRI as an index test. The studies varied as to whether noninvasive, invasive, or allergic fungal RS was suspected. Sample sizes ranged from 21 to 615 patients. Patient age ranged from 4 to 76 years, but mean or median age, where reported, ranged from 25 to 53. In 1 study, standard radiographs were used as the initial imaging modality prior to referral for CT scans. Two studies enrolled patients that were immunocompromised or had hematological malignancies.

Six studies that assessed *CT* against *histopathology* found that CT had *very low to high sensitivity*, *moderately high to high specificity*, *very low to high PPV*, *and moderately high to high NPV for detecting various forms of fungal RS*, using histopathology as the reference standard. The 2 studies with very low prevalence (8% to 9%) and very low PPV (56%) were conducted with a large number of patients undergoing sinonasal surgery for CRS. In this population, fungal RS may not have been suspected. In another 2 studies with both high prevalence (71% to74%) and high PPV (93% to 91%), all patients were at high risk for fungal infection. In 1 study, patients had recently undergone endodontic work and had plain radiographic evidence of concretions believed to be related to both aspergillosis and dental root filling material. In the other study all patients were immunocompromised. The remaining 2 studies were case-control studies and thus did not provide valid figures for prevalence or PPV, but patients in 1 of the case-control studies had hematologic malignancies and were considered to be at high risk because of immunosuppression due to aggressive chemotherapy. The evidence was considered to be of low quality because of the small quantity of data for each specific indication and unexplained inconsistency with respect to sensitivity.

One very small study found that *MRI* had *moderately high sensitivity and moderate specificity for diagnosing suspected invasive fungal RS*, using histopathology as the reference standard. The evidence regarding *diagnostic performance of MRI* was considered to be of very low quality because of the quantity of data.

Evidence of the *clinical performance of imaging for prognosis of surgical outcomes* in patients with fungal RS is insufficient due to the lack of studies. Evidence of the *clinical performance of any imaging modality other than CT and MRI for diagnosis* in patients with fungal RS is insufficient due to the lack of studies.

Differential Clinical Performance by Imaging Modality for Fungal RS (Key Question #1a)

The study that assessed MRI also assessed CT against the same reference standard. *MRI and CT had nearly comparable specificity and comparable PPV for detecting invasive fungal RS, but MRI was superior to CT in sensitivity and NPV*. The evidence regarding *the comparative clinical performance of MRI and CT* was considered to be of very low quality because of the quantity of data. Evidence regarding the *variation in clinical performance according to imaging modalities other than MRI and CT and for any indication other than invasive fungal RS* is insufficient due to the lack of studies.

Table 3. Summary of Findings, Key Questions #1 and #1a: Fungal RS

Key: CT, computed tomography; dx, diagnosis; MRI, magnetic resonance imaging; NPV, negative predictive value; PICO, population-intervention-comparator-outcome; PPV, positive predictive value; pt(s), patient(s); RS, rhinosinusitis

Number, Size, and Quality of Studies	Quality of Evidence	Direction of Findings	Key Study Results
KQ #1. Clinical Performance of CT for Dx			
6 studies (n=1244) Lenglinger 1996 Broglie 2009 Groppo 2011 (cohort, fair) Dhiwakar 2003 Finkelstein 2011 (case-control, 1 poor, 1 fair) Yoon 1999 (cross-sectional, fair)	**OVERALL: LOW** **Study quality:** Generally fair **Quantity and precision:** Few studies, most had small sample sizes **Consistency:** Unexplained inconsistency for sensitivity **Applicability to PICO:** ✓ **Reference standard:** Histopathology **Publication Bias:** Unknown	CT has moderately high to high specificity and variable sensitivity	***Lenglinger 1996 (dx of maxillary sinus aspergillosis, following screening by x-ray in pts w/ recent endodontic work) (n=21):*** *Diagnostic accuracy of CT:* Overall accuracy: 90.5% Sensitivity: 93.3% Specificity: 83.3% PPV: 93.3% NPV: 83.3% ***Yoon 1999 (dx of fungal RS) (n=510):*** *Diagnostic accuracy of CT:* Accuracy: 93.1% Sensitivity: 51.3% Specificity: 96.6% PPV: 55.6% NPV: 96% ***Dhiwakar 2003 (differentiation of allergic fungal RS from ethmoidal polyposis or invasive fungal RS) (n=41):*** *Diagnostic accuracy of CT:* Sensitivity: 70% Specificity: 100% ***Broglie 2009 (dx of sinus fungal ball) (n=615):*** *Diagnostic accuracy of CT:*

Number, Size, and Quality of Studies	Quality of Evidence	Direction of Findings	Key Study Results
			Sensitivity: 83% Specificity: 94% PPV: 56% NPV: 98% ***Finkelstein 2011 (dx of invasive fungal RS, pts w/ hematologic malignancies) (n=34):*** *Diagnostic accuracy of CT:* Sensitivity: 36% Specificity: 100% ***Groppo 2011 (dx of invasive fungal RS, immunocompromised pts) (n=23):*** *Diagnostic performance of CT (Observer 1, Observer 2):* Sensitivity: 69%, 57% Specificity: 83%, 83% PPV: 92%, 91% NPV: 48%, 40%
KQ #1. Clinical Performance of Imaging for Prognosis of Surgical Outcomes: *Insufficient (no studies)*			
KQ #1. Clinical Performance of MRI for Dx of Invasive Fungal RS			
1 study (n=23) Groppo 2011 (cohort, fair)	**OVERALL: VERY LOW** **Study quality:** Fair **Quantity and precision:** Very sparse data **Consistency:** Unknown **Applicability to PICO:** ✓ **Reference standard:** Histopathology **Publication Bias:** Unknown	MRI has high sensitivity and moderate specificity	***Groppo 2011:*** *Diagnostic performance of MRI (Observer 1, Observer 2):* Sensitivity: 86%, 85% Specificity: 75%, 75% PPV: 90%, 91% NPV: 65%, 64%
KQ #1. Clinical Performance of Any Modality Other Than CT and MRI for Diagnosis: *Insufficient (no studies)*			
KQ #1a. Variation in Clinical Performance by Imaging Modality, MRI vs CT for Dx of Invasive Fungal RS			
1 study (n=23) Groppo 2011 (cohort, fair)	**OVERALL: VERY LOW** **Study quality:** Fair **Quantity and precision:** Very sparse data **Consistency:** Unknown **Applicability to PICO:** ✓ **Reference standard:** Histopathology **Publication Bias:** Unknown	Compared w/ MRI, CT has lower sensitivity and nearly comparable specificity	***Groppo 2011:*** *Diagnostic performance of MRI (Observer 1, Observer 2):* Sensitivity: 86%, 85% Specificity: 75%, 75% PPV: 90%, 91% NPV: 65%, 64% *Diagnostic performance of CT (Observer 1, Observer 2):* Sensitivity: 69%, 57% Specificity: 83%, 83% PPV: 92%, 91% NPV: 48%, 40%
KQ #1a. Variation in Clinical Performance by Imaging Modality, Comparisons Other Than MRI vs CT and Indications Other Than Invasive Fungal RS: *Insufficient (no studies)*			

Key Question #2

Key Question #2: What is the clinical utility of imaging for rhinosinusitis, i.e., what is the impact on clinical management decisions, on utilization (Key Question #2a) and on health outcomes (Key Question #2b), and according to different imaging modalities (Key Question #2c)?

Findings are summarized in **Table 4**.

Impact On Clinical Management Decisions and Utilization (Key Question #2a)

One cross-sectional survey, 1 observational study with historical controls, and 1 RCT (total n=157) assessed the impact of CT scans on treatment decisions in patients with CRS. These studies were very poor, very poor, and fair in quality, respectively.

One study assessing clinical utility found that CT may be an important factor in surgeons' decision to offer surgery in patients with refractory CRS, while 2 other studies suggested that CT prior to medical treatment may reduce the use of antibiotics in patients with persistent symptoms but a negative endoscopy. Only 1 of the studies assessing antibiotic use demonstrated a substantial difference in antibiotic use. Due to the paucity of research regarding clinical utility of imaging, no strong conclusions may be drawn.

The quality of the body of evidence regarding the *clinical utility of imaging with respect to clinical management decisions and utilization in patients with CRS* is of very low quality, due to study quality, sample sizes, and the quantity of studies addressing each outcome. The main outcome measures of the studies were related to treatment decisions, and did not directly assess effects of treatment decisions on health outcomes. Thus, no conclusions may be made regarding whether change in treatment decisions following imaging studies lead to improved patient outcomes. Evidence concerning the *impact on clinical management of imaging modalities other than CT* or concerning the *impact on clinical management of any form of imaging for indications other than CRS* is *insufficient* due to the lack of studies.

Impact on Health Outcomes (Key Question #2b)

Evidence pertaining to *clinical utility in terms of impact on health outcomes* was *insufficient* due to a lack of studies.

Impact According to Different Imaging Modalities (Key Question #2c)

Evidence pertaining to *clinical utility in terms of impact according to different imaging modalities* was *insufficient* due to a lack of studies investigating the utility of modalities other than CT.

Indirect Evidence of Impact Based on Treatment Effectiveness

The overall uncertainty of the effectiveness and necessity of treatment, as described in the **CLINICAL BACKGROUND** section, adds to the uncertainty regarding the clinical utility of imaging. Subgroup analyses in 2 meta-analyses have indicated that the use of imaging for diagnostic confirmation may not be associated with better treatment outcomes. A meta-analysis of 17 double-blind, placebo-controlled RCTs of antibiotics for acute RS in adults or children found that the odds of cure or improvement were better in studies where imaging was used, but the difference was small and nonsignificant. A Cochrane Review of 9 placebo-controlled RCTs of antibiotics for acute maxillary RS in adults detected no differential effect when comparing studies based on clinical diagnosis alone and studies where radiological or bacteriological confirmation was also required. No systematic reviews of medical treatment for CRS or recurrent RS or for surgery reported an analysis differential effect according to whether imaging had been used.

Other Potentially Policy-Relevant Evidence, Key Question #2

One of the cost analyses reviewed for this report (see **Key Question #5**) found that the cost savings associated with upfront CT might be especially high if an optimal combination of symptoms was used to select patients for the upfront CT scan and if endoscopy results were not taken into account (Tan et al., 2013). The symptoms that were considered included not only those recommended by the American Otolaryngology Association–Head and Neck Surgery (AAO-HNS) but also symptoms recommended by other professional groups for evaluating headache and rhinitis symptoms. The authors also found that if endoscopy results were used to form the initial working diagnosis rather than symptoms alone, upfront CT prior to medical treatment would *increase* costs.

Table 4. Summary of Findings for Key Question #2

Key: Abx, antibiotics; CRS, chronic rhinosinusitis; CT, computed tomography; EMT, empiric medical therapy; f/u, follow-up; NR, not reported; PICO, population-intervention-comparator-outcome; POC, point-of-care; pt(s), patient(s); RCT, randomized controlled trial; sx, symptoms; tx, treatment or therapy; uCT, upfront CT

Number, Size, and Quality of Studies	Quality of Evidence	Direction of Findings	Key Study Results
KQ #2a: Impact of CT on Clinical Management Decision and Utilization for CRS			
3 studies (157 pts) Anzai 2004 (cross-sectional; very poor) Conley 2011 (observational w/ historical controls; very poor)	**OVERALL: VERY LOW** **Study quality:** 2 of 3 studies very poor **Quantity and precision:** Very small studies, 1 or 2 per outcome **Consistency:** Unknown **Applicability to PICO:** ✓ **Publication Bias:** Unknown	CT imaging may alter decisions regarding surgery; uCT may reduce use of Abx in pts w/ negative endoscopy	***Anzai 2004 (persistent CRS):*** *% pts for whom surgeon made change in tx decision from surgery to no surgery following review of CT:* Surgeon A: 33%. Recommendation for surgery increased from 37% to 56%; decision for surgery was reversed in 2 pts. Surgeon B: 26% Surgeon C: 37% (*P*=0.002) ***Conley 2011 (POC-CT prior to medical tx vs CT as f/u to medical tx; pts had persistent sx and negative endoscopy):*** *Medical tx at initial visit (POC-CT era, pre-POC-CT era) (% pts):* Abx, overall: 35%, 37.5%

Number, Size, and Quality of Studies	Quality of Evidence	Direction of Findings	Key Study Results
Tan 2011 (single-blind RCT; fair)			Oral steroid, overall: 35%, 5% (*P*=0.0021) (Statistical testing NR except where noted.) *Medical tx by CT results (POC-CT, pre-POC-CT) (% pts):* Abx, positive CT: 51.9%, 54.2% Oral steroid, positive CT: 51.9%, 8.3% Abx, negative CT: 0, 12.5% Oral steroid, negative CT: 0, 0 (Statistical testing NR.) ***Tan 2011 (uCT vs EMT in pts w/ sx ≥ 12 wks and negative endoscopy):*** *Utilization (uCT, EMT) (% all pts unless otherwise noted):* CT scans: 100%, 45% Neurological referral for negative CT (% negative scans): 75% (9/12); 29% (2/7) Neurological referral for negative CT: 45% (9/20); 10% (2/20) (*P*=0.031*)* Allergist referral: 35%, 25% Otolaryngology visits (mean # pts): 1.55, 1.71 Abx: 40%, 100% Antihistamine: 60%, 30% Proton pump inhibitor: 0, 5% Antileukotriene: 5%, 10% Nasal steroid: 80%, 75% Oral steroid: 30%, 35% (Significance NR for most outcomes.)
KQ #2a: Impact on Clinical Management/Utilization of Imaging Modalities Other Than CT or for Indications Other than CRS: *Insufficient (no studies).*			
KQ#2b: Impact on Health Outcomes: *Insufficient (no studies)*			
KQ#2c: Impact According to Different Imaging Modalities: *Insufficient (no studies)*			

Key Question #3

Key Question #3: What are the safety issues associated with different forms of imaging technologies?

As noted in the **SUMMARY OF CLINICAL BACKGROUND** section, the risks associated with CT, MRI, x-ray, and US scans are minimal. These are all established technologies that have long been used for many applications. However, unnecessary repeated use of CT and x-ray in a patient would be of concern because of the radiation exposure.

No studies directly assessed adverse events during or following imaging. One study assessing the clinical utility of imaging found that CT may be an important factor in surgeons' decision to offer surgery in patients with CRS, while 2 other studies suggested that CT may reduce the use of antibiotics. However,

these studies did not report surgical complications or adverse events attributable to medications. Thus, no definitive conclusions can be made regarding whether change in treatment decisions following imaging studies leads to better or poorer safety outcomes.

One of the modeling studies reviewed as evidence for Key Question #5 estimated that upfront CT, compared with empiric medical therapy, for CRS would result in an increased radiation exposure of 0.09 millisieverts (mSv) or 0.48 mSv, depending on whether a low-dose CT scanner or only a conventional multidetector CT scanner were available. To put this increase into perspective, the authors cited sources regarding the risk of lung and colon cancer, which are the cancers most likely to be caused by radiation. The estimated lifetime risk of lung cancer due to a 10 mSv exposure is 0.2%, and the estimated risk for colon cancer is 0.01%.

In summary, use of imaging to evaluate RS *does not pose major safety concerns*, but evidence of *extent to which radiation exposure may be increased by the use of CT or x-ray* in patients with RS is of very low quality due to the lack of direct evidence.

Key Question #4

Key Question #4: Does the diagnostic performance, impact on clinical management, impact on health outcomes, or incidence of adverse events vary by clinical history or patient characteristics (e.g., comorbidities, subtypes of rhinosinusitis)?

Eight of the 14 studies analyzed for Key Question #1 enrolled children and adolescents as well as adults. These studies did not report results separately for children and adults. None of the studies analyzed for Key Question #2 enrolled children. In general, the studies did not report data separately according to other patient characteristics (e.g., immunosuppression, comorbidities, type of RS, treatment history or number of previous episodes), nor was variation according to patient characteristics noted across studies.

Direct evidence of *varying diagnostic performance*, *impact on clinical management*, *impact on health outcomes*, *and incidence of adverse events according to patient characteristics or clinical history* is insufficient due to the lack of studies.

However, the evidence for Key Question #1 demonstrated low-quality positive evidence of the clinical performance of imaging for the following indications. Evidence for all other populations and indications was insufficient (no studies), of very low quality, or suggested poor clinical performance.

- **For detecting CRS**, there was low-quality evidence that plain radiograph views of the maxillary sinuses assessed against CT had moderate to moderately high overall accuracy, moderate to high PPV, and low to moderately high NPV. Indirect evidence from 2 small studies suggested a

positive association between the severity of CRS, as measured by CT scanning, and histopathological evidence of infection.

- **For detecting fungal RS**, there was evidence from 6 studies that CT assessed against histopathology had moderately high to high specificity regardless of patient population. Two studies that involved patients who either had recent endodontic work or were immunocompromised also reported moderately high to high PPV, and the prevalence of fungal RS was high in these patient groups. Another study that involved patients with hematological malignancies, and who were immunocompromised due to treatment, found CT to be 100% specific for detecting invasive fungal RS, but neither prevalence nor PPV could be calculated because it was a case-control study. The estimates of good specificity and PPV suggest that CT is a good test for selecting symptomatic patients for follow-up investigation and biopsy for possible fungal infection, particularly when risk factors are present. However, the variable sensitivity reported across studies suggests that CT would not be a reliable test for ruling out fungal infection.

Key Question #5

Key Question #5: What are the cost and cost-effectiveness of imaging modalities in the diagnosis of sinusitis, including comparative costs and incremental cost-effectiveness when comparing modalities?

See **Table 5** for a summary of findings.

Cost of CT Sinus Scan

Three cost comparison studies conducted at the same institution assumed a cost of $272 for a CT sinus scan, based on 2010 Medicare reimbursement rates (Leung et al., 2011; Tan et al., 2011; Leung et al., 2014).

Cost of Upfront CT Compared with Empiric Medical Therapy

Four studies, all conducted by researchers in the Department of Otolaryngology–Head and Neck Surgery at Northwestern University in Chicago, compared utilization and/or direct costs associated with upfront CT scanning with costs associated with a presumption of CRS and empiric medical therapy.

NOTE: For the following currency conversions, the CCEMG-EPPI-Centre web-based cost converter with the International Monetary Fund (IMF) dataset for Purchasing Power Parity (PPP) values was used on December 18, 2014, with 2010 or 2011 as the price years and 2014 as the target price year at: CCEMG-EPPI-Centre Cost Converter (last updated on January 27, 2014). These conversions represent an *approximate* translation of the procedural cost and/or product price *values* to current U.S. *values*. These conversions do NOT provide an estimate of the current cost and do not directly reflect the U.S. healthcare system.

Study Descriptions

The primary perspective of all 4 studies was healthcare payer. Three of the studies were modeling studies. The other study was a trial-based evaluation in which patients were randomized to upfront CT or empiric medical therapy; the trial was funded by the National Institute on Deafness and Communication Disorders (NIDCD). No commercial funding was reported for any of the studies.

The trial-based evaluation and 2 of the modeling studies evaluated upfront CT for patients being seen at a tertiary specialist clinic with or without referral by another physician, while the other modeling study evaluated upfront CT for patients being seen in a primary care clinic. In the studies conducted in or assuming a tertiary care setting, upfront CT was performed if endoscopy at the initial visit was negative, but in the primary care study, CT was assumed to be the first step for the upfront CT strategy. CT-based diagnoses of CRS were made if the Lund-Mackay score was ≥ 4 (modeling studies) or ≥ 3 (trial-based study). All studies made several assumptions in favor of the null hypothesis (no advantage to upfront CT).

Findings

Four cost comparisons concluded that upfront CT would save overall costs or, at a minimum, reduce medication costs in certain situations. Two modeling studies suggested that upfront CT in a tertiary care setting results in a reduction of direct medical costs associated with an episode of CRS, but only when the working diagnosis is made on the basis of symptoms without the use of endoscopy or when endoscopy is negative. Costs and utilization rates collected during an RCT suggested that upfront CT following a negative endoscopy would reduce the use of antibiotics and possibly overall medication costs in a tertiary care setting. Sensitivity analysis in 1 of the modeling studies for tertiary care also supported the use of upfront CT after negative endoscopy in settings other than tertiary care. Another modeling study that assumed a primary care setting for the base case estimated reduced costs from the use of upfront CT without endoscopy, compared with referral to an otolaryngology practice for endoscopy. The estimates from the 4 studies apply to a single episode of CRS, starting with initial presentation and ending with final evaluation of CRS after first-line treatment or referral for alternative diagnoses; surgical costs were not included. No assumptions were made regarding whether patients had been previously treated for CRS.

The chief limitations of the modeling studies were the use of Medicare reimbursement rates for non-medication costs, even though other model parameters did not assume age ≥ 65 years, and the use of treatment response estimates that were not based on systematic reviews. The trial-based study collected costs only for CRS medications. As noted in the ***Treatment of RS*** section of the **SUMMARY OF CLINICAL BACKGROUND**, the effectiveness of antibiotic therapy for CRS has not been precisely defined. However, the authors attempted to compensate for this deficiency by assuming rates of response to antibiotic therapy at the high end of reported estimates. Overall, the evidence concerning cost savings is weakened by the lack of at least moderate-quality empirical evidence that upfront CT reduces antibiotic use without diminishing health benefits. Furthermore, since all studies were conducted at the same institution, corroboration of findings by other researchers is needed. See the section on ***Objective***

***Confirmation of RS**, Endoscopy* in the **SUMMARY OF CLINICAL BACKGROUND** section for a description of a systematic review of the relationship between endoscopy and CT in patients with CRS.

Other Possible Cost Comparisons

No studies compared costs between different imaging strategies for any form of RS other than CRS; evaluated imaging strategies involving x-ray, MRI, or US; or addressed pediatric populations. Thus, the evidence for *the cost implications of CT scanning for the evaluation of fungal RS or acute RS*, the evidence for the *comparative cost of imaging in the form of x-ray, MRI, or US for evaluation of RS versus no imaging*, and the evidence for the *comparative cost of imaging in children with RS* is insufficient due to lack of studies.

Cost-Effectiveness

No studies evaluated the cost of a particular imaging strategy per unit of clinical benefit. Thus, evidence of the *cost-effectiveness of imaging for evaluation of RS* is insufficient due to the lack of studies. However, it should be noted that it might be considered difficult to construct a reasonable comparator strategy for a cost-effectiveness analysis. The rationale for imaging is primarily to prevent the unnecessary use of antibiotics and steroids. Imaging would not necessarily be expected to improve sinusitis-related outcomes.

Table 5. Summary of Findings, Key Question #5

Key: AAO-HNS, American Academy of Otolaryngology-Head and Neck Surgery; AE, adverse event; AFP, atypical face pain; AR/NAR, allergic/nonallergic rhinitis; CRS, chronic rhinosinusitis; CT, computed tomography; dx, diagnosis; EMT, empiric medical therapy; NS, statistically nonsignificant; PCP, primary care physician; pt(s), patient(s); RCT, randomized controlled trial; sx, symptom(s); tx, treatment; uCT, upfront CT

Number and Type of Studies	Limitations	Direction of Findings	Study Results*
uCT vs EMT for Evaluation of CRS			
4 cost comparisons, uCT vs EMT, all from U.S. payer perspective Leung 2011, Tan 2011, Leung 2014 (modeling studies) Tan 2013 (trial-based analysis; RCT w/ blinded evaluation of CT scans; n=40)	*Modeling studies:* Non-medication costs based on Medicare reimbursement rates; tx response rates not based on systematic reviews *Trial-based study:* Total costs not computed	uCT is cost-saving in the absence of endoscopy or for pts w/ negative endoscopy	***Cost savings per pt w/ negative endoscopy, median assumptions for CRS medication costs, rates of AEs, and medical tx response rates (Leung 2011):*** Same-day CT available: $321 ($343 in 2014 USD) Same-day CT not available: $297 ($317 savings in 2014 USD) ***Medication costs for pts w/ negative endoscopy (uCT, EMT) (mean±variance) (Tan 2011):*** All: $218±$139, $253±$89 (NS) Abx: $53±$88, $153±$36 (*P*<0.05) ***Cost savings per pt, median assumptions for CRS medication costs, rates of AEs, and***

Number and Type of Studies	Limitations	Direction of Findings	Study Results*
All studies except Leung 2014 assumed tertiary care center in base case.			***medical tx response rates (Tan 2013):*** Same-day CT available: Dx based on individual sx (from set of 13 AR/NAR and AFP sx): $64-$415 ($68-$444 in 2014 USD) Dx based on AAO-HNS sx for CRS: $186 ($199 in 2014 USD) Various combinations of sx: –$121 to $504 Pts w/ endoscopy+: –$133 Same-day CT not available: Dx based on individual sx (from set of 13 AR/NAR and AFP sx): –$100 to $229 (–$107 to $245 in 2014 USD) Dx based on AAO-HNS sx for CRS: $20 ($21 in 2014 USD) Various combinations of sx: –$276 to $332 Pts w/ positive endoscopy: –$288 ***Cost savings per pt, uCT w/o endoscopy in primary care vs EMT for positive endoscopy after otolaryngology referral (Leung 2014):*** PCP treats CRS: >$503 ($538 in 2014 USD) (use of '>' unclear) PCP refers for tx of CRS: $326 ($348 in 2014 USD)
Imaging Modalities Other than CT, Indications Other Than CRS, Children: *Insufficient (no studies)*			
Cost-Effectiveness: *Insufficient (no studies)*			

Practice Guidelines

The search of the core sources and relevant specialty groups identified 6 guidelines with relevant recommendations regarding rhinosinusitis (RS) and published within the past 10 years. The general recommendations provided by the guidelines are summarized in **Table 6**. Additional details, by guideline, are presented in **Appendix V**. See also **Practice Guidelines** in the **TECHNICAL REPORT** for additional background information on guidelines.

Classification and Diagnosis of RS

Two (2) guidelines addressed the classification of RS according to symptom duration. These included guidelines from the American Academy of Allergy, Asthma, and Immunology (AAAAI) and American College of Allergy, Asthma & Immunology (ACAAI), and the American College of Radiology (ACR). These guidelines were of fair quality. Both of these guidelines classified acute RS as lasting < 4 weeks and subacute RS as lasting 4 to 8 weeks. The guidelines differed slightly on their classification of chronic and recurrent RS. The AAAAI/ACAAI defined chronic RS (CRS) as lasting > 8 weeks, and the ACR defined CRS as lasting > 90 days (12.8 weeks). The AAAAI/ACAAI defined recurrent RS as ≥ 3 episodes of acute RS per

year, and the ACR defined recurrent RS as episodes lasting < 30 days each and separated by intervals of > 10 asymptomatic days.

Six (6) guidelines addressed criteria for diagnosing acute bacterial rhinosinusitis (ABRS) based on symptoms. These included guidelines from the AAAAI/ACAAI, American Academy of Otolaryngology–Head and Neck Surgery Foundation (AAO-HNSF), American Academy of Pediatrics (AAP), Institute for Clinical Systems Improvement (ICSI), and the Infectious Diseases Society of America (IDSA). All guidelines were of fair or good quality. The guidelines were generally in good agreement for criteria for diagnosing ABRS. These criteria include: (1) upper respiratory infection (URI) symptoms lasting > 10 days, (2) symptoms that worsen after an initial improvement, or (3) severe symptoms or high fever (≥ 39°C/102°F). Prominent symptoms of ABRS include nasal congestion, purulent rhinorrhea, facial-dental pain, postnasal drainage, headache, and cough.

