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Cohen JF, Bertille N, Cohen R, Chalumeau M

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[Diagnostic Test Accuracy Review]

Rapid antigen detection test for group A streptococcus in children with pharyngitis

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ABSTRACT

Background

Group A streptococcus (GAS) accounts for 20% to 40% of cases of pharyngitis in children; the remaining cases are caused by viruses. Compared with throat culture, rapid antigen detection tests (RADTs) offer diagnosis at the point of care (within five to 10 minutes).

Objectives

To determine the diagnostic accuracy of RADTs for diagnosing GAS in children with pharyngitis. To assess the relative diagnostic accuracy of the two major types of RADTs (enzyme immunoassays (EIA) and optical immunoassays (OIA)) by indirect and direct comparison.

Search methods

We searched CENTRAL, MEDLINE, EMBASE, Web of Science, CDSR, DARE, MEDION and TRIP (January 1980 to July 2015). We also conducted related citations tracking via PubMed, handsearched reference lists of included studies and relevant review articles, and screened all articles citing included studies via Google Scholar.

Selection criteria

We included studies that compared RADT for GAS pharyngitis with throat culture on a blood agar plate in a microbiology laboratory in children seen in ambulatory care.

Data collection and analysis

Two review authors independently screened titles and abstracts for relevance, assessed full texts for inclusion, and carried out data extraction and quality assessment using the QUADAS-2 tool. We used bivariate meta-analysis to estimate summary sensitivity and specificity, and to investigate heterogeneity across studies. We compared the accuracy of EIA and OIA tests using indirect and direct evidence.

Main results

We included 98 unique studies in the review (116 test evaluations; 101,121 participants). The overall methodological quality of included studies was poor, mainly because many studies were at high risk of bias regarding patient selection and the reference standard used (in 73% and 43% of test evaluations, respectively). In studies in which all participants underwent both RADT and throat culture (105

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test evaluations; 58,244 participants; median prevalence of participants with GAS was 29.5%), RADT had a summary sensitivity of 85.6%; 95% confidence interval (CI) 83.3 to 87.6 and a summary specificity of 95.4%; 95% CI 94.5 to 96.2. There was substantial heterogeneity in sensitivity across studies; specificity was more stable. There was no evidence of a trade-off between sensitivity and specificity. Heterogeneity in accuracy was not explained by study-level characteristics such as whether an enrichment broth was used before plating, mean age and clinical severity of participants, and GAS prevalence. The sensitivity of EIA and OIA tests was comparable (summary sensitivity 85.4% versus 86.2%). Sensitivity analyses showed that summary estimates of sensitivity and specificity were stable in low risk of bias studies.

Authors' conclusions

In a population of 1000 children with a GAS prevalence of 30%, 43 patients with GAS will be missed. Whether or not RADT can be used as a stand-alone test to rule out GAS will depend mainly on the epidemiological context. The sensitivity of EIA and OIA tests seems comparable. RADT specificity is sufficiently high to ensure against unnecessary use of antibiotics. Based on these results, we would expect that amongst 100 children with strep throat, 86 would be correctly detected with the rapid test while 14 would be missed and not receive antibiotic treatment.

PLAIN LANGUAGE SUMMARY

What is the performance of rapid tests for the diagnosis of strep throat in children?

Background and aims

Sore throat is very common in children. It can be caused by viruses or bacteria. The bacterium most frequently identified during sore throat in children is group A streptococcus ('strep throat'). Amongst children with sore throat, antibiotic treatment is only useful in those with strep throat.

Simple, rapid tests for the diagnosis of strep throat have been available since the 1980s. Physicians can do a rapid test at the point of care by swabbing the throat. Based on the result of the rapid test, they can then decide if antibiotics are needed.

We reviewed the evidence about the performance of rapid tests for correctly detecting strep throat in children seen in Outpatient departments with a main complaint of sore throat.

Study characteristics

We searched for studies published in any language from January 1980 to July 2015. We found 98 unique studies, for a total of 116 test evaluations, involving 101,121 children. The number of participants ranged from 42 to 11,644 across test evaluations. The proportion of children with strep throat ranged from 9.5% to 66.6% across test evaluations.

Quality of the evidence

Important study design features were frequently not reported. The overall methodological quality of included studies was poor. For most studies, we had concerns about the ways in which participants were selected.

Key results

On average, rapid tests for strep throat had a sensitivity (ability to correctly detect people with the disease) of 86% and a specificity (ability to correctly identify people who do not have the disease) of 95%. There was substantial variability in rapid test performance across studies, which was not explained by study characteristics, including methodological quality. The two types of rapid tests under evaluation seemed to have comparable sensitivity (85.4% versus 86.2% for enzyme immunoassays and optical immunoassays, respectively). Based on these results, we would expect that amongst 100 children with strep throat, 86 would be correctly detected with the rapid test while 14 would be missed and not receive antibiotic treatment. Of 100 children with non-streptococcal sore throat, 95 would be correctly classified as such with the rapid test while 5 would be misdiagnosed as having strep throat and receive unnecessary antibiotics.

SUMMARY OF FINDINGS

Summary of findings 1. Summary of findings table

Review questions	What is the diagnostic accuracy of rapid antigen detection tests (RADT) for detecting group A streptococcus (GAS)? What is the relative diagnostic accuracy of the two major types of RADTs (enzyme immunoassays (EIA) and optical immunoassays (OIA))?						
Patients/population	Children with acute pharyngitis						
Prior testing	Physical examination establishing the diagnosis of pharyngitis, with or without evaluating the likelihood of a streptococcal origin						
Settings	Ambulatory care settings: mainly private offices, emergency departments and walk-in clinics						
Index tests	EIA and OIA test for GAS						
Reference standard	Throat culture on a blood agar plate						
Importance	Compared with culture, RADTs offer diagnosis at the point of care. Whether negative RADTs should be backed up by throat culture depends mainly on the reported sensitivity of the test						
Studies	Cross-sectional studies						
Quality concerns	Methodological quality was generally poor, but quality appraisal was impeded by suboptimal reporting. Patient selection and reference standard methods were common risk of bias concerns (in 73% and 43% of test evaluations, respectively)						
Heterogeneity	There was substantial heterogeneity in the results of the individual studies, especially for sensitivity, which could not be explained by the investigations						
	Quantity of evidence		Average diagnostic accuracy		Consequences in a cohort of 1000 patients...		
	Studies (n)	Participants (n)	Sensitivity (95% CI)	Specificity (95% CI)	...given 20% prevalence of GAS cases?	...given 30% prevalence of GAS cases?	...given 40% prevalence of GAS cases?
RADT for the diagnosis of GAS pharyngitis in children (EIA and OIA tests)	105	58,244	85.6% (83.3 to 87.6)	95.4% (94.5 to 96.2)	200 children will have a positive culture for GAS. Of these, 171 will be identified (TP); 29 will be missed (FN). Of the 800 children without GAS, 763 will not be treated (TN);	300 children will have a positive culture for GAS. Of these, 257 will be identified (TP); 43 will be missed (FN). Of the 700 children without GAS, 668 will not be treated (TN);	400 children will have a positive culture for GAS. Of these, 342 will be identified (TP); 58 will be missed (FN). Of the 600 children without GAS, 572 will not be treated (TN);

37 may receive unnecessary antibiotics (FP) 32 may receive unnecessary antibiotics (FP) 28 may receive unnecessary antibiotics (FP)

Comparison of EIA versus OIA tests					
EIA tests	86	48,808	85.4% (82.7 to 87.8)	95.8% (94.8 to 96.6)	Interpretation: EIA and OIA tests seem to have comparable accuracy (P value = 0.23)
OIA tests	19	9436	86.2% (82.7 to 89.2)	93.7% (91.5 to 95.4)	

CI: confidence interval
 EIA: enzyme immunoassay
 FN: false negative
 FP: false positive
 GAS: group A streptococcus
 OIA: optical immunoassay
 RADT: rapid antigen detection test
 TN: true negative
 TP: true positive

BACKGROUND

Target condition being diagnosed

Pharyngitis is defined as an acute inflammation of the pharynx, tonsils or both. A sore throat is the most common symptom of pharyngitis. The terms 'pharyngitis', 'tonsillitis' and 'sore throat' are often used interchangeably. In this review, the more general term 'pharyngitis' is used. Viruses are the most common cause of pharyngitis but the bacterium most frequently identified during acute pharyngitis is *Streptococcus pyogenes* (*S. pyogenes*), also known as group A β -haemolytic streptococcus (GAS). GAS is estimated to account for 20% to 40% of cases of pharyngitis in children and 5% to 15% in adults (Shaikh 2010; Wessels 2011). The estimated number of cases of GAS pharyngitis in children is 450 million/year worldwide (Carapetis 2005a). Most cases are benign and self limiting within a week but suppurative complications (cervical lymphadenitis, retropharyngeal abscess, peritonsillar cellulitis or abscess (quinsy), sinusitis, acute otitis media and mastoiditis) or non-suppurative post-streptococcal diseases (acute rheumatic fever and rheumatic heart disease, acute glomerulonephritis, Sydenham's chorea, scarlet fever, streptococcal toxic shock syndrome and paediatric autoimmune neuropsychiatric disorder associated with group A streptococci) can occur (Gerber 2005; Shulman 2009).

Acute rheumatic fever is an autoimmune disorder resulting from infection with group A streptococcus, in which heart valves may be severely damaged (rheumatic heart disease). In low-income countries, rheumatic heart disease remains the most commonly acquired heart disease in children, adolescents and young adults: a recent estimate of the number of deaths from rheumatic heart disease is 233,000 per year worldwide (Carapetis 2005a). In high-income countries, acute rheumatic fever and rheumatic heart disease are rare (e.g., ≤ 10 cases/year/100,000 children for acute rheumatic fever) (Carapetis 2005b; Seckeler 2011), because of improvements in living conditions, hygiene, increased antibiotic usage, increased access to primary care providers and changes in GAS epidemiology (Carapetis 2007). In the US, about 50% to 70% of the visits by children with pharyngitis result in antibiotic agents being prescribed (Linder 2005). As a result, the public health goal is shifting from preventing rare GAS complications to minimising inappropriate use of antibiotics.

Index test(s)

Simple rapid antigen detection tests (RADTs) were developed in the 1980s to provide an immediate indication for the clinician about the presence or absence of GAS in children with pharyngitis. RADTs do not require any special equipment and can be performed at the point of care with a throat swab (Gerber 2004). They can provide immediate results and are calibrated to produce binary results (positive or negative).

All available RADTs involve the detection of the Lancefield group A carbohydrate, a GAS-specific cell-wall antigen. Different immunologic techniques are available for carbohydrate detection (Gerber 2004); from older to most recent:

- Latex agglutination (LA) assay: the sample is placed in the presence of latex beads coupled with GAS-specific antibodies; the result is determined by observing the agglutination of the beads if they are related to the specific antigen in the sample.

These first-generation tests are no longer used in clinical practice and were not considered in this review.

- Enzyme immunoassay (EIA): the sample is placed at the end of a nitrocellulose strip and then migrates to an area where it forms an antigen-antibody complex. These second-generation tests are also known as immunochromatographic, sandwich or lateral-flow assays. They are the most widespread and most used RADTs in clinical practice.
- Optical immunoassay (OIA): the sample is placed on a silicon membrane in the presence of the reagent. The result is based on the change in optical properties of the inert membrane in the presence of an antigen-antibody complex. These third-generation tests seem to be more sensitive than EIAs but their use is limited because of their high cost.

Clinical pathway

Many experts recommend the prescription of antibiotics for children with GAS-suspected or GAS-proven pharyngitis (Matthys 2007). The goal of antibiotic treatment is to reduce the individual risk of suppurative or non-suppurative complications, the duration of symptoms and the spread of the condition (Spinks 2013). Correct identification of GAS ensures against missing GAS-positive cases that can lead to complications. The correct exclusion of GAS ensures against unnecessary use of antibiotics (thus reducing the incidence of adverse drug reactions, antibiotic resistance and associated costs).

There is a lack of consensus on the most suitable diagnostic method for GAS in children with pharyngitis and the 'standard' diagnostic practice varies greatly amongst countries. The signs and symptoms of GAS and viral pharyngitis overlap broadly (Shaikh 2011), therefore most guidelines that recommend antibiotic treatment of GAS also recommend confirmation of the presence of GAS on the basis of a throat swab (Matthys 2007). However, throat swabs are explicitly not recommended in some countries (e.g., the United Kingdom, Belgium and the Netherlands) (Matthys 2007). International discrepancies might be explained by academic reasons and 'clinical traditions', different targets of sensitivity and specificity because of local epidemiological differences (i.e., rheumatic fever and rheumatic heart disease prevalence), international differences in health systems and policies, and the sparseness of recent data on the incidence of GAS complications and the efficacy of antibiotic treatment for their prevention.

The standard criterion for the diagnosis of GAS in children with pharyngitis is a throat culture on a blood agar plate in a microbiology laboratory (AAP 2012). The major advantage of laboratory throat culture is its detection of GAS from swabs with a very low number of bacteria, but the major limitation is the 48-hour delay in obtaining results. In addition, throat cultures cannot distinguish true GAS infection from GAS carriage with intercurrent viral pharyngitis. Asymptomatic pharyngeal GAS carriage is usually defined as positive throat culture results for GAS without a GAS-specific immune response (anti-streptolysin O and anti-DNase B antibodies) (Tanz 2007). Asymptomatic GAS carriage occurs in 10% to 15% of healthy children (Shaikh 2010), and does not require antibiotic treatment (Tanz 2007). Agreement is lacking on the most suitable culture technique for diagnosing GAS in children with pharyngitis. Several parameters are likely to affect the sensitivity of the test (culture medium, atmosphere of incubation, duration of incubation, group A identification technique and the number

of plates inoculated) (Kellogg 1990; Tanz 1997). These variables affect the diagnostic accuracy of the throat culture and thus the diagnostic accuracy of RADTs as compared to throat culture.

RADTs are widely used for diagnosing GAS pharyngitis at the point of care. In children, the reported sensitivity of RADTs is about 85% (Gerber 2004), but varies greatly amongst studies (from 66% (Van Limbergen 2006) to 99% (Harbeck 1993)), and the specificity is high and stable, about 95% (Gerber 2004). Due to this high specificity, most experts agree on prescribing antibiotics with positive RADT results, even if RADTs cannot differentiate GAS true infection from GAS carriage. However, the consequences of a negative RADT result depend on national guidelines. North American guidelines recommend backing up negative RADT results with throat culture to avoid not treating RADT false-negative cases (Gerber 2009; Shulman 2012), but most recent European guidelines recommend relying on negative RADT results without culture confirmation (Pelucchi 2012). In low-income countries, the clinical consequences of RADT results might be the same as in high-income countries (treat RADT-positive cases only) but resources for testing might be limited and practices may vary from generalised empiric antibiotic treatment to selective antibiotic treatment or selective rapid testing based on clinical scoring systems (Joachim 2010; Steinhoff 2005; WHO 1995).

Alternative test(s)

Office culture

Another test for the diagnosis of GAS in children with pharyngitis is a throat culture performed in the physician's office (office culture). Office culture has the same disadvantage as a laboratory culture (a 48-hour delay in obtaining results), with the major limitation being insufficient sensitivity (from 50% to 85%) (Battle 1971; Mondzac 1967; Rosenstein 1970; Tanz 2009; Wegner 1992). Office culture is almost completely abandoned and was not considered in this review.

Streptococcal antibody tests

Assessment of GAS-specific antibodies is the traditional reference test to differentiate true GAS infection and GAS carriage. The most commonly used GAS-specific antibody assays tests are for anti-streptolysin O and anti-DNase B antibodies. Increased antibody titre assessment diagnoses true GAS infection better than a single absolute titre assessment (Gerber 1986b; Johnson 2010). Streptococcal antibody tests are not used for the diagnosis of GAS in children with pharyngitis because of the need for repeat blood samples. Moreover, the information about the kinetics of the immune response to GAS in children with pharyngitis is very limited and the most recent data show that the interpretation of streptococcal antibody test results is not straightforward (Johnson 2010). Therefore, their use is usually limited to documenting recent GAS infection in patients suspected of having GAS non-suppurative complications or to epidemiologic studies (Gerber 1986b; Johnson 2010).

Clinical scoring systems

Clinical scoring systems have been developed to diagnose GAS on clinical grounds. The most popular of these scores are the Centor score (Centor 1981) and the McIsaac score (McIsaac 1998). The scores are based on assessing simple clinical criteria (history of fever, cough, tonsillar swelling or exudate, tender cervical

adenopathy and age). Their use is recommended in adults but might be inappropriate in children; several authors have reported a lack of diagnostic accuracy in this population (Cohen 2012; Cohen 2015; Fischer Walker 2006; Shaikh 2011). Clinical scoring systems were not considered in this review.

Rapid molecular biology assays

Rapid molecular biology assays for GAS in children with pharyngitis have been recently developed (Group A Streptococcus Direct Test; GenProbe Inc., San Diego, CA; and LightCycler Strep-A assay; Roche Applied Science, Indianapolis, IN) (Chapin 2002; Heelan 1996; Pokorski 1994; Uhl 2003). These techniques, based on DNA-rRNA hybridisation or polymerase chain reaction (PCR), are highly sensitive but are not currently used widely because of their cost, the need for highly specialised equipment and personnel, and the two-hour delay in results (Gerber 2004). Molecular assays are not antigen-detection tests and were not considered in this review.

Rationale

Childhood pharyngitis is a significant public health problem with, on the one hand, suppurative and non-suppurative complications of GAS pharyngitis (especially acute rheumatic fever and rheumatic heart disease) and, on the other, costly diagnostic tests and unnecessary antibiotics. RADTs for GAS are now widely available and their use in children with pharyngitis might increase accurate diagnosis and reduce antibiotic consumption.

According to local clinical guidelines, RADTs may be used as stand-alone diagnostic tests in replacement of throat culture (e.g., in contexts where throat culture is unavailable or not used), or as triage tests, with negative results being supported by a throat culture. These international discrepancies might be explained in part by persistent gaps in knowledge regarding the diagnostic accuracy of RADTs:

- What is the accuracy of RADTs for GAS in children with pharyngitis compared to the most consensual reference test (throat culture on a blood agar plate)?
- Are there significant differences in diagnostic accuracy between EIAs and OIAs?
- Which study-level factors could explain variations in diagnostic accuracy across clinical studies?

We did not address in this review the questions of whether RADTs should be performed in all patients presenting with signs and symptoms of pharyngitis or only in selected patients on the basis of a clinical score (selective testing strategies), and whether clinical protocols that incorporate RADTs are sufficient to reduce antibiotic prescription. We aimed to provide information to help clinicians and public health decision makers better define the precise role of RADTs in the diagnosis of GAS in children with pharyngitis on the basis of unbiased evidence.

OBJECTIVES

To determine the diagnostic accuracy of RADTs for diagnosing GAS in children with pharyngitis. To assess the relative diagnostic accuracy of the two major types of RADTs (enzyme immunoassays (EIA) and optical immunoassays (OIA)) by indirect and direct comparison.

Secondary objectives

To assess the relative diagnostic accuracy of EIA and OIA tests by indirect and direct comparison.

METHODS

Criteria for considering studies for this review

Types of studies

We included reports of cross-sectional studies reporting the diagnostic accuracy of one or more RADTs for the diagnosis of GAS in children with pharyngitis, with laboratory throat culture as the reference standard. Reports of randomised controlled trials (RCTs) were also eligible if we could extract 2 x 2 tables for children. Reports of studies in which throat culture was selectively performed in participants with a positive or negative RADT result were included in the review but excluded from the meta-analysis of sensitivity and specificity estimates.

Participants

We included reports of studies of children (age ≤ 21 years, according to the upper limit used by the American Academy of Pediatrics) seeking ambulatory medical care because of a sore throat or with a diagnosis of pharyngitis, who provided a throat swab for a RADT and laboratory throat culture. In this review, ambulatory care settings included private physicians' offices (general practitioners and paediatricians), walk-in clinics, hospital outpatient clinics, emergency departments and family medicine centres; we excluded studies performed by specialised physicians (e.g., ear, nose and throat specialists).

We also included reports of studies with only a subgroup of participants eligible for inclusion in the review, provided that we could extract relevant data specific to that subgroup. Reports of studies were not excluded on the basis of whether studies were performed in high-income or low-income countries because no data exist to support variations in the accuracy of RADTs according to this criterion.

Index tests

We included only studies of EIA or OIA RADTs for GAS in children with pharyngitis, including those no longer marketed.

Target conditions

GAS in children with pharyngitis (dichotomous).

Reference standards

Studies were required to diagnose GAS with throat culture on a blood agar plate in a microbiology laboratory used as the reference test. Several parameters may affect the accuracy of throat culture. For studies involving more than one throat culture technique (different medium, duration or atmosphere of incubation), we a priori chose to extract data related to the culture technique recommended by a panel of North American content experts, i.e., simple blood agar plate (versus selective or enriched media), incubation 48 hours total (versus 18 to 24 hours only), aerobic atmosphere (versus other) (Shulman 2000), in order to avoid data-driven approaches.

Search methods for identification of studies

Electronic searches

We searched MEDLINE via Ovid (1980 to May week 5, 2013) using the search strategy described in [Appendix 1](#). The search strategy was developed in consultation with a medical librarian and the Trials Search Co-ordinator for the Acute Respiratory Infections Group and was adapted to search EMBASE via Elsevier (1980 to June 2013) ([Appendix 2](#)) and Web of Science (1980 to June 2013) ([Appendix 3](#)). We did not use any filter related to age because many RADT studies enrol adults and children and could provide extractable data for children. We did not use methodological filters to identify diagnostic studies because such filters may result in omission of relevant studies (Leeflang 2006; Whiting 2011b). The searches were run from 1980 onwards because RADTs were not available prior to this date. We searched the Cochrane Central Register of Controlled Trials (CENTRAL) for relevant studies.

We searched the following databases to identify potentially relevant studies referenced in reviews and guidelines:

- the Cochrane Database of Systematic Reviews (2013, Issue 5);
- DARE (Database of Abstracts of Reviews of Effects) (2013, Issue 2 of 4);
- the MEDION database (for Systematic Reviews of Diagnostic Studies) (23 May 2013); and
- TRIP (Turning Research Into Practice) (23 May 2013).

We also searched Conference Proceedings Citation Index (CPCI) and SCI-Expanded for conference proceedings and abstracts. The literature search was updated by the Trials Search Co-ordinator for the Acute Respiratory Infections Group on 7 July 2015.

Searching other resources

We handsearched reference lists of included articles and relevant review articles identified through the search and the 'related articles' function in PubMed (20 first related articles of each included article) for eligible articles. We used Google Scholar to search for reports that cited included articles. We contacted manufacturers of the most common RADTs to seek additional or unpublished studies. Manufacturers included Abbott, Beckman Coulter, Becton Dickinson, Genzyme, Inverness Medical, Polymedco and Quidel.

Data collection and analysis

Selection of studies

We considered studies published in any language. Two review authors (JFC, NB) independently excluded studies that were not related to pharyngitis or RADT on the basis of the titles and abstracts identified by the search strategy. Two review authors (JFC, NB) retrieved the full text of relevant articles and independently evaluated them for inclusion by using a pro forma as a guide. One review author (MC) acted as arbiter in case of discrepancies between two review authors (JFC, NB) who discussed the inclusion of the studies.

We selected the most recent or most complete report in cases of multiple reports for a given study or when we could not exclude the possibility of overlapping populations. We produced a flowchart to report the search process. We reported reasons for excluding studies but we did not report their references.

Data extraction and management

We extracted the number of true positives, true negatives, false positives and false negatives for each index test evaluated in each study to construct 2 x 2 tables. If such data were not provided by the trial authors, we calculated the number of true positives, true negatives, false positives and false negatives from the summary estimates of sensitivity and specificity of the index test, if available. For studies for which only a subgroup of patients were included in the review, we extracted, analysed and presented data for this subgroup only. If some data were unclear or missing, we attempted to contact study authors to obtain additional data.

Two authors (JFC, NB) independently extracted the data used for study quality assessment and statistical analysis (data from 2 x 2 tables and covariates used for investigations of heterogeneity) and resolved discrepancies by discussion until a consensus was reached; other descriptive data were extracted by one review author (JFC). See [Table 1](#) for a description of which data were extracted for each study. Non-English language reports were not translated: for reports in French, Italian, Spanish and German, members of our team extracted data; for other languages, the Cochrane Acute Respiratory Infections Group identified collaborators who kindly agreed to extract the data.

Assessment of methodological quality

Methodological quality assessment involved use of a four-domain tool adapted from QUADAS-2 ([Whiting 2011a](#)). Two review authors (JFC, NB) independently collected the information needed to assess the methodological quality of each study using signalling questions (yes/no/unclear). We resolved disagreements on the signalling questions by discussion with a third author (MC) until a consensus was reached. One author (JFC) used this information to judge the risk of bias and concerns about applicability using pre-defined rules. We tailored the quality assessment tool to our review question. We developed review-specific guidance on how to assess each signalling question and how to use this information to judge the risk of bias and applicability. We refined the tool until satisfactory inter-rater agreement on signalling questions was achieved. We summarised the methodological quality assessment in tables. See [Table 2](#).

Statistical analysis and data synthesis

We entered data for the 2 x 2 tables into [RevMan 2014](#) and plotted estimates of sensitivity and specificity on forest plots and in the receiver-operating characteristic (ROC) space to represent the variability in diagnostic test accuracy within and between studies.

We fitted the hierarchical bivariate model described by [Reitsma 2005](#) by use of Stata/SE version 13 (using the user written program 'metandi'), which allowed for calculating summary estimates of sensitivity and specificity and the associated 95% confidence intervals (CIs). We also reported the estimate of correlation between sensitivity and specificity (ρ). We put the results from the bivariate model into [RevMan 2014](#) to provide plots of the estimated summary points and confidence regions, superimposed on the study-specific estimates of sensitivity and specificity in the ROC space.

We included the same study in the same meta-analysis more than once if needed, i.e., if one study reported different index tests. We presented results in groups according to commercial test name.

Investigations of heterogeneity

We initially visually inspected the forest plots and ROC space to check for heterogeneity between study results. To investigate sources of heterogeneity, we incorporated covariates in the bivariate model, i.e., meta-regression (using the built in program 'xtmelogit' and routines available at <http://methods.cochrane.org/sdt/software-meta-analysis-dta-studies>). We assessed the significance of the difference in covariate by likelihood ratio test comparing the bivariate model with and without the covariate. We used a P value of less than 0.05 to denote statistical significance. With a significant test result, we assessed effects of covariates on sensitivity and specificity separately by testing the significance of the change in -2 log-likelihood of the model (i.e., change in model deviance) with or without corresponding terms. We addressed the five following sources of heterogeneity by adding variables to the meta-analysis model:

a. Effect of test type

Some authors have suggested that OIA may be more sensitive than EIA tests ([Gerber 2004](#)). Therefore, we tried to indirectly compare the RADT tests by using test type as a categorical covariate in the models (EIA versus OIA); in indirect comparisons, data originate from different studies in which participants underwent either the EIA or the OIA test. We also tried to perform direct comparisons of EIA versus OIA by restricting the analysis to studies in which all patients underwent both EIA and OIA tests.

b. Effect of the reference standard

In this review, the reference standard was throat culture on a blood agar plate. However, several parameters may affect the accuracy of throat culture on blood agar, including whether an enrichment broth was used before plating. We added this variable as a categorical covariate (yes/no) in the model.

c. Effect of age

The sensitivity of RADTs is known to be higher in younger children than in older ones ([Cohen 2012](#); [Edmonson 2005](#)). This might be explained by higher GAS prevalence in school-age children with pharyngitis than in older children. Therefore, we explored age as a potential source of heterogeneity by using the mean age of patients in the study as a categorised covariate in the model (i.e., below or above median of mean age across studies).

d. Effect of disease severity

Spectrum effect has been demonstrated for RADTs, with increasing sensitivity with increasing disease severity, usually assessed by the Mclsaac score ([Cohen 2012](#); [Edmonson 2005](#); [Hall 2004](#); [Tanz 2009](#)). Therefore, disease severity might be a relevant source of heterogeneity to explore. We used the proportion of patients with a Mclsaac score greater than two as a categorical covariate in the model; we compared studies with less than 70% of patients with a Mclsaac score greater than two to studies with more than 70% of patients with a Mclsaac score greater than two (arbitrary).

e. Effect of GAS prevalence

Diagnostic accuracy may vary with disease prevalence ([Leeflang 2009](#); [Leeflang 2013](#)), usually with better performances in a population with higher disease prevalence. We considered GAS prevalence as a dichotomised covariate to define low-risk versus

high-risk study populations (i.e., below or above median of GAS prevalence across studies).

Sensitivity analyses

We carried out the following sensitivity analyses to explore the robustness of the results:

- include only studies judged at low risk of bias in each QUADAS-2 domain;
- include only studies judged at low risk of bias in at least 3 of 4 QUADAS-2 domains (arbitrary);
- include only studies judged to have low concerns about applicability in each QUADAS-2 domain.

Additional analyses

We performed univariate logitnormal random-effects meta-analysis of the negative predictive value of RADTs (using the user written command 'metan') combining studies with complete verification and studies in which RADT results were selectively verified by throat culture only in RADT-negative participants.

Assessment of reporting bias

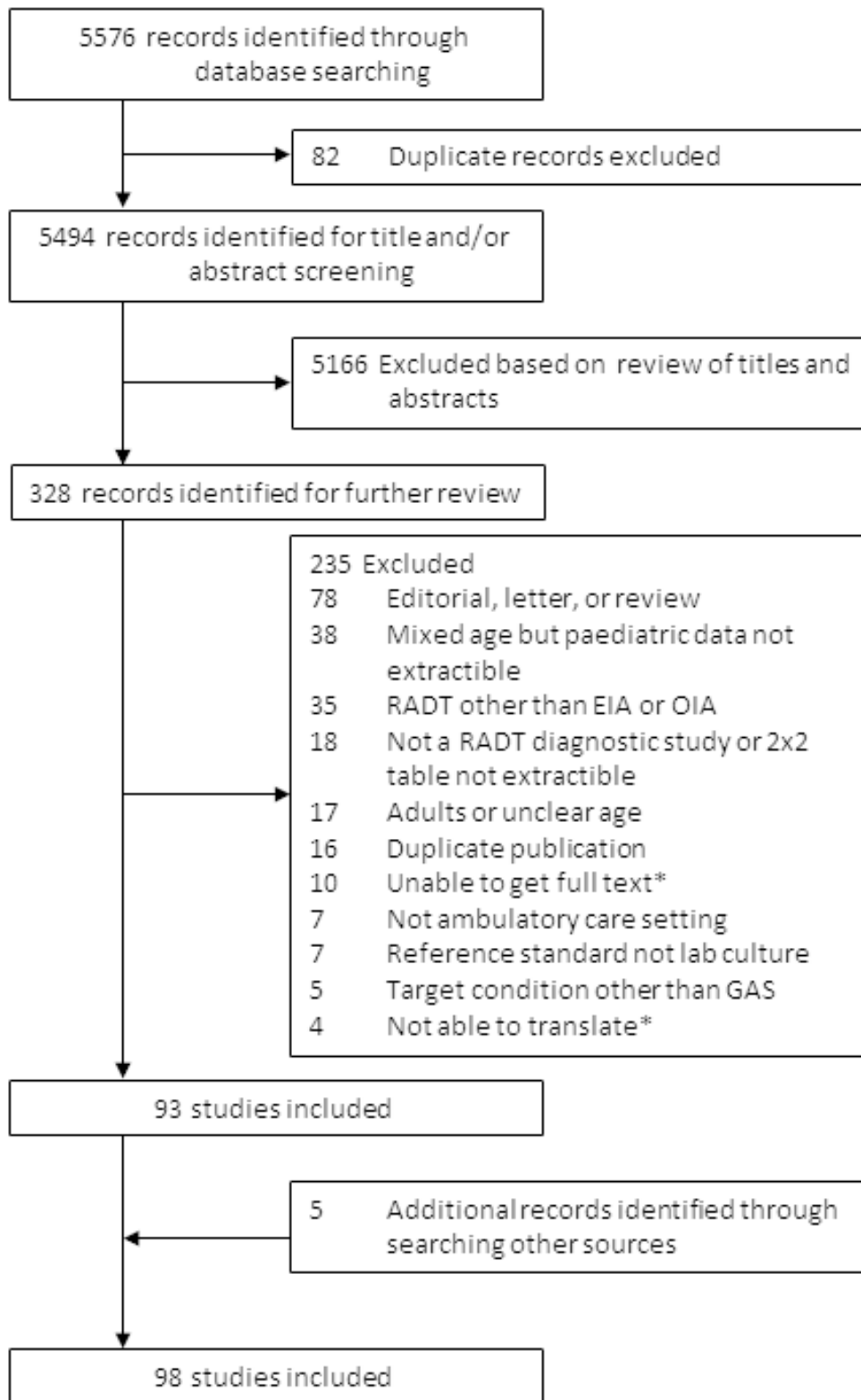
We did not try to assess reporting bias (Macaskill 2010).

RESULTS

Results of the search

The electronic search was performed on 7 July 2015. The search identified 5576 titles, of which we identified 82 as duplicates. We further excluded a total of 5166 titles on the basis of their title, abstract or both (Figure 1). After assessment of the full text of 328 articles, we excluded 235. Using the 'PubMed related articles' function and Google Scholar, and checking the references of included studies or reviews on the same topic (Gerber 2004; Lean 2014; Ruiz-Aragon 2010; Stewart 2014), allowed us to include five additional studies (Nitsch-Osuch 2010; Pauchard 2012; Sedki 2010; Tellechea 2012; Wong 1989). When possible, we contacted by email and postal mail authors of studies that included children and adults or in which the age of participants was unclear; eight trial authors shared or clarified paediatric data (Arribas Blanco 1988; Drulak 1991; Llor 2008; Mezghani Maleej 2010; Mlejnek 2014; Pauchard 2012; Pauchard 2013; Schwabe 1987; Schwabe 1991; Toepfner 2013). All included studies were cross-sectional. Manufacturers of RADTs did not respond. Thus, this review includes a total of 98 unique study reports.

Figure 1. Flow diagram of studies in the review. *Studies awaiting classification (n = 14)



Included studies

Some studies were subdivided for the purpose of the review. One multi-centre study conducted in four different countries was subdivided into four study cohorts (Rimoin 2010a). Some studies were also subdivided because they evaluated more than one RADT: nine studies compared two tests (Donatelli 1992a; Egger 1990a; Gieseke 2002a; Kaufhold 1991a; Mayes 2001a; Mirza 2007a; Roe 1995a; Schwartz 1997a; Wright 2007a), one compared three tests (Rogo 2010a), and one compared five tests (Chiadmi 2004a). Thus, this review includes a total of 116 test evaluations reporting a total of 101,121 test results. We performed descriptive analysis, methodological quality assessment and meta-analysis at the test evaluation level.

Included studies came from a variety of countries (n = 25); 53 (46%) test evaluations were conducted in the US. Forty-two different commercial RADT kits were evaluated, and three studies mentioned evaluating an EIA test without providing any commercial name (further referred to as "EIA (no name)"). Six commercial kits were evaluated in at least five paediatric cohorts: OSOM Strep A, QuickVue InLine Strep A, Strep A OIA, Strep A OIA Max, TestPack Strep A and TestPack Plus.

Excluded studies

Amongst 328 full-text articles assessed, we excluded 235 trials. Thirty-five assessed RADTs relying on other technologies than EIA or OIA. We excluded 38 studies because they included children and adults but did not report specific data for children, and we could not obtain additional data by contacting the trial authors. The status of 10 studies is uncertain because we were unable to obtain articles in full text. The status of four articles is uncertain as they have not yet been translated (two articles in Turkish, one in Polish and one in Czech).

Methodological quality of included studies

The overall methodological quality of included study cohorts is summarised in Figure 2. The quality assessment results for the individual studies is shown in Figure 3. The median sample size per study cohort was 297 participants (interquartile range (IQR) 196 to 539). The median mean age of participants was 6.6 (IQR 5.8 to 7.7) years, as reported in 32 studies. The majority of study cohorts (82 of 116, 71%) did not clearly report whether participants formed a consecutive, random or convenience series. Fifty-eight study cohorts (50%) avoided clinical selection of participants and therefore included a representative spectrum of patients.

Figure 2. Risk of bias and applicability concerns graph: review authors' judgements about each domain across all included study cohorts (n = 116).

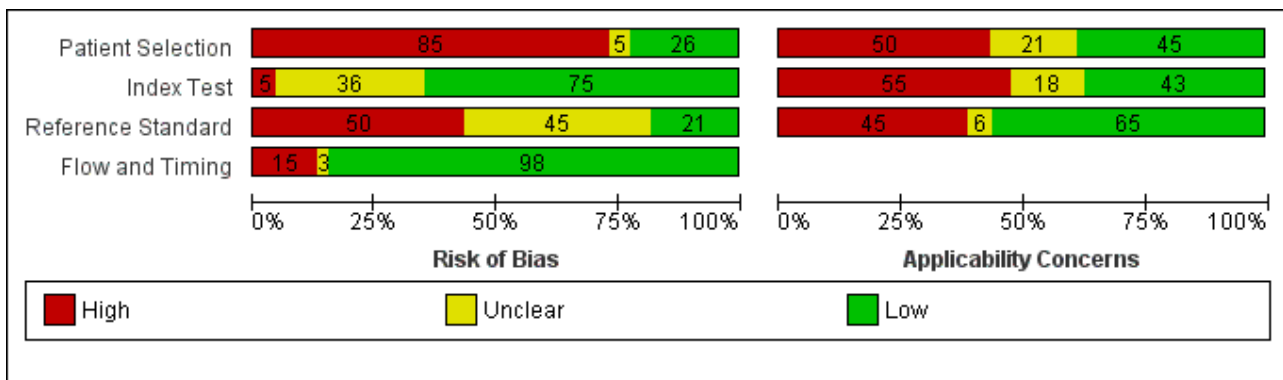


Figure 3. Risk of bias and applicability concerns summary: review authors' judgements about each domain for each included study cohort (n = 116).

	Risk of Bias				Applicability Concerns		
	Patient Selection	Index Test	Reference Standard	Flow and Timing	Patient Selection	Index Test	Reference Standard
Al-Najjar 2008	-	?	?	?	-	?	?
Alper 2013	+	?	-	+	+	-	-
Altun 2015	-	-	-	+	-	-	-
Arribas Blanco 1988	+	+	?	+	+	+	+
Attia 2001	+	?	?	+	+	-	+
Ayanruoh 2009	+	+	-	-	+	+	+
Begovac 1993	-	+	+	+	+	-	+
Buchbinder 2007	-	+	-	+	-	+	-
Camurdan 2008	-	?	-	+	+	?	-
Chapin 2002	-	+	+	+	+	-	+
Chiadmi 2004a	-	?	?	+	-	-	+
Chiadmi 2004b	-	?	?	+	-	-	+
Chiadmi 2004c	-	?	?	+	-	-	+
Chiadmi 2004d	-	?	?	+	-	-	+
Chiadmi 2004e	-	?	?	+	-	-	+
Chu 1990	+	?	-	+	+	-	-
Clegg 1987	-	+	-	+	+	?	-
Cohen 1988	-	+	-	-	-	+	-
Cohen 1998	-	+	-	-	+	+	+
Cohen 2004	-	-	-	-	+	+	-
Cohen 2012	+	+	+	+	+	+	+
Cohen 2013	+	+	+	+	+	+	+
Contessotto 2000	+	+	-	+	+	+	-
Dagnelie 1998	+	?	?	+	+	?	+
Daly 1994	-	?	?	+	+	-	+
Della-Latta 1994	+	+	?	+	+	-	+

Figure 3. (Continued)

Della-Latta 1994	+	+	?	+	+	-	+
Ding 2011	+	+	-	+	+	?	-
Dobkin 1987	-	?	?	+	?	-	+
Donatelli 1992a	-	?	+	+	-	?	+
Donatelli 1992b	-	?	+	+	-	?	+
dos Santos 2005	-	+	?	+	-	+	+
Drulak 1988	+	+	?	+	+	-	+
Drulak 1991	+	?	-	+	+	-	-
Edmonson 2005	-	+	+	-	?	+	+
Egger 1990a	-	+	?	+	-	-	+
Egger 1990b	-	+	?	+	-	-	+
Enright 2011	+	+	-	+	+	+	-
Ezike 2005	-	+	+	+	-	-	+
Faverge 2004	-	+	-	+	-	+	-
Felsenstein 2014	-	-	?	+	+	-	+
Finger 1999	+	+	-	+	+	+	-
Flores Mateo 2010	+	+	?	+	+	+	+
Forward 2006	-	?	?	+	?	-	+
Fourati 2009	-	?	-	+	+	-	-
Gerber 1990	-	+	?	+	-	+	+
Gerber 1997	-	+	-	+	-	-	-
Giesecker 2002a	-	+	?	+	-	-	+
Giesecker 2002b	-	+	?	+	-	-	+
Giesecker 2003	-	+	+	+	-	-	+
Gurol 2010	-	?	-	+	?	-	-
Hall 2004	-	+	?	-	-	+	+
Harris 1995	+	+	?	+	+	-	+
Hart 1997	-	+	?	+	-	-	+
Henderson 1988	-	?	-	+	?	+	-
Kaltwasser 1997	-	+	?	+	-	-	+
Kaufhold 1991a	-	?	-	+	-	-	-

Figure 3. (Continued)

Kaufhold 1991 a	-	?	-	+	-	-	-
Kaufhold 1991 b	-	?	-	+	-	-	-
Kellog 1987	-	+	?	+	+	-	+
Kellog 1991	-	+	-	-	+	-	+
Kim 2009	-	?	-	+	-	-	-
Küçük 2014	-	-	?	+	-	-	?
Kuhn 1999	-	+	?	+	-	-	+
Kurtz 2000	-	+	+	+	-	-	+
Laubscher 1995	-	+	+	+	+	+	+
Lewey 1988	-	+	-	+	-	+	-
Llor 2008	-	+	+	+	-	+	+
Macknin 1988	-	?	-	+	-	?	-
Maltezou 2008	?	+	-	+	-	+	-
Mayes 2001 a	-	+	-	-	-	+	-
Mayes 2001 b	-	+	-	-	?	+	-
Mazur 2014	-	+	+	+	-	+	+
Mclsaac 2004	-	?	-	+	-	?	-
Menozzi 1992	-	+	-	+	+	?	-
Mezghani Maleej 2010	-	+	?	+	-	+	+
Mirza 2007 a	-	+	-	-	?	+	-
Mirza 2007 b	-	+	-	-	?	-	-
Mlejnek 2014	?	+	-	-	?	+	+
Moyer 1990	-	+	?	+	?	-	+
Needham 1998	-	+	?	+	?	-	+
Nitsch-Osuch 2010	-	?	-	+	-	?	-
Nonaka 1988	?	?	?	+	?	?	?
Pauchard 2012	+	+	+	+	+	+	+
Pauchard 2013	+	+	+	+	+	+	+
Pitetti 1998	-	?	+	+	?	?	+
Ramos 2011	-	+	-	+	?	+	-
Regueras De Lorenzo 2012	+	+	?	+	+	+	+

Figure 3. (Continued)

Regueras De Lorenzo 2012	+	+	?	+	+	+	+
Reinert 1988	-	+	-	?	-	+	-
Rimoin 2010a	+	?	?	+	+	-	+
Rimoin 2010b	+	?	?	+	+	-	+
Rimoin 2010c	+	?	?	+	+	-	+
Rimoin 2010d	+	?	?	+	+	-	+
Roddey 1995	-	+	?	+	-	-	+
Roe 1995a	-	+	+	+	+	-	+
Roe 1995b	-	+	+	-	+	-	+
Rogo 2010a	-	+	-	+	-	+	-
Rogo 2010b	-	+	-	+	-	+	-
Rogo 2010c	-	+	-	+	-	+	-
Savoia 1994	+	?	?	+	?	-	+
Schlager 1996	-	+	+	+	-	-	+
Schwabe 1987	-	+	?	+	?	-	+
Schwabe 1991	-	?	?	+	?	-	+
Schwartz 1997a	-	+	-	+	?	+	-
Schwartz 1997b	-	+	-	+	?	+	-
Sedki 2010	-	?	-	+	-	?	-
Strandjord 1987	-	+	-	+	-	+	-
Subashini 2015	-	-	?	+	?	-	?
Tanz 2009	+	+	+	+	+	+	+
Tellechea 2012	-	?	?	?	-	?	?
Tenjarla 1991	-	+	-	+	+	-	-
Toepfner 2013	-	+	?	+	?	?	?
Van Limbergen 2006	-	+	-	-	+	+	-
Wong 1989	-	+	+	+	+	-	+
Wright 2007a	?	+	-	+	-	?	-
Wright 2007b	?	+	-	+	-	?	-
Yuckienuz 1988	-	+	-	-	+	+	+
Zanacca 1992	-	+	-	+	+	+	-

- High
 ? Unclear
 + Low

Interpretation of the results of the RADT was done with blinding of the result of throat culture in 84 of 116 cases (72%). An appropriate reference standard (i.e., laboratory throat culture on a blood agar plate during 48 hours) was used in 72 study cohorts (62%). Interpretation of the results of the reference standard was done with blinding of the result of the RADT in 23 of 116 cases (20%).

