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Diagnosis of acute rhinosinusitis in primary care:

a systematic review of test accuracy

Abstract

Background
Acute rhinosinusitis (ARS) is a common primary care infection, but there have been no recent, comprehensive diagnostic meta-analyses.

Aim
To determine the accuracy of laboratory and imaging studies for the diagnosis of ARS.

Design and setting
Systematic review of diagnostic tests in outpatient, primary care, and specialty settings.

Method
The authors included studies of patients presenting with or referred for suspected ARS, and used bivariate meta-analysis to calculate summary estimates of test accuracy and the area under the receiver operating characteristic (ROC) curve. The authors also plotted summary ROC curves to explore heterogeneity, cutoffs, and the impact of different reference standards.

Results
Using antral puncture as the reference standard, A mode ultrasound (positive likelihood ratio [LR+] 1.71, negative likelihood ratio [LR–] 0.41), B mode ultrasound (LR+ 1.64, LR– 0.69), and radiography (LR+ 2.01, LR– 0.28) had only modest accuracy. Accuracy was higher using imaging as the reference standard for both ultrasound (LR+ 12.4, LR– 0.35) and radiography (LR+ 9.4, LR– 0.27), although this likely overestimates accuracy. C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR) both had clear threshold effects, and modest overall accuracy. The LR+ for ESR >30 and >40 were 4.08 and 7.40, respectively. A dipstick of nasal secretions for leucocyte esterase was highly accurate (LR+ 18.4, LR– 0.17) but has not been validated.

Conclusion
In general, tests were of limited value in the diagnosis of ARS. Normal radiography helps rule out sinusitis when negative, whereas CRP and ESR help rule in sinusitis when positive, although, given their limited accuracy as individual tests, they cannot be routinely recommended. Prospective studies integrating signs and symptoms with point-of-care CRP, dipstick, and/or handheld B-mode ultrasound are needed.

Keywords
acute sinusitis; acute rhinosinusitis; clinical diagnosis; clinical decision-making; primary care; rhinosinusitis; sinusitis.

INTRODUCTION

Acute rhinosinusitis (ARS) accounts for more than 30 million outpatient visits per year in the US.[1] It is defined as inflammation of the paranasal sinuses caused by viral or bacterial infection, and typically presents with facial pain or pressure, purulent nasal discharge, fever, cacosmia or hyposmia, and double-sickening (symptoms that worsen after an initial improvement).[2] Although most episodes of ARS are viral, they may also be caused by a bacterial infection.[3] A Cochrane review concluded that, in patients diagnosed with ARS based on signs and symptoms, antibiotics increased the likelihood of a cure at 7 to 14 days (number needed to treat = 18), although this was balanced by an increased risk of adverse events (number needed to harm = 8).[4] Physicians often treat ARS with antibiotics based on the history and the physical examination, resulting in the widespread use of antibiotics for what is predominantly a viral condition.[3] Recent guidelines recommend that clinicians only prescribe antibiotics when acute bacterial rhinosinusitis (ABRS) is suspected because it persists for at least 10 days, or based on double-sickening.[3]

One strategy to reduce inappropriate antibiotic use is to encourage the use of point-of-care tests such as C-reactive protein (CRP) or imaging to improve diagnostic accuracy. Use of CRP has been shown to reduce antibiotic prescribing rates for acute respiratory tract infections.[5] However, practice guidelines generally recommend against the use of imaging because the accuracy of radiography is thought to be poor, ultrasound and radiography are not widely available in the primary care setting, and computed tomography (CT) is expensive and results in potentially harmful radiation exposure.[6] In addition, imaging primarily detects fluid in the sinuses and may not distinguish bacterial from viral sinusitis.[3,7–9] Antral puncture is the preferred reference standard test, but is not widely used due to the discomfort it causes and a lack of expertise in performing antral puncture in the primary care setting.

Previous systematic reviews have been limited by focusing only on children,[10,11] have not identified all relevant studies,[11] or are ≥10 years old.[10,12] The goal of the current study is to perform an updated, comprehensive systematic review of the accuracy of imaging and laboratory tests for the diagnosis of ARS and ABRS.

METHOD

Inclusion and exclusion criteria

The authors included studies of adults and children with clinically suspected sinusitis or acute respiratory tract infection that reported the accuracy of at least one blood test or imaging study for ARS or ABRS. Acceptable reference standards included radiography, ultrasound, computed tomography (CT), or magnetic resonance imaging (MRI) for ARS, and antral puncture revealing purulent fluid or fluid yielding a positive culture for ABRS. Only studies in which all patients

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How this fits in

This report represents the most comprehensive and methodologically-rigorous systematic review to date of laboratory and imaging studies to diagnose acute rhinosinusitis (ARS). When clinically suspected, the prevalence of sinusitis is approximately 50%. The authors found that C-reactive protein >20 mg/L (LR+ 2.9) and erythrocyte sedimentation rate >30 (LR+ 4.1) or >40 (LR+ 7.4) significantly increase the likelihood of ARS, whereas normal radiography decreases the likelihood of ARS somewhat (LR– 0.28). The accuracy of ultrasound varied depending on whether it was A or B mode technology, and on the reference standard. B mode ultrasound using antral puncture as the reference standard was not helpful (LR+ 1.6, LR– 0.69). Given the limitations of the evidence base, imaging cannot be routinely recommended for patients with suspected ARS.

received the same reference standard were included, to avoid verification bias. Studies involving hospitalised patients or that recruited patients from highly specialised populations (for example, patients with immunodeficiency, odontogenic sinusitis, or children with brain cancer) were excluded. The authors did not impose any temporal or language limits. Case-control studies were excluded.

In studies that reported findings separately by maxillary, frontal, or ethmoid sinus, only maxillary sinus findings are shown. Whenever individual sinuses as well as results by person are reported, diagnostic accuracy and prevalence are reported by person where possible. Whenever it was possible to use different thresholds (definitions of abnormal) for a test, the threshold that yielded the highest diagnostic odds ratio (DOR, calculated by dividing the positive likelihood ratio [LR+] by the negative likelihood ratio [LR–]) was selected.

Search strategy and data abstraction

The authors used the strategy shown in Appendix 1 to search MEDLINE®. The reference lists of previous meta-analyses, review articles, and practice guidelines for additional articles were also searched. All abstracts were reviewed by at least two investigators, and any article deemed potentially useful by either investigator was reviewed in full. Full articles were also each reviewed by at least two investigators, who evaluated them for inclusion criteria. Two investigators abstracted data regarding study quality and test accuracy. Any disagreements regarding inclusion criteria, quality, or accuracy were resolved via consensus discussion with the principal investigator. The PRISMA flow diagram describing the search is shown in Appendix 2.

Quality assessment

The authors adapted the QUADAS-2 criteria for the study (Appendix 3).[13] Quality assessment was done in parallel by two investigators, and any discrepancies were resolved by consensus discussion.

Analytic strategy

The metaprop procedure in R version 3.2.2 was used to perform random effects meta-analysis of the prevalence of sinusitis, stratified by age group, clinical presentation, and reference standard. The authors used the meta-analysis of diagnostic accuracy (mada) procedure in R version 3.2.2 to perform bivariate meta-analysis for each test using the Reitsma procedure, stratified by imaging technology and reference standard where appropriate. Summary measures of sensitivity, specificity, LR+, and LR– are reported. Summary receiver operating characteristic (ROC) curves were drawn to explore sources of heterogeneity and threshold effects for key tests, and the area under the receiver operating characteristic curve (AUC) was calculated for selected tests. Formal testing for heterogeneity was not performed, as it is unreliable when there are small numbers of studies,[14] and in particular for diagnostic meta-analysis as it does not account for threshold effects. For example, sensitivity and specificity vary inversely as the threshold for diagnosis changes, often implicitly, and do not necessarily represent heterogeneity of populations.[15]

RESULTS

Study characteristics

The characteristics of included studies are summarised in Appendix 4. The authors identified a total of 30 studies, 16 enrolling adults,[16–31] eight both adults and children,[32–39] four enrolling only children,[40–43] and two that did not report the age of participants.[44,45] Two were retrospective cohort studies,[36,44] and the remainder were prospective cohort studies. Two studies enrolled patients with the common cold or a 'runny nose',[30,40] while the remaining 28 enrolled patients with clinically suspected acute sinusitis. Only four studies were at a low overall risk of bias.[19,20,23,40] The remainder were at moderate (n = 11) or high (n = 9) overall risk of bias (Appendix 5).

Table 1. Prevalence of acute rhinosinusitis in the included studies, by population, inclusion criteria, and reference standard[a]

Population	Reference standard	Patients, *n* (studies, *n*)	Prevalence of ARS, % (95% CI)
Adults or adults and children with clinically suspected ARS	Antral puncture	1971 (11)	49 (42 to 57)
Adults or adults and children with clinically suspected ARS	CT	487 (5)	44 (23 to 67)
Adults or adults and children with clinically suspected ARS	Rad	1345 (9)	48 (39 to 57)
Adults with acute respiratory tract infection	AP (1), MRI (1)	501 (2)	20 (14 to 29)
All studies in adults			49 (43 to 55)
All studies in children	CT (1), Rad (2)	260 (3)	41 (19 to 67)
All studies in adults and children			47 (41 to 53)

[a]If a study reports different numbers of patients with different signs and symptoms, the data for the greatest number of patients reported were used. AP = antral puncture revealing purulence. ARS = acute rhinosinusitis. CT = computed tomography. MRI = magnetic resonance imaging. Rad = radiography.