Imaging for RS

Six (6) guidelines addressed the use of imaging technology to confirm diagnosis of uncomplicated ABRS. These included guidelines from the AAAAI/ACAAI, AAO-HNSF, AAP, ACR, ICSI, and the IDSA. Five (5) of these guidelines recommend against the use of imaging for differentiating ABRS from viral infection. However, the sixth guideline published by the AAAAI/ACAAI recommends use of imaging to support diagnosis of RS when symptoms are vague, physical findings are equivocal, or clinical disease persists despite optimal medical treatment.

The 6 guidelines also addressed the use of imaging technology when complications are suspected and/or symptoms do not improve in response to medical treatment. All 6 guidelines recommend the use of computed tomography (CT) of the sinuses, as CT accurately depicts the sinus anatomy. Two of the guidelines recommend the use of contrast-enhanced CT, 1 guideline recommends against contrast enhancement, and 3 do not address CT with contrast enhancement.

The guidelines differ somewhat in their recommendations regarding magnetic resonance imaging (MRI). Two of the guidelines state that although MRI is limited in its ability to define bone anatomy, it may be useful for evaluating suspected fungal RS or complications of RS. One guideline recommends the use of CT instead of MRI, 1 recommends MRI as a complementary imaging study to CT, and 2 guidelines recommend MRI as an alternative to CT in certain situations. However, 1 of these guidelines does not mention MRI in the algorithm of practice parameters. Guidelines produced by the AAO-HNS do not provide any recommendations concerning MRI.

Only 3 of the guidelines discussed imaging modalities other than CT or MRI. The AAAAI/ACAAI stated that ultrasound has limited utility but might be useful in pregnant women or for determining amounts of retained sinus secretions. However, this guideline did not mention ultrasound in the algorithm of practice parameters. Two guidelines stated that standard radiographs are limited in the evaluation of the paranasal sinuses because they cannot localize the pathology well. One guideline stated that although standard radiographs are nonspecific due to many false-positives, they are fairly sensitive in detecting maxillary sinusitis.

Repeated imaging for RS

None of the guidelines addressed recommendations for repeated imaging for RS. However, 1 guideline stated that CT findings provide an objective method for monitoring.

Endoscopy

Five (5) practice guidelines state that endoscopy may be performed either as an alternative or in addition to CT in the case of recurrent RS or CRS, after empiric medical therapy has failed. The use of nasal endoscopy is offered as an option, and not a formal recommendation, in these guidelines.

Choosing Wisely

In addition to guidelines, AAAAI mentions imaging for acute RS in its "List" of *10 Things Physicians and Patients Should Question* as part of the Choosing Wisely initiative of the American Board of Internal Medicine (ABIM). Each participating specialty society voluntarily supplies a list. Item number 2 on the AAAAI list reads as follows:

> Don't order sinus computed tomography (CT) or indiscriminately prescribe antibiotics for uncomplicated acute rhinosinusitis. (#2 on the list).

The following rationale for this advice is offered: (a) only a very small percentage of acute RS cases (0.5% to 2%) advance from a viral infection to a bacterial infection, (b) most cases resolve without treatment in 2 weeks, and (3) uncomplicated cases generally can be diagnosed clinically without imaging. The AAO-HNS is not a current participant in Choosing Wisely. The AAP does not include an item related to imaging and RS in its list, and although it is a Choosing Wisely partner, the IDSA has not submitted a list.

Table 6. Summary of Practice Guideline Recommendations

Key: AAAAI, American Academy of Allergy, Asthma, and Immunology; AAO-HNSF, American Academy of Otolaryngology–Head and Neck Surgery Foundation; AAP, American Academy of Pediatrics; ABRS, acute bacterial rhinosinusitis; ACAAI, American College of Allergy, Asthma & Immunology; ACR, American College of Radiology; CRS, chronic rhinosinusitis; CT, computed tomography; dx, diagnosis; GL(s), guideline(s); ICSI, Institute for Clinical Systems Improvement; IDSA, Infectious Diseases Society of America; MRI, magnetic resonance imaging; RS, rhinosinusitis; sx, symptoms; URI, upper respiratory infection; US, ultrasound

Quantity of Individual GLs*	Individual GL Quality	Recommendations
Classification of RS		
2 (AAAAI/ACAAI, ACR)	2 Fair	Acute RS: Lasting <4 wks Subacute RS: Lasting 4-8 wks CRS: 1 GL defines as lasting >8 wks (AAAAI/ACAAI), the second defines as lasting >90 days (12.8 wks) (ACR) Recurrent RS: 1 GL defines as ≥3 episodes of acute RS per year (AAAAI/ACAAI), the second defines as episodes lasting <30 days each and separated by intervals of >10 asymptomatic days

Quantity of Individual GLs*	Individual GL Quality	Recommendations
Criteria for Clinical Dx of ABRS		
6 (AAAAI/ACAAI, AAO-HNSF, AAP, ACR, ICSI, IDSA)	3 Good 3 Fair	Presumed ABRS based on the following criteria: (1) URI sx lasting >10 days, (2) sx that worsen after an initial improvement, or (3) severe sx or high fever (≥39°C/102°F). Prominent sx of ABRS include nasal congestion, purulent rhinorrhea, facial-dental pain, postnasal drainage, headache, and cough.
Imaging for RS		
6 (AAAAI/ACAAI, AAO-HNSF, AAP, ACR, ICSI, IDSA)	3 Good 3 Fair	Most of these GLs recommend against the use of imaging for differentiating ABRS from viral URI. However, 1 GL recommends use of imaging to support dx of ABRS when sx are vague, physical findings are equivocal, or clinical disease persists despite optimal medical treatment (AAAAI/ACAAI). CT: When complications are suspected and/or sx do not improve, CT of the sinuses is recommended, as CT accurately depicts the sinus anatomy. MRI: 1 GL recommends the use of CT instead of MRI (IDSA), 1 recommends MRI as a complementary imaging study to CT (ACR), and 2 recommend MRI as an alternative to CT in certain situations (AAAAI/ACAAI, AAP). US: 1 GL states that US might be useful in pregnant women or for determining amounts of retained sinus secretions (AAAAI/ACAAI). Standard radiographs: 2 GLs state that standard radiographs are limited in the evaluation of the sinuses because they cannot localize the pathology well (AAAAI/ACAAI, ACR). 1 GL states that although standard radiographs are nonspecific due to many false-positives, they are fairly sensitive in detecting maxillary sinusitis (ICSI).
Repeated Imaging for RS		
1 (AAO-HNSF)	1 Good	None of the GLs addressed recommendations for repeated imaging for RS. However, 1 GL stated that CT findings provide an objective method for monitoring (AAO-HNSF). Evidence is insufficient to support a recommendation.

* The AAO-HNSF is scheduled to publish an update to the adult sinusitis guidelines in April 2015.

Selected Payer Policies

At the direction of WA State HCA, the coverage policies for the following organizations were reviewed: Aetna, Centers for Medicare & Medicaid Services (CMS), Oregon Health Evidence Review Commission (HERC), GroupHealth, and Regence Blue Cross/Blue Shield. The only payer found to have a policy was Aetna.

Aetna considers paranasal sinus US experimental and investigational for the evaluation of sinusitis and other indications because of a lack of clinical studies demonstrating that this procedure improves clinical outcomes. Aetna covers *magnetic resonance venography (MRV)* for evaluation of thrombosis or compression by tumor of the cerebral venous sinus in members who are at risk; sinusitis is considered a risk factor. No policies regarding CT, x-ray, or any other form of imaging for RS were identified.

See **Selected Payer Policies** in the **TECHNICAL REPORT** for additional details and links to policy documents.

Overall Summary and Discussion

Evidence-Based Summary Statement

The accuracy of imaging for diagnosing acute or chronic rhinosinusitis (RS) has not been established. Computed tomography (CT) is considered the technology of choice for confirming a suspicion of RS, but the accuracy of CT scans with respect to an objective reference standard such as histopathology has not been studied for general cases of acute or chronic RS (CRS). Metaregression analyses of randomized controlled trials (RCTs) of antibiotics for *acute* RS have found that treatment effect does not vary according to whether imaging was used in the diagnosis. Practice guidelines imply that CT would be reserved for patients with CRS or recurrent RS who have not responded to antibiotic therapy or who may be at risk for serious complications. A very small quantity of evidence has shown a correlation between the Lund-Mackay score on preoperative CT scans and the results of histopathological analysis of specimens obtained during surgery in adults undergoing surgery for CRS.

Two studies suggested that CT *prior* to medical treatment may reduce the use of antibiotics in patients with suspected CRS and negative endoscopy. However, only 1 of the studies demonstrated a substantial difference in antibiotic use, and the ability of upfront imaging to reduce antibiotic use without diminishing the positive health benefits of antibiotic treatment is unknown. Several studies from a single institution have concluded that use of upfront CT (prior to empiric medical therapy) saves costs in patients with persistent symptoms of RS. These analyses applied to patients with a negative endoscopy or without endoscopy results. Most of these analyses were based on modeling rather than on empirical evidence.

Several accuracy studies suggested that CT has good specificity but variable sensitivity for detecting different forms of fungal RS. Two studies that included only immunocompromised patients or patients with recent endodontic work had a high prevalence of fungal infection and CT had a high positive predictive value (PPV). Because invasive fungal RS has a very high morbidity and mortality rate, prompt diagnosis and treatment is necessary in this patient population. Therefore, it may be reasonable to utilize imaging at an earlier stage in symptomatic patients who have risk factors for fungal infection.

A small body of evidence suggests that plain radiographs (x-ray) may be sensitive to CT-defined acute RS and may be both sensitive and specific to CT-defined CRS. However, practice guidelines do not support the use of x-ray for evaluation of RS. There is no evidence or professional consensus to support the use of ultrasound (US) for evaluating RS or to support the use of magnetic resonance imaging (MRI) for routine evaluation of acute RS or CRS. Practice guidelines cite special situations in which MRI may be needed in addition to or instead of CT. These include suspicion of invasive fungal infection, pregnancy, and craniofacial abnormalities in children. Very sparse evidence suggests that MRI may be more sensitive than CT for detecting fungal RS.

One large study suggested that preoperative CT has sufficient discriminatory power for predicting perioperative complications or revisions following sinonasal surgery for CRS. These findings suggest that CT has potential for helping to select patients for surgery to improve refractory CRS. A single very-poor-quality study suggested that surgeons might frequently change their recommendations regarding

surgery based on preoperative CT scans. No studies were identified that assessed the impact of preoperative imaging on health outcomes. However, practice guidelines advise that imaging prior to surgery is mandatory for surgical planning, and the guidelines describe CT of the sinuses as the imaging method of choice.

The risks associated with CT, MRI, plain radiographs, and US scans are minimal, but unnecessary repeated use of CT and plain radiographs would be of concern because of the radiation exposure, especially in children.

Gaps in the Evidence

The following evidence is needed to better answer the Key Questions of this report:

- Large observational studies (cohort or cross-sectional design) designed to measure the accuracy of imaging for diagnosis of acute RS and CRS, and for detecting fungal infection, especially those assessing use of CT and MRI.
- RCTs assessing the clinical utility of imaging with respect to clinical management decisions, utilization, and health outcomes.
- Large observational studies (cohort or cross-sectional design) designed to assess the clinical performance of imaging for selection of patients for surgery through prognosis of surgical outcomes.
- Studies designed to assess the relative clinical performance and clinical utility of different imaging modalities for the same application.
- Studies designed to assess the differential accuracy and clinical utility of imaging for subpopulations defined by demographic characteristics and clinical history.
- RCTs designed to measure the impact of specific imaging strategies on costs.

TECHNICAL REPORT

Clinical Background

Rhinosinusitis: Prevalence and Clinical Definition

Sinusitis is a condition that is characterized by inflammation of the lining of the paranasal sinuses. Because the nasal mucosa is simultaneously involved and because sinusitis rarely occurs without concurrent rhinitis (i.e., irritation and inflammation of the mucous membrane inside the nose), rhinosinusitis (RS) is now the preferred term for this condition. RS affects an estimated 35 million people per year in the United States and accounts for close to 16 million office visits per year. Chronic RS (CRS) is one of the top 20 reasons for office visits per year (NCHS, 2009). Sinusitis is more common from early fall to early spring. RS can be caused by or associated with viral, bacterial, or fungal infection. Alternatively, RS can be due to allergy. Acute bacterial rhinosinusitis (ABRS) develops in 0.5% to 2% of adults and 6% to 13% of children with upper respiratory tract infections (URIs). The prevalence of RS is greater in women (20.3%) than in men (11.5%). The diagnosis of RS historically has been made based on symptom-based criteria. Symptomatic criteria for a presumptive diagnosis of bacterial RS include: (1) URI symptoms lasting > 10 days, (2) symptoms that worsen after an initial improvement, or (3) severe symptoms or high fever (≥ 39°C/102°F). Prominent symptoms of bacterial RS include nasal congestion, purulent rhinorrhea, facial-dental pain, postnasal drainage, headache, and cough (ACR, 2012a; ACR, 2012b; Slavin et al., 2005; Rosenfeld et al., 2007; Chow et al., 2012; Smith et al., 2013; Snellman et al., 2013; Wald et al., 2013).

Although there is some variability in the literature, duration of RS is characterized as acute when lasting less than 4 weeks, subacute when lasting 4 to 8 weeks, and chronic when lasting longer than 8 weeks. Recurrent sinusitis consists of 3 or more episodes of acute sinusitis per year, with the patient being asymptomatic between episodes (Slavin et al., 2005; Rosenfeld et al., 2007; Brook et al., 2014). RS may be further classified according to the pathogenic organism (viral, bacterial, or fungal) and presence of associated factors (e.g., nasal polyposis, immunosuppression). Most RS episodes are caused by viral infection, which may become bacterial. Rarely, sinusitis is caused by fungi Fungal RS can be seen in both immunocompetent and immunocompromised patients (Slavin et al., 2005). Immunocompetent patients with CRS may develop a noninvasive form of fungal RS that may manifest as either a fungus ball or allergic fungal RS. Immunocompromised patients may develop an invasive fungal RS, which is a rapidly progressive disease. Prompt diagnosis and treatment is necessary in this patient population, as invasive fungal RS has a very high morbidity and mortality rate (ACR, 2012a).

Predisposing Factors

Allergies, trauma, environmental factors, cystic fibrosis, anatomic abnormalities, recent dental work, or, as previously noted, an immunocompromised state may predispose individuals to bacterial RS. Anatomic abnormalities that are thought to potentially contribute to RS are abnormalities of the ostiomeatal complex (channels linking the sinuses) and various nasal anatomic variants, including septal

deviation and polyps. Nasal polyps, which can cause nasal obstruction, congestion, facial pressure, and diminished sense of smell, often accompany CRS. Polyposis may be the result of chronic inflammation of the nasal lining (Rimmer et al., 2014).

Objective Confirmation of RS

Objective confirmation of RS is challenging due to symptomatic overlap with many other diseases or conditions (e.g., septal deviation, migraine disorders, atypical facial pain). Many studies have found that self-reported symptoms do not correlate well with extent of imaging abnormality (stage) in CRS.

Lab Testing

The gold standard for diagnosis of a bacterial infection of the sinuses involves aspiration of a mucosal specimen from the parasinuses and analysis of the microbiology of the specimen. However, the invasive and painful nature of the procedure and the time required to complete the process make sinus aspiration impractical for daily practice. Therefore, aspiration is not recommended prior to empiric treatment with antibiotics. Endoscopically guided culture of the middle meatus are considered reasonable alternatives to sinus puncture, but such a procedure is beyond the skills of a typical primary care physician (Slavin et al., 2005; Chow et al., 2012). Accurate diagnosis of fungal RS also depends on histopathology, which includes surgical biopsy of the sinonasal tissue (Groppo et al., 2011). Optimal objective diagnostic technologies for RS remain elusive.

Endoscopy

Endoscopy is sometimes used by otolaryngology specialists to provide objective confirmation of a clinical diagnosis of RS. The procedure provides a complete view of the nose and sinuses. Endoscopic findings that are considered consistent with a diagnosis of CRS are purulent mucus and edema at the middle meatus or ethmoid region or polyps. Endoscopy has high specificity for RS but low sensitivity. (Tichenor et al., 2008; Leung et al., 2011; Wuister et al., 2014). Practice guidelines recommend that either computed tomography (CT) or nasal endoscopy be considered if antibiotic treatment for RS is not effective, especially for recurrent RS or CRS, but they do not recommend endoscopy prior to empiric treatment (Slavin et al., 2005; Rosenfeld et al., 2007; Wald et al., 2013).

A recent systematic review of 3 studies (585 patients) of the diagnostic accuracy of endoscopy for CRS reported positive predictive values (PPVs) of 65% to 84% at prevalences (according to the reference standard) ranging from 40% to 56% and negative predictive values (NPVs) of 30% to 39% (Wuister et al., 2014). Put in other terms, endoscopy added value to a clinical diagnosis of 25% to 28% for *ruling in* CRS and added a value of 5% to 30% to a clinical diagnosis for *ruling out* CRS (Wuister et al., 2014). However, the reference standard in all 3 studies was CT, which the review authors described as the usual reference standard for endoscopy. Based on their findings, the review authors recommended *against* follow-up CT in patients with *positive* endoscopy findings since CT cannot provide conclusive results. (The review authors further expressed the opinion that a follow-up CT in patients with *negative* endoscopy findings should be reserved only for patients with a prolonged or complicated course of RS.

(The use of follow-up CT after endoscopy only where endoscopy findings are negative was also assumed in the economic evaluations reviewed as evidence for Key Question #5 in the present report.)

Imaging

In the case of acute RS, current guidelines recommend against the use of imaging for differentiating uncomplicated ABRS from viral infection (Rosenfeld et al., 2007; ACR, 2012a; ACR, 2012b; Chow et al., 2012; Smith et al., 2013; Snellman et al., 2013; Wald et al., 2013). Although nasal endoscopy is considered a standard means of corroborating an uncertain clinical diagnosis of RS, this technology is not widely available to primary care, allergy, and infectious disease care providers (Bhattacharyya, 2010; Chow et al., 2012). Therefore, CT of the paranasal sinuses, with its widespread availability and ability to accurately depict sinus anatomy, is most commonly used to support a clinical diagnosis of *chronic* RS and the potential utility of antibiotic treatment (Bhattacharyya, 2010). Approximately 20% to 36% of patients with symptoms of CRS have CT-confirmed disease. Depending on the accuracy of CT for diagnosing CRS, these prevalence estimates suggest that a large proportion of patients treated empirically might be taking antibiotics unnecessarily. Bacterial resistance is a concern when antibiotics are overused (Leung et al., 2011).

Imaging may be particularly helpful in the diagnosis of fungal RS, and CT is considered an option (Slavin et al., 2005). Magnetic resonance imaging (MRI) has been suggested as an alternative to CT in the diagnosis of CRS. However, there are concerns that MRI may overestimate the presence of mucosal abnormalities and provide insufficient bone detail required for surgical planning (Bhattacharyya, 2010). Although MRI is limited in its ability to define bone anatomy, it may be useful for evaluating suspected fungal RS or complications of RS (Slavin et al., 2005; ACR, 2012a; ACR, 2012b).

The use of plain radiographs (x-ray) and ultrasound (US) for the diagnosis of RS has also been investigated. US has limited utility but might be useful in pregnant women in order to avoid radiation exposure or for determining amounts of retained sinus secretions (Slavin et al., 2005). Standard radiographs are limited in the evaluation of the paranasal sinuses because they cannot localize the pathology well (Slavin et al., 2005; ACR, 2012a; ACR, 2012b). In addition, although standard radiographs are nonspecific due to many false-positives, they have been found to be fairly sensitive in detecting maxillary sinusitis (Snellman et al., 2013).

The purpose of imaging in refractory RS is primarily to identify anatomic abnormalities that might explain continued disease or to investigate suspicion of serious problems such as fungal infection, a threat to nearby structures, abscess, or tumor. These situations represent causes or sequelae of RS that might be addressed by surgery or biopsy. Sinus CT is considered mandatory for presurgical planning (Slavin et al., 2005). (See **Treatment of RS** for a summary of systematic reviews of the effectiveness of surgery for RS.)

See **Appendix V** for detail on the recommendations of professional associations regarding imaging for RS, or **PRACTICE GUIDELINES** in the **EXECUTIVE SUMMARY** for a synthesis of recommendations.

An analysis of data from the National Ambulatory Medical Care Survey (NAMCS) for the years 2005 through 2008 found that advanced radiographic imaging (CT, MRI, or positron emission tomography [PET]) for evaluation of CRS was much more common in otolaryngology practice than in primary care practice: 16.0% versus 1.9%, *P*<0.001 (Pynnonen et al., 2012). Use of basic radiology occurred with similar frequency between otolaryngology and primary care practices: 4.0% versus 3.4%. The majority of office visits for CRS were in primary care practices.

Radiographic Staging

The most commonly used system for grading the severity of CRS according to imaging findings is the Lund-Mackay system. The system can be used with any form of imaging. The scale ranges from 0 (absence of any radiographic opacification of the sinuses) to 24 (all sinuses completely opacified). A study of asymptomatic individuals from the general population found a mean Lund-Mackay score of 4.3 (95% CI, 3.5 to 4.1). Accordingly, a typical cutoff value for diagnosing the presence of RS is 4 (Bhattacharya, 2010).

Safety of Imaging

Potential adverse effects associated with radiation exposure are an important factor to consider when utilizing imaging examinations. The American College of Radiology (ACR) provides a relative radiation level (RRL) for CT and MRI based on effective dose (i.e., the radiation dose quantity that is used to estimate population total radiation risk) (ACR, 2013). Because children are at higher risk from exposure, the RRL dose estimate ranges for children are lower compared with those specified for adults. The primary risk associated with exposure to ionizing radiation is cancer. It is estimated that approximately 1 in 1000 individuals will develop cancer from an exposure of 10 millisieverts (mSv). Although the overall risk of cancer from a diagnostic imaging procedure involving ionizing radiation is small, it is not 0. Therefore, care should be taken to limit patient radiation exposure (ACR, 2012a; ACR, 2013).

The RRLs for various imaging modalities of the paranasal sinuses are as follows (ACR, 2012a; ACR, 2012b; ACR, 2013):

- US: 0 mSv
- MRI: 0 mSv
- CT: 0.1-1 mSv (adults) and 0.3-3.0 mSv (children)
- X-ray: < 0.1 mSv (adults) and < 0.03 mSv (children)

Some authors have suggested that the rationale for empiric medical therapy and a postponement of CT scanning is no longer valid since CT scans deliver lower doses of radiation, are more readily available, and are less expensive than when current practices were established (Leung et al., 2011; Leung et al., 2014). Cone beam CT (CBCT) technologies provide high-spatial-resolution visualization of high-contrast structures in the head and neck areas, at a significantly lower level of radiation than a conventional CT scanner. CBCT scanning of the maxillofacial region can be obtained with effective dosing in the range of

30 to 80 microsieverts (μSv), and imaging of the paranasal sinuses requires a delivery of ~0.2 mSv (Miracle and Mukherji, 2009).

Treatment of RS

The potential clinical utility of imaging in the evaluation of RS depends in part on whether treatments recommended on the basis of imaging findings are effective. The spontaneous cure for viral sinusitis is 98%. Four of the reviewed practice guidelines issued a recommendation or option that antibiotics should only be prescribed in patients with severe or worsening symptoms of acute RS (ARS), who have failed decongestant therapy, or who have complications of RS (Rosenfeld et al., 2007; Smith et al., 2013; Snellman et al., 2013; Wald et al., 2013). One guideline stated that concern has been raised about the overdiagnosis of RS and unnecessary treatment with antibiotics (Slavin et al., 2005). In a discussion section, this guideline stated that appropriate criteria for the prescription of antibiotics are RS symptoms lasting 10 to 14 days, or severe symptoms of acute sinus infection, including fever with purulent nasal discharge, facial pain or tenderness, and periorbital swelling. However, 1 guideline made a strong recommendation to initiate antibiotic treatment as soon as the clinical diagnosis of ABRS is made (Chow et al., 2012). Patients with acute RS, when treated with appropriate antibiotics, usually improve quickly. The relapse rate after successful treatment is less than 5% (Brook et al., 2014). Practice guidelines recommend that if the patient fails to improve within 3 to 14 days of initiation of the antibiotic, the clinician should change to a second-line antibiotic (Slavin et al., 2005; Rosenfeld et al., 2007; Smith et al., 2013; Snellman et al., 2013; Wald et al., 2013). Estimates of the rate of adverse events due to antibiotic use for patients with symptoms of CRS range from 1% to 10% (Leung et al., 2011). However, the appropriateness of antibiotics has not been well established for either acute or chronic RS (see discussion below).

Other possible treatments include antihistamines for allergic RS, decongestants, and oral and topical steroids. Adjunctive treatments include saline, mucolytics, and expectorants. Surgery for purposes of removing infected mucosal material or correcting a complication such as abscess or polyps is sometimes considered necessary for refractory RS. Surgery may also be considered in a patient who is immunosuppressed and at greater risk of invasive infection (Slavin et al., 2005). Functional endoscopic surgery (FESS), sometimes referred to simply as endoscopy surgery (ESS), is the current approach to sinus surgery and comprises a variety of techniques (Khalil and Nunez, 2009). Surgery is much less likely to be performed in children than in adults (Vlastarakos et al., 2013).

The following discussion of different forms of treatment for RS includes findings from several systematic reviews and meta-analyses. In the reviews that provided a description of how RS was diagnosed or confirmed, study protocols represented a mix of RS diagnosed clinically and RS diagnosed on the basis of imaging and/or endoscopy in addition to clinical assessment. Subgroup analyses of treatment effectiveness according to method of diagnostic confirmation are discussed as indirect evidence for **Key Question #2** in the **LITERATURE REVIEW**.

Antibiotics

Three systematic reviews of antibiotics for acute RS concluded that they are modestly effective in adults and children but that they should be used with caution (Falagas et al., 2008; Cronin et al., 2013; Ahovuo-Saloranta et al., 2014). A review of antibiotics for acute RS found that 80% of adults in placebo groups improved within 2 weeks. There is no evidence that antibiotic therapy for recurrent RS should differ from that of sporadic acute RS (Kaper et al., 2013). One systematic review assessed the use of macrolides for CRS (Pynnonen et al., 2013), but no comprehensive review of antibiotics for CRS was identified. Antibiotics were not found to be effective for RS in patients with cystic fibrosis (Liang et al., 2014). As noted earlier, a large proportion of patients treated empirically might be taking antibiotics unnecessarily. Bacterial resistance is a concern when antibiotics are overused.

Additional Detail from Systematic Reviews:

- Falagas et al. (2008): This systematic review and meta-analysis of antibiotics for acute RS in adults and children analyzed 17 double-blind, placebo-controlled, randomized controlled trials (RCTs) (> 2648 patients), and found that antibiotics are modestly effective in resolving acute RS, but should be restricted to patients with high probability of bacterial infection. No advantage of the use of imaging for diagnosis was demonstrated in subgroup analysis.

- Pynnonen et al. (2012): This systematic review of macrolide treatment for CRS analyzed 3 RCTs (183 patients). This review found no differences for any nasal symptoms in macrolide versus amoxicillin in 1 RCT, and mixed results in the 2 RCTS that compared macrolide with placebo. Thus, there is limited scientific evidence to support the use of long-term macrolide treatment for CRS.