Partial verification was avoided in a majority (105 of 116, 91%) of cases. In 10 study cohorts (42,319 participants), RADT results were verified by throat culture only in RADT negative participants (Ayanruoh 2009; Cohen 2004; Edmonson 2005; Hall 2004; Mayes 2001a; Mirza 2007a; Mlejnek 2014; Van Limbergen 2006); in one

study (558 participants) RADT results were verified only in RADT positive participants (Cohen 1998).

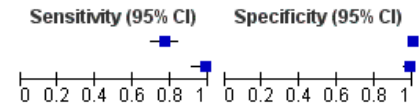
Findings

Across the 116 study cohorts included in the review, the sensitivity of rapid antigen detection tests (RADTs) ranged from 38.6% to 100% and the specificity from 54.1% to 100% (Figure 4). We excluded 11 study cohorts from the meta-analysis of sensitivity and specificity estimates for a final dataset containing 105 pairs of sensitivity and specificity (58,244 participants), where partial verification was not avoided.

Figure 4. Forest plots of RADT sensitivity and specificity for GAS detection, ordered by commercial kit. TP = True Positive; FP = False Positive; FN = False Negative; TN = True Negative.

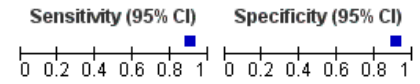
Acceava Strep A (Biostar)

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Hall 2004	117	0	35	409	0.77 [0.69, 0.83]	1.00 [0.99, 1.00]
Rogo 2010a	63	2	1	162	0.98 [0.92, 1.00]	0.99 [0.96, 1.00]



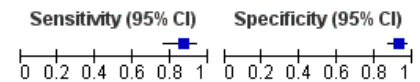
ACON Strep A Rapid Test Strip

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Tellechea 2012	1981	290	210	3024	0.90 [0.89, 0.92]	0.91 [0.90, 0.92]



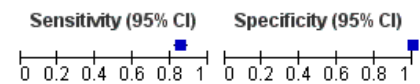
BioNexia Strep A (BioMerieux)

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Pauchard 2013	59	8	9	107	0.87 [0.76, 0.94]	0.93 [0.87, 0.97]



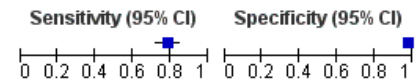
CARDS QS Strep A (Quidel)

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Edmonson 2005	384	0	65	735	0.86 [0.82, 0.89]	1.00 [0.99, 1.00]



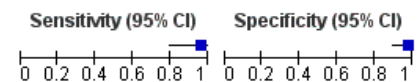
Clearview Exact Strep A

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Ding 2011	146	9	40	435	0.78 [0.72, 0.84]	0.98 [0.96, 0.99]



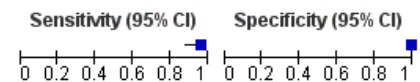
Clearview Strep A

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Chiadmi 2004c	24	1	1	49	0.96 [0.80, 1.00]	0.98 [0.89, 1.00]



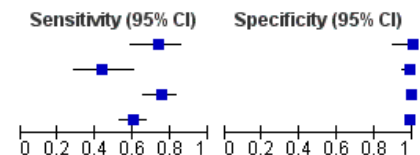
Diaquick Strep A Test (Dialab)

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Al-Najjar 2008	68	3	3	422	0.96 [0.88, 0.99]	0.99 [0.98, 1.00]



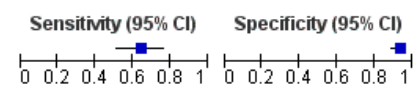
Directgen 1-2-3 Group A Strep (Becton Dickinson)

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Dagnelie 1998	34	0	12	33	0.74 [0.59, 0.86]	1.00 [0.89, 1.00]
Donatelli 1992a	18	2	23	137	0.44 [0.28, 0.60]	0.99 [0.95, 1.00]
Moyer 1990	78	2	26	218	0.75 [0.66, 0.83]	0.99 [0.97, 1.00]
Zanacca 1992	120	6	79	401	0.60 [0.53, 0.67]	0.99 [0.97, 0.99]



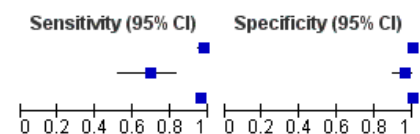
Direct Strep A EIA

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Egger 1990b	38	16	21	218	0.64 [0.51, 0.76]	0.93 [0.89, 0.96]



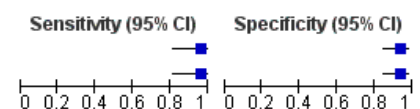
EIA (no name)

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Cohen 2004	268	0	7	329	0.97 [0.95, 0.99]	1.00 [0.99, 1.00]
Henderson 1988	27	3	12	75	0.69 [0.52, 0.83]	0.96 [0.89, 0.99]
Mayes 2001b	1743	0	68	4696	0.96 [0.95, 0.97]	1.00 [1.00, 1.00]



Group A Strep Test (Quidel)

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Cohen 1988	26	4	1	61	0.96 [0.81, 1.00]	0.94 [0.85, 0.98]
Reinert 1988	26	4	1	61	0.96 [0.81, 1.00]	0.94 [0.85, 0.98]



IM Strep A (International Microbio)

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
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Figure 4. (Continued)

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Buchbinder 2007	44	29	13	130	0.77 [0.64, 0.87]	0.82 [0.75, 0.87]
Chiadmi 2004b	24	2	1	48	0.96 [0.80, 1.00]	0.96 [0.86, 1.00]

Meridian Bioscience

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Alper 2013	19	10	0	85	1.00 [0.82, 1.00]	0.89 [0.81, 0.95]

OSOM Strep A (Genzyme)

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Flores Mateo 2010	65	30	7	109	0.90 [0.81, 0.96]	0.78 [0.71, 0.85]
Llor 2008	7	3	1	31	0.88 [0.47, 1.00]	0.91 [0.76, 0.98]
Mezghani Maleej 2010	138	14	10	283	0.93 [0.88, 0.97]	0.95 [0.92, 0.97]
Mlejnek 2014	0	0	0	0	Not estimable	Not estimable
Ramos 2011	50	3	2	110	0.96 [0.87, 1.00]	0.97 [0.92, 0.99]
Rogo 2010b	65	1	1	161	0.98 [0.92, 1.00]	0.99 [0.97, 1.00]
Schwartz 1997a	98	0	5	155	0.95 [0.89, 0.98]	1.00 [0.98, 1.00]

OSOM Ultra Strep A (Genzyme)

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Felsenstein 2014	32	3	26	300	0.55 [0.42, 0.68]	0.99 [0.97, 1.00]
Gieseke 2002b	84	18	3	197	0.97 [0.90, 0.99]	0.92 [0.87, 0.95]
Gieseke 2003	181	19	29	658	0.86 [0.81, 0.91]	0.97 [0.96, 0.98]
Wright 2007a	76	7	13	242	0.85 [0.76, 0.92]	0.97 [0.94, 0.99]

QuickVue Dipstick Strep A (Quidel)

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Rogo 2010c	60	6	5	157	0.92 [0.83, 0.97]	0.96 [0.92, 0.99]
Tanz 2009	385	29	168	1261	0.70 [0.66, 0.73]	0.98 [0.97, 0.98]

QuickVue Flex Strep A (Quidel)

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Contessotto 2000	103	11	10	277	0.91 [0.84, 0.96]	0.96 [0.93, 0.98]
Finger 1999	212	42	27	496	0.89 [0.84, 0.92]	0.92 [0.90, 0.94]

QuickVue In-Line Strep A (Quidel)

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Enright 2011	27	2	11	137	0.71 [0.54, 0.85]	0.99 [0.95, 1.00]
Kü ç ü k 2014	128	19	87	658	0.60 [0.53, 0.66]	0.97 [0.96, 0.98]
Pauchard 2012	571	153	180	1036	0.76 [0.73, 0.79]	0.87 [0.85, 0.89]
Schwartz 1997b	90	0	13	155	0.87 [0.79, 0.93]	1.00 [0.98, 1.00]
Toepfner 2013	94	20	5	398	0.95 [0.89, 0.98]	0.95 [0.93, 0.97]
Wright 2007b	70	13	18	237	0.80 [0.70, 0.87]	0.95 [0.91, 0.97]

QuickVue+ Strep A (Quidel)

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
dos Santos 2005	89	16	3	268	0.97 [0.91, 0.99]	0.94 [0.91, 0.97]
Guro 2010	28	3	12	135	0.70 [0.53, 0.83]	0.98 [0.94, 1.00]
Mazur 2014	45	2	0	43	1.00 [0.92, 1.00]	0.96 [0.85, 0.99]
Van Limbergen 2006	21	1	11	168	0.66 [0.47, 0.81]	0.99 [0.97, 1.00]

Sacks Biological Farms

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Ayanruoh 2009	1474	0	2	5081	1.00 [1.00, 1.00]	1.00 [1.00, 1.00]

SD Bioline Strep A

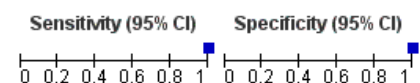
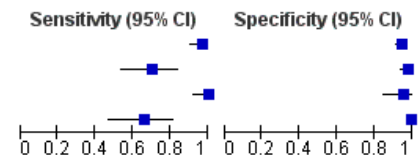
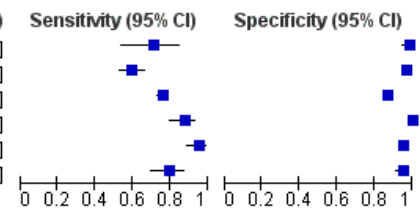
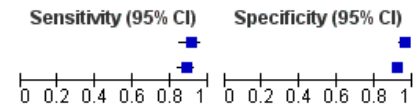
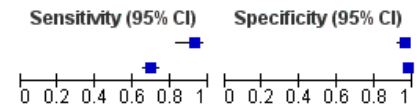
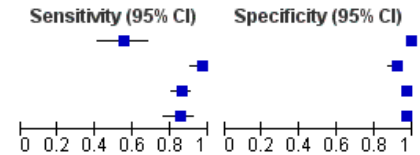
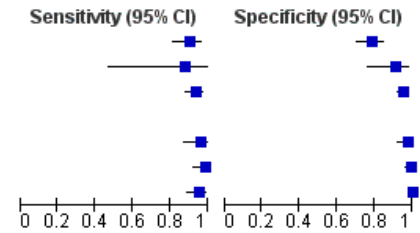
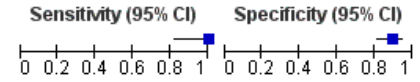
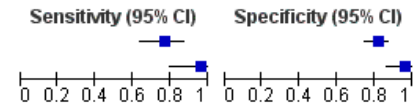


Figure 4. (Continued)

SD Bioline Strep A

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Kim 2009	187	8	8	90	0.96 [0.92, 0.98]	0.92 [0.85, 0.96]
Subashini 2015	15	0	12	84	0.56 [0.35, 0.75]	1.00 [0.96, 1.00]

Signify Strep A (Abbott)

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Mirza 2007b	1730	0	280	4855	0.86 [0.84, 0.88]	1.00 [1.00, 1.00]

SMART Group A Strep (New Horizons)

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Kellog 1991	302	8	121	604	0.71 [0.67, 0.76]	0.99 [0.97, 0.99]

Strep A Abon kit

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Altun 2015	224	30	83	906	0.73 [0.68, 0.78]	0.97 [0.95, 0.98]

Strep A OIA (Biostar)

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Chapin 2002	149	10	24	337	0.86 [0.80, 0.91]	0.97 [0.95, 0.99]
Daly 1994	64	15	12	333	0.84 [0.74, 0.92]	0.96 [0.93, 0.98]
Della-Latta 1994	89	35	3	563	0.97 [0.91, 0.99]	0.94 [0.92, 0.96]
Gerber 1997	844	78	161	1030	0.84 [0.82, 0.86]	0.93 [0.91, 0.94]
Harris 1995	109	24	5	381	0.96 [0.90, 0.99]	0.94 [0.91, 0.96]
Hart 1997	13	23	3	36	0.81 [0.54, 0.96]	0.61 [0.47, 0.73]
Kaltwasser 1997	47	18	10	125	0.82 [0.70, 0.91]	0.87 [0.81, 0.92]
Kuhn 1999	120	9	12	222	0.91 [0.85, 0.95]	0.96 [0.93, 0.98]
Needham 1998	75	7	11	183	0.87 [0.78, 0.93]	0.96 [0.93, 0.99]
Pitetti 1998	58	5	15	155	0.79 [0.68, 0.88]	0.97 [0.93, 0.99]
Roddey 1995	107	8	10	176	0.91 [0.85, 0.96]	0.96 [0.92, 0.98]
Roe 1995a	126	38	25	311	0.83 [0.77, 0.89]	0.89 [0.85, 0.92]
Schlager 1996	48	7	14	193	0.77 [0.65, 0.87]	0.96 [0.93, 0.99]

Strep A OIA Max (Biostar)

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Ezike 2005	73	4	6	103	0.92 [0.84, 0.97]	0.96 [0.91, 0.99]
Gieseke 2002a	65	12	17	208	0.79 [0.69, 0.87]	0.95 [0.91, 0.97]
Rimoin 2010a	39	5	6	134	0.87 [0.73, 0.95]	0.96 [0.92, 0.99]
Rimoin 2010b	146	23	13	222	0.92 [0.86, 0.96]	0.91 [0.86, 0.94]
Rimoin 2010c	321	82	109	1114	0.75 [0.70, 0.79]	0.93 [0.92, 0.95]
Rimoin 2010d	55	26	21	156	0.72 [0.61, 0.82]	0.86 [0.80, 0.90]

Strep A Rapid Test Device

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Forward 2006	80	23	38	349	0.68 [0.59, 0.76]	0.94 [0.91, 0.96]

Strep A Sign

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Chiadmi 2004d	22	3	3	47	0.88 [0.69, 0.97]	0.94 [0.83, 0.99]

Strep A test II (INTEX Diagnostica)

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Camurdan 2008	426	22	49	751	0.90 [0.87, 0.92]	0.97 [0.96, 0.98]

StreptAtest (Dectrapharm)

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
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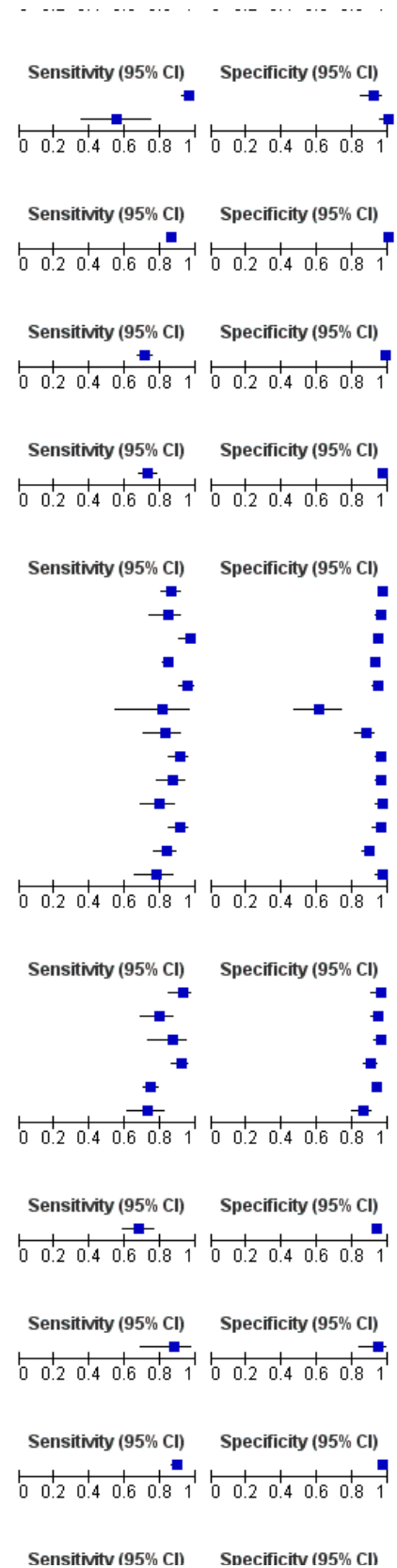
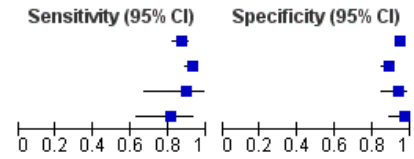


Figure 4. (Continued)

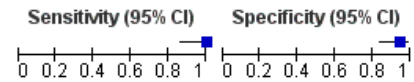
Streptest (Becton Dickinson)

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Cohen 2012	247	27	38	473	0.87 [0.82, 0.90]	0.95 [0.92, 0.96]
Cohen 2013	259	46	21	350	0.93 [0.89, 0.95]	0.88 [0.85, 0.91]
Faverge 2004	17	4	2	61	0.89 [0.67, 0.99]	0.94 [0.85, 0.98]
Sedki 2010	25	2	6	62	0.81 [0.63, 0.93]	0.97 [0.89, 1.00]



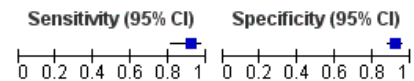
Streptavit

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Chiadmi 2004e	25	3	0	47	1.00 [0.86, 1.00]	0.94 [0.83, 0.99]



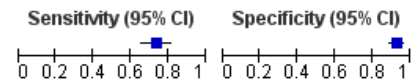
Streptop A (ALL-Diag)

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Fourati 2009	54	18	5	215	0.92 [0.81, 0.97]	0.92 [0.88, 0.95]



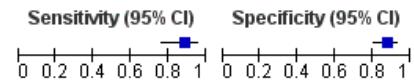
SUDS Group A Strep

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Yuckienuz 1988	93	15	33	200	0.74 [0.65, 0.81]	0.93 [0.89, 0.96]



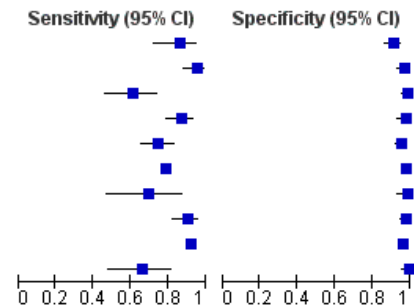
SureScreen Test Strep A

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Nitsch-Osuch 2010	46	17	6	119	0.88 [0.77, 0.96]	0.88 [0.81, 0.93]



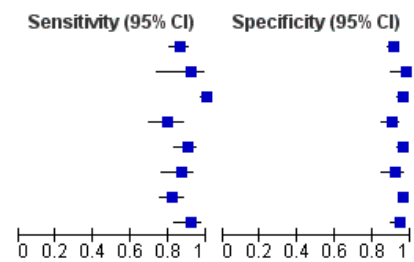
TestPack Strep A (Abbott)

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Arribas Blanco 1988	37	18	6	179	0.86 [0.72, 0.95]	0.91 [0.86, 0.94]
Dobkin 1987	65	5	3	148	0.96 [0.88, 0.99]	0.97 [0.93, 0.99]
Egger 1990a	31	4	20	231	0.61 [0.46, 0.74]	0.98 [0.96, 1.00]
Kaufhold 1991a	91	3	14	122	0.87 [0.79, 0.93]	0.98 [0.93, 1.00]
Kellog 1987	80	11	27	240	0.75 [0.65, 0.83]	0.96 [0.92, 0.98]
Menozi 1992	1007	54	269	2328	0.79 [0.77, 0.81]	0.98 [0.97, 0.98]
Nonaka 1988	16	1	7	76	0.70 [0.47, 0.87]	0.99 [0.93, 1.00]
Schwabe 1987	90	7	10	258	0.90 [0.82, 0.95]	0.97 [0.95, 0.99]
Tenjarla 1991	1389	305	125	7342	0.92 [0.90, 0.93]	0.96 [0.96, 0.96]
Wong 1989	23	1	12	111	0.66 [0.48, 0.81]	0.99 [0.95, 1.00]



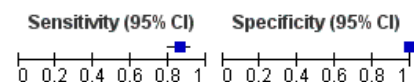
TestPack Plus (Abbott)

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Attia 2001	187	33	31	336	0.86 [0.80, 0.90]	0.91 [0.88, 0.94]
Chiadmi 2004a	23	1	2	49	0.92 [0.74, 0.99]	0.98 [0.89, 1.00]
Cohen 1998	121	19	0	418	1.00 [0.97, 1.00]	0.96 [0.93, 0.97]
Kurtz 2000	63	18	16	159	0.80 [0.69, 0.88]	0.90 [0.84, 0.94]
Laubscher 1995	106	14	12	322	0.90 [0.83, 0.95]	0.96 [0.93, 0.98]
Regueras De Lorenzo 2012	64	10	10	108	0.86 [0.77, 0.93]	0.92 [0.85, 0.96]
Roe 1995b	124	14	27	335	0.82 [0.75, 0.88]	0.96 [0.93, 0.98]
Schwabe 1991	65	11	6	179	0.92 [0.83, 0.97]	0.94 [0.90, 0.97]



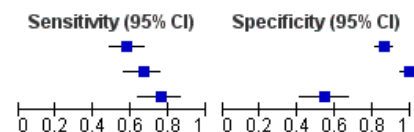
TestPack Plus Strep A with OBC II (Abbott)

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Mclsaac 2004	133	3	22	296	0.86 [0.79, 0.91]	0.99 [0.97, 1.00]



Ventrescreen Strep A (Ventrex Lab)

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Begovac 1993	70	37	51	231	0.58 [0.49, 0.67]	0.86 [0.81, 0.90]
Clegg 1987	66	1	33	105	0.67 [0.56, 0.76]	0.99 [0.95, 1.00]
Macknin 1988	45	28	14	33	0.76 [0.63, 0.86]	0.54 [0.41, 0.67]



Visual Strep A (ADN)

Figure 4. (Continued)

Macknin 1988 45 28 14 33 0.76 [0.63, 0.86] 0.54 [0.41, 0.67]

Visuwell Strep A (ADI)

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Chu 1990	37	23	5	379	0.88 [0.74, 0.96]	0.94 [0.92, 0.96]
Drulak 1988	43	26	14	197	0.75 [0.62, 0.86]	0.88 [0.83, 0.92]
Drulak 1991	43	22	11	126	0.80 [0.66, 0.89]	0.85 [0.78, 0.90]

Icon Strep A

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Donatelli 1992b	17	0	27	158	0.39 [0.24, 0.55]	1.00 [0.98, 1.00]
Kaufhold 1991b	90	12	20	139	0.82 [0.73, 0.89]	0.92 [0.87, 0.96]
Lewey 1988	41	21	6	196	0.87 [0.74, 0.95]	0.90 [0.86, 0.94]
Strandjord 1987	46	6	6	80	0.88 [0.77, 0.96]	0.93 [0.85, 0.97]

Qtest (Becton Dickinson)

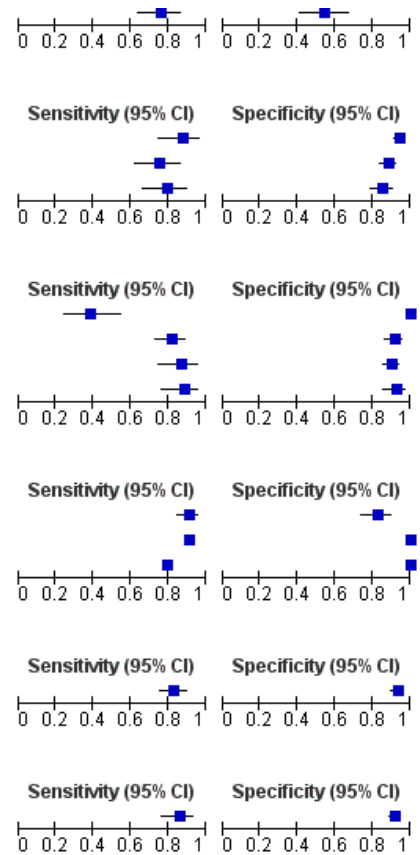
Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Gerber 1990	123	16	12	77	0.91 [0.85, 0.95]	0.83 [0.74, 0.90]
Mayes 2001a	1299	0	132	3342	0.91 [0.89, 0.92]	1.00 [1.00, 1.00]
Mirza 2007a	2612	0	688	8344	0.79 [0.78, 0.81]	1.00 [1.00, 1.00]

Link 2 Strep A Rapid Test (Becton Dickinson)

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Maltezou 2008	98	21	20	293	0.83 [0.75, 0.89]	0.93 [0.90, 0.96]

Event Test Strip Strep A

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Savoia 1994	63	36	10	401	0.86 [0.76, 0.93]	0.92 [0.89, 0.94]

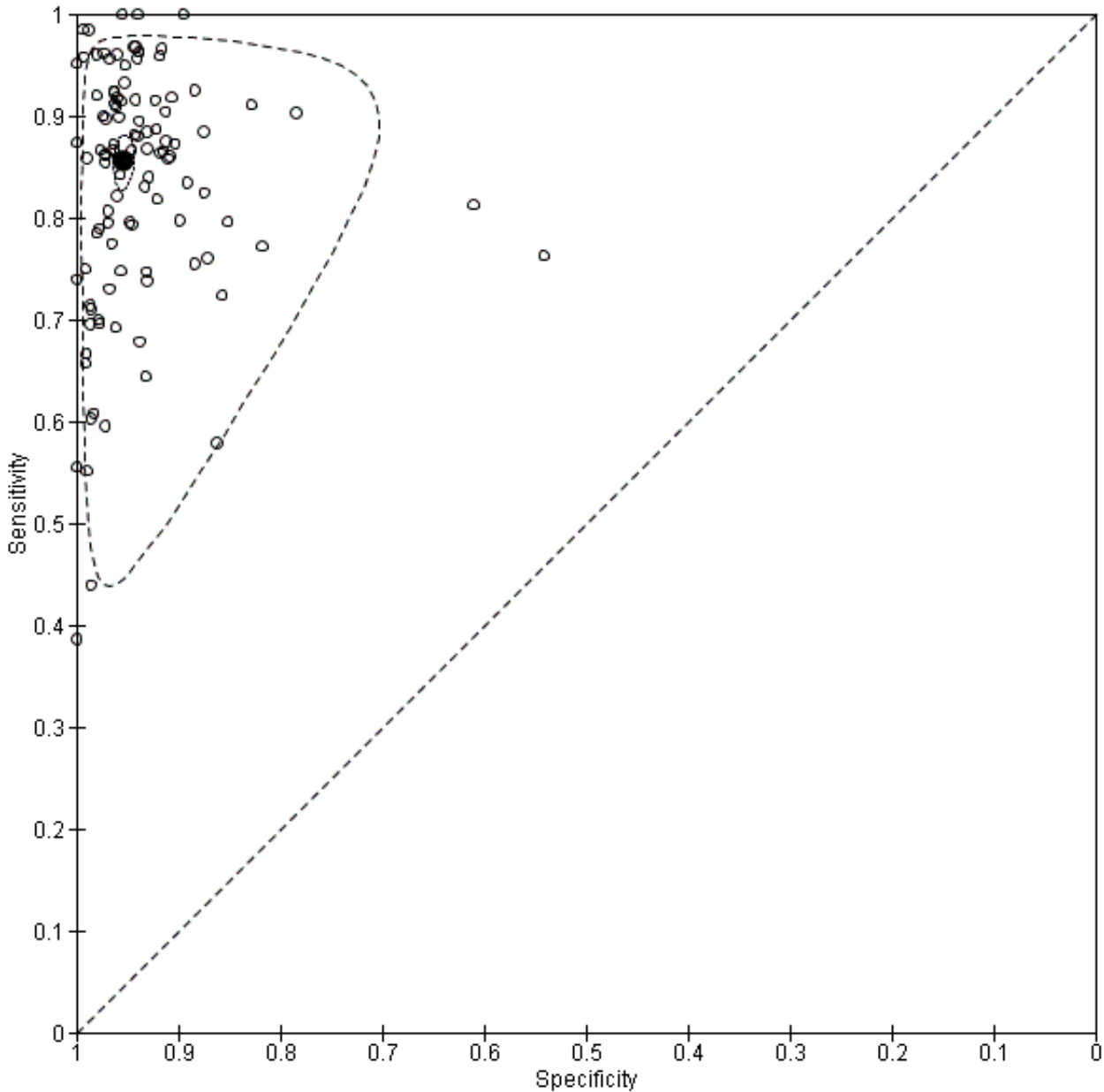


Summary estimates of sensitivity and specificity

Amongst 105 test evaluations included in the meta-analysis (58,244 participants), the summary estimates of sensitivity and specificity

were 85.6%; 95% confidence interval (CI) 83.3 to 87.6; and 95.4%; 95% CI 94.5 to 96.2, respectively (Figure 5). There was no statistical evidence of a correlation between sensitivity and specificity (correlation coefficient -0.17; 95% CI -0.39 to 0.07).

Figure 5. Summary ROC plot of RADT sensitivity and specificity for GAS detection (n = 105). Each individual study cohort is represented by an empty circle. The filled circle is the pooled summary estimate for sensitivity and specificity. The solid curve represents the 95% confidence region around the summary estimate; the dashed curve represents the 95% prediction region.

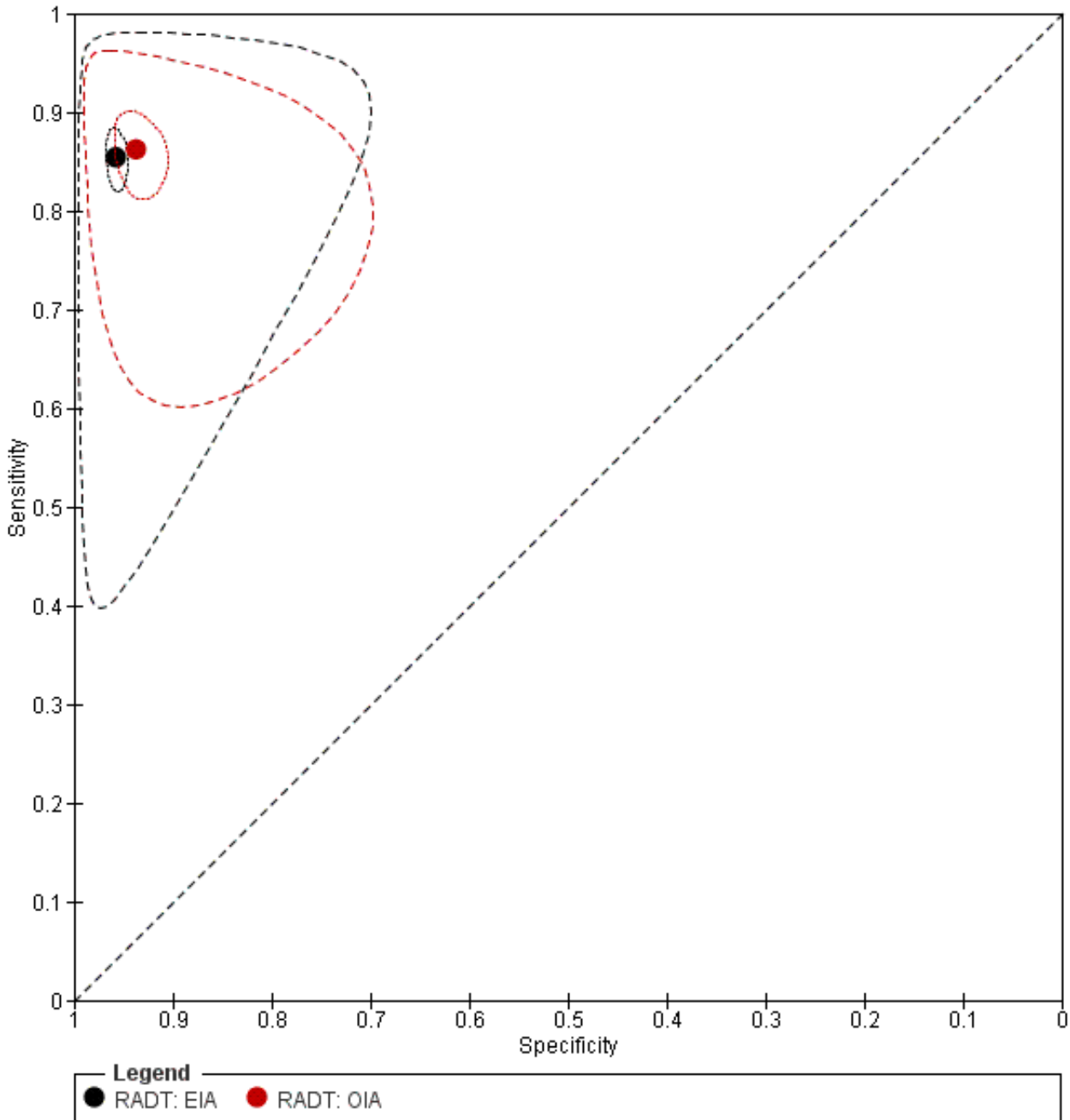


Enzyme immunoassay (EIA) tests

We included 86 evaluations of EIA RADTs (48,808 participants). The median sample size was 263 (IQR 178 to 454) and the median prevalence of group A streptococcus (GAS) on throat culture was

29.5% (IQR 23.8% to 34.9%). Sensitivity of EIA RADTs ranged from 38.6% to 100%, and specificity from 54.1% to 100%. The summary estimates of sensitivity and specificity for EIA tests were 85.4% (82.7 to 87.8) and 95.8% (94.8 to 96.6), respectively (Figure 6).

Figure 6. Summary ROC plot of RADT sensitivity and specificity for GAS detection: EIA (n = 86) versus OIA (n = 19). The filled black circle is the pooled summary estimate for sensitivity and specificity of EIA tests; the filled red circle is the pooled summary estimate for sensitivity and specificity of OIA tests. The solid curves represent the 95% confidence region around the summary estimate; the dashed curves represent the 95% prediction region.



Optical immunoassay (OIA) tests

We included 19 evaluations of OIA RADTs (9436 participants). The median sample size was 302 (IQR 233 to 519), and the median prevalence of GAS on throat culture was 29.5% (IQR 23.7% to 36.4%). Sensitivity of OIA RADTs ranged from 72.4% to 96.7%, specificity from 61.0% to 97.1%. The summary estimates of

sensitivity and specificity for OIA tests were 86.2% (82.7 to 89.2) and 93.7% (91.5 to 95.4), respectively (Figure 6).

Investigations of heterogeneity

Visual inspection of the forests plots and ROC space suggested substantial heterogeneity in accuracy estimates, especially amongst estimates of sensitivity, as reflected by the wide prediction

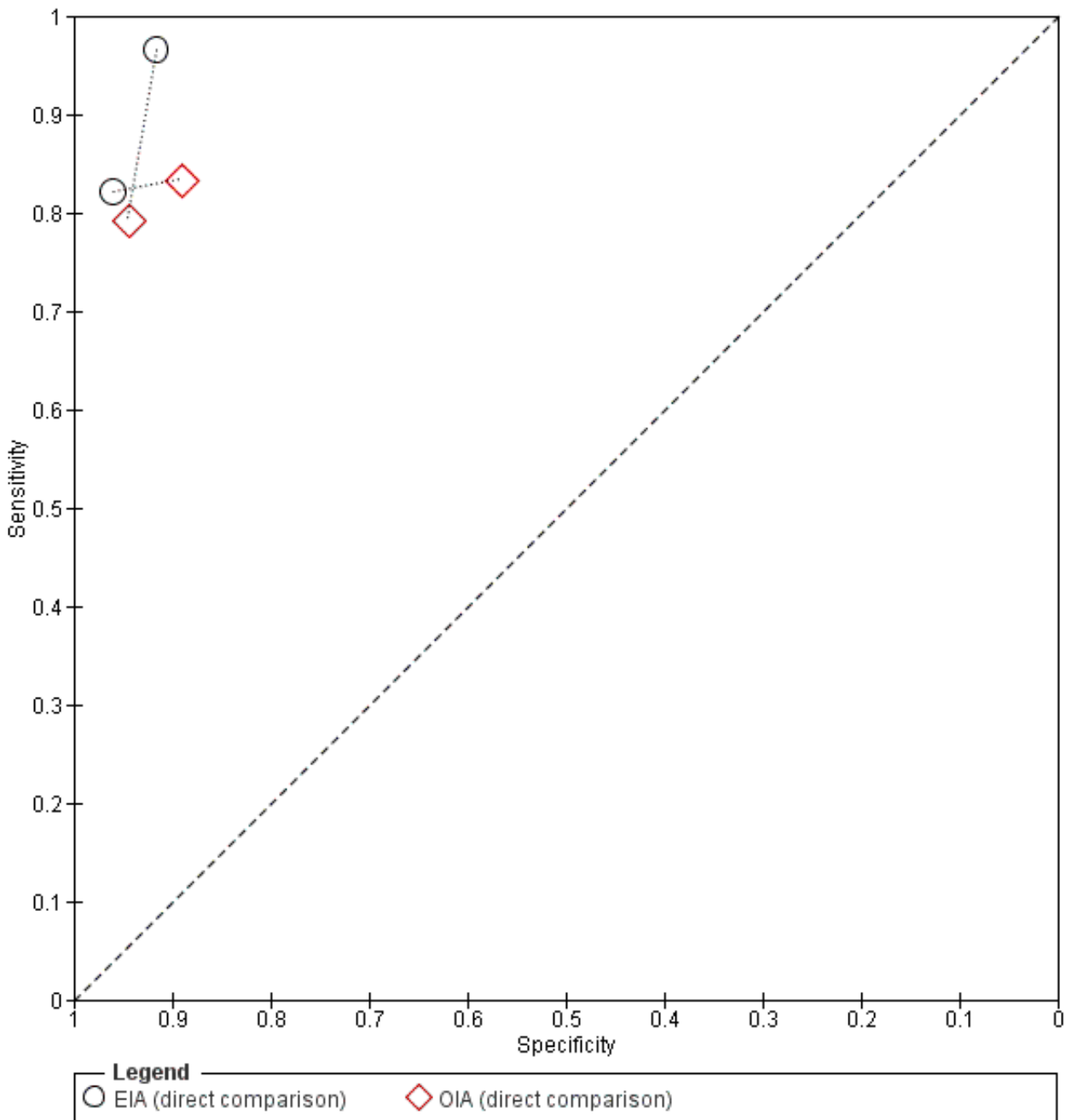
areas around summary estimates. The results of investigations of heterogeneity are summarised in [Table 3](#).

a. Effect of test type

There were 86 evaluations of EIA tests (48,808 participants) and 19 evaluations of OIA tests (9436 participants). Based on analysis of all available data, there was no statistical evidence that sensitivity and/or specificity differed between EIA and OIA tests (sensitivity 85.4% versus 86.2%, respectively; specificity 95.8% versus 93.7%, respectively; change in model deviance = 2.90; P value = 0.23) ([Figure 6](#)).

Two studies directly compared EIA to OIA tests by applying both tests to each individual (802 participants; [Figure 7](#)) ([Giesekeker 2002a](#); [Roe 1995a](#)); data were too limited to perform additional statistical analysis. In [Giesekeker 2002a](#), EIA and OIA tests had comparable specificity (92% (87 to 95) versus 95% (91 to 97), respectively), and the EIA test had the highest sensitivity (97% (90 to 99) versus 79% (69 to 87), respectively). Contrarily, [Roe 1995a](#) found that EIA and OIA tests had comparable sensitivity (82% (75 to 88) versus 83% (77 to 89), respectively), with the specificity of EIA being higher than that of the OIA test under evaluation (96% (93 to 98) versus 89% (85 to 92)).

Figure 7. Summary ROC plot of RADT sensitivity and specificity for GAS detection: direct comparison of EIA versus OIA (n = 2). Each individual study cohort is represented by an empty black circle (EIA) and an empty red diamond (OIA), connected by a dotted line.



b. Effect of the reference standard

An enrichment broth was used before plating in 10 test evaluations; this was not done in 88 study cohorts, and the information was unclear for seven. Using an enrichment broth before plating was not associated with significantly different estimates of sensitivity and/or specificity (sensitivity 86.3% versus 85.5%, respectively; specificity 92.7% versus 95.6%, respectively; change in model deviance = 3.79; P value = 0.15).

c. Effect of age

Twenty-nine studies reported the mean age of participants. The median of the mean age of participants was 6.6 years (IQR 5.8 to 7.4). Mean age was not associated with significantly different estimates of sensitivity and/or specificity (sensitivity 87.1% versus 83.7%, respectively; specificity 93.2% versus 95.0%, respectively; change in model deviance = 1.87; P value = 0.39).

d. Effect of disease severity

Twelve studies assessed clinical severity using the Mclsaac score. The median proportion of severe patients (patients with a Mclsaac score greater than two) was 85% (IQR 63% to 91%). The proportion of severe patients was below 70% in four study cohorts. Meta-regression did not show evidence of significant associations between clinical severity and sensitivity and/or specificity (change in model deviance = 2.10; P value = 0.35).

e. Effect of GAS prevalence

Based on the proportion of throat culture results positive for GAS, the median prevalence of participants with streptococcal pharyngitis was 29.5% (IQR 23.8% to 34.9%). There was no significant effect of GAS prevalence on sensitivity and/or specificity when GAS prevalence was tested as a covariate in the bivariate model (change in model deviance = 0.71; P value = 0.70).

Sensitivity analysis

Compared with the overall results (summary sensitivity 85.6%), sensitivity was lower in the 20 studies at low risk of bias for the reference standard (81.0%), higher in the 33 studies with low concerns about applicability in the index test domain (89.1%), but stable in the 20 studies at low risk of bias in at least three QUADAS-2 domains (84.0%) (Table 4). Summary estimates of specificity were robust across subgroups, at around 95%.

Additional analysis

We excluded 10 studies from the main meta-analysis of sensitivity and specificity estimates because RADT results were selectively verified by throat culture only in RADT negative participants (partial verification); four were very large studies (more than 3000 participants) (Ayanruoh 2009; Mayes 2001a; Mirza 2007a; Mlejnek 2014). We performed a meta-analysis of the negative predictive value of RADTs, including those 10 additional studies. Across 115 test evaluations, the median prevalence of participants with streptococcal pharyngitis was 29.4%. Negative predictive value ranged from 70.2% to 100%; the summary estimate of negative predictive value was 93.9% (93.1 to 94.6).

DISCUSSION

Summary of main results

In this systematic review, we included 116 cohorts (98 unique studies; 101,121 participants) that evaluated rapid antigen detection tests (RADTs) for the detection of group A streptococcus (GAS) in children with pharyngitis. The overall methodological quality of included studies was poor. Across 105 study cohorts (58,244 participants) in which all participants underwent both RADT and throat culture, the summary estimates of sensitivity and specificity were 85.6% (83.3 to 87.6) and 95.4% (94.5 to 96.2), respectively. There were substantial variations in sensitivity across studies, but specificity was more stable; there was no statistical evidence of a trade-off between sensitivity and specificity. Heterogeneity in accuracy was not explained by study-level characteristics such as test type (enzyme immunoassay (EIA) versus optical immunoassay (OIA)), use of an enrichment broth before plating, mean age and clinical severity of participants, and GAS prevalence. Summary estimates of sensitivity and specificity were stable in low risk of bias studies (84.0% and 95.0%, respectively). Across 115 test evaluations in which all negative RADT results were

verified by throat culture, the negative predictive value of RADT was 93.9% (93.1 to 94.6).

Summary of findings

The [Summary of findings 1](#) summarises the findings of the review by applying the results to a hypothetical cohort of 1000 children with pharyngitis, considering three scenarios where GAS prevalence varies from 20% to 40%. The consequence of a false negative result is that the patient may not receive antibiotic treatment, and thus may experience symptoms for a longer period and be at higher risk of developing non-suppurative and suppurative complications of GAS infection (Spinks 2013). The consequence of a false positive result is that the patient may receive unnecessary antibiotics, which could result in adverse reactions and unwilling exposure to antibiotic-resistant bacteria.

Comparison with previous findings

Our findings are in line with those from three published systematic reviews about the accuracy of RADTs for the diagnosis of streptococcal pharyngitis (Table 5) (Lean 2014; Ruiz-Aragon 2010; Stewart 2014). Summary estimates of sensitivity and specificity were comparable across reviews, at around 85% and 95%, respectively.