The authors identified studies of the accuracy of imaging including radiography, screening coronal computed tomography, and ultrasound (both A and B mode). A mode ultrasound is amplitude modulation and is no longer in wide use, whereas B mode or brightness modulation is the more commonly used two-dimensional study. Blood tests studied included CRP, white blood cell count (WBC), and the erythrocyte sedimentation rate (ESR), and other tests included rhinoscopy, a test of nasal secretions, and the accuracy of scintigraphy.

Prevalence of acute rhinosinusitis

The prevalence of acute rhinosinusitis in the included studies is summarised in Table 1 (a more complete version of these results are shown in Appendix 6). It is stratified by population, reference standard, and presenting symptoms. In studies enrolling adults, or a mix of adults and children with clinically suspected acute rhinosinusitis, the prevalence ranged from 16% to 80%, with a pooled prevalence of 48% (95% confidence interval [CI] = 42 to 54). There was no significant difference in prevalence by type of reference standard (antral puncture, radiography, or CT). Studies in children with clinically suspected rhinosinusitis had prevalences between 19% and 57%, with a pooled prevalence of 41% (95% CI = 19 to 67). Two studies enrolled all patients with a cold or runny nose and found a lower prevalence of acute rhinosinusitis of 20% (95% CI = 14 to 29).[30,40]

Table 2. Accuracy of imaging studies for acute rhinosinusitis

Test	Reference standard	Patients, *n* (studies, *n*)	Sensitivity (95% CI)	Specificity (95% CI)	LR+ (95% CI)	LR– (95% CI)	AUC
Radiography	AP	1564 (9)	0.85 (0.77 to 0.90)	0.56 (0.38 to 0.73)	2.01 (1.40 to 3.05)	0.28 (0.19 to 0.39)	0.820
Radiography	Imaging	350 (3)	0.80 (0.66 to 0.89)	0.84 (0.31 to 0.98)	9.37 (1.27 to 39.6)	0.27 (0.16 to 0.48)	0.841
Radiography	Any	1914 (12)	0.84 (0.78 to 0.89)	0.63 (0.44 to 0.78)	2.36 (1.57 to 3.68)	0.27 (0.20 to 0.34)	0.836
Radiography[a]	Any	1592 (9)	0.82 (0.74 to 0.88)	0.69 (0.45 to 0.86)	2.96 (1.51 to 5.7)	0.27 (0.19 to 0.37)	0.84
Ultrasound, A mode	AP	552 (4)	0.79 (0.52 to 0.93)	0.54 (0.36 to 0.71)	1.71 (1.42 to 2.08)	0.41 (0.19 to 0.68)	0.679
Ultrasound, B mode	AP	262 (2)	0.53 (0.03 to 0.98)	0.69 (0.61 to 0.77)	1.64 (0.10 to 3.2)	0.69 (0.03 to 1.36)	0.693
Ultrasound, A mode	Imaging	713 (6)	0.62 (0.55 to 0.69)	0.91 (0.79 to 0.96)	7.64 (2.95 to 17.1)	0.42 (0.32 to 0.54)	0.702
Ultrasound, B mode	Imaging	351 (4)	0.75 (0.67 to 0.81)	0.98 (0.94 to 0.99)	38.4 (12.7 to 88.3)	0.26 (0.20 to 0.34)	0.897
Ultrasound[b]	Any	1060 (8)	0.68 (0.45 to 0.85)	0.72 (0.50 to 0.87)	2.58 (1.4 to 4.6)	0.46 (0.22 to 0.73)	0.76
Limited CT scan	CT	(2)	0.88 (0.71 to 0.96)	0.89 (0.77 to 0.95)	9.01 (3.77 to 18.3)	0.15 (0.05 to 0.33)	0.895

[a]Radiography, excluding studies at high risk of bias. [b]Ultrasound, excluding studies at high risk of bias. AP = antral puncture showing purulent fluid. AUC = area under the receiver operating characteristic curve. CT = computed tomography. LR+ = positive likelihood ratio. LR– = negative likelihood ratio.

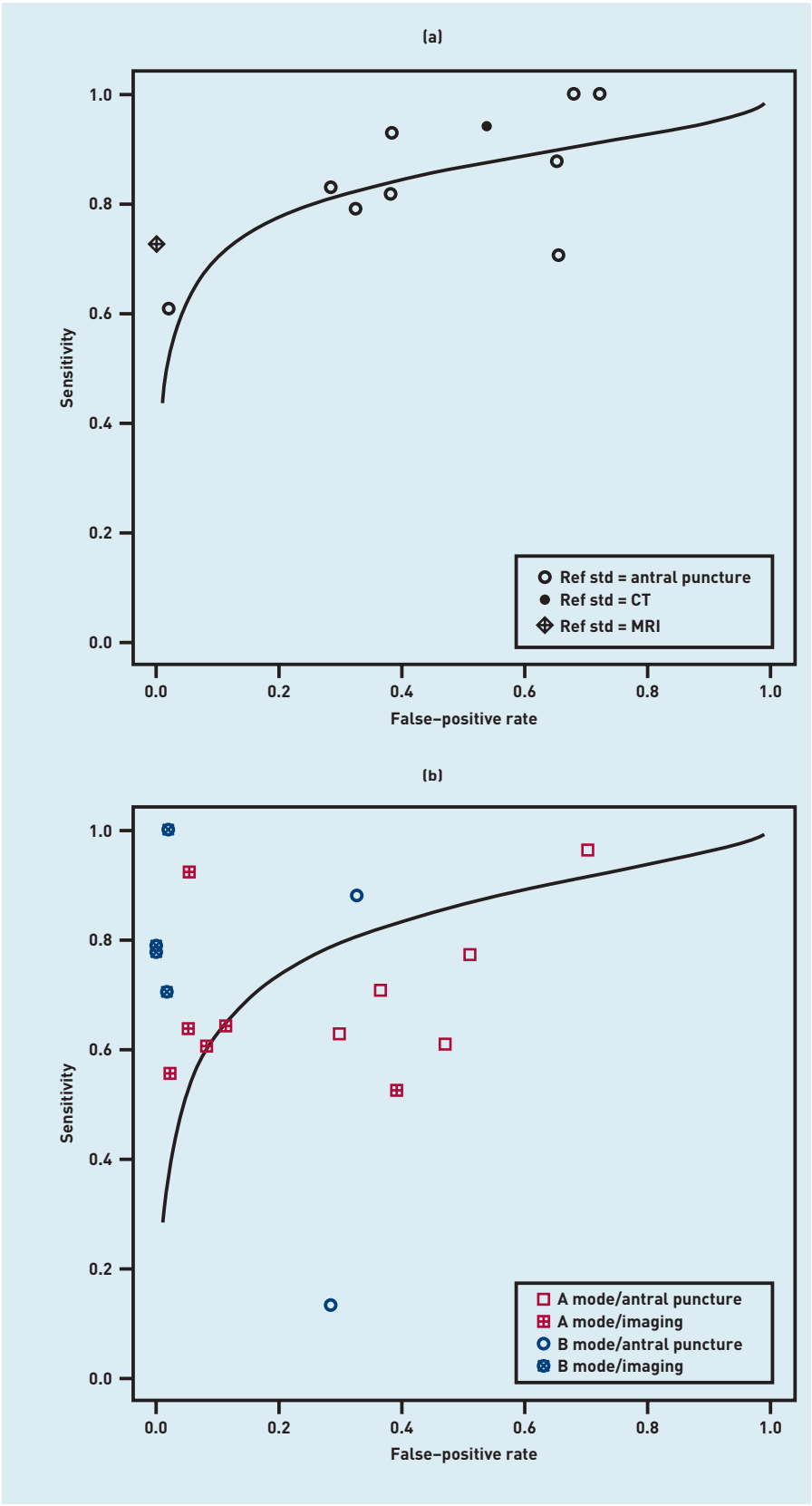


Figure 1. (a) Summary receiver operating characteristic curve for radiography, with accuracy stratified by the reference standard. (b) Summary receiver operating characteristic curve for ultrasound, with accuracy stratified by the reference standard for A and B mode. CT = computed tomography. MRI = magnetic resonance imaging. Ref std = reference standard.

Accuracy of imaging

The accuracy of imaging studies is summarised in Table 2 (Appendix 7). Because there was no clear pattern of accuracy with regard to studies of children and adults, and due to the small number of studies in children, their results are combined in Table 2.

The most accurate imaging test was limited or screening CT (LR+ 9.01, LR– 0.15, AUC 0.895), but was only evaluated in two small studies at high risk of bias that used full CT as the reference standard.[36,44] Radiography was fairly sensitive when compared with antral puncture, but lacked specificity, and was therefore more helpful when negative (LR– 0.28) than when positive (LR+ 2.01). Figure 1a shows a summary ROC curve for radiography.