- Cronin et al. (2013): This meta-analysis of outcomes in children after 10 to 14 days of antibiotic treatment for acute RS included 4 placebo-controlled RCTs (382 patients). Results support the use of antibiotics for acute RS in children, but the authors did not believe that efficacy was established because of inconsistent diagnostic and inclusion criteria.

- Liang et al. (2013): This systematic review of various medical treatments of CRS in adults and children with cystic fibrosis analyzed 12 studies (701 patients) of various designs. Treatments included antibiotics (4 studies), topical steroids (4 studies), dornase alfa (3 studies), and ibuprofen (1 study). Dornase alfa and, to a lesser extent, topical steroids demonstrated significant benefits. There was a lack of evidence to support antibiotics treatment in the outcomes assessed.

- Kaper et al. (2013): This systematic review of antibiotics for recurrent acute RS (≥ 4 acute episodes per year with no symptoms between episodes) identified no placebo-controlled RCTs with data specific to recurrent RS. The authors concluded that decisions for or against initial antibiotics treatment in patients with recurring episodes of acute RS should be based on the same criteria used in managing primary or sporadic RS.

- Ahovuo-Saloranta et al. (2014): This Cochrane Review analyzed 9 placebo-controlled RCTs and 54 head-to-head comparator trials (1915 patients) of antibiotics for acute maxillary RS in adults. The authors found moderate evidence that antibiotics provide a small benefit for clinical outcomes in immunocompetent primary care patients with uncomplicated acute RS. However, since approximately 80% of patients in non-antibiotics groups improved within 2 weeks, clinicians were encouraged to weigh the small benefits against the potential for adverse events.

Steroids

Small bodies of evidence suggest that topical (intranasal) steroids may be effective for acute RS either as monotherapy or as adjunctive therapy combined with antibiotics (Zalmanovici Trestioreanu and Yaphe, 2013) and that oral (systemic) steroids have modest benefit for acute RS only when used as adjunctive therapy (Venekamp et al., 2014). Topical steroids have been found to be effective for CRS with nasal polyps (Joe et al., 2008), but their benefit for CRS without nasal polyps (Kalish et al., 2009) is uncertain. Similarly, oral steroids may be more beneficial for CRS with polyps than for CRS without polyps, but data are sparse (Poetker et al., 2013). Preliminary evidence suggests that topical steroids are effective for allergic RS (Van Loon et al., 2013). A large body of RCTs has shown that topical and oral steroids improve olfactory symptoms due to CRS with polyps (Banglawala et al., 2014).

Additional Detail from Systematic Reviews:

- Joe et al. (2008): This systematic review of intranasal steroids for adults with CRS with nasal polyps pooled data from 6 double-blind, placebo-controlled RCTs (1256 patients). The authors found that intranasal steroids alone are beneficial for treatment of sinonasal polyps occurring in patients with CRS.

- Kalish et al. (2009): This meta-analysis of topical steroids for adults with CRS without nasal polyps analyzed 9 RCTs (675 patients). This review found that there was insufficient evidence to demonstrate a clear overall benefit for topical steroids in adults with CRS without nasal polyps. However, their use appears safe and may show some symptomatic benefit.

- Poetker et al. (2013): This systematic review of oral steroids for adults with CRS with or without nasal polyps analyzed 4 case series (167 patients). The authors strongly recommended oral steroids for short-term management of CRS with nasal polyps, recommended them for acute fungal RS, and recommended them as an option for patients with CRS without nasal polyps (due to insufficient evidence). At least 2 studies reported concomitant use of antibiotics. In addition, the strength of recommendations is at odds with the recommendation-rating scheme that took study design into account.

- Van Loon et al. (2013): This systematic review of intranasal corticosteroids for recurrent allergic RS in adolescents and adults analyzed 3 placebo-controlled RCTs (542 patients). The authors concluded that although initial evidence suggests that intranasal corticosteroids may facilitate recovery of symptoms, evidence is limited.

- Zalmanovici Trestioreanu and Yaphe (2013): This Cochrane Review of intranasal steroids for adults and children with acute RS included 4 RCTs (1943 patients). This review found that 73% of steroid patients versus 66% of placebo or no-treatment patients improved or were cured following 15 to 21 days of treatments. Thus, there is limited evidence supporting the use of intranasal steroids as monotherapy or adjuvant therapy to antibiotics. The authors suggest that clinicians should weigh the modest but clinically important benefits against possible minor adverse events when prescribing treatment.

- Banglawala et al. (2014): This systematic review-meta-analysis of medical treatment for improvement of olfactory dysfunction in adults with CRS with nasal polyps included 28 RCTs (sample sizes, 14 to 246 patients). Results suggested that oral and topical steroids, but not antibiotics, significantly improved olfaction in patients.

- Venekamp et al. (2014): This Cochrane Review of systemic corticosteroids for acute RS in adults included 5 RCTs (1193 pts). Results suggested that oral corticosteroids as monotherapy appear to be ineffective for adult patients with clinically diagnosed acute RS. Current data on adjunctive treatment are limited, and almost all of the trials were performed in secondary care settings and carried a significant risk of bias. Results suggest that oral corticosteroids in combination with antibiotics may be modestly beneficial for short-term relief of symptoms in acute RS.

Immunotherapy

A systematic review of adjunctive immunotherapy for allergic rhinitis in presence of CRS or acute fungal RS included 7 studies (3 prospective controlled studies, 2 cross-sectional analyses of same study, 1 retrospective case series, and 1 retrospective chart review) in 353 atopic patients with CRS with nasal polyps, CRS without nasal polyps, or acute fungal RS (DeYoung et al., 2014). Generally, symptom scores improved compared with baseline or control patients.

Ancillary Treatments

A systematic review of decongestants, antihistamines, and nasal irrigation for acute RS in children found no RCTs or quasi-RCTs that met inclusion criteria (Shaikh et al., 2012). Thus, there was no evidence to determine effects of ancillary treatments on RS.

Surgery

Evidence collected by 4 recent systematic reviews failed to clearly demonstrate an advantage of endoscopic surgery over medical therapy in adults or children with CRS (Khalil and Nunez, 2006; Liang et al., 2013; Vlastarakos et al., 2013; Rimmer et al., 2014). The reviews did not provide detail on the specific surgical procedures performed. No systematic reviews of surgery for recurrent RS or for fungal RS were identified.

- Khalil and Nunez (2009): This systematic review of FESS for CRS in adults and children included 3 RCTs (212 patients). The studies compared FESS with medical treatment, FESS with conventional sinus surgery, FESS plus medical treatment versus medical treatment alone, or FESS plus medical

treatment versus conventional sinus surgery plus medical treatment. Results for all comparisons and all outcome measures were not significant. Results suggest that as currently practiced, FESS is safe but has not been demonstrated to provide additional benefit to that provided by medical treatment with or without sinus irrigation in CRS.

- Liang et al. (2013): This systematic review of ESS for CRS in children and adults with cystic fibrosis included 28 studies of various designs (680 patients). ESS yielded clinical improvement, measured primarily by symptoms and endoscopic findings. However, quantitative data were not reported. The authors stated that future prospective studies with predetermined, objective, and validated outcome measures are needed to determine the effectiveness of surgical intervention for cystic fibrosis–related CRS.

- Vlastarokos et al. (2013): This systematic review of FESS for CRS in children included 15 studies of mixed designs (1301 patients). No high-quality RCTs were identified. Results suggested that surgical management in children with CRS is effective when optimal medical treatment proves unsuccessful, is associated with improvement in the children's quality of life, and also improves symptoms and quality of life in children with cystic fibrosis.

- Rimmer et al. (2014): This Cochrane Review of surgery versus medical interventions for adults with CRS with nasal polyps included 4 RCTs (231 patients). Results suggest that evidence was of very low quality and did not demonstrate that surgery or medical treatment is better than the other.

Washington Agency Utilization Data

Review Objectives and Analytic Framework

Scope

The scope of this report is defined as:

Population: Adults and children diagnosed with or suspected of having chronic, acute, or recurrent rhinosinusitis (RS).

Interventions: Imaging technologies, including computed tomography (CT), magnetic resonance imaging (MRI), x-ray (plain radiography), and ultrasound (US).

Comparisons: Clinical diagnosis without imaging; another imaging modality.

Outcomes: Diagnostic performance (accuracy) in terms of sensitivity/specificity, positive/negative predictive value, and positive/negative likelihood ratios; change in clinical management decisions or utilization; health outcomes such as improvement in symptoms, reduced incidence of episodes, improved quality of life (QOL), and prevention of disease-related complications; adverse events associated with imaging (e.g., radiation exposure); cost and cost-effectiveness.

Key Questions

The following key questions will be addressed:

1. What is the clinical performance (accuracy) of imaging technologies such as CT, MRI, x-ray, and US for evaluation of RS or related complications?
   1a. Does the clinical performance vary by imaging modality or technique?
2. What is the clinical utility of imaging for RS, i.e., what is the impact:
   2a. on clinical management decisions and utilization?
   2b. on health outcomes?
   2c. according to different imaging modalities?
3. What are the safety issues associated with different forms of imaging technologies?
4. Does the diagnostic performance, impact on clinical management, impact on health outcomes, or incidence of adverse events vary by clinical history or patient characteristics (e.g., comorbidities, subtypes of RS)?
5. What are the cost and cost-effectiveness of imaging modalities in the diagnosis of sinusitis, including comparative costs and incremental cost-effectiveness when comparing modalities?

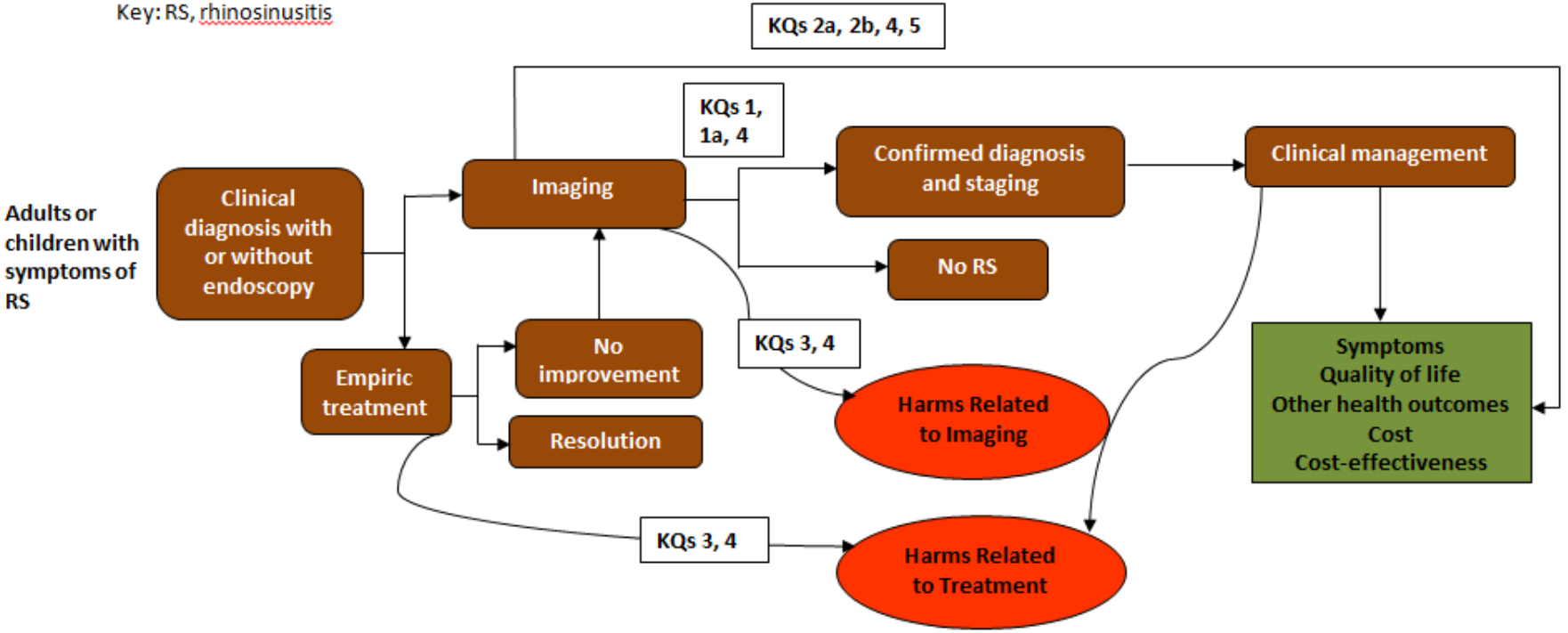
Analytic Framework

Figure 1 depicts the relationship of the PICO statement with the Key Questions.

Figure 1. Analytic Framework: Imaging for Rhinosinusitis
(Key Questions referenced by number in the graphic)

1. What is the clinical performance (accuracy) of imaging technologies such as x-ray, US, MRI, and CT for evaluation of rhinosinusitis or related complications?
   1a. Does the clinical performance vary by imaging modality or technique?
2. What is the impact of imaging for rhinosinusitis on outcomes (clinical utility)?
   2a. On clinical management decisions and utilization?
   2b. On health outcomes?
   2c. According to different imaging modalities?
3. What are the safety issues associated with different forms of imaging technologies?
4. Does the diagnostic performance, impact on clinical management, impact on health outcomes, or incidence of adverse events vary by clinical history or patient characteristics (e.g., comorbidities, subtypes of rhinosinusitis)?
5. What are the cost and cost-effectiveness of imaging modalities in the diagnosis of sinusitis, including comparative costs and incremental cost-effectiveness when comparing modalities?

Key: RS, rhinosinusitis



Methods

Search Strategy and Selection Criteria

See **Appendix I** for additional search details.

Systematic Reviews and Guidelines

These sources were searched on September 15, 2014, for systematic reviews, meta-analyses, economic evaluations, and practice guidelines published in the last 10 years:

- Core online databases such as the Agency for Healthcare Research and Quality (AHRQ), Centre for Reviews and Dissemination (York University), and National Guidelines Clearinghouse (NGC).
- Websites of relevant professional societies.
- PubMed, using filters for Practice Guidelines, Guidelines, Meta-analyses, and Systematic Reviews.

Systematic reviews were selected if they reviewed studies considered eligible for answering the Key Questions or if they provided useful background information. However, no systematic reviews of direct evidence pertinent to the Key Questions were discovered.

Primary Studies

The PubMed (searched on October 24, 2014) and OVID-Embase (searched on November 7, 2014) databases were searched for primary studies and economic evaluations designed to answer the Key Questions. Update searches were conducted on January 14, 2015 and March 20, 2015. Specific search strings are documented in **Appendix I**.

Inclusion/Exclusion Criteria

Detailed inclusion and exclusion criteria, along with their rationale, are presented in **Table 7**.

Table 7. Inclusion/Exclusion Criteria

Key: Abx, antibiotics; CT, computed tomography; RCT(s), randomized controlled trial(s); RS, rhinosinusitis

KQ #1, #4. Accuracy of Imaging to Confirm or Refine Diagnosis or to Make a Prognosis	
For CT studies, include if all of the following were true	**Rationale**
All patients in the study group originally presented with symptoms suggestive of RS.	This is the appropriate clinical population in which the intervention of interest would be used.
Patients differed from each other with respect to true RS or no RS, the presence or absence of a complication (e.g., invasive infection), or some other factor that has implications for clinical management. Patients also had to differ according	The accuracy of a medical test relates to its discriminatory power—the ability to distinguish between patients with and without disease. Inclusion of patients without disease allows calculation of specificity as well as sensitivity.

KQ #1, #4. Accuracy of Imaging to Confirm or Refine Diagnosis or to Make a Prognosis	
to imaging results.	
The study measured the accuracy of CT-detected features or the comparative accuracy of a diagnosis based on clinical evaluation plus CT features versus diagnosis-based clinical evaluation alone, and assessed CT against 1 of these reference standards: • Histopathology (including eosinophilia of nasal specimen*) or mycology • Skin prick for allergy • Surgical findings • Clinical follow-up (CT as a prognostic tool or response to Abx as a confirmation of the CT-based dx) • Intraoperative/postoperative outcomes (CT as a prognostic tool) Clinical evaluation was assumed to include evaluation of symptoms or symptoms plus nasal endoscopy.	Accuracy is best measured against a gold standard (a test known to be highly accurate) if possible, or otherwise against a reference standard that represents usual practice. Histopathology is considered the gold standard for diagnosing a sinus infection, and skin prick is the standard for diagnosing allergic reaction. Compared with imaging, surgical confirmation would be considered a more accurate and direct assessment of anatomic variants and disease complications. Clinical follow-up can confirm the appropriateness of the diagnosis and subsequent treatment.
Accuracy was calculated based on a global CT score or 1 or 2 features that are specific to the complication in question.	Sensitivity/specificity of individual features does not express the overall clinical performance of imaging. The particular features that a clinician would take into account are unknown, and their relative prevalence in clinical populations would also have to be factored into an assessment of clinical performance. Furthermore, measuring the accuracy of multiple features creates the risk of multiplicity (high accuracy or statistically significant associations by chance alone).
For non-CT (MRI, US, x-ray), include if	
Either all of the above were true. Or all of the above were true except that the reference standard was CT. Or all of the above were true except that the reference standard was endoscopy and the modality of interest was considered an alternative (not an add-on) to endoscopy.	Although histopathology was the preferred reference standard for all imaging modalities, CT was considered an acceptable reference standard since, in practice, CT is considered the standard imaging choice for confirming or refining a diagnosis of RS. Using CT as the reference standard for alternative imaging modalities was thought to represent an indirect comparison with usual care.

KQ #1, #4. Accuracy of Imaging to Confirm or Refine Diagnosis or to Make a Prognosis	
Exclude if any of the following were true:	**Rationale**
Symptoms were the reference standard.	Imaging is used to confirm or strengthen confidence in a clinical diagnosis based on symptoms or symptoms and nasal endoscopy. It is illogical to use symptoms as the measure of the accuracy of CT. CT is known to have poor correlation with symptoms (Rosenfeld et al., 2007; Bhattacharyya, 2010; Chow et al., 2012).
Statistical association alone (e.g., correlation, chi-squared analysis of differences in prevalence) between imaging measures and any other measure, without calculation of accuracy, even if that other measure is objective.	Statistical association alone shows a relationship but does not express the magnitude of new information provided by CT imaging.
Case-control studies in which the controls were "healthy controls", i.e., individuals who were not showing signs or symptoms of RS.	Imaging would not be performed in patients with no symptoms; sensitivity/specificity would be overestimated in such a study.
Studies that used imaging to describe or explore characteristics of RS or patients with RS, and that did not include a reference standard.	Such studies have made an assumption that CT findings are accurate.

KQ #2, #3, #4: Impact on Health Outcomes and Safety	
Inclusion criteria	**Rationale**
RCTs, nonrandomized trials, or observational studies comparing a group treated according to imaging results with a group treated without imaging, or comparing groups treated according to different imaging modalities.	The impact of diagnostic strategies is evaluated in the same manner as the impact of therapeutic interventions.
Exclusion criteria	**Rationale**
Case reports, case series.	Studies without control groups cannot measure the effect of a diagnostic strategy.
KQ #5: Cost, Cost-Effectiveness	
Inclusion criteria	**Rationale**
Any study or modeling evaluation that reported cost or cost-effectiveness outcomes.	---
Exclusion criteria	**Rationale**

Studies published prior to October 2004.	Studies published more than 10 years prior to the search date were considered to have limited relevance to the current economy.
All Questions	
Exclusion criteria	**Rationale**
Use of imaging in inpatient settings (e.g., ventilator-induced sinusitis).	Not relevant to coverage decisions.
Non-English-language publications.	The high volume of English-language literature suggests that there would be little bias in omitting non-English-language publications. Exceptions were to be made if hand searching or consultation with experts revealed pivotal studies not published in English.

Quality Assessment

Clinical Studies

Appendix II outlines the process used by Hayes for assessing the quality of individual primary studies and the quality of bodies of evidence. This process is in alignment with the methods recommended by the Grading of Recommendations Assessment, Development and Evaluation (GRADE) Working Group. Quality checklists for individual studies address study design, integrity of execution, completeness of reporting, and the appropriateness of the data analysis approach. Individual studies are labeled as *good*, *fair*, *poor*, or *very poor*. For individual studies included in systematic reviews, this report relies on the quality assessment by review authors. To aid in interpreting the assessment by review authors, a systematic review quality checklist, the Assessment of Multiple Systematic Reviews (AMSTAR) tool (Shea et al., 2007), was used.

Like the GRADE Working Group, Hayes uses the phrase *quality of evidence* to describe bodies of evidence in the same manner that other groups, such as AHRQ, use the phrase *strength of evidence*. The Hayes Evidence-Grading Guides ensure that assessment of the quality of bodies of evidence takes into account the following considerations:

- Methodological quality of individual studies, with an emphasis on the risk of bias within studies.
- Applicability to the population(s), intervention(s), comparator(s), and outcome(s) of interest, i.e., applicability to the PICO statement.
- Consistency of the results across studies.
- Quantity of data (number of studies and sample sizes).
- Publication bias, if relevant information or analysis is available.

NOTE: Two terms related to applicability are *directness* and *generalizability*. *Directness* refers to how applicable the evidence is to the outcomes of interest (i.e., health outcomes versus surrogate or

intermediate outcomes) or to the comparator of interest (indirect comparison of 2 treatments versus head-to-head trials). *Generalizability* usually refers to whether study results are applicable to real-world practice. If the setting is not specified in a PICO (population-interventions-comparator-outcomes) statement, the issue of generalizability to real-world settings is not typically treated as an evidence quality issue. Another term used by some organizations is *imprecision*, which refers to findings based on such a small quantity of data that the CI surrounding a pooled estimate includes both clinically important benefits and clinically important harms, or such a small quantity of data that any results other than large statistically significant effects should be considered unreliable.

Bodies of evidence for particular outcomes are labeled as being of *high*, *moderate*, *or low quality*, or they are deemed to be *insufficient* to permit conclusions. These labels can be interpreted in the following manner:

High: Suggests that we can have high confidence that the evidence found is reliable, reflecting the true effect, and is very unlikely to change with the publication of future studies.

Moderate: Suggests that we can have reasonable confidence that the results represent the true direction of effect but that the effect estimate might well change with the publication of new studies.

Low: We have very little confidence in the results obtained, which often occurs when the quality of the studies is poor, the results are mixed, and/or there are few available studies. Future studies are likely to change the estimates and possibly the direction of the results.

Insufficient: Suggests no confidence in any result found, which often occurs when there is a paucity of data or the data are such that we cannot make a statement on the findings.

Economic Evaluations

A tool created for internal use at Hayes was used to guide interpretation and critical appraisal of economic evaluations. The tool for economic evaluations was based on best practices as identified in the literature and addresses issues such as the reliability of effectiveness estimates, transparency of the report, quality of analysis (e.g., the inclusion of all relevant costs, benefits, and harms), generalizability/applicability, and conflicts of interest. Sources are listed in **Appendix II**.

Guidelines

The Rigor of Development domain of the Appraisal of Guidelines Research and Evaluation (AGREE) tool (AGREE Enterprise, 2013), along with a consideration of the items related to commercial funding and conflicts of interest among the guideline authors, was used to assess the quality of practice guidelines. Use of the AGREE tool was limited to these areas because they relate most directly to the link between guideline recommendations and evidence.

Search Results

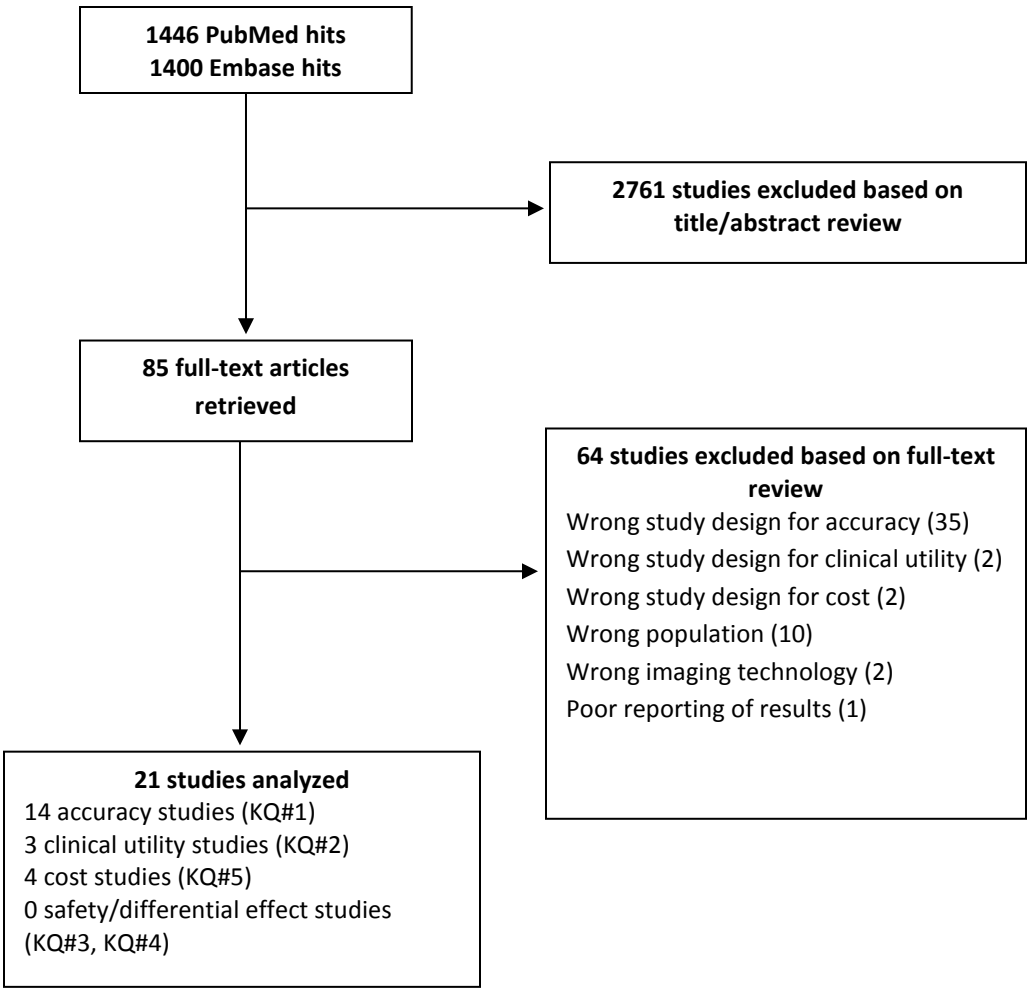
Included Studies

Twenty-one studies were selected for detailed analysis as evidence pertaining to the Key Questions. **Figure 2** summarizes the systematic identification and selection of these studies, which included 14 accuracy studies, 3 clinical utility studies, and 4 cost studies. No unique studies were identified for Key Question #3 (safety) and Key Question #4 (differential effectiveness). The accuracy studies addressed acute RS, CRS, or fungal RS. No studies specifically addressing imaging for cases of recurrent RS were identified. However, guidelines do not make different recommendations regarding imaging for recurrent acute RS and CRS.

Excluded Studies

See **Appendix III** for a listing of the 64 studies that were excluded from analysis after full-text review.