Strengths and weaknesses of the review

We believe this dataset constitutes a fair representation of diagnostic accuracy studies evaluating RADTs in children with pharyngitis. However, it is known that studies of diagnostic test accuracy tend to be poorly indexed in electronic databases and we may therefore have missed some eligible studies. Moreover, we used an extensive literature search but we did not look systematically in conference abstracts, whereas it has been estimated that at least one-fourth of abstracts of diagnostic accuracy studies presented at conferences are not published (Brazzelli 2009). Thirty-eight studies did not differentiate between adults and children and so whilst they were identified, eligible subsets of data could not be included in the review.

The overall methodological quality of studies included in the review was poor, with less than one-fifth (17%) of studies being judged at low risk of bias for at least three of four QUADAS-2 domains, and half (50%) of estimates of diagnostic accuracy obtained from unselected groups of children presenting with signs and symptoms of pharyngitis. Poor quality mainly arose from high risk of selection bias and high risk of bias in the reference standard used (in 73% and 43% of test evaluations, respectively). Poor study reporting frequently impeded quality appraisal. Whether or not participants formed a consecutive or random series was reported in only 29% of cases, inclusion criteria in 46%, and whether readers of the reference standard were blinded to the result of the rapid test in 28%. We used QUADAS-2 to assess the quality of included studies but did not use GRADE to rate the overall quality of the body of evidence; we will undertake GRADE assessment in future updates of this review.

We included sufficient numbers of studies and participants to obtain precise summary estimates. However, we were not able to identify sources of heterogeneity in accuracy through meta-regression. It is known that sensitivity of RADTs is likely to vary across patient subgroups within a study; several studies, for example, found evidence of increasing sensitivity with increasing

Centor or McIsaac scores (Cohen 2012; Edmonson 2005; Hall 2004; Tanz 2009). Due to aggregation bias, relationships across studies may not reflect relationships within studies; the relationship between accuracy and patient characteristics such as age and disease severity may be adequately estimated only using individual patient data; we strongly recommend such a future work. We dichotomised variables such as age and clinical severity when investigating heterogeneity, mostly because we lack routines for bivariate meta-regression with continuous variables in Stata, but this may be at the cost of loss of information and statistical power. Study setting could also be a relevant source of heterogeneity to explore in future trials.

Other well described sources of variability in RADT sensitivity could not be explored in this review. For example, several studies reported increasing sensitivity with increasing amount of GAS found on culture (Cohen 2012; Kuhn 1999; Kurtz 2000), but we could not evaluate and compare such effects across studies because of the absence of any standard method to measure bacterial inoculum size. Also the level of expertise of the person performing the throat sample seems to affect the sensitivity of RADTs; several studies have shown improvement in sensitivity following dedicated training sessions (Fox 2006; Toepfner 2013).

The analysis was carried out at the test evaluation level, therefore some studies were included more than once in the meta-analysis. This means that the summary estimates are partially based on duplicate use of individuals. This is likely to have introduced bias. However, we anticipate that the implications are rather marginal because such studies represent only a minority when compared to the total number of included studies (11 out of 98).

Applicability of findings to the review question

Included studies came from a variety of countries ($n = 25$) and ambulatory care settings (private offices, walk-in clinics, emergency departments). However, only half of studies avoided clinical selection of participants; investigators often used clinical criteria, such as McIsaac's, as inclusion criteria. Thus, the included studies may provide a distorted reflection of the diagnostic performance of RADT in unselected children with pharyngitis seen in ambulatory care. From the 41 studies judged at low risk of applicability concerns for patient selection, the summary estimate of sensitivity was slightly lower than the overall estimate (83.1% versus 85.6%, respectively).

We evaluated 42 different commercial kits in this review. All of them are binary tests giving either a positive or negative result, but the different commercial kits may not share a common positivity threshold (Charlier-Bret 2004; Lasseter 2009). The absence of evidence for a significant correlation between sensitivity and specificity suggests that threshold effects may be negligible when evaluating the accuracy of RADTs. Recently, molecular rapid tests relying on DNA probes, polymerase chain reaction (PCR) and fluorescence in situ methods have been commercialised (Chapin 2002; Ding 2011; Slinger 2011). Their accuracy seems promising but they have rarely been evaluated in children and require specialised equipment and personnel.

Amongst 105 test evaluations included in the meta-analysis of sensitivity and specificity estimates, we judged about one-third (31%) to be of low concern regarding applicability in the index test domain because the RADT was processed and interpreted

during consultation time. In this subgroup of studies, the summary estimate of sensitivity was higher than that from the overall analysis (89.1% versus 85.6%, respectively).

An appropriate reference standard (laboratory throat culture on a blood agar plate during 48 hours) was used in about two-thirds (62%) of test evaluations. An enrichment broth was used to improve recovery of GAS on culture in 10% of test evaluations; this did not have any effect on RADT sensitivity on meta-regression.

AUTHORS' CONCLUSIONS

Implications for practice

The high specificity of rapid antigen detection tests (RADTs) implies that positive results may not require throat culture confirmation and could be used as a basis to prescribe antibiotics in children with pharyngitis. On average, RADT sensitivity and negative predictive value were 85.6% and 93.9%, respectively. Whether such performances are sufficient to use RADTs without backup culture of RADT negative results depends mainly on the epidemiological context. This includes the prevalence of group A streptococcus (GAS) pharyngitis, the rate of asymptomatic GAS carriage and the incidence of GAS complications such as acute rheumatic fever and quinsy. Clinicians and guideline developers should also take into account other elements that were beyond the scope of this review, such as effectiveness of antibiotics to prevent complications of GAS infection, accessibility of diagnostic tests, cost-effectiveness and patient preferences. Our findings challenge the common view that optical immunoassay (OIA) tests may perform better than enzyme immunoassay (EIA) tests (AAP 2012; Gerber 2004).

Implications for research

Further research should aim to define the minimal sensitivity that RADTs should achieve before such diagnostic tests would be accepted as stand-alone tests in replacement of throat culture. This could be done by inviting a panel of experts or through simulation of patient outcomes. We also need to obtain consensus on which is the most appropriate reference standard to diagnose GAS pharyngitis in children. It remains controversial whether or not throat cultures yielding low GAS colony counts (less than 10 per plate) reflect true GAS infection or GAS carriage. Similarly, weakly positive results on molecular tests such as polymerase chain reaction (PCR) assays may reflect GAS carriage rather than true GAS infection.

Future accuracy studies should include more direct comparisons between different kits and types of RADTs. The best study design might be to randomise participants rather than to compare the accuracy of different tests in the same participants. Indeed, if a unique swab is used to perform two rapid tests, it is likely that the bacterial inoculum available for the second test will be insufficient to give a positive result. Thus, the first rapid test will look more sensitive than the second. Future diagnostic accuracy studies of RADTs should be reported according to the STARD reporting guideline to enhance data extraction and critical appraisal (Bossuyt 2003; Bossuyt 2015).

Beyond accuracy, further research is required to assess the impact of implementing RADTs on antibiotic prescribing and patient outcomes (Llor 2011). We need more test-and-treat randomised trials to evaluate whether rapid testing and/or antibiotics are beneficial to patients. Accuracy is only a proxy for more important

outcomes such as pharyngitis-related morbidity (e.g., quinsy, acute rheumatic fever, rheumatic heart disease) and mortality.

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* Indicates the major publication for the study

CHARACTERISTICS OF STUDIES
Characteristics of included studies [ordered by study ID]

Al-Najjar 2008
Study characteristics

Patient sampling	Cross-sectional study Prospective design Sample: unclear Direct comparison of different RADTs: no Direct comparison of several throat culture techniques: no Person performing the throat sample: unclear Exclusion if recent antibiotics use before inclusion: yes (exclusion if antibiotics during the preceding week) Clinical selection of patients: explicit criteria but not a score Presenting signs and symptoms: fever, acute catarrh and acutely inflamed throat/tonsils with or without exudates Age range for inclusion: not reported ("children")
Patient characteristics and setting	Sample size: 505 (but the contingency table includes 496 participants) Age (distribution): 81% under 5 years of age (mean or median not reported) GAS prevalence according to culture (with 95% confidence interval): 14.1% (95% CI not reported) Country of study: United Arab Emirates Sex (% of girls): 45% Clinical severity assessment: none Clinical setting: walk-in clinics Multi-centre study
Index tests	Throat swab: 1 double swab Commercial name of the RADT: Diaquick Strep A Test (Dialab) Type of RADT: EIA
Target condition and reference standard(s)	Throat culture medium: not reported Atmosphere of incubation: not reported Duration of incubation: not reported GAS confirmation: not reported Number of plates inoculated: not reported Assessment of GAS antibody response: no Relevant details: throat culture technique not described
Flow and timing	No follow-up
Comparative	
Type of study	Journal article

Al-Najjar 2008 (Continued)

Notes -

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient Selection			
Was a consecutive or random sample of patients enrolled?	Unclear		
Was it a cross-sectional study or a RCT?	Yes		
Were selection criteria clearly described (at least presenting signs and symptoms and age limits for inclusion)?	No		
Was clinical selection of patients avoided?	No		
Were patients seen in an ambulatory care setting?	Yes		
		High	High
DOMAIN 2: Index Test All tests			
Were the RADT results interpreted with blinding of the results of culture?	Unclear		
Was the type of the RADT mentioned (EIA or OIA)?	Yes		
Were RADTs conducted during consultation time?	Unclear		
		Unclear	Unclear
DOMAIN 3: Reference Standard			
Were culture results interpreted with blinding of the results of the RADT?	Unclear		
Is the throat culture method likely to correctly identify GAS (laboratory culture on a blood agar plate during 48 hr)?	Unclear		
Were the culture medium, atmosphere, duration of incubation and GAS-confirmation technique described?	No		
		Unclear	Unclear
DOMAIN 4: Flow and Timing			
Was the delay between the performance of the RADT and throat culture plating less than 48 hours?	Unclear		
Did all patients receive a throat culture?	Yes		
Did patients receive the same throat culture method?	Unclear		

Al-Najjar 2008 (Continued)

Were undetermined/uninterpretable results reported? No

Were withdrawals from the study explained? No

Unclear

Alper 2013
Study characteristics

Patient sampling	<p>Cross-sectional study Prospective design Sample: unclear Direct comparison of different RADTs: no Direct comparison of several throat culture techniques: no Person performing the throat sample: unclear</p> <p>Exclusion if recent antibiotics use before inclusion: yes (within 3 days before inclusion)</p> <p>Clinical selection of patients: none</p> <p>Presenting signs and symptoms: patients with a chief complaint of sore throat</p> <p>Age range for inclusion: 7 to 15 years</p>
Patient characteristics and setting	<p>Sample size: 114 Age (distribution): mean (SD) = 10.0 (0.24) years</p> <p>GAS prevalence according to culture (with 95% confidence interval): 16.7% (95% CI not reported) Country of study: Turkey Sex (% of girls): not reported Clinical severity assessment: Centor score Clinical setting: walk-in clinic (family practice centre) Single-centre study</p>
Index tests	<p>Throat swab: unclear</p> <p>Commercial name of the RADT: only the name of the manufacturer was reported (Meridian Bioscience) Type of RADT: EIA</p>
Target condition and reference standard(s)	<p>Throat culture medium: standard Atmosphere of incubation: not reported Duration of incubation: 48 hours GAS confirmation: bacitracin disk Number of plates inoculated: not reported Assessment of GAS antibody response: no Relevant details: -</p>
Flow and timing	No follow-up
Comparative	
Type of study	Journal article

Alper 2013 (Continued)

Notes

Supported by academic funding (Uludag University Scientific Research Projects)

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient Selection			
Was a consecutive or random sample of patients enrolled?	Unclear		
Was it a cross-sectional study or a RCT?	Yes		
Were selection criteria clearly described (at least presenting signs and symptoms and age limits for inclusion)?	Yes		
Was clinical selection of patients avoided?	Yes		
Were patients seen in an ambulatory care setting?	Yes		
		Low	Low
DOMAIN 2: Index Test All tests			
Were the RADT results interpreted with blinding of the results of culture?	Unclear		
Was the type of the RADT mentioned (EIA or OIA)?	Yes		
Were RADTs conducted during consultation time?	No		
		Unclear	High
DOMAIN 3: Reference Standard			
Were culture results interpreted with blinding of the results of the RADT?	Unclear		
Is the throat culture method likely to correctly identify GAS (laboratory culture on a blood agar plate during 48 hr)?	Yes		
Were the culture medium, atmosphere, duration of incubation and GAS-confirmation technique described?	No		
		High	High
DOMAIN 4: Flow and Timing			
Was the delay between the performance of the RADT and throat culture plating less than 48 hours?	Unclear		
Did all patients receive a throat culture?	Yes		
Did patients receive the same throat culture method?	Yes		

Alper 2013 (Continued)

Were undetermined/uninterpretable results reported?	No
Were withdrawals from the study explained?	Yes
Low	

Altun 2015
Study characteristics

Patient sampling	Cross-sectional study Retrospective design Sample: non-consecutive Direct comparison of different RADTs: no Direct comparison of several throat culture techniques: no Person performing the throat sample: not reported Exclusion if recent antibiotics use before inclusion: no Clinical selection of patients: explicit criteria but not a score Presenting signs and symptoms: clinical exudative tonsillopharyngitis Age range for inclusion: 0 to 18 years
Patient characteristics and setting	Sample size: 1243 Age (distribution): mean (SD) = 5.5 (3.1) years GAS prevalence according to culture (with 95% confidence interval): 24.7% (95% CI not reported) Country of study: Turkey Sex (% of girls): 48.5% Clinical severity assessment: none Clinical setting: paediatric outpatient clinic Single-centre study
Index tests	Throat swab: 2 different swabs Commercial name of the RADT: Strep A Abon kit Type of RADT: EIA
Target condition and reference standard(s)	Throat culture medium: standard Atmosphere of incubation: not reported Duration of incubation: < 24 hours GAS confirmation: bacitracin disk Number of plates inoculated: 1 Assessment of GAS antibody response: no Relevant details: -
Flow and timing	No follow-up
Comparative	
Type of study	Journal article
Notes	—

Altun 2015 (Continued)

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient Selection			
Was a consecutive or random sample of patients enrolled?	No		
Was it a cross-sectional study or a RCT?	Yes		
Were selection criteria clearly described (at least presenting signs and symptoms and age limits for inclusion)?	Yes		
Was clinical selection of patients avoided?	No		
Were patients seen in an ambulatory care setting?	Yes		
		High	High
DOMAIN 2: Index Test All tests			
Were the RADT results interpreted with blinding of the results of culture?	Yes		
Was the type of the RADT mentioned (EIA or OIA)?	Yes		
Were RADTs conducted during consultation time?	No		
		High	High
DOMAIN 3: Reference Standard			
Were culture results interpreted with blinding of the results of the RADT?	Unclear		
Is the throat culture method likely to correctly identify GAS (laboratory culture on a blood agar plate during 48 hr)?	No		
Were the culture medium, atmosphere, duration of incubation and GAS-confirmation technique described?	No		
		High	High
DOMAIN 4: Flow and Timing			
Was the delay between the performance of the RADT and throat culture plating less than 48 hours?	Unclear		
Did all patients receive a throat culture?	Yes		
Did patients receive the same throat culture method?	Yes		
Were undetermined/uninterpretable results reported?	Yes		
Were withdrawals from the study explained?	Yes		

Altun 2015 (Continued)

Low

Arribas Blanco 1988
Study characteristics

Patient sampling	<p>Cross-sectional study Prospective design Sample: consecutive Direct comparison of different RADTs: no Direct comparison of several throat culture techniques: no Person performing the throat sample: physician (most of the time) or nurse (sometimes)</p> <p>Exclusion if recent antibiotics use before inclusion: no</p> <p>Clinical selection of patients: none</p> <p>Presenting signs and symptoms: acute pharyngo-tonsillitis</p> <p>Age range for inclusion: < 21 years</p>
Patient characteristics and setting	<p>Sample size: 240 Age (distribution): not reported</p> <p>GAS prevalence according to culture (with 95% confidence interval): 18.9% (95% CI not reported) Country of study: Spain Sex (% of girls): not reported Clinical severity assessment: none Clinical setting: walk-in clinic Single-centre study</p>
Index tests	<p>Throat swab: 2 different swabs</p> <p>Commercial name of the RADT: TestPack Strep A (Abbott) Type of RADT: EIA</p>
Target condition and reference standard(s)	<p>Throat culture medium: standard Atmosphere of incubation: aerobic Duration of incubation: 48 hours GAS confirmation: bacitracin disk Number of plates inoculated: not reported Assessment of GAS antibody response: no Relevant details: -</p>
Flow and timing	No follow-up
Comparative	
Type of study	Journal article (in Spanish)
Notes	We thank Dr JM Arribas Blanco for sharing unpublished paediatric data

Methodological quality

Arribas Blanco 1988 (Continued)

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient Selection			
Was a consecutive or random sample of patients enrolled?	Yes		
Was it a cross-sectional study or a RCT?	Yes		
Were selection criteria clearly described (at least presenting signs and symptoms and age limits for inclusion)?	Yes		
Was clinical selection of patients avoided?	Yes		
Were patients seen in an ambulatory care setting?	Yes		
		Low	Low
DOMAIN 2: Index Test All tests			
Were the RADT results interpreted with blinding of the results of culture?	Yes		
Was the type of the RADT mentioned (EIA or OIA)?	Yes		
Were RADTs conducted during consultation time?	Yes		
		Low	Low
DOMAIN 3: Reference Standard			
Were culture results interpreted with blinding of the results of the RADT?	Unclear		
Is the throat culture method likely to correctly identify GAS (laboratory culture on a blood agar plate during 48 hr)?	Yes		
Were the culture medium, atmosphere, duration of incubation and GAS-confirmation technique described?	Yes		
		Unclear	Low
DOMAIN 4: Flow and Timing			
Was the delay between the performance of the RADT and throat culture plating less than 48 hours?	Unclear		
Did all patients receive a throat culture?	Yes		
Did patients receive the same throat culture method?	Yes		
Were undetermined/uninterpretable results reported?	No		
Were withdrawals from the study explained?	Yes		
		Low	

Attia 2001
Study characteristics

Patient sampling	<p>Cross-sectional study Prospective design Sample: unclear Direct comparison of different RADTs: no Direct comparison of several throat culture techniques: no Person performing the throat sample: physicians</p> <p>Exclusion if recent antibiotics use before inclusion: yes (within 5 days of enrollment)</p> <p>Clinical selection of patients: none</p> <p>Presenting signs and symptoms: patients with signs and symptoms of acute pharyngitis</p> <p>Age range for inclusion: 1 to 18 years</p>		
Patient characteristics and setting	<p>Sample size: 587 Age (distribution): mean (SD) = 6.7 (3.9) years</p> <p>GAS prevalence according to culture (with 95% confidence interval): 37.1% (95% CI not reported) Country of study: USA Sex (% of girls): 51% Clinical severity assessment: other (Attia score) Clinical setting: mixed (paediatric emergency department and 2 paediatric outpatient clinics) Multi-centre study</p>		
Index tests	<p>Throat swab: 2 different swabs (1 swab for culture, 1 swab for the RADT)</p> <p>Commercial name of the RADT: TestPack Plus (Abbott) Type of RADT: EIA</p>		
Target condition and reference standard(s)	<p>Throat culture medium: inhibitory Atmosphere of incubation: aerobic with CO₂ enrichment Duration of incubation: 48 hours GAS confirmation: latex test Number of plates inoculated: 2 Assessment of GAS antibody response: no Relevant details: -</p>		
Flow and timing	No follow-up		
Comparative			
Type of study	Journal article		
Notes	Funded by a grant from the Nemours Research Programmes		
Methodological quality			
Item	Authors' judgement	Risk of bias	Applicability concerns

Attia 2001 (Continued)

DOMAIN 1: Patient Selection

Was a consecutive or random sample of patients enrolled?	Unclear		
Was it a cross-sectional study or a RCT?	Yes		
Were selection criteria clearly described (at least presenting signs and symptoms and age limits for inclusion)?	Yes		
Was clinical selection of patients avoided?	Yes		
Were patients seen in an ambulatory care setting?	Yes		
		Low	Low

DOMAIN 2: Index Test All tests

Were the RADT results interpreted with blinding of the results of culture?	Unclear		
Was the type of the RADT mentioned (EIA or OIA)?	Yes		
Were RADTs conducted during consultation time?	No		
		Unclear	High

DOMAIN 3: Reference Standard

Were culture results interpreted with blinding of the results of the RADT?	Unclear		
Is the throat culture method likely to correctly identify GAS (laboratory culture on a blood agar plate during 48 hr)?	Yes		
Were the culture medium, atmosphere, duration of incubation and GAS-confirmation technique described?	Yes		
		Unclear	Low

DOMAIN 4: Flow and Timing

Was the delay between the performance of the RADT and throat culture plating less than 48 hours?	Unclear		
Did all patients receive a throat culture?	Yes		
Did patients receive the same throat culture method?	Yes		
Were undetermined/uninterpretable results reported?	No		
Were withdrawals from the study explained?	Yes		
		Low	

Ayanruoh 2009
Study characteristics

Patient sampling	<p>Cross-sectional study Retrospective design Sample: consecutive Direct comparison of different RADTs: no Direct comparison of several throat culture techniques: no Person performing the throat sample: physicians</p> <p>Exclusion if recent antibiotics use before inclusion: yes (within 14 days of presentation)</p> <p>Clinical selection of patients: none</p> <p>Presenting signs and symptoms: patients with clinical signs of pharyngitis</p> <p>Age range for inclusion: 3 to 18 years</p>
Patient characteristics and setting	<p>Sample size: 6557 Age (distribution): not reported</p> <p>GAS prevalence according to culture (with 95% confidence interval): 22.5% (95% CI not reported) Country of study: USA Sex (% of girls): not reported Clinical severity assessment: none Clinical setting: emergency department Single-centre study</p>
Index tests	<p>Throat swab: not reported</p> <p>Commercial name of the RADT: only the name of the manufacturer was reported (Sacks Biological Farms) Type of RADT: EIA</p>
Target condition and reference standard(s)	<p>Throat culture medium: standard Atmosphere of incubation: anaerobic Duration of incubation: 48 hours GAS confirmation: latex test Number of plates inoculated: not reported Assessment of GAS antibody response: no Relevant details: -</p>
Flow and timing	No follow-up
Comparative	
Type of study	Journal article
Notes	Throat culture performed only for children with negative RADT results (partial verification)

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
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Ayanruoh 2009 (Continued)

DOMAIN 1: Patient Selection

Was a consecutive or random sample of patients enrolled?	Yes		
Was it a cross-sectional study or a RCT?	Yes		
Were selection criteria clearly described (at least presenting signs and symptoms and age limits for inclusion)?	Yes		
Was clinical selection of patients avoided?	Yes		
Were patients seen in an ambulatory care setting?	Yes		
		Low	Low

DOMAIN 2: Index Test All tests

Were the RADT results interpreted with blinding of the results of culture?	Yes		
Was the type of the RADT mentioned (EIA or OIA)?	Yes		
Were RADTs conducted during consultation time?	Yes		
		Low	Low

DOMAIN 3: Reference Standard

Were culture results interpreted with blinding of the results of the RADT?	No		
Is the throat culture method likely to correctly identify GAS (laboratory culture on a blood agar plate during 48 hr)?	Yes		
Were the culture medium, atmosphere, duration of incubation and GAS-confirmation technique described?	Yes		
		High	Low

DOMAIN 4: Flow and Timing

Was the delay between the performance of the RADT and throat culture plating less than 48 hours?	Unclear		
Did all patients receive a throat culture?	No		
Did patients receive the same throat culture method?	Yes		
Were undetermined/uninterpretable results reported?	No		
Were withdrawals from the study explained?	No		
		High	

Begovac 1993
Study characteristics

Patient sampling	Cross-sectional study Prospective design Sample: unclear Direct comparison of different RADTs: no Direct comparison of several throat culture techniques: no Person performing the throat sample: not reported Exclusion if recent antibiotics use before inclusion: no Clinical selection of patients: none Presenting signs and symptoms: symptoms and signs of pharyngitis Age range for inclusion: not reported
Patient characteristics and setting	Sample size: 389 (age < 15 years = 389, age > 15 years = 115) Age (distribution): mean or median not reported GAS prevalence according to culture (with 95% confidence interval): 31.1% (95% CI not reported) Country of study: Croatia Sex (% of girls): not reported Clinical severity assessment: none Clinical setting: walk-in clinic (outpatient clinic of a University Hospital) Single-centre study
Index tests	Throat swab: 1 double swab Commercial name of the RADT: Venterscreen Strep A Type of RADT: EIA
Target condition and reference standard(s)	Throat culture medium: standard and inhibitory (2 plates) Atmosphere of incubation: aerobic with CO ₂ enrichment Duration of incubation: 48 hours GAS confirmation: latex test Number of plates inoculated: 2 Assessment of GAS antibody response: no Relevant details: -
Flow and timing	No follow-up
Comparative	
Type of study	Journal article
Notes	—

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient Selection			
Was a consecutive or random sample of patients enrolled?	Unclear		

Begovac 1993 *(Continued)*

Was it a cross-sectional study or a RCT?	Yes
Were selection criteria clearly described (at least presenting signs and symptoms and age limits for inclusion)?	No
Was clinical selection of patients avoided?	Yes
Were patients seen in an ambulatory care setting?	Yes

High
Low
DOMAIN 2: Index Test All tests

Were the RADT results interpreted with blinding of the results of culture?	Yes
Was the type of the RADT mentioned (EIA or OIA)?	Yes
Were RADTs conducted during consultation time?	No

Low
High
DOMAIN 3: Reference Standard

Were culture results interpreted with blinding of the results of the RADT?	Yes
Is the throat culture method likely to correctly identify GAS (laboratory culture on a blood agar plate during 48 hr)?	Yes
Were the culture medium, atmosphere, duration of incubation and GAS-confirmation technique described?	Yes

Low
Low
DOMAIN 4: Flow and Timing

Was the delay between the performance of the RADT and throat culture plating less than 48 hours?	Yes
Did all patients receive a throat culture?	Yes
Did patients receive the same throat culture method?	Yes
Were undetermined/uninterpretable results reported?	No
Were withdrawals from the study explained?	Yes

Low
Buchbinder 2007
Study characteristics

Patient sampling	Cross-sectional study
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Buchbinder 2007 (Continued)

	Prospective design Sample: random Direct comparison of different RADTs: no Direct comparison of several throat culture techniques: no Person performing the throat sample: physicians Exclusion if recent antibiotics use before inclusion: yes (time frame not reported) Clinical selection of patients: explicit criteria but not a score (see below) Presenting signs and symptoms: sore throat associated with pharyngeal erythema or exudate and fever Age range for inclusion: not reported ("children")
Patient characteristics and setting	Sample size: 216 Age (distribution): mean (SD) = 4.8 (3.6) years GAS prevalence according to culture (with 95% confidence interval): 26.4% (95% CI not reported) Country of study: France Sex (% of girls): not reported Clinical severity assessment: none Clinical setting: emergency department Single-centre study
Index tests	Throat swab: 2 different swabs (1 swab for culture, 1 swab for the RADT) Commercial name of the RADT: IM Strep A (International Microbio) Type of RADT: EIA
Target condition and reference standard(s)	Throat culture medium: standard (no details) Atmosphere of incubation: not reported Duration of incubation: not reported GAS confirmation: not reported Number of plates inoculated (n): not reported Assessment of GAS antibody response: no Relevant details: -
Flow and timing	No follow-up
Comparative	
Type of study	Journal article (in French)
Notes	—

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient Selection			
Was a consecutive or random sample of patients enrolled?	Yes		
Was it a cross-sectional study or a RCT?	Yes		

Buchbinder 2007 *(Continued)*

Were selection criteria clearly described (at least presenting signs and symptoms and age limits for inclusion)?	No		
Was clinical selection of patients avoided?	No		
Were patients seen in an ambulatory care setting?	Yes		
		High	High

DOMAIN 2: Index Test All tests

Were the RADT results interpreted with blinding of the results of culture?	Yes		
Was the type of the RADT mentioned (EIA or OIA)?	Yes		
Were RADTs conducted during consultation time?	Yes		
		Low	Low

DOMAIN 3: Reference Standard

Were culture results interpreted with blinding of the results of the RADT?	No		
Is the throat culture method likely to correctly identify GAS (laboratory culture on a blood agar plate during 48 hr)?	Unclear		
Were the culture medium, atmosphere, duration of incubation and GAS-confirmation technique described?	No		
		High	High

DOMAIN 4: Flow and Timing

Was the delay between the performance of the RADT and throat culture plating less than 48 hours?	Unclear		
Did all patients receive a throat culture?	Yes		
Did patients receive the same throat culture method?	Yes		
Were undetermined/uninterpretable results reported?	No		
Were withdrawals from the study explained?	No		
		Low	

Camurdan 2008
Study characteristics

Patient sampling	Cross-sectional study Prospective design
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Rapid antigen detection test for group A streptococcus in children with pharyngitis (Review)

Camurdan 2008 (Continued)

	Sample: unclear Direct comparison of different RADTs: no Direct comparison of several throat culture techniques: no Person performing the throat sample: physician Exclusion if recent antibiotics use before inclusion: no Clinical selection of patients: none Presenting signs and symptoms: signs and symptoms of acute upper respiratory tract infections Age range for inclusion: not reported ("children")
Patient characteristics and setting	Sample size: 1248 Age (distribution): mean (SD) = 6.3 (3.6) years GAS prevalence according to culture (with 95% confidence interval): 38.1% (95% CI not reported) Country of study: Turkey Sex (% of girls): 48% Clinical severity assessment: none Clinical setting: walk-in clinic Single-centre study
Index tests	Throat swab (1 single, 1 double, 2 different): unclear Commercial name of the RADT: Strep A Test II (Intex Diagnostica) Type of RADT: EIA
Target condition and reference standard(s)	Throat culture medium: standard Atmosphere of incubation: aerobic with CO ₂ enrichment Duration of incubation: 24 hours GAS confirmation: latex test Number of plates inoculated: not reported Assessment of GAS antibody response: no Relevant details: -
Flow and timing	No follow-up
Comparative	
Type of study	Journal article
Notes	—

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient Selection			
Was a consecutive or random sample of patients enrolled?	Unclear		
Was it a cross-sectional study or a RCT?	Yes		
Were selection criteria clearly described (at least presenting signs and symptoms and age limits for inclusion)?	No		

Camurdan 2008 *(Continued)*

Was clinical selection of patients avoided?	Yes		
Were patients seen in an ambulatory care setting?	Yes		
		High	Low
DOMAIN 2: Index Test All tests			
Were the RADT results interpreted with blinding of the results of culture?	Unclear		
Was the type of the RADT mentioned (EIA or OIA)?	Yes		
Were RADTs conducted during consultation time?	Unclear		
		Unclear	Unclear
DOMAIN 3: Reference Standard			
Were culture results interpreted with blinding of the results of the RADT?	Unclear		
Is the throat culture method likely to correctly identify GAS (laboratory culture on a blood agar plate during 48 hr)?	No		
Were the culture medium, atmosphere, duration of incubation and GAS-confirmation technique described?	Yes		
		High	High
DOMAIN 4: Flow and Timing			
Was the delay between the performance of the RADT and throat culture plating less than 48 hours?	Yes		
Did all patients receive a throat culture?	Yes		
Did patients receive the same throat culture method?	Yes		
Were undetermined/uninterpretable results reported?	No		
Were withdrawals from the study explained?	Yes		
		Low	

Chapin 2002
Study characteristics

Patient sampling	Cross-sectional study Prospective design Sample: consecutive Direct comparison of different RADTs: no (comparison of a RADT with a DNA probe test) Direct comparison of several throat culture techniques: no
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Chapin 2002 (Continued)

	Person performing the throat sample: physicians Exclusion if recent antibiotics use before inclusion: no Clinical selection of patients: none Presenting signs and symptoms: symptoms of pharyngitis Age range for inclusion: not reported ("paediatric outpatient clinics")
Patient characteristics and setting	Sample size: 520 Age (distribution): not reported GAS prevalence according to culture (with 95% confidence interval): 33.1% (95% CI not reported) Country of study: USA Sex (% of girls): not reported Clinical severity assessment: none Clinical setting: walk-in clinic ("paediatric outpatient clinics") Multi-centre study
Index tests	Throat swab: 1 double swab (1 swab was used for the RADT, 1 swab for the DNA probe technique, and the pledget was used for culture) Commercial name of the RADT: Strep A OIA (Thermo Biostar) Type of RADT: OIA
Target condition and reference standard(s)	Throat culture medium: enrichment Atmosphere of incubation: anaerobic Duration of incubation: 48 hours GAS confirmation: latex test Number of plates inoculated: 1 Assessment of GAS antibody response: no Relevant details: -
Flow and timing	No follow-up
Comparative	
Type of study	Journal article
Notes	The RADT was compared to a DNA probe technique; such molecular tests are not in the scope of this review. Travel grant support provided by Gen-Probe, manufacturer of the DNA probe assay under evaluation

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient Selection			
Was a consecutive or random sample of patients enrolled?	Yes		
Was it a cross-sectional study or a RCT?	Yes		

Chapin 2002 *(Continued)*

Were selection criteria clearly described (at least presenting signs and symptoms and age limits for inclusion)?	No
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Was clinical selection of patients avoided?	Yes
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Were patients seen in an ambulatory care setting?	Yes
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High
Low
DOMAIN 2: Index Test All tests

Were the RADT results interpreted with blinding of the results of culture?	Yes
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Was the type of the RADT mentioned (EIA or OIA)?	Yes
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Were RADTs conducted during consultation time?	No
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Low
High
DOMAIN 3: Reference Standard

Were culture results interpreted with blinding of the results of the RADT?	Yes
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Is the throat culture method likely to correctly identify GAS (laboratory culture on a blood agar plate during 48 hr)?	Yes
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Were the culture medium, atmosphere, duration of incubation and GAS-confirmation technique described?	Yes
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Low
Low
DOMAIN 4: Flow and Timing

Was the delay between the performance of the RADT and throat culture plating less than 48 hours?	Yes
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Did all patients receive a throat culture?	Yes
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Did patients receive the same throat culture method?	Yes
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Were undetermined/uninterpretable results reported?	No
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Were withdrawals from the study explained?	Yes
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Low
Chiadmi 2004a
Study characteristics
Rapid antigen detection test for group A streptococcus in children with pharyngitis (Review)

Chiadmi 2004a (Continued)

Patient sampling	<p>Cross-sectional study Prospective design Sample: unclear Direct comparison of different RADTs: yes Direct comparison of several throat culture techniques: no Person performing the throat sample: unclear</p> <p>Exclusion if recent antibiotics use before inclusion: yes (within 7 days before inclusion)</p> <p>Clinical selection of patients: explicit criteria but not a score (see below)</p> <p>Presenting signs and symptoms: signs and symptoms of pharyngitis or pharyngo-tonsillitis (fever, sore throat, inflammation of pharynx)</p> <p>Age range for inclusion: 8 to 14 years</p>
Patient characteristics and setting	<p>Sample size: 75 Age (distribution): not reported</p> <p>GAS prevalence according to culture (with 95% confidence interval): 33.3% (95% CI not reported) Country of study: France Sex (% of girls): not reported Clinical severity assessment: none Clinical setting: other ("paediatric consultation") Single-centre study</p>
Index tests	<p>Throat swab (1 single, 1 double, 2 different): unclear</p> <p>Commercial name of the RADT: Test Pack Plus (Abbott) Type of RADT: EIA</p>
Target condition and reference standard(s)	<p>Throat culture medium: inhibitory Atmosphere of incubation: aerobic Duration of incubation: 48 hours GAS confirmation: latex test Number of plates inoculated: 1 Assessment of GAS antibody response: no Relevant details: -</p>
Flow and timing	No follow-up
Comparative	
Type of study	Journal article (in French)
Notes	A total of 7 RADTs were performed in the same sample of children (5 EIAs and 2 LAs). We only extracted data regarding the evaluation of EIA tests

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient Selection			
Was a consecutive or random sample of patients enrolled?	Unclear		

Chiadmi 2004a (Continued)

Was it a cross-sectional study or a RCT?	Yes		
Were selection criteria clearly described (at least presenting signs and symptoms and age limits for inclusion)?	Yes		
Was clinical selection of patients avoided?	No		
Were patients seen in an ambulatory care setting?	Yes		
		High	High

DOMAIN 2: Index Test All tests

Were the RADT results interpreted with blinding of the results of culture?	Unclear		
Was the type of the RADT mentioned (EIA or OIA)?	Yes		
Were RADTs conducted during consultation time?	No		
		Unclear	High

DOMAIN 3: Reference Standard

Were culture results interpreted with blinding of the results of the RADT?	Unclear		
Is the throat culture method likely to correctly identify GAS (laboratory culture on a blood agar plate during 48 hr)?	Yes		
Were the culture medium, atmosphere, duration of incubation and GAS-confirmation technique described?	Yes		
		Unclear	Low

DOMAIN 4: Flow and Timing

Was the delay between the performance of the RADT and throat culture plating less than 48 hours?	Unclear		
Did all patients receive a throat culture?	Yes		
Did patients receive the same throat culture method?	Yes		
Were undetermined/uninterpretable results reported?	No		
Were withdrawals from the study explained?	Yes		
		Low	

Chiadmi 2004b
Study characteristics

Patient sampling	See Chiadmi 2004a
Patient characteristics and setting	See Chiadmi 2004a
Index tests	Throat swab (1 single, 1 double, 2 different): unclear Commercial name of the RADT: IM Strep A (International Microbio) Type of RADT: EIA
Target condition and reference standard(s)	See Chiadmi 2004a
Flow and timing	No follow-up
Comparative	
Type of study	Journal article (in French)
Notes	A total of 7 RADTs were performed in the same sample of children (5 EIAs and 2 LAs). We only extracted data regarding the evaluation of EIA tests

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient Selection			
Was a consecutive or random sample of patients enrolled?	Unclear		
Was it a cross-sectional study or a RCT?	Yes		
Were selection criteria clearly described (at least presenting signs and symptoms and age limits for inclusion)?	Yes		
Was clinical selection of patients avoided?	No		
Were patients seen in an ambulatory care setting?	Yes		
		High	High
DOMAIN 2: Index Test All tests			
Were the RADT results interpreted with blinding of the results of culture?	Unclear		
Was the type of the RADT mentioned (EIA or OIA)?	Yes		
Were RADTs conducted during consultation time?	No		
		Unclear	High
DOMAIN 3: Reference Standard			

Chiadmi 2004b (Continued)

Were culture results interpreted with blinding of the results of the RADT?	Unclear
Is the throat culture method likely to correctly identify GAS (laboratory culture on a blood agar plate during 48 hr)?	Yes
Were the culture medium, atmosphere, duration of incubation and GAS-confirmation technique described?	Yes
	Unclear Low

DOMAIN 4: Flow and Timing

Was the delay between the performance of the RADT and throat culture plating less than 48 hours?	Unclear
Did all patients receive a throat culture?	Yes
Did patients receive the same throat culture method?	Yes
Were undetermined/uninterpretable results reported?	No
Were withdrawals from the study explained?	Yes
	Low

Chiadmi 2004c
Study characteristics

Patient sampling	See Chiadmi 2004a
Patient characteristics and setting	See Chiadmi-a
Index tests	Throat swab (1 single, 1 double, 2 different): unclear Commercial name of the RADT: Clearview Strep A Type of RADT: EIA
Target condition and reference standard(s)	See Chiadmi 2004a
Flow and timing	No follow-up
Comparative	
Type of study	Journal article (in French)
Notes	A total of 7 RADTs were performed in the same sample of children (5 EIAs and 2 LAs). We only extracted data regarding the evaluation of EIA tests

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
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Chiadmi 2004c (Continued)

DOMAIN 1: Patient Selection

Was a consecutive or random sample of patients enrolled?	Unclear		
Was it a cross-sectional study or a RCT?	Yes		
Were selection criteria clearly described (at least presenting signs and symptoms and age limits for inclusion)?	Yes		
Was clinical selection of patients avoided?	No		
Were patients seen in an ambulatory care setting?	Yes		
		High	High

DOMAIN 2: Index Test All tests

Were the RADT results interpreted with blinding of the results of culture?	Unclear		
Was the type of the RADT mentioned (EIA or OIA)?	Yes		
Were RADTs conducted during consultation time?	No		
		Unclear	High

DOMAIN 3: Reference Standard

Were culture results interpreted with blinding of the results of the RADT?	Unclear		
Is the throat culture method likely to correctly identify GAS (laboratory culture on a blood agar plate during 48 hr)?	Yes		
Were the culture medium, atmosphere, duration of incubation and GAS-confirmation technique described?	Yes		
		Unclear	Low

DOMAIN 4: Flow and Timing

Was the delay between the performance of the RADT and throat culture plating less than 48 hours?	Unclear		
Did all patients receive a throat culture?	Yes		
Did patients receive the same throat culture method?	Yes		
Were undetermined/uninterpretable results reported?	No		
Were withdrawals from the study explained?	Yes		
		Low	

Chiadmi 2004d
Study characteristics

Patient sampling	See Chiadmi 2004a
Patient characteristics and setting	See Chiadmi 2004a
Index tests	Throat swab (1 single, 1 double, 2 different): unclear Commercial name of the RADT: Strep A Sign Type of RADT: EIA
Target condition and reference standard(s)	See Chiadmi 2004a
Flow and timing	No follow-up
Comparative	
Type of study	Journal article (in French)
Notes	A total of 7 RADTs were performed in the same sample of children (5 EIAs and 2 LAs). We only extracted data regarding the evaluation of EIA tests

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient Selection			
Was a consecutive or random sample of patients enrolled?	Unclear		
Was it a cross-sectional study or a RCT?	Yes		
Were selection criteria clearly described (at least presenting signs and symptoms and age limits for inclusion)?	Yes		
Was clinical selection of patients avoided?	No		
Were patients seen in an ambulatory care setting?	Yes		
		High	High
DOMAIN 2: Index Test All tests			
Were the RADT results interpreted with blinding of the results of culture?	Unclear		
Was the type of the RADT mentioned (EIA or OIA)?	Yes		
Were RADTs conducted during consultation time?	No		
		Unclear	High
DOMAIN 3: Reference Standard			

Chiadmi 2004d (Continued)

Were culture results interpreted with blinding of the results of the RADT?	Unclear
Is the throat culture method likely to correctly identify GAS (laboratory culture on a blood agar plate during 48 hr)?	Yes
Were the culture medium, atmosphere, duration of incubation and GAS-confirmation technique described?	Yes
	Unclear Low

DOMAIN 4: Flow and Timing

Was the delay between the performance of the RADT and throat culture plating less than 48 hours?	Unclear
Did all patients receive a throat culture?	Yes
Did patients receive the same throat culture method?	Yes
Were undetermined/uninterpretable results reported?	No
Were withdrawals from the study explained?	Yes
	Low

Chiadmi 2004e
Study characteristics

Patient sampling	See Chiadmi 2004a
Patient characteristics and setting	See Chiadmi 2004a
Index tests	Throat swab (1 single, 1 double, 2 different): unclear Commercial name of the RADT: Streptavit Type of RADT: EIA
Target condition and reference standard(s)	See Chiadmi 2004a
Flow and timing	No follow-up
Comparative	
Type of study	Journal article (in French)
Notes	A total of 7 RADTs were performed in the same sample of children (5 EIAs and 2 LAs). We only extracted data regarding the evaluation of EIA tests

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
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Chiadmi 2004e (Continued)

DOMAIN 1: Patient Selection

Was a consecutive or random sample of patients enrolled?	Unclear		
Was it a cross-sectional study or a RCT?	Yes		
Were selection criteria clearly described (at least presenting signs and symptoms and age limits for inclusion)?	Yes		
Was clinical selection of patients avoided?	No		
Were patients seen in an ambulatory care setting?	Yes		
		High	High

DOMAIN 2: Index Test All tests

Were the RADT results interpreted with blinding of the results of culture?	Unclear		
Was the type of the RADT mentioned (EIA or OIA)?	Yes		
Were RADTs conducted during consultation time?	No		
		Unclear	High

DOMAIN 3: Reference Standard

Were culture results interpreted with blinding of the results of the RADT?	Unclear		
Is the throat culture method likely to correctly identify GAS (laboratory culture on a blood agar plate during 48 hr)?	Yes		
Were the culture medium, atmosphere, duration of incubation and GAS-confirmation technique described?	Yes		
		Unclear	Low

DOMAIN 4: Flow and Timing

Was the delay between the performance of the RADT and throat culture plating less than 48 hours?	Unclear		
Did all patients receive a throat culture?	Yes		
Did patients receive the same throat culture method?	Yes		
Were undetermined/uninterpretable results reported?	No		
Were withdrawals from the study explained?	Yes		
		Low	