The accuracy of ultrasound varied depending on the mode (A or B) and the reference standard (antral puncture or imaging). In general, B mode was more accurate than A mode, and studies using antral puncture as the reference standard found much lower accuracy (particularly specificity) than those using imaging. Using antral puncture as the reference standard, both A mode (LR+ 1.71, LR– 0.41, AUC 0.679) and B mode (LR+ 1.64, LR– 0.69, AUC 0.693) ultrasound had only modest accuracy. Figure 1b shows a summary ROC curve for ultrasound, stratified by mode and reference standard.

A sensitivity analysis excluding studies at high risk of bias found no significant difference regarding the accuracy of radiography (LR+ 2.88, LR– 0.27). High-quality studies of ultrasound had a positive likelihood ratio of 2.58 and negative likelihood ratio of 0.46, reflecting the fact that antral puncture was used as the reference standard rather than imaging.

Accuracy of laboratory tests

The accuracy of blood tests and other tests for ARS are shown in Table 3 (study-level data shown in more detail are available from the authors). Summary ROC curves for CRP and ESR are shown in Figures 2a and 2b. Both show clear threshold effects. That is, differences in accuracy are likely to be related to differences in the cutoff or threshold. It was therefore not appropriate to calculate a summary estimate of accuracy for these tests as a group. An ESR <10 is limited evidence against a diagnosis of acute rhinosinusitis (LR– 0.57), while an ESR >30 (LR+ 4.08) or >40 (LR+ 7.40) provide moderate evidence in favour of the diagnosis. Similarly, a CRP <10 mg/L was limited evidence against a

Table 3. Accuracy of blood tests for the diagnosis of acute rhinosinusitis in adults[a]

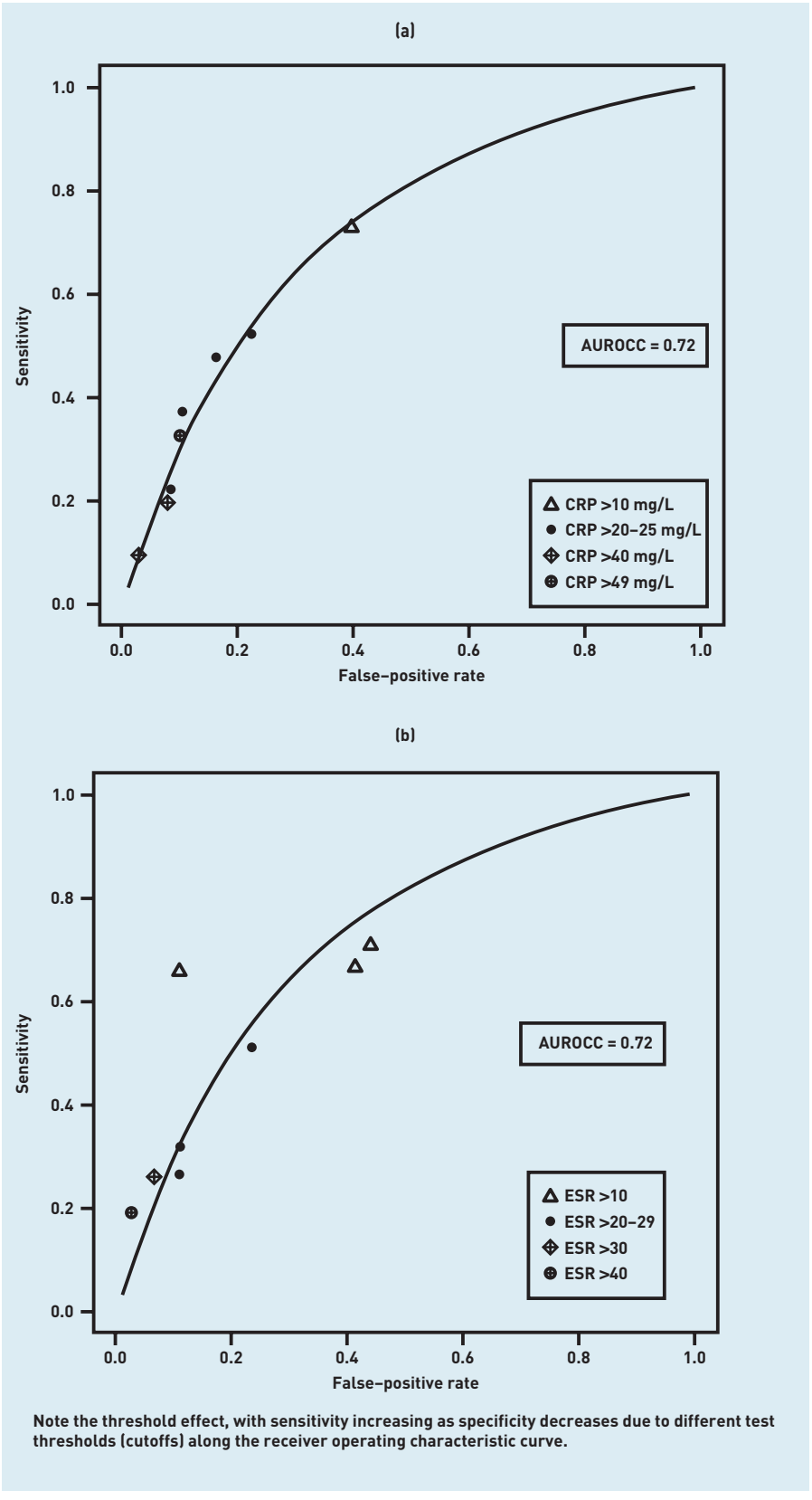
Test	Total patients, *n* reference	Sensitivity (95% CI)	Specificity (95% CI)	LR+ (95% CI)	LR– (95% CI)	DOR	AUC
Blood tests							
CRP							
CRP >10 mg/L	173[19]	0.73	0.60	1.84	0.45	4.09	
CRP >20–25 mg/L	789[19,21,24,29]	0.39 (0.29 to 0.50)	0.87 (0.80 to 0.91)	2.92 (2.17 to 3.98)	0.71 (0.60 to 0.80)	4.11	
CRP >40–49 mg/L	548[19,21,24]	0.22 (0.15 to 0.30)	0.91 (0.84 to 0.95)	2.46 (1.45 to 3.91)	0.86 (0.77 to 0.93)	2.86	
Summary		**0.34 (0.21 to 0.51)**	**0.88 (0.79 to 0.94)**	**2.92 (2.21 to 3.80)**	**0.74 (0.60 to 0.85)**	**3.95**	**0.720**
ESR							
ESR >10	426[19,21,24]	0.68 (0.63 to 0.72)	0.58 (0.50 to 0.65)	1.60 (1.33 to 1.97)	0.57 (0.46 to 0.68)	2.81	
ESR >20	425[19,23,24]	0.36 (0.23 to 0.51)	0.86 (0.75 to 0.92)	2.55 (1.68 to 3.74)	0.74 (0.61 to 0.85)	3.45	
ESR >30	168[19]	0.26	0.94	4.08	0.79	5.16	
ESR >40	176[21]	0.19	0.97	7.40	0.83	8.91	
Summary		**0.43 (0.29 to 0.58)**	**0.83 (0.70 to 0.92)**	**2.61 (1.85 to 3.68)**	**0.68 (0.58 to 0.78)**	**3.84**	**0.685**
WBC							
WBC >10	375[21,24]	0.25 (0.20 to 0.31)	0.88 (0.81 to 0.93)	2.23 (1.29 to 3.66)	0.85 (0.78 to 0.94)	2.62	0.710
Other tests							
Clinical nasal secretion score ≥4	217[39]	0.95	1.00	95	0.05	1900	
Leucocyte esterase ≥1+	217[39]	0.83	0.95	18.4	0.17	108	
Protein >2.0	217[39]	0.96	0.79	4.5	0.05	91	
Nitrite >1.0	217[39]	0.52	0.93	7.6	0.52	14.7	
pH >7	217[39]	0.96	0.42	1.7	0.09	18.6	
Leucocytes in sinus washings	187[23]	0.84	0.78	3.7	0.21	17.7	
Leucocytes in sinus washings	93[40]	0.31	0.94	4.9	0.74	6.6	
Leucocytes in nasal secretions	30[41]	0.94	0.69	3.1	0.08	38.3	
Flexible endoscopy	104[25]	0.83	0.67	2.5	0.26	9.7	
Rhinoscopy, pus in nasal cavity	241[29]	0.82	0.38	1.3	0.47	2.8	
Rhinoscopy, pus in throat	242[29]	0.25	0.81	1.3	0.93	1.4	
Scintigraphy (probably or definitely abnl)	48[17]	0.91	0.92	11.4	0.09	127	
Diode gas laser spectroscopy (frontal sinus)	80[31]	0.86	0.94	14.1	0.15	94	
Diode gas laser spectroscopy (maxillary sinus)	7531	0.39	0.93	5.5	0.66	8.4	

[a]No studies with children were identified. Where results for more than one study are presented, a summary estimate is shown. Abnl = abnormal. AP = antral puncture revealing purulent fluid. AUC = area under the receiver operating characteristic curve. CRP = C-reactive protein. DOR = diagnostic odds ratio (positive likelihood ratio divided by negative likelihood ratio). ESR = erythrocyte sedimentation rate. LR+ = positive likelihood ratio. LR– = negative likelihood ratio. WBC = white blood cells. (Individual-study level data and the reference standard used for each test is shown in Appendix 8 and Appendix 9)

diagnosis of ARS (LR– 0.45), while a CRP >20 is limited evidence in favour of the diagnosis (LR+ 2.92). Only one of the four studies of CRP used antral puncture as the reference standard, and it had generally similar results to the imaging studies.[19]

A single study evaluated the accuracy of a test strip of the sort ordinarily used for diagnosis of urinary tract infection.[39] The researchers found that leucocyte esterase and nitrite were highly specific, while pH and protein were highly sensitive. A score that assigned 0 to 3 points to each of these tests successfully identified patients at low (0%), moderate (33%), and high (100%) risk of ARS. However, this study was at high risk of bias because it used imaging rather than antral puncture as the reference standard, and the thresholds for low-, moderate-, and high-risk groups were established post hoc.