Figure 2. Summary of Search Results



Literature Review

Key Question #1

Key Question #1: *What is the clinical performance (accuracy) of imaging technologies such as CT, MRI, x-ray, and US for evaluation of rhinosinusitis or related complications? #1a: Does the clinical performance vary by imaging modality or technique?*

Fourteen studies involving primarily adult patients were selected. Several studies involved a mix of adults and children but did not report results separately for the 2 populations. The studies evaluated CT, MRI, x-ray, or US for acute RS, chronic RS (CRS), or fungal RS. When an imaging modality other than CT was the index test, then CT was the reference standard. Results were mixed regarding the accuracy of sinus radiographs for diagnosis of acute RS (3 studies) and suggested moderately high sensitivity, but were variable with respect to specificity. Results were mixed for the use of various modalities for evaluation of CRS (5 studies). Six studies reported mixed results for sensitivity but moderately high to high specificity of CT in patients with suspected fungal RS. See **Appendix IV** for details regarding selected studies. No studies compared the clinical performance of different imaging modalities.

Acute RS (3 studies)

Clinical Performance of Imaging for Acute RS (Key Question #1)

KQ#1, Acute RS:
X-ray for Diagnosis of Acute RS: Burke 1994, Aaløkken 2003, Chiu 2010

Three studies reported consistently good results for sensitivity, but mixed results for the specificity of maxillary sinus radiographs in patients with clinical suspicion of acute RS (Burke et al., 1994; Aaløkken et al., 2003; Chiu et al., 2010). All 3 studies evaluated the use of radiographs as the index test assessed against CT scans as the reference standard. One study took place in an emergency department and 2 studies took place in a radiology department. Prevalence of acute RS ranged from 17% to 83% in the maxillary sinus alone and 72% to 100% in all sinuses. Sample sizes ranged from 30 to 47 patients. Patient age ranged from 5 to 83 years, but mean age ranged from 37 to 52 years. Only 1 of the 3 studies specified symptoms that were required for suspicion of RS, which included nasal obstruction, postnasal drip, mucus or pus-like nasal discharge, and halitosis in the nasal cavity (Chiu et al., 2010). In all 3 studies, radiographs and CT scans were obtained within 2 weeks of each other. Study details are presented in **Appendix IVa**.

The selected studies included 1 good-quality cohort study, 1 fair-quality cohort study, and 1 fair-quality cross-sectional study (Burke et al., 1994; Aaløkken et al., 2003; Chiu et al., 2010). All 3 studies found that maxillary sinus radiographs had moderate to moderately high sensitivity (70% to 83%) for detecting acute RS. However, specificity varied across studies. Two studies found that radiographs of the maxillary sinuses had high specificity (92% to 100%) (Burke et al., 1994; Aaløkken et al., 2003). The third study found that specificity for radiographs of the maxillary sinuses was very low (43%) (Chiu et al., 2010).

Positive predictive value (PPV) and negative predictive value (NPV) for detection of RS in the maxillary sinuses were variable. PPV was very low (PPV 14%; prevalence 17%) in 1 study (Burke et al.) and high (89% to 90% with prevalences of 83% and 48%, respectively) in the other 2 studies. NPV in the maxillary sinuses was low in 2 studies (NPV 43%, prevalence 83%; NPV 62%, prevalence 17%) and moderately high in 1 study (NPV 83%; prevalence 48%). Low PPV was at least partially attributable to low prevalence of acute RS in the 1 study with low PPV: 17%, compared with 48% to 90% in the other 2 studies. The variability in NPV is also consistent with the variability in prevalence. A high prevalence of true disease increases PPV but decreases NPV. Taking into account patient characteristics and setting, no pattern could be detected across studies that might account for the discrepant findings with regard to specificity. The diagnostic performance of sinus radiograph views other than maxillary sinuses was variable. Two studies assessed the overall diagnostic performance of all radiograph sinus views considered collective. The first study found all sinus views had low sensitivity (57% to 62%), moderately high specificity (88%), high PPV (92% to 93%), and very low NPV (44% to 47%) (Burke et al., 1994). The second study found that all sinus views had high sensitivity (93%) and high PPV (100%). Because prevalence (according to CT scans) was 100% in this study, specificity and NPV could not be calculated (Chiu et al., 2010). One study that calculated diagnostic performance variables for individual sinuses reported very low sensitivity (25% to 41%), high specificity (97% to 100%), moderate to high PPV (75% to 100%), and moderate to moderately high NPV (70% to 86%) using imaging of the frontal, ethmoid, and sphenoid sinuses (Aaløkken et al., 2003).

Summary of Clinical Performance of Imaging for Acute RS:

Three small studies that assessed *radiographs against CT* found that views of the maxillary sinuses had *moderate to moderately high sensitivity*, *very low to high specificity*, *very low to high PPV*, *and very low to moderately high NPV for detecting acute RS*. The evidence was considered to be of low quality because of the small quantity of data, unexplained inconsistency with respect to specificity, inconsistency with respect to PPV and NPV due possibly to variation in prevalence, and the studies' use of another imaging modality as the reference standard. The variable specificity is especially relevant to an assessment of the value of imaging for diagnosis of acute RS, given that one component of the rationale for imaging in patients with suspected RS is to avoid unnecessary use of antibiotics. A low risk of false-negative results (missed cases), i.e., high sensitivity, might be deemed to be relatively less important than a low risk of false-positive results, i.e., high specificity, since acute RS is not typically a serious disorder and there are harms associated with antibiotics. Furthermore, according to a Cochrane Review of antibiotics for acute maxillary sinusitis, approximately 80% of clinical research patients who were *not* treated with antibiotics improved spontaneously within 2 weeks after administration of a placebo (Ahovuo-Saloranta et al., 2014). Thus, high sensitivity is not as important as high specificity for diagnosis of acute RS. Similarly, a high PPV might be valued over high NPV for acute RS since a high PPV would indicate that most patients with positive imaging results would be true candidates for treatment. Although a low NPV would indicate that a high proportion of patients with negative imaging results might be candidates for treatment, the risks associated with missed treatment are relatively low.

Evidence of the *clinical performance of imaging for prognosis of surgical outcomes* in patients with acute RS is insufficient due to the lack of studies. Evidence of the *clinical performance of any imaging modality other than radiographs for diagnosis* in patients with acute RS is insufficient due to the lack of studies.

Differential Clinical Performance by Imaging Modality for Acute RS (Key Question #1a)

Evidence regarding the *relative clinical performance of different imaging modalities for the same application to acute RS* is insufficient due to the lack of studies evaluating different modalities against the same reference standard.

CRS (5 Studies)

Clinical Performance of Imaging for CRS (Key Question #1)

KQ#1, CRS:
CT for Preoperative Planning: Hopkins 2007
X-ray for Diagnosis of CRS: Konen 2000, Timmenga 2002, Kasapoğlu 2009
US for Diagnosis of CRS: Vento 1999

Five studies reported mixed results with respect to the clinical performance of imaging in patients with suspected CRS (Vento et al., 1999; Konen et al., 2000; Timmenga et al., 2002; Hopkins et al., 2007; Kasapoğlu et al., 2009). The studies evaluated different imaging modalities for different purposes. Three studies assessed the diagnostic performance of radiographs using CT as the reference standard. One study assessed the diagnostic performance of US using CT as the reference standard. One study assessed the use of CT for predicting perioperative complications or revisions following sinonasal surgery. Four studies took place in a Department of Otolaryngology, 1 study took place in multiple head and neck surgery hospitals, and 1 study took place in a Department of Diagnostic Imaging following referral from an otolaryngologist. Prevalence of CRS ranged from 25% to 83%. Sample sizes ranged from 40 to 1840 patients. Patient age ranged from 6 to 88 years, but mean or median age ranged from 37 to 59 years. Only 1 of the 5 studies specified symptoms that were required for suspicion of RS, which included pain in the paranasal sinus, recurrent mucopurulent rhinorrhea, and nasal congestion lasting at least 3 months (Timmenga et al., 2002). Another study noted that patients must have experienced symptoms for at least 3 months; however, the symptoms were not specified (Kasapoğlu et al., 2009). Study details are presented in **Appendix IVa**.

One fair-quality cohort study (n=1840) used logistic regression to determine whether Lund-Mackay scores could predict perioperative complications or revisions following sinonasal surgery (Hopkins et al., 2007). A 1-point increase in Lund-Mackay score was significantly associated with complication rates (odds ratio [OR], 1.08; 95% CI, 1.06 to 1.1; $P<0.001$) and revision surgery within 36 months (OR, 1.03; 95% CI, 1.001 to 1.06; $P=0.046$). Although the authors controlled for the potential confounders of extent of surgery and allergic status, no other factors were included as potential confounders in the regression analysis. In addition, there was no assessment of overall prognostic performance based on a cutoff score. The authors found that only 2.1% of patients had a Lund-Mackay score of 0 to 4 (4 is a common cutoff value for a positive CT scan) and thus concluded that there was no evidence of a threshold Lund-Mackey score below which patients would not be offered surgery. Thus, results suggested that CT Lund-Mackey scores would not be useful in predicting overall complication and revision rates of surgery.

Two good-quality cross-sectional studies (n=174) and 1 fair-quality cohort study (n=43) assessed the diagnostic performance of radiography using CT scans as the reference standard in patients with suspected CRS (Konen et al., 2000; Timmenga et al., 2002; Kasapoğlu et al., 2009). Three studies found that maxillary sinus radiographs had moderate to moderately high overall accuracy (77% to 87%) for detecting CRS (Konen et al., 2000; Timmenga et al., 2002; Kasapoğlu et al., 2009). However, the relative values of sensitivity and specificity varied. One study found that the maxillary sinus radiographs had low sensitivity (68%) and moderately high specificity (88%) (Konen et al., 2000). A second study found that radiographs of the maxillary sinuses had moderately high to high sensitivity (83% to 95%) and very low to low specificity (53% to 69%) (Timmenga et al., 2002). The third study found that both sensitivity (87%) and specificity (88%) were moderately high (Kasapoğlu et al., 2009). PPV ranged from moderately high to high (73% to 95%), and NPV ranged from low to moderately high (69% to 89%). No pattern could be detected across studies that may account for the discrepant findings with regard to specificity and NPV. In general, sensitivity (15% to 66%) was very low and specificity (81% to 95%) was moderately high using imaging of the frontal, ethmoid, and sphenoid sinuses.

One good-quality cohort study (n=40) suggested that in patients with a history of CRS and recurrent polyposis, US had very low sensitivity (28% to 30% for fluid level and 40% to 50% for mucosal thickening) and generally low specificity (69% to 81% for fluid level and 40% to 50% for mucosal thickening) in predicting overall results of CT scanning (Vento et al., 1999). The study reported results for 2 independent evaluators. PPV was low: 23% to 35% for fluid level and 44% to 53% for mucosal thickening. NPV was moderately high for fluid level (74% to 77%) and low for mucosal thickening (44% to 53%). Overall accuracy was also low: 59% to 68% for fluid level and 44% to 54% for mucosal thickening. Although the 2 independent investigators had poor agreement in interpreting the US (50%), sensitivity and specificity were similar between the investigators.

Summary of the Clinical Performance of Imaging for CRS:

No studies evaluated the clinical performance of *CT for diagnosis of CRS*; thus, the evidence for this application of CT is insufficient. One large fair-quality study found that *CT was not useful in predicting complications and the need for revision surgery* following sinonasal surgery. The evidence was considered to be of low quality because of study quality, the lack of overall clinical performance calculations, and the availability of only a single study.

Three small studies that assessed *radiographs* against CT found that views of the maxillary sinuses had *moderate to moderately high overall accuracy*, *moderate to high PPV*, *and low to moderately high NPV for detecting CRS*. The evidence was considered to be of low quality because of the small quantity of data, inconsistency with respect to specificity and NPV, and the studies' use of another imaging modality of unknown accuracy as the reference standard.

One very small study found that *US has low overall accuracy, PPV, and NPV for detecting CRS* when CT scans were used as the reference standard. The evidence was considered to be of very low quality because of the quantity of data and the studies' use of another imaging modality of unknown accuracy as the reference standard.

Evidence of the clinical performance of *any imaging modality other than CT for prognosis of surgical outcomes* in patients with CRS is insufficient due to the lack of studies.

Differential Clinical Performance by Imaging Modality for CRS (Key Question #1a)

Evidence regarding the *relative clinical performance of different imaging modalities for the same application* is insufficient due to the lack of studies evaluating different modalities against the same reference standard.

Indirect Evidence Regarding the Clinical Performance of CT for CRS

Since no studies meeting inclusion criteria were identified for assessing the accuracy of CT in the evaluation of CRS and since CT is the standard imaging modality for evaluation of CRS, other evidence that might shed light on the potential clinical performance of CT was considered. The following discussion reviews several studies that measured the association between CT results and other objective measures but were excluded because they did not report data that could be used to compute sensitivity and specificity.

Association Between CT Scores and Histopathology:

Two studies investigated the relationship between the Lund-Mackay score on preoperative CT scans and the results of histopathological analysis of specimens obtained during surgery in adults undergoing endoscopic sinus surgery (ESS) for CRS (Jiang et al., 2005; Bhattacharyya, 2008). CRS was defined as persistence of symptoms for > 3 months despite maximal medical therapy, which included at least 2 trials of antibiotics in the study by Jiang et al. CT scanning had been used as part of the process for diagnosing RS, but the CT criteria were not reported.

In the first study (79 patients) (Jiang et al., 2005) the culture rates of middle meatus specimens were moderately and positively correlated with the Lund-Mackay scores (Pearson's correlation coefficient r=0.3984), while culture rates of the ethmoid sinus specimens were weakly but positively correlated with scores (r=0.2244). If *Staphylococcus epidermidis* and corynebacteria were considered normal flora, the comparison of CT with middle meatus culture rates indicated a stronger correlation (r=0.6427), while the correlation with the ethmoid sinus specimens declined (r=0.0467). The authors concluded that the severity of CRS, as measured by the Lund-Mackay scale for CT scans, increased as the extent of infection increased. The statistical significance of the r values was not reported. The Pearson's correlation coefficient can have a value ranging from –1 (perfect negative correlation) to 1 (perfect positive correlation).

In the second study (Bhattacharyya, 2008) (115 patients), total Lund-Mackay CT score was compared, through linear regression, with pathology severity, which was graded according to a 5-point Likert scale (0 = absence of inflammation to 4 = maximum inflammation, i.e., severe eosinophilia, lymphoplasmacytic infiltrate, etc.). Total weeks of intranasal steroid use, total weeks of nonsedating antihistamine use, and number of weeks of antibiotic use in the previous 12 weeks were included in the linear regression model to control for confounding by differences in medication use. The CT and

pathology scores were positively correlated (linear regression coefficient, 3.28; *P*<0.001). The authors also analyzed the relationship between symptom score and pathology score and observed small, negative regression coefficients, but all coefficients were statistically nonsignificant.

Although neither set of authors commented on the implication of their findings for the use of CT in diagnosing CRS, the study findings suggest the possibility that CT would add information to symptom assessment and improve the accuracy of CRS diagnoses. This conclusion is supported by the positive and statistically significant association between CT scores and severity of inflammation according to pathology. Additionally, 1 study found no statistically significant association between symptoms and pathology. However, neither study performed an analysis that would allow an assessment of the magnitude of the discriminatory power of CT. In other words, the sensitivity and specificity of CT for diagnosing CRS remains unknown.

Association Between Changes on CT and Outcome of Treatment:

Five studies evaluated whether disease severity, as measured by CT scan, was associated with better treatment outcome. One study compared change in CT severity score (stage) with improvement according to multiple outcome measures after treatment with triamcinolone, and reported a statistically significant positive relationship. In other words, a greater reduction in CT severity score was associated with generally better outcomes from antibiotic treatment (Pallanch et al., 2013). Four other studies compared pretreatment CT stage with treatment outcomes and reported mixed findings (Sharp et al., 1999; Stewart et al., 2000; Bradley and Kountakis, 2005; Bhattacharyya, 2006). Sample sizes ranged from 57 to 202, with the larger studies failing to find a relationship.

The study evaluating change in CT as a predictor of outcome involved 48 adult patients being treated with triamcinolone for CRS (Pallanch et al., 2013). Assessment of outcome variables and CT scanning were performed prior to treatment and at 1 month after administration of the triamcinolone. Changes in both the Lund-Mackay CT score and a score based on 3-dimensional (3D) volume-based CT were significantly correlated with various measures of clinical improvement. Change in 1 or both types of CT score were significantly and positively correlated with improvement in scores for 2 of 5 endoscopic features, 4 of 8 symptoms, and 4 of 8 disease-specific QOL measures. QOL measures were defined as either the frequency or the bothersomeness of various symptoms, such as thick nasal drainage. The Pearson's correlation coefficient (*r*) values, where statistically significant, were ≥ 0.29, but nearly all correlation coefficients were < 0.50. Volumetric CT was more likely than the Lund-Mackay score to be correlated with outcomes.

The 4 studies evaluating the association between pretreatment CT and treatment outcomes reported mixed findings. One study found a statistically significant positive correlation between pretreatment CT score and the percentage improvement in overall symptom score after adjusting for several disease-related variables such as polyps and allergic rhinitis. The study involved patients undergoing either maximal medical treatment or surgery. No subgroup analysis by type of treatment was performed; however, confounding due to type of treatment was controlled by including treatment type in the multivariate model (Stewart et al., 2000). The other 3 studies involved only patients undergoing surgery.

They either found no correlation in univariate analysis between pretreatment CT and surgical outcome (Bradley and Kountakis, 2005; Bhattacharyya, 2006), or found that the relationship between pretreatment CT and outcome was nonsignificant after adjusting for the presence of a systemic comorbidity (Sharp et al., 1999). The systemic comorbidities considered were asthma, aspirin-sensitive asthma, atopy, bronchiectasis, cystic fibrosis, immunoglobulin deficiency, primary ciliary dyskinesia, sarcoidosis, Young's disease, and diabetes mellitus.

The authors of studies that detected significant associations concluded that their findings support the use of CT scoring to evaluate the effect of medical therapy or that CT scanning has a potential role in predicting treatment outcomes. However, the inconsistent findings across all 5 studies preclude a conclusion about the potential of pretreatment CT scanning as a predictive tool. The studies varied considerably in terms of type of treatment; duration of follow-up; scale used for CT scoring; outcome measurement scale; whether change in CT score or simply pretreatment score was evaluated; whether CT score was compared with percent change in symptoms, absolute change in symptoms, or final symptom score; and the type of statistical test used to measure an association. The volume of data is too small to allow an assessment of the variation in findings according to differences in study methods.

Fungal RS (6 studies)

Clinical Performance of Imaging for Fungal RS (Key Question #1)

KQ#1, Fungal RS:
CT for Suspected Fungal RS: Lenglinger 1996, Yoon 1999, Broglie 2009
CT for Suspected Invasive Fungal RS: Finkelstein 2011, Groppo 2011
CT for Diagnosis of Allergic Fungal RS: Dhiwaker 2003

Six studies reported mixed results for sensitivity and moderately high to high specificity of imaging in patients with suspected fungal RS (Lenglinger et al., 1996; Yoon et al., 1999; Dhiwakar et al., 2003; Broglie et al., 2009; Finkelstein et al., 2011; Groppo et al., 2011). All 6 studies evaluated the use of CT as the index test assessed against histopathology as the reference standard. In addition to CT, 1 study also assessed the use of MRI as an index test. The studies varied as to whether noninvasive, invasive, or allergic fungal RS was suspected. Five studies took place in a Department of Otolaryngology, 1 study took place in a Department of Radiology following referral from an otolaryngologist, and 1 study took place in a Department of Oral and Maxillofacial Surgery. Prevalence of fungal RS ranged from 8% to 74%. Sample sizes ranged from 21 to 615 patients. Patient age ranged from 4 to 76 years, but mean or median age, where reported, ranged from 25 to 53. In 1 study, standard radiographs were used as the initial imaging modality prior to referral for CT scans (Lenglinger et al., 1996). Two studies enrolled patients that were immunocompromised or had hematological malignancies (Finkelstein et al., 2011; Groppo et al., 2011). Study details are presented in **Appendix IVa**.

Three fair-quality cohort studies (n=659), 2 fair-quality case-control studies (n=75), and 1 poor-quality cross-sectional study (n=510) assessed the diagnostic performance of CT scans using histopathology as the reference standard in patients with suspected fungal RS. All 6 of these studies found CT scans had moderately high to high specificity (83% to 100%) for detecting fungal RS. Results regarding the

sensitivity of CT were mixed. Three studies found CT scans had very low to low sensitivity (36% to 69%) for detecting fungal RS (Yoon et al., 1999; Finkelstein et al., 2011; Groppo et al., 2011), while the other 3 studies reported moderate to high sensitivity (70% to 93%) for detecting fungal RS (Lenglinger et al., 1996; Broglie et al., 2009) or for differentiating allergic fungal RS from polyposis or invasive sinus aspergillosis (Dhiwakar et al., 2003). The variable sensitivity could not be explained in terms of study quality, specific indication, the limited data provided concerning patient characteristics, or whether a contrast agent was used. Where PPV and NPV could be calculated, results were also variable: PPV was 56% in 2 studies and 90% to 93% in 2 studies; NPV was 40% to 48% in 1 study (2 observers) and 83% to 98% in 3 studies. Low PPV was at least partially attributable to low prevalence of fungal infection in the 2 studies with low PPV: 7.6% and 8.6%, compared with 71% to 74% in the other 2 studies where prevalence could be calculated. Low NPV might be explained by the form of fungal infection being explored: invasive fungal infection in the study with low NPV, and maxillary sinus aspergillosis or sinus fungal ball in the studies with moderately high to high NPV. However, the number of studies does not allow firm conclusions about the reason for variable NPV.

Study-specific findings, in order of increasing sensitivity, can be summarized as follows:

- The first study was conducted in 34 patients with suspected invasive fungal RS and underlying hematological malignancies (Finkelstein et al., 2011). Sensitivity was very low (36%) and specificity was high (100%). In this study, significantly more invasive fungal RS patients than control patients had previous antibiotic treatment.

- In the second study, 510 patients underwent sinonasal surgery to treat CRS (Yoon et al., 1999). Sensitivity was very low (51%) and specificity was high (97%). Only 39 (7.6%) of these patients were found to have fungal RS. Overall accuracy was high (93%), PPV was very low (56%), and NPV was high (96%) in this study.

- The third study was conducted in 23 immunocompromised patients with suspected invasive fungal RS (Groppo et al., 2011). Sensitivity was very low to low across 2 observers (57% to 69%), and specificity was high (83%). PPV was high (91% to 92%) and NPV was low (40% to 48%).

- A fourth study, in contrast to the other 5 studies, evaluated the ability of CT scans to specifically identify allergic RS (Dhiwakar et al., 2003). The study found that CT scans had moderate sensitivity (70%) in differentiating allergic fungal RS from polyposis or invasive sinus aspergillosis in 41 patients. Patients with allergic fungal RS were significantly younger, more likely to be female, and more likely to have had previous surgery than control patients.

- Two of the 6 studies found moderately high to high sensitivity (83% to 93%) for detecting fungal RS (Lenglinger et al., 1996; Broglie et al., 2009). Lenglinger et al. (1996) assessed the diagnostic accuracy of CT in 21 patients with a history of endodontic work and radiological signs of aspergillosis. Overall accuracy was high (90.5%), PPV was high (93%), and NPV was moderately high (83%) in this study. In the second study, 615 patients underwent functional ESS (FESS) to treat CRS (Broglie et al., 2009). Only 53 (8.6%) of these patients were found to have sinus fungus ball. PPV was very low (56%) and NPV was high (98%) in this study.

One fair-quality cohort study (n=23) assessed both MRI and CT for evaluating suspected invasive fungal RS in immunocompromised patients (Groppo et al., 2011). MRI had moderately high sensitivity (85% to 86%), while CT had very low to low sensitivity (57% to 69%). MRI had moderate specificity (75%), while CT had moderately high specificity (83%). The 2 forms of imaging had very similar PPV, but NPV somewhat favored MRI (64% to 65% versus 40% to 48%). The study reported results for 2 independent evaluators. Although the 2 independent investigators had moderate agreement in interpreting the US (κ=0.40-0.77), sensitivity and specificity were similar between the investigators.

Summary of Accuracy of Imaging for Fungal RS:

Six studies that assessed *CT* against *histopathology* found that CT had *very low to high sensitivity*, *moderately high to high specificity*, *very low to high PPV*, *and moderately high to high NPV for detecting various forms of fungal RS*, using histopathology as the reference standard. The 2 studies with very low prevalence (8% to 9%) and very low PPV (56%) were conducted with a large number of patients undergoing sinonasal surgery for CRS (Yoon et al., 1999; Broglie et al., 2009). In this population, fungal RS may not have been suspected prior to surgery. In another 2 studies with both high prevalence (71% to 74%) and high PPV (93% to 91%) (Lenlinger et al., 1996; Groppo et al., 2011), all patients were at high risk for fungal infection. In 1 study patients had recently undergone endodontic work, and the authors explained that evidence of concretions in patients' plain radiography films was not only considered to be evidence of aspergillosis but that previous research had suggested a connection between dental root filling material and sinus concretions. In the other study, all patients were immunocompromised. The remaining 2 studies were case-control studies and thus did not provide valid figures for prevalence or PPV, but 1 of the case-control studies had hematologic malignancies and patients were considered to be at high risk because of immunosuppression due to aggressive chemotherapy (Finkelstein et al., 2011). The evidence was considered to be of low quality because of the small quantity of data for each specific indication and unexplained inconsistency with respect to sensitivity.

One very small study found that *MRI* had *moderately high sensitivity and moderate specificity for diagnosing suspected invasive fungal RS,* using histopathology as the reference standard. The evidence regarding *diagnostic performance of MRI* was considered to be of very low quality because of the quantity of data.

Evidence of the *clinical performance of imaging for prognosis of surgical outcomes* in patients with fungal RS is insufficient due to the lack of studies. Evidence of the *clinical performance of any imaging modality other than CT and MRI for diagnosis* in patients with fungal RS is insufficient due to the lack of studies. Evidence regarding the *variation in clinical performance according to imaging modalities other than MRI and CT and for any indication other than invasive fungal RS* is insufficient due to the lack of studies.

Differential Clinical Performance by Imaging Modality for Fungal RS (Key Question #1a)

The study that assessed MRI also assessed CT against the same reference standard. *MRI and CT had nearly comparable specificity and comparable PPV for detecting invasive fungal RS, but MRI was superior*

to CT in sensitivity and NPV. The evidence regarding *the comparative clinical performance of MRI and CT* was considered to be of very low quality because of the quantity of data.

Evidence regarding the *relative clinical performance of different imaging modalities for the same application* is insufficient due to the lack of studies evaluating different modalities against the same reference standard.

Key Question #2

Key Question #2: *What is the clinical utility of imaging for rhinosinusitis, i.e., what is the impact on clinical management decisions, on utilization (Key Question #2a) and on health outcomes (Key Question #2b), and according to different imaging modalities (Key Question #2c)?*

Impact On Clinical Management Decisions and Utilization (Key Question #2a)

One cross-sectional survey, 1 observational study with historical controls, and 1 randomized controlled trial (RCT) (total n=157) assessed the impact of CT scans on treatment decisions in patients with CRS (Anzai et al., 2004; Conley et al., 2011; Tan et al., 2011).These studies were very poor, very poor, and fair in quality, respectively. Study details are presented in **Appendix IVb**.