Chu 1990
Study characteristics

Patient sampling	Cross-sectional study Prospective design Sample: consecutive Direct comparison of different RADTs: no Direct comparison of several throat culture techniques: no Person performing the throat sample: not reported Exclusion if recent antibiotics use before inclusion: no Clinical selection of patients: explicit criteria but not a score (see below) Presenting signs and symptoms: one or more of the following: sore throat, tonsil exudate, pharyngeal erythema, enlarged anterior cervical lymph node, fever or skin rash suggestive of scarlet fever Age range for inclusion: 3 to 18 years
Patient characteristics and setting	Sample size: 444 Age (distribution): mean = 9.8 years GAS prevalence according to culture (with 95% confidence interval): 9.5% (95% CI not reported) Country of study: Taiwan Sex (% of girls): not reported Clinical severity assessment: none Clinical setting: mixed (hospital outpatient clinics, emergency department and a private office clinic) Multi-centre study
Index tests	Throat swab: 2 different swabs Commercial name of the RADT: Visuwell Strep A (ADI) Type of RADT: EIA
Target condition and reference standard(s)	Throat culture medium: standard Atmosphere of incubation: anaerobic Duration of incubation: 24 hours GAS confirmation: bacitracin disk Number of plates inoculated: 1 Assessment of GAS antibody response: no Relevant details: -
Flow and timing	No follow-up
Comparative	
Type of study	Journal article
Notes	—

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
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DOMAIN 1: Patient Selection

Chu 1990 (Continued)

Was a consecutive or random sample of patients enrolled?	Yes
Was it a cross-sectional study or a RCT?	Yes
Were selection criteria clearly described (at least presenting signs and symptoms and age limits for inclusion)?	Yes
Was clinical selection of patients avoided?	Yes
Were patients seen in an ambulatory care setting?	Yes

Low
Low
DOMAIN 2: Index Test All tests

Were the RADT results interpreted with blinding of the results of culture?	Unclear
Was the type of the RADT mentioned (EIA or OIA)?	Yes
Were RADTs conducted during consultation time?	No

Unclear
High
DOMAIN 3: Reference Standard

Were culture results interpreted with blinding of the results of the RADT?	Unclear
Is the throat culture method likely to correctly identify GAS (laboratory culture on a blood agar plate during 48 hr)?	No
Were the culture medium, atmosphere, duration of incubation and GAS-confirmation technique described?	No

High
High
DOMAIN 4: Flow and Timing

Was the delay between the performance of the RADT and throat culture plating less than 48 hours?	Unclear
Did all patients receive a throat culture?	Yes
Did patients receive the same throat culture method?	Yes
Were undetermined/uninterpretable results reported?	No
Were withdrawals from the study explained?	No

Low

Clegg 1987
Study characteristics

Patient sampling	Cross-sectional study Prospective design Sample: unclear Direct comparison of different RADTs: no Direct comparison of several throat culture techniques: no Person performing the throat sample: not reported Exclusion if recent antibiotics use before inclusion: no Clinical selection of patients: none Presenting signs and symptoms: acute pharyngitis Age range for inclusion: not reported ("paediatric patients")
Patient characteristics and setting	Sample size: 205 Age (distribution): not reported GAS prevalence according to culture (with 95% confidence interval): 48.3% (95% CI not reported) Country of study: USA Sex (% of girls): not reported Clinical severity assessment: none Clinical setting: office-based Single-centre study
Index tests	Throat swab: 1 single swab (used for culture and then for the RADT) Commercial name of the RADT: Ventrescreen (Ventrex Laboratories) Type of RADT: EIA
Target condition and reference standard(s)	Throat culture medium: standard Atmosphere of incubation: aerobic Duration of incubation: not reported GAS confirmation: bacitracin disk Number of plates inoculated: 1 Assessment of GAS antibody response: no Relevant details: -
Flow and timing	No follow-up
Comparative	
Type of study	Journal article
Notes	—

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient Selection			

Clegg 1987 (Continued)

Was a consecutive or random sample of patients enrolled?	Unclear
Was it a cross-sectional study or a RCT?	Yes
Were selection criteria clearly described (at least presenting signs and symptoms and age limits for inclusion)?	No
Was clinical selection of patients avoided?	Yes
Were patients seen in an ambulatory care setting?	Yes

High
Low
DOMAIN 2: Index Test All tests

Were the RADT results interpreted with blinding of the results of culture?	Yes
Was the type of the RADT mentioned (EIA or OIA)?	Yes
Were RADTs conducted during consultation time?	Unclear

Low
Unclear
DOMAIN 3: Reference Standard

Were culture results interpreted with blinding of the results of the RADT?	Yes
Is the throat culture method likely to correctly identify GAS (laboratory culture on a blood agar plate during 48 hr)?	Unclear
Were the culture medium, atmosphere, duration of incubation and GAS-confirmation technique described?	No

High
High
DOMAIN 4: Flow and Timing

Was the delay between the performance of the RADT and throat culture plating less than 48 hours?	Yes
Did all patients receive a throat culture?	Yes
Did patients receive the same throat culture method?	Yes
Were undetermined/uninterpretable results reported?	No
Were withdrawals from the study explained?	No

Low

Cohen 1988
Study characteristics

Patient sampling	Cross-sectional study Prospective design Sample: unclear Direct comparison of different RADTs: no Direct comparison of several throat culture techniques: no Person performing the throat sample: not reported Exclusion if recent antibiotics use before inclusion: no Clinical selection of patients: explicit criteria but not a score (see below) Presenting signs and symptoms: pharyngitis with fever Age range for inclusion: 2 to 14 years
Patient characteristics and setting	Sample size: 92 Age (distribution): mean age = 6.3 years GAS prevalence according to culture (with 95% confidence interval): 29.3% (95% CI not reported) Country of study: France Sex (% of girls): not reported Clinical severity assessment: none Clinical setting: mixed (office-based and hospital) Multi-centre study
Index tests	Throat swab: 2 different swabs Commercial name of the RADT: Group A Strep Test (Quidel) Type of RADT: EIA
Target condition and reference standard(s)	Throat culture medium: enrichment and inhibitory Atmosphere of incubation: aerobic Duration of incubation: not reported GAS confirmation: not reported Number of plates inoculated: 1 Assessment of GAS antibody response: no Relevant details: -
Flow and timing	No follow-up
Comparative	
Type of study	Journal article (in French)
Notes	—

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient Selection			
Was a consecutive or random sample of patients enrolled?	Unclear		

Cohen 1988 (Continued)

Was it a cross-sectional study or a RCT?	Yes		
Were selection criteria clearly described (at least presenting signs and symptoms and age limits for inclusion)?	Yes		
Was clinical selection of patients avoided?	No		
Were patients seen in an ambulatory care setting?	Yes		
		High	High

DOMAIN 2: Index Test All tests

Were the RADT results interpreted with blinding of the results of culture?	Yes		
Was the type of the RADT mentioned (EIA or OIA)?	Yes		
Were RADTs conducted during consultation time?	Yes		
		Low	Low

DOMAIN 3: Reference Standard

Were culture results interpreted with blinding of the results of the RADT?	Unclear		
Is the throat culture method likely to correctly identify GAS (laboratory culture on a blood agar plate during 48 hr)?	Unclear		
Were the culture medium, atmosphere, duration of incubation and GAS-confirmation technique described?	No		
		High	High

DOMAIN 4: Flow and Timing

Was the delay between the performance of the RADT and throat culture plating less than 48 hours?	Yes		
Did all patients receive a throat culture?	Yes		
Did patients receive the same throat culture method?	No		
Were undetermined/uninterpretable results reported?	No		
Were withdrawals from the study explained?	No		
		High	

Cohen 1998
Study characteristics

Patient sampling	Cross-sectional study
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Cohen 1998 (Continued)

	<p>Prospective design Sample: unclear Direct comparison of different RADTs: no Direct comparison of several throat culture techniques: no Person performing the throat sample: physician</p> <p>Exclusion if recent antibiotics use before inclusion: yes (within 7 days before inclusion)</p> <p>Clinical selection of patients: implicit criteria (see below)</p> <p>Presenting signs and symptoms: acute pharyngitis or tonsillitis with dysphagia or fever</p> <p>Age range for inclusion: 4 to 15 years</p>
Patient characteristics and setting	<p>Sample size: 563 Age (distribution): not reported</p> <p>GAS prevalence according to culture (with 95% confidence interval): 21.5% (95% CI not reported) Country of study: France Sex (% of girls): not reported Clinical severity assessment: none Clinical setting: office-based Multi-centre study</p>
Index tests	<p>Throat swab: 2 different (first one for the RADT, second one only if RADT+)</p> <p>Commercial name of the RADT: TestPack Plus Strep A (Abbott) Type of RADT: EIA</p>
Target condition and reference standard(s)	<p>Throat culture medium: inhibitory Atmosphere of incubation: anaerobic Duration of incubation: 48 hours GAS confirmation: latex test Number of plates inoculated: 1 Assessment of GAS antibody response: no Relevant details: -</p>
Flow and timing	No follow-up
Comparative	
Type of study	Journal article (in French)
Notes	The study was supported by ASTRA laboratories

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient Selection			
Was a consecutive or random sample of patients enrolled?	Unclear		
Was it a cross-sectional study or a RCT?	Yes		

Cohen 1998 (Continued)

Were selection criteria clearly described (at least presenting signs and symptoms and age limits for inclusion)?	Yes		
Was clinical selection of patients avoided?	No		
Were patients seen in an ambulatory care setting?	Yes		
		High	Low
DOMAIN 2: Index Test All tests			
Were the RADT results interpreted with blinding of the results of culture?	Yes		
Was the type of the RADT mentioned (EIA or OIA)?	Yes		
Were RADTs conducted during consultation time?	Yes		
		Low	Low
DOMAIN 3: Reference Standard			
Were culture results interpreted with blinding of the results of the RADT?	No		
Is the throat culture method likely to correctly identify GAS (laboratory culture on a blood agar plate during 48 hr)?	Yes		
Were the culture medium, atmosphere, duration of incubation and GAS-confirmation technique described?	Yes		
		High	Low
DOMAIN 4: Flow and Timing			
Was the delay between the performance of the RADT and throat culture plating less than 48 hours?	Yes		
Did all patients receive a throat culture?	No		
Did patients receive the same throat culture method?	Yes		
Were undetermined/uninterpretable results reported?	Yes		
Were withdrawals from the study explained?	Yes		
		High	

Cohen 2004
Study characteristics

Patient sampling	Cross-sectional study Prospective design Sample: unclear
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Cohen 2004 (Continued)

Direct comparison of different RADTs: no
 Direct comparison of several throat culture techniques: no
 Person performing the throat sample: not reported

 Exclusion if recent antibiotics use before inclusion: no

 Clinical selection of patients: none

 Presenting signs and symptoms: signs and symptoms of pharyngitis

 Age range for inclusion: not reported ("children")

Patient characteristics and setting	Sample size: 604 Age (distribution): median age = 5.5 years GAS prevalence according to culture (with 95% confidence interval): 45.5% (95% CI not reported) Country of study: France Sex (% of girls): not reported Clinical severity assessment: Mclsaac score and Wald score Clinical setting: mixed (office-based and emergency department) Multi-centre study
Index tests	Throat swab: 2 different swabs (1 swab for the RADT, 1 swab for culture) Commercial name of the RADT: not reported ("EIA no name") Type of RADT: EIA
Target condition and reference standard(s)	Throat culture medium: not reported Atmosphere of incubation: not reported Duration of incubation: not reported GAS confirmation: not reported Number of plates inoculated: not reported Assessment of GAS antibody response: no Relevant details: -
Flow and timing	No follow-up
Comparative	
Type of study	Journal article
Notes	Throat culture performed only for children with negative RADT results (partial verification)

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient Selection			
Was a consecutive or random sample of patients enrolled?	Unclear		
Was it a cross-sectional study or a RCT?	Yes		
Were selection criteria clearly described (at least presenting signs and symptoms and age limits for inclusion)?	No		

Cohen 2004 (Continued)

Was clinical selection of patients avoided?	Yes		
Were patients seen in an ambulatory care setting?	Yes		
		High	Low
DOMAIN 2: Index Test All tests			
Were the RADT results interpreted with blinding of the results of culture?	Yes		
Was the type of the RADT mentioned (EIA or OIA)?	No		
Were RADTs conducted during consultation time?	Yes		
		High	Low
DOMAIN 3: Reference Standard			
Were culture results interpreted with blinding of the results of the RADT?	No		
Is the throat culture method likely to correctly identify GAS (laboratory culture on a blood agar plate during 48 hr)?	Unclear		
Were the culture medium, atmosphere, duration of incubation and GAS-confirmation technique described?	No		
		High	High
DOMAIN 4: Flow and Timing			
Was the delay between the performance of the RADT and throat culture plating less than 48 hours?	Yes		
Did all patients receive a throat culture?	No		
Did patients receive the same throat culture method?	Yes		
Were undetermined/uninterpretable results reported?	No		
Were withdrawals from the study explained?	No		
		High	

Cohen 2012
Study characteristics

Patient sampling	Cross-sectional study Prospective design Sample: unclear Direct comparison of different RADTs: no Direct comparison of several throat culture techniques: no
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Cohen 2012 (Continued)

	Person performing the throat sample: physician Exclusion if recent antibiotics use before inclusion: yes (within 7 days before inclusion) Clinical selection of patients: none Presenting signs and symptoms: pharyngitis (inflammation of the pharynx and/or tonsils) Age range for inclusion: 3 to 15 years
Patient characteristics and setting	Sample size: 785 Age (distribution): mean (SD) = 6.1 (2.5) years GAS prevalence according to culture (with 95% confidence interval): 36.3% (95% CI 32.9 to 39.8) Country of study: France Sex (% of girls): 44.7% Clinical severity assessment: Mclsaac score Clinical setting: office-based Multi-centre study
Index tests	Throat swab: 1 double swab (1 swab for the RADT, 1 swab for culture) Commercial name of the RADT: StreptAtest (Dectrapharm) Type of RADT: EIA
Target condition and reference standard(s)	Throat culture medium: standard Atmosphere of incubation: anaerobic Duration of incubation: 48 hours GAS confirmation: latex agglutination (Prolex) Number of plates inoculated: 1 Assessment of GAS antibody response: no Relevant details: -
Flow and timing	No follow-up
Comparative	
Type of study	Journal article
Notes	Funded by Dectrapharm (manufacturer of the RADT) and educational grants

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient Selection			
Was a consecutive or random sample of patients enrolled?	Unclear		
Was it a cross-sectional study or a RCT?	Yes		
Were selection criteria clearly described (at least presenting signs and symptoms and age limits for inclusion)?	Yes		
Was clinical selection of patients avoided?	Yes		

Cohen 2012 (Continued)

Were patients seen in an ambulatory care setting?	Yes		
		Low	Low
DOMAIN 2: Index Test All tests			
Were the RADT results interpreted with blinding of the results of culture?	Yes		
Was the type of the RADT mentioned (EIA or OIA)?	Yes		
Were RADTs conducted during consultation time?	Yes		
		Low	Low
DOMAIN 3: Reference Standard			
Were culture results interpreted with blinding of the results of the RADT?	Yes		
Is the throat culture method likely to correctly identify GAS (laboratory culture on a blood agar plate during 48 hr)?	Yes		
Were the culture medium, atmosphere, duration of incubation and GAS-confirmation technique described?	Yes		
		Low	Low
DOMAIN 4: Flow and Timing			
Was the delay between the performance of the RADT and throat culture plating less than 48 hours?	No		
Did all patients receive a throat culture?	Yes		
Did patients receive the same throat culture method?	Yes		
Were undetermined/uninterpretable results reported?	Yes		
Were withdrawals from the study explained?	Yes		
		Low	

Cohen 2013
Study characteristics

Patient sampling	Cross-sectional study Prospective design Sample: consecutive Direct comparison of different RADTs: no Direct comparison of several throat culture techniques: no Person performing the throat sample: physician
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Cohen 2013 (Continued)

	Exclusion if recent antibiotics use before inclusion: yes (within 7 days before inclusion) Clinical selection of patients: none Presenting signs and symptoms: children with a diagnosis of pharyngitis Age range for inclusion: 3 to 14 years
Patient characteristics and setting	Sample size: 676 Age (distribution): mean (SD) = 6.1 (2.5) years GAS prevalence according to culture (with 95% confidence interval): 41.4% (95% CI 37.7 to 45.2) Country of study: France Sex (% of girls): 46.3% Clinical severity assessment: none Clinical setting: office-based Multi-centre study
Index tests	Throat swab: 1 double swab (1 swab for the RADT, 1 swab for culture) Commercial name of the RADT: StreptAtest (Dectrapharm) Type of RADT: EIA
Target condition and reference standard(s)	Throat culture medium: inhibitory and enrichment Atmosphere of incubation: anaerobic Duration of incubation: 48 hours GAS confirmation: latex test Number of plates inoculated: 2 (the second plate was inoculated if the first one was negative after 48 hours of incubation) Assessment of GAS antibody response: no Relevant details: -
Flow and timing	No follow-up
Comparative	
Type of study	Journal article
Notes	Funded by Dectrapharm (manufacturer of the RADT)

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient Selection			
Was a consecutive or random sample of patients enrolled?	Yes		
Was it a cross-sectional study or a RCT?	Yes		
Were selection criteria clearly described (at least presenting signs and symptoms and age limits for inclusion)?	Yes		
Was clinical selection of patients avoided?	Yes		

Cohen 2013 (Continued)

Were patients seen in an ambulatory care setting?	Yes		
		Low	Low
DOMAIN 2: Index Test All tests			
Were the RADT results interpreted with blinding of the results of culture?	Yes		
Was the type of the RADT mentioned (EIA or OIA)?	Yes		
Were RADTs conducted during consultation time?	Yes		
		Low	Low
DOMAIN 3: Reference Standard			
Were culture results interpreted with blinding of the results of the RADT?	Yes		
Is the throat culture method likely to correctly identify GAS (laboratory culture on a blood agar plate during 48 hr)?	Yes		
Were the culture medium, atmosphere, duration of incubation and GAS-confirmation technique described?	Yes		
		Low	Low
DOMAIN 4: Flow and Timing			
Was the delay between the performance of the RADT and throat culture plating less than 48 hours?	No		
Did all patients receive a throat culture?	Yes		
Did patients receive the same throat culture method?	Yes		
Were undetermined/uninterpretable results reported?	Yes		
Were withdrawals from the study explained?	Yes		
		Low	

Contessotto 2000
Study characteristics

Patient sampling	Cross-sectional study Prospective design Sample: unclear Direct comparison of different RADTs: no Direct comparison of several throat culture techniques: no Person performing the throat sample: not reported
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Contessotto 2000 (Continued)

	Exclusion if recent antibiotics use before inclusion: yes (within 3 days before inclusion) Clinical selection of patients: none Presenting signs and symptoms: acute pharyngitis and/or tonsillitis Age range for inclusion: 6 months to 14 years
Patient characteristics and setting	Sample size: 401 Age (distribution): not reported GAS prevalence according to culture (with 95% confidence interval): 28.2% (95% CI +/- 4.4%) Country of study: Spain Sex (% of girls): not reported Clinical severity assessment: none Clinical setting: mixed (office-based and emergency department) Multi-centre study
Index tests	Throat swab: 1 double swab (1 swab for the RADT, 1 swab for culture) Commercial name of the RADT: QuickVue Flex Strep A (Quidel) Type of RADT: EIA
Target condition and reference standard(s)	Throat culture medium: standard Atmosphere of incubation (aerobic, aerobic with CO ₂ enrichment, anaerobic): not reported Duration of incubation: 48 hours GAS confirmation: bacitracin disk and latex test Number of plates inoculated: 1 Assessment of GAS antibody response: no Relevant details: -
Flow and timing	No follow-up
Comparative	
Type of study	Journal article (Spanish)
Notes	—

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient Selection			
Was a consecutive or random sample of patients enrolled?	Unclear		
Was it a cross-sectional study or a RCT?	Yes		
Were selection criteria clearly described (at least presenting signs and symptoms and age limits for inclusion)?	Yes		
Was clinical selection of patients avoided?	Yes		
Were patients seen in an ambulatory care setting?	Yes		

Contessotto 2000 (Continued)

		Low	Low
DOMAIN 2: Index Test All tests			
Were the RADT results interpreted with blinding of the results of culture?	Yes		
Was the type of the RADT mentioned (EIA or OIA)?	Yes		
Were RADTs conducted during consultation time?	Yes		
		Low	Low
DOMAIN 3: Reference Standard			
Were culture results interpreted with blinding of the results of the RADT?	Unclear		
Is the throat culture method likely to correctly identify GAS (laboratory culture on a blood agar plate during 48 hr)?	Yes		
Were the culture medium, atmosphere, duration of incubation and GAS-confirmation technique described?	No		
		High	High
DOMAIN 4: Flow and Timing			
Was the delay between the performance of the RADT and throat culture plating less than 48 hours?	Yes		
Did all patients receive a throat culture?	Yes		
Did patients receive the same throat culture method?	Yes		
Were undetermined/uninterpretable results reported?	No		
Were withdrawals from the study explained?	Yes		
		Low	

Dagnelie 1998

Study characteristics	
Patient sampling	Cross-sectional study Prospective design Sample: unclear Direct comparison of different RADTs: no Direct comparison of several throat culture techniques: no Person performing the throat sample: physicians Exclusion if recent antibiotics use before inclusion: no Clinical selection of patients: none

Dagnelie 1998 (Continued)

	Presenting signs and symptoms: sore throat for less than 15 days Age range for inclusion: 4 to 14 years
Patient characteristics and setting	Sample size: 79 (total of 558 patients but only 79 children) Age (distribution): not reported GAS prevalence according to culture (with 95% confidence interval): 58.2% (95% CI not reported) Country of study: the Netherlands Sex (% of girls): not reported Clinical severity assessment: Centor score Clinical setting: office-based Multi-centre study
Index tests	Throat swab: 2 different swabs (1 swab for the RADT, 1 swab for culture) Commercial name of the RADT: Directgen 1-2-3 (Becton Dickinson) Type of RADT: EIA (liposomal test)
Target condition and reference standard(s)	Throat culture medium: standard Atmosphere of incubation: aerobic and anaerobic Duration of incubation: 48 hours GAS confirmation: latex test Number of plates inoculated: unclear Assessment of GAS antibody response: yes Relevant details: -
Flow and timing	No follow-up
Comparative	
Type of study	Journal article
Notes	The study included children and adults; we extracted data only for children

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient Selection			
Was a consecutive or random sample of patients enrolled?	Unclear		
Was it a cross-sectional study or a RCT?	Yes		
Were selection criteria clearly described (at least presenting signs and symptoms and age limits for inclusion)?	Yes		
Was clinical selection of patients avoided?	Yes		
Were patients seen in an ambulatory care setting?	Yes		
		Low	Low

DOMAIN 2: Index Test All tests
Rapid antigen detection test for group A streptococcus in children with pharyngitis (Review)

Dagnelie 1998 (Continued)

Were the RADT results interpreted with blinding of the results of culture?	Unclear		
Was the type of the RADT mentioned (EIA or OIA)?	Yes		
Were RADTs conducted during consultation time?	Unclear		
		Unclear	Unclear

DOMAIN 3: Reference Standard

Were culture results interpreted with blinding of the results of the RADT?	Unclear		
Is the throat culture method likely to correctly identify GAS (laboratory culture on a blood agar plate during 48 hr)?	Yes		
Were the culture medium, atmosphere, duration of incubation and GAS-confirmation technique described?	Yes		
		Unclear	Low

DOMAIN 4: Flow and Timing

Was the delay between the performance of the RADT and throat culture plating less than 48 hours?	Yes		
Did all patients receive a throat culture?	Yes		
Did patients receive the same throat culture method?	Yes		
Were undetermined/uninterpretable results reported?	No		
Were withdrawals from the study explained?	Yes		
		Low	

Daly 1994
Study characteristics

Patient sampling	Cross-sectional study Prospective design Sample: unclear Direct comparison of different RADTs: no Direct comparison of several throat culture techniques: yes Person performing the throat sample: unclear Exclusion if recent antibiotics use before inclusion: no Clinical selection of patients: none Presenting signs and symptoms: pharyngitis Age range for inclusion: not reported ("children")
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Daly 1994 (Continued)

Patient characteristics and setting	Sample size: 424 Age (distribution): not reported GAS prevalence according to culture (with 95% confidence interval): 17.9% (95% CI not reported) Country of study: USA Sex (% of girls): not reported Clinical severity assessment: none Clinical setting: child medical centre Single-centre study
Index tests	Throat swab: 1 single swab (used for culture and then for the RADT) Commercial name of the RADT: Strep A OIA (Biostar) Type of RADT: OIA
Target condition and reference standard(s)	Throat culture medium: enrichment in a Todd-Hewitt broth followed by culture on a selective medium Atmosphere of incubation: 35°C, aerobic with CO ₂ enrichment Duration of incubation: 48 hours GAS confirmation: bacitracin disk and latex test (and PYR test) Number of plates inoculated: 1 Assessment of GAS antibody response: no Relevant details: -
Flow and timing	No follow-up
Comparative	
Type of study	Journal article
Notes	Supported by a grant from Biostar (manufacturer of the RADT)

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient Selection			
Was a consecutive or random sample of patients enrolled?	Unclear		
Was it a cross-sectional study or a RCT?	Unclear		
Were selection criteria clearly described (at least presenting signs and symptoms and age limits for inclusion)?	No		
Was clinical selection of patients avoided?	Yes		
Were patients seen in an ambulatory care setting?	Yes		
		High	Low
DOMAIN 2: Index Test All tests			
Were the RADT results interpreted with blinding of the results of culture?	Unclear		

Daly 1994 (Continued)

Was the type of the RADT mentioned (EIA or OIA)?	Yes	
Were RADTs conducted during consultation time?	No	
		Unclear High

DOMAIN 3: Reference Standard

Were culture results interpreted with blinding of the results of the RADT?	Unclear	
Is the throat culture method likely to correctly identify GAS (laboratory culture on a blood agar plate during 48 hr)?	Yes	
Were the culture medium, atmosphere, duration of incubation and GAS-confirmation technique described?	Yes	
		Unclear Low

DOMAIN 4: Flow and Timing

Was the delay between the performance of the RADT and throat culture plating less than 48 hours?	Unclear	
Did all patients receive a throat culture?	Yes	
Did patients receive the same throat culture method?	Yes	
Were undetermined/uninterpretable results reported?	No	
Were withdrawals from the study explained?	Yes	
		Low

Della-Latta 1994
Study characteristics

Patient sampling	Cross-sectional study Prospective design Sample: unclear Direct comparison of different RADTs: no Direct comparison of several throat culture techniques: yes Person performing the throat sample: unclear Exclusion if recent antibiotics use before inclusion: no Clinical selection of patients: none Presenting signs and symptoms: acute pharyngitis Age range for inclusion: 2 to 19 years
Patient characteristics and setting	Sample size: 690 Age (distribution): not reported

Della-Latta 1994 (Continued)

	GAS prevalence according to culture (with 95% confidence interval): 13.3% (95% CI not reported) Country of study: USA Sex (% of girls): not reported Clinical severity assessment: none Clinical setting: emergency department Single-centre study
Index tests	Throat swab: 1 single swab (used for culture and then for the RADT) Commercial name of the RADT: Strep A OIA (BioStar) Type of RADT: OIA
Target condition and reference standard(s)	Throat culture medium: standard Atmosphere of incubation: aerobic Duration of incubation: 48 hours GAS confirmation: latex agglutination Number of plates inoculated: 1 Assessment of GAS antibody response: no Relevant details: pledgets were also incubated in a Todd-Hewitt broth to improve GAS recovery (data not extracted)
Flow and timing	No follow-up
Comparative	
Type of study	Journal article
Notes	—

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient Selection			
Was a consecutive or random sample of patients enrolled?	Yes		
Was it a cross-sectional study or a RCT?	Yes		
Were selection criteria clearly described (at least presenting signs and symptoms and age limits for inclusion)?	Yes		
Was clinical selection of patients avoided?	Yes		
Were patients seen in an ambulatory care setting?	Yes		
		Low	Low
DOMAIN 2: Index Test All tests			
Were the RADT results interpreted with blinding of the results of culture?	Yes		
Was the type of the RADT mentioned (EIA or OIA)?	Yes		
Were RADTs conducted during consultation time?	No		

Della-Latta 1994 (Continued)

	Low	High
DOMAIN 3: Reference Standard		
Were culture results interpreted with blinding of the results of the RADT?	Unclear	
Is the throat culture method likely to correctly identify GAS (laboratory culture on a blood agar plate during 48 hr)?	Yes	
Were the culture medium, atmosphere, duration of incubation and GAS-confirmation technique described?	Yes	
	Unclear	Low
DOMAIN 4: Flow and Timing		
Was the delay between the performance of the RADT and throat culture plating less than 48 hours?	Yes	
Did all patients receive a throat culture?	Yes	
Did patients receive the same throat culture method?	Yes	
Were undetermined/uninterpretable results reported?	No	
Were withdrawals from the study explained?	No	
	Low	

Ding 2011
Study characteristics

Patient sampling	Cross-sectional study Prospective design Sample: unclear Direct comparison of different RADTs: no Direct comparison of several throat culture techniques: no Person performing the throat sample: physicians Exclusion if recent antibiotics use before inclusion: no Clinical selection of patients: none Presenting signs and symptoms: signs and symptoms of acute upper respiratory infection Age range for inclusion: 6 months to 14 years
Patient characteristics and setting	Sample size: 630 Age (distribution): not reported GAS prevalence according to culture (with 95% confidence interval): 29.5% (95% CI not reported) Country of study: China Sex (% of girls): 39.5%

Ding 2011 (Continued)

	Clinical severity assessment: none Clinical setting: walk-in clinic Multi-centre study
Index tests	Throat swab: 1 double swab (1 swab was used for the RADT, 1 swab for a FISH technique, and the pledget for culture) Commercial name of the RADT: Clearview Exact Strep A Type of RADT: EIA
Target condition and reference standard(s)	Throat culture medium: standard Atmosphere of incubation: aerobic with CO ₂ enrichment Duration of incubation: 24 hours GAS confirmation: bacitracin disk and latex test Number of plates inoculated: 1 Assessment of GAS antibody response: no Relevant details: -
Flow and timing	No follow-up
Comparative	
Type of study	Journal article
Notes	The RADT was compared to a FISH technique; such techniques were out of the scope of this review

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient Selection			
Was a consecutive or random sample of patients enrolled?	Unclear		
Was it a cross-sectional study or a RCT?	Yes		
Were selection criteria clearly described (at least presenting signs and symptoms and age limits for inclusion)?	Yes		
Was clinical selection of patients avoided?	Yes		
Were patients seen in an ambulatory care setting?	Yes		
		Low	Low
DOMAIN 2: Index Test All tests			
Were the RADT results interpreted with blinding of the results of culture?	Yes		
Was the type of the RADT mentioned (EIA or OIA)?	Yes		
Were RADTs conducted during consultation time?	Unclear		
		Low	Unclear

Ding 2011 (Continued)

DOMAIN 3: Reference Standard

Were culture results interpreted with blinding of the results of the RADT? Yes

Is the throat culture method likely to correctly identify GAS (laboratory culture on a blood agar plate during 48 hr)? No

Were the culture medium, atmosphere, duration of incubation and GAS-confirmation technique described? Yes

High
High
DOMAIN 4: Flow and Timing

Was the delay between the performance of the RADT and throat culture plating less than 48 hours? Unclear

Did all patients receive a throat culture? Yes

Did patients receive the same throat culture method? Yes

Were undetermined/uninterpretable results reported? No

Were withdrawals from the study explained? Yes

Low
Dobkin 1987
Study characteristics

Patient sampling

Cross-sectional study
 Prospective design
 Sample: unclear
 Direct comparison of different RADTs: no
 Direct comparison of several throat culture techniques: no
 Person performing the throat sample: not reported

Exclusion if recent antibiotics use before inclusion: no

Clinical selection of patients: none

Presenting signs and symptoms: patients with acute pharyngitis

Age range for inclusion: not reported

Patient characteristics and setting

Sample size: 221
 Age (distribution): not reported ("Almost all swabs were obtained from children younger than 16 years of age")

GAS prevalence according to culture (with 95% confidence interval): 30.8% (95% CI not reported)
 Country of study: USA
 Sex (% of girls): not reported
 Clinical severity assessment: none
 Clinical setting: unclear

Dobkin 1987 (Continued)

	Single-centre study
Index tests	Throat swab: not reported Commercial name of the RADT: Test Pack Strep A (Abbott) Type of RADT: EIA
Target condition and reference standard(s)	Throat culture medium: standard Atmosphere of incubation: aerobic Duration of incubation: 48 hours GAS confirmation: bacitracin disk and latex test Number of plates inoculated: 1 Assessment of GAS antibody response: no Relevant details: -
Flow and timing	No follow-up
Comparative	
Type of study	Journal article
Notes	Supported by a grant from Abbott (manufacturer of the RADT)

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient Selection			
Was a consecutive or random sample of patients enrolled?	Unclear		
Was it a cross-sectional study or a RCT?	Yes		
Were selection criteria clearly described (at least presenting signs and symptoms and age limits for inclusion)?	No		
Was clinical selection of patients avoided?	Yes		
Were patients seen in an ambulatory care setting?	Unclear		
		High	Unclear
DOMAIN 2: Index Test All tests			
Were the RADT results interpreted with blinding of the results of culture?	Unclear		
Was the type of the RADT mentioned (EIA or OIA)?	Yes		
Were RADTs conducted during consultation time?	No		
		Unclear	High
DOMAIN 3: Reference Standard			

Dobkin 1987 (Continued)

Were culture results interpreted with blinding of the results of the RADT?	Unclear	
Is the throat culture method likely to correctly identify GAS (laboratory culture on a blood agar plate during 48 hr)?	Yes	
Were the culture medium, atmosphere, duration of incubation and GAS-confirmation technique described?	Yes	
	Unclear	Low

DOMAIN 4: Flow and Timing

Was the delay between the performance of the RADT and throat culture plating less than 48 hours?	No	
Did all patients receive a throat culture?	Yes	
Did patients receive the same throat culture method?	Yes	
Were undetermined/uninterpretable results reported?	No	
Were withdrawals from the study explained?	Yes	
		Low

Donatelli 1992a
Study characteristics

Patient sampling	Cross-sectional study Prospective design Sample: unclear Direct comparison of different RADTs: yes Direct comparison of several throat culture techniques: no Person performing the throat sample: laboratory personnel (data from nurses not extracted) Exclusion if recent antibiotics use before inclusion: no Clinical selection of patients: none Presenting signs and symptoms: patients presenting with and symptoms of acute pharyngitis Age range for inclusion: not reported (performed in a children's hospital)
Patient characteristics and setting	Sample size: 180 Age (distribution): not reported GAS prevalence according to culture (with 95% confidence interval): 22.8% (95% CI not reported) Country of study: USA Sex (% of girls): not reported Clinical severity assessment: none Clinical setting: mixed (general paediatric clinic and emergency department)

Donatelli 1992a (Continued)

	Single-centre study
Index tests	Throat swab: 2 different swabs Commercial name of the RADT: Directgen 1-2-3 Type of RADT: EIA (liposome assay)
Target condition and reference standard(s)	Throat culture medium: standard Atmosphere of incubation: anaerobic Duration of incubation: 48 hours GAS confirmation: other (PYR test during first third of the study, then latex test) Number of plates inoculated: 1 Assessment of GAS antibody response: no Relevant details: -
Flow and timing	No follow-up
Comparative	
Type of study	Journal article
Notes	The study compared results obtained by nurses and by laboratory technologists; we extracted data only for laboratory technologists. This study was funded in part by Health and Welfare Canada

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient Selection			
Was a consecutive or random sample of patients enrolled?	Unclear		
Was it a cross-sectional study or a RCT?	Yes		
Were selection criteria clearly described (at least presenting signs and symptoms and age limits for inclusion)?	No		
Was clinical selection of patients avoided?	Yes		
Were patients seen in an ambulatory care setting?	Yes		
		High	High
DOMAIN 2: Index Test All tests			
Were the RADT results interpreted with blinding of the results of culture?	Yes		
Was the type of the RADT mentioned (EIA or OIA)?	Yes		
Were RADTs conducted during consultation time?	Unclear		
		Unclear	Unclear

Donatelli 1992a *(Continued)*
DOMAIN 3: Reference Standard

Were culture results interpreted with blinding of the results of the RADT?	Unclear
Is the throat culture method likely to correctly identify GAS (laboratory culture on a blood agar plate during 48 hr)?	Yes
Were the culture medium, atmosphere, duration of incubation and GAS-confirmation technique described?	Yes
	Low Low

DOMAIN 4: Flow and Timing

Was the delay between the performance of the RADT and throat culture plating less than 48 hours?	Unclear
Did all patients receive a throat culture?	Yes
Did patients receive the same throat culture method?	Yes
Were undetermined/uninterpretable results reported?	No
Were withdrawals from the study explained?	Yes
	Low

Donatelli 1992b
Study characteristics

Patient sampling	Cross-sectional study Prospective design Sample: unclear Direct comparison of different RADTs: yes Direct comparison of several throat culture techniques: no Person performing the throat sample: laboratory personnel (data from nurses not extracted) Exclusion if recent antibiotics use before inclusion: no Clinical selection of patients: none Presenting signs and symptoms: patients presenting with and symptoms of acute pharyngitis Age range for inclusion: not reported
Patient characteristics and setting	Sample size: 203 Age (distribution): not reported GAS prevalence according to culture (with 95% confidence interval): 21.7% (95% CI not reported) Country of study: USA Sex (% of girls): not reported

Donatelli 1992b (Continued)

Clinical severity assessment: none
Clinical setting: mixed (general paediatric clinic and emergency department)
Single-centre study

Index tests

Throat swab: 2 different swabs
Commercial name of the RADT: ICON Strep A
Type of RADT: EIA

Target condition and reference standard(s)

Throat culture medium: standard
Atmosphere of incubation: anaerobic
Duration of incubation: 48 hours
GAS confirmation: other (PYR test during first third of the study, then latex test)
Number of plates inoculated: 1
Assessment of GAS antibody response: no
Relevant details: -

Flow and timing

No follow-up

Comparative

Type of study

Journal article

Notes

The study compared results obtained by nurses and by laboratory technologists; we extracted data only for laboratory technologists. This study was funded in part by Health and Welfare Canada

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient Selection			
Was a consecutive or random sample of patients enrolled?	Unclear		
Was it a cross-sectional study or a RCT?	Yes		
Were selection criteria clearly described (at least presenting signs and symptoms and age limits for inclusion)?	No		
Was clinical selection of patients avoided?	Yes		
Were patients seen in an ambulatory care setting?	Yes		
		High	High
DOMAIN 2: Index Test All tests			
Were the RADT results interpreted with blinding of the results of culture?	Yes		
Was the type of the RADT mentioned (EIA or OIA)?	Yes		

Donatelli 1992b (Continued)

Were RADTs conducted during consultation time?	Unclear		
		Unclear	Unclear
DOMAIN 3: Reference Standard			
Were culture results interpreted with blinding of the results of the RADT?	Unclear		
Is the throat culture method likely to correctly identify GAS (laboratory culture on a blood agar plate during 48 hr)?	Yes		
Were the culture medium, atmosphere, duration of incubation and GAS-confirmation technique described?	Yes		
		Low	Low
DOMAIN 4: Flow and Timing			
Was the delay between the performance of the RADT and throat culture plating less than 48 hours?	Unclear		
Did all patients receive a throat culture?	Yes		
Did patients receive the same throat culture method?	Yes		
Were undetermined/uninterpretable results reported?	No		
Were withdrawals from the study explained?	Yes		
		Low	

dos Santos 2005

Study characteristics	
Patient sampling	Cross-sectional study Prospective design Sample: consecutive Direct comparison of different RADTs: no Direct comparison of several throat culture techniques: no Person performing the throat sample: the "researcher" Exclusion if recent antibiotics use before inclusion: no Clinical selection of patients: explicit criteria but not a score (see below) Presenting signs and symptoms: children with a painful throat and evidence of inflammation of throat or tonsils and no sign of viral respiratory infection (rhinorrhoea, coryza, conjunctivitis, coughing and/or sneezing) Age range for inclusion: 2 to 13 years
Patient characteristics and setting	Sample size: 376 Age (distribution): not reported

dos Santos 2005 (Continued)

GAS prevalence according to culture (with 95% confidence interval): 24.5%
 (95% CI not reported)
 Country of study: Brazil
 Sex (% of girls): 54%
 Clinical severity assessment: none
 Clinical setting: emergency department
 Single-centre study

Index tests	Throat swab: 1 double swab (1 swab for the RADT, 1 swab for culture) Commercial name of the RADT: QuickVue Plus Strep A (Quidel) Type of RADT: EIA
Target condition and reference standard(s)	Throat culture medium: standard Atmosphere of incubation: aerobic Duration of incubation: 48 hours GAS confirmation: bacitracin disk (and PYR test) Number of plates inoculated: 1 Assessment of GAS antibody response: no Relevant details: -
Flow and timing	No follow-up
Comparative	
Type of study	Journal article
Notes	The first author received public funding (Coordination for the Improvement of Higher Education Personnel, Brazilian Ministry of Higher Education)

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient Selection			
Was a consecutive or random sample of patients enrolled?	Yes		
Was it a cross-sectional study or a RCT?	Yes		
Were selection criteria clearly described (at least presenting signs and symptoms and age limits for inclusion)?	Yes		
Was clinical selection of patients avoided?	No		
Were patients seen in an ambulatory care setting?	Yes		
		High	High
DOMAIN 2: Index Test All tests			
Were the RADT results interpreted with blinding of the results of culture?	Yes		
Was the type of the RADT mentioned (EIA or OIA)?	Yes		

dos Santos 2005 (Continued)

Were RADTs conducted during consultation time?	Yes		
		Low	Low
DOMAIN 3: Reference Standard			
Were culture results interpreted with blinding of the results of the RADT?	Unclear		
Is the throat culture method likely to correctly identify GAS (laboratory culture on a blood agar plate during 48 hr)?	Yes		
Were the culture medium, atmosphere, duration of incubation and GAS-confirmation technique described?	Yes		
		Unclear	Low
DOMAIN 4: Flow and Timing			
Was the delay between the performance of the RADT and throat culture plating less than 48 hours?	Unclear		
Did all patients receive a throat culture?	Yes		
Did patients receive the same throat culture method?	Yes		
Were undetermined/uninterpretable results reported?	Yes		
Were withdrawals from the study explained?	Yes		
		Low	

Drulak 1988

Study characteristics	
Patient sampling	Cross-sectional study Prospective design Sample: unclear Direct comparison of different RADTs: no Direct comparison of several throat culture techniques: no Person performing the throat sample: other ("staff") Exclusion if recent antibiotics use before inclusion: no Clinical selection of patients: none Presenting signs and symptoms: pharyngitis Age range for inclusion: < 18 years
Patient characteristics and setting	Sample size: 280 Age (distribution): not reported

Drulak 1988 (Continued)

GAS prevalence according to culture (with 95% confidence interval): 20.4% (95% CI not reported)
 Country of study: Canada
 Sex (% of girls): not reported
 Clinical severity assessment: none
 Clinical setting: outpatient clinic ("outpatient department of a large paediatric institution")
 Single-centre study

Index tests	Throat swab: 1 double swab (1 swab for the RADT, 1 swab for culture) Commercial name of the RADT: Visuwel Strep A (ADI) Type of RADT: EIA
Target condition and reference standard(s)	Throat culture medium: standard Atmosphere of incubation: anaerobic during 24 hours then aerobic with CO ₂ enrichment during 24 hours Duration of incubation: 48 hours GAS confirmation: other (capillary tube precipitation) Number of plates inoculated: 1 Assessment of GAS antibody response: no Relevant details: -
Flow and timing	No follow-up
Comparative	
Type of study	Journal article
Notes	The study had 2 parts: 1 with adults and children (n = 585), the second with children only (n = 280). The data used for this systematic review were restricted to the second part because paediatric data were not extractable from the first part of the study Study conducted by the manufacturer of the RADT under investigation (Visuwel, ADI)

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient Selection			
Was a consecutive or random sample of patients enrolled?	Unclear		
Was it a cross-sectional study or a RCT?	Yes		
Were selection criteria clearly described (at least presenting signs and symptoms and age limits for inclusion)?	Yes		
Was clinical selection of patients avoided?	Yes		
Were patients seen in an ambulatory care setting?	Yes		
		Low	Low

Drulak 1988 (Continued)