The presence of leucocytes in nasal washings was evaluated in three studies, with LR+ ranging from 3.06 to 4.92, and LR– from 0.08 to 0.74.[24,40,41] Rhinoscopy for pus in the nasal cavity or throat (LR+ 1.32, LR– 0.47 to 0.93) and the white blood cell



Note the threshold effect, with sensitivity increasing as specificity decreases due to different test thresholds (cutoffs) along the receiver operating characteristic curve.

Figure 2. (a) Summary receiver operating characteristic curve for the accuracy of C-reactive protein as a test for acute rhinosinusitis. (b) Summary receiver operating characteristic curve for the accuracy of erythrocyte sedimentation rate as a test for acute rhinosinusitis. AUROCC = area under the receiver operating characteristic curve. CRP = C-reactive protein. ESR = erythrocyte sedimentation rate.

count (LR+ 2.23, LR– 0.85) both lacked accuracy for the diagnosis of acute rhinosinusitis.[21,24,29]

DISCUSSION

Despite being a very common complaint in the outpatient setting, the evidence base for imaging and laboratory tests to diagnose ARS is limited. Many of the studies are ≥20 years old and few are at low risk of bias. Using antral puncture as a reference standard, sinus radiographs are fairly sensitive but have poor specificity. However, they are useful for reducing the likelihood of ARS when negative (LR– 0.28). Although studies comparing ultrasound to imaging (largely radiography) found good accuracy, those using antral puncture as the reference standard found that, like radiography, it lacked specificity. That is likely to be because imaging studies are limited to detection of fluid in the sinuses, which is commonly seen in viral upper respiratory tract infections as well.

Although CT is often recommended as the imaging study of choice for patients with persistent symptoms, chronic sinusitis, or when surgery is being considered,[3] the authors identified only two small studies comparing limited or screening CT with full CT of the sinuses,[36,44] and no studies directly comparing CT to antral puncture.

C-reactive protein and the erythrocyte sedimentation rate performed similarly as tests for acute rhinosinusitis. In both cases there was no clearly preferred single threshold for defining an abnormal test. A potentially useful strategy would be to define two thresholds and three risk groups, for example, CRP or ESR <10 defining a low-risk group, 10 to 30 a moderate-risk group, and >30 a high-risk group. However, as originally reported in the relevant studies, it is not possible to determine stratum-specific likelihood ratios and predictive values as part of this meta-analysis.

The study by Huang and Small suggests an innovative approach to diagnosis of acute rhinosinusitis, using a dipstick normally used for urinalysis.[39] It deserves replication, in particular the very promising risk score based on the dipstick findings.

Strengths and limitations

The authors' conclusions are limited by the relatively poor quality of many studies, many of which are quite old. There was significant unexplained heterogeneity, for example, among studies of radiography using antral puncture as the reference standard, and therefore summary estimates of accuracy should

be interpreted cautiously. An unexpected finding was the similar prevalence of acute rhinosinusitis when using antral puncture as the reference standard compared with imaging. Although the authors expected a lower prevalence with antral puncture as the reference standard, because it was presumably largely detecting only ABRS, it may be that the spectrum of patients in the Scandinavian countries where the antral puncture studies were largely performed may be different, with patients not seeking care unless symptoms are more severe.

Strengths of the current study include: an updated and comprehensive search identifying more studies than previous systematic reviews; use of a bivariate meta-analysis; and the use of summary ROC curves to allow a better understanding of heterogeneity due to different reference standard and diagnostic cutoffs.

Implications for research

A condition as common as acute rhinosinusitis deserves a better evidence base. A particular challenge is the choice of a reference standard. Radiography and ultrasound lack specificity, and CT is costly, exposes patients to radiation, and is likely to mistakenly classify many patients with viral respiratory infection as having ARS. Antral puncture revealing purulent fluid is arguably the preferred reference standard. Although some might argue that bacterial culture of antral fluid revealing a bacterial pathogen is the optimal reference standard, cultures may lack sensitivity.

Use of C-reactive protein in particular is promising because it is available as a rapid and relatively inexpensive point-of-care test that has been shown in randomised controlled trials to reduce the use of inappropriate antibiotics for respiratory infections in the primary care setting.[46,47] Trials of its use in patients with clinically suspected sinusitis are needed, using clinically helpful cutoffs to identify low-, moderate-, and high-risk patients.

Physicians increasingly have access to high-resolution B mode ultrasound in a handheld device at the point of care.[48,49] To date, these devices have not been evaluated for their ability to diagnose ARS. A study evaluating the accuracy of signs and symptoms as well as handheld B mode ultrasound, C-reactive protein, and/or dipstick for leucocyte esterase, nitrite, pH, and protein, and using antral puncture as the reference standard, would be an important contribution to the literature. This could lead to the development and validation of a decision support tool that integrates signs and symptoms with one of these point-of-care tests, to help physicians limit antibiotic therapy to only those patients most likely to benefit.

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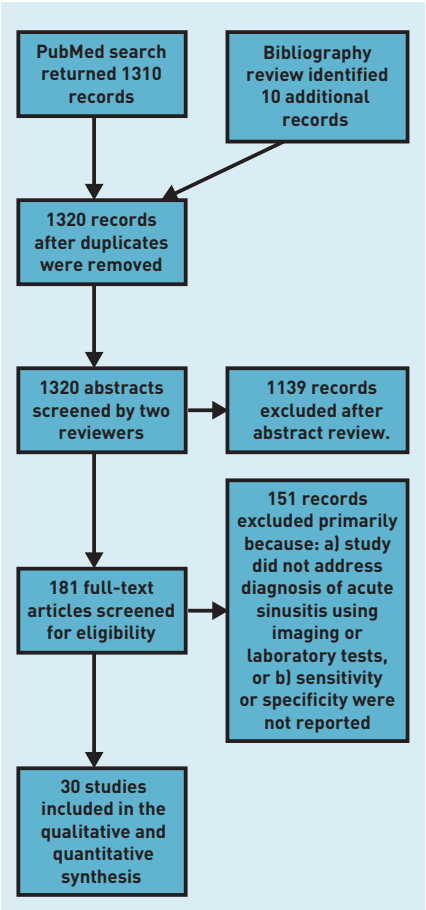
Appendix 1. Search strategy used in MEDLINE

(rhinosinusitis[Title/Abstract] OR sinusitis[Title/Abstract] OR sinus infection[Title/Abstract] OR sinusitis[MeSH Terms] OR "Paranasal Sinus Diseases"[MeSH Terms]) AND ("medical history taking"[MeSH Terms] OR "physical examination"[MeSH Terms] OR "signs and symptoms"[Title/Abstract] OR "symptoms and signs"[Title/Abstract] OR symptom[Title/Abstract] OR "history and physical" OR "physical examination" OR "physical exam"[Title/Abstract] OR "clinical examination"[Title/Abstract] OR ultrasound[Title/Abstract] OR "computed tomogram"[Title/Abstract] OR "computed tomographic"[Title/Abstract] OR "radiograph"[Title/Abstract] OR "radiographic"[Title/Abstract] OR "x-ray"[Title/Abstract] OR "computed tomography"[Title/Abstract] OR "radiological"[Title/Abstract] OR "CRP"[Title/Abstract] OR "C-reactive protein"[Title/Abstract] OR "white blood cell count"[Title/Abstract] OR "white cell count"[Title/Abstract] OR"leucocytosis"[Title/Abstract] OR "leucocyte count"[Title/Abstract] OR Westergren"[Title/Abstract] OR "sed rate"[Title/Abstract] OR "sedimentation rate") NOT ("carotid sinus" OR "sinus rhythm" OR "sinus arrest" OR "aortic sinus" OR "aortic sinuses" OR "cavernous sinus" OR "sinus tachycardia" OR "sinus arrhythmia" OR "cavernous sinuses" OR "sinus tract" OR "sinus tracts" OR "coronary sinus" OR "renalsinus" OR "sinus node" OR "sinusoidal" OR "non-sinus" OR "petrosal sinus" OR "sinus rate" OR "sinus rhythm" OR "sinus cardiac rhythm" OR "sinus cyst" OR "sinusoid") NOT chronic[Title/Abstract] OR surgery[Title] OR surgical[Title] OR lymphoma OR mycosis OR "sphenoid" OR Wegener's OR sarcoidosis OR cancer OR post-operative OR myositis OR HIV OR tuberculosis OR fasciitis OR periodontitis OR "dental implant").



Appendix 2. PRISMA flow diagram of studies selected for meta-analysis.