Anzai et al. (2004) administered questionnaires regarding treatment decisions to 3 otolaryngology surgeons before and after the surgeons reviewed sinus CT scans for 27 patients with refractory CRS. Only 1 of the otolaryngologists physically examined the patients; the other 2 otolaryngologists made hypothetical decisions based on medical records. The main outcome measure was dichotomous decisions regarding surgical versus nonsurgical treatment. The surgeon who examined the patients made a change in treatment decision for one-third (9 of 27) of the patients after the sinus CT scans were reviewed, but this result was statistically nonsignificant. Of these 9 patients, a surgery decision was reversed for 2 while a new decision in favor of surgery was made for the other 7. The other 2 surgeons changed their decisions for 26% and 37% of patients. The 3 surgeons' agreement regarding treatment decisions improved after the sinus CT scans were reviewed. CT findings were found to be the predominant determinant of a decision to offer surgery. Limitations of this study included small sample size (the study was likely underpowered), potential bias toward delaying decision for surgery until after CT (which may have overestimated the impact of the CT on clinical decisions), and nonrandomized study design.

Conley et al. (2011) evaluated the impact of point-of-care (POC)-CT by comparing patients seen after POC-CT was introduced (POC-CT era) with historical controls who did not receive POC-CT (pre-POC-CT era). All patients presented with symptoms of CRS but had negative endoscopic findings. At their initial visit, 35% of the POC-CT group and 37.5% of the pre-POC-CT group received antibiotic treatment, a difference that favored POC-CT in terms of reducing antibiotics, but only slightly. Significantly more patients in the POC-CT group (35%) than in the pre-POC-CT group (5%; P=0.0021) received steroid treatment in addition to antibiotics at the first visit. The authors interpreted this finding to suggest that

less aggressive treatment was pursued for some patients in the pre-POC-CT group due to the lack of objective evidence of disease. In those patients with positive CT results, which were obtained at the initial visit for the POC-CT group and at the posttreatment follow-up visit for the pre-POC-CT group, 51.9% of the POC-CT group and 54.2% of the pre-POC-CT group received antibiotic treatment. In addition to antibiotics, 51.9% of the CT-positive POC-CT group and 8.3% of the pre-POC-CT group received oral steroids. Among those patients with CT-negative results, no POC-CT patients but 12.5% pre-POC-CT patients received antibiotics. The authors interpreted this finding as suggesting that 2 of 40 patients in the pre-POC-CT group received antibiotics unnecessarily since their CT scans were normal at 3 weeks after initiation of treatment. No CT-negative patients received oral steroids. Thus, in patients who were negative for CT-based CRS signs, POC-CT may have reduced unnecessary antibiotic use. However, the overall difference in antibiotic use between groups was very small, the authors did not report statistical analyses for this outcome, and the negative CT findings in the pre-POC-CT group would partially have reflected the effects of treatment. Other study limitations included a moderate loss to follow-up (20%) in the pre-POC-CT group, retrospective study design, and a control group that comprised historical patients (i.e., chronology bias may be present).

The study by Tan et al. (2011) recruited patients with persistent symptoms of CRS (≥ 12 weeks) and negative endoscopic findings. Patients were then randomized to upfront CT or empiric medical therapy (EMT). Because patients in the upfront CT group who had a negative CT scan were not followed, and a substantial proportion of patients in the EMT group failed to return for follow-up, the impact on clinical outcomes could not be assessed. Utilization data collected as part of the trial showed upfront CT to result in greater use of CT scans and higher rates of referral for neurologic consultation. However, antibiotic use was substantially reduced with the use of upfront CT: 40% versus 100% of patients (statistical testing was not reported, but use of an online power calculator suggests that results were statistically significant). Use of most other medications did not differ between groups.

In summary, 1 study assessing clinical utility found that CT may be an important factor in surgeons' decision to offer surgery in patients with refractory CRS, while 2 other studies suggested that CT prior to medical treatment may reduce the use of antibiotics in patients with persistent symptoms but a negative endoscopy. Only 1 of the studies assessing antibiotic use demonstrated a substantial difference in antibiotic use. Due to the paucity of research regarding clinical utility of imaging, no strong conclusions may be drawn. The quality of the body of evidence regarding the *clinical utility of imaging with respect to clinical management decisions and utilization* is of very low quality, due to study quality, sample sizes, and the quantity of studies addressing each outcome. *In patients with CRS*, main outcome measures of the studies were related to treatment decisions, and did not directly assess effects of treatment decisions on health outcomes. Thus, no conclusions may be made regarding whether change in treatment decisions following imaging studies leads to improved patient outcomes. Evidence concerning the *impact on clinical management of imaging modalities other than CT* or concerning the *impact on clinical management of any form of imaging for indications other than CRS* is insufficient due to the lack of studies.

Impact on Health Outcomes (Key Question #2b)

Evidence pertaining to *clinical utility in terms of impact on health outcomes* was *insufficient* due to a lack of studies.

Impact According to Different Imaging Modalities (Key Question #2c)

Evidence pertaining to *clinical utility in terms of impact according to different imaging modalities* was *insufficient* due to a lack of studies investigating the utility of modalities other than CT.

Indirect Evidence Based on Treatment Effectiveness

The overall uncertainty of the effectiveness and necessity of treatment, as described in the **CLINICAL BACKGROUND** section, adds to the uncertainty regarding the clinical utility of imaging. Subgroup analyses in 2 meta-analyses have indicated that the use of imaging for diagnostic confirmation of acute RS may not be associated with better treatment outcomes. A meta-analysis of 17 double-blind, placebo-controlled RCTs of antibiotics for acute RS in adults or children found that the odds of cure or improvement were better in studies where imaging was used, but the difference was small and nonsignificant (Falagas et al., 2008). A Cochrane Review of 9 placebo-controlled RCTs of antibiotics for acute maxillary RS in adults detected no differential effect when comparing studies based on clinical diagnosis alone and studies where radiological or bacteriological confirmation was also required (Ahovuo-Saloranta et al., 2014). No systematic reviews reported an analysis of differential effect of medical treatment for CRS or recurrent RS, or for surgical treatment of any form of RS according to whether imaging had been used.

Other Potentially Policy-Relevant Evidence, Key Question #2

One of the cost analyses reviewed for this report (see **Key Question #5**) found that the cost savings associated with upfront CT might be especially high if an optimal combination of symptoms were used to select patients for the upfront CT scan and if endoscopy results were not taken into account (Tan et al., 2013). The symptoms that were considered included not only those recommended by the American Otolaryngology Association–Head and Neck Surgery (AAO-HNS), but also symptoms recommended by other professional groups for evaluating headache and rhinitis symptoms. The authors also found that if endoscopy results were used to form the initial working diagnosis rather than symptoms alone, upfront CT prior to medical treatment would *increase* costs.

Key Question #3

Key Question #3: *What are the safety issues associated with different forms of imaging technologies?*

As noted in the **CLINICAL BACKGROUND** section, the risks associated with CT, MRI, x-ray, and US scans are minimal. These are all established technologies that have long been used for many applications.

However, unnecessary repeated use of CT and x-ray in a patient would be of concern because of the radiation exposure.

No studies directly assessed adverse events during or following imaging. One study assessing the clinical utility of imaging found that CT may be an important factor in surgeons' decision to offer surgery in patients with CRS, while 2 other studies suggested that CT may reduce the use of antibiotics. However, these studies did not report surgical complications or adverse events attributable to medications. Thus, no definitive conclusions can be made regarding whether change in treatment decisions following imaging studies leads to better or poorer safety outcomes.

One of the modeling studies reviewed as evidence for Key Question #5 estimated that upfront CT, compared with EMT, for CRS would result in an increased radiation exposure of 0.09 millisieverts (mSv) or 0.48 mSv, depending on whether a low-dose CT scanner or only a conventional multidetector CT scanner were available (Leung et al., 2011). To put this increase into perspective, the authors cited sources regarding the risk of lung and colon cancer, which are the cancers most likely to be caused by radiation. The estimated lifetime risk of lung cancer due to a 10 mSv exposure is 0.2%, and the estimated risk for colon cancer is 0.01%.

In summary, use of imaging to evaluate RS *does not pose major safety concerns*, but evidence of the *extent to which radiation exposure may be increased by the use of CT or x-ray* in patients with RS is of very low quality due to the lack of direct evidence.

Key Question #4

Key Question #4: *Does the diagnostic performance, impact on clinical management, impact on health outcomes, or incidence of adverse events vary by clinical history or patient characteristics (e.g., comorbidities, subtypes of rhinosinusitis)?*

Eight of the 14 studies analyzed for Key Question #1 enrolled children and adolescents as well as adults (Lenglinger et al, 1996; Yoon et al., 1999; Konen et al., 2000; Aaløkken et al., 2004; Hopkins et al., 2007; Kasapoğlu et al., 2009; Chiu et al., 2010; Finkelstein et al., 2011). These studies did not report results separately for children and adults. None of the studies analyzed for Key Question #2 enrolled children. In general, the studies did not report data separately according to other patient characteristics (e.g., immunosuppression, comorbidities, type of RS, treatment history or number of previous episodes), nor was variation according to patient characteristics noted across studies.

Direct evidence of *varying diagnostic performance, impact on clinical management, impact on health outcomes, and incidence of adverse events according to patient characteristics or clinical history* is insufficient due to the lack of studies.

However, the evidence for Key Question #1 demonstrated low-quality positive evidence of the diagnostic performance of imaging for the following indications. Evidence for all other populations and indications was insufficient (no studies), of very low quality, or suggested poor clinical performance.

- **For detecting CRS**, there was low-quality evidence that plain radiograph views of the maxillary sinuses assessed against CT had moderate to moderately high overall accuracy, moderate to high PPV, and low to moderately high NPV. Indirect evidence from 2 small studies suggested a positive association between the severity of CRS, as measured by CT scanning, and histopathological evidence of infection.
- **For detecting fungal RS**, there was evidence from 6 studies that CT assessed against histopathology had moderately high to high specificity regardless of patient population. Two studies that involved patients who either had recent endodontic work or were immunocompromised also reported moderately high to high PPV, and the prevalence of fungal RS was high in these patient groups. Another study that involved patients with hematological malignancies, and who were immunocompromised due to treatment, found CT to be 100% specific for detecting invasive fungal RS, but neither prevalence nor PPV could be calculated because it was a case-control study. The estimates of good specificity and PPV suggest that CT is a good test for selecting symptomatic patients for follow-up investigation and biopsy for possible fungal infection, particularly when risk factors are present. However, the variable sensitivity reported across studies suggests that CT would not be a reliable test for ruling out fungal infection.

Key Question #5

Key Question #5: *What are the cost and cost-effectiveness of imaging modalities in the diagnosis of sinusitis, including comparative costs and incremental cost-effectiveness when comparing modalities?*

Cost of CT Sinus Scan

Three cost comparison studies conducted at the same institution assumed a cost of $272 for a CT sinus scan, based on 2010 Medicare reimbursement rates (Leung et al., 2011; Tan et al., 2011; Leung et al., 2014).

Cost of Upfront CT Compared with EMT

Four studies, all conducted by researchers in the Department of Otolaryngology–Head and Neck Surgery at Northwestern University in Chicago, compared utilization and/or direct costs associated with upfront CT scanning with costs associated with a presumption of CRS and EMT (Leung et al., 2011; Tan

KQ #5:
Tertiary care center: Leung 2011, Tan 2011, Tan 2013
Primary care center: Leung 2014

et al., 2011; Tan et al., 2013; Leung et al., 2014). See **Appendix IVc** for the details of these studies.

NOTE: For the following currency conversions, the CCEMG-EPPI-Centre web-based cost converter with the International Monetary Fund (IMF) dataset for Purchasing Power Parity (PPP) values was used on December 18, 2014, with 2010 or 2011 as the price year and 2014 as the target price year: CCEMG-EPPI-Centre Cost Converter (last updated on January 27, 2014) (Shemilt et al., 2010). These conversions represent an *approximate* translation of the procedural cost and/or product price *values* to current U.S. *values*. These conversions do NOT provide an estimate of the current cost and do not directly reflect the U.S. healthcare system.

Study Descriptions

The primary perspective of all 4 studies was healthcare payer. Three of the studies were modeling studies. The study by Tan et al. (2011) was a trial-based evaluation in which patients were randomized to upfront CT or EMT; the trial was funded by the National Institute on Deafness and Communication Disorders (NIDCD). No commercial funding was reported for any of the studies.

The trial-based evaluation (Tan et al., 2011) and 2 of the modeling studies (Leung et al., 2011; Tan et al., 2011) evaluated upfront CT for patients being seen at a tertiary specialist clinic with or without referral by another physician, while the other modeling study (Leung et al., 2014) evaluated upfront CT for patients being seen in a primary care clinic. Symptom-based suspicion of CRS, allergic/nonallergic rhinitis (AR/NAR), or atypical facial pain (possible migraine) was based on criteria defined by the AAO-HNS and other relevant professional societies. Various assumptions were made regarding the prevalence of these pretest (pre-CT) symptom-based diagnoses. In the studies conducted in or assuming a tertiary care setting, upfront CT was performed if endoscopy at the initial visit was negative, but in the primary care study (Leung et al., 2014), CT was assumed to be the first step for the upfront CT strategy. CT-based diagnoses of CRS were made if the Lund-Mackay score was ≥ 4 (modeling studies) or ≥ 3 (trial-based study [Tan et al., 2011]). The 2011 study by Tan et al. used cone beam CT (CBCT), delivered at point of care (POC-CT) for upfront CT. The other studies did not make these assumptions, but the authors of another study (Leung et al., 2014) pointed out that compared with conventional CT, CBCT delivers a smaller radiation dose and is more commonly accessible in an outpatient setting. **Table 8** provides additional details on how the 4 studies defined the upfront CT and EMT strategies for evaluating and managing patients who present with symptoms supporting a clinical diagnosis of CRS. All studies made the following assumptions in favor of the null hypothesis (no advantage to upfront CT): routine repeat CT in upfront CT strategy, use of the cheapest available medications, no inclusion of adverse events associated with steroids, no accounting for antibiotic resistance, valuation of partial response to medical treatment the same as full response, no return of symptoms after resolution, no addition of oral steroids to intranasal steroids for allergic rhinitis.

The time horizon of the 4 studies was a single episode of CRS, starting with initial presentation and ending with final evaluation of CRS after first-line treatment or referral for alternative diagnoses; surgical costs were not included. No assumptions were made regarding whether patients had been previously treated for CRS. The 3 modeling studies also included costs associated with consultation for

and first-line treatment for an alternate diagnosis (AR/NAR or atypical face pain). The primary care modeling study by Leung et al. (2014) considered 2 scenarios: one where the primary care physician was comfortable managing medical treatment for CRS and one where the primary care physician preferred to refer patients diagnosed with CRS to an otolaryngologist.

Table 8. General Protocols in Studies Comparing Costs of Upfront CT and EMT for the Management of Patients with Symptoms of CRS (Leung et al., 2011; Tan et al., 2011; Tan et al., 2013; Leung et al., 2014)

Key: CRS, chronic rhinosinusitis; CT, computed tomography; EMT, empiric medical treatment

Upfront CT	EMT

• New visit with endoscopy*
• CT if endoscopy is negative*
• Follow-up visit (unless same-day CT is possible)
• Action following CT
  ○ *CT suggests CRS:* antibiotics, prednisone, and fluticasone propionate if CT-based diagnosis is CRS; a second antibiotic if adverse events occur with first antibiotic
  ○ *CT rules out CRS:* referral for allergy or neurology consultation
• Posttreatment follow-up visit for patients receiving antibiotics for CRS
  ○ Follow-up CT for CRS medication nonresponders (for surgical planning)†
	• New visit with endoscopy
	• Action following endoscopy
	  ○ *Positive endoscopy:* antibiotics, prednisone, and fluticasone propionate if endoscopy is positive; a second antibiotic if adverse events occur with first antibiotic†
	  ○ *Negative endoscopy:* CT; then referral/treatment according to CT diagnosis
	• Posttreatment follow-up visit for patients receiving antibiotics for CRS
	• CT for CRS treatment nonresponders (for surgical planning)†

*Exceptions: One of the tertiary care studies (Tan et al., 2013) assumed that in the upfront CT scenario, the CT scan might or might not be preceded by endoscopy, and the primary care study (Leung et al., 2014) assumed that endoscopy would not precede upfront CT (but would precede follow-up CT in the EMT group).

†The authors of the Leung studies acknowledged that a second CT might not be considered necessary but stated that including the costs of a second CT was intentional so that results would be biased in favor of EMT.

Findings

Two of the modeling studies (Leung et al., 2011; Tan et al., 2013) and the trial-based analysis (Tan et al., 2011) reported findings suggesting cost advantages to upfront CT in a tertiary care setting, but only when the working diagnosis is made on the basis of symptoms without the use of endoscopy or when endoscopy is negative. Sensitivity analyses in the 2011 Leung study also suggested that upfront CT for patients with a negative endoscopy would save costs in a range of practice settings, using various prevalence estimates from the literature. Another modeling study (Leung et al., 2014) estimated reduced costs from the use of upfront CT in a primary care setting.

Modeling Study by Leung et al. (2011) – Tertiary care, negative endoscopy, non-medication costs based on Medicare reimbursement rates, medication costs based on Redbook:

Assuming the availability of same-day CT, total costs saved were $321 per patient in 2010 dollars (approximately $343 in 2014 USD) in the base case, using median values for medication costs and treatment response. Assuming that same-day CT were *not* available and that patients would require an extra follow-up visit, cost savings were estimated to be $297 ($317 in 2014 USD) in the base case. As a form of sensitivity analysis, the authors computed cost differences with medication cost and treatment response assumptions that were the most favorable to EMT (EMT optimized) and with assumptions that were most favorable to upfront CT) (upfront CT optimized). Under these scenarios, upfront CT still reduced costs, even when EMT was optimized. Thus, the base case results were found to be robust. Other sensitivity analyses using various prevalence estimates from the literature for a variety of practice settings resulted in similar conclusions. Costs included otolaryngology office visits, endoscopy, CT scans, skin prick for allergy, antibiotics, and oral and nasal steroids.

Trial-Based Evaluation by Tan et al. (2011) – Tertiary care, negative endoscopy, non-medication costs excluded, medication costs based on Walgreen prices:

Total medication costs were somewhat smaller in the upfront CT group ($218 versus $253 per patient; difference nonsignificant), but antibiotic costs were substantially lower in the upfront CT group compared with the EMT group ($53 versus $153; $P<0.05$). The base year for cost estimates was not reported. If a base year of 2011 is assumed, comparative antibiotic costs would be $56 in 2014 USD versus $160 in 2014 USD. The authors offered no analysis of total costs.

Modeling Study by Tan et al. (2013) – Tertiary care, no restriction by endoscopy results, non-medication costs based on Medicare reimbursement rates, medication costs based on Redbook:

Total direct costs were estimated to be either reduced or increased by the use of upfront CT, depending on varying assumptions regarding the availability of same-day CT (POC-CT), response to medical treatment, the cost of CRS medications, and the symptoms or findings taken into account during the initial diagnosis. Assuming the availability of same-day CT and a working diagnosis based simply on 1 of 13 possible symptoms of CRS or atypical face pain (pre-endoscopy), the model predicted base case savings ranging from $64 ($68 in 2014 USD) per patient if the working diagnosis were made according to the presence of hyposmia, to $415 ($444 in 2014 USD) per patient if the working diagnosis were made according to the presence of forehead pain. Assuming same-day CT were *not* available, the model predicted corresponding estimates ranging from an *increase* of $100 ($107 in 2014 USD) per patient (working diagnosis based on hyposmia) to a savings of $229 ($245 in 2014 USD) per patient (working diagnosis based on forehead pain). Upfront CT following a working diagnosis based on the symptom set recommended by the AAO-HNS would result in a savings of $186 ($199 in 2014 USD), or $20 per patient ($21 in 2014 USD), depending on whether same-day CT were available.

An important finding from this analysis is that when the working diagnosis was based on positive endoscopy, median value (base case) assumptions suggested that upfront CT would *increase* costs. Upfront CT was also associated with increased costs when the model assumed initial diagnoses based on novel combinations of symptoms.

Cost assumptions were the same as those for the study by Leung et al. (2011). As in the study by Leung et al. (2011), the authors computed cost differences for medication cost and treatment response assumptions that were the most favorable to EMT (EMT optimized) and for assumptions that were most favorable to upfront CT (upfront CT optimized). When EMT was optimized, cost differences ranged from substantially favoring EMT to marginally favoring upfront CT if same-day CT were available, and consistently favored EMT if same-day CT were not available. Thus, in contrast to the 2011 Leung study, the base case results were *not* found to be robust. Tan and colleagues did not discuss the differences between their findings and those of the 2011 Leung study. The differences in assumptions between the 2 studies were the response rates to atypical facial pain treatment (higher rates assumed in the 2013 Tan study) and the pretest (pre-CT) prevalence of CRS, AR/NAR, and atypical face pain (20% in the 2011 Leung study; 50% in the 2013 Tan study for working diagnosis based on AAO-HNS criteria). The latter difference reflects the fact that the Leung study assumed that all patients had a negative endoscopy whereas pretest prevalence figures in the 2013 Tan study were for patients who had not yet undergone endoscopy.

Modeling Study by Leung et al. (2014) – Primary care, endoscopy performed after positive upfront CT or instead of upfront CT, non-medication costs based on Medicare reimbursement rates, medication costs based on Redbook:

Total direct costs were estimated to be reduced by the use of upfront CT. The model predicted median cost savings of > $503 (> $538 in 2014 USD) for primary care physicians who were comfortable managing the medical treatment of patients diagnosed with CRS and median cost savings of $326 ($348 in 2014 USD) for primary care physicians who preferred to refer patients to an otolaryngologist for medical treatment of CRS. Results continued to suggest substantial cost savings when the various parameters were varied in multiway sensitivity analysis. Cost assumptions were the same as for the study by Leung et al. (2011).

Summary, Cost Implications of Upfront CT Versus EMT

Four cost comparisons concluded that upfront CT would save overall costs or, at a minimum, reduce medication costs in certain situations. Two modeling studies suggested that upfront CT in a tertiary care setting results in a reduction of direct medical costs associated with an episode of CRS, but only when the working diagnosis is made on the basis of symptoms without the use of endoscopy or when endoscopy is negative. Costs and utilization rates collected during an RCT suggested that upfront CT following a negative endoscopy would reduce the use of antibiotics and possibly overall medication costs in a tertiary care setting. Sensitivity analysis in 1 of the modeling studies for tertiary care supported the use of upfront CT after negative endoscopy in settings other than tertiary care. Another modeling study that assumed a primary care setting for the base case estimated reduced costs from the use of upfront CT without endoscopy, compared with referral for endoscopy in an otolaryngology practice. The estimates apply to a single episode of CRS, starting with initial presentation and ending with final evaluation of CRS after first-line treatment or referral for alternative diagnoses; surgical costs

were not included. No assumptions were made regarding whether patients had been previously treated for CRS.

The chief limitations of the modeling studies were the use of Medicare reimbursement rates for non-medication costs, even though other model parameters did not assume age ≥ 65 years, and the use of treatment response estimates that were not based on systematic reviews. The trial-based study collected costs only for CRS medications. As noted in the ***Treatment of RS*** section of the **CLINICAL BACKGROUND**, the effectiveness of antibiotic therapy for CRS has not been precisely defined. However, the authors attempted to compensate for this deficiency by assuming rates of response to antibiotic therapy at the high end of reported estimates. Overall, the evidence concerning cost savings is weakened by the lack of at least moderate-quality empirical evidence that upfront CT reduces antibiotic use without diminishing health benefits. Furthermore, since all studies were conducted at the same institution, corroboration of findings by other researchers is needed. See the section on ***Objective Confirmation of RS****, Endoscopy* in the **CLINICAL BACKGROUND** section for a description of a systematic review of the relationship between endoscopy and CT in patients with CRS.

Other Possible Cost Comparisons

No studies compared costs between different imaging strategies for any form of RS other than CRS; evaluated imaging strategies involving x-ray, MRI, or US; or addressed pediatric populations. Thus, the evidence for *the cost implications of CT scanning for the evaluation of fungal RS or acute RS*, the evidence for the *comparative cost of imaging in the form of x-ray, MRI, or US for evaluation of RS versus no imaging*, and the evidence for the *comparative cost of imaging in children with RS* are insufficient due to lack of studies.

Cost-Effectiveness

No studies evaluated the cost of a particular imaging strategy per unit of clinical benefit. Thus, evidence of the *cost-effectiveness of imaging for evaluation of RS* is insufficient due to the lack of studies. However, it should be noted that it might be considered difficult to construct a reasonable comparator strategy for a cost-effectiveness analysis. The rationale for imaging is primarily to prevent the unnecessary use of antibiotics and steroids. Imaging would not necessarily be expected to improve sinusitis-related outcomes.

Practice Guidelines

Six practice guidelines with relevant recommendations were identified. **Appendix V** presents the recommendations of each guideline.

In addition to guidelines, the American Academy of Allergy, Asthma and Immunology (AAAAI) mentions imaging for RS in its "List" of *10 Things Physicians and Patients Should Question* as part of the Choosing Wisely initiative of the American Board of Internal Medicine (ABIM). Each participating specialty society voluntarily supplies a list (ChoosingWisely, 2015). Item number 2 on the AAAAI list reads as follows:

> Don't order sinus computed tomography (CT) or indiscriminately prescribe antibiotics for uncomplicated acute rhinosinusitis. (#2 on the list).

The following rationale for this advice is offered: (a) only a very small percentage of acute RS cases (0.5% to 2%) advance from a viral infection to a bacterial infection, (b) most cases resolve without treatment in 2 weeks, and (3) uncomplicated cases generally can be diagnosed clinically without imaging. The AAO-HNS is not a current participant in Choosing Wisely. The American Academy of Pediatrics (AAP) does not include an item related to imaging and RS in its list, and although it is a Choosing Wisely partner, the Infectious Diseases Society of America (IDSA) has not submitted a list.

Selected Payer Policies

The terms used in searching the payer databases were *rhinosinusitis* and *sinusitis* without restriction to title.

Aetna

Aetna considers paranasal sinus US experimental and investigational for the evaluation of sinusitis and other indications because of a lack of clinical studies demonstrating that this procedure improves clinical outcomes.

See Paranasal Sinus Ultrasound for the Evaluation of Sinusitis: Aetna Clinical Policy Bulletin No. 0694.

Aetna considers magnetic resonance venography (MRV) medically necessary for *any* of the following indications:

1. For evaluation of thrombosis or compression by tumor of the cerebral venous sinus in members who are at risk (e.g., hypercoagulable disorders, meningitis, oral contraceptive use, otitis media, sinusitis, underlying malignant process) or have signs or symptoms (e.g., drowsiness and confusion accompanying a headache, focal motor or sensory deficits, papilledema, or seizures); *or*
2. For evaluation of venous thrombosis or occlusion in the large systemic veins (e.g., superior vena cava, subclavian, or other deep veins in the chest); *or*
3. For evaluation of venous thrombosis or occlusion in the portal and/or hepatic venous system (e.g., Budd-Chiari syndrome).

See Magnetic Resonance Angiography (MRA) and Magnetic Resonance Venography (MRV): Clinical Policy Bulletin No. 0094. NOTE: Neither MRA nor MRV was mentioned in any of the review articles or practice guidelines reviewed for the present report.