DOMAIN 2: Index Test All tests

Were the RADT results interpreted with blinding of the results of culture?	Yes		
Was the type of the RADT mentioned (EIA or OIA)?	Yes		
Were RADTs conducted during consultation time?	No		
		Low	High

DOMAIN 3: Reference Standard

Were culture results interpreted with blinding of the results of the RADT?	Unclear		
Is the throat culture method likely to correctly identify GAS (laboratory culture on a blood agar plate during 48 hr)?	Yes		
Were the culture medium, atmosphere, duration of incubation and GAS-confirmation technique described?	Yes		
		Unclear	Low

DOMAIN 4: Flow and Timing

Was the delay between the performance of the RADT and throat culture plating less than 48 hours?	Unclear		
Did all patients receive a throat culture?	Yes		
Did patients receive the same throat culture method?	Yes		
Were undetermined/uninterpretable results reported?	No		
Were withdrawals from the study explained?	Yes		
		Low	

Drulak 1991
Study characteristics

Patient sampling	Cross-sectional study Prospective design Sample: unclear Direct comparison of different RADTs: no Direct comparison of several throat culture techniques: no Person performing the throat sample: not reported Exclusion if recent antibiotics use before inclusion: no
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Drulak 1991 (Continued)

	Clinical selection of patients: none
	Presenting signs and symptoms: pharyngitis
	Age range for inclusion: < 18 years
Patient characteristics and setting	Sample size: 202 Age (distribution): not reported GAS prevalence according to culture (with 95% confidence interval): 26.7% (95% CI not reported) Country of study: USA Sex (% of girls): not reported Clinical severity assessment: none Clinical setting: outpatient clinic Single-centre study
Index tests	Throat swab: 1 swab (used for culture and then for the RADT) Commercial name of the RADT: Visuwell Strep A Type of RADT: EIA
Target condition and reference standard(s)	Throat culture medium: standard Atmosphere of incubation: aerobic with CO ₂ enrichment Duration of incubation: 24 hours GAS confirmation: bacitracin disk followed by latex test Number of plates inoculated: unclear Assessment of GAS antibody response: no Relevant details: -
Flow and timing	No follow-up
Comparative	
Type of study	Journal article
Notes	First and last author affiliated with the manufacturer. We thank Dr M Drulak for sharing unpublished paediatric data

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient Selection			
Was a consecutive or random sample of patients enrolled?	Unclear		
Was it a cross-sectional study or a RCT?	Yes		
Were selection criteria clearly described (at least presenting signs and symptoms and age limits for inclusion)?	Yes		
Was clinical selection of patients avoided?	Yes		
Were patients seen in an ambulatory care setting?	Yes		
		Low	Low

Drulak 1991 (Continued)

DOMAIN 2: Index Test All tests

Were the RADT results interpreted with blinding of the results of culture?	Unclear		
Was the type of the RADT mentioned (EIA or OIA)?	Yes		
Were RADTs conducted during consultation time?	No		
		Unclear	High

DOMAIN 3: Reference Standard

Were culture results interpreted with blinding of the results of the RADT?	Unclear		
Is the throat culture method likely to correctly identify GAS (laboratory culture on a blood agar plate during 48 hr)?	No		
Were the culture medium, atmosphere, duration of incubation and GAS-confirmation technique described?	Yes		
		High	High

DOMAIN 4: Flow and Timing

Was the delay between the performance of the RADT and throat culture plating less than 48 hours?	Unclear		
Did all patients receive a throat culture?	Yes		
Did patients receive the same throat culture method?	Yes		
Were undetermined/uninterpretable results reported?	No		
Were withdrawals from the study explained?	Yes		
		Low	

Edmonson 2005
Study characteristics

Patient sampling	Cross-sectional study Retrospective design Sample: consecutive Direct comparison of different RADTs: no Direct comparison of several throat culture techniques: no Person performing the throat sample: unclear Exclusion if recent antibiotics use before inclusion: no (exclusion only if current antimicrobial therapy) Clinical selection of patients: patients enrolled retrospectively if they had a diagnostic test to detect GAS
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Edmonson 2005 (Continued)

	Presenting signs and symptoms: n/a (see above)
	Age range for inclusion: < 24 years
Patient characteristics and setting	Sample size: 1184 Age (distribution): 63% between 5 and 15 years of age GAS prevalence according to culture (with 95% confidence interval): 38% (95% CI 35 to 41) Country of study: USA Sex (% of girls): 53% Clinical severity assessment: McIsaac score Clinical setting: walk-in clinic Single-centre study
Index tests	Throat swab: 1 single swab for culture and then for the RADT during first 11 months then 1 double swab (1 swab for the RADT, 1 swab for culture) Commercial name of the RADT: CARDS QS Strep A (Quidel) Type of RADT: EIA
Target condition and reference standard(s)	Throat culture medium: standard Atmosphere of incubation: anaerobic Duration of incubation: 48 hours GAS confirmation: latex test Number of plates inoculated: 1 Assessment of GAS antibody response: no Relevant details: -
Flow and timing	No follow-up
Comparative	
Type of study	Journal article
Notes	Throat culture performed only for children with negative RADT results (partial verification)

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient Selection			
Was a consecutive or random sample of patients enrolled?	Yes		
Was it a cross-sectional study or a RCT?	Yes		
Were selection criteria clearly described (at least presenting signs and symptoms and age limits for inclusion)?	No		
Was clinical selection of patients avoided?	Unclear		
Were patients seen in an ambulatory care setting?	Yes		
		High	Unclear

Edmonson 2005 (Continued)

DOMAIN 2: Index Test All tests

Were the RADT results interpreted with blinding of the results of culture?	Yes		
Was the type of the RADT mentioned (EIA or OIA)?	Yes		
Were RADTs conducted during consultation time?	Yes		
		Low	Low

DOMAIN 3: Reference Standard

Were culture results interpreted with blinding of the results of the RADT?	Yes		
Is the throat culture method likely to correctly identify GAS (laboratory culture on a blood agar plate during 48 hr)?	Yes		
Were the culture medium, atmosphere, duration of incubation and GAS-confirmation technique described?	Yes		
		Low	Low

DOMAIN 4: Flow and Timing

Was the delay between the performance of the RADT and throat culture plating less than 48 hours?	Unclear		
Did all patients receive a throat culture?	No		
Did patients receive the same throat culture method?	Yes		
Were undetermined/uninterpretable results reported?	Yes		
Were withdrawals from the study explained?	Yes		
		High	

Egger 1990a
Study characteristics

Patient sampling	Cross-sectional study Prospective design Sample: unclear Direct comparison of different RADTs: yes Direct comparison of several throat culture techniques: no Person performing the throat sample: not reported Exclusion if recent antibiotics use before inclusion: no Clinical selection of patients: none Presenting signs and symptoms: clinical pharyngitis
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Egger 1990a (Continued)

	Age range for inclusion: not reported ("children")
Patient characteristics and setting	Sample size: 579 Age (distribution): range 9 months to 14 years 1 month GAS prevalence according to culture (with 95% confidence interval): 19.0% (95% CI not reported) Country of study: Switzerland Sex (% of girls): not reported Clinical severity assessment: none Clinical setting: walk-in clinic Single-centre study
Index tests	Throat swab: 2 different swabs (1 swab for the RADT, 1 swab for culture) Commercial name of the RADTs: Test Pack Strep A Type of RADTs: EIA
Target condition and reference standard(s)	Throat culture medium: standard Atmosphere of incubation: anaerobic during 24 hours and if negative reincubated during 24 hours in CO ₂ enriched atmosphere Duration of incubation: 48 hours GAS confirmation: latex test Number of plates inoculated: 1 Assessment of GAS antibody response: no Relevant details: -
Flow and timing	No follow-up
Comparative	
Type of study	Journal article
Notes	Supported by grants from the manufacturers of the RADTs (Abbott and Hoffmann-La Roche)

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient Selection			
Was a consecutive or random sample of patients enrolled?	Unclear		
Was it a cross-sectional study or a RCT?	Yes		
Were selection criteria clearly described (at least presenting signs and symptoms and age limits for inclusion)?	No		
Was clinical selection of patients avoided?	Yes		
Were patients seen in an ambulatory care setting?	Yes		
		High	High

DOMAIN 2: Index Test All tests

Egger 1990a (Continued)

Were the RADT results interpreted with blinding of the results of culture?	Yes	
Was the type of the RADT mentioned (EIA or OIA)?	Yes	
Were RADTs conducted during consultation time?	No	
		Low High

DOMAIN 3: Reference Standard

Were culture results interpreted with blinding of the results of the RADT?	Unclear	
Is the throat culture method likely to correctly identify GAS (laboratory culture on a blood agar plate during 48 hr)?	Yes	
Were the culture medium, atmosphere, duration of incubation and GAS-confirmation technique described?	Yes	
		Unclear Low

DOMAIN 4: Flow and Timing

Was the delay between the performance of the RADT and throat culture plating less than 48 hours?	No	
Did all patients receive a throat culture?	Yes	
Did patients receive the same throat culture method?	Yes	
Were undetermined/uninterpretable results reported?	Yes	
Were withdrawals from the study explained?	Yes	
		Low

Egger 1990b
Study characteristics

Patient sampling	See Egger 1990a
Patient characteristics and setting	See Egger 1990a
Index tests	Throat swab: 2 different swabs (1 swab for the RADT, 1 swab for culture) Commercial name of the RADTs: Direct Strep A Type of RADTs: EIA
Target condition and reference standard(s)	See Egger 1990a
Flow and timing	No follow-up

Egger 1990b (Continued)

Comparative

Type of study	Journal article
Notes	Supported by grants from the manufacturers of the RADTs (Abbott and Hoffmann-La Roche)

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient Selection			
Was a consecutive or random sample of patients enrolled?	Unclear		
Was it a cross-sectional study or a RCT?	Yes		
Were selection criteria clearly described (at least presenting signs and symptoms and age limits for inclusion)?	No		
Was clinical selection of patients avoided?	Yes		
Were patients seen in an ambulatory care setting?	Yes		
		High	High
DOMAIN 2: Index Test All tests			
Were the RADT results interpreted with blinding of the results of culture?	Yes		
Was the type of the RADT mentioned (EIA or OIA)?	Yes		
Were RADTs conducted during consultation time?	No		
		Low	High
DOMAIN 3: Reference Standard			
Were culture results interpreted with blinding of the results of the RADT?	Unclear		
Is the throat culture method likely to correctly identify GAS (laboratory culture on a blood agar plate during 48 hr)?	Yes		
Were the culture medium, atmosphere, duration of incubation and GAS-confirmation technique described?	Yes		
		Unclear	Low
DOMAIN 4: Flow and Timing			
Was the delay between the performance of the RADT and throat culture plating less than 48 hours?	No		

Egger 1990b *(Continued)*

Did all patients receive a throat culture?	Yes
Did patients receive the same throat culture method?	Yes
Were undetermined/uninterpretable results reported?	Yes
Were withdrawals from the study explained?	Yes
Low	

Enright 2011
Study characteristics

Patient sampling	Cross-sectional study Prospective design Sample: unclear Direct comparison of different RADTs: no Direct comparison of several throat culture techniques: no Person performing the throat sample: nurse Exclusion if recent antibiotics use before inclusion: no Clinical selection of patients: none Presenting signs and symptoms: presentation consistent with symptomatic pharyngitis Age range for inclusion: 0 to 13 years
Patient characteristics and setting	Sample size: 177 Age (distribution): not reported GAS prevalence according to culture (with 95% confidence interval): 21.5% (95% CI not reported) Country of study: Scotland Sex (% of girls): not reported Clinical severity assessment: none Clinical setting: emergency department Single-centre study
Index tests	Throat swab: 2 different swabs (1 swab for the RADT, 1 swab for culture) Commercial name of the RADT: QuickVue In-Line Strep A (Quidel) Type of RADT: EIA
Target condition and reference standard(s)	Throat culture medium: not reported Atmosphere of incubation: not reported Duration of incubation: not reported GAS confirmation: not reported Number of plates inoculated: not reported Assessment of GAS antibody response: no Relevant details: throat culture technique not described
Flow and timing	No follow-up

Enright 2011 (Continued)

Comparative

Type of study	Journal article		
Notes	No specific funding reported but the RADTs were made available by the manufacturer (Quidel)		
Methodological quality			
Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient Selection			
Was a consecutive or random sample of patients enrolled?	Unclear		
Was it a cross-sectional study or a RCT?	Yes		
Were selection criteria clearly described (at least presenting signs and symptoms and age limits for inclusion)?	Yes		
Was clinical selection of patients avoided?	Yes		
Were patients seen in an ambulatory care setting?	Yes		
		Low	Low
DOMAIN 2: Index Test All tests			
Were the RADT results interpreted with blinding of the results of culture?	Yes		
Was the type of the RADT mentioned (EIA or OIA)?	Yes		
Were RADTs conducted during consultation time?	Yes		
		Low	Low
DOMAIN 3: Reference Standard			
Were culture results interpreted with blinding of the results of the RADT?	Unclear		
Is the throat culture method likely to correctly identify GAS (laboratory culture on a blood agar plate during 48 hr)?	Unclear		
Were the culture medium, atmosphere, duration of incubation and GAS-confirmation technique described?	No		
		High	High
DOMAIN 4: Flow and Timing			
Was the delay between the performance of the RADT and throat culture plating less than 48 hours?	Unclear		

Enright 2011 (Continued)

Did all patients receive a throat culture?	Yes
Did patients receive the same throat culture method?	Yes
Were undetermined/uninterpretable results reported?	Yes
Were withdrawals from the study explained?	Yes
Low	

Ezike 2005
Study characteristics

Patient sampling	<p>Cross-sectional study Prospective design Sample: convenience Direct comparison of different RADTs: no Direct comparison of several throat culture techniques: no Person performing the throat sample: physician</p> <p>Exclusion if recent antibiotics use before inclusion: yes</p> <p>Clinical selection of patients: explicit criteria but not a score (see below)</p> <p>Presenting signs and symptoms: acute pharyngitis without rhinorrhoea or conjunctivitis (considered suggestive of viral infection)</p> <p>Age range for inclusion: 5 to 18 years</p>
Patient characteristics and setting	<p>Sample size: 186 (group 2) Age (distribution): mean (SD) = 9.9 (3.7) years</p> <p>GAS prevalence according to culture (with 95% confidence interval): 42.5% (95% CI not reported) Country of study: USA Sex (% of girls): not reported Clinical severity assessment: McIsaac score Clinical setting: emergency department Single-centre study</p>
Index tests	<p>Throat swab: 2 different swabs</p> <p>Commercial name of the RADT: Strep A OIA MAX Type of RADT: OIA</p>
Target condition and reference standard(s)	<p>Throat culture medium: enrichment Atmosphere of incubation: aerobic with CO₂ enrichment Duration of incubation: 48 hours GAS confirmation: latex test Number of plates inoculated: 1 Assessment of GAS antibody response: no Relevant details: -</p>
Flow and timing	No follow-up
Comparative	

Ezike 2005 (Continued)

Type of study	Journal article
Notes	This study was supported by the Sarnaik Endowment Resident and Fellow Research Fund, Children's Hospital of Michigan, Detroit. Some rapid test kits were provided by Thermo Electron Corporation

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient Selection			
Was a consecutive or random sample of patients enrolled?	No		
Was it a cross-sectional study or a RCT?	Yes		
Were selection criteria clearly described (at least presenting signs and symptoms and age limits for inclusion)?	Yes		
Was clinical selection of patients avoided?	No		
Were patients seen in an ambulatory care setting?	Yes		
		High	High
DOMAIN 2: Index Test All tests			
Were the RADT results interpreted with blinding of the results of culture?	Yes		
Was the type of the RADT mentioned (EIA or OIA)?	Yes		
Were RADTs conducted during consultation time?	No		
		Low	High
DOMAIN 3: Reference Standard			
Were culture results interpreted with blinding of the results of the RADT?	Unclear		
Is the throat culture method likely to correctly identify GAS (laboratory culture on a blood agar plate during 48 hr)?	Yes		
Were the culture medium, atmosphere, duration of incubation and GAS-confirmation technique described?	Yes		
		Low	Low
DOMAIN 4: Flow and Timing			
Was the delay between the performance of the RADT and throat culture plating less than 48 hours?	Yes		

Ezike 2005 *(Continued)*

Did all patients receive a throat culture?	Yes
Did patients receive the same throat culture method?	Yes
Were undetermined/uninterpretable results reported?	Yes
Were withdrawals from the study explained?	Yes
Low	

Faverge 2004
Study characteristics

Patient sampling	Cross-sectional study Prospective design Sample: unclear Direct comparison of different RADTs: no Direct comparison of several throat culture techniques: no Person performing the throat sample: not reported Exclusion if recent antibiotics use before inclusion: no Clinical selection of patients: unclear Presenting signs and symptoms: not reported Age range for inclusion: not reported ("children")
Patient characteristics and setting	Sample size: 84 Age (distribution): range 7 months to 14 years GAS prevalence according to culture (with 95% confidence interval): 22.6% (95% CI not reported) Country of study: France Sex (% of girls): 42% Clinical severity assessment: none Clinical setting: mixed (paediatric ward, outpatient clinic, emergency department from a general hospital) Single-centre study
Index tests	Throat swab: 2 different swabs Commercial name of the RADT: StreptAtest Type of RADT: EIA
Target condition and reference standard(s)	Throat culture medium: not reported Atmosphere of incubation: not reported Duration of incubation: not reported GAS confirmation: not reported Number of plates inoculated: not reported Assessment of GAS antibody response: no Relevant details: throat culture technique not described
Flow and timing	No follow-up
Comparative	

Faverge 2004 (Continued)

Type of study	Journal article (in French)		
Notes	—		
Methodological quality			
Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient Selection			
Was a consecutive or random sample of patients enrolled?	Unclear		
Was it a cross-sectional study or a RCT?	Yes		
Were selection criteria clearly described (at least presenting signs and symptoms and age limits for inclusion)?	No		
Was clinical selection of patients avoided?	Unclear		
Were patients seen in an ambulatory care setting?	Unclear		
		High	High
DOMAIN 2: Index Test All tests			
Were the RADT results interpreted with blinding of the results of culture?	Yes		
Was the type of the RADT mentioned (EIA or OIA)?	Yes		
Were RADTs conducted during consultation time?	Yes		
		Low	Low
DOMAIN 3: Reference Standard			
Were culture results interpreted with blinding of the results of the RADT?	Unclear		
Is the throat culture method likely to correctly identify GAS (laboratory culture on a blood agar plate during 48 hr)?	Unclear		
Were the culture medium, atmosphere, duration of incubation and GAS-confirmation technique described?	No		
		High	High
DOMAIN 4: Flow and Timing			
Was the delay between the performance of the RADT and throat culture plating less than 48 hours?	Unclear		
Did all patients receive a throat culture?	Yes		
Did patients receive the same throat culture method?	Yes		

Faverge 2004 (Continued)

Were undetermined/uninterpretable results reported?	No
Were withdrawals from the study explained?	No
Low	

Felsenstein 2014
Study characteristics

Patient sampling	<p>Cross-sectional study Retrospective design Sample: unclear Direct comparison of different RADTs: no Direct comparison of several throat culture techniques: no Person performing the throat sample: nurse</p> <p>Exclusion if recent antibiotics use before inclusion: no</p> <p>Clinical selection of patients: none</p> <p>Presenting signs and symptoms: pharyngitis, fever of unknown origin, upper respiratory tract symptoms, or subjective complaints of throat pain or discomfort on swallowing</p> <p>Age range for inclusion: not reported ("paediatric patients")</p>
Patient characteristics and setting	<p>Sample size: 361 Age (distribution): mean (SD) = 7.4 (4.2) years</p> <p>GAS prevalence according to culture (with 95% confidence interval): 16.1% (95% CI not reported) Country of study: USA Sex (% of girls): not reported Clinical severity assessment: Centor and McIsaac scores (only in those with positive throat culture or RADT result) Clinical setting: emergency department Single-centre study</p>
Index tests	<p>Throat swab: 2 different swabs</p> <p>Commercial name of the RADT: OSOM Ultra Strep A Type of RADT: EIA</p>
Target condition and reference standard(s)	<p>Throat culture medium: standard Atmosphere of incubation: aerobic Duration of incubation: 48 hours GAS confirmation: latex test Number of plates inoculated: 1 Assessment of GAS antibody response: no Relevant details: -</p>
Flow and timing	No follow-up
Comparative	
Type of study	Journal article

Felsenstein 2014 (Continued)

Notes

No specific funding reported but the manufacturer of a rapid molecular test also evaluated in the study (illumigene, Meridian Biosciences) supplied assay kits, incubator and reader for the study

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient Selection			
Was a consecutive or random sample of patients enrolled?	Unclear		
Was it a cross-sectional study or a RCT?	Yes		
Were selection criteria clearly described (at least presenting signs and symptoms and age limits for inclusion)?	No		
Was clinical selection of patients avoided?	Yes		
Were patients seen in an ambulatory care setting?	Yes		
		High	Low
DOMAIN 2: Index Test All tests			
Were the RADT results interpreted with blinding of the results of culture?	Yes		
Was the type of the RADT mentioned (EIA or OIA)?	Yes		
Were RADTs conducted during consultation time?	No		
		High	High
DOMAIN 3: Reference Standard			
Were culture results interpreted with blinding of the results of the RADT?	Unclear		
Is the throat culture method likely to correctly identify GAS (laboratory culture on a blood agar plate during 48 hr)?	Yes		
Were the culture medium, atmosphere, duration of incubation and GAS-confirmation technique described?	Yes		
		Unclear	Low
DOMAIN 4: Flow and Timing			
Was the delay between the performance of the RADT and throat culture plating less than 48 hours?	Yes		
Did all patients receive a throat culture?	Yes		

Felsenstein 2014 (Continued)

Did patients receive the same throat culture method?	Yes
Were undetermined/uninterpretable results reported?	No
Were withdrawals from the study explained?	Yes
Low	

Finger 1999
Study characteristics

Patient sampling	<p>Cross-sectional study</p> <p>Prospective design</p> <p>Sample: unclear</p> <p>Direct comparison of different RADTs: no</p> <p>Direct comparison of several throat culture techniques: no</p> <p>Person performing the throat sample: unclear</p> <p>Exclusion if recent antibiotics use before inclusion: no</p> <p>Clinical selection of patients: none</p> <p>Presenting signs and symptoms: complaint of sore throat with at least one sign of pharyngitis (redness of throat, purulent exudate in throat, or anterior cervical lymphadenopathy)</p> <p>Age range for inclusion: 3 to 16 years</p>
Patient characteristics and setting	<p>Sample size: 777</p> <p>Age (distribution): not reported</p> <p>GAS prevalence according to culture (with 95% confidence interval): 30.8% (95% CI not reported)</p> <p>Country of study: Vietnam</p> <p>Sex (% of girls): not reported</p> <p>Clinical severity assessment: none</p> <p>Clinical setting: mixed (emergency department and outpatient clinics)</p> <p>Multi-centre study</p>
Index tests	<p>Throat swab: 2 different swabs (1 swab for the RADT, 1 swab for culture)</p> <p>Commercial name of the RADT: QuickVue Flex Strep A (Quidel)</p> <p>Type of RADT: EIA</p>
Target condition and reference standard(s)	<p>Throat culture medium: standard</p> <p>Atmosphere of incubation: not reported</p> <p>Duration of incubation: 48 hours</p> <p>GAS confirmation: bacitracin disk</p> <p>Number of plates inoculated: 1</p> <p>Assessment of GAS antibody response: no</p> <p>Relevant details: during the first half of the study, the laboratory investigators read cultures with knowledge of the result of the RADT</p>
Flow and timing	No follow-up

Finger 1999 (Continued)

Comparative

Type of study	Journal article		
Notes	No specific funding reported but the manufacturer of the RADT (Quidel) provided the RADTs		
Methodological quality			
Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient Selection			
Was a consecutive or random sample of patients enrolled?	Unclear		
Was it a cross-sectional study or a RCT?	Yes		
Were selection criteria clearly described (at least presenting signs and symptoms and age limits for inclusion)?	Yes		
Was clinical selection of patients avoided?	Yes		
Were patients seen in an ambulatory care setting?	Yes		
		Low	Low
DOMAIN 2: Index Test All tests			
Were the RADT results interpreted with blinding of the results of culture?	Yes		
Was the type of the RADT mentioned (EIA or OIA)?	Yes		
Were RADTs conducted during consultation time?	Yes		
		Low	Low
DOMAIN 3: Reference Standard			
Were culture results interpreted with blinding of the results of the RADT?	Yes		
Is the throat culture method likely to correctly identify GAS (laboratory culture on a blood agar plate during 48 hr)?	Yes		
Were the culture medium, atmosphere, duration of incubation and GAS-confirmation technique described?	No		
		High	High
DOMAIN 4: Flow and Timing			

Finger 1999 (Continued)

Was the delay between the performance of the RADT and throat culture plating less than 48 hours?	Yes
Did all patients receive a throat culture?	Yes
Did patients receive the same throat culture method?	Yes
Were undetermined/uninterpretable results reported?	No
Were withdrawals from the study explained?	No
Low	

Flores Mateo 2010
Study characteristics

Patient sampling	<p>Cross-sectional study Prospective design Sample: consecutive Direct comparison of different RADTs: no Direct comparison of several throat culture techniques: no Person performing the throat sample: physicians</p> <p>Exclusion if recent antibiotics use before inclusion: yes (within 15 days before enrollment)</p> <p>Clinical selection of patients: none</p> <p>Presenting signs and symptoms: sore throat for less than 5 days</p> <p>Age range for inclusion: 1 to 14 years</p>
Patient characteristics and setting	<p>Sample size: 211 Age (distribution): mean (SD) = 6.6 (3.8) years</p> <p>GAS prevalence according to culture (with 95% confidence interval): 34.1% (95% CI not reported) Country of study: Spain Sex (% of girls): 55.8% Clinical severity assessment: McIsaac score Clinical setting: walk-in clinic Multi-centre study</p>
Index tests	<p>Throat swab: 2 different swabs (1 swab for the RADT, 1 swab for culture)</p> <p>Commercial name of the RADT: OSOM Strep A (Gemzyme) Type of RADT: EIA</p>
Target condition and reference standard(s)	<p>Throat culture medium: standard Atmosphere of incubation: aerobic with CO₂ enrichment Duration of incubation: 48 hours GAS confirmation: bacitracin disk and latex test</p> <p>Number of plates inoculated: 1 Assessment of GAS antibody response: no</p>

Flores Mateo 2010 (Continued)

Relevant details: -

Flow and timing	No follow-up
Comparative	
Type of study	Journal article (in Spanish)
Notes	—

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient Selection			
Was a consecutive or random sample of patients enrolled?	Yes		
Was it a cross-sectional study or a RCT?	Yes		
Were selection criteria clearly described (at least presenting signs and symptoms and age limits for inclusion)?	Yes		
Was clinical selection of patients avoided?	Yes		
Were patients seen in an ambulatory care setting?	Yes		
		Low	Low
DOMAIN 2: Index Test All tests			
Were the RADT results interpreted with blinding of the results of culture?	Yes		
Was the type of the RADT mentioned (EIA or OIA)?	Yes		
Were RADTs conducted during consultation time?	Yes		
		Low	Low
DOMAIN 3: Reference Standard			
Were culture results interpreted with blinding of the results of the RADT?	Unclear		
Is the throat culture method likely to correctly identify GAS (laboratory culture on a blood agar plate during 48 hr)?	Yes		
Were the culture medium, atmosphere, duration of incubation and GAS-confirmation technique described?	Yes		
		Unclear	Low
DOMAIN 4: Flow and Timing			

Flores Mateo 2010 *(Continued)*

Was the delay between the performance of the RADT and throat culture plating less than 48 hours?	Unclear
Did all patients receive a throat culture?	Yes
Did patients receive the same throat culture method?	Yes
Were undetermined/uninterpretable results reported?	No
Were withdrawals from the study explained?	Yes
Low	

Forward 2006
Study characteristics

Patient sampling	Cross-sectional study Prospective design Sample: unclear Direct comparison of different RADTs: no Direct comparison of several throat culture techniques: no Person performing the throat sample: not reported Exclusion if recent antibiotics use before inclusion: no Clinical selection of patients: none Presenting signs and symptoms: not reported ("pharyngeal swabs received from children") Age range for inclusion: < 16 years
Patient characteristics and setting	Sample size: 490 Age (distribution): not reported GAS prevalence according to culture (with 95% confidence interval): 24.1% (95% CI not reported) Country of study: Canada Sex (% of girls): not reported Clinical severity assessment: none Clinical setting: unclear (laboratory study) Single-centre study
Index tests	Throat swab: 1 single swab (used for culture and then for the RADT) Commercial name of the RADT: Strep A Rapid test Device Type of RADT: EIA
Target condition and reference standard(s)	Throat culture medium: standard Atmosphere of incubation: anaerobic Duration of incubation: 48 hours GAS confirmation: PYR test Number of plates inoculated: 1 Assessment of GAS antibody response: no Relevant details: -

Forward 2006 (Continued)

Flow and timing	No follow-up
Comparative	
Type of study	Journal article
Notes	—

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient Selection			
Was a consecutive or random sample of patients enrolled?	Unclear		
Was it a cross-sectional study or a RCT?	Yes		
Were selection criteria clearly described (at least presenting signs and symptoms and age limits for inclusion)?	No		
Was clinical selection of patients avoided?	Unclear		
Were patients seen in an ambulatory care setting?	Unclear		
		High	Unclear
DOMAIN 2: Index Test All tests			
Were the RADT results interpreted with blinding of the results of culture?	Unclear		
Was the type of the RADT mentioned (EIA or OIA)?	Yes		
Were RADTs conducted during consultation time?	No		
		Unclear	High
DOMAIN 3: Reference Standard			
Were culture results interpreted with blinding of the results of the RADT?	Unclear		
Is the throat culture method likely to correctly identify GAS (laboratory culture on a blood agar plate during 48 hr)?	Yes		
Were the culture medium, atmosphere, duration of incubation and GAS-confirmation technique described?	Yes		
		Unclear	Low
DOMAIN 4: Flow and Timing			
Was the delay between the performance of the RADT and throat culture plating less than 48 hours?	Unclear		

Forward 2006 *(Continued)*

Did all patients receive a throat culture?	Yes
Did patients receive the same throat culture method?	Yes
Were undetermined/uninterpretable results reported?	No
Were withdrawals from the study explained?	Yes
Low	

Fourati 2009
Study characteristics

Patient sampling	Cross-sectional study Prospective design Sample: unclear Direct comparison of different RADTs: no Direct comparison of several throat culture techniques: no Person performing the throat sample: not reported Exclusion if recent antibiotics use before inclusion: no Clinical selection of patients: none Presenting signs and symptoms: pharyngotonsillitis Age range for inclusion: not reported ("children")
Patient characteristics and setting	Sample size: 292 Age (distribution): mean (SD) = 6.7 (3.5) years GAS prevalence according to culture (with 95% confidence interval): 20.2% (95% CI not reported) Country of study: Tunisia Sex (% of girls): 39% Clinical severity assessment: none Clinical setting: mixed (emergency department and walk-in clinics) Multi-centre study
Index tests	Throat swab: 2 different swabs (1 swab for the RADT, 1 swab for culture) Commercial name of the RADT: Streptop A (ALL-Diag) Type of RADT: EIA
Target condition and reference standard(s)	Throat culture medium: standard Atmosphere of incubation: aerobic with CO ₂ enrichment Duration of incubation: 24 hours GAS confirmation: not reported Number of plates inoculated: 1 Assessment of GAS antibody response: no Relevant details: -
Flow and timing	No follow-up
Comparative	

Fourati 2009 (Continued)

Type of study	Journal article (in French)		
Notes	—		
Methodological quality			
Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient Selection			
Was a consecutive or random sample of patients enrolled?	Unclear		
Was it a cross-sectional study or a RCT?	Yes		
Were selection criteria clearly described (at least presenting signs and symptoms and age limits for inclusion)?	No		
Was clinical selection of patients avoided?	Yes		
Were patients seen in an ambulatory care setting?	Yes		
		High	Low
DOMAIN 2: Index Test All tests			
Were the RADT results interpreted with blinding of the results of culture?	Unclear		
Was the type of the RADT mentioned (EIA or OIA)?	Yes		
Were RADTs conducted during consultation time?	No		
		Unclear	High
DOMAIN 3: Reference Standard			
Were culture results interpreted with blinding of the results of the RADT?	Unclear		
Is the throat culture method likely to correctly identify GAS (laboratory culture on a blood agar plate during 48 hr)?	No		
Were the culture medium, atmosphere, duration of incubation and GAS-confirmation technique described?	No		
		High	High
DOMAIN 4: Flow and Timing			
Was the delay between the performance of the RADT and throat culture plating less than 48 hours?	Unclear		
Did all patients receive a throat culture?	Yes		
Did patients receive the same throat culture method?	Yes		

Fourati 2009 (Continued)

Were undetermined/uninterpretable results reported?	No
Were withdrawals from the study explained?	Yes
Low	

Gerber 1990
Study characteristics

Patient sampling	Cross-sectional study Prospective design Sample: consecutive Direct comparison of different RADTs: no Direct comparison of several throat culture techniques: no Person performing the throat sample: not reported Exclusion if recent antibiotics use before inclusion: no Clinical selection of patients: implicit criteria (see below) Presenting signs and symptoms: "clinical findings suggestive of GA(BH)S pharyngitis" Age range for inclusion: not reported ("private pediatric practice")
Patient characteristics and setting	Sample size: 228 Age (distribution): not reported GAS prevalence according to culture (with 95% confidence interval): 59.2% (95% CI not reported) Country of study: USA Sex (% of girls): not reported Clinical severity assessment: none Clinical setting: office-based Single-centre study
Index tests	Throat swab: 2 different swabs (1 swab for the RADT, 1 swab for culture) Commercial name of the RADT: QTest Strep (Becton Dickinson) Type of RADT: EIA (liposomal assay)
Target condition and reference standard(s)	Throat culture medium: standard Atmosphere of incubation: aerobic Duration of incubation: 48 hours GAS confirmation: bacitracin disk and latex test Number of plates inoculated: 1 Assessment of GAS antibody response: no Relevant details: -
Flow and timing	No follow-up
Comparative	
Type of study	Journal article

Gerber 1990 (Continued)

Notes —

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient Selection			
Was a consecutive or random sample of patients enrolled?	Yes		
Was it a cross-sectional study or a RCT?	Yes		
Were selection criteria clearly described (at least presenting signs and symptoms and age limits for inclusion)?	No		
Was clinical selection of patients avoided?	No		
Were patients seen in an ambulatory care setting?	Yes		
		High	High
DOMAIN 2: Index Test All tests			
Were the RADT results interpreted with blinding of the results of culture?	Yes		
Was the type of the RADT mentioned (EIA or OIA)?	Yes		
Were RADTs conducted during consultation time?	Yes		
		Low	Low
DOMAIN 3: Reference Standard			
Were culture results interpreted with blinding of the results of the RADT?	Unclear		
Is the throat culture method likely to correctly identify GAS (laboratory culture on a blood agar plate during 48 hr)?	Yes		
Were the culture medium, atmosphere, duration of incubation and GAS-confirmation technique described?	Yes		
		Unclear	Low
DOMAIN 4: Flow and Timing			
Was the delay between the performance of the RADT and throat culture plating less than 48 hours?	Yes		
Did all patients receive a throat culture?	Yes		
Did patients receive the same throat culture method?	Yes		
Were undetermined/uninterpretable results reported?	No		

Gerber 1990 (Continued)

Were withdrawals from the study explained? No

Low

Gerber 1997
Study characteristics

Patient sampling	<p>Cross-sectional study Prospective design Sample: consecutive Direct comparison of different RADTs: no Direct comparison of several throat culture techniques: yes Person performing the throat sample: unclear</p> <p>Exclusion if recent antibiotics use before inclusion: no</p> <p>Clinical selection of patients: none</p> <p>Presenting signs and symptoms: acute pharyngitis</p> <p>Age range for inclusion: not reported ("children")</p>
Patient characteristics and setting	<p>Sample size: 2113 Age (distribution): not reported</p> <p>GAS prevalence according to culture (with 95% confidence interval): 47.6% (95% CI not reported) Country of study: USA Sex (% of girls): not reported Clinical severity assessment: none Clinical setting: office-based Multi-centre study</p>
Index tests	<p>Throat swab: 1 single swab (used for culture and then for the RADT)</p> <p>Commercial name of the RADT: Strep A OIA (Biostar) Type of RADT: OIA</p>
Target condition and reference standard(s)	<p>Throat culture medium: standard culture and culture following incubation in a Todd-Hewitt enrichment broth Atmosphere of incubation: aerobic Duration of incubation: 48 hours GAS confirmation: bacitracin disk +/- latex test Number of plates inoculated: 2 Assessment of GAS antibody response: no Relevant details: composite reference standard (office standard culture + laboratory enriched culture). Office tests (culture and RADT) were reviewed in the laboratory. The same swab was used for multiple purposes (office culture, RADT and lab culture).</p>
Flow and timing	No follow-up
Comparative	
Type of study	Journal article

Gerber 1997 (Continued)

Notes

Supported by a grant from Biostar (manufacturer of the RADT)

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient Selection			
Was a consecutive or random sample of patients enrolled?	Yes		
Was it a cross-sectional study or a RCT?	Yes		
Were selection criteria clearly described (at least presenting signs and symptoms and age limits for inclusion)?	No		
Was clinical selection of patients avoided?	Yes		
Were patients seen in an ambulatory care setting?	Yes		
		High	High
DOMAIN 2: Index Test All tests			
Were the RADT results interpreted with blinding of the results of culture?	Yes		
Was the type of the RADT mentioned (EIA or OIA)?	Yes		
Were RADTs conducted during consultation time?	No		
		Low	High
DOMAIN 3: Reference Standard			
Were culture results interpreted with blinding of the results of the RADT?	Unclear		
Is the throat culture method likely to correctly identify GAS (laboratory culture on a blood agar plate during 48 hr)?	Yes		
Were the culture medium, atmosphere, duration of incubation and GAS-confirmation technique described?	Yes		
		High	High
DOMAIN 4: Flow and Timing			
Was the delay between the performance of the RADT and throat culture plating less than 48 hours?	Unclear		
Did all patients receive a throat culture?	Yes		
Did patients receive the same throat culture method?	Yes		

Gerber 1997 (Continued)

Were undetermined/uninterpretable results reported?	No
Were withdrawals from the study explained?	Yes
Low	

Gieseke 2002a
Study characteristics

Patient sampling	<p>Cross-sectional study Prospective design Sample: unclear Direct comparison of different RADTs: yes Direct comparison of several throat culture techniques: yes Person performing the throat sample: unclear</p> <p>Exclusion if recent antibiotics use before inclusion: no</p> <p>Clinical selection of patients: implicit criteria ("children suspected of having <i>S. pyogenes</i> pharyngitis")</p> <p>Presenting signs and symptoms: not reported</p> <p>Age range for inclusion: not reported ("children")</p>
Patient characteristics and setting	<p>Sample size: 302 Age (distribution): not reported</p> <p>GAS prevalence according to culture (with 95% confidence interval): 28.8% (plate 1) Country of study: USA Sex (% of girls): not reported Clinical severity assessment: none Clinical setting: mixed (child health clinic and emergency department) Multi-centre study</p>
Index tests	<p>Throat swab: 2 different swabs</p> <p>Commercial name of the RADTs: Strep A OIA Max (Biostar) Type of RADTs: OIA</p>
Target condition and reference standard(s)	<p>Throat culture medium: inhibitory Atmosphere of incubation: aerobic with CO₂ enrichment Duration of incubation: 48 hours GAS confirmation: latex test Number of plates inoculated: 4 Assessment of GAS antibody response: no</p> <p>Relevant details: the study used a composite reference standard relying on 4 media plated for each culture but we only extracted the data corresponding to the "same swab single plate standard", i.e., single inhibitory plate using the same swab first for culture and then for performing the RADT. This standard may resemble what is used in practice in most settings.</p>
Flow and timing	No follow-up

Gieseke 2002a (Continued)

Comparative

Type of study	Journal article
Notes	Supported by a grant from one of the manufacturers of the RADTs under evaluation (Genzyme)

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient Selection			
Was a consecutive or random sample of patients enrolled?	Unclear		
Was it a cross-sectional study or a RCT?	Yes		
Were selection criteria clearly described (at least presenting signs and symptoms and age limits for inclusion)?	No		
Was clinical selection of patients avoided?	No		
Were patients seen in an ambulatory care setting?	Yes		
		High	High
DOMAIN 2: Index Test All tests			
Were the RADT results interpreted with blinding of the results of culture?	Yes		
Was the type of the RADT mentioned (EIA or OIA)?	Yes		
Were RADTs conducted during consultation time?	No		
		Low	High
DOMAIN 3: Reference Standard			
Were culture results interpreted with blinding of the results of the RADT?	Unclear		
Is the throat culture method likely to correctly identify GAS (laboratory culture on a blood agar plate during 48 hr)?	Yes		
Were the culture medium, atmosphere, duration of incubation and GAS-confirmation technique described?	Yes		
		Unclear	Low
DOMAIN 4: Flow and Timing			

Gieseke 2002a *(Continued)*

Was the delay between the performance of the RADT and throat culture plating less than 48 hours?	No
Did all patients receive a throat culture?	Yes
Did patients receive the same throat culture method?	Yes
Were undetermined/uninterpretable results reported?	No
Were withdrawals from the study explained?	Yes
Low	

Gieseke 2002b
Study characteristics

Patient sampling	See Gieseke 2002a
Patient characteristics and setting	See Gieseke 2002a
Index tests	Throat swab: 2 different swabs Commercial name of the RADTs: OSOM Ultra Strep A (Genzyme) Type of RADTs: EIA
Target condition and reference standard(s)	See Gieseke 2002a
Flow and timing	No follow-up
Comparative	
Type of study	Journal article
Notes	Supported by a grant from one of the manufacturers of the RADTs under evaluation (Genzyme)

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient Selection			
Was a consecutive or random sample of patients enrolled?	Unclear		
Was it a cross-sectional study or a RCT?	Yes		
Were selection criteria clearly described (at least presenting signs and symptoms and age limits for inclusion)?	No		
Was clinical selection of patients avoided?	No		

Gieseke 2002b *(Continued)*

Were patients seen in an ambulatory care setting?	Yes		
		High	High
DOMAIN 2: Index Test All tests			
Were the RADT results interpreted with blinding of the results of culture?	Yes		
Was the type of the RADT mentioned (EIA or OIA)?	Yes		
Were RADTs conducted during consultation time?	No		
		Low	High
DOMAIN 3: Reference Standard			
Were culture results interpreted with blinding of the results of the RADT?	Unclear		
Is the throat culture method likely to correctly identify GAS (laboratory culture on a blood agar plate during 48 hr)?	Yes		
Were the culture medium, atmosphere, duration of incubation and GAS-confirmation technique described?	Yes		
		Unclear	Low
DOMAIN 4: Flow and Timing			
Was the delay between the performance of the RADT and throat culture plating less than 48 hours?	No		
Did all patients receive a throat culture?	Yes		
Did patients receive the same throat culture method?	Yes		
Were undetermined/uninterpretable results reported?	No		
Were withdrawals from the study explained?	Yes		
		Low	

Gieseke 2003
Study characteristics

Patient sampling	Cross-sectional study Prospective design Sample: consecutive Direct comparison of different RADTs: no Direct comparison of several throat culture techniques: no Person performing the throat sample: unclear Exclusion if recent antibiotics use before inclusion: no
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Gieseke 2003 (Continued)

	<p>Clinical selection of patients: implicit criteria (see below)</p> <p>Presenting signs and symptoms: patients suspected of having <i>S. pyogenes</i> pharyngitis</p> <p>Age range for inclusion: not reported</p>
Patient characteristics and setting	<p>Sample size: 887</p> <p>Age (distribution): not reported</p> <p>GAS prevalence according to culture (with 95% confidence interval): 23.7% (95% CI not reported)</p> <p>Country of study: USA</p> <p>Sex (% of girls): not reported</p> <p>Clinical severity assessment: none</p> <p>Clinical setting: office-based</p> <p>Single-centre study</p>
Index tests	<p>Throat swab: 1 single swab (used for culture and then for the RADT)</p> <p>Commercial name of the RADT: OSOM Ultra Strep A</p> <p>Type of RADT: EIA</p>
Target condition and reference standard(s)	<p>Throat culture medium: inhibitory</p> <p>Atmosphere of incubation: aerobic with CO₂ enrichment</p> <p>Duration of incubation: 48 hours</p> <p>GAS confirmation: latex test</p> <p>Number of plates inoculated: 2</p> <p>Assessment of GAS antibody response: no</p> <p>Relevant details: 2 swabs were taken for each participant. We extracted the data corresponding to Swab #2 because it was fully processed in the microbiology laboratory whereas Swab #1 was processed in the paediatrician's office.</p>
Flow and timing	No follow-up
Comparative	
Type of study	Journal article
Notes	The study was funded by Genzyme (manufacturer of the RADT)

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient Selection			
Was a consecutive or random sample of patients enrolled?	Yes		
Was it a cross-sectional study or a RCT?	Yes		
Were selection criteria clearly described (at least presenting signs and symptoms and age limits for inclusion)?	No		
Was clinical selection of patients avoided?	No		

Gieseke 2003 (Continued)

Were patients seen in an ambulatory care setting?	Yes		
		High	High
DOMAIN 2: Index Test All tests			
Were the RADT results interpreted with blinding of the results of culture?	Yes		
Was the type of the RADT mentioned (EIA or OIA)?	Yes		
Were RADTs conducted during consultation time?	No		
		Low	High
DOMAIN 3: Reference Standard			
Were culture results interpreted with blinding of the results of the RADT?	Yes		
Is the throat culture method likely to correctly identify GAS (laboratory culture on a blood agar plate during 48 hr)?	Yes		
Were the culture medium, atmosphere, duration of incubation and GAS-confirmation technique described?	Yes		
		Low	Low
DOMAIN 4: Flow and Timing			
Was the delay between the performance of the RADT and throat culture plating less than 48 hours?	Yes		
Did all patients receive a throat culture?	Yes		
Did patients receive the same throat culture method?	Yes		
Were undetermined/uninterpretable results reported?	No		
Were withdrawals from the study explained?	Yes		
		Low	

Gurol 2010
Study characteristics

Patient sampling	Cross-sectional study Retrospective design Sample: consecutive Direct comparison of different RADTs: no Direct comparison of several throat culture techniques: no Person performing the throat sample: unclear
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Gurol 2010 (Continued)

	<p>Exclusion if recent antibiotics use before inclusion: no</p> <p>Clinical selection of patients: patients for whom RADT and culture were requested</p> <p>Presenting signs and symptoms: not reported</p> <p>Age range for inclusion: not reported ("all patients", i.e., adults and children; data extractable for children 0 to 9 years of age)</p>
Patient characteristics and setting	<p>Sample size: 178 (total sample 453, paediatric sample 0 to 9 years 178) Age (distribution): not reported in this age group (0 to 9 years)</p> <p>GAS prevalence according to culture (with 95% confidence interval): 22.5% (95% CI not reported) Country of study: Turkey Sex (% of girls): not reported Clinical severity assessment: none Clinical setting: outpatient clinic of a university hospital Single-centre study</p>
Index tests	<p>Throat swab: unclear</p> <p>Commercial name of the RADT: QuickVue Plus Strep A (Quidel) Type of RADT: EIA</p>
Target condition and reference standard(s)	<p>Throat culture medium: standard Atmosphere of incubation: not reported Duration of incubation: not reported GAS confirmation: bacitracin disk Number of plates inoculated: 1 Assessment of GAS antibody response: no Relevant details: -</p>
Flow and timing	No follow-up
Comparative	
Type of study	Journal article
Notes	<p>The RADT is referred to as "QuickVue Strep A cassette test" from Quidel. Quidel manufactures 2 cassette 2: QuickVue In-Line and QuickVue Plus. The accuracy mentioned by the authors as being reported in the package insert corresponds to those from the QuickVue Plus test.</p>

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient Selection			
Was a consecutive or random sample of patients enrolled?	Yes		
Was it a cross-sectional study or a RCT?	Yes		

Gurol 2010 (Continued)

Were selection criteria clearly described (at least presenting signs and symptoms and age limits for inclusion)?	No		
Was clinical selection of patients avoided?	Unclear		
Were patients seen in an ambulatory care setting?	Yes		
		High	Unclear
DOMAIN 2: Index Test All tests			
Were the RADT results interpreted with blinding of the results of culture?	Unclear		
Was the type of the RADT mentioned (EIA or OIA)?	Yes		
Were RADTs conducted during consultation time?	No		
		Unclear	High
DOMAIN 3: Reference Standard			
Were culture results interpreted with blinding of the results of the RADT?	Unclear		
Is the throat culture method likely to correctly identify GAS (laboratory culture on a blood agar plate during 48 hr)?	Unclear		
Were the culture medium, atmosphere, duration of incubation and GAS-confirmation technique described?	No		
		High	High
DOMAIN 4: Flow and Timing			
Was the delay between the performance of the RADT and throat culture plating less than 48 hours?	Unclear		
Did all patients receive a throat culture?	Yes		
Did patients receive the same throat culture method?	Yes		
Were undetermined/uninterpretable results reported?	No		
Were withdrawals from the study explained?	Yes		
		Low	

Hall 2004
Study characteristics

Patient sampling	<p>Cross-sectional study Retrospective design Sample: consecutive Direct comparison of different RADTs: no Direct comparison of several throat culture techniques: no Person performing the throat sample: nurse or medical assistant</p> <p>Exclusion if recent antibiotics use before inclusion: no</p> <p>Clinical selection of patients: implicit criteria ("all children with suspected GAS pharyngitis")</p> <p>Presenting signs and symptoms: unclear (see above)</p> <p>Age range for inclusion: 2 to 17 years</p>
Patient characteristics and setting	<p>Sample size: 561 Age (distribution): median age = 9 years</p> <p>GAS prevalence according to culture (with 95% confidence interval): 27.1% (95% CI not reported) Country of study: USA Sex (% of girls): 53% Clinical severity assessment: Centor score (modified) Clinical setting: mixed ("departments of pediatrics, family medicine, urgent care, and emergency medicine and primary care satellite centers") Multi-centre study</p>
Index tests	<p>Throat swab: 2 different swabs (1 swab for culture, 1 swab for the RADT)</p> <p>Commercial name of the RADT: Acceava Strep A (Biostar) Type of RADT: EIA</p>
Target condition and reference standard(s)	<p>Throat culture medium: standard (plate 1) and inhibitory (plate 2) Atmosphere of incubation: aerobic (plate 1) and aerobic with CO₂ enrichment (plate 2) Duration of incubation: 48 hours GAS confirmation: latex test Number of plates inoculated: 1 Assessment of GAS antibody response: no Relevant details: -</p>
Flow and timing	No follow-up
Comparative	
Type of study	Journal article
Notes	Throat culture performed only for children with negative RADT results (partial verification). Funded by the US Centers for Disease Control and Prevention.