Appendix 3. QUADAS-2 instrument, adapted for systematic review of the accuracy of signs and symptoms for the diagnosis of acute sinusitis[a]

	QUADAS-2 study design questions																	
	Patient selection					Index test				Reference std				Flow & timing				
Study, year	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	Overall
	Consecutive	Not case-control	Exclusion criteria	Risk of bias	Applicability	Index blinded	Threshold pre-specified	Risk of bias	Applicability	Antral puncture used	Reference blinded	Risk of bias	Applicability	All got reference standard	All had same ref standard	All accounted for	Risk of bias	L = 0, M = 1, and H = 2+ with high likelihood of bias
Adults																		
Hansen, 1995	Y	Y	Y	L	L	Y	U	L	L	Y	U	L	L	Y	Y	Y	L	L
van Buchem, 1995	Y	Y	Y	L	L	Y	U	L	L	Y	Y	L	L	Y	Y	Y	L	L
Laine, 1998	Y	Y	Y	L	L	Y	Y	L	L	Y	Y	L	L	Y	Y	Y	L	L
Bergstedt,1980	N	Y	Y	H	L	Y	Y	L	L	Y	Y	L	L	Y	Y	Y	L	M
Savolainen, 1997a	N	Y	Y	H	L	Y	U	L	L	Y	Y	L	L	Y	Y	Y	L	M
Savolainen, 1997b	N	Y	Y	H	L	Y	U	L	L	Y	Y	L	L	Y	Y	Y	L	M
Puhakka, 2000	Y	Y	Y	L	L	Y	Y	L	L	N	Y	H	L	Y	Y	Y	L	M
Young, 2003	Y	Y	Y	L	L	Y	Y	L	L	N	Y	H	L	Y	Y	Y	L	M
Kuusela, 1983	Y	Y	Y	L	L	U	Y	H	L	Y	U	L	L	Y	Y	Y	L	M
Berg, 1981	N	Y	Y	H	L	U	Y	H	L	Y	Y	L	L	Y	Y	Y	L	H
Rohr, 1986	U	Y	Y	H	L	Y	Y	L	L	N	Y	H	L	Y	Y	Y	L	H
Jensen, 1987	U	Y	Y	H	L	Y	Y	L	L	N	U	H	L	Y	Y	Y	L	H
Lindbaek, 1996	U	Y	Y	H	L	Y	Y	L	L	N	U	H	L	Y	Y	Y	L	H
Varonen, 2003	N	Y	Y	H	L	Y	Y	L	L	N	Y	H	L	Y	Y	Y	L	H
Berger, 2011	N	Y	Y	H	L	Y	Y	L	L	N	Y	H	L	Y	Y	Y	L	H
Lewander, 2012	N	Y	Y	H	L	Y	Y	L	L	N	Y	H	L	Y	Y	Y	L	H
Adults and children																		
Watt-Boolsen, 1977	N	Y	Y	H	L	Y	Y	L	L	Y	U	L	L	Y	Y	Y	L	M
Shapiro, 1986	Y	Y	Y	L	L	Y	Y	L	L	N	Y	H	L	Y	Y	Y	L	M
McNeill, 1963	N	Y	Y	H	L	Y	Y	L	L	Y	N	H	L	Y	Y	N	H	H
Berg, 1985	N	Y	Y	H	L	Y	Y	L	L	Y	U	L	L	Y	Y	N	H	H
Gianoli,1992	N	Y	Y	H	L	Y	Y	L	L	N	Y	H	L	Y	Y	Y	L	H
Ghatasheh, 2000	N	Y	Y	H	L	Y	U	L	L	N	Y	H	L	Y	Y	Y	L	H
Awaida, 2004	N	Y	Y	H	L	Y	Y	L	L	N	Y	H	L	Y	Y	Y	L	H
Huang, 2008	Y	Y	Y	L	L	Y	N	H	L	N	U	H	L	Y	Y	Y	L	H
Children																		
van Buchem, 1992	Y	Y	Y	L	L	Y	Y	L	L	Y	U	L	L	Y	Y	Y	L	L
Reilly, 1989	Y	Y	Y	L	L	Y	Y	L	L	N	Y	H	L	Y	Y	Y	L	M
Visca, 1995	N	Y	U	H	U	Y	U	L	N	Y	U	H	L	Y	Y	Y	L	H
Fufezan, 2010	U	Y	Y	H	L	Y	Y	L	L	N	Y	H	L	Y	Y	Y	L	H
Not reported																		
Dobson, 1996	N	Y	Y	H	L	U	Y	H	L	N	U	H	L	Y	Y	Y	L	H
Goodman, 1995	N	Y	Y	H	L	Y	Y	L	L	N	Y	H	L	Y	Y	Y	L	H

[a]Overall risk of bias was low (L) if all domains were at low risk of bias, moderate (M) if one domain was at high risk of bias, and high (H) if two or more domains were at high risk of bias. Ref = reference. Std = standard.

Appendix 3 continued. QUADAS-2 instrument, adapted for systematic review of the accuracy of signs and symptoms for the diagnosis of acute sinusitis.[a] Definitions of questions 1–17 for QUADAS-2

Patient selection, questions 1–5

1. Was a consecutive or random sample of patients enrolled? (Y/N/U)
   - Y: Study enrolled consecutive patients or a random sample of consecutive patients from a primary care, urgent care, or emergency department setting
   - N: A convenience sample or other non-consecutive or non-random sample was used, or it only included patients referred for diagnostic imaging or to an ENT clinic (this does not address exclusion criteria, see question 3)
   - U: Uncertain

2. Was the study designed to avoid a case-control design? (Y/N/U)
   - Y: The study population was drawn from a cohort that included patients with a spectrum of disease
   - N: The study population consisted of patients with known disease and healthy controls
   - U: Uncertain

3. Did the study design avoid inappropriate exclusion criteria? (Y/N/U)
   - Y: There were no inappropriate exclusion criteria, such as excluding those with uncertain findings
   - N: The study used inappropriate exclusion criteria
   - U: Uncertain

4. *Patient selection risk of bias:* What is the likelihood that patient selection could have introduced bias? (L/H/U)
   - L: Low likelihood of bias due to patient selection or enrolment ('Yes' to question 1, 2, and 3)
   - H: High likelihood of bias due to patient selection ('No' to question 1, 2, or 3)
   - U: Unable to judge degree of bias

5. *Concerns about patient selection applicability:* Are there concerns that included patients and setting do not match the review question? (L/H/U)
   - L: Low risk of bias — the patients or settings are from the outpatient setting and have clinically suspected acute sinusitis or acute respiratory tract infection
   - H: High risk of bias — the patients or settings do not match the review question, for example, a group of patients hospitalised, or from a specialised population, or patients with subacute or chronic sinusitis
   - U: Uncertain

Index test, questions 6–9

6. Were index test results interpreted without knowledge of the reference standard? (Y/N/U)
   - Y: Yes
   - N: No (including when index and reference standard were performed by the same observer, although blinding was not addressed)
   - U: Uncertain

7. If a threshold was used for the index test, was it pre-specified? (Y/N/U)
   - Y: The threshold was pre-specified, or there was no threshold mentioned
   - N: The threshold was established post hoc
   - U: A threshold was used but it is not clear when it was specified

8. *Index test risk of bias:* What is the likelihood that conduct of the index test could have introduced bias? (L/H/U)
   - L: Low likelihood of bias — 'Yes' to question 6, and 'Yes' or 'Uncertain' to question 7
   - H: High likelihood of bias due to failure to mask to reference standard — 'No' or 'Uncertain' to question 6 or 'No' to question 7
   - U: Uncertain

9. *Concerns regarding index test applicability:* Are there concerns that the index test differs from those specified in the review question? (L/H/U)
   - L: Low likelihood — the index test in this study is a laboratory or imaging test
   - H: High likelihood — the index test in this study may not be a laboratory or imaging test
   - U: Uncertain

Reference standard test, questions 10–13

10. Is the reference standard likely to correctly classify patients as having acute sinusitis? (Y/N/U)
    - Y: Yes, used antral puncture
    - N: No, used another reference standard
    - U: Uncertain

11. Was the reference standard interpreted without knowledge of the index test? (Y/N/U)
    - Y: Yes, reference standard interpretation masked to index test results
    - N: No, reference standard interpretation not masked to index test results
    - U: Uncertain

12. *Reference standard risk of bias:* Could conduct or interpretation of the reference standard have introduced bias? (L/H/U)
    - L: Low likelihood of bias due to the reference standard ('Yes' to question 9, 'Yes' or 'Uncertain' to question 10)
    - H: High likelihood of bias due to inadequate reference standard ('No' to question 9 or 10)
    - U: Uncertain

13. *Concerns regarding applicability of the reference standard:* Are there concerns that the target conditions defined by the reference standard do not match the review question? (L/H/U)
    - L: Low likelihood of bias — that is, the reference standard was intended to detect acute sinusitis
    - H: High likelihood of bias — that is, the reference standard was not intended to detect acute sinusitis
    - U: Uncertain

... continued

Appendix 3 continued. QUADAS-2 instrument, adapted for systematic review of the accuracy of signs and symptoms for the diagnosis of acute sinusitis.[a] Definitions of questions 1–17 for QUADAS-2