Centers for Medicare & Medicaid Services (CMS)

No CMS National Coverage Determination (NCD) was identified for imaging for RS on January 7, 2015 (search National Coverage Documents in National Coverage Determinations and Medicare Coverage Documents at: CMS Advanced Search Database). In the absence of an NCD, coverage decisions are left to the discretion of local Medicare carriers.

GroupHealth

No coverage policy for imaging for RS was identified on the GroupHealth website (GroupHealth Providers) on January 7, 2015.

Oregon Health Evidence Review Commission (HERC)

No coverage policy for imaging for RS was identified on the Oregon HERC website (HERC Coverage Guidances) on January 7, 2015.

Regence

No coverage policy for imaging for RS was identified on the Regence website (Regence Group Medical Policies) on January 7, 2015.

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APPENDICES

APPENDIX I. Search Strategy

INITIAL SEARCH, SYSTEMATIC REVIEWS AND PRACTICE GUIDELINES (conducted September 15, 2014)

Initially, evidence for this report was obtained by searching for systematic reviews, meta-analyses, practice guidelines, and economic evaluations that had been published in the past 10 years. Searches were conducted in the following databases using the terms *rhinosinusitis* or *sinusitis*: Agency for Healthcare Research and Quality (AHRQ), Blue Cross Blue Shield TEC Assessments, Canadian Agency for Drugs and Technology in Health (CADTH), Centre for Reviews and Dissemination (CRD) (York University), Hayes Knowledge Center, Institute for Clinical Systems Improvement (ICSI), National Institute for Health Research Health Technology Assessment (NIHR HTA) Programme (UK), United States Preventive Services Task Force (USPSTF), National Guidelines Clearinghouse (NGC), National Institute for Health and Care Excellence (NICE), and Veterans Affairs Technology Assessment Program (VA TAP). (NOTE: The CRD search strategy includes a search for Cochrane Reviews.)

The websites for the American Academy of Otolaryngology–Head and Neck Surgery (AAO-HNS); American Academy of Allergy, Asthma, and Immunology (AAAAI); American College of Physicians; American College of Radiology (ACR); Infectious Diseases Society of America (IDSA); and International Headache Society were also searched.

Additional systematic reviews were sought from a search of the PubMed database using filters for Practice Guidelines, Guidelines, Meta-Analyses, and Systematic Reviews, according to this search:

1. rhinosinusitis or sinusitis

   Filters: Meta-Analysis; Systematic Reviews; Publication date from 2009/01/01 to 2014/12/31; English

SEARCH FOR PRIMARY CLINICAL STUDIES AND ECONOMIC EVALUATIONS

Since no systematic reviews were identified that addressed the Key Questions for this report, the main literature search was designed to identify all relevant primary studies.

PubMed search on October 24, 2014

1. sinusitis [MeSH]
2. Tomography, X-ray computed [MeSH] or Radiography [MeSH] or Ultrasonography [MeSH] or Magnetic Resonance Imaging [MeSH]
3. 1 AND 2

4. "addresses"[Publication Type] OR "autobiography"[Publication Type] OR "bibliography"[Publication Type] OR "biography"[Publication Type] OR "book illustrations"[Publication Type] OR "classical article"[Publication Type] OR "clinical conference"[Publication Type] OR "collected works"[Publication Type] OR "comment"[Publication Type] OR "congresses"[Publication Type] OR "consensus development conference"[Publication Type] OR "consensus development conference, nih"[Publication Type] OR "dictionary"[Publication Type] OR "directory"[Publication Type] OR "duplicate publication"[Publication Type] OR "editorial"[Publication Type] OR "[Publication Type] OR "festschrift"[Publication Type] OR "guideline"[Publication Type] OR "historical article"[Publication Type] OR "in vitro"[Publication Type] OR "interactive tutorial"[Publication Type] OR "interview"[Publication Type] OR "lectures"[Publication Type] OR "legal cases"[Publication Type] OR "legislation"[Publication Type] OR "letter"[Publication Type] OR "news"[Publication Type] OR "newspaper article"[Publication Type] OR "overall"[Publication Type] OR "patient education handout"[Publication Type] OR "periodical index"[Publication Type] OR "personal narratives"[Publication Type] OR "pictorial works"[Publication Type] OR "popular works"[Publication Type] OR "portraits"[Publication Type] OR "practice guideline"[Publication Type] OR "review"[Publication Type] OR "scientific integrity review"[Publication Type] OR "video audio media"[Publication Type] OR "webcasts"[Publication Type]
5. 3 NOT 4

Filters: Humans; English

OVID-Embase search on November 7, 2014

The following search was run in both the Embase and MEDLINE databases. Only search results in Embase were reviewed.

1. exp *sinusitis/
2. exp *rhinosinusitis/
3. 1 or 2
4. exp computer assisted tomography/
5. exp nuclear magnetic resonance imaging/
6. exp radiography/
7. exp ultrasound/
8. 4 or 5 or 6 or 7
9. 3 and 8
10. remove duplicates from 9
11. limit 10 to human
12. limit 11 to humans

13. limit 12 to (book or book series or conference abstract or conference paper or conference proceeding or "conference review" or editorial or letter or note or short survey or trade journal or addresses or autobiography or bibliography or biography or case reports or dataset or dictionary or directory or duplicate publication or festschrift or in vitro or interactive tutorial or interview or lectures or legal cases or legislation or news or newspaper article or patient education handout or periodical index or portraits or video-audio media or webcasts)
14. 12 not 13
15. limit 14 to "review"
16. 14 not 15

Update Searches

Update searches were conducted on January 14, 2015 and March 20, 2015.

APPENDIX II. Overview of Evidence Quality Assessment Methods

Clinical Studies

Tools used include internally developed Quality Checklists for evaluating the quality (internal validity) of different types of studies, a checklist for judging the adequacy of systematic reviews used instead of de novo analysis, and Hayes Evidence-Grading Guides for evaluating bodies of evidence for different types of technologies. Hayes methodology is in alignment with the GRADE (Grading of Recommendations, Assessment, Development, and Evaluation) system, which was developed by the GRADE Working Group, an international collaborative body.

Step 1	Individual study appraisal: a. Initial rating according to study design *Good:* Randomized Controlled Trials *Fair:* Nonrandomized Trial (controlled, parallel-group, quasirandomized) *Poor:* Observational Analytic Studies (prospective or retrospective trials involving historical controls, pretest-posttest control trial [patients legitimately serve as their own controls], case-control, registry/chart/database analysis involving a comparison group) *Very Poor:* Descriptive Uncontrolled Studies (case reports, case series, cross-sectional surveys [individual-level data], correlation studies [group-level data]) b. Consider the methodological rigor of study execution according to items in a proprietary Quality Checklist c. Repeat for each study
Step 2	Evaluation of each body of evidence by outcome, key question, or application: a. Initial quality designation according to best study design in a body of evidence b. Downgrade/upgrade *Downgrade factors:* Study weaknesses (Quality Checklists), small quantity of evidence, lack of applicability, inconsistency of results, publication bias *Possible upgrade factors:* Strong association, dose-response effect, bias favoring no effect c. Assign final rating: High-Moderate-Low-Insufficient d. Repeat for each outcome/question/application
Step 3	Evaluation of overall evidence: a. Rank outcomes by clinical importance b. Consider overall quality of evidence for each critical outcome c. Assign overall rating based on lowest-quality body: High-Moderate-Low-Insufficient
Step 4	Evidence-based conclusion: Overall quality of evidence + Balance of benefits and harms

Practice Guidelines (checklist taken from AGREE Tool and approach to scoring used in this report)

Rank each item on a scale of 1-7.

Decide on overall quality (1 = lowest to 7 = highest), giving strongest weight to items 7-14 (Rigor of Development Domain) and items 22-23 (Editorial Independence).

For qualitative labels:

Very poor = 1
Poor = 2-3
Fair = 4-5
Good = 6-7

1. The overall objective(s) of the guideline is (are) specifically described.
2. The health question(s) covered by the guideline is (are) specifically described.
3. The population (patients, public, etc.) to whom the guideline is meant to apply is specifically described.
4. The guideline development group includes individuals from all relevant professional groups.
5. The views and preferences of the target population (patients, public, etc.) have been sought.
6. The target users of the guideline are clearly defined.
7. Systematic methods were used to search for evidence.
8. The criteria for selecting the evidence are clearly described.
9. The strengths and limitations of the body of evidence are clearly described.
10. The methods for formulating the recommendations are clearly described.
11. The health benefits, side effects, and risks have been considered in formulating the recommendations.
12. There is an explicit link between the recommendations and the supporting evidence.
13. The guideline has been externally reviewed by experts prior to its publication.
14. A procedure for updating the guideline is provided.
15. The recommendations are specific and unambiguous.
16. The different options for management of the condition or health issue are clearly presented.
17. Key recommendations are easily identifiable.
18. The guideline describes facilitators and barriers to its application.
19. The guideline provides advice and/or tools on how the recommendations can be put into practice.
20. The potential resource implications of applying the recommendations have been considered.
21. The guideline presents monitoring and/or auditing criteria.
22. The views of the funding body have not influenced the content of the guideline.

Competing interests of guideline development group members have been recorded and addressed.

Economic Evaluations

A tool developed by Hayes for internal use guides interpretation and critical appraisal of economic evaluations. The tool includes a checklist of items addressing issues such as the reliability of effectiveness assumptions, transparency of reporting, quality of analysis, generalizability/applicability, and conflicts of interest. The following publications served as sources of best practice.

Brunetti M, Shemilt I, Pregno S, et al. GRADE guidelines: 10. Considering resource use and rating the quality of economic evidence. J Clin Epidemiol. 2013;66(2):140-150. PMID: 22863410.

Drummond MF, Jefferson TO. Guidelines for authors and peer reviewers of economic submissions to the BMJ. The BMJ Economic Evaluation Working Party. BMJ. 1996;313(7052):275-283. PMID: 8704542.

Drummond M, Sculpher M. Common methodological flaws in economic evaluations. Med Care. 2005;43(7 Suppl):5-14. PMID: 16056003.

Evers S, Goossens M, de Vet H, van Tulder M, Ament A. Criteria list for assessment of methodological quality of economic evaluations: Consensus on Health Economic Criteria. Int J Technol Assess Health Care. 2005;21(2):240-245. PMID: 15921065.

Gerkens S, Crott R, Cleemput I, et al. Comparison of three instruments assessing the quality of economic evaluations: a practical exercise on economic evaluations of the surgical treatment of obesity. Int J Technol Assess Health Care. 2008;24(3):318-325. PMID: 18601800.

Hutubessy R, Chisholm D, Edejer TT. Generalized cost-effectiveness analysis for national-level priority-setting in the health sector. Cost Eff Resour Alloc. 2003;1(1):8. PMID: 14687420.

Shemilt I, Thomas J, Morciano M. A web-based tool for adjusting costs to a specific target currency and price year. Evid Policy. 2010;6(1):51-59.

Smith KA, Rudmik L. Cost collection and analysis for health economic evaluation. Otolaryngol Head Neck Surg. 2013;149(2):192-199. PMID: 23641023.

Ubel PA, Hirth RA, Chernew ME, Fendrick AM. What is the price of life and why doesn't it increase at the rate of inflation? Arch Intern Med. 2003;163(14):1637-1641. PMID: 12885677.

Books

Drummond MF, O'Brien BJ, Stoddart GL, Torrance GW. Methods for the Economic Evaluation of Health Care Programmes. 2nd Edition. Oxford, UK: Oxford University Press; 1997.

Gold MR, Siegel JE, Russell LB, Weinstein MC, eds. Cost-Effectiveness in Health and Medicine. 1996. Oxford, UK: Oxford University Press; 1996.

Other

Canadian Agency for Drugs and Technologies in Health (CADTH). Guidelines for the Economic Evaluation of Health Technologies. 3rd Edition. Ottawa, Canada: Canadian Agency for Drugs and Technologies in Health; 2006. Available at: http://www.cadth.ca/media/pdf/186_EconomicGuidelines_e.pdf. Accessed January 26, 2015.

APPENDIX III. Excluded Studies

The following 64 studies were excluded during full-text review.

Wrong Study Design for Assessing Accuracy

Typical reasons for excluding studies were wrong reference standard, measurement of statistical association only, failure to include patients with and without disease according to the reference standard, and accuracy calculated individually for numerous imaging features.

Awaida JP, Woods SE, Doerzbacher M, Gonzales Y, Miller TJ. Four-cut sinus computed tomographic scanning in screening for sinus disease. South Med J. 2004;97(1):18-20. PMID: 14746416.

Berger G, Steinberg DM, Popovtzer A, Ophir D. Endoscopy versus radiography for the diagnosis of acute bacterial rhinosinusitis. Eur Arch Otorhinolaryngol. 2005;262(5):416-422. PMID: 15378314.

Bhattacharyya N. Radiographic stage fails to predict symptom outcomes after endoscopic sinus surgery for chronic rhinosinusitis. Laryngoscope. 2006;116(1):18-22. PMID: 16481802.

Chandrasekharan R, Thomas M, Rupa V. Comparative study of orbital involvement in invasive and non-invasive fungal sinusitis. J Laryngol Otol. 2012;126(2):152-158. PMID: 22182506.

Chen JC, Ho CY. The significance of computed tomographic findings in the diagnosis of fungus ball in the paranasal sinuses. Am J Rhinol Allergy. 2012;26(2):117-119. PMID: 22487287.

De Sutter A, Lemiengre M, Van Maele G, et al. Predicting prognosis and effect of antibiotic treatment in rhinosinusitis. Ann Fam Med. 2006;4(6):486-493. PMID: 17148625.

Dufour X, Kauffmann-Lacroix C, Ferrie JC, Goujon JM, Rodier MH, Klossek JM. Paranasal sinus fungus ball: epidemiology, clinical features and diagnosis. A retrospective analysis of 173 cases from a single medical center in France, 1989-2002. Med Mycol. 2006;44(1):61-67. PMID: 16805094.

Ezeanolue BC, Aneke EC, Nwagbo DF. Correlation of plain radiological diagnostic features with antral lavage results in chronic maxillary sinusitis. West Afr J Med. 2000;19(1):16-18. PMID: 10821080.

Fakhran S, Alhilali L, Sreedher G, et al. Comparison of simulated cone beam computed tomography to conventional helical computed tomography for imaging of rhinosinusitis. Laryngoscope. 2014;124(9):2002-2006. PMID: 24449524.

Garcia DP, Corbett ML, Eberly SM, et al. Radiographic imaging studies in pediatric chronic sinusitis. J Allergy Clin Immunol. 1994;94(3 Pt 1):523-530. PMID: 8083458.

Gheriani H, Curran A, Timon C. Endoscopic sinus surgery outcome in patients with symptomatic chronic rhinosinusitis and minimal changes on computerised tomography. Ir Med J. 2006;99(1):15-16. PMID: 16506684.

Gutowski WM, Mulbury PE, Hengerer AS, Kido DK. The role of C.T. scans in managing the orbital complications of ethmoiditis. Int J Pediatr Otorhinolaryngol. 1988;15(2):117-128. PMID: 3397230.

Herrmann BW, Forsen JW Jr. Simultaneous intracranial and orbital complications of acute rhinosinusitis in children. Int J Pediatr Otorhinolaryngol. 2004;68(5):619-625. PMID: 15081240.

Iqbal A., Khan B., Ahmed M. Early radiological diagnosis of chronic sinusitis prevents complications. Journal of Medical and Health Sciences. 2013:1070-1076.

Jain R, Stow N, Douglas R. Comparison of anatomical abnormalities in patients with limited and diffuse chronic rhinosinusitis. Int Forum Allergy Rhinol. 2013;3(6):493-496. 00001 PMID: 23281312.

Jiang RS, Lin PK, Lin JF. Correlation between bacteriology and computed tomography staging for chronic sinusitis. J Laryngol Otol. 2005;119(3):193-197. PMID: 15845190.

Jiannetto DF, Pratt MF. Correlation between preoperative computed tomography and operative findings in functional endoscopic sinus surgery. Laryngoscope. 1995;105(9 Pt 1):924-927. PMID: 7666726.

Joshua BZ, Sachs O, Shelef I, et al. Comparison of clinical data, CT, and bone histopathology in unilateral chronic maxillary sinusitis. Otolaryngol Head Neck Surg. 2013;148(1):145-150. PMID: 23112270.

Kaplan BA, Kountakis SE. Diagnosis and pathology of unilateral maxillary sinus opacification with or without evidence of contralateral disease. Laryngoscope. 2004a;114(6):981-985. PMID: 15179199.

Kaplan BA, Kountakis SE. Role of nasal endoscopy in patients undergoing endoscopic sinus surgery. Am J Rhinol. 2004b;18(3):161-164. PMID: 15283490.

Katz RM, Friedman S, Diament M, et al. A comparison of imaging techniques in patients with chronic sinusitis (X-ray, MRI, A-mode ultrasound). Allergy Proc. 1995;16(3):123-127. PMID: 7557370.

Kolo ES. The role of plain radiographs in the diagnosis of chronic maxillary rhinosinusitis in adults. Afr Health Sci. 2012;12(4):459-463. PMID: 23515592.

Lazar RH, Younis RT, Parvey LS. Comparison of plain radiographs, coronal CT, and intraoperative findings in children with chronic sinusitis. Otolaryngol Head Neck Surg. 1992;107(1):29-34. PMID: 1528599.

Leo G, Triulzi F, Consonni D, Cazzavillan A, Incorvaia C. Reappraising the role of radiography in the diagnosis of chronic rhinosinusitis. Rhinology. 2009;47(3):271-274. PMID: 19839249.

Lindbaek M, Melby KK, Schøyen R, Hjortdahl P. Bacteriological findings in nasopharynx specimens from patients with a clinical diagnosis of acute sinusitis. Scand J Prim Health Care. 2001;19(2):126-130. PMID: 11482414.

McAlister WH, Lusk R, Muntz HR. Comparison of plain radiographs and coronal CT scans in infants and children with recurrent sinusitis. AJR Am J Roentgenol. 1989;153(6):1259-1264. PMID: 2816644.

Pokharel M, Karki S, Shrestha BL, Shrestha I, Amatya RC. Correlations between symptoms, nasal endoscopy computed tomography and surgical findings in patients with chronic rhinosinusitis. Kathmandu Univ Med J (KUMJ). 2013;11(43):201-205. PMID: 24442166.

Pokorny A, Tataryn R. Clinical and radiologic findings in a case series of maxillary sinusitis of dental origin. Int Forum Allergy Rhinol. 2013;3(12):973-979. PMID: 24039196.

Ragab A, Samaka RM, Salem M. Impact of fungal load on diagnosis and outcome of allergic fungal rhinosinusitis. Eur Arch Otorhinolaryngol. 2014;271(1):93-101. PMID: 23568040.

Rasmussen J, Aanæs K, Norling R, Nielsen KG, Johansen HK, von Buchwald C. CT of the paranasal sinuses is not a valid indicator for sinus surgery in CF patients. J Cyst Fibros. 2012;11(2):93-99. PMID: 22018629.

Sakuma Y, Ishitoya J, Komatsu M, et al. New clinical diagnostic criteria for eosinophilic chronic rhinosinusitis. Auris Nasus Larynx. 2011;38(5):583-588. PMID: 21371840.

Schwartz RH, Pitkaranta A, Winther B. Computed tomography imaging of the maxillary and ethmoid sinuses in children with short-duration purulent rhinorrhea. Otolaryngol Head Neck Surg. 2001;124(2):160-163. PMID: 11226949.

Sedaghat AR, Bhattacharyya N. Chronic rhinosinusitis symptoms and computed tomography staging: improved correlation by incorporating radiographic density. Int Forum Allergy Rhinol. 2012;2(5):386-391. PMID: 22550029.

Sharp HR, Rowe-Jones JM, Mackay IS. The outcome of endoscopic sinus surgery: correlation with computerized tomography score and systemic disease. Clin Otolaryngol Allied Sci. 1999;24(1):39-42. PMID: 10196646.

Sil A, Mackay I, Rowe-Jones J. Assessment of predictive prognostic factors for functional endoscopic sinus surgery in a 5-year prospective outcome study. Am J Rhinol. 2007;21(3):289-296. PMID: 17621811.

Smith TL, Mendolia-Loffredo S, Loehrl TA, Sparapani R, Laud PW, Nattinger AB. Predictive factors and outcomes in endoscopic sinus surgery for chronic rhinosinusitis. Laryngoscope. 2005;115(12):2199-2205. PMID: 16369166.

Snidvongs K, Chin D, Sacks R, Earls P, Harvey RJ. Eosinophilic rhinosinusitis is not a disease of ostiomeatal occlusion. Laryngoscope. 2013a;123(5):1070-1074. PMID: 23553255.

Snidvongs K, McLachlan R, Sacks R, Earls P, Harvey RJ. Correlation of the Kennedy Osteitis Score to clinico-histologic features of chronic rhinosinusitis. Int Forum Allergy Rhinol. 2013b;3(5):369-375. PMID: 23136070.

Som PM, Shapiro MD, Biller HF, Sasaki C, Lawson W. Sinonasal tumors and inflammatory tissues: differentiation with MR imaging. Radiology. 1988;167(3):803-808. PMID: 3363145.

Suonpää J, Revonta M. Diagnosis of frontal sinusitis: one-dimensional ultrasonography versus radiography. J Laryngol Otol. 1989;103(8):765-767. PMID: 2671221.

Suzuki H, Ikeda K, Honma R, et al. Prognostic factors of chronic rhinosinusitis under long-term low-dose macrolide therapy. ORL J Otorhinolaryngol Relat Spec. 2000;62(3):121-127. PMID: 10810255.

Wang PC, Chu CC, Liang SC, Tai CJ. Outcome predictors for endoscopic sinus surgery. Otolaryngol Head Neck Surg. 2002;126(2):154-159. PMID: 11870345.

Wang M, Yuan F, Qi W, et al. Anatomy, classification of intersinus septal cell and its clinical significance in frontal sinus endoscopic surgery in Chinese subjects. Chin Med J (Engl). 2012;125(24):4470-4473. PMID: 23253722.

Watelet JB, Annicq B, van Cauwenberge P, Bachert C. Objective outcome after functional endoscopic sinus surgery: prediction factors. Laryngoscope. 2004;114(6):1092-1097. PMID: 15179219.

Younis RT, Anand VK, Davidson B. The role of computed tomography and magnetic resonance imaging in patients with sinusitis with complications. Laryngoscope. 2002;112(2):224-229. PMID: 11889374.

Excluded Because of Wrong Study Design For Assessing Clinical Utility

Ramadan HH, Makary CA. Can computed tomography score predict outcome of adenoidectomy for chronic rhinosinusitis in children. Am J Rhinol Allergy. 2014;28(1):e80-e82. PMID: 24717893.

Stewart MG, Donovan DT, Parke RB, Bautista MH. Does the severity of sinus computed tomography findings predict outcome in chronic sinusitis? Otolaryngol Head Neck Surg. 2000;123(1 Pt 1):81-84. PMID: 10889486.

Wrong Design for Assessing Economic Impact

Franzese CB, Stringer SP. Economic analysis of the use of limited coronal computed tomography scans in the management of sinusitis. Am J Rhinol. 2004;18(5):329-334. PMID: 15586806. (wrong comparison)

Sedaghat AR, Gray ST, Kieff DA. Preapproval of sinus computed tomography for otolaryngologic evaluation of chronic rhinosinusitis does not save health care costs. Laryngoscope. 2014;124(2):373-377. PMID: 23794515. (wrong type of cost)

Wrong Population

These studies were excluded because either the entire study group or the control group were selected for some reason other than clinical suspicion of rhinosinusitis.

Carter JM, Johnson BT, Patel A, Palacios E, Rodriguez KH. Lund-mackay staging system in cystic fibrosis: a prognostic factor for revision surgery? Ochsner J. 2014;14(2):184-187. PMID: 24940127.

Clary RA, Cunningham MJ, Eavey RD. Orbital complications of acute sinusitis: comparison of computed tomography scan and surgical findings. Ann Otol Rhinol Laryngol. 1992;101(7):598-600. PMID: 1626907.

Dhong HJ, Jung JY, Park JH. Diagnostic accuracy in sinus fungus balls: CT scan and operative findings. Am J Rhinol. 2000;14(4):227-231. PMID: 10979495.

Jones NS, Strobl A, Holland I. A study of the CT findings in 100 patients with rhinosinusitis and 100 controls. Clin Otolaryngol Allied Sci. 1997;22(1):47-51. PMID: 9088680.

Lichtenstein D, Biderman P, Mezière G, Gepner A. The “sinusogram”, a real-time ultrasound sign of maxillary sinusitis. Intensive Care Med. 1998;24(10):1057-1061. PMID: 9840240.

Lin HW, Bhattacharyya N. Diagnostic and staging accuracy of magnetic resonance imaging for the assessment of sinonasal disease. Am J Rhinol Allergy. 2009;23(1):36-39. PMID: 19379610.

Karantanas AH, Sandris V. Maxillary sinus inflammatory disease: ultrasound compared to computed tomography. Comput Med Imaging Graph. 1997;21(4):233-241. PMID: 9402236.

Krzeski A, Kapiszewska-Dzedzej D, Jakubczyk I, Jedrusik A, Held-Ziółkowska M. Extent of pathological changes in the paranasal sinuses of patients with cystic fibrosis: CT analysis. Am J Rhinol. 2001;15(3):207-210. PMID: 11453510.

Pfister R, Lütolf M, Schapowal A, Glatte B, Schmitz M, Menz G. Screening for sinus disease in patients with asthma: a computed tomography-controlled comparison of A-mode ultrasonography and standard radiography. J Allergy Clin Immunol. 1994;94(5):804-809. PMID: 7963148.

Sadr SM, Ahmadinejad M, Saedi B, Razaghian F, Rafiee M. Anatomical variations in sinus imaging in sinusitis: a case control study. B-ENT. 2012;8(3):185-189. PMID: 23113381.

Revonta M, Suonpää J. Diagnosis of subacute maxillary sinusitis in children. J Laryngol Otol. 1981;95(2):133-140. PMID: 7462783.

Wrong Imaging Modality

Javer AR, Stevens HE, Stillwell M, Jafar AM. Efficacy of nuclear scintigraphy in the diagnosis and management of sinusitis. J Otolaryngol. 1996;25(6):375-382. PMID: 8972429.

Saylam G, Görgülü O, Korkmaz H, Dursun E, Ortapamuk H, Eryilmaz A. Do single-photon emission computerized tomography findings predict severity of chronic rhinosinusitis: a pilot study. Am J Rhinol Allergy. 2009;23(2):172-176. PMID: 19401044.

Poor Reporting of Results

Pfleiderer AG, Drake-Lee AB, Lowe D. Ultrasound of the sinuses: a worthwhile procedure? A comparison of ultrasound and radiography in predicting the findings of proof puncture on the maxillary sinuses. Clin Otolaryngol Allied Sci. 1984;9(6):335-339. PMID: 6398149.