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
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Hall 2004 (Continued)

DOMAIN 1: Patient Selection

Was a consecutive or random sample of patients enrolled?	Yes		
Was it a cross-sectional study or a RCT?	Yes		
Were selection criteria clearly described (at least presenting signs and symptoms and age limits for inclusion)?	No		
Was clinical selection of patients avoided?	No		
Were patients seen in an ambulatory care setting?	Yes		
		High	High

DOMAIN 2: Index Test All tests

Were the RADT results interpreted with blinding of the results of culture?	Yes		
Was the type of the RADT mentioned (EIA or OIA)?	Yes		
Were RADTs conducted during consultation time?	Yes		
		Low	Low

DOMAIN 3: Reference Standard

Were culture results interpreted with blinding of the results of the RADT?	Unclear		
Is the throat culture method likely to correctly identify GAS (laboratory culture on a blood agar plate during 48 hr)?	Yes		
Were the culture medium, atmosphere, duration of incubation and GAS-confirmation technique described?	Yes		
		Unclear	Low

DOMAIN 4: Flow and Timing

Was the delay between the performance of the RADT and throat culture plating less than 48 hours?	Yes		
Did all patients receive a throat culture?	No		
Did patients receive the same throat culture method?	Yes		
Were undetermined/uninterpretable results reported?	No		
Were withdrawals from the study explained?	Yes		
		High	

Harris 1995
Study characteristics

Patient sampling	Cross-sectional study Prospective design Sample: unclear Direct comparison of different RADTs: no Direct comparison of several throat culture techniques: no Person performing the throat sample: physician Exclusion if recent antibiotics use before inclusion: no Clinical selection of patients: none Presenting signs and symptoms: signs of pharyngitis Age range for inclusion: 2 to 18 years
Patient characteristics and setting	Sample size: 519 Age (distribution): not reported GAS prevalence according to culture (with 95% confidence interval): 22.0% (95% CI not reported) Country of study: USA Sex (% of girls): not reported Clinical severity assessment: other (in-house score) Clinical setting: walk-in clinic Single-centre study
Index tests	Throat swab: 1 single swab (used for culture and then for the RADT) Commercial name of the RADT: Strep A OIA (Biostar) Type of RADT: OIA
Target condition and reference standard(s)	Throat culture medium: standard Atmosphere of incubation: aerobic with CO ₂ enrichment Duration of incubation: 48 hours GAS confirmation: latex test Number of plates inoculated: 1 Assessment of GAS antibody response: no Relevant details: -
Flow and timing	No follow-up
Comparative	
Type of study	Journal article
Notes	RADT kits were provided by the manufacturer (Biostar)

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient Selection			
Was a consecutive or random sample of patients enrolled?	Unclear		

Harris 1995 (Continued)

Was it a cross-sectional study or a RCT?	Yes		
Were selection criteria clearly described (at least presenting signs and symptoms and age limits for inclusion)?	Yes		
Was clinical selection of patients avoided?	Yes		
Were patients seen in an ambulatory care setting?	Yes		
		Low	Low

DOMAIN 2: Index Test All tests

Were the RADT results interpreted with blinding of the results of culture?	Yes		
Was the type of the RADT mentioned (EIA or OIA)?	Yes		
Were RADTs conducted during consultation time?	No		
		Low	High

DOMAIN 3: Reference Standard

Were culture results interpreted with blinding of the results of the RADT?	Unclear		
Is the throat culture method likely to correctly identify GAS (laboratory culture on a blood agar plate during 48 hr)?	Yes		
Were the culture medium, atmosphere, duration of incubation and GAS-confirmation technique described?	Yes		
		Unclear	Low

DOMAIN 4: Flow and Timing

Was the delay between the performance of the RADT and throat culture plating less than 48 hours?	Yes		
Did all patients receive a throat culture?	Yes		
Did patients receive the same throat culture method?	Yes		
Were undetermined/uninterpretable results reported?	No		
Were withdrawals from the study explained?	Yes		
		Low	

Hart 1997
Study characteristics

Patient sampling	Cross-sectional study
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Hart 1997 (Continued)

	<p>Prospective design Sample: unclear Direct comparison of different RADTs: no Direct comparison of several throat culture techniques: yes Person performing the throat sample: nurses</p> <p>Exclusion if recent antibiotics use before inclusion: no</p> <p>Clinical selection of patients: none</p> <p>Presenting signs and symptoms: patients presenting with pharyngitis</p> <p>Age range for inclusion: not reported ("adults" and "children"; data extractable for patients ≤ 18 years)</p>
Patient characteristics and setting	<p>Sample size: total sample 263, paediatric sample 75 Age (distribution): not reported</p> <p>GAS prevalence according to culture (with 95% confidence interval): 21% (95% CI not reported) Country of study: USA Sex (% of girls): not reported Clinical severity assessment: none Clinical setting: walk-in clinic ("family practice clinic") Single-centre study</p>
Index tests	<p>Throat swab: 1 double swab (each swab was used first for culture and then for performing the RADT; paired swabs were collected to study swab-to-swab variability but only the result from one randomly selected swab was used for estimating diagnostic accuracy)</p> <p>Commercial name of the RADT: Strep A OIA (Biostar) Type of RADT: OIA</p>
Target condition and reference standard(s)	<p>Throat culture medium: inhibitory and enrichment (using the pledget) Atmosphere of incubation: anaerobic Duration of incubation: 48 hours GAS confirmation: bacitracin disk Number of plates inoculated: 2 plates per swab (1 selective plate and 1 selective plate following Todd-Hewitt enrichment) Assessment of GAS antibody response: no Relevant details: 2 swabs were collected to study swab-to-swab variability but only the result from one randomly selected swab was used for estimating accuracy measurements</p>
Flow and timing	No follow-up
Comparative	
Type of study	Journal article
Notes	Technical and partial financial assistance was provided by Biostar (manufacturer of the RADT)

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient Selection			

Hart 1997 (Continued)

Was a consecutive or random sample of patients enrolled?	Unclear		
Was it a cross-sectional study or a RCT?	Yes		
Were selection criteria clearly described (at least presenting signs and symptoms and age limits for inclusion)?	No		
Was clinical selection of patients avoided?	Yes		
Were patients seen in an ambulatory care setting?	Yes		
		High	High
DOMAIN 2: Index Test All tests			
Were the RADT results interpreted with blinding of the results of culture?	Yes		
Was the type of the RADT mentioned (EIA or OIA)?	Yes		
Were RADTs conducted during consultation time?	No		
		Low	High
DOMAIN 3: Reference Standard			
Were culture results interpreted with blinding of the results of the RADT?	Unclear		
Is the throat culture method likely to correctly identify GAS (laboratory culture on a blood agar plate during 48 hr)?	Yes		
Were the culture medium, atmosphere, duration of incubation and GAS-confirmation technique described?	Yes		
		Unclear	Low
DOMAIN 4: Flow and Timing			
Was the delay between the performance of the RADT and throat culture plating less than 48 hours?	Unclear		
Did all patients receive a throat culture?	Yes		
Did patients receive the same throat culture method?	Yes		
Were undetermined/uninterpretable results reported?	Yes		

Hart 1997 (Continued)

Were withdrawals from the study explained? No

Low
Henderson 1988
Study characteristics

Patient sampling	Cross-sectional study Prospective design Sample: unclear Direct comparison of different RADTs: yes (EIA versus LA) Direct comparison of several throat culture techniques: no Person performing the throat sample: physician Exclusion if recent antibiotics use before inclusion: no Clinical selection of patients: unclear Presenting signs and symptoms: unclear Age range for inclusion: birth to 17 years
Patient characteristics and setting	Sample size: 117 (total sample 218; 117 were tested by EIA) Age (distribution): not reported GAS prevalence according to culture (with 95% confidence interval): 33.3% (95% CI not reported) Country of study: USA Sex (% of girls): not reported Clinical severity assessment: none Clinical setting: emergency department Single-centre study
Index tests	Throat swab: unclear Commercial name of the RADT: not reported ("EIA no name") Type of RADT: EIA
Target condition and reference standard(s)	Throat culture medium: not reported Atmosphere of incubation: not reported Duration of incubation: not reported GAS confirmation: not reported Number of plates inoculated: unclear Assessment of GAS antibody response: no Relevant details: throat culture technique not described
Flow and timing	No follow-up
Comparative	
Type of study	Conference abstract (published in the American Journal of Diseases in Children)
Notes	The study compared an EIA rapid test to a LA test and compared the accuracy of both tests performed in the emergency room or in the microbiology

Henderson 1988 (Continued)

laboratory. We extracted data only for the EIA test performed in the emergency room.

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient Selection			
Was a consecutive or random sample of patients enrolled?	Unclear		
Was it a cross-sectional study or a RCT?	Yes		
Were selection criteria clearly described (at least presenting signs and symptoms and age limits for inclusion)?	No		
Was clinical selection of patients avoided?	Unclear		
Were patients seen in an ambulatory care setting?	Yes		
		High	Unclear
DOMAIN 2: Index Test All tests			
Were the RADT results interpreted with blinding of the results of culture?	Yes		
Was the type of the RADT mentioned (EIA or OIA)?	Yes		
Were RADTs conducted during consultation time?	Yes		
		Unclear	Low
DOMAIN 3: Reference Standard			
Were culture results interpreted with blinding of the results of the RADT?	Unclear		
Is the throat culture method likely to correctly identify GAS (laboratory culture on a blood agar plate during 48 hr)?	Unclear		
Were the culture medium, atmosphere, duration of incubation and GAS-confirmation technique described?	No		
		High	High
DOMAIN 4: Flow and Timing			
Was the delay between the performance of the RADT and throat culture plating less than 48 hours?	Unclear		
Did all patients receive a throat culture?	Yes		

Henderson 1988 (Continued)

Did patients receive the same throat culture method?	Yes
Were undetermined/uninterpretable results reported?	No
Were withdrawals from the study explained?	No
Low	

Kaltwasser 1997
Study characteristics

Patient sampling	<p>Cross-sectional study Prospective design Sample: unclear Direct comparison of different RADTs: no Direct comparison of several throat culture techniques: yes (and culture versus PCR) Person performing the throat sample: other ("emergency department personnel")</p> <p>Exclusion if recent antibiotics use before inclusion: no</p> <p>Clinical selection of patients: implicit criteria (enrollment if "the medical staff evaluating the patient determined that detection of GAS was needed")</p> <p>Presenting signs and symptoms: pharyngitis</p> <p>Age range for inclusion: not reported ("children")</p>
Patient characteristics and setting	<p>Sample size: 200 Age (distribution): not reported</p> <p>GAS prevalence according to culture (with 95% confidence interval): 28.5% (95% CI not reported) Country of study: USA Sex (% of girls): not reported Clinical severity assessment: none Clinical setting: emergency department Single-centre study</p>
Index tests	<p>Throat swab: 1 double swab (1 swab used first for culture and then for the RADT, 1 swab used for broth-enhanced culture and PCR)</p> <p>Commercial name of the RADT: Strep A OIA (Biostar) Type of RADT: OIA</p>
Target condition and reference standard(s)	<p>Throat culture medium: inhibitory and enrichment Atmosphere of incubation: aerobic with CO₂ enrichment Duration of incubation: 48 hours GAS confirmation: bacitracin disk +/- latex test Number of plates inoculated: 2 Assessment of GAS antibody response: no Relevant details: only data for the simple selective plate were extracted (no enrichment)</p>
Flow and timing	No follow-up

Kaltwasser 1997 (Continued)

Comparative

Type of study	Journal article
Notes	<p>The study compared the RADT to 2 types of culture and to PCR. We extracted data regarding OIA versus simple agar plating.</p> <p>Study supported in part by an unrestricted grant from Biostar (manufacturer of the RADT).</p>

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient Selection			
Was a consecutive or random sample of patients enrolled?	Unclear		
Was it a cross-sectional study or a RCT?	Yes		
Were selection criteria clearly described (at least presenting signs and symptoms and age limits for inclusion)?	No		
Was clinical selection of patients avoided?	No		
Were patients seen in an ambulatory care setting?	Yes		
		High	High
DOMAIN 2: Index Test All tests			
Were the RADT results interpreted with blinding of the results of culture?	Yes		
Was the type of the RADT mentioned (EIA or OIA)?	Yes		
Were RADTs conducted during consultation time?	No		
		Low	High
DOMAIN 3: Reference Standard			
Were culture results interpreted with blinding of the results of the RADT?	Unclear		
Is the throat culture method likely to correctly identify GAS (laboratory culture on a blood agar plate during 48 hr)?	Yes		
Were the culture medium, atmosphere, duration of incubation and GAS-confirmation technique described?	Yes		
		Unclear	Low

Kaltwasser 1997 (Continued)

DOMAIN 4: Flow and Timing

Was the delay between the performance of the RADT and throat culture plating less than 48 hours?	Unclear
Did all patients receive a throat culture?	Yes
Did patients receive the same throat culture method?	Yes
Were undetermined/uninterpretable results reported?	Yes
Were withdrawals from the study explained?	No
Low	

Kaufhold 1991a
Study characteristics

Patient sampling	<p>Cross-sectional study Retrospective or prospective design: unclear Sample: unclear Direct comparison of different RADTs: yes Direct comparison of several throat culture techniques: no Person performing the throat sample: not reported</p> <p>Exclusion if recent antibiotics use before inclusion: data not extracted</p> <p>Clinical selection of patients: none</p> <p>Presenting signs and symptoms: suspicion of streptococcal pharyngitis</p> <p>Age range for inclusion: 0 to 16 years</p>
Patient characteristics and setting	<p>Sample size: 230 Age (distribution): not reported</p> <p>GAS prevalence according to culture (with 95% confidence interval): 45.6% (95% CI not reported) Country of study: Germany Sex (% of girls): not reported Clinical severity assessment: none Clinical setting: mixed (paediatric hospital and private offices) Multi-centre study</p>
Index tests	<p>Throat swab: 1 double swab</p> <p>Commercial name of the RADT: TestPack Strep A Type of RADT: EIA</p>
Target condition and reference standard(s)	<p>Throat culture medium: standard Atmosphere of incubation: aerobic Duration of incubation: 24 to 48 hours GAS confirmation: latex test Number of plates inoculated (n): data not extracted Assessment of GAS antibody response: data not extracted</p>

Kaufhold 1991a (Continued)

Relevant details: -

Flow and timing	No follow-up
Comparative	
Type of study	Journal article (in German)
Notes	The manufacturers provided the rapid test kits. We thank Dr A Leis for translating this study report.

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient Selection			
Was a consecutive or random sample of patients enrolled?	Unclear		
Was it a cross-sectional study or a RCT?	Yes		
Were selection criteria clearly described (at least presenting signs and symptoms and age limits for inclusion)?	No		
Was clinical selection of patients avoided?	Yes		
Were patients seen in an ambulatory care setting?	Yes		
		High	High
DOMAIN 2: Index Test All tests			
Were the RADT results interpreted with blinding of the results of culture?	Unclear		
Was the type of the RADT mentioned (EIA or OIA)?	Yes		
Were RADTs conducted during consultation time?	No		
		Unclear	High
DOMAIN 3: Reference Standard			
Were culture results interpreted with blinding of the results of the RADT?	Unclear		
Is the throat culture method likely to correctly identify GAS (laboratory culture on a blood agar plate during 48 hr)?	No		
Were the culture medium, atmosphere, duration of incubation and GAS-confirmation technique described?	Yes		
		High	High

Kaufhold 1991a (Continued)

DOMAIN 4: Flow and Timing

Was the delay between the performance of the RADT and throat culture plating less than 48 hours?	Unclear
Did all patients receive a throat culture?	Yes
Did patients receive the same throat culture method?	Yes
Were undetermined/uninterpretable results reported?	No
Were withdrawals from the study explained?	No
Low	

Kaufhold 1991b
Study characteristics

Patient sampling	<p>Cross-sectional study Retrospective or prospective design: unclear Sample: unclear Direct comparison of different RADTs: yes Direct comparison of several throat culture techniques: no Person performing the throat sample: not reported</p> <p>Exclusion if recent antibiotics use before inclusion: data not extracted</p> <p>Clinical selection of patients: none</p> <p>Presenting signs and symptoms: suspicion of streptococcal pharyngitis</p> <p>Age range for inclusion: 0 to 16 years</p>
Patient characteristics and setting	<p>Sample size: 261 Age (distribution): not reported</p> <p>GAS prevalence according to culture (with 95% confidence interval): 42.1% (95% CI not reported) Country of study: Germany Sex (% of girls): not reported Clinical severity assessment: none Clinical setting: mixed (paediatric hospital and private offices) Multi-centre study</p>
Index tests	<p>Throat swab: 1 double swab</p> <p>Commercial name of the RADT: Tandem Icon Strep A Type of RADT: EIA</p>
Target condition and reference standard(s)	<p>Throat culture medium: standard Atmosphere of incubation: aerobic Duration of incubation: 24 to 48 hours GAS confirmation: latex test Number of plates inoculated (n): data not extracted Assessment of GAS antibody response: data not extracted Relevant details: -</p>

Kaufhold 1991b (Continued)

Flow and timing	No follow-up
Comparative	
Type of study	Journal article (in German)
Notes	The manufacturers provided the rapid test kits. We thank Dr A Leis for translating this study report.

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient Selection			
Was a consecutive or random sample of patients enrolled?	Unclear		
Was it a cross-sectional study or a RCT?	Yes		
Were selection criteria clearly described (at least presenting signs and symptoms and age limits for inclusion)?	No		
Was clinical selection of patients avoided?	Yes		
Were patients seen in an ambulatory care setting?	Yes		
		High	High
DOMAIN 2: Index Test All tests			
Were the RADT results interpreted with blinding of the results of culture?	Unclear		
Was the type of the RADT mentioned (EIA or OIA)?	Yes		
Were RADTs conducted during consultation time?	No		
		Unclear	High
DOMAIN 3: Reference Standard			
Were culture results interpreted with blinding of the results of the RADT?	Unclear		
Is the throat culture method likely to correctly identify GAS (laboratory culture on a blood agar plate during 48 hr)?	No		
Were the culture medium, atmosphere, duration of incubation and GAS-confirmation technique described?	Yes		
		High	High
DOMAIN 4: Flow and Timing			

Kaufhold 1991b *(Continued)*

Was the delay between the performance of the RADT and throat culture plating less than 48 hours?	Unclear
Did all patients receive a throat culture?	Yes
Did patients receive the same throat culture method?	Yes
Were undetermined/uninterpretable results reported?	No
Were withdrawals from the study explained?	No
Low	

Kellog 1987
Study characteristics

Patient sampling	Cross-sectional study Prospective design Sample: unclear Direct comparison of different RADTs: no Direct comparison of several throat culture techniques: yes (office versus laboratory culture) Person performing the throat sample: not reported Exclusion if recent antibiotics use before inclusion: no Clinical selection of patients: none Presenting signs and symptoms: patients with symptoms of pharyngitis Age range for inclusion: not reported (only age range of included patients)
Patient characteristics and setting	Sample size: 358 Age (distribution): mean 7.2 years (range 7 months to 19 years) GAS prevalence according to culture (with 95% confidence interval): 29.9% (95% CI not reported) Country of study: USA Sex (% of girls): not reported Clinical severity assessment: none Clinical setting: office-based Single-centre study
Index tests	Throat swab: 1 single swab (used for culture and then for the RADT) Commercial name of the RADT: TestPack Strep A (Abbott) Type of RADT: EIA
Target condition and reference standard(s)	Throat culture medium: standard Atmosphere of incubation: anaerobic Duration of incubation: 48 hours GAS confirmation: latex test or direct fluorescent antibody procedure Number of plates inoculated: 1 Assessment of GAS antibody response: no Relevant details: 2 swabs were taken from each patient. Swab #1 was used in the office for culture (office culture) and then for performing the RADT. Swab #2 was

Kellog 1987 (Continued)

sent to the laboratory for culture and then for performing the RADT. We only extracted data related to analyses performed in the microbiology laboratory.

Flow and timing	No follow-up
Comparative	
Type of study	Journal article
Notes	2 swabs were taken from each patient. Swab #1 was used in the office for culture (office culture) and then for performing the RADT. Swab #2 was sent to the laboratory for culture and then for performing the RADT. We only extracted data related to analyses performed in the microbiology laboratory.

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient Selection			
Was a consecutive or random sample of patients enrolled?	Unclear		
Was it a cross-sectional study or a RCT?	Yes		
Were selection criteria clearly described (at least presenting signs and symptoms and age limits for inclusion)?	No		
Was clinical selection of patients avoided?	Yes		
Were patients seen in an ambulatory care setting?	Yes		
		High	Low
DOMAIN 2: Index Test All tests			
Were the RADT results interpreted with blinding of the results of culture?	Yes		
Was the type of the RADT mentioned (EIA or OIA)?	Yes		
Were RADTs conducted during consultation time?	No		
		Low	High
DOMAIN 3: Reference Standard			
Were culture results interpreted with blinding of the results of the RADT?	Unclear		
Is the throat culture method likely to correctly identify GAS (laboratory culture on a blood agar plate during 48 hr)?	Yes		

Kellog 1987 *(Continued)*

Were the culture medium, atmosphere, duration of incubation and GAS-confirmation technique described? Yes

Unclear

Low

DOMAIN 4: Flow and Timing

Was the delay between the performance of the RADT and throat culture plating less than 48 hours? Yes

Did all patients receive a throat culture? Yes

Did patients receive the same throat culture method? Yes

Were undetermined/uninterpretable results reported? No

Were withdrawals from the study explained? No

Low

Kellog 1991
Study characteristics

Patient sampling

Cross-sectional study
 Prospective design
 Sample: unclear
 Direct comparison of different RADTs: no
 Direct comparison of several throat culture techniques: yes (office culture versus laboratory culture)
 Person performing the throat sample: physician

Exclusion if recent antibiotics use before inclusion: no

Clinical selection of patients: none

Presenting signs and symptoms: symptoms of pharyngitis

Age range for inclusion: not reported ("pediatric offices")

Patient characteristics and setting

Sample size: 1035
 Age (distribution): mean = 8.0 years (1030 children and 5 parents included)

GAS prevalence according to culture (with 95% confidence interval): 40.9% (95% CI not reported)
 Country of study: USA
 Sex (% of girls): not reported
 Clinical severity assessment: none
 Clinical setting: office-based
 Multi-centre study

Kellog 1991 (Continued)

Index tests	Throat swab: 1 duplicate swab (swab #1 used first for culture and then for performing the RADT in the office; swab #2 used first for culture and then for performing the RADT in the microbiology laboratory) Commercial name of the RADT: SMART Group A test (New Horizons) Type of RADT: EIA
Target condition and reference standard(s)	Throat culture medium: standard Atmosphere of incubation: aerobic Duration of incubation: 48 hours GAS confirmation: latex test Number of plates inoculated: 1 Assessment of GAS antibody response: no Relevant details: when the SMART result was positive but the culture was negative, the primary inoculum zone was subcultured to both an aerobically incubated standard blood agar plate and aerobically (with CO ₂ enrichment) selective blood agar plate.
Flow and timing	No follow-up.
Comparative	
Type of study	Journal article
Notes	Swab #1 was used first for culture and then for performing the RADT in the office and swab #2 was used first for culture and then for performing the RADT in the microbiology laboratory. In the laboratory, RADTs were read after 5 minutes of incubation and tests with negative results were reincubated overnight and reread. We extracted data only for the RADT performed in the laboratory and read after 5 minutes of incubation. RADT kits were provided by the manufacturer (New Horizons).

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient Selection			
Was a consecutive or random sample of patients enrolled?	Unclear		
Was it a cross-sectional study or a RCT?	Yes		
Were selection criteria clearly described (at least presenting signs and symptoms and age limits for inclusion)?	No		
Was clinical selection of patients avoided?	Yes		
Were patients seen in an ambulatory care setting?	Yes		
		High	Low
DOMAIN 2: Index Test All tests			
Were the RADT results interpreted with blinding of the results of culture?	Yes		

Kellog 1991 (Continued)

Was the type of the RADT mentioned (EIA or OIA)?	Yes		
Were RADTs conducted during consultation time?	No		
		Low	High
DOMAIN 3: Reference Standard			
Were culture results interpreted with blinding of the results of the RADT?	No		
Is the throat culture method likely to correctly identify GAS (laboratory culture on a blood agar plate during 48 hr)?	Yes		
Were the culture medium, atmosphere, duration of incubation and GAS-confirmation technique described?	Yes		
		High	Low
DOMAIN 4: Flow and Timing			
Was the delay between the performance of the RADT and throat culture plating less than 48 hours?	Yes		
Did all patients receive a throat culture?	Yes		
Did patients receive the same throat culture method?	No		
Were undetermined/uninterpretable results reported?	Yes		
Were withdrawals from the study explained?	Yes		
		High	

Kim 2009
Study characteristics

Patient sampling	Cross-sectional study Prospective design Sample: unclear Direct comparison of different RADTs: no Direct comparison of several throat culture techniques: no Person performing the throat sample: unclear Exclusion if recent antibiotics use before inclusion: no Clinical selection of patients: implicit criteria (see below)
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Kim 2009 (Continued)

	Presenting signs and symptoms: patients with "suspected bacterial pharyngitis on the basis of the symptoms or signs" Age range for inclusion: not reported ("children")
Patient characteristics and setting	Sample size: 293 Age (distribution): not reported GAS prevalence according to culture (with 95% confidence interval): 66.6% (95% CI not reported) Country of study: Korea Sex (% of girls): 44.7% Clinical severity assessment: none Clinical setting: mixed (office-based and walk-in clinics) Multi-centre study
Index tests	Throat swab: 2 different swabs (unclear how they were used) Commercial name of the RADT: SD Bioline Strep A Type of RADT: EIA
Target condition and reference standard(s)	Throat culture medium: standard Atmosphere of incubation: aerobic Duration of incubation: 24 hours GAS confirmation: bacitracin disk and latex test Number of plates inoculated: 1 Assessment of GAS antibody response: no Relevant details: -
Flow and timing	No follow-up
Comparative	
Type of study	Journal article
Notes	The manufacturer of the RADT (SD) provided the kits for this study

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient Selection			
Was a consecutive or random sample of patients enrolled?	Unclear		
Was it a cross-sectional study or a RCT?	Yes		
Were selection criteria clearly described (at least presenting signs and symptoms and age limits for inclusion)?	No		
Was clinical selection of patients avoided?	No		
Were patients seen in an ambulatory care setting?	Yes		
		High	High

DOMAIN 2: Index Test All tests

Kim 2009 (Continued)

Were the RADT results interpreted with blinding of the results of culture?	Unclear		
Was the type of the RADT mentioned (EIA or OIA)?	Yes		
Were RADTs conducted during consultation time?	No		
		Unclear	High

DOMAIN 3: Reference Standard

Were culture results interpreted with blinding of the results of the RADT?	Yes		
Is the throat culture method likely to correctly identify GAS (laboratory culture on a blood agar plate during 48 hr)?	No		
Were the culture medium, atmosphere, duration of incubation and GAS-confirmation technique described?	Yes		
		High	High

DOMAIN 4: Flow and Timing

Was the delay between the performance of the RADT and throat culture plating less than 48 hours?	Unclear		
Did all patients receive a throat culture?	Yes		
Did patients receive the same throat culture method?	Yes		
Were undetermined/uninterpretable results reported?	Yes		
Were withdrawals from the study explained?	No		
		Low	

Kuhn 1999
Study characteristics

Patient sampling	Cross-sectional study Prospective design Sample: unclear Direct comparison of different RADTs: no Direct comparison of several throat culture techniques: yes Person performing the throat sample: not reported Exclusion if recent antibiotics use before inclusion: yes (within the previous 72 hours) Clinical selection of patients: explicit criteria but not a score (see below) Presenting signs and symptoms: sore throat and one of the following signs: pharyngeal injection or exudate, fever > 38.4°C, or cervical lymphadenopathy
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Kuhn 1999 (Continued)

Age range for inclusion: 2 to 18 years

Patient characteristics and setting	<p>Sample size: 363 throat swabs from 248 children (multiple visits allowed) Age (distribution): median 6.6 years (range 2.2 to 15.9 years)</p> <p>GAS prevalence according to culture (with 95% confidence interval): 36.4% (95% CI not reported) Country of study: Canada Sex (% of girls): 49.2% Clinical severity assessment: none Clinical setting: mixed (emergency department and office-based) Multi-centre study</p>
Index tests	<p>Throat swab: 1 single swab (used for culture and then for the RADT)</p> <p>Commercial name of the RADT: Strep A OIA (Biostar) Type of RADT: OIA</p>
Target condition and reference standard(s)	<p>Throat culture medium: standard Atmosphere of incubation: anaerobic Duration of incubation: 48 hours GAS confirmation: bacitracin disk and latex test Number of plates inoculated: 1 standard (+1 after broth enrichment, data not extracted) Assessment of GAS antibody response: no Relevant details: the throat swab was used for standard culture and the pledget was used for a broth-enriched culture. We only extracted data relevant to the standard agar culture technique.</p>
Flow and timing	No follow-up
Comparative	
Type of study	Journal article
Notes	<p>The throat swab was used for standard culture and the pledget was used for a broth-enriched culture. We only extracted data relevant to the standard agar culture technique. The first author was supported by the Canadian Infectious Diseases Society Glaxo Wellcome Research Fellowship Award. The study was supported by a grant from the Alberta Children's Hospital Foundation.</p>

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient Selection			
Was a consecutive or random sample of patients enrolled?	Unclear		
Was it a cross-sectional study or a RCT?	Yes		
Were selection criteria clearly described (at least presenting signs and symptoms and age limits for inclusion)?	Yes		
Was clinical selection of patients avoided?	No		

Kuhn 1999 *(Continued)*

Were patients seen in an ambulatory care setting? Yes

High
High
DOMAIN 2: Index Test All tests

Were the RADT results interpreted with blinding of the results of culture? Yes

Was the type of the RADT mentioned (EIA or OIA)? Yes

Were RADTs conducted during consultation time? No

Low
High
DOMAIN 3: Reference Standard

Were culture results interpreted with blinding of the results of the RADT? Unclear

Is the throat culture method likely to correctly identify GAS (laboratory culture on a blood agar plate during 48 hr)? Yes

Were the culture medium, atmosphere, duration of incubation and GAS-confirmation technique described? Yes

Unclear
Low
DOMAIN 4: Flow and Timing

Was the delay between the performance of the RADT and throat culture plating less than 48 hours? Yes

Did all patients receive a throat culture? Yes

Did patients receive the same throat culture method? Yes

Were undetermined/uninterpretable results reported? No

Were withdrawals from the study explained? No

Low
Kurtz 2000
Study characteristics

Kurtz 2000 (Continued)

Patient sampling	<p>Cross-sectional study Prospective design Sample: unclear Direct comparison of different RADTs: no (but comparison of single-swab versus double-swab antigen extraction) Direct comparison of several throat culture techniques: yes (standard blood agar versus selective medium) Person performing the throat sample: not reported</p> <p>Exclusion if recent antibiotics use before inclusion: yes (previous 7 days)</p> <p>Clinical selection of patients: explicit criteria but not a score (see below)</p> <p>Presenting signs and symptoms: children with clinical signs of <i>S. pyogenes</i> pharyngitis ("fever, sore throat, and/or cervical adenitis and the absence of cough, rhinorrhea, lower respiratory infection, and otitis media")</p> <p>Age range for inclusion: 4 to 15 years</p>
Patient characteristics and setting	<p>Sample size: 256 Age (distribution): not reported</p> <p>GAS prevalence according to culture (with 95% confidence interval): 30.9% (95% CI not reported) Country of study: USA Sex (% of girls): not reported Clinical severity assessment: none Clinical setting: office-based Single-centre study</p>
Index tests	<p>Throat swab: 2 different swabs (each used first for culture and then for performing the RADT; we randomly chose to extract data for swab B)</p> <p>Commercial name of the RADT: Test Pack Plus (Abbott) Type of RADT: EIA</p>
Target condition and reference standard(s)	<p>Throat culture medium: standard and inhibitory (composite 2-plate reference standard) Atmosphere of incubation: aerobic Duration of incubation: 48 hours GAS confirmation: bacitracin disk and latex test Number of plates inoculated: 2 Assessment of GAS antibody response: no Relevant details: 2 swabs were taken (A and B). Each swab was first inoculated onto a culture plate (standard or selective) and then used for performing the RADT. Culture positivity was defined as growth from either of the 2 plates. For the results of the RADT, we only extracted data for 1 swab, which was randomly chosen to be swab B.</p>
Flow and timing	No follow-up
Comparative	
Type of study	Journal article
Notes	2 swabs were taken (A and B). Each swab was inoculated onto a culture plate (standard or selective) and then used for antigen detection. Culture positivity was defined as growth from either of the 2 plates. For the results of the RADT, we only extracted data for 1 swab, which was randomly chosen to be swab B. Funded in part by Abbott (manufacturer of the RADT).

Methodological quality

Kurtz 2000 (Continued)

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient Selection			
Was a consecutive or random sample of patients enrolled?	Unclear		
Was it a cross-sectional study or a RCT?	Yes		
Were selection criteria clearly described (at least presenting signs and symptoms and age limits for inclusion)?	Yes		
Was clinical selection of patients avoided?	No		
Were patients seen in an ambulatory care setting?	Yes		
		High	High
DOMAIN 2: Index Test All tests			
Were the RADT results interpreted with blinding of the results of culture?	Yes		
Was the type of the RADT mentioned (EIA or OIA)?	Yes		
Were RADTs conducted during consultation time?	No		
		Low	High
DOMAIN 3: Reference Standard			
Were culture results interpreted with blinding of the results of the RADT?	Yes		
Is the throat culture method likely to correctly identify GAS (laboratory culture on a blood agar plate during 48 hr)?	Yes		
Were the culture medium, atmosphere, duration of incubation and GAS-confirmation technique described?	Yes		
		Low	Low
DOMAIN 4: Flow and Timing			
Was the delay between the performance of the RADT and throat culture plating less than 48 hours?	Unclear		
Did all patients receive a throat culture?	Yes		

Kurtz 2000 (Continued)

Did patients receive the same throat culture method? Yes

Were undetermined/uninterpretable results reported? Yes

Were withdrawals from the study explained? Yes

Low

Küçük 2014
Study characteristics

Patient sampling	<p>Cross-sectional study Retrospective design Sample: consecutive Direct comparison of different RADTs: no Direct comparison of several throat culture techniques: no Person performing the throat sample: not reported</p> <p>Exclusion if recent antibiotics use before inclusion: yes (without precision)</p> <p>Clinical selection of patients: explicit criteria but not a score</p> <p>Presenting signs and symptoms: acute sore throat, fever and acutely inflamed throat/tonsils with or without exudates</p> <p>Age range for inclusion: 0 to 17 years</p>
Patient characteristics and setting	<p>Sample size: 892 Age (distribution): mean = 5.3 years</p> <p>GAS prevalence according to culture (with 95% confidence interval): 24.1% (95% CI not reported) Country of study: Turkey Sex (% of girls): 42% Clinical severity assessment: none Clinical setting: mixed (paediatric emergency department and outpatient clinics) Multi-centre study</p>
Index tests	<p>Throat swab: 2 different swabs</p> <p>Commercial name of the RADT: QuickVue In-Line Strep A (Quidel) Type of RADT: EIA</p>
Target condition and reference standard(s)	<p>Throat culture medium: standard Atmosphere of incubation: not reported Duration of incubation: not reported GAS confirmation: bacitracin disk Number of plates inoculated: 1 Assessment of GAS antibody response: no Relevant details: -</p>
Flow and timing	No follow-up

Küçük 2014 (Continued)

Comparative

Type of study	Journal article
Notes	The authors reported using the "QuickVue Strep A (Quidel) cassette". Quidel manufactures several RADTs that use a cassette; we assumed the study evaluated the most simple one, QuickVue In-Line Strep A kit.