Patient flow and timing, questions 14–17

14. Did all patients receive a reference standard? (Y/N/U)
    - Y: Yes, all patients received some sort of reference standard (no partial verification bias)
    - N: No, some patients did not receive any reference standard (partial verification bias)
    - U: Uncertain

15. Did all patients receive the same reference standard? (Y/N/U)
    - Y: Yes, all used the same reference standard (no differential verification bias)
    - N: No, the reference standard varied depending on the results of the index test (differential verification bias)
    - U: Uncertain

16. Were all patients included in the analysis? (Y/N/U)
    - Y: Yes, all patients were properly accounted for in the analysis
    - N: No, some patients were not accounted for or dropped out for unclear reasons
    - U: Uncertain

17. *Patient flow risk of bias:* Could patient flow have introduced bias? (L/H/U)
    - L: Low likelihood of bias based on absence of partial verification bias and good follow-up ('Yes' to question 14 and 15, 'Yes' or 'Uncertain' to question 16)
    - H: High likelihood of bias based on partial verification bias or poor follow-up ('No' to question 14 or 15, or significant number of patients lost to follow-up in question 16)
    - U: Uncertain

Appendix 4. Characteristics of included studies, by population and sorted by year of publication (with individual study-level data)

Study, year	Population	Setting	Number in study	Mean age and/or age range, years	Reference standard	Country	Year(s)
Adults							
Bergstedt, 1980[17]	Adults with clinically suspected maxillary sinusitis	ENT clinic	48	Range 17 to 79	Antral aspiration showing purulent aspirate	Sweden	NR
Berg, 1981[16]	Adults with clinically suspected sinusitis of at least 3 weeks' duration	ENT clinic	50	Mean age 46	AP revealing purulent discharge	Sweden	NR
Kuusela, 1983[18]	Young adults (largely male) with clinically suspected acute sinusitis	Military clinic	105	NR	AP showing purulent fluid	Finland	NR
Rohr, 1986[27]	Adults with clinically suspected acute sinusitis	Medicine outpatient clinic	99	Range 18 to 74	Radiograph showing mucosal thickening or opacification >4 mm	US	NR
Jensen, 1987[26]	Adults with clinically suspected acute sinusitis	ENT clinic	138 (253 sinuses)	Mean age 33	Radiograph showing mucosal thickening >6 mm, fluid, or complete opacification	Sweden	NR
Hansen, 1995[a19]	Consecutive adults suspected of having acute maxillary sinusitis by their GP	Primary care clinic	174	Median 35, range 18 to 65	CT scan abnormal and purulent or mucopurulent material from AP	Denmark	1992 to 1994
van Buchem, 1995[23]	Adults with clinically suspected acute maxillary sinusitis	Primary care with referral to ENT clinic	113	42% 18 to 29, 34% 30 to 44, 16% 45 to 59, and 9% 60 or older	AP showing fluid or floccules	Netherlands	NR
Lindbaek, 1996[24]	Adults clinically diagnosed by a primary care doctor with acute sinusitis requiring antibiotics	Primary care	201	Mean 37.8, range 15 to 83	CT scan showing air-fluid level or complete opacification	Norway	1993
Savolainen, 1997[21]	Young adult men with suspected acute maxillary sinusitis <3 weeks' duration	ENT clinic (military)	176	Mean 20.5	AP with positive bacterial culture	Finland	NR
Savolainen, 1997[22]	Young adult men with suspected acute maxillary sinusitis <30 days' duration	ENT clinic (military)	161 (322 sinuses)	Mean 29, range 17 to 68	AP yields fluid	Finland	NR

... continued

Appendix 4 continued. Characteristics of included studies, by population and sorted by year of publication (with individual study-level data)

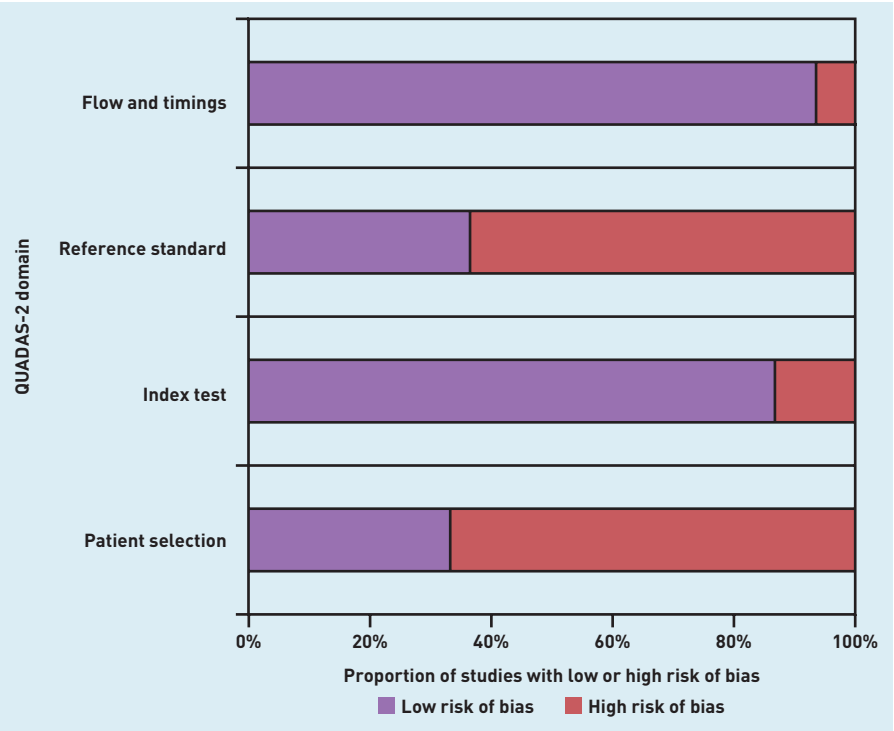
Laine, 1998[20]	Consecutive adult patients with clinically suspected acute maxillary sinusitis, duration <30 days	Primary care clinic	39	Median 37, range 16 to 68	Nasal aspirate with purulent or mucopurulent material	Finland	1992 to 1993
Puhakka, 2000[b30]	Convenience sample of young adult students with symptoms of common cold <48 hours	Primary care clinic	200 (394 sinuses)	Mean 24	MRI using same criteria for accuracy of ultrasound and radiographs	Finland	NR
Young, 2003[29]	Adults with clinically suspected sinusitis (purulent nasal discharge and maxillary pain) of 2 to 28 days' duration, median 4 days' duration	Primary care clinic	251	Median 34	Latent class model incorporating CRP, radiographs (air-fluid levels or opacity), and clinical findings	Switzerland	NR
Varonen, 2003[28]	Consecutive adults with clinically suspected acute sinusitis <30 days' duration, 72% more than 5 days	Primary care clinic	148	Mean 39.7, range 18 to 75	Sinus radiographs (AP and Waters' view) showing total opacification, air-fluid level, or mucosal thickening ≥6 mm	Finland	1998 to 1999
Berger, 2011[25]	Consecutive adults with clinically suspected acute bacterial rhinosinusitis between 5 days' and 4 weeks' duration	ENT clinic	104	Mean 44	Abnormal sinus radiograph (AP and Waters' view with air-fluid level, complete opacification, or ≥6 mm mucosal thickening)	Israel	2003 to 2006
Lewander, 2012[31]	Adults referred for CT for clinically suspected sinus disease	Radiology clinic	40	57 for men, 54 for women, range 22 to 84	CT scan showing any opacification or obstruction of the ostiomeatal complex	Sweden	2008 to 2009
Adults and children							
McNeill, 1963[33]	Adults and children referred for clinically suspected sinusitis	ENT clinic	150 (242 sinuses)	Inclusion range 10 and older. Age 10–19 (*n* = 22), 20–29 (*n* = 35), 30–39 (39), 40–49 (*n* = 31), 50 and older (*n* = 23)	For radiography: AP showing mucopus, or pus. For clinical signs: radiography showing mucosal thickening or any opacity	Northern Ireland	NR
Watt-Boolsen, 1977[34]	Adults and children with clinically suspected maxillary sinusitis	ENT clinic	286 (468 sinuses)	Range 3 to 93	AP with return of cloudy fluid	Denmark	NR
Berg, 1985[32]	Adults and children with clinically suspected sinusitis	ENT clinic	90	Mean 37, range 10 to 75	AP showing purulent fluid	Sweden	NR

... continued

Appendix 4 continued. Characteristics of included studies, by population and sorted by year of publication (with individual study-level data)