APPENDIX IV. Evidence Tables

Appendix IVa. Studies Assessing the Clinical Performance of Imaging for RS

Key: AFIFS, acute fulminant invasive fungal sinusitis; AFS, allergic fungal sinusitis; ARS, acute rhinosinusitis; btwn, between; CRS, chronic rhinosinusitis; CT, computed tomography; dx, diagnosis(es); FESS, functional endoscopic sinus surgery; grp(s), group(s); HIV, human immunodeficiency virus; hx, history; IFRS, invasive fungal rhinosinusitis; LR, likelihood ratio; MRI, magnetic resonance imaging; NPV, negative predictive value; NR, not reported; OR, odds ratio; PPV, positive predictive value; preop, preoperative(ly); pt(s), patient(s); RS, rhinosinusitis; SD, standard deviation; SFB, sinus fungus ball; SNOT, Sinonasal Outcome Test; sx, symptoms; tx, treatment or therapy; US, ultrasound

Authors/Study Design/ Protocol	Pts/Follow-Up from DXA Scan	Main Findings	Quality/Comments
ARS			
Burke et al. (1994) Retrospective cohort study ***Index Test:*** Radiographs ***Reference Standard:*** CT	30 pts w/ ARS sx (mean age 37 yrs) ***Criteria for suspicion of ARS:*** NR ***Setting:*** Emergency department ***Previous tx:*** NR	***Prevalence of ARS:*** 72% All sinuses: 21 of 29 (72%) Maxillary sinus: 10 of 58 (17%) ***Diagnostic accuracy of radiographs for all sinuses (Radiologist 1, Radiologist 2) (%, 95% CI):*** Sensitivity: 57% (34%-78%), 62% (38%-82%) Specificity: 88% (47%-100%), 88% (47%-100%) PPV:* 92%, 93% NPV:* 44%, 47% ***Diagnostic accuracy of radiographs for maxillary sinuses (Radiologist 1, Radiologist 2) (%, 95% CI):*** Sensitivity: 70% (35%-93%), 70% (35%-93%) Specificity: 100% (93%-100%), 100% (93%-100%) PPV:* 14%, 14% NPV:* 62%, 62%	Good Small sample size. Reference standard was different imaging modality.
Aaløkken et al. (2003) Cross-sectional study ***Index Test:*** Radiographs ***Reference Standard:*** CT	47 pts w/ ARS sx (mean age 43 yrs) ***Criteria for suspicion of ARS:*** NR ***Setting:*** Radiology department; referring specialist NR ***Previous tx:*** NR	***Prevalence of ARS:*** Maxillary sinus: 48% Ethmoid sinus: 42% Frontal sinus: 21% Sphenoid sinus: 26% ***Diagnostic accuracy of radiographs:*** Sensitivity (%, 95% CI): Maxillary sinus (94 sinuses): 80% (65%-90%)	Fair Small sample size. Reference standard was different imaging modality. Whether examiners were blinded to results of index and reference standard NR.

Authors/Study Design/ Protocol	Pts/Follow-Up from DXA Scan	Main Findings	Quality/Comments
		Ethmoid sinus (94 sinuses): 41% (26%-58%) Frontal sinus (84 sinuses): 39% (17%-64%) Sphenoid sinus (47 sinuses): 25% (5%-57%) Specificity (%, 95% CI): Maxillary sinus (94 sinuses): 92% (80%-98%) Ethmoid sinus (94 sinuses): 100% (94%-100%) Frontal sinus (84 sinuses): 97% (89%-100%) Sphenoid sinus (47 sinuses): 97% (85%-100%) PPV:* Maxillary sinus (94 sinuses): 90% Ethmoid sinus (94 sinuses): 100% Frontal sinus (84 sinuses): 78% Sphenoid sinus (47 sinuses): 75% NPV:* Maxillary sinus (94 sinuses): 83% Ethmoid sinus (94 sinuses): 70% Frontal sinus (84 sinuses): 86% Sphenoid sinus (47 sinuses): 79%	
Chiu et al. (2010) Prospective cohort study ***Index Test:*** Radiographs ***Reference Standard:*** CT	42 pts w/ ARS sx (mean age 52 yrs) ***Criteria for suspicion of ARS:*** Nasal obstruction, postnasal drip, mucus or pus-like nasal discharge, halitosis in the nasal cavity ***Setting:*** Radiology department; referring specialist NR ***Previous tx:*** NR	***Prevalence of ARS:*** All sinuses: 100% Maxillary sinus: 83% ***Diagnostic accuracy of radiographs for all sinuses (%, 95% CI):*** Sensitivity: 93% PPV:* 100% Specificity and NPV could not be calculated because of 100% prevalence. ***Diagnostic accuracy of radiographs for maxillary sinuses (%, 95% CI):*** Sensitivity: 89% Specificity: 43 PPV:* 89% NPV:* 43%	Fair Small sample size. Reference standard was different imaging modality. Whether examiners were blinded to results of index and reference standard NR. The study group was of insufficient size and diversity to allow assessment of specificity for all sinuses.
CRS			
Vento et al. (1999) Cohort study, dx of CRS in pts w/ recurrent polyposis	40 pts (79 sinuses) w/ hx of CRS w/ recurrent polyposis (mean age 59 yrs) ***Criteria for suspicion of RS:*** NR	***Prevalence of CT-based RS dx:*** Fluid level: 25% Mucosal thickening: 51% ***Diagnostic accuracy of US assessed against CT for fluid level***	Good Small sample size. No assessment of statistical

Authors/Study Design/ Protocol	Pts/Follow-Up from DXA Scan	Main Findings	Quality/Comments
Index Test: US ***Reference Standard:*** CT	***Setting:*** Department of Otolaryngology ***Previous tx:*** 1 maxillary sinus had medial maxillectomy, 30 maxillary sinuses had Caldwell-Luc operation	***(Investigator 1, Investigator 2):*** Overall accuracy: 68%, 59% Sensitivity: 30%, 28% Specificity: 81%, 69% PPV: 35%, 23% NPV: 77%, 74% ***Diagnostic accuracy of US assessed against CT for mucosal thickening (Investigator 1, Investigator 2):*** Overall accuracy: 44%, 54% Sensitivity: 40%, 50% Specificity: 48% 58% PPV: 44%, 55% NPV: 44%, 53% ***Reproducibility:*** There was 50% agreement btwn the 2 investigators	uncertainty.
Konen et al. (2000) Cross-sectional study, dx of CRS ***Index Test:*** Radiography using Waters' view ***Reference Standard:*** CT	134 pts w/ suspected CRS (110 adults, 24 children; mean age 36.6 yrs) ***Criteria for suspicion of RS:*** NR ***Setting:*** Referred to Department of Diagnostic Imaging by otolaryngologist ***Previous tx:*** NR	***Prevalence of RS dx*:** 72.4% ***Diagnostic accuracy of radiography assessed against CT for maxillary sinuses (weighted mean±SD):*** Accuracy: 78.6±1.9 Sensitivity: 67.7±8.4 Specificity: 87.6±4.7 PPV: 82.5±4.5 NPV: 76.9±4.1 ***Diagnostic accuracy of radiography assessed against CT for frontal sinuses (weighted mean±SD):*** Accuracy: 78.5±4.9 Sensitivity: 14.6±16.3 Specificity: 94.5±9.3 PPV: 49.2±18.0 NPV: 81.7±2.6	Good Tx NR.
Timmenga et al. (2002) Cross-sectional study, dx of CRS ***Index Test:*** Radiography using Waters' view ***Reference Standard:*** CT	40 consecutive pts w/ suspected CRS (mean age 46.5 yrs) ***Criteria for suspicion of RS:*** Sx of pain in paranasal sinus; recurrent mucopurulent rhinorrhea; nasal congestion/obstruction for ≥3 mos ***Setting:*** Department of Otolaryngology ***Previous tx:*** Conservative tx (antibiotics,	***Prevalence of abnormal CT findings:*** Observer 1: 20 of 35 pts (57%) Observer 2: 24 of 37 pts (65%) ***Diagnostic accuracy of radiography assessed against CT (Investigator 1, Investigator 2):*** Overall accuracy: 77%, 81% Sensitivity: 95.0%, 83.3% Specificity: 53.0%, 69.2%	Good No assessment of statistical uncertainty.

Authors/Study Design/ Protocol	Pts/Follow-Up from DXA Scan	Main Findings	Quality/Comments
	decongestants)	PPV: 73.1%, 83.3% NPV: 88.9%, 68.6% LR+/LR─: 2.02/0.094, 2.7/0.24 ***Reproducibility (Cohen's kappa):*** Intraobserver agreement: >0.80 Interobserver agreement: >0.75	
Hopkins et al. (2007) Multicenter prospective cohort study, prognosis of surgical outcomes following nasal surgery ***Index Test:*** CT ***Reference Standard:*** Surgical confirmation	1840 pts scheduled to undergo procedures to treat CRS and/or nasal polyposis (mean age 47.2 yrs) ***Criteria for suspicion of RS:*** NR ***Setting:*** 87 participating Neck and Head Surgery Hospitals ***Mean SNOT score according to Lund-Mackey score range:*** 0-4 (358 pts): 41.8 5-9 (469 pts): 43.5 10-14 (515 pts): 42.8 15-24 (471 pts): 45.5 ***Previous tx:*** 45.4% had previous sinonasal surgery, 89.1% had previous steroid tx	1288 of an original 3128 pts did not undergo a preop CT scan, and therefore could not be assigned a Lund-Mackay score. 7% pts underwent simple polypectomy and no sinus surgery. ***Prognostic accuracy (adjusted OR for 1-point increase in Lund-Mackey score, 95% CI):*** Occurrence of complication (corrected for extent of surgery): 1.09 (1.06-1.13), *P*=0.001 Revision surgery w/in 12 mos: 1.006 (0.96-1.05), NS Revision surgery w/in 36 mos: 1.03 (1.001-1.06), *P*=0.046 Authors found no evidence of a threshold Lund-Mackey score below which pts are not offered surgery; 2 1% had a score of 0-4.	Fair Authors did not explain why factors other than extent of surgery and allergic status were not included as potential confounders in regression analysis. No assessment of overall prognostic performance based on a cutoff score.
Kasapoğlu et al. (2009) Cohort study, preop evaluation of CRS or recurrent RS ***Index Test:*** Radiographs ***Reference Standard:*** CT	43 pts (86 sinuses) undergoing evaluation prior to surgery for CRS or recurrent RS ***Criteria for suspicion of RS:*** Sx of RS for ≥3 mos ***Setting:*** Department of Otolaryngology ***Previous tx:*** Amoxicillin-clavulanic acid, second-generation cephalosporins or macrolides for 3 wks w/ systemic and local decongestant	***Prevalence (maxillary, frontal, ethmoid, sphenoid)*:** 70.9%, 70.9%, 82.6%, 38.4% ***Diagnostic performance of radiography for different sinuses (maxillary, frontal, ethmoid, sphenoid):*** Overall accuracy: 87.2%, 87.2%, 69.8%, 70.9% Sensitivity: 86.9%, 57.4%, 66.2%, 54.5% Specificity: 88.0%, 92.3%, 86.7%, 81.1% PPV: 94.6%, 90.0%, 95.9%, 64.3% NPV: 73.3%, 64.3%, 35.1%, 74.1%	Fair No assessment of statistical uncertainty. Whether radiographs and CT scans were assessed in a blinded manner NR. Details on grading of imaging NR.
Fungal RS			
Lenglinger et al. (1996) Prospective cohort study, suspected aspergillosis ***Index Test:*** CT	21 pts w/ sx and radiology results suggesting maxillary sinus aspergillosis (mean age 37 yrs) ***Criteria for suspicion of fungal RS:*** Unilateral concretions in the maxillary sinus detected in standard radiographs	***Prevalence of fungal infection confirmed by histopathology:*** 15 of 21 pts (71.4%) ***Diagnostic accuracy of CT assessed against histopathology:*** Overall accuracy: 90.5% Sensitivity:* 93.3% Specificity:* 83.3%	Fair Small sample size. No measure of statistical uncertainty. Whether coding of imaging and

Authors/Study Design/ Protocol	Pts/Follow-Up from DXA Scan	Main Findings	Quality/Comments
Reference Standard: Histopathology	***Setting:*** Department of Oral and Maxillofacial Surgery; referring physician specialty NR ***Previous tx:*** Hx of endodontic work in the adjacent upper alveolar ridge; radiographs ***Reason for surgery:*** NR	PPV: 93.3% NPV: 83.3%	histopathology was blinded NR.
Yoon et al. (1999) Cross-sectional study, dx of fungal RS ***Index Test:*** CT ***Reference Standard:*** Histopathology	510 pts w/ CRS who underwent sinonasal surgery (451 pts had FESS and 59 pts had Caldwell-Luc operations) (age range 18-77 yrs) ***Criteria for suspicion of fungal RS:*** NR ***Setting:*** Departments of Radiology and Otolaryngology ***Previous tx:*** NR ***Reason for surgery:*** Chronic maxillary RS	***Prevalence of fungal infection confirmed by histopathology:*** 39 of 510 (7.6%) pts ***Diagnostic accuracy of CT assessed against histopathology:*** Accuracy:* 93.1% Sensitivity:* 51.3% Specificity:* 96.6% PPV:* 55.6% NPV:* 96%	Fair Examiners not blinded to results of CT when interpreting results of the reference standard. No measure of statistical uncertainty.
Dhiwakar et al. (2003) Case-control study, dx of AFS ***Index Test:*** CT ***Reference Standard:*** Histopathology	41 pts that underwent sinonasal surgery categorized into 3 grps based on histopathological examination of the surgical specimen. Cases: AFS (20 pts) Controls: Ethmoidal polyposis (16 pts), invasive aspergillosis (5 pts) AFS pts: Mean age 24.9 yrs; 11 previous sinonasal surgery Polyposis pts: Mean age 44.8 yrs; 3 previous sinonasal surgery Aspergillosis pts: Mean age 38.2 yrs; 3 previous sinonasal surgery Pts w/ AFS were significantly younger than pts w/ ethmoidal polyposis, more likely to be female, and more likely to have had previous surgery. ***Criteria for suspicion of AFS:*** NR ***Setting:*** Department of Otolaryngology ***Reason for surgery:*** Previous surgery in some pts	***Diagnostic accuracy of CT for differentiating AFS from ethmoidal polyposis or invasive aspergillosis, assessed against histopathology:*** Sensitivity: 70% Specificity: 100% PPV and NPV are invalid.	Poor Case-control design. Examiners not blinded to results of CT when interpreting results of the reference standard. AFS pts were younger, more likely to be female, and more likely to have had previous surgery. No measure of statistical uncertainty.

Authors/Study Design/ Protocol	Pts/Follow-Up from DXA Scan	Main Findings	Quality/Comments
Broglie et al. (2009) Retrospective cohort study, dx of SFB ***Index Test:*** CT ***Reference Standard:*** Histopathology	615 pts who underwent FESS for CRS (age range 27-94 yrs) ***Criteria for suspicion of SFB:*** NR ***Setting:*** Department of Otolaryngology ***Previous tx:*** NR ***Reason for surgery:*** CRS	***Prevalence of SFB confirmed by histopathology:*** 53 of 615 (8.6%) pts ***Diagnostic accuracy of CT assessed against histopathology:*** Sensitivity: 83% Specificity: 94% PPV: 56% NPV: 98%	Fair No assessment of statistical uncertainty. Examiners not blinded to results of the CT when interpreting results of the reference standard.
Finkelstein et al. (2011) Retrospective case-control study, dx of IFRS in presence of hematological malignancies ***Index Test:*** CT ***Reference Standard:*** Histopathology	n=34 pts w/ hematological malignancies. 14 pts developed IFRS (cases). 20 pts did not have IFRS (control grp). IFRS grp: Median age 35.5 yrs; acute lymphatic leukemia (5 pts), acute myelocytic leukemia (4 pts), other disease (4 pts) Control grp: Median age 38.5 yrs; acute lymphatic leukemia (8 pts), acute myelocytic leukemia (9 pts), other disease (3 pts) ***Criteria for suspicion of IFRS:*** NR ***Setting:*** Department of Otolaryngology ***Previous tx:*** 71% of IFRS pts and 30% of control pts had antibiotic tx ($P<0.05$) ***Reason for surgery:*** NR	***Diagnostic accuracy of CT assessed against confirmed cases:*** Sensitivity:* 36% Specificity:* 100% PPV and NPV are invalid.	Fair Case-control design. No assessment of statistical uncertainty. Significantly more IFRS pts had previous antibiotic tx.
Groppo et al. (2011) Retrospective cohort study, dx of AFIFS in immunocompromised pts ***Index Test:*** CT ***Reference Standard:*** Histopathology	n=23 immunocompromised pts. 17 pts had confirmed AFIFS. 6 pts did not have AFIFS (control grp). AFIFS grp: Median age 53 yrs; diabetes (29%), acute lymphoblastic leukemia (18%), acute myelogenous leukemia (18%), HIV (12%), end-stage liver disease (0%) Control grp: Median age 33 yrs; diabetes (17%), acute lymphatic leukemia (50%), acute myelocytic leukemia (17%), HIV (0%), end-stage liver disease (17%)	***Prevalence of AFIFS confirmed by histopathology:*** 17 of 23 (74%) pts ***Diagnostic performance of MRI (Observer 1, Observer 2):*** Sensitivity: 86%, 85% Specificity: 75%, 75% PPV:* 90%, 91% NPV:* 65%, 64% ***Diagnostic performance of CT (Observer 1, Observer 2):*** Sensitivity: 69%, 57% Specificity: 83%, 83% PPV:* 92%, 91% NPV:* 48%, 40% ***Agreement btwn observers (k, 95% CI):***	Fair No assessment of statistical uncertainty. Examiners likely not blinded to the results of imaging when interpreting the results of the reference standard.

Authors/Study Design/ Protocol	Pts/Follow-Up from DXA Scan	Main Findings	Quality/Comments
	Criteria for suspicion of AFIFS: NR ***Setting:*** Department of Otolaryngology ***Previous tx:*** 17 pts had a hx of hematopoietic malignancy, solid organ transplant, or bone marrow transplant ***Reason for surgery:*** Underwent operative endoscopy to rule out or diagnose AFIFS	CT: 0.50 (0.19-0.80), *P*=0.006 MRI: 0.75 (0.48-1.00), *P*=0.001	

*Values were calculated using information provided in the article.

Appendix IVb. Studies Assessing the Clinical Utility of Imaging for RS

Key: Abx, antibiotic treatment; btwn, between; CRS, chronic rhinosinusitis; CT, computed tomography; EMT, empiric medical therapy; f/u, follow-up; grp(s), group(s); NR, not reported; NS, not statistically significant; OMC-CT, obstruction of ostiomeatal complex on CT; OR, odds ratio; POC-CT, point-of-care computed tomography; pt(s), patient(s); RCT, randomized controlled trial; sx, symptom(s); tx, treatment or therapy; uCT, upfront computed tomography

Authors/Study Design & Protocol	Study Population	Main Findings	Quality/Comments
Anzai et al. (2004) Cross-sectional survey 3 otolaryngology surgeons (Surgeon A was the only surgeon to examine pts) were administered questionnaires regarding tx decisions, before and after reviewing sinus CT scans in pts suspected of having CRS.	27 pts w/ suspected CRS (mean age 50 yrs) 74% of pts had sinus surgery prior to the study. Recent Abx for 89% of pts and oral steroids for 59%. Duration of sx in current episode NR.	***% pts for whom surgeon made change in tx decision from surgery to no surgery following review of C (surgical vs nonsurgical):*** Surgeon A: 9 of 27 pts (33%) (NS). Recommendation for surgery increased from 37% (10/27) to 56% (15/27); decision for surgery was reversed in 2 pts. Surgeon B: 7 of 27 pts (26%) Surgeon C: 10 of 27 pts (37%) (*P*=0.002) ***Agreement btwn surgeons:*** Agreement btwn treating physician (Surgeon A) and the other 2 surgeons (Surgeons B and C) before sinus CT scans were reviewed was poor (Cohen's κ=0.14), but improved significantly after the CT scans were seen (κ=0.46). ***Significant predictors of surgical tx after CT, OR (95% CI):*** CT findings were the predominant determinant of a decision to offer surgery. Surgeon A: Concordance, 153 (8.6-2730); *P*=0.001 Surgeon B: Total CT score, 1.13 (1.01-1.3); *P*=0.03 Surgeon C: OMC-CT, 18 (1.25-262); *P*=0.03 No other clinical factors, including previous Abx or demographic factors were significant.	Very poor Small sample size (likely underpowered). Bias toward delaying decision for surgery prior to CT may have overestimated the impact of the CT on clinical decisions.
Conley et al. (2011) Observational study w/ historical controls Compared the impact of POC-CT, on diagnostic and therapeutic decisions, using historical controls who did not receive POC-CT (pre-POC-CT). Pts presented w/ CRS sx and had negative endoscopic findings.	90 pts w/ suspected CRS and no previous surgery (pt characteristics NR) Evidence of CRS was found in 24 (60%) pts in the pre-POC-CT grp and 27 (67.5%) pts in the POC-CT grp.	***W/drawal or loss to f/u:*** 10 (20%) pts in the pre-POC-CT grp did not return for f/u CT, including 2 Abx pts, and were excluded from analysis. ***Medical tx at initial visit (POC-CT, pre-POC-CT) (% pts):*** Abx, overall: 35%, 37.5% Oral steroid, overall: 35%, 5% (*P*=0.0021) (Statistical testing NR except where noted.) ***Medical tx by CT results (POC-CT, pre-POC-CT) (% pts):*** Abx, positive CT: 51.9%, 54.2% Oral steroid, positive CT: 51.9%, 8.3% Abx, negative CT: 0%, 12.5% Oral steroid, negative CT: 0%, 0% (CT results were from initial visit for POC-CT grp; from posttx f/u visit for	Very poor Moderate loss to f/u in pre-POC-CT grp; retrospective study design; control grp was historical pts (chronology bias may be present); statistical analyses for Abx NR; utilization rates by CT results in the pre-POC-CT grp were confounded by medication effects; no

Authors/Study Design & Protocol	Study Population	Main Findings	Quality/Comments
Positive CT defined by Lund-Mackay score ≥5. Pre-POC-CT grp returned for CT at 3-wk, posttx f/u. No f/u data for POC-CT grp.		pre-POC-CT grp. Statistical testing NR.)	comparison of final surgery rates; source of funding NR.
Tan et al. (2011) Single-blind RCT Compared uCT w/ EMT in pts w/ negative endoscopy seen in a tertiary care setting. In uCT grp, only pts w/ positive CT received medical tx; in EMT grp, all pts received medical tx. Positive CT defined by Lund-Mackay score ≥3. F/u at 4-6 wks for pts who received medical tx (55% of uCT grp; 100% of EMT grp).	40 adults w/ sx of CRS for ≥12 wks and negative endoscopy (an unknown proportion of pts had already undergone a trial of medical tx) 60% of pts in uCT grp had positive CT.	***Missing f/u data:*** 45% (9/20) of uCT grp (no instructions to return because of negative CT), 30% (6/20) of EMT grp (low to f/u despite instructions to return after tx) ***Clinical response (uCT, EMT) (% contactable pts w/ some relief):*** 73% (8/11), 43% (6/14) (NS) 1 pt in each grp required surgery ***Utilization (uCT, EMT) (% all pts unless otherwise noted):*** CT scans (% pts): 100%, 45% Neurological referral for negative CT (% negative scans): 75% (9 /12), 29% (2/7) Neurological referral for negative CT: 45% (9 /20), 10% (2/20) (*P*=0.031*)* Allergist referral: 35%, 25% Otolaryngology visits (mean n): 1.55, 1.71 Abx: 40%, 100% Antihistamine: 60%, 30% Proton pump inhibitor: 0%, 5% Antileukotriene: 5%, 10% Nasal steroid: 80%, 75% Oral steroid: 30%, 35% Significance NR for most outcomes.	Fair (tx decisions) Very poor (clinical outcomes) Pts in uCT grp w/ negative CT were not followed; 30% of EMT grp did not return for f/u. Use of online power calculator (http://www.stat.ubc.ca/~rollin/stats/ssize/b2.html) suggests that Abx differences are statistically significant.

Appendix IVc. Cost Comparisons of Different Strategies for Using Computed Tomography (CT) in the Diagnosis of Rhinosinusitis (Key Question #5)

NOTE: All of the following studies were conducted by investigators in the Department of Otolaryngology–Head and Neck Surgery at Northwestern University in Chicago, Illinois. All studies made the following assumptions in favor of the null hypothesis (no advantage to upfront CT): repeat CT always necessary in upfront CT strategy, cheapest available medications, no inclusion of adverse events associated with steroids, no accounting for antibiotic resistance, estimates of response to medical treatment counting partial as full, no return of symptoms after resolution, no addition of oral steroids to intranasal steroids for allergic rhinitis.

Key: AAO-HNS, American Association of Otolaryngology–Head and Neck Surgery; Abx, antibiotic treatment; AE(s), adverse event(s); AFP, atypical facial pain/migraine/headache disorder; AR, allergic rhinitis; AR/NAR, allergic/nonallergic rhinitis; CRS, chronic rhinosinusitis; CT, computed tomography; dx, diagnosis; EE, economic evaluation; EMT, empiric medical therapy; f/u, follow-up; NIDCD, National Institute on Deafness and Communication Disorders; NR, not reported; PCP, primary care physician; POC-CT, point-of-care computed tomography; pt(s), patient(s); sx, symptoms; tx, treatment or therapy; uCT, upfront CT

Authors/Study Type/Population	Inputs, Assumptions, and Calculations	Findings/Sensitivity Analysis	Author Conclusions/Comments
Leung et al. (2011) U.S. ***Type of EE:*** Cost comparison of uCT vs EMT ***Design:*** Markov model ***Perspective:*** Payer and societal ***Time horizon:*** Until completed evaluation and first-line tx of CRS or referred evaluation and first-line tx of AR/NAR or AFP ***Participants:*** Pts who presented to tertiary care center w/ sx of CRS (defined by 2007 AAO-HNS guidelines; see **Appendix V**) but have negative endoscopy	***Pre-CT, sx-based prevalence in pts w/ negative endoscopy:*** CRS, 20%; AR/NAR, 30%; AFP, 50% ***Prevalence of CT-based dx:*** Unclear ***Tx protocol (services listed in order of delivery):*** uCT: CT if endoscopy is negative Abx, prednisone, and fluticasone propionate for CRS if CT positive (Lund-Mackay score ≥4) (plus second Abx if AEs occur); otherwise, allergy consultation for AR, and neurology consultation for AFP F/u CT for nonresponders to CRS medications. EMT: Abx, prednisone, and fluticasone propionate (plus second Abx if AEs occur) if endoscopy is positive CT for nonresponders Referral if CT-based dx is AR or AFP.	***Cost savings per pt w/ negative endoscopy, median assumptions for CRS medication costs, rates of AEs, and medical tx response rates:*** Same-day CT available: $321 ($343 in 2014 USD) Same-day CT not available: $297 ($317 savings in 2014 USD) ***Optimization of alternative strategies:*** Cost savings also predicted when either uCT or EMT was optimized (optimization = most favorable assumptions for CRS medication costs, rates of AEs, and medical tx response rates), regardless of whether same-day CT available. ***Multiway sensitivity analyses based on simulation:*** uCT represented a cost savings across the range of probabilities for various combinations of pretest probabilities (to reflect different practice settings) and alternative optimization of uCT vs EMT. ***Impact on society (uCT, EMT):*** Half-days of productivity loss, same-day CT available: 2, 2.6	***Authors' conclusions:*** The uCT strategy is favorable under various circumstances and could yield substantial savings to the healthcare system. ***Limitations:*** Findings may not be generalizable to pts who are diagnosed w/o endoscopy, or have health insurance other than Medicare; unclear assumptions regarding prevalence of CT-based dx of CRS; tx response assumptions not based on a systematic review.