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient Selection			
Was a consecutive or random sample of patients enrolled?	Yes		
Was it a cross-sectional study or a RCT?	Yes		
Were selection criteria clearly described (at least presenting signs and symptoms and age limits for inclusion)?	Yes		
Was clinical selection of patients avoided?	No		
Were patients seen in an ambulatory care setting?	Yes		
		High	High
DOMAIN 2: Index Test All tests			
Were the RADT results interpreted with blinding of the results of culture?	Yes		
Was the type of the RADT mentioned (EIA or OIA)?	Yes		
Were RADTs conducted during consultation time?	No		
		High	High
DOMAIN 3: Reference Standard			
Were culture results interpreted with blinding of the results of the RADT?	Unclear		
Is the throat culture method likely to correctly identify GAS (laboratory culture on a blood agar plate during 48 hr)?	Unclear		
Were the culture medium, atmosphere, duration of incubation and GAS-confirmation technique described?	No		
		Unclear	Unclear
DOMAIN 4: Flow and Timing			

Küçük 2014 (Continued)

Was the delay between the performance of the RADT and throat culture plating less than 48 hours?	Yes
Did all patients receive a throat culture?	Yes
Did patients receive the same throat culture method?	Yes
Were undetermined/uninterpretable results reported?	No
Were withdrawals from the study explained?	Yes
Low	

Laubscher 1995
Study characteristics

Patient sampling	<p>Cross-sectional study Prospective design Sample: consecutive Direct comparison of different RADTs: no Direct comparison of several throat culture techniques: no Person performing the throat sample: unclear</p> <p>Exclusion if recent antibiotics use before inclusion: yes (within the last 5 days)</p> <p>Clinical selection of patients: none</p> <p>Presenting signs and symptoms: all patients with a clinical diagnosis of pharyngitis</p> <p>Age range for inclusion: not reported ("pediatric patients")</p>
Patient characteristics and setting	<p>Sample size: 454 Age (distribution): not reported</p> <p>GAS prevalence according to culture (with 95% confidence interval): 26.0% (95% CI not reported) Country of study: Switzerland Sex (% of girls): not reported Clinical severity assessment: none Clinical setting: walk-in clinic Single-centre study</p>
Index tests	<p>Throat swab: 2 different swabs (1 swab for culture, 1 swab for performing the RADT)</p> <p>Commercial name of the RADT: Test Pack Strep A Plus (Abbott) Type of RADT: EIA</p>
Target condition and reference standard(s)	<p>Throat culture medium: standard Atmosphere of incubation: aerobic with CO₂ enrichment Duration of incubation: 48 hours GAS confirmation: bacitracin disk and latex test Number of plates inoculated: 1 Assessment of GAS antibody response: no</p>

Laubscher 1995 (Continued)

Relevant details: -

Flow and timing	No follow-up
Comparative	
Type of study	Journal article
Notes	Supported by the manufacturer of the RADT (Abbott), which provided the kits

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient Selection			
Was a consecutive or random sample of patients enrolled?	Yes		
Was it a cross-sectional study or a RCT?	Yes		
Were selection criteria clearly described (at least presenting signs and symptoms and age limits for inclusion)?	No		
Was clinical selection of patients avoided?	Yes		
Were patients seen in an ambulatory care setting?	Yes		
		High	Low
DOMAIN 2: Index Test All tests			
Were the RADT results interpreted with blinding of the results of culture?	Yes		
Was the type of the RADT mentioned (EIA or OIA)?	Yes		
Were RADTs conducted during consultation time?	Yes		
		Low	Low
DOMAIN 3: Reference Standard			
Were culture results interpreted with blinding of the results of the RADT?	Yes		
Is the throat culture method likely to correctly identify GAS (laboratory culture on a blood agar plate during 48 hr)?	Yes		
Were the culture medium, atmosphere, duration of incubation and GAS-confirmation technique described?	Yes		
		Low	Low

Laubscher 1995 *(Continued)*
DOMAIN 4: Flow and Timing

Was the delay between the performance of the RADT and throat culture plating less than 48 hours?	Unclear
Did all patients receive a throat culture?	Yes
Did patients receive the same throat culture method?	Yes
Were undetermined/uninterpretable results reported?	Yes
Were withdrawals from the study explained?	Yes
Low	

Lewey 1988
Study characteristics

Patient sampling	Cross-sectional study Prospective design Sample: unclear Direct comparison of different RADTs: no Direct comparison of several throat culture techniques: no Person performing the throat sample: physician Exclusion if recent antibiotics use before inclusion: no Clinical selection of patients: explicit criteria but not a score (see below) Presenting signs and symptoms: sore throat and fever Age range for inclusion: 1 to 21 years
Patient characteristics and setting	Sample size: 264 Age (distribution): mean = 10.4 years GAS prevalence according to culture (with 95% confidence interval): 17.8% (95% CI not reported) Country of study: USA Sex (% of girls): 59% Clinical severity assessment: none Clinical setting: walk-in clinic Single-centre study
Index tests	Throat swab: 1 double swab (2 double swabs were taken, for a total of 4 swabs, but we extracted data only for swab #1) Commercial name of the RADT: Icon Strep A (Hybritech) Type of RADT: EIA
Target condition and reference standard(s)	Throat culture medium: standard Atmosphere of incubation: aerobic with CO ₂ enrichment Duration of incubation: 24 hours GAS confirmation: latex test Number of plates inoculated: 1 Assessment of GAS antibody response: no

Lewey 1988 (Continued)

Relevant details: 2 double swabs (swab #1 and #2) were taken for each patient, for a total of 4 swabs per participant. For each double swab, swab A was used for the RADT and swab B was used for culture. We randomly chose 1 double swab for which we extracted data (swab #1).

Flow and timing	No follow-up
Comparative	
Type of study	Journal article
Notes	2 double swabs (swab #1 and #2) were taken for each patient, for a total of 4 swabs per participant. For each double swab, swab A was used for the RADT and swab B was used for culture. We randomly chose 1 double swab for which we extracted data (swab #1).

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient Selection			
Was a consecutive or random sample of patients enrolled?	Unclear		
Was it a cross-sectional study or a RCT?	Yes		
Were selection criteria clearly described (at least presenting signs and symptoms and age limits for inclusion)?	Yes		
Was clinical selection of patients avoided?	No		
Were patients seen in an ambulatory care setting?	Yes		
		High	High
DOMAIN 2: Index Test All tests			
Were the RADT results interpreted with blinding of the results of culture?	Yes		
Was the type of the RADT mentioned (EIA or OIA)?	Yes		
Were RADTs conducted during consultation time?	Yes		
		Low	Low
DOMAIN 3: Reference Standard			
Were culture results interpreted with blinding of the results of the RADT?	Unclear		
Is the throat culture method likely to correctly identify GAS (laboratory culture on a blood agar plate during 48 hr)?	No		

Lewey 1988 (Continued)

Were the culture medium, atmosphere, duration of incubation and GAS-confirmation technique described? Yes

High
High
DOMAIN 4: Flow and Timing

Was the delay between the performance of the RADT and throat culture plating less than 48 hours? Unclear

Did all patients receive a throat culture? Yes

Did patients receive the same throat culture method? Yes

Were undetermined/uninterpretable results reported? Yes

Were withdrawals from the study explained? Yes

Low
Llor 2008
Study characteristics

Patient sampling

Cross-sectional study
 Prospective design
 Sample: consecutive
 Direct comparison of different RADTs: no
 Direct comparison of several throat culture techniques: no
 Person performing the throat sample: physician

Exclusion if recent antibiotics use before inclusion: yes

Clinical selection of patients: clinical score (Centor score)

Presenting signs and symptoms: clinical symptoms of odynophagia and 2 or more of Centor criteria

Age range for inclusion: 14 to 21 years

Patient characteristics and setting

Sample size: 42
 Age (distribution): not reported, in patients 14 to 21 years

GAS prevalence according to culture (with 95% confidence interval): 19.0% (95% CI not reported)
 Country of study: Spain
 Sex (% of girls): not reported, in patients 14 to 21 years
 Clinical severity assessment: Centor score
 Clinical setting: walk-in clinic
 Single-centre study

Index tests

Throat swab: 2 different swabs

Commercial name of the RADT: OSOM Strep A

Llor 2008 (Continued)

	Type of RADT: EIA
Target condition and reference standard(s)	Throat culture medium: standard Atmosphere of incubation: aerobic with CO ₂ enrichment Duration of incubation: 48 hours GAS confirmation: latex test Number of plates inoculated: 1 Assessment of GAS antibody response: no Relevant details: -
Flow and timing	No follow-up
Comparative	
Type of study	Journal article
Notes	The manufacturer provided the rapid test kits. We thank Dr C Llor for sharing unpublished paediatric data.

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient Selection			
Was a consecutive or random sample of patients enrolled?	Yes		
Was it a cross-sectional study or a RCT?	Yes		
Were selection criteria clearly described (at least presenting signs and symptoms and age limits for inclusion)?	Yes		
Was clinical selection of patients avoided?	No		
Were patients seen in an ambulatory care setting?	Yes		
		High	High
DOMAIN 2: Index Test All tests			
Were the RADT results interpreted with blinding of the results of culture?	Yes		
Was the type of the RADT mentioned (EIA or OIA)?	Yes		
Were RADTs conducted during consultation time?	Yes		
		Low	Low
DOMAIN 3: Reference Standard			
Were culture results interpreted with blinding of the results of the RADT?	Unclear		
Is the throat culture method likely to correctly identify GAS (laboratory culture on a blood agar plate during 48 hr)?	Yes		

Llor 2008 (Continued)

Were the culture medium, atmosphere, duration of incubation and GAS-confirmation technique described? Yes

Low
Low
DOMAIN 4: Flow and Timing

Was the delay between the performance of the RADT and throat culture plating less than 48 hours? Unclear

Did all patients receive a throat culture? Yes

Did patients receive the same throat culture method? Yes

Were undetermined/uninterpretable results reported? No

Were withdrawals from the study explained? Yes

Low
Macknin 1988
Study characteristics

Patient sampling	Cross-sectional study Prospective design Sample: unclear Direct comparison of different RADTs: yes (EIA versus LA, data extracted only for EIA) Direct comparison of several throat culture techniques: no Person performing the throat sample: not reported Exclusion if recent antibiotics use before inclusion: no Clinical selection of patients: explicit criteria but not a score (see below) Presenting signs and symptoms: patients with fever and sore throat Age range for inclusion: 2 to 18 years
Patient characteristics and setting	Sample size: 120 Age (distribution): not reported GAS prevalence according to culture (with 95% confidence interval): 49.2% (95% CI not reported) Country of study: USA Sex (% of girls): not reported Clinical severity assessment: none Clinical setting: walk-in clinic Single-centre study
Index tests	Throat swab: 3 different swabs (1 for each RADT and 1 for culture) Commercial name of the RADT: Ventrescreen Strep A Type of RADT: EIA

Macknin 1988 (Continued)

Target condition and reference standard(s)	Throat culture medium: not reported Atmosphere of incubation: anaerobic Duration of incubation: not reported GAS confirmation: bacitracin disk and latex test Number of plates inoculated: 1 Assessment of GAS antibody response: no Relevant details: -
Flow and timing	No follow-up
Comparative	
Type of study	Journal article
Notes	—

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient Selection			
Was a consecutive or random sample of patients enrolled?	Unclear		
Was it a cross-sectional study or a RCT?	Yes		
Were selection criteria clearly described (at least presenting signs and symptoms and age limits for inclusion)?	Yes		
Was clinical selection of patients avoided?	No		
Were patients seen in an ambulatory care setting?	Yes		
		High	High
DOMAIN 2: Index Test All tests			
Were the RADT results interpreted with blinding of the results of culture?	Unclear		
Was the type of the RADT mentioned (EIA or OIA)?	Yes		
Were RADTs conducted during consultation time?	Unclear		
		Unclear	Unclear
DOMAIN 3: Reference Standard			
Were culture results interpreted with blinding of the results of the RADT?	Unclear		
Is the throat culture method likely to correctly identify GAS (laboratory culture on a blood agar plate during 48 hr)?	Unclear		
Were the culture medium, atmosphere, duration of incubation and GAS-confirmation technique described?	No		

Macknin 1988 (Continued)

High
High
DOMAIN 4: Flow and Timing

Was the delay between the performance of the RADT and throat culture plating less than 48 hours?	Unclear
Did all patients receive a throat culture?	Yes
Did patients receive the same throat culture method?	Yes
Were undetermined/uninterpretable results reported?	No
Were withdrawals from the study explained?	Yes
Low	

Maltezou 2008
Study characteristics

Patient sampling	<p>Cross-sectional study Prospective design Sample: unclear Direct comparison of different RADTs: no Direct comparison of several throat culture techniques: no Person performing the throat sample: unclear</p> <p>Exclusion if recent antibiotics use before inclusion: yes (within the previous week)</p> <p>Clinical selection of patients: clinical score (Centor)</p> <p>Presenting signs and symptoms: clinical evidence of pharyngitis including one of the 4 Centor criteria (fever, tonsillar exudate, tender enlarged anterior cervical lymph nodes and absence of cough)</p> <p>Age range for inclusion: 2 to 14 years</p>
Patient characteristics and setting	<p>Sample size: 432 Age (distribution): mean = 6.8 years (calculated from data in table 1)</p> <p>GAS prevalence according to culture (with 95% confidence interval): 27.3% (95% CI not reported) Country of study: Greece Sex (% of girls): 53.9% Clinical severity assessment: Centor score Clinical setting: mixed (office-based and hospital outpatient clinic) Multi-centre study</p>
Index tests	<p>Throat swab: 2 different swabs (1 swab for culture, 1 swab for performing the RADT)</p> <p>Commercial name of the RADT: Link 2 Strep A Rapid Test (Becton Dickinson) Type of RADT: EIA</p>
Target condition and reference standard(s)	<p>Throat culture medium: standard Atmosphere of incubation: not reported</p>

Maltezou 2008 (Continued)

Duration of incubation: 48 hours
 GAS confirmation: bacitracin disk and latex test
 Number of plates inoculated: not reported
 Assessment of GAS antibody response: no
 Relevant details: -

Flow and timing	No follow-up
Comparative	
Type of study	Journal article
Notes	Funded by the Hellenic Center for Disease Control and Prevention

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient Selection			
Was a consecutive or random sample of patients enrolled?	Unclear		
Was it a cross-sectional study or a RCT?	Yes		
Were selection criteria clearly described (at least presenting signs and symptoms and age limits for inclusion)?	Yes		
Was clinical selection of patients avoided?	No		
Were patients seen in an ambulatory care setting?	Yes		
		Unclear	High
DOMAIN 2: Index Test All tests			
Were the RADT results interpreted with blinding of the results of culture?	Yes		
Was the type of the RADT mentioned (EIA or OIA)?	Yes		
Were RADTs conducted during consultation time?	Yes		
		Low	Low
DOMAIN 3: Reference Standard			
Were culture results interpreted with blinding of the results of the RADT?	Unclear		
Is the throat culture method likely to correctly identify GAS (laboratory culture on a blood agar plate during 48 hr)?	Yes		

Maltezou 2008 (Continued)

Were the culture medium, atmosphere, duration of incubation and GAS-confirmation technique described? No

High
High
DOMAIN 4: Flow and Timing

Was the delay between the performance of the RADT and throat culture plating less than 48 hours? Yes

Did all patients receive a throat culture? Yes

Did patients receive the same throat culture method? Yes

Were undetermined/uninterpretable results reported? No

Were withdrawals from the study explained? Yes

Low
Mayes 2001a
Study characteristics

Patient sampling	Cross-sectional study Retrospective design Sample: unclear Direct comparison of different RADTs: no Direct comparison of several throat culture techniques: no Person performing the throat sample: not reported Exclusion if recent antibiotics use before inclusion: no Clinical selection of patients: implicit criteria (RADTs were not used for all patients presenting with pharyngitis; different physicians used varying individual criteria to determine whether or not to use the RADT or throat culture as the primary diagnostic test) Presenting signs and symptoms: unclear Age range for inclusion: not reported
Patient characteristics and setting	Sample size: total 4847 Age (distribution): not reported GAS prevalence according to culture (with 95% confidence interval): 28.8% (assuming all RADT positive results are true positives; 95CI not reported) Country of study: USA Sex (% of girls): 45% Clinical severity assessment: none Clinical setting: office-based (laboratory records of the Elmwood Pediatric Group) Single-centre study
Index tests	Throat swab: 2 different swabs (1 swab for performing the RADT, 1 swab for culture) Commercial name of the RADT: Qtest (Becton Dickinson)

Mayes 2001a (Continued)

Type of RADT: EIA (liposomal test)

Target condition and reference standard(s)	Throat culture medium: not reported Atmosphere of incubation: not reported Duration of incubation: not reported GAS confirmation: not reported Number of plates inoculated: not reported Assessment of GAS antibody response: no Relevant details: throat culture technique not described
Flow and timing	No follow-up
Comparative	
Type of study	Journal article
Notes	We sub-divided the study into 2 time periods (Mayes 2001a and Mayes 2001b) to take into account the fact that different criteria were used to determine whether or not a RADT should be performed, and because different RADTs were used during those 2 time periods. Funded in part by an academic grant (Strong Children's Research Center, Summer Student Scholar Program, University of Rochester). Throat culture performed only for children with negative RADT results (partial verification).

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient Selection			
Was a consecutive or random sample of patients enrolled?	No		
Was it a cross-sectional study or a RCT?	Yes		
Were selection criteria clearly described (at least presenting signs and symptoms and age limits for inclusion)?	No		
Was clinical selection of patients avoided?	No		
Were patients seen in an ambulatory care setting?	Yes		
		High	High
DOMAIN 2: Index Test All tests			
Were the RADT results interpreted with blinding of the results of culture?	Yes		
Was the type of the RADT mentioned (EIA or OIA)?	Yes		
Were RADTs conducted during consultation time?	Yes		
		Low	Low

Mayes 2001a *(Continued)*
DOMAIN 3: Reference Standard

Were culture results interpreted with blinding of the results of the RADT?	Unclear	
Is the throat culture method likely to correctly identify GAS (laboratory culture on a blood agar plate during 48 hr)?	Unclear	
Were the culture medium, atmosphere, duration of incubation and GAS-confirmation technique described?	No	
		High
		High

DOMAIN 4: Flow and Timing

Was the delay between the performance of the RADT and throat culture plating less than 48 hours?	Unclear	
Did all patients receive a throat culture?	No	
Did patients receive the same throat culture method?	Unclear	
Were undetermined/uninterpretable results reported?	No	
Were withdrawals from the study explained?	Yes	
		High

Mayes 2001b
Study characteristics

Patient sampling	Cross-sectional study Retrospective design Sample: unclear Direct comparison of different RADTs: no (different RADTs used but not compared) Direct comparison of several throat culture techniques: no Person performing the throat sample: not reported Exclusion if recent antibiotics use before inclusion: no Clinical selection of patients: unclear Presenting signs and symptoms: unclear Age range for inclusion: not reported
Patient characteristics and setting	Sample size: total 6580 Age (distribution): not reported

Mayes 2001b (Continued)

GAS prevalence according to culture (with 95% confidence interval): 27.8% (assuming all RADT positive results are true positives: 95% CI not reported)
 Country of study: USA
 Sex (% of girls): 45%
 Clinical severity assessment: none
 Clinical setting: office-based
 Single-centre study

Index tests	Throat swab: 2 different swabs (1 swab for performing the RADT, 1 swab for culture) Commercial name of the RADT: Signify (Abbott) and Aceava (Biostar), data aggregated and test further referred to as "EIA (no name)" Type of RADT: EIA
Target condition and reference standard(s)	See Mayes 2001a
Flow and timing	No follow-up
Comparative	
Type of study	Journal article
Notes	See Mayes 2001a

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient Selection			
Was a consecutive or random sample of patients enrolled?	Unclear		
Was it a cross-sectional study or a RCT?	Yes		
Were selection criteria clearly described (at least presenting signs and symptoms and age limits for inclusion)?	No		
Was clinical selection of patients avoided?	Unclear		
Were patients seen in an ambulatory care setting?	Yes		
		High	Unclear
DOMAIN 2: Index Test All tests			
Were the RADT results interpreted with blinding of the results of culture?	Yes		
Was the type of the RADT mentioned (EIA or OIA)?	Yes		
Were RADTs conducted during consultation time?	Yes		
		Low	Low

Mayes 2001b (Continued)

DOMAIN 3: Reference Standard

Were culture results interpreted with blinding of the results of the RADT?	Unclear
Is the throat culture method likely to correctly identify GAS (laboratory culture on a blood agar plate during 48 hr)?	Unclear
Were the culture medium, atmosphere, duration of incubation and GAS-confirmation technique described?	No
	High
	High

DOMAIN 4: Flow and Timing

Was the delay between the performance of the RADT and throat culture plating less than 48 hours?	Unclear
Did all patients receive a throat culture?	No
Did patients receive the same throat culture method?	Unclear
Were undetermined/uninterpretable results reported?	No
Were withdrawals from the study explained?	Yes
	High

Mazur 2014
Study characteristics

Patient sampling	Cross-sectional study Prospective design Sample: unclear Direct comparison of different RADTs: no Direct comparison of several throat culture techniques: no Person performing the throat sample: physician Exclusion if recent antibiotics use before inclusion: yes (within the previous 2 weeks) Clinical selection of patients: clinical score (Mclsaac) Presenting signs and symptoms: clinical and epidemiological signs of acute pharyngitis suggesting GAS aetiology and Mclsaac score ≥ 2 Age range for inclusion: 2 to 15 years
Patient characteristics and setting	Sample size: 90 Age (distribution): mean (SD) = 6.6 (3.4) years GAS prevalence according to culture (with 95% confidence interval): 50.0% (95% CI not reported) Country of study: Poland Sex (% of girls): 42.2% Clinical severity assessment: Mclsaac score

Mazur 2014 (Continued)

 Clinical setting: paediatric outpatient clinic
 Single-centre study

Index tests	Throat swab: 2 different swabs Commercial name of the RADT: QuickVue+ Strep A Test (Quidel) Type of RADT: EIA
Target condition and reference standard(s)	Throat culture medium: standard Atmosphere of incubation: not reported Duration of incubation: 48 hours GAS confirmation: latex test Number of plates inoculated: 1 Assessment of GAS antibody response: no Relevant details: -
Flow and timing	No follow-up
Comparative	
Type of study	Journal article
Notes	Academic funding (Medical University of Lublin, Poland)

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient Selection			
Was a consecutive or random sample of patients enrolled?	Unclear		
Was it a cross-sectional study or a RCT?	Yes		
Were selection criteria clearly described (at least presenting signs and symptoms and age limits for inclusion)?	Yes		
Was clinical selection of patients avoided?	No		
Were patients seen in an ambulatory care setting?	Yes		
		High	High
DOMAIN 2: Index Test All tests			
Were the RADT results interpreted with blinding of the results of culture?	Yes		
Was the type of the RADT mentioned (EIA or OIA)?	Yes		
Were RADTs conducted during consultation time?	Yes		
		Low	Low
DOMAIN 3: Reference Standard			

Mazur 2014 (Continued)

Were culture results interpreted with blinding of the results of the RADT? Yes

Is the throat culture method likely to correctly identify GAS (laboratory culture on a blood agar plate during 48 hr)? Yes

Were the culture medium, atmosphere, duration of incubation and GAS-confirmation technique described? No

Low

Low

DOMAIN 4: Flow and Timing

Was the delay between the performance of the RADT and throat culture plating less than 48 hours? Yes

Did all patients receive a throat culture? Yes

Did patients receive the same throat culture method? Yes

Were undetermined/uninterpretable results reported? No

Were withdrawals from the study explained? Yes

Low

Mclsaac 2004
Study characteristics

Patient sampling	RCT (comparing 2 different antibacterial therapies for pharyngitis) Prospective design Sample: unclear Direct comparison of different RADTs: no Direct comparison of several throat culture techniques: no Person performing the throat sample: unclear Exclusion if recent antibiotics use before inclusion: no Clinical selection of patients: implicit criteria ("a throat swab was collected when the physician believed it was warranted") Presenting signs and symptoms: patients with acute sore throat Age range for inclusion: 3 to 17 years (adults also included in the study but data extracted only for children)
Patient characteristics and setting	Sample size: total 787; children 454 Age (distribution): not reported among children GAS prevalence according to culture (with 95% confidence interval): 34.1% (95% CI not reported) Country of study: Canada Sex (% of girls): not reported Clinical severity assessment: Mclsaac score Clinical setting: walk-in clinic Single-centre study

Mclsaac 2004 (Continued)

Index tests	Throat swab: 2 different swabs (1 swab for culture, 1 swab for performing the RADT) Commercial name of the RADT: TestPack Plus Strep A with OBC II (Abbott) Type of RADT: EIA
Target condition and reference standard(s)	Throat culture medium: standard Atmosphere of incubation: anaerobic Duration of incubation: not reported GAS confirmation: latex test Number of plates inoculated: 1 Assessment of GAS antibody response: no Relevant details: -
Flow and timing	No follow-up
Comparative	
Type of study	Journal article
Notes	The study was funded by Abbott (manufacturer of the RADT)

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient Selection			
Was a consecutive or random sample of patients enrolled?	Unclear		
Was it a cross-sectional study or a RCT?	Yes		
Were selection criteria clearly described (at least presenting signs and symptoms and age limits for inclusion)?	Yes		
Was clinical selection of patients avoided?	No		
Were patients seen in an ambulatory care setting?	Yes		
		High	High
DOMAIN 2: Index Test All tests			
Were the RADT results interpreted with blinding of the results of culture?	Unclear		
Was the type of the RADT mentioned (EIA or OIA)?	Yes		
Were RADTs conducted during consultation time?	Unclear		
		Unclear	Unclear
DOMAIN 3: Reference Standard			

Mclsaac 2004 (Continued)

Were culture results interpreted with blinding of the results of the RADT? Unclear

Is the throat culture method likely to correctly identify GAS (laboratory culture on a blood agar plate during 48 hr)? Unclear

Were the culture medium, atmosphere, duration of incubation and GAS-confirmation technique described? No

High
High
DOMAIN 4: Flow and Timing

Was the delay between the performance of the RADT and throat culture plating less than 48 hours? Unclear

Did all patients receive a throat culture? Yes

Did patients receive the same throat culture method? Yes

Were undetermined/uninterpretable results reported? No

Were withdrawals from the study explained? Yes

Low
Menozzi 1992
Study characteristics

Patient sampling

Cross-sectional study
 Prospective design
 Sample: unclear
 Direct comparison of different RADTs: no
 Direct comparison of several throat culture techniques: no
 Person performing the throat sample: physicians and nurses

Exclusion if recent antibiotics use before inclusion: no

Clinical selection of patients: none

Presenting signs and symptoms: patients with symptoms of pharyngitis

Age range for inclusion: unclear

Patient characteristics and setting

Sample size: 3658
 Age (distribution): not reported

GAS prevalence according to culture (with 95% confidence interval): 34.9% (95% CI not reported)
 Country of study: Italy
 Sex (% of girls): not reported
 Clinical severity assessment: none
 Clinical setting: paediatric outpatient clinic
 Single- or multi-centre study: unclear

Menozzi 1992 (Continued)

Index tests	Throat swab: 2 different swabs (1 swab for culture, 1 swab for performing the RADT) Commercial name of the RADT: TestPack Strep A (Abbott) Type of RADT: EIA
Target condition and reference standard(s)	Throat culture medium: inhibitory Atmosphere of incubation: not reported Duration of incubation: not reported GAS confirmation: not reported Number of plates inoculated: not reported Assessment of GAS antibody response: no Relevant details: -
Flow and timing	No follow-up
Comparative	
Type of study	Conference abstract
Notes	—

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient Selection			
Was a consecutive or random sample of patients enrolled?	Unclear		
Was it a cross-sectional study or a RCT?	Yes		
Were selection criteria clearly described (at least presenting signs and symptoms and age limits for inclusion)?	No		
Was clinical selection of patients avoided?	Yes		
Were patients seen in an ambulatory care setting?	Yes		
		High	Low
DOMAIN 2: Index Test All tests			
Were the RADT results interpreted with blinding of the results of culture?	Yes		
Was the type of the RADT mentioned (EIA or OIA)?	Yes		
Were RADTs conducted during consultation time?	Unclear		
		Low	Unclear
DOMAIN 3: Reference Standard			
Were culture results interpreted with blinding of the results of the RADT?	Unclear		

Menziozi 1992 *(Continued)*

Is the throat culture method likely to correctly identify GAS (laboratory culture on a blood agar plate during 48 hr)?	Unclear		
Were the culture medium, atmosphere, duration of incubation and GAS-confirmation technique described?	No		
		High	High
DOMAIN 4: Flow and Timing			
Was the delay between the performance of the RADT and throat culture plating less than 48 hours?	Unclear		
Did all patients receive a throat culture?	Yes		
Did patients receive the same throat culture method?	Yes		
Were undetermined/uninterpretable results reported?	No		
Were withdrawals from the study explained?	No		
		Low	

Mezghani Maleej 2010
Study characteristics

Patient sampling	Cross-sectional study Prospective design Sample: consecutive Direct comparison of different RADTs: no Direct comparison of several throat culture techniques: no Person performing the throat sample: physician Exclusion if recent antibiotics use before inclusion: yes Clinical selection of patients: implicit criteria (see below) Presenting signs and symptoms: acute pharyngitis, excluding those with signs suggesting viral aetiology Age range for inclusion: 2 to 10 years
Patient characteristics and setting	Sample size: 504 (445 participants in the contingency table) Age (distribution): mean = 5.7 years (range 2 years and 2 months to 10 years) GAS prevalence according to culture (with 95% confidence interval): 32.9% (95% CI not reported) Country of study: Tunisia Sex (% of girls): 46% Clinical severity assessment: Mclsaac score Clinical setting: walk-in clinic Single-centre study
Index tests	Throat swab: 2 different swabs

Mezghani Maleej 2010 (Continued)

 Commercial name of the RADT: OSOM Strep A
 Type of RADT: EIA

Target condition and reference standard(s)	Throat culture medium: standard and inhibitory (2 plates) Atmosphere of incubation: aerobic with CO ₂ enrichment Duration of incubation: 48 hours GAS confirmation: latex test Number of plates inoculated: 2 Assessment of GAS antibody response: no Relevant details: -
Flow and timing	No follow-up
Comparative	
Type of study	Journal article (in French)
Notes	We thank Prof. A Hammami for providing data from the contingency table (not extractable in the original publication)

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient Selection			
Was a consecutive or random sample of patients enrolled?	Yes		
Was it a cross-sectional study or a RCT?	Yes		
Were selection criteria clearly described (at least presenting signs and symptoms and age limits for inclusion)?	Yes		
Was clinical selection of patients avoided?	No		
Were patients seen in an ambulatory care setting?	Yes		
		High	High
DOMAIN 2: Index Test All tests			
Were the RADT results interpreted with blinding of the results of culture?	Yes		
Was the type of the RADT mentioned (EIA or OIA)?	Yes		
Were RADTs conducted during consultation time?	Yes		
		Low	Low
DOMAIN 3: Reference Standard			
Were culture results interpreted with blinding of the results of the RADT?	Unclear		

Mezghani Maleej 2010 (Continued)

Is the throat culture method likely to correctly identify GAS (laboratory culture on a blood agar plate during 48 hr)?

Yes

Were the culture medium, atmosphere, duration of incubation and GAS-confirmation technique described?

Yes

Unclear
Low
DOMAIN 4: Flow and Timing

Was the delay between the performance of the RADT and throat culture plating less than 48 hours?

Unclear

Did all patients receive a throat culture?

Yes

Did patients receive the same throat culture method?

Yes

Were undetermined/uninterpretable results reported?

Yes

Were withdrawals from the study explained?

Yes

Low
Mirza 2007a
Study characteristics

Patient sampling

Cross-sectional study
 Retrospective design
 Sample: unclear
 Direct comparison of different RADTs: no
 Direct comparison of several throat culture techniques: no
 Person performing the throat sample: nurses and medical assistants

 Exclusion if recent antibiotics use before inclusion: no

 Clinical selection of patients: unclear

 Presenting signs and symptoms: unclear

 Age range for inclusion: < 18 years

Patient characteristics and setting

Sample size: total 11,644 (only 9032 included in the meta-analysis, i.e., those with RADT negative results also cultured)
 Age (distribution): not reported

 GAS prevalence according to culture (with 95% confidence interval): 28.3% (95% CI not reported)
 Country of study: USA
 Sex (% of girls): not reported
 Clinical severity assessment: none
 Clinical setting: office-based
 Multi-centre study

Index tests

Throat swab: 2 different swabs (1 swab for culture, 1 swab for performing the RADT)

Mirza 2007a (Continued)

 Commercial name of the RADT: QTest (Becton Dickinson)
 Type of RADT: EIA (liposomal test)

Target condition and reference standard(s)	Throat culture medium: standard Atmosphere of incubation: aerobic with CO ₂ enrichment Duration of incubation: not reported GAS confirmation: not reported Number of plates inoculated: 1 Assessment of GAS antibody response: no Relevant details: -
Flow and timing	No follow-up
Comparative	
Type of study	Journal article
Notes	The study was sub-divided into 2 study cohorts (Mirza 2007a and Mirza 2007b). In Mirza 2007a, the data came from 3 paediatric practices and the RADT used was the QTest (Abbott). In Mirza 2007b, the data came from a children's hospital and the RADT used was the Signify (Abbott). Throat culture performed only for children with negative RADT results (partial verification).

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient Selection			
Was a consecutive or random sample of patients enrolled?	Unclear		
Was it a cross-sectional study or a RCT?	Yes		
Were selection criteria clearly described (at least presenting signs and symptoms and age limits for inclusion)?	No		
Was clinical selection of patients avoided?	Unclear		
Were patients seen in an ambulatory care setting?	Yes		
		High	Unclear
DOMAIN 2: Index Test All tests			
Were the RADT results interpreted with blinding of the results of culture?	Yes		
Was the type of the RADT mentioned (EIA or OIA)?	Yes		
Were RADTs conducted during consultation time?	Yes		
		Low	Low
DOMAIN 3: Reference Standard			

Mirza 2007a (Continued)

Were culture results interpreted with blinding of the results of the RADT?	No
Is the throat culture method likely to correctly identify GAS (laboratory culture on a blood agar plate during 48 hr)?	Unclear
Were the culture medium, atmosphere, duration of incubation and GAS-confirmation technique described?	No
	High
	High

DOMAIN 4: Flow and Timing

Was the delay between the performance of the RADT and throat culture plating less than 48 hours?	Unclear
Did all patients receive a throat culture?	No
Did patients receive the same throat culture method?	Yes
Were undetermined/uninterpretable results reported?	No
Were withdrawals from the study explained?	Yes
	High

Mirza 2007b
Study characteristics

Patient sampling	Cross-sectional study Retrospective design Sample: unclear Direct comparison of different RADTs: no Direct comparison of several throat culture techniques: no Person performing the throat sample: nurses Exclusion if recent antibiotics use before inclusion: no Clinical selection of patients: unclear Presenting signs and symptoms: unclear Age range for inclusion: < 18 years
Patient characteristics and setting	Sample size: total 6865 (only 5135 included in the meta-analysis, i.e., those with RADT negative results also cultured) Age (distribution): not reported GAS prevalence according to culture (with 95% confidence interval): 29.3% (95% CI not reported) Country of study: USA Sex (% of girls): not reported

Mirza 2007b (Continued)

 Clinical severity assessment: none
 Clinical setting: unclear ("children's hospital")
 Single-centre study

Index tests	Throat swab: 2 different swabs (1 swab for performing the RADT, 1 swab for culture) Commercial name of the RADT: Signify Strep A (Abbott) Type of RADT: EIA
Target condition and reference standard(s)	Throat culture medium: inhibitory Atmosphere of incubation: not reported Duration of incubation: not reported GAS confirmation: not reported Number of plates inoculated: 1 Assessment of GAS antibody response: no Relevant details: -
Flow and timing	No follow-up
Comparative	
Type of study	Journal article
Notes	See Mirza 2007a

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient Selection			
Was a consecutive or random sample of patients enrolled?	Unclear		
Was it a cross-sectional study or a RCT?	Yes		
Were selection criteria clearly described (at least presenting signs and symptoms and age limits for inclusion)?	No		
Was clinical selection of patients avoided?	Unclear		
Were patients seen in an ambulatory care setting?	Unclear		
		High	Unclear
DOMAIN 2: Index Test All tests			
Were the RADT results interpreted with blinding of the results of culture?	Yes		
Was the type of the RADT mentioned (EIA or OIA)?	Yes		
Were RADTs conducted during consultation time?	No		
		Low	High

DOMAIN 3: Reference Standard

Mirza 2007b (Continued)

Were culture results interpreted with blinding of the results of the RADT?	No		
Is the throat culture method likely to correctly identify GAS (laboratory culture on a blood agar plate during 48 hr)?	Unclear		
Were the culture medium, atmosphere, duration of incubation and GAS-confirmation technique described?	No		
		High	High

DOMAIN 4: Flow and Timing

Was the delay between the performance of the RADT and throat culture plating less than 48 hours?	Unclear		
Did all patients receive a throat culture?	No		
Did patients receive the same throat culture method?	Yes		
Were undetermined/uninterpretable results reported?	No		
Were withdrawals from the study explained?	Yes		
		High	

Mlejnek 2014
Study characteristics

Patient sampling	Cross-sectional study Retrospective design Sample: consecutive Direct comparison of different RADTs: no Direct comparison of several throat culture techniques: no Person performing the throat sample: not reported Exclusion if recent antibiotics use before inclusion: no Clinical selection of patients: unclear Presenting signs and symptoms: not reported ("all patients who had rapid strep screens") Age range for inclusion: < 21 years
Patient characteristics and setting	Sample size: 3423 Age (distribution): not reported GAS prevalence according to culture (with 95% confidence interval): 16.8% (95% CI not reported) Country of study: USA Sex (% of girls): not reported Clinical severity assessment: none Clinical setting: emergency department Single-centre study

Mlejnek 2014 (Continued)

Index tests	Throat swab (1 single, 1 double, 2 different): not reported Commercial name of the RADT: OSOM Strep A Type of RADT: EIA
Target condition and reference standard(s)	Throat culture medium: standard Atmosphere of incubation: aerobic with CO ₂ enrichment Duration of incubation: 48 hours GAS confirmation: not reported Number of plates inoculated: 1 Assessment of GAS antibody response: no Relevant details: -
Flow and timing	No follow-up
Comparative	
Type of study	Conference abstract (Annual Meeting of the Society for Academic Emergency Medicine, Dallas, Texas, USA, May 2014)
Notes	We thank Dr. JR Mlejnek for sharing additional information that was not part of the original conference abstract

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient Selection			
Was a consecutive or random sample of patients enrolled?	Yes		
Was it a cross-sectional study or a RCT?	Yes		
Were selection criteria clearly described (at least presenting signs and symptoms and age limits for inclusion)?	No		
Was clinical selection of patients avoided?	Unclear		
Were patients seen in an ambulatory care setting?	Yes		
		Unclear	Unclear
DOMAIN 2: Index Test All tests			
Were the RADT results interpreted with blinding of the results of culture?	Yes		
Was the type of the RADT mentioned (EIA or OIA)?	Yes		
Were RADTs conducted during consultation time?	Yes		
		Low	Low
DOMAIN 3: Reference Standard			

Mlejnek 2014 (Continued)

Were culture results interpreted with blinding of the results of the RADT?	No	
Is the throat culture method likely to correctly identify GAS (laboratory culture on a blood agar plate during 48 hr)?	Yes	
Were the culture medium, atmosphere, duration of incubation and GAS-confirmation technique described?	Yes	
		High Low

DOMAIN 4: Flow and Timing

Was the delay between the performance of the RADT and throat culture plating less than 48 hours?	Unclear	
Did all patients receive a throat culture?	No	
Did patients receive the same throat culture method?	Yes	
Were undetermined/uninterpretable results reported?	No	
Were withdrawals from the study explained?	Yes	
		High

Moyer 1990
Study characteristics

Patient sampling	Cross-sectional study Prospective design Sample: unclear Direct comparison of different RADTs: no Direct comparison of several throat culture techniques: yes (24 versus 48 hour reading) Person performing the throat sample: physician or nurse Exclusion if recent antibiotics use before inclusion: yes (within 2 weeks prior to the onset of pharyngitis) Clinical selection of patients: not reported Presenting signs and symptoms: not reported Age range for inclusion: not reported ("children")
Patient characteristics and setting	Sample size: total 649, children 324 Age (distribution): range 7 months to 16 years GAS prevalence according to culture (with 95% confidence interval): 32.1% (95% CI not reported) Country of study: USA Sex (% of girls): not reported Clinical severity assessment: none Clinical setting: office-based

Moyer 1990 (Continued)

	Single-centre study
Index tests	Throat swab: 1 single swab (used for culture and then for the RADT) Commercial name of the RADT: Directgen 1-2-3 Group A Strep Test Type of RADT: EIA (liposomal test)
Target condition and reference standard(s)	Throat culture medium: standard Atmosphere of incubation: aerobic Duration of incubation: 48 hours GAS confirmation: latex test Number of plates inoculated: 1 Assessment of GAS antibody response: no Relevant details: plates were examined at 24 and 48 hours and variations in the accuracy of the RADT by incubation time were evaluated. We only extracted data related to the 48 hour reference standard.
Flow and timing	No follow-up
Comparative	
Type of study	Journal article
Notes	The study included children and adults. We extracted data for paediatric participants. RADT kits were provided by the manufacturer (BBL).

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient Selection			
Was a consecutive or random sample of patients enrolled?	Unclear		
Was it a cross-sectional study or a RCT?	Yes		
Were selection criteria clearly described (at least presenting signs and symptoms and age limits for inclusion)?	No		
Was clinical selection of patients avoided?	Unclear		
Were patients seen in an ambulatory care setting?	Yes		
		High	Unclear
DOMAIN 2: Index Test All tests			
Were the RADT results interpreted with blinding of the results of culture?	Yes		
Was the type of the RADT mentioned (EIA or OIA)?	Yes		
Were RADTs conducted during consultation time?	No		
		Low	High

Moyer 1990 (Continued)

DOMAIN 3: Reference Standard

Were culture results interpreted with blinding of the results of the RADT?	Unclear
Is the throat culture method likely to correctly identify GAS (laboratory culture on a blood agar plate during 48 hr)?	Yes
Were the culture medium, atmosphere, duration of incubation and GAS-confirmation technique described?	Yes
	Unclear Low

DOMAIN 4: Flow and Timing

Was the delay between the performance of the RADT and throat culture plating less than 48 hours?	Yes
Did all patients receive a throat culture?	Yes
Did patients receive the same throat culture method?	Yes
Were undetermined/uninterpretable results reported?	Yes
Were withdrawals from the study explained?	Yes
	Low

Needham 1998
Study characteristics

Patient sampling	Cross-sectional study Prospective design Sample: consecutive Direct comparison of different RADTs: no Direct comparison of several throat culture techniques: yes (standard versus enriched) Person performing the throat sample: physician Exclusion if recent antibiotics use before inclusion: no Clinical selection of patients: unclear Presenting signs and symptoms: unclear Age range for inclusion: not reported
Patient characteristics and setting	Sample size: 276 Age (distribution): mean = 6.4 years GAS prevalence according to culture (with 95% confidence interval): 31.2% (95% CI not reported)

Needham 1998 (Continued)

Country of study: USA
 Sex (% of girls): not reported
 Clinical severity assessment: none
 Clinical setting: office-based
 Single-centre study (regarding paediatric participants)

Index tests	Throat swab: 1 single swab (used for culture and then for the RADT) Commercial name of the RADT: Strep A OIA (Biostar) Type of RADT: OIA
Target condition and reference standard(s)	Throat culture medium: standard and enrichment Atmosphere of incubation: aerobic Duration of incubation: 48 hours GAS confirmation: latex test Number of plates inoculated: 1 Assessment of GAS antibody response: no Relevant details: swabs were inoculated on a standard blood agar plate and the pledget from the transport tube was used for culture following incubation in a Todd-Hewitt enrichment broth. Enriched culture did not identify additional positive specimens as compared to standard culture. The results of the 2 culture techniques were considered equivalent.
Flow and timing	No follow-up
Comparative	
Type of study	Journal article
Notes	The study was funded in part by Biostar (manufacturer of the RADT)

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient Selection			
Was a consecutive or random sample of patients enrolled?	Yes		
Was it a cross-sectional study or a RCT?	Yes		
Were selection criteria clearly described (at least presenting signs and symptoms and age limits for inclusion)?	No		
Was clinical selection of patients avoided?	Unclear		
Were patients seen in an ambulatory care setting?	Yes		
		High	Unclear
DOMAIN 2: Index Test All tests			
Were the RADT results interpreted with blinding of the results of culture?	Yes		

Needham 1998 *(Continued)*

Was the type of the RADT mentioned (EIA or OIA)?	Yes
Were RADTs conducted during consultation time?	No
Low High	

DOMAIN 3: Reference Standard

Were culture results interpreted with blinding of the results of the RADT?	Unclear
Is the throat culture method likely to correctly identify GAS (laboratory culture on a blood agar plate during 48 hr)?	Yes
Were the culture medium, atmosphere, duration of incubation and GAS-confirmation technique described?	Yes
Unclear Low	

DOMAIN 4: Flow and Timing

Was the delay between the performance of the RADT and throat culture plating less than 48 hours?	Yes
Did all patients receive a throat culture?	Yes
Did patients receive the same throat culture method?	Yes
Were undetermined/uninterpretable results reported?	No
Were withdrawals from the study explained?	No
Low	

Nitsch-Osuch 2010
Study characteristics

Patient sampling	Cross-sectional study Prospective design Sample: unclear Direct comparison of different RADTs: no Direct comparison of several throat culture techniques: no Person performing the throat sample: unclear Exclusion if recent antibiotics use before inclusion: yes Clinical selection of patients: explicit criteria but not a score (see below) Presenting signs and symptoms: fever > 38°C and sore throat, no cough and sneezing Age range for inclusion: 2 to 15 years
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Nitsch-Osuch 2010 (Continued)

Patient characteristics and setting	Sample size: 188 Age (distribution): mean (SD) = 5.5 (2.6) years GAS prevalence according to culture (with 95% confidence interval): 33.5% (95% CI not reported) Country of study: Poland Sex (% of girls): 48% Clinical severity assessment: none Clinical setting: unclear Single- or multi-centre study: unclear
Index tests	Throat swab (1 single, 1 double, 2 different): not reported Commercial name of the RADT: Test Strep A (SureScreen) Type of RADT: EIA
Target condition and reference standard(s)	Throat culture medium: not reported Atmosphere of incubation: not reported Duration of incubation: not reported GAS confirmation: not reported Number of plates inoculated: not reported Assessment of GAS antibody response: no Relevant details: throat culture technique not described
Flow and timing	No follow-up
Comparative	
Type of study	Conference abstract
Notes	—

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient Selection			
Was a consecutive or random sample of patients enrolled?	Unclear		
Was it a cross-sectional study or a RCT?	Yes		
Were selection criteria clearly described (at least presenting signs and symptoms and age limits for inclusion)?	Yes		
Was clinical selection of patients avoided?	No		
Were patients seen in an ambulatory care setting?	Yes		
		High	High
DOMAIN 2: Index Test All tests			
Were the RADT results interpreted with blinding of the results of culture?	Unclear		
Was the type of the RADT mentioned (EIA or OIA)?	Yes		

Nitsch-Osuch 2010 *(Continued)*

Were RADTs conducted during consultation time?	Unclear		
		Unclear	Unclear
DOMAIN 3: Reference Standard			
Were culture results interpreted with blinding of the results of the RADT?	Unclear		
Is the throat culture method likely to correctly identify GAS (laboratory culture on a blood agar plate during 48 hr)?	Unclear		
Were the culture medium, atmosphere, duration of incubation and GAS-confirmation technique described?	No		
		High	High
DOMAIN 4: Flow and Timing			
Was the delay between the performance of the RADT and throat culture plating less than 48 hours?	Unclear		
Did all patients receive a throat culture?	Yes		
Did patients receive the same throat culture method?	Yes		
Were undetermined/uninterpretable results reported?	No		
Were withdrawals from the study explained?	No		
		Low	

Nonaka 1988

Study characteristics	
Patient sampling	Cross-sectional study Retrospective or prospective design: unclear Sample: unclear Direct comparison of different RADTs: yes Direct comparison of several throat culture techniques: no Person performing the throat sample: unclear Exclusion if recent antibiotics use before inclusion: unclear Clinical selection of patients: unclear Presenting signs and symptoms: pharyngitis or tonsillitis Age range for inclusion: 0 to 16 years
Patient characteristics and setting	Sample size: 100 Age (distribution): unclear GAS prevalence according to culture (with 95% confidence interval): 23% (95% CI not reported) Country of study: Japan

Nonaka 1988 (Continued)

Sex (% of girls): 42%
 Clinical severity assessment: none
 Clinical setting: hospital paediatric outpatient clinic
 Single-centre study

Index tests	Throat swab: unclear Commercial name of the RADT: TestPack Strep A Type of RADT: EIA
Target condition and reference standard(s)	Throat culture medium: unclear Atmosphere of incubation: unclear Duration of incubation: unclear GAS confirmation: bacitracin disk Number of plates inoculated: not extracted Assessment of GAS antibody response: not extracted Relevant details: -
Flow and timing	No follow-up
Comparative	
Type of study	Journal article (in Japanese)
Notes	The study was funded by Tokyo Kosei-Nenkin Hospital. We thank Prof. Ryuki Kassai for translating this article.