Shapiro, 1986[37]	Consecutive adults and children with clinically suspected acute sinusitis	Allergy and paediatric clinics	75	Median age 10, range 2 to 72	Radiograph showing at least 3 mm mucosal thickening, clouding, opacification, or air-fluid level	US	NR
Gianoli, 1992[35]	Adults and children undergoing CT for evaluation of clinically suspected sinusitis	Radiology clinic	41	Mean 40, range 5 to 80	CT scan abnormal (>4 mm mucosal thickening or opacification, excluding solitary polyps)	US	NR
Ghatasheh, 2000[38]	Adults and children with suspected acute maxillary sinusitis referred from emergency department, primary care, or ENT clinics for sinus radiography	Radiology clinic	50 (100 sinuses)	Mean 23.4, range 6 to 50	Sinus radiograph (Waters' view only) showing mucosal thickening, air-fluid levels, or complete opacification	Jordan	NR
Awaida, 2004[36]	Adults and children referred for sinus CT scan	Radiology clinic	51	Mean 40.7, range 11 to 70	CT scan abnormal	US	1999 to 2000
Huang, 2008[39]	Consecutive adults and children with clinically suspected acute sinusitis less than 3 weeks' duration	Allergy clinic	217	Range 4 to 61. Age 4 to 9 (n = 89), age 10 to 19 (n = 101), age 20 and older (n = 27)	Sinus radiograph (n = 151), or CT scan (n = 12) with >4 mm mucosal thickening, air-fluid levels, and/or increased opacity or retention cyst	US	NR
Children							
Reilly, 1989[43]	Children with clinically suspected acute sinusitis	ENT clinic	53 (106 sinuses)	Median age 6, age range 2 to 16	Radiograph showing opacification or mucosal thickening >4 mm	US	1985
van Buchem, 1992[40]	Consecutive children presenting with runny nose	Primary care clinic	46 (93 sinuses)	Range 2 to 12	AP showing purulent fluid or positive bacterial culture	Netherlands	1984 to 1985
Visca, 1995[41]	Children with clinically suspected sinusitis	Respiratory clinic at paediatric hospital	30	Range 5 to 15	CT scan abnormal in coronal projection	Italy	NR
Fufezan, 2010[42]	Children with clinically suspected sinusitis, including poorly controlled asthma	Paediatric clinic	67	Range 4 to 16	Sinus radiographs with total opacity of the maxillary sinus, air-fluid level, or mucosal thickening	Romania	NR
Not reported							
Goodman, 1995[44]	Convenience sample of patients with clinically suspected sinusitis	Sinus referral clinic	44	NR	CT scan showing incomplete aeration, air-fluid level, or mucosal thickening	US	NR
Dobson, 1996[45]	Patients with clinically suspected maxillary sinusitis	ENT clinic	25 (50 sinuses)	NR	Sinus radiographs showing mucosal thickening, air-fluid level, or complete opacification	UK	NR

[a] *Two other publications by Hansen are excluded as they used the same group of patients.* [b] *Reported results for both MRI and radiography as reference standard for ultrasound. Only MRI results are used. AP = antral puncture. CRP = C-reactive protein. CT = computed tomography. MRI = magnetic resonance imaging. NR = not reported.*



Appendix 5. The risk of bias in QUADAS-2 study design domains.

Appendix 6. Prevalence of acute sinusitis in the included studies, by population, inclusion criteria, and reference standard[a]

Study	Reference standard	Sinusitis/ total	Prevalence, % (95% CI)
Adults, or adults and children with clinically suspected sinusitis			
Berg, 1981	AP	25/50	50.0
Berg, 1985	AP	43/90	47.8
Bergstedt, 1980	AP	23/48	47.9
Hansen, 1995	AP	92/174	52.9
Kuusela, 1983	AP	82/156	52.6
Laine, 1998	AP	23/72	31.9
McNeill, 1963	AP	100/242	41.3
Savolainen, 1997a	AP	165/234	70.5
Savolainen, 1997b	AP	187/234	79.9
van Buchem, 1995	AP	71/203	35.0
Watt-Boolsen, 1997	AP	221/468	47.2
Pooled subtotal:			**49 (42 to 57)**
Gianoli, 1992	CT	11/67	16.4
Goodman, 1995	CT	60/88	68.2
Lewander, 2012	CT	14/80	17.5
Awaida, 2004	CT	32/51	62.7
Lindbaek, 1996	CT	127/201	63.2
Pooled subtotal:			**44 (23 to 67)**
Berger, 2011	Rad	52/104	50.0
Shapiro, 1986	Rad	63/150	42.0
Jensen, 1987	Rad	120/253	47.4
Rohr, 1986	Rad	91/198	46.0
Dobson, 1996	Rad	28/50	56.0
Ghatasheh, 2000	Rad	54/100	54.0
Huang, 2008	Rad	151/217	69.6
Varonen, 2003	Rad	13/32	40.6
Young, 2003	Rad	67/241	27.8
Pooled subtotal:			**48 (39 to 57)**
Pooled subtotal, any reference standard:			**48 (42 to 54)**
Children with clinically suspected sinusitis			
Visca, 1995	CT	17/30	56.7
Fufezan, 2010	Rad	71/134	53.0
Reilly, 1989	Rad	18/96	18.8
Pooled subtotal:			**41 (19 to 67)**
Patients with acute respiratory tract infection			
van Buchem, 1992 (children)	AP	17/107	15.9
Puhakka, 2000 (adults)	MRI	94/394	23.9
Pooled subtotal:			**20 (14 to 29)**
Overall total			**46 (40 to 53)**

[a]*Subtotals pooled using a random effects model. If a study reports different numbers of patients with different signs and symptoms, the data for the greatest number of patients reported were used. AP = antral puncture revealing purulence. CT = computed tomography. MRI = magnetic resonance imaging. Rad = radiography.*

Appendix 7. Accuracy of imaging studies for diagnosis of acute sinusitis

Study	Ref std		Pop'n	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)	LR+ (95% CI)	LR– (95% CI)	AUC
Radiography												
Antral puncture as reference standard												
Berg, 1981	AP		A	25	17	0	8	1.00	0.32	1.47	0.00	
Bergstedt, 1980	AP		A	23	18	0	7	1.00	0.28	1.39	0.00	
Laine, 1998	AP		A	14	1	9	48	0.61	0.98	29.83	0.40	
Savolainen, 1997b	AP		A	174	18	13	29	0.93	0.62	2.43	0.11	
van Buchem, 1995	AP		A	53	39	14	81	0.79	0.68	2.43	0.31	
McNeill, 1963	AP		B	82	54	18	88	0.82	0.62	2.16	0.29	
Watt-Boolsen, 1977	AP		B	194	161	27	86	0.88	0.35	1.35	0.35	
Kuusela, 1983	AP		A	68	21	14	53	0.83	0.72	2.96	0.24	
van Buchem, 1992	AP		C	12	59	5	31	0.71	0.34	1.08	0.85	
Summary								**0.85 (0.77 to 0.90)**	**0.56 (0.38 to 0.73)**	**2.01 (1.40 to 3.05)**	**0.28 (0.19 to 0.39)**	**0.820**
Imaging as reference standard												
Young, 2003	LC		A	54	36	13	137	0.81	0.79	3.87	0.25	
Puhakka, 2000	MRI		A	16	0	6	58	0.73	1.00	73.00	0.27	
Visca, 1995	CT		C	16	7	1	6	0.94	0.46	1.75	0.13	
Summary								**0.80 (0.66 to 0.89)**	**0.84 (0.31 to 0.98)**	**9.37 (1.27 to 39.6)**	**0.27 (0.16 to 0.48)**	**0.841**
Summary (all)								**0.84 (0.78 to 0.89)**	**0.63 (0.44 to 0.78)**	**2.36 (1.57 to 3.68)**	**0.27 (0.20 to 0.34)**	**0.836**
Ultrasound		**Mode**										
A mode, AP as reference standard												
Laine, 1998	AP	A (Sinuscan 101)	A	14	23	9	26	0.61	0.53	1.30	0.74	
Savolainen, 1997b	AP	A (Sinuscan 102)	A	180	33	7	14	0.96	0.30	1.37	0.13	
Kuusela, 1983	AP	A (Sinuscan 101)	A	58	27	24	47	0.71	0.64	1.97	0.45	
Berg, 1985	AP	A (Sinuson 810)	B	27	14	16	33	0.63	0.70	2.11	0.53	
Summary								**0.79 (0.52 to 0.93)**	**0.54 (0.36 to 0.71)**	**1.71 (1.42 to 2.08)**	**0.41 (0.19 to 0.68)**	**0.679**
B mode, AP as reference standard												
van Buchem, 1992[a]	AP	B (3.5 Mhz sector scanner Philips SP 3000)	C	2	25	13	63	0.13	0.72	0.47	1.21	
van Buchem, 1995	AP	B (5 Mhz sectorscan)	A	51	33	7	68	0.88	0.67	2.69	0.18	
Summary								**0.53 (0.03 to 0.98)**	**0.69 (0.61 to 0.77)**	**1.64 (0.10 to 3.2)**	**0.69 (0.03 to 1.36)**	**0.693**
A mode, imaging as reference standard												
Varonen, 2003	Rad	A (Sinuscan 102)	A	12	1	1	18	0.92	0.95	17.5	0.08	

... continued

Appendix 7 continued. Accuracy of imaging studies for diagnosis of acute sinusitis