Authors/Study Type/Population	Inputs, Assumptions, and Calculations	Findings/Sensitivity Analysis	Author Conclusions/Comments
Funding source: NR	***Tx response rates from literature (base case, minimum, maximum):*** CRS: 55%, 40%, 72% AR/NAR: 63%, 40%, 87% AFP: 8%, 5.5%, 11% (definitions of response unclear) ***Abx AE rates from literature:*** Median, 5%; minimum, 1%; maximum, 10% ***Costs:*** Office visits, endoscopy at initial visit, CT scan, CRS medications, and skin prick for allergy. Specific cost assumptions for AR/NAR and AFP medical txs NR. Derived from Redbook (2010) and Medicare (2010).	Half-days of productivity loss, same-day CT not available: 3, 3.2	
Tan et al. (2011) U.S. ***Type of EE:*** Utilization comparison of uCT vs EMT ***Design:*** Trial-based (single-blind [CT interpretation] RCT) ***Perspective:*** Unclear (most likely combined pt-payer) ***Time horizon:*** 4-6 wks after initial office visit (costs associated w/ referral and surgical planning not included) ***Participants:*** Pts referred to or self-referred to a tertiary specialist clinic w/ CRS sx lasting ≥12 wks, excluding those w/ positive endoscopy ***Funding source:*** NIDCD	***Prevalence of CT-diagnosed CRS in uCT grp:*** 60% (all pts had negative endoscopy) ***Tx protocol (services listed in order of delivery):*** See Leung et al. (2011). Exceptions: (1) Cutoff for positive CT was Lund-Mackay score ≥3. (2) CBCT used for uCT. ***Tx response and AE rates:*** As observed in trial ***Costs:*** CRS medications; derived from local Walgreens charges, calculated for pts' actual prescriptions. Base year NR.	All pts in uCT grp for whom posttx f/u was recommended returned; only 10 pts in EMT grp returned for f/u, although all 20 were advised to return (*P=0.004*). ***Medication costs for pts w/ negative endoscopy (uCT, EMT) (mean±variance):*** All: $218±$139, $253±$89 (NS) Abx: $53±$88, $153±$36 (*P*<0.05)	***Authors' conclusions:*** uCT w/ POC-CT reduced use of Abx and Abx costs but not overall medication costs. There are intangible benefits from minimizing risk of Abx resistance. ***Limitations:*** Findings not generalizable to pts who are diagnosed w/o endoscopy or are seen where POC-CT is unavailable; unclear whether Walgreens costs were unnegotiated prices or actual charges; high loss to f/u. ***Comments:*** Study does not allow a comparison of total costs or overall clinical outcomes.

Authors/Study Type/Population	Inputs, Assumptions, and Calculations	Findings/Sensitivity Analysis	Author Conclusions/Comments
Tan et al. (2013) U.S. ***Type of EE:*** Cost comparison of uCT vs EMT ***Design:*** Decision analysis using previous cross-sectional study of correlation between sx- and CT-based dx ***Perspective:*** Payer ***Time horizon:*** Until completed evaluation and first-line tx of CRS or referred evaluation and first-line tx of AR/NAR or AFP ***Participants:*** Pts referred to or self-referred to a tertiary specialist clinic, excluding those whose initial exam suggested dxs other than CRS, AFP, or AR/NAR (set of possible sx drawn from multi-specialty guidelines). ***Funding source:*** NR	***Pre-CT, pre-endoscopy prevalence of CRS, AR/NAR, and AFP based on AAO-HNS criteria:*** CRS, 50%; AR/NAR, 28%; AFP, 22%. Derived from a previous cross-sectional study by same authors. ***Prevalence of CT-based dx:*** Unclear ***Tx protocol:*** See Leung et al. (2011) ***Tx response rates from literature:*** Same as for Leung et al. (2011) except response rates for AFP (19%, 16%, and 34%) were reported for placebo tx. ***Abx AE rates from literature:*** Same as for Leung et al. (2011) ***Costs:*** Same as in Leung et al. (2011).	***Cost savings per pt, median assumptions for CRS medication costs, rates of AEs, and medical tx response rates:*** *Same-day CT available:* Dx based on individual sx (from set of 13 AR/NAR and AFP sx): $64-$415 ($68-$444 in 2014 USD) Dx based on AAO sx for CRS: $186 ($199 in 2014 USD) Various combinations of sx: –$121 to $504 Pts w/ endoscopy+: –$133 *Same-day CT NOT available:* Dx based on individual sx (from set of 13 AR/NAR and AFP sx): –$100 to $229 (–$107 to $245 in 2014 USD) Dx based on AAO-HNS sx for CRS: $20 ($21 in 2014 USD) Various combinations of sx: –$276 to $332 Pts w/ endoscopy+: –$288 ***Optimization of alternative strategies (same method as for Leung et al., 2011):*** When EMT was optimized, cost differences ranged from substantially favoring EMT to marginally favoring uCT if same-day CT were available, and consistently favored EMT if same-day CT were not available.	***Authors' conclusion:*** According to median costs, uCT is less costly unless an endoscopy is added. However, a multi-symptom-based risk-stratification model can potentially change costs and reduce the need for nasal endoscopy or CT for the dx of CRS. ***Limitations:*** Findings may not be generalizable to pts who have health insurance other than Medicare, or are seen in non-academic or primary care settings; unclear assumptions regarding prevalence of CT-based dx of CRS; tx response assumptions not based on a systematic review
Leung et al. (2014) U.S. ***Type of EE:*** Cost comparison of uCT vs EMT ***Design:*** Decision analysis ***Perspective:*** Payer ***Time horizon:*** Until completed evaluation and	***Prevalence of endoscopy- or CT-based CRS:*** 88% AFP, 12% CRS. From estimates in the literature, using L-M score ≥4 or positive endoscopy as the basis of CRS dx. Values in studies of specialty-based practice were extrapolated (methods NR) to primary care practice. ***Tx protocol:*** Limited detail suggests protocol	***Cost savings per pt, uCT w/o endoscopy in primary care vs EMT for positive endoscopy after otolaryngology referral:*** Scenario 1: >$503* ($538 in 2014 USD) Scenario 2: $326 ($348 in 2014 USD) ***Cost savings in multiway sensitivity analyses:*** Scenario 1: $296-$761 ($248-$813 in 2014 USD) Scenario 2: $299-$353 ($320-$377 in 2014 USD)	***Authors' conclusions****:* uCT is less costly than tx of presumed CRS based on sx alone for pts w/ CRS sx seen in a PCP office. ***Limitations:*** *Persistence* not defined; methods of extrapolation of sx-based

Authors/Study Type/Population	Inputs, Assumptions, and Calculations	Findings/Sensitivity Analysis	Author Conclusions/Comments
first-line tx of CRS or referred evaluation and first-line tx of AR/NAR or AFP ***Participants:*** Pts presenting to PCP office w/ sx of CRS ***Funding source:*** NR	was same as that for Leung et al. (2011), modified to account for possibility of referring pts to a specialist for CRS tx. ***Scenario 1 (PCPs comfortable managing medical tx):*** uCT grp: CT at first visit. CRS diagnosed if endoscopy and/or CT is positive; otherwise, chronic AR. Referral to otolaryngologist if sx persist after first-line tx. Presumed CRS grp: Tx at first visit. Referral to otolaryngologist if sx persist after tx. CT follows to confirm CRS if endoscopy is negative. CT for surgical planning for all pts w/ CRS dx (unclear whether second-line tx would be considered by otolaryngologist prior to preop CT). ***Scenario 2 (PCP prefers referral):*** uCT grp: CT at first visit, followed by referral to otolaryngologist. Second-line tx considered if necessary. Presumed CRS grp: Referred directly to otolaryngologist and treated medically if endoscopy is positive. If endoscopy is negative, CT is ordered for confirmation. ***Tx response rates from literature (median, minimum, maximum):*** CRS and AR: Same as for Leung et al. (2011) AFP (placebo): 19%, 16%, 34% AFP (appropriate): 55%, 72%, 32% ***Abx AE rates****:* Same as Leung et al. (2011) ***Costs:*** Same as for Leung et al. (2011) plus explicit consideration of costs for AR and AFP medications.	*Use of '>' unclear.	prevalence from specialty to PCP setting not described; findings may not be generalizable to pts who are treated for presumptive CRS w/o endoscopy or who do not have Medicare coverage.

APPENDIX V. Summary of Practice Guidelines

Key: α, alpha; ABRS, acute bacterial rhinosinusitis; Abx, antibiotics; AR, allergic rhinitis; btwn, between; CT, computed tomography; dx, diagnosis; hx, history; IVIG, intravenous immunoglobulin; MRI, magnetic resonance imaging; pt(s), patient(s); RS, rhinosinusitis; sx, symptoms; tx, treatment/therapy; URI, upper respiratory tract infection; US, ultrasound; VRS, viral rhinosinusitis

Sponsor, Title	Relevant Recommendations			Quality/Main Limitations
	Diagnosis	Treatment	Repeat Testing	
American Academy of Allergy, Asthma, and Immunology (AAAAI); American College of Allergy, Asthma & Immunology (ACAAI) (Slavin et al., 2005) *The Diagnosis and Management of Sinusitis: A Practice Parameter Update*	***Classification of RS:*** Acute: Sx lasting <4 wks; sx may include persistent sx of URI, purulent rhinorrhea, postnasal drainage, anosmia, nasal congestion, facial pain, headache, fever, cough, and purulent discharge Subacute: Sx lasting 4-8 wks Chronic RS: Sx lasting ≥8 wks; there should be abnormal CT or MRI findings Recurrent RS: ≥3 episodes of acute RS per yr ***Presumed ABRS:*** ABRS is suspected in pts w/ URI lasting >10-14 days. A hx of persistent purulent rhinorrhea, postnasal drainage, and facial pain correlates w/ increased likelihood of ABRS. (Grade A recommendation) Prominent sx of ABRS include nasal congestion, purulent rhinorrhea, facial-dental pain, postnasal drainage, headache, and cough. (Grade C recommendation) ***Imaging:*** To confirm dx when sx are vague, physical findings are equivocal, or clinical disease persists despite optimal medical tx. (Grade B recommendation) *US:* Limited utility but might be useful in pregnant women or for determining amounts of retained sinus secretions. (Grade C recommendation) (Not mentioned in algorithm) *Standard radiographs:* Might be used to detect acute	***Abx:*** Primary tx for bacterial RS. (Grade A recommendation). Inappropriate and discouraged strongly for uncomplicated viral URI. (Grade D recommendation) Duration not well defined. (Grade D recommendation) Concern has been raised about the overdiagnosis of RS and unnecessary tx w/ Abx. Appropriate criteria for the use of Abx are sx of RS for 10-14 days or severe sx of acute sinus infection, including fever w/ purulent nasal discharge, facial pain or tenderness, and periorbital swelling. Extended Abx tx or a different Abx to be considered if initial trial is unsuccessful. (Not formal recommendations) ***Antihistamines:*** No data to recommend the use of H_1 antihistamines in acute bacterial RS. (Grade D recommendation) Possible role for antihistamines in chronic RS if the underlying risk factor is AR. (Grade D recommendation) ***α-Adrenergic decongestants:*** Topical and oral decongestants are often used in the tx of acute or chronic RS because they decrease nasal resistance and theoretically increase ostial patency. (Grade D recommendation) Prospective studies are lacking and are needed to assess the value of α-adrenergic agents in the prevention or tx of RS. (Grade D recommendation)	No recommendations	4.5—Fair (criteria for selecting evidence not described, methods for formulating recommendations not described, guideline review and update process not described)

Sponsor, Title	Relevant Recommendations			Quality/Main Limitations
	Diagnosis	Treatment	Repeat Testing	
	ABRS; not sensitive, particularly for ethmoid disease. (Grade C recommendation) (Not mentioned in algorithm) *CT:*[1,2] Optimal technique for evaluating ethmoid sinuses and for preoperative evaluation of nose and paranasal sinuses, including assessment of the ostiomeatal complex areas. (Grade C recommendation) NOTE: Algorithm advises to *consider* CT and/or nasal endoscopy if Abx tx is not successful; no distinction btwn acute and chronic RS. *MRI:*[3] Sensitive technique for evaluating suspected fungal RS and for differentiating btwn inflammatory disease and malignant tumors. Limited in its ability to define bony anatomy. (Grade C recommendation) (Not mentioned in algorithm)	***Glucocorticosteroids:*** The use of systemic corticosteroid tx for sinus disease has not been studied systematically in a well-controlled or blinded manner. (Grade D recommendation) A few recent studies suggest that the addition of intranasal corticosteroids as an adjunct to Abx tx might be modestly beneficial in the tx of pts w/ recurrent acute or chronic RS. (Grade C recommendation) ***Adjunctive tx:*** *Saline, mucolytics, and expectorants:* There are several scientific studies that imply but do not directly confirm a role for these agents in RS. (Grade D recommendation) Use of all these agents as prophylaxis for exacerbations of chronic RS is empiric and not supported by clinical data. (Grade D recommendation) These agents are commonly used and in some instances might be beneficial in some pts. (Grade D recommendation) ***IVIG:*** Immunodeficiency might be an underlying risk factor for the development of recurrent acute or chronic RS. (Grade B recommendation)		

[1]Indications for CT: recurrent acute sinusitis, chronic sinusitis, preoperative evaluation prior to sinus surgery, nasal polyposis, persistent and nasal congestion-obstruction, immunocompromised pt w/ fever, dentomaxillary pain, facial pressure-headache unresponsive to medical tx.
[2]Indications for CT w/ contrast: complications of sinusitis (periorbital edema, subperiosteal abscess), sinonasal tumor.
[3]Indications for MRI w/ contrast: skull base dehiscence with opacification, unilateral sinonasal opacification (on CT), sinonasal process with cranial extension, expansile sinonasal mass with bony erosion, sinonasal mass with orbital extension, biopsy-proven tumor, fungal sinusitis.

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		IVIG is approved as a replacement tx for antibody deficiency disorders (e.g., X-linked agammaglobulinemia, common variable immunodeficiency). (Grade A recommendation) Appropriate use of IVIG can prevent complications from chronic RS, including subperiosteal and intracranial abscesses, meningitis, sepsis, and death. (Grade B recommendation) ***Aspirin-desensitization tx****:* Beneficial effects of aspirin desensitization on pts w/ aspirin-exacerbated respiratory disease (AERD) have been reported. (Grade A recommendation) ***Surgery:*** Antral puncture and irrigation is an office procedure that has a place in the management of acute ethmomaxillary RS refractory to medical tx, or in acute RS in an immunosuppressed pt in which early identification of pathogenic organisms is paramount. (Grade D recommendation) Surgical intervention might be required in acute RS to provide drainage when there is a significant risk of intracranial complication or in a pt w/ periorbital or intraorbital abscess or visual compromise. (Grade D recommendation) Functional endoscopic sinus surgery, in combination w/ appropriate medical tx, has been shown in uncontrolled studies to have long-term efficacy in reducing disease-specific sx and in improving overall quality of life. (Grade C recommendation)		
American Academy of Otolaryngology–Head and Neck Surgery Foundation (AAO-	*Presumed ABRS:* Diagnose ABRS when (a) sx or signs of acute RS are present >10 days beyond the onset of upper respiratory sx, or (b) sx or signs of acute RS worsen w/in 10 days after an initial improvement	Symptomatic relief for managing VRS or ABRS*. Option* Analgesic tx for presumed ABRS based on severity of pain. *Strong recommendation*	No recommendations. (However, discussion states	6—Good (source of funding NR)

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HNSF) (Rosenfeld et al., 2007) *Clinical Practice Guideline: Adult Sinusitis* The AAO-HNSF is scheduled to publish an update to the adult sinusitis guidelines in April 2015.	(double worsening). *Strong recommendation* ***Endoscopy/Radiographic imaging:*** Acute: *Not* recommended unless a complication or alternative dx is suspected. *Recommendation against* Chronic or recurrent acute: Nasal endoscopy. *Option* CT of the paranasal sinuses. *Recommendation* (A dx of chronic RS requires documentation of inflammation by rhinoscopy, nasal endoscopy, or radiographic imaging.) Clinicians should distinguish chronic RS and recurrent acute RS from isolated episodes of ABRS and other causes of sinonasal sx. *Recommendation* Clinicians should assess the pt w/ chronic RS or recurrent acute RS for factors that modify management, such as AR, cystic fibrosis, immunocompromised state, ciliary dyskinesia, and anatomic variation. *Recommendation* The clinician should corroborate a dx and/or investigate for underlying causes of chronic RS and recurrent acute RS. *Recommendation* The clinician may obtain testing for allergy and immune function in evaluating a pt w/ chronic RS or recurrent acute RS. *Option based on observational studies w/ an unclear balance of benefit vs harm*	Observation w/o use of Abx for adults w/ uncomplicated ABRS who have mild illness (mild pain and temperature <38.3°C/101°F) and assurance of f/u. *Option* If a decision is made to treat ABRS w/ an Abx agent, the clinician should prescribe amoxicillin as first-line tx for most adults. If the pt worsens or fails to improve w/ the initial management option by 7 days after dx, the clinician should reassess the pt to confirm ABRS, exclude other causes of illness, and detect complications. If ABRS is confirmed in the pt initially managed w/ observation, the clinician should begin Abx tx. If the pt was initially managed w/ an Abx, the clinician should change the antibiotic. *Recommendation* ***Surgery:*** No recommendations on surgery are made in the guidelines.	that CT findings provide an objective method for monitoring.)	
American Academy of Pediatrics (Smith et al., 2013; Wald et al., 2013) *Clinical Practice Guideline for the*	***Presumed ABRS:*** Diagnose ABRS when child w/ URI presents w/ (a) persistent illness >10 days w/o improvement, (b) worsening course after initial improvement, (c) severe onset (temperature ≥39°C/102.2°F) and purulent nasal discharge for ≥3 days. *Recommendation* Reassessment: If caregiver reports worsening	***Severe onset and worsening course ABRS:*** Abx for acute ABRS w/ severe or worsening sx. *Strong recommendation* Persistent illness: Abx or additional observation for 3 days for persistent illness (nasal discharge and/or cough for ≥10 days w/o improvement). *Strong recommendation*	No recommendations	6.5—Good (methods for formulating consensus recommendations not described, procedure for

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Diagnosis and Management of Acute Bacterial Sinusitis in Children Aged 1 to 18 Years	(progression of initial sx or appearance of new sx) *or* failure to improve (lack of reduction in all presenting sx) w/in 72 hrs of initial management. *Recommendation* ***Radiographic imaging:*** Dx: *Not* recommended to distinguish ABRS from viral URI. *Strong recommendation against* Suspected complications: Clinicians should obtain a contrast-enhanced CT scan of the paranasal sinuses and/or an MRI w/ contrast if a child is suspected of having orbital or central nervous system complications of ABRS. *Strong recommendation* Recurrent ABRS: Contrast-enhanced CT, MRI, or endoscopy, or all 3 should be performed for detection of obstructive conditions, particularly in children w/ craniofacial abnormalities. (Not a formal, graded recommendation)	First-line: Amoxicillin w/ or w/o clavulanate. *Recommendation* Reassessment: If the dx of ABRS is confirmed in a child w/ worsening sx or failure to improve in 72 hrs, consider changing Abx for the child initially managed w/ Abx or initiate Abx tx of the child initially managed w/ observation. *Option* Adjuvant tx: No recommendation for ABRS, including intranasal corticosteroids, saline nasal irrigation or lavage, topical or oral decongestants, mucolytics, and topical or oral antihistamines. *No recommendation* *Recurrent ABRS:* ABRS episodes lasting <30 days and separated by intervals of ≥10 days. Some experts require ≥4 episodes/yr to diagnose. Pt should be evaluated for underlying allergies, quantitative and functional immunologic defect(s), dysmotile cilia syndrome, and anatomic abnormalities. *No recommendation*		update of guideline NR)
American College of Radiology (ACR) (ACR, 2012a; ACR, 2012b) *ACR Appropriateness Criteria: Sinusitis (Child and Adult)*	Gold standard for dx of ABRS is recovery of high-density bacteria ($\geq 10^4$ colony-forming units/mL) from sinus aspirate. However, this method is not feasible for the primary care practitioner and is invasive, time-consuming, and potentially painful. ***ABRS:*** Bacterial RS that lasts <30 days and whose sx resolve completely. A common sx of ABRS is URI w/ purulent nasal drainage. Severe ABRS is associated w/ high fever and headache that is typically above or behind the eyes. ***Subacute RS:*** Sx lasting 4-12 wks (28-84 days) ***Recurrent ABRS:*** Episodes lasting <30 days each and separated by intervals of ≥10 asymptomatic days. ***Chronic RS:*** Lasts >90 days and pts have persistent	The differentiation btwn viral and bacterial RS and the decision about whether to treat w/ Abx may be difficult. Adjuvant tx may include saline nasal irrigation, antihistamines, decongestants, mucolytic agents, and topical intranasal steroids.	No recommendations	4—Fair (systematic search methods and criteria for selecting evidence not described, methods for formulating recommendations not described, guideline not reviewed by external experts, guideline review and update process not described,

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	residual respiratory sx (cough, rhinorrhea, or nasal obstruction) ***Imaging:*** Routine imaging of the paranasal sinuses in children and adults w/ ABRS w/o complications is not recommended. It is not useful for differentiating btwn viral and bacterial RS and usually does not change management in uncomplicated ABRS. Imaging should be reserved for pts who develop recurrent ABRS, complicated RS, or chronic RS w/ atypical sx, or for defining sinus anatomy prior to surgery. In adults, clinical evaluation combined w/ nasal endoscopy may obviate the need for CT imaging in some cases of chronic RS. ***Radiography:*** Radiographs are limited in the evaluation of the paranasal sinuses because they cannot localize the pathology well and cannot evaluate the ostiomeatal complex. Sinus radiographs are inaccurate in a high % of pts and have been supplanted by CT imaging. ***CT:*** CT scans are the gold standard for guiding management of RS because they accurately depict the sinus anatomy and complications. Contrast enhancement is not generally needed for routine sinus imaging. CT is the study of choice in children w/ persistent, recurrent, or chronic RS. If suspicion exists for complications of RS, then intravenous contrast CT, including the brain and sinuses, is indicated. ***MRI:*** Not as good as CT for depicting bone details but more sensitive for evaluating intracranial complications not demonstrated on initial CT scan. MRI of the sinuses should not be the primary imaging for evaluation of RS.			competing interests of grp members not declared)

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	Fungal RS: Invasive fungal RS is a rapidly progressive disease seen in immunosuppressed pts and poorly controlled diabetics. Both CT (w/ contrast) and MRI (w/ or w/o contrast) of the sinuses, brain, and orbits may be needed to fully define the extent of orbital or intracranial extension of disease. ***Suspected Sinonasal Mass:*** If seen on sinus CT or if pts have persistent sx of pain, nasal obstruction, or epistaxis, complete evaluation of the extent of disease usually requires both CT and MRI evaluation.			
Institute for Clinical Systems Improvement (ICSI) (Snellman et al., 2013) *Diagnosis and Treatment of Respiratory Illness in Children and Adults*	***Presumed ABRS:*** URI present ≥10 days w/o improvement; sx are severe or pt has fever ≥102°F w/ purulent nasal discharge or facial pain that lasts ≥3-4 days; sx are worsening or new onset of fever, headache, or increased nasal discharge after initial improvement Gold standard for dx of ABRS: Sinus aspiration (>10,000 colony-forming units/mL). However, routine sinus aspiration is not practical. ***Presumed allergic RS:*** Pruritus of eyes, nose, palate, ears; watery rhinorrhea; sneezing; seasonal sx; family hx of allergies; sensitivity to specific allergens; asthma or eczema Reassessment: An alternative management strategy is recommended if sx worsen after 48-72 hrs of initial Abx tx or fail to improve despite 3-5 days of initial empiric Abx tx. ***Imaging:*** Not to be used for dx of ABRS Reassessment: X-ray, although nonspecific due to many false-positives, is fairly sensitive in detecting maxillary sinusitis. An abnormal sinus x-ray, especially if opacification or an air-fluid level is present, suggests ABRS. A sinus CT scan could also be obtained to verify	***Abx for ABRS:*** Abx for pts who failed decongestant tx; have sx of more severe illness; have complications of acute RS. Amoxicillin-clavulanate is considered first-line tx. The duration of Abx tx is controversial, ranging 3-14 days. ***Reassessment*:** If sx worsen after 48-72 hrs of initial Abx tx or fail to improve despite 3-5 days of initial empiric Abx tx, either: (1) switch to second-line Abx, (2) refer to specialist, (3) reinforce comfort and prevention measures. If pt has no or little sx improvement after 10-day course of Abx tx, either treat w/ (1) high-dose amoxicillin-clavulanate, (2) cephalosporin w/ intramuscular ceftriaxone, (3) fluoroquinolone w/ pneumococcal coverage (except for pts who are skeletally immature)	No recommendations	4—Fair (systematic search methods and criteria for selecting evidence not described, strength of recommendations not given, methods for formulating recommendations not described, guideline not reviewed by external experts)

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	disease. It is somewhat more expensive, but has greater accuracy and is often recommended as the imaging test of choice. Failure of Abx tx: If no response to 3 wks of Abx tx, consider limited coronal CT scan of sinuses and/or referral to specialist.			
Infectious Diseases Society of America (IDSA) (Chow et al., 2012) *IDSA Clinical Practice Guideline for Acute Bacterial Rhinosinusitis in Children and Adults*	***Presumed ABRS:*** Diagnose ABRS vs VRS when pt presents w/ (a) persistent sx lasting ≥10 days w/o improvement, (b) severe sx or high fever (≥39°C/102°F), (c) worsening sx after initial improvement. *Strong recommendation* Reassessment: An alternative management strategy is recommended if sx worsen after 48-72 hrs of initial Abx tx or fail to improve despite 3-5 days of initial empiric Abx tx. *Strong recommendation* Histopathology: Obtain cultures by direct sinus aspiration rather than by nasopharyngeal swab in pts who have failed to respond to Abx tx. *Strong recommendation* ***Imaging:*** Dx: *Not* recommended to distinguish ABRS from VRS. *Weak recommendation against* Suspected complications: Axial and coronal views of contrast-enhanced CT rather than MRI to localize the infection and to guide further tx. *Weak recommendation*	***Abx tx for ABRS:*** Initiated as soon as the clinical dx of ABRS is made. *Strong recommendation* Amoxicillin-clavulanate rather than amoxicillin alone is recommended as antimicrobial tx for ABRS in children. *Strong recommendation* Amoxicillin-clavulanate rather than amoxicillin alone is recommended as antimicrobial tx for ABRS in adults. *Weak recommendation* Abx tx duration: 5-7 days for uncomplicated ABRS in adults; 10-14 days in children. *Weak recommendation* Intranasal saline irrigation is recommended as an adjunctive tx in adults w/ ABRS. *Weak recommendation* Intranasal corticosteroids are recommended as an adjunct tx, primarily in pts w/ a hx of AR. *Weak recommendation* Topical and oral decongestants and/or antihistamines are *not* recommended as adjunctive tx in pts w/ ABRS. *Strong recommendation against*	No recommendations	6—Good (literature search was limited to systematic reviews; several panel members served as consultants or received research funding from pharmaceutical companies)

*According to the Rigor of Development domain of the Appraisal of Guidelines Research and Evaluation (AGREE) tool, along with a consideration of commercial funding and conflicts of interest among the guideline authors. Guidelines were scored on scale of 1 to 7 and judged to be good (6-7), fair (4-5), or poor (1-3).