Puhakka, 2000	MRI	A (Sinuscan 102)	A	14	3	8	55	0.64	0.95	12.3	0.38	
Shapiro, 1986	Rad	A (Echosine)	B	33	34	30	53	0.52	0.61	1.34	0.78	
Jensen, 1987	Rad	A (Sinuson 810)	A	77	15	43	118	0.64	0.89	5.69	0.40	
Reilly, 1989	Rad	A (Sinus V)	C	10	2	8	86	0.56	0.98	24.4	0.45	
Rohr, 1986	Rad	A (Echosine)	A	26	4	17	45	0.60	0.92	7.41	0.43	
Summary								**0.62 (0.55 to 0.69)**	**0.91 (0.79 to 0.96)**	**7.64 (2.95 to 17.1)**	**0.42 (0.32 to 0.54)**	**0.702**
B mode, imaging as reference standard												
Ghatasheh, 2000	Rad	B (not stated)	B	42	0	12	46	0.78	1.00	78.00	0.22	
Fufezan, 2010	Rad	B (Sonoace 8000 EX)	C	50	1	21	62	0.70	0.98	44.37	0.30	
Dobson, 1996	Rad	B (Acuson 128)	NR	22	0	6	22	0.79	1.00	79.00	0.21	
Gianoli, 1992	CT	B (5 Mhz sectorscan)	B	11	1	0	55	1.00	0.98	56.00	0.00	
Summary								**0.75 (0.67 to 0.81)**	**0.98 (0.94 to 0.99)**	**38.4 (12.7 to 88.3)**	**0.26 (0.20 to 0.34)**	**0.897**
Summary (AP)	**AP**							**0.73 (0.49 to 0.88)**	**0.58 (0.47 to 0.69)**	**1.72 (1.32 to 2.12)**	**0.48 (0.24 to 0.81)**	**0.659**
Summary (imaging)	**Imaging**							**0.68 (0.61 to 0.73)**	**0.94 (0.88 to 0.97)**	**12.4 (5.1 to 26.0)**	**0.35 (0.28 to 0.43)**	**0.796**
Summary (all)								**0.71 (0.61 to 0.79)**	**0.83 (0.71 to 0.91)**	**4.40 (2.46 to 7.48)**	**0.35 (0.25 to 0.48)**	**0.820**
Screening CT												
Goodman, 1995	CT		NR	56	3	4	25	0.93	0.89	8.71	0.07	
Awaida, 2004	CT		B	26	2	6	17	0.81	0.89	7.36	0.21	
Summary (all)								**0.88 (0.71 to 0.96)**	**0.89 (0.77 to 0.95)**	**9.01 (3.77 to 18.3)**	**0.15 (0.05 to 0.33)**	**0.895**

[a]*Excluding this study as an outlier due to its very low sensitivity, the results for the remaining studies using antral puncture as the reference standard are: sensitivity 0.80 (95% CI = 0.60 to 0.92), specificity 0.58 (95% CI = 0.43 to 0.71), positive likelihood ratio 1.89 (95% CI = 1.48 to 2.45), and negative likelihood ratio 0.35 (95% CI = 0.16 to 0.60). A = patient population of adults. AP = antral puncture showing purulent fluid. AUC = area under the receiver operating characteristic curve. B = patient population of both adults and children. C = patient population of children. CT = computed tomography. FN = false negative. FP = false positive. LC = latent class analysis. LR+ = positive likelihood ratio. LR– = negative likelihood ratio. NR = not reported. MRI = magnetic resonance imaging. Pop'n = population. Rad = radiography. Ref std = reference standard. TN = true negative. TP = true positive*

Appendix 8. Accuracy of blood tests for the diagnosis of acute sinusitis in adults[a]

Study	Ref std	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)	LR+ (95% CI)	LR– (95% CI)	DOR	AUC
CRP >10 mg/L											
Hansen, 1995	AP	67	32	25	49	0.73	0.60	1.84	0.45	4.09	
CRP >20–25 mg/L											
Hansen, 1995	AP	48	18	44	63	0.52	0.78	2.35	0.61		
Lindbaek, 1996	CT	28	6	98	67	0.22	0.92	2.70	0.85		
Savolainen, 1997a	BC	51	4	86	35	0.37	0.90	3.63	0.70		
Young, 2003	Rad	32	28	35	146	0.48	0.84	2.97	0.62		
Summary						**0.39 (0.29 to 0.50)**	**0.87 (0.80 to 0.91)**	**2.92 (2.17 to 3.98)**	**0.71 (0.60 to 0.80)**	**4.11**	
CRP >40–49 mg/L											
Lindbaek, 1996	CT	12	2	114	71	0.10	0.97	3.48	0.93		
Savolainen, 1997a	BC	27	3	110	36	0.20	0.92	2.56	0.87		
Hansen, 1995	AP	30	8	62	73	0.33	0.90	3.30	0.75		
Summary						**0.22 (0.15 to 0.30)**	**0.91 (0.84 to 0.95)**	**2.46 (1.45 to 3.91)**	**0.86 (0.77 to 0.93)**	**2.86**	**0.721**
ESR >10											
Lindbaek, 1996	CT	89	32	37	41	0.71	0.56	1.61	0.52		
Savolainen, 1997a	BC	91	16	46	23	0.66	0.59	1.62	0.57		
Hansen, 1995	AP	21	2	11	17	0.66	0.89	6.23	0.38		
Summary						**0.68 (0.63 to 0.72)**	**0.58 (0.50 to 0.65)**	**1.60 (1.33 to 1.97)**	**0.57 (0.46 to 0.68)**	**2.81**	
ESR >20											
Lindbaek, 1996	CT	40	8	86	65	0.32	0.89	2.90	0.77		
van Buchem, 1995	AP	14	6	39	50	0.26	0.89	2.47	0.82		
Hansen, 1995	AP	29	14	28	46	0.51	0.77	2.18	0.64		
Summary						**0.36 (0.23 to 0.51)**	**0.86 (0.75 to 0.92)**	**2.55 (1.68 to 3.74)**	**0.74 (0.61 to 0.85)**	**3.45**	
ESR >30											
Hansen, 1995	AP	23	5	66	74	0.26	0.94	4.08	0.79	5.16	
ESR >40											
Savolainen, 1997a	BC	26	1	111	38	0.19	0.97	7.40	0.83	8.91	0.684
WBC >10											
Lindbaek, 1996	CT	31	8	95	65	0.25	0.89	2.25	0.85		
Savolainen, 1997a	BC	35	5	102	34	0.26	0.87	1.99	0.85		
Summary						**0.25 (0.20 to 0.31)**	**0.88 (0.81 to 0.93)**	**2.23 (1.29 to 3.66)**	**0.85 (0.78 to 0.94)**	**2.62**	**0.710**

[a]No studies with children were identified. Where results for more than one study are presented, a summary estimate is shown. AP = antral puncture revealing purulent fluid. AUC = area under the receiver operating characteristic curve. BC = bacterial culture of antral fluid positive for pathogenic bacteria. CRP = C-reactive protein. CT = computed tomography. DOR = diagnostic odds ratio (positive likelihood ratio divided by negative likelihood ratio). ESR = erythrocyte sedimentation rate. FN = false negative. FP = false positive. LR+ = positive likelihood ratio. LR– = negative likelihood ratio. Rad = radiography. Ref std = reference standard. TN = true negative. TP = true positive. WBC = white blood cells.

Appendix 9. Accuracy of miscellaneous tests for the diagnosis of acute sinusitis

Test	Study	Ref std	Pop'n	TP	FP	FN	TN	Sens	Spec	LR+	LR–
Clinical nasal secretion score ≥4	Huang, 2008	Rad	B	144	0	7	66	0.95	1.00	95.00	0.05
Leucocyte esterase ≥1+ in nasal secretions	Huang, 2008	Rad	B	126	3	25	63	0.83	0.95	18.36	0.17
Nitrite >1.0 in nasal secretions	Huang, 2008	Rad	B	78	4	73	55	0.52	0.93	7.62	0.52
pH >7 in nasal secretions	Huang, 2008	Rad	B	145	38	6	28	0.96	0.42	1.67	0.09
Protein >2.0 in nasal secretions	Huang, 2008	Rad	B	145	14	6	52	0.96	0.79	4.53	0.05
Leucocytes in sinus washings	van Buchem, 1995	AP	A	56	27	11	93	0.84	0.78	3.71	0.21
Leucocytes in sinus washings	van Buchem, 1992	AP	C	4	5	9	75	0.31	0.94	4.92	0.74
Leucocytes in nasal secretions	Visca, 1995	CT	C	16	4	1	9	0.94	0.69	3.06	0.08
Flexible endoscopy	Berger, 2011	Rad	A	43	17	9	35	0.83	0.67	2.53	0.26
Rhinoscopy — pus in nasal cavity	Young, 2003	Rad	A	55	108	12	66	0.82	0.38	1.32	0.47
Rhinoscopy — pus in throat	Young, 2003	Rad	A	17	33	51	141	0.25	0.81	1.32	0.93
Scintigraphy (probably or definitely abnl)	Bergstedt, 1980	AP	A	21	2	2	23	0.91	0.92	11.41	0.09
Diode gas laser spectroscopy (frontal sinus)	Lewander, 2012	CT	A	12	4	2	62	0.86	0.94	14.14	0.15
Diode gas laser spectroscopy (maxillary sinus)	Lewander, 2012	CT	A	7	4	11	53	0.39	0.93	5.54	0.66

A = patient population of adults. Abnl = abnormal. AP = antral puncture showing purulent fluid. B = patient population of both adults and children. C = patient population of children. CT = computed tomography. FN = false negative. FP = false positive. LR+ = positive likelihood ratio. LR– = negative likelihood ratio. Pop'n = population. Rad = radiography. Ref std = reference standard. Sens = sensitivity. Spec = specificity. TP = true positive. TN = true negative.