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient Selection			
Was a consecutive or random sample of patients enrolled?	Unclear		
Was it a cross-sectional study or a RCT?	Yes		
Were selection criteria clearly described (at least presenting signs and symptoms and age limits for inclusion)?	Unclear		
Was clinical selection of patients avoided?	Unclear		
Were patients seen in an ambulatory care setting?	Yes		
		Unclear	Unclear
DOMAIN 2: Index Test All tests			
Were the RADT results interpreted with blinding of the results of culture?	Unclear		
Was the type of the RADT mentioned (EIA or OIA)?	Yes		
Were RADTs conducted during consultation time?	Unclear		
		Unclear	Unclear

Nonaka 1988 (Continued)

DOMAIN 3: Reference Standard

Were culture results interpreted with blinding of the results of the RADT?	Unclear
Is the throat culture method likely to correctly identify GAS (laboratory culture on a blood agar plate during 48 hr)?	Unclear
Were the culture medium, atmosphere, duration of incubation and GAS-confirmation technique described?	Unclear
	Unclear Unclear

DOMAIN 4: Flow and Timing

Was the delay between the performance of the RADT and throat culture plating less than 48 hours?	Unclear
Did all patients receive a throat culture?	Yes
Did patients receive the same throat culture method?	Yes
Were undetermined/uninterpretable results reported?	Yes
Were withdrawals from the study explained?	Unclear
	Low

Pauchard 2012
Study characteristics

Patient sampling	Cross-sectional study Prospective design Sample: consecutive Direct comparison of different RADTs: no Direct comparison of several throat culture techniques: no Person performing the throat sample: not reported Exclusion if recent antibiotics use before inclusion: yes (within the previous week) Clinical selection of patients: none Presenting signs and symptoms: sore throat Age range for inclusion: 3 to 18 years
Patient characteristics and setting	Sample size: 1940 Age (distribution): not reported GAS prevalence according to culture (with 95% confidence interval): 38.7% (95% CI not reported for this group) Country of study: Switzerland Sex (% of girls): not reported Clinical severity assessment: Mclsaac score Clinical setting: emergency department

Pauchard 2012 (Continued)

	Single-centre study
Index tests	Throat swab: 2 different swabs Commercial name of the RADT: QuickVue In-Line Strep A (Quidel) Type of RADT: EIA
Target condition and reference standard(s)	Throat culture medium: standard Atmosphere of incubation: aerobic with CO ₂ enrichment Duration of incubation: 48 hours GAS confirmation: latex test Number of plates inoculated: 1 Assessment of GAS antibody response: no Relevant details: -
Flow and timing	No follow-up
Comparative	
Type of study	Conference abstract (Annual Meeting of the Swiss Society of Paediatrics, Lucerne, Switzerland, June 2012)
Notes	We thank Dr. JY Pauchard for sharing additional information that was not part of the original conference abstract

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient Selection			
Was a consecutive or random sample of patients enrolled?	Yes		
Was it a cross-sectional study or a RCT?	Yes		
Were selection criteria clearly described (at least presenting signs and symptoms and age limits for inclusion)?	Yes		
Was clinical selection of patients avoided?	Yes		
Were patients seen in an ambulatory care setting?	Yes		
		Low	Low
DOMAIN 2: Index Test All tests			
Were the RADT results interpreted with blinding of the results of culture?	Yes		
Was the type of the RADT mentioned (EIA or OIA)?	Yes		
Were RADTs conducted during consultation time?	Yes		
		Low	Low

Pauchard 2012 (Continued)

DOMAIN 3: Reference Standard

Were culture results interpreted with blinding of the results of the RADT?	Yes	
Is the throat culture method likely to correctly identify GAS (laboratory culture on a blood agar plate during 48 hr)?	Yes	
Were the culture medium, atmosphere, duration of incubation and GAS-confirmation technique described?	Yes	
		Low
		Low

DOMAIN 4: Flow and Timing

Was the delay between the performance of the RADT and throat culture plating less than 48 hours?	Unclear	
Did all patients receive a throat culture?	Yes	
Did patients receive the same throat culture method?	Yes	
Were undetermined/uninterpretable results reported?	Yes	
Were withdrawals from the study explained?	Yes	
		Low

Pauchard 2013
Study characteristics

Patient sampling	Cross-sectional study Prospective design Sample: consecutive Direct comparison of different RADTs: no Direct comparison of several throat culture techniques: no Person performing the throat sample: not reported Exclusion if recent antibiotics use before inclusion: yes (within the previous week) Clinical selection of patients: none Presenting signs and symptoms: sore throat Age range for inclusion: 3 to 18 years
Patient characteristics and setting	Sample size: 183 Age (distribution): not reported GAS prevalence according to culture (with 95% confidence interval): 37.2% (95% CI not reported for this group) Country of study: Switzerland Sex (% of girls): not reported Clinical severity assessment: Mclsaac

Pauchard 2013 (Continued)

	Clinical setting: emergency department Single-centre study
Index tests	Throat swab: 2 different swabs Commercial name of the RADT: BioNexia Strep A (BioMerieux) Type of RADT: EIA
Target condition and reference standard(s)	Throat culture medium: standard Atmosphere of incubation: aerobic with CO ₂ enrichment Duration of incubation: 48 hours GAS confirmation: latex test Number of plates inoculated: 1 Assessment of GAS antibody response: no Relevant details: -
Flow and timing	No follow-up
Comparative	
Type of study	Conference abstract (Annual Meeting of the Swiss Society of Paediatrics, Geneva, Switzerland, June 2012).
Notes	We thank Dr. JY Pauchard for sharing additional information that was not part of the original conference abstract.

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient Selection			
Was a consecutive or random sample of patients enrolled?	Yes		
Was it a cross-sectional study or a RCT?	Yes		
Were selection criteria clearly described (at least presenting signs and symptoms and age limits for inclusion)?	Yes		
Was clinical selection of patients avoided?	Yes		
Were patients seen in an ambulatory care setting?	Yes		
		Low	Low
DOMAIN 2: Index Test All tests			
Were the RADT results interpreted with blinding of the results of culture?	Yes		
Was the type of the RADT mentioned (EIA or OIA)?	Yes		
Were RADTs conducted during consultation time?	Yes		
		Low	Low

Pauchard 2013 (Continued)

DOMAIN 3: Reference Standard

Were culture results interpreted with blinding of the results of the RADT?	Yes	
Is the throat culture method likely to correctly identify GAS (laboratory culture on a blood agar plate during 48 hr)?	Yes	
Were the culture medium, atmosphere, duration of incubation and GAS-confirmation technique described?	Yes	
		Low
		Low

DOMAIN 4: Flow and Timing

Was the delay between the performance of the RADT and throat culture plating less than 48 hours?	Unclear	
Did all patients receive a throat culture?	Yes	
Did patients receive the same throat culture method?	Yes	
Were undetermined/uninterpretable results reported?	Yes	
Were withdrawals from the study explained?	Yes	
		Low

Pitetti 1998
Study characteristics

Patient sampling	<p>Cross-sectional study Prospective design Sample: unclear Direct comparison of different RADTs: no Direct comparison of several throat culture techniques: no Person performing the throat sample: not reported</p> <p>Exclusion if recent antibiotics use before inclusion: yes (within one week before presentation)</p> <p>Clinical selection of patients: explicit criteria but not a score (see below)</p> <p>Presenting signs and symptoms: patients with a sore throat with erythematous posterior pharynx, tonsillar exudate or scarlatiniform rash; or patients without a complaint of sore throat but with either an erythematous posterior pharynx, with or without exudate, or a scarlatiniform rash</p> <p>Age range for inclusion: 1 to 18 years</p>
Patient characteristics and setting	<p>Sample size: 233 Age (distribution): mean = 8.6 years (range 1.5 to 18.9 years)</p> <p>GAS prevalence according to culture (with 95% confidence interval): 31.3% (95% CI not reported)</p>

Pitetti 1998 (Continued)

Country of study: USA
 Sex (% of girls): 44.6%
 Clinical severity assessment: none
 Clinical setting: mixed (emergency department, walk-in clinic and acute concern clinic of a children hospital)
 Single-centre study

Index tests	Throat swab: 1 single swab (used for culture and then for the RADT) Commercial name of the RADT: Strep A OIA (Biostar) Type of RADT: OIA
Target condition and reference standard(s)	Throat culture medium: standard Atmosphere of incubation: aerobic with CO ₂ enrichment Duration of incubation: 48 hours GAS confirmation: latex test Number of plates inoculated: 1 Assessment of GAS antibody response: no Relevant details: -
Flow and timing	No follow-up
Comparative	
Type of study	Journal article
Notes	Funded in part by a grant from Biostar (manufacturer of the RADT)

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient Selection			
Was a consecutive or random sample of patients enrolled?	Unclear		
Was it a cross-sectional study or a RCT?	Yes		
Were selection criteria clearly described (at least presenting signs and symptoms and age limits for inclusion)?	Yes		
Was clinical selection of patients avoided?	No		
Were patients seen in an ambulatory care setting?	Yes		
		High	Unclear
DOMAIN 2: Index Test All tests			
Were the RADT results interpreted with blinding of the results of culture?	Unclear		
Was the type of the RADT mentioned (EIA or OIA)?	Yes		
Were RADTs conducted during consultation time?	Unclear		

Pitetti 1998 (Continued)

		Unclear	Unclear
DOMAIN 3: Reference Standard			
Were culture results interpreted with blinding of the results of the RADT?	Yes		
Is the throat culture method likely to correctly identify GAS (laboratory culture on a blood agar plate during 48 hr)?	Yes		
Were the culture medium, atmosphere, duration of incubation and GAS-confirmation technique described?	Yes		
		Low	Low
DOMAIN 4: Flow and Timing			
Was the delay between the performance of the RADT and throat culture plating less than 48 hours?	Yes		
Did all patients receive a throat culture?	Yes		
Did patients receive the same throat culture method?	Yes		
Were undetermined/uninterpretable results reported?	No		
Were withdrawals from the study explained?	Yes		
		Low	

Ramos 2011

Study characteristics	
Patient sampling	Cross-sectional study Prospective design Sample: unclear Direct comparison of different RADTs: no Direct comparison of several throat culture techniques: no Person performing the throat sample: not reported Exclusion if recent antibiotics use before inclusion: no Clinical selection of patients: unclear Presenting signs and symptoms: unclear Age range for inclusion: not reported ("pediatric services")
Patient characteristics and setting	Sample size: 165 Age (distribution): not reported

Ramos 2011 (Continued)

GAS prevalence according to culture (with 95% confidence interval): 31.5% (95% CI not reported)
 Country of study: Spain
 Sex (% of girls): not reported
 Clinical severity assessment: none
 Clinical setting: other ("pediatric services")
 Multi-centre study

Index tests	Throat swab: unclear Commercial name of the RADT: OSOM Strep A Type of RADT: EIA
Target condition and reference standard(s)	Throat culture medium: not reported Atmosphere of incubation: not reported Duration of incubation: not reported GAS confirmation: not reported Number of plates inoculated: not reported Assessment of GAS antibody response: no Relevant details: throat culture technique not described
Flow and timing	No follow-up
Comparative	
Type of study	Conference abstract
Notes	Funding not reported

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient Selection			
Was a consecutive or random sample of patients enrolled?	Unclear		
Was it a cross-sectional study or a RCT?	Yes		
Were selection criteria clearly described (at least presenting signs and symptoms and age limits for inclusion)?	No		
Was clinical selection of patients avoided?	Unclear		
Were patients seen in an ambulatory care setting?	Yes		
		High	Unclear
DOMAIN 2: Index Test All tests			
Were the RADT results interpreted with blinding of the results of culture?	Yes		
Was the type of the RADT mentioned (EIA or OIA)?	Yes		
Were RADTs conducted during consultation time?	Yes		

Ramos 2011 (Continued)

Low
Low
DOMAIN 3: Reference Standard

Were culture results interpreted with blinding of the results of the RADT? Unclear

Is the throat culture method likely to correctly identify GAS (laboratory culture on a blood agar plate during 48 hr)? Unclear

Were the culture medium, atmosphere, duration of incubation and GAS-confirmation technique described? No

High
High
DOMAIN 4: Flow and Timing

Was the delay between the performance of the RADT and throat culture plating less than 48 hours? Unclear

Did all patients receive a throat culture? Yes

Did patients receive the same throat culture method? Yes

Were undetermined/uninterpretable results reported? No

Were withdrawals from the study explained? No

Low
Regueras De Lorenzo 2012
Study characteristics

Patient sampling	Cross-sectional study Prospective design Sample: consecutive Direct comparison of different RADTs: no Direct comparison of several throat culture techniques: no Person performing the throat sample: physicians Exclusion if recent antibiotics use before inclusion: yes (within a week before enrollment) Clinical selection of patients: none Presenting signs and symptoms: acute tonsillitis and/or pharyngitis Age range for inclusion: 2 to 14 years
Patient characteristics and setting	Sample size: 192 Age (distribution): mean (SD) = 7.2 (2.8) years GAS prevalence according to culture (with 95% confidence interval): 38.5% (95% CI not reported) Country of study: Spain

Regueras De Lorenzo 2012 (Continued)

Sex (% of girls): 48.4%
 Clinical severity assessment: Centor score
 Clinical setting: office-based
 Multi-centre study

Index tests	Throat swab: 2 different swabs (1 for culture, 1 for performing the RADT) Commercial name of the RADT: TestPack Plus (Inverness) Type of RAD: EIA
Target condition and reference standard(s)	Throat culture medium: inhibitory Atmosphere of incubation: aerobic with CO ₂ enrichment Duration of incubation: 48 hours GAS confirmation: latex test Number of plates inoculated: 1 Assessment of GAS antibody response: no Relevant details: -
Flow and timing	No follow-up
Comparative	
Type of study	Journal article (in Spanish)
Notes	Supported by a public research grant (Institute of Health Carlos III) and EU funding (FEDER)

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient Selection			
Was a consecutive or random sample of patients enrolled?	Yes		
Was it a cross-sectional study or a RCT?	Yes		
Were selection criteria clearly described (at least presenting signs and symptoms and age limits for inclusion)?	Yes		
Was clinical selection of patients avoided?	Yes		
Were patients seen in an ambulatory care setting?	Yes		
		Low	Low
DOMAIN 2: Index Test All tests			
Were the RADT results interpreted with blinding of the results of culture?	Yes		
Was the type of the RADT mentioned (EIA or OIA)?	Yes		
Were RADTs conducted during consultation time?	Yes		
		Low	Low

Regueras De Lorenzo 2012 *(Continued)*
DOMAIN 3: Reference Standard

Were culture results interpreted with blinding of the results of the RADT?	Unclear
Is the throat culture method likely to correctly identify GAS (laboratory culture on a blood agar plate during 48 hr)?	Yes
Were the culture medium, atmosphere, duration of incubation and GAS-confirmation technique described?	Yes
	Unclear Low

DOMAIN 4: Flow and Timing

Was the delay between the performance of the RADT and throat culture plating less than 48 hours?	Unclear
Did all patients receive a throat culture?	Yes
Did patients receive the same throat culture method?	Yes
Were undetermined/uninterpretable results reported?	No
Were withdrawals from the study explained?	No
	Low

Reinert 1988
Study characteristics

Patient sampling	Cross-sectional study Prospective design Sample: unclear Direct comparison of different RADTs: no Direct comparison of several throat culture techniques: no Person performing the throat sample: not reported Exclusion if recent antibiotics use before inclusion: no Clinical selection of patients: none Presenting signs and symptoms: febrile sore throat Age range for inclusion: 2 to 14 years
Patient characteristics and setting	Sample size: 92 Age (distribution): mean age = 6 years and 4 months GAS prevalence according to culture (with 95% confidence interval): 29.4% (95% CI not reported) Country of study: France Sex (% of girls): not reported Clinical severity assessment: none Clinical setting: office-based

Reinert 1988 (Continued)

	Multi-centre study
Index tests	Throat swab: 2 different swabs (1 swab for performing the RADT, 1 swab for culture) Commercial name of the RADT: Group A Strep Test (Quidel) Type of RADT: EIA
Target condition and reference standard(s)	Throat culture medium: enrichment and inhibitory Atmosphere of incubation: aerobic Duration of incubation: not reported GAS confirmation: not reported Number of plates inoculated: 1 Assessment of GAS antibody response: no Relevant details: -
Flow and timing	No follow-up
Comparative	
Type of study	Journal article
Notes	—

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient Selection			
Was a consecutive or random sample of patients enrolled?	Unclear		
Was it a cross-sectional study or a RCT?	Yes		
Were selection criteria clearly described (at least presenting signs and symptoms and age limits for inclusion)?	Yes		
Was clinical selection of patients avoided?	No		
Were patients seen in an ambulatory care setting?	Yes		
		High	High
DOMAIN 2: Index Test All tests			
Were the RADT results interpreted with blinding of the results of culture?	Yes		
Was the type of the RADT mentioned (EIA or OIA)?	Yes		
Were RADTs conducted during consultation time?	Yes		
		Low	Low
DOMAIN 3: Reference Standard			

Reinert 1988 *(Continued)*

Were culture results interpreted with blinding of the results of the RADT?	Unclear
Is the throat culture method likely to correctly identify GAS (laboratory culture on a blood agar plate during 48 hr)?	Unclear
Were the culture medium, atmosphere, duration of incubation and GAS-confirmation technique described?	No
	High
	High

DOMAIN 4: Flow and Timing

Was the delay between the performance of the RADT and throat culture plating less than 48 hours?	Yes
Did all patients receive a throat culture?	Yes
Did patients receive the same throat culture method?	Unclear
Were undetermined/uninterpretable results reported?	No
Were withdrawals from the study explained?	No
	Unclear

Rimoin 2010a
Study characteristics

Patient sampling	<p>Cross-sectional study Prospective design Sample: consecutive Direct comparison of different RADTs: no Direct comparison of several throat culture techniques: no Person performing the throat sample: unclear</p> <p>Exclusion if recent antibiotics use before inclusion: yes (oral use in the 3 days prior to screening or parenteral use in the 28 days before screening)</p> <p>Clinical selection of patients: none</p> <p>Presenting signs and symptoms: sore throat</p> <p>Age range for inclusion: 2 to 12 years</p>
Patient characteristics and setting	<p>Sample size: 184 Age (distribution): mean (SD) = 5.8 (0.21) years</p> <p>GAS prevalence according to culture (with 95% confidence interval): 24.5% (95% CI not reported) Country of study: Brazil Sex (% of girls): 43.3% Clinical severity assessment: Centor score Clinical setting: walk-in clinic</p> <p>Multi-centre study (see Rimoin 2010b-d)</p>

Rimoin 2010a (Continued)

Index tests	Throat swab: 2 different swabs (1 swab for performing the RADT, 1 swab for culture) Commercial name of the RADT: Strep A OIA Max (Biostar) Type of RADT: OIA
Target condition and reference standard(s)	Throat culture medium: standard Atmosphere of incubation: anaerobic Duration of incubation: 48 hours GAS confirmation: bacitracin disk Number of plates inoculated: 1 Assessment of GAS antibody response: no Relevant details: -
Flow and timing	No follow-up
Comparative	
Type of study	Journal article
Notes	Multi-centre study conducted in Brazil, Croatia, Egypt and Latvia (see Rimoin 2010b-d). This study was supported by USAID and WHO. The rapid test kits were provided by Biostar (manufacturer of the RADT).

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient Selection			
Was a consecutive or random sample of patients enrolled?	Yes		
Was it a cross-sectional study or a RCT?	Yes		
Were selection criteria clearly described (at least presenting signs and symptoms and age limits for inclusion)?	Yes		
Was clinical selection of patients avoided?	Yes		
Were patients seen in an ambulatory care setting?	Yes		
		Low	Low
DOMAIN 2: Index Test All tests			
Were the RADT results interpreted with blinding of the results of culture?	Unclear		
Was the type of the RADT mentioned (EIA or OIA)?	Yes		
Were RADTs conducted during consultation time?	No		
		Unclear	High

Rimoin 2010a (Continued)

DOMAIN 3: Reference Standard

Were culture results interpreted with blinding of the results of the RADT?	Unclear
Is the throat culture method likely to correctly identify GAS (laboratory culture on a blood agar plate during 48 hr)?	Yes
Were the culture medium, atmosphere, duration of incubation and GAS-confirmation technique described?	Yes
	Unclear
	Low

DOMAIN 4: Flow and Timing

Was the delay between the performance of the RADT and throat culture plating less than 48 hours?	Unclear
Did all patients receive a throat culture?	Yes
Did patients receive the same throat culture method?	Yes
Were undetermined/uninterpretable results reported?	No
Were withdrawals from the study explained?	Yes
	Low

Rimoin 2010b
Study characteristics

Patient sampling	See Rimoin 2010a
Patient characteristics and setting	Sample size: 404 Age (distribution): mean (SD) = 5.8 (0.14) years GAS prevalence according to culture (with 95% confidence interval): 39.4% (95% CI not reported) Country of study: Croatia Sex (% of girls): 51.6% Clinical severity assessment: Centor score Clinical setting: walk-in clinic Multi-centre study (see Rimoin 2010a)
Index tests	See Rimoin 2010a
Target condition and reference standard(s)	See Rimoin 2010a
Flow and timing	No follow-up
Comparative	
Type of study	Journal article

Rimoin 2010b (Continued)

Notes

See Rimoin 2010a

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient Selection			
Was a consecutive or random sample of patients enrolled?	Yes		
Was it a cross-sectional study or a RCT?	Yes		
Were selection criteria clearly described (at least presenting signs and symptoms and age limits for inclusion)?	Yes		
Was clinical selection of patients avoided?	Yes		
Were patients seen in an ambulatory care setting?	Yes		
		Low	Low
DOMAIN 2: Index Test All tests			
Were the RADT results interpreted with blinding of the results of culture?	Unclear		
Was the type of the RADT mentioned (EIA or OIA)?	Yes		
Were RADTs conducted during consultation time?	No		
		Unclear	High
DOMAIN 3: Reference Standard			
Were culture results interpreted with blinding of the results of the RADT?	Unclear		
Is the throat culture method likely to correctly identify GAS (laboratory culture on a blood agar plate during 48 hr)?	Yes		
Were the culture medium, atmosphere, duration of incubation and GAS-confirmation technique described?	Yes		
		Unclear	Low
DOMAIN 4: Flow and Timing			
Was the delay between the performance of the RADT and throat culture plating less than 48 hours?	Unclear		
Did all patients receive a throat culture?	Yes		
Did patients receive the same throat culture method?	Yes		
Were undetermined/uninterpretable results reported?	No		

Rimoin 2010b (Continued)

Were withdrawals from the study explained? Yes

Low

Rimoin 2010c
Study characteristics

Patient sampling	See Rimoin 2010a
Patient characteristics and setting	Sample size: 1626 Age (distribution): mean (SD) = 4.8 (0.06) years GAS prevalence according to culture (with 95% confidence interval): 26.4% (95% CI not reported) Country of study: Egypt Sex (% of girls): 42.3% Clinical severity assessment: Centor score Clinical setting: walk-in clinic Multi-centre study (see Rimoin 2010a)
Index tests	See Rimoin 2010a
Target condition and reference standard(s)	See Rimoin 2010a
Flow and timing	No follow-up
Comparative	
Type of study	Journal article
Notes	See Rimoin 2010a

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient Selection			
Was a consecutive or random sample of patients enrolled?	Yes		
Was it a cross-sectional study or a RCT?	Yes		
Were selection criteria clearly described (at least presenting signs and symptoms and age limits for inclusion)?	Yes		
Was clinical selection of patients avoided?	Yes		
Were patients seen in an ambulatory care setting?	Yes		
		Low	Low

DOMAIN 2: Index Test All tests

Rimoin 2010c (Continued)

Were the RADT results interpreted with blinding of the results of culture?	Unclear
Was the type of the RADT mentioned (EIA or OIA)?	Yes
Were RADTs conducted during consultation time?	No
	Unclear High

DOMAIN 3: Reference Standard

Were culture results interpreted with blinding of the results of the RADT?	Unclear
Is the throat culture method likely to correctly identify GAS (laboratory culture on a blood agar plate during 48 hr)?	Yes
Were the culture medium, atmosphere, duration of incubation and GAS-confirmation technique described?	Yes
	Unclear Low

DOMAIN 4: Flow and Timing

Was the delay between the performance of the RADT and throat culture plating less than 48 hours?	Unclear
Did all patients receive a throat culture?	Yes
Did patients receive the same throat culture method?	Yes
Were undetermined/uninterpretable results reported?	No
Were withdrawals from the study explained?	Yes
	Low

Rimoin 2010d
Study characteristics

Patient sampling	See Rimoin 2010a
Patient characteristics and setting	Sample size: 258 Age (distribution): mean (SD) = 6.6 (1.9) years GAS prevalence according to culture (with 95% confidence interval): 29.5% (95% CI not reported) Country of study: Latvia Sex (% of girls): 46.1% Clinical severity assessment: Centor score Clinical setting: walk-in clinic Multi-centre study (see Rimoin 2010a)
Index tests	See Rimoin 2010a

Rimoin 2010d (Continued)

Target condition and reference standard(s)	See Rimoin 2010a
Flow and timing	No follow-up
Comparative	
Type of study	Journal article
Notes	See Rimoin 2010a

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient Selection			
Was a consecutive or random sample of patients enrolled?	Yes		
Was it a cross-sectional study or a RCT?	Yes		
Were selection criteria clearly described (at least presenting signs and symptoms and age limits for inclusion)?	Yes		
Was clinical selection of patients avoided?	Yes		
Were patients seen in an ambulatory care setting?	Yes		
		Low	Low
DOMAIN 2: Index Test All tests			
Were the RADT results interpreted with blinding of the results of culture?	Unclear		
Was the type of the RADT mentioned (EIA or OIA)?	Yes		
Were RADTs conducted during consultation time?	No		
		Unclear	High
DOMAIN 3: Reference Standard			
Were culture results interpreted with blinding of the results of the RADT?	Unclear		
Is the throat culture method likely to correctly identify GAS (laboratory culture on a blood agar plate during 48 hr)?	Yes		
Were the culture medium, atmosphere, duration of incubation and GAS-confirmation technique described?	Yes		
		Unclear	Low
DOMAIN 4: Flow and Timing			

Rimoin 2010d (Continued)

Was the delay between the performance of the RADT and throat culture plating less than 48 hours?	Unclear
Did all patients receive a throat culture?	Yes
Did patients receive the same throat culture method?	Yes
Were undetermined/uninterpretable results reported?	No
Were withdrawals from the study explained?	Yes
Low	

Roddey 1995

Study characteristics

Patient sampling	<p>Cross-sectional study Prospective design Sample: unclear Direct comparison of different RADTs: no Direct comparison of several throat culture techniques: yes (standard versus enriched culture) Person performing the throat sample: unclear</p> <p>Exclusion if recent antibiotics use before inclusion: yes (during the precedent week)</p> <p>Clinical selection of patients: none</p> <p>Presenting signs and symptoms: acute pharyngitis</p> <p>Age range for inclusion: not reported</p>
Patient characteristics and setting	<p>Sample size: 301 Age (distribution): not reported</p> <p>GAS prevalence according to culture (with 95% confidence interval): 38.9% (95% CI not reported) Country of study: USA Sex (% of girls): not reported Clinical severity assessment: none Clinical setting: paediatric office Single-centre study</p>
Index tests	<p>Throat swab: 2 throat swabs were taken for each patient. Swab #1 was used for standard culture and then for performing the RADT. Swab #2 was incubated in a Todd-Hewitt enrichment broth and subsequently inoculated on a blood agar plate. We extracted data only for swab #1.</p> <p>Commercial name of the RADT: Strep A OIA (Biostar) Type of RADT: OIA</p>
Target condition and reference standard(s)	<p>Throat culture medium: standard and enrichment (data extracted only for standard culture) Atmosphere of incubation: aerobic Duration of incubation: 48 hours GAS confirmation: bacitracin disk</p>

Roddey 1995 (Continued)

 Number of plates inoculated: 1
 Assessment of GAS antibody response: no
 Relevant details: -

Flow and timing No follow-up

Comparative

Type of study Journal article

Notes The study was funded by a research grant from the American Academy of Pediatrics and the manufacturer of the RADT (Biostar) provided the test kits

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient Selection			
Was a consecutive or random sample of patients enrolled?	Unclear		
Was it a cross-sectional study or a RCT?	Yes		
Were selection criteria clearly described (at least presenting signs and symptoms and age limits for inclusion)?	No		
Was clinical selection of patients avoided?	Yes		
Were patients seen in an ambulatory care setting?	Yes		
		High	High
DOMAIN 2: Index Test All tests			
Were the RADT results interpreted with blinding of the results of culture?	Yes		
Was the type of the RADT mentioned (EIA or OIA)?	Yes		
Were RADTs conducted during consultation time?	No		
		Low	High
DOMAIN 3: Reference Standard			
Were culture results interpreted with blinding of the results of the RADT?	Unclear		
Is the throat culture method likely to correctly identify GAS (laboratory culture on a blood agar plate during 48 hr)?	Yes		
Were the culture medium, atmosphere, duration of incubation and GAS-confirmation technique described?	Yes		

Roddey 1995 (Continued)

	Unclear	Low
DOMAIN 4: Flow and Timing		
Was the delay between the performance of the RADT and throat culture plating less than 48 hours?	Yes	
Did all patients receive a throat culture?	Yes	
Did patients receive the same throat culture method?	Yes	
Were undetermined/uninterpretable results reported?	No	
Were withdrawals from the study explained?	No	
Low		

Roe 1995a

Study characteristics	
Patient sampling	Cross-sectional study Prospective design Sample: unclear Direct comparison of different RADTs: yes Direct comparison of several throat culture techniques: yes (1 plate versus 2 plates versus enrichment broth) Person performing the throat sample: other ("clinical personnel") Exclusion if recent antibiotics use before inclusion: no Clinical selection of patients: none Presenting signs and symptoms: symptomatic pharyngitis Age range for inclusion: not reported ("children")
Patient characteristics and setting	Sample size: 500 Age (distribution): not reported GAS prevalence according to culture (with 95% confidence interval): 30.2% (95% CI not reported) Country of study: USA Sex (% of girls): not reported Clinical severity assessment: none Clinical setting: mixed (children's hospital clinic and emergency department) Single-centre study
Index tests	Throat swab: 2 different swabs (each swab used for culture and then for the RADT) Commercial name of the RADT: Strep A OIA (Biostar) Type of RADT: OIA
Target condition and reference standard(s)	Throat culture medium: inhibitory and enrichment Atmosphere of incubation: aerobic Duration of incubation: 48 hours

Roe 1995a (Continued)

GAS confirmation: latex test
 Number of plates inoculated: 2 or 3
 Assessment of GAS antibody response: no
 Relevant details: 2 swabs were taken for each patient. Each swab was used for culture on a selective medium and then for antigen detection by one or the other RADTs. If both selective plates were negative for GAS, the pledgets were incubated in a Todd-Hewitt enrichment broth with subsequent culture. The reference standard was the isolation of GAS by any one (or more than one) of the plates.

Flow and timing	No follow-up
Comparative	
Type of study	Journal article
Notes	A co-author was affiliated with the manufacturer of one of the RADTs under evaluation (Abbott)

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient Selection			
Was a consecutive or random sample of patients enrolled?	Unclear		
Was it a cross-sectional study or a RCT?	Yes		
Were selection criteria clearly described (at least presenting signs and symptoms and age limits for inclusion)?	No		
Was clinical selection of patients avoided?	Yes		
Were patients seen in an ambulatory care setting?	Yes		
		High	Low
DOMAIN 2: Index Test All tests			
Were the RADT results interpreted with blinding of the results of culture?	Yes		
Was the type of the RADT mentioned (EIA or OIA)?	Yes		
Were RADTs conducted during consultation time?	No		
		Low	High
DOMAIN 3: Reference Standard			
Were culture results interpreted with blinding of the results of the RADT?	Yes		

Roe 1995a *(Continued)*

Is the throat culture method likely to correctly identify GAS (laboratory culture on a blood agar plate during 48 hr)?	Yes
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Were the culture medium, atmosphere, duration of incubation and GAS-confirmation technique described?	Yes
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Low
Low
DOMAIN 4: Flow and Timing

Was the delay between the performance of the RADT and throat culture plating less than 48 hours?	Yes
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Did all patients receive a throat culture?	Yes
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Did patients receive the same throat culture method?	No
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Were undetermined/uninterpretable results reported?	No
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Were withdrawals from the study explained?	Yes
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Low
Roe 1995b
Study characteristics

Patient sampling	See Roe 1995a
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Patient characteristics and setting	See Roe 1995a
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Index tests	Throat swab: 2 different swabs (each swab used for culture and then for the RADT) Commercial name of the RADT: Test Pack Plus Strep A (Abbott) Type of RADT: EIA
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Target condition and reference standard(s)	See Roe 1995a
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Flow and timing	No follow-up
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Comparative	
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Type of study	Journal article
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Notes	See Roe 1995a
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Methodological quality

Roe 1995b (Continued)

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient Selection			
Was a consecutive or random sample of patients enrolled?	Unclear		
Was it a cross-sectional study or a RCT?	Yes		
Were selection criteria clearly described (at least presenting signs and symptoms and age limits for inclusion)?	No		
Was clinical selection of patients avoided?	Yes		
Were patients seen in an ambulatory care setting?	Yes		
		High	Low
DOMAIN 2: Index Test All tests			
Were the RADT results interpreted with blinding of the results of culture?	Yes		
Was the type of the RADT mentioned (EIA or OIA)?	Yes		
Were RADTs conducted during consultation time?	No		
		Low	High
DOMAIN 3: Reference Standard			
Were culture results interpreted with blinding of the results of the RADT?	Yes		
Is the throat culture method likely to correctly identify GAS (laboratory culture on a blood agar plate during 48 hr)?	Yes		
Were the culture medium, atmosphere, duration of incubation and GAS-confirmation technique described?	Yes		
		Low	Low
DOMAIN 4: Flow and Timing			
Was the delay between the performance of the RADT and throat culture plating less than 48 hours?	Yes		
Did all patients receive a throat culture?	Yes		
Did patients receive the same throat culture method?	No		
Were undetermined/uninterpretable results reported?	No		
Were withdrawals from the study explained?	Yes		
		High	

Rogo 2010a
Study characteristics

Patient sampling	Cross-sectional study Prospective design Sample: unclear Direct comparison of different RADTs: yes Direct comparison of several throat culture techniques: no Person performing the throat sample: not reported Exclusion if recent antibiotics use before inclusion: no Clinical selection of patients: none Presenting signs and symptoms: signs and symptoms of pharyngitis Age range for inclusion: not reported ("pediatric office setting")
Patient characteristics and setting	Sample size: 228 Age (distribution): not reported GAS prevalence according to culture (with 95% confidence interval): 28.1% (95% CI not reported) Country of study: USA Sex (% of girls): not reported Clinical severity assessment: none Clinical setting: office-based Multi-centre study
Index tests	Throat swab: 3 different swabs (each swab used for culture and then for the RADT) Commercial name of the RADT: Acceava Strep A Type of RADT: EIA
Target condition and reference standard(s)	Throat culture medium: standard Atmosphere of incubation: not reported Duration of incubation: 24 hours GAS confirmation: latex test Number of plates inoculated: 1 Assessment of GAS antibody response: no Relevant details: -
Flow and timing	No follow-up
Comparative	
Type of study	Journal article
Notes	The study was funded by the manufacturer of one of the 3 RADTs under evaluation (Acceava)

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
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DOMAIN 1: Patient Selection

Rogo 2010a (Continued)

Was a consecutive or random sample of patients enrolled?	Unclear		
Was it a cross-sectional study or a RCT?	Yes		
Were selection criteria clearly described (at least presenting signs and symptoms and age limits for inclusion)?	No		
Was clinical selection of patients avoided?	Yes		
Were patients seen in an ambulatory care setting?	Yes		
		High	High

DOMAIN 2: Index Test All tests

Were the RADT results interpreted with blinding of the results of culture?	Yes		
Was the type of the RADT mentioned (EIA or OIA)?	Yes		
Were RADTs conducted during consultation time?	Yes		
		Low	Low

DOMAIN 3: Reference Standard

Were culture results interpreted with blinding of the results of the RADT?	Unclear		
Is the throat culture method likely to correctly identify GAS (laboratory culture on a blood agar plate during 48 hr)?	No		
Were the culture medium, atmosphere, duration of incubation and GAS-confirmation technique described?	No		
		High	High

DOMAIN 4: Flow and Timing

Was the delay between the performance of the RADT and throat culture plating less than 48 hours?	Yes		
Did all patients receive a throat culture?	Yes		
Did patients receive the same throat culture method?	Yes		
Were undetermined/uninterpretable results reported?	No		
Were withdrawals from the study explained?	Yes		
		Low	

Rogo 2010b
Study characteristics

Patient sampling	See Rogo 2010a
Patient characteristics and setting	See Rogo 2010a
Index tests	Throat swab: 3 different swabs (each swab used for culture and then for the RADT) Commercial name of the RADT: OSOM Strep A (Genzyme) Type of RADT: EIA
Target condition and reference standard(s)	See Rogo 2010a
Flow and timing	No follow-up
Comparative	
Type of study	Journal article
Notes	The study was funded by the manufacturer of one of the 3 RADTs under evaluation (Acceava)

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient Selection			
Was a consecutive or random sample of patients enrolled?	Unclear		
Was it a cross-sectional study or a RCT?	Yes		
Were selection criteria clearly described (at least presenting signs and symptoms and age limits for inclusion)?	No		
Was clinical selection of patients avoided?	Yes		
Were patients seen in an ambulatory care setting?	Yes		
		High	High
DOMAIN 2: Index Test All tests			
Were the RADT results interpreted with blinding of the results of culture?	Yes		
Was the type of the RADT mentioned (EIA or OIA)?	Yes		
Were RADTs conducted during consultation time?	Yes		
		Low	Low
DOMAIN 3: Reference Standard			

Rogo 2010b (Continued)

Were culture results interpreted with blinding of the results of the RADT?	Unclear
Is the throat culture method likely to correctly identify GAS (laboratory culture on a blood agar plate during 48 hr)?	No
Were the culture medium, atmosphere, duration of incubation and GAS-confirmation technique described?	No
	High
	High

DOMAIN 4: Flow and Timing

Was the delay between the performance of the RADT and throat culture plating less than 48 hours?	Yes
Did all patients receive a throat culture?	Yes
Did patients receive the same throat culture method?	Yes
Were undetermined/uninterpretable results reported?	No
Were withdrawals from the study explained?	Yes
	Low

Rogo 2010c
Study characteristics

Patient sampling	See Rogo 2010a
Patient characteristics and setting	See Rogo 2010a
Index tests	Throat swab: 3 different swabs (each swab used for culture and then for the RADT) Commercial name of the RADT: QuickVue Dipstick (Quidel) Type of RADT: EIA
Target condition and reference standard(s)	See Rogo 2010a
Flow and timing	No follow-up
Comparative	
Type of study	Journal article
Notes	The study was funded by the manufacturer of one of the 3 RADTs under evaluation (Acceava)

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
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Rogo 2010c (Continued)

DOMAIN 1: Patient Selection

Was a consecutive or random sample of patients enrolled?	Unclear		
Was it a cross-sectional study or a RCT?	Yes		
Were selection criteria clearly described (at least presenting signs and symptoms and age limits for inclusion)?	No		
Was clinical selection of patients avoided?	Yes		
Were patients seen in an ambulatory care setting?	Yes		
		High	High

DOMAIN 2: Index Test All tests

Were the RADT results interpreted with blinding of the results of culture?	Yes		
Was the type of the RADT mentioned (EIA or OIA)?	Yes		
Were RADTs conducted during consultation time?	Yes		
		Low	Low

DOMAIN 3: Reference Standard

Were culture results interpreted with blinding of the results of the RADT?	Unclear		
Is the throat culture method likely to correctly identify GAS (laboratory culture on a blood agar plate during 48 hr)?	No		
Were the culture medium, atmosphere, duration of incubation and GAS-confirmation technique described?	No		
		High	High

DOMAIN 4: Flow and Timing

Was the delay between the performance of the RADT and throat culture plating less than 48 hours?	Yes		
Did all patients receive a throat culture?	Yes		
Did patients receive the same throat culture method?	Yes		
Were undetermined/uninterpretable results reported?	No		
Were withdrawals from the study explained?	Yes		
		Low	

Savoia 1994
Study characteristics

Patient sampling	Cross-sectional study Prospective design Sample: unclear Direct comparison of different RADTs: no Direct comparison of several throat culture techniques: no Person performing the throat sample: not reported Exclusion if recent antibiotics use before inclusion: no Clinical selection of patients: none Presenting signs and symptoms: patients with pharyngotonsillitis Age range for inclusion: 1 to 14 years
Patient characteristics and setting	Sample size: 510 Age (distribution): not reported GAS prevalence according to culture (with 95% confidence interval): 14.3% (95% CI not reported) Country of study: Italy Sex (% of girls): not reported Clinical severity assessment: none Clinical setting: not reported Single- or multi-centre study: not reported
Index tests	Throat swab: 2 different swabs Commercial name of the RADT: Event test strip Strep A Type of RADT: EIA
Target condition and reference standard(s)	Throat culture medium: inhibitory Atmosphere of incubation: aerobic with CO ₂ enrichment Duration of incubation: 48 hours GAS confirmation: latex test Number of plates inoculated: 2 Assessment of GAS antibody response: no Relevant details: -
Flow and timing	No follow-up
Comparative	
Type of study	Journal article
Notes	—

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient Selection			
Was a consecutive or random sample of patients enrolled?	Unclear		
Was it a cross-sectional study or a RCT?	Yes		

Savoia 1994 (Continued)

Were selection criteria clearly described (at least presenting signs and symptoms and age limits for inclusion)?	Yes		
Was clinical selection of patients avoided?	Yes		
Were patients seen in an ambulatory care setting?	Unclear		
		Low	Unclear

DOMAIN 2: Index Test All tests

Were the RADT results interpreted with blinding of the results of culture?	Unclear		
Was the type of the RADT mentioned (EIA or OIA)?	Yes		
Were RADTs conducted during consultation time?	No		
		Unclear	High

DOMAIN 3: Reference Standard

Were culture results interpreted with blinding of the results of the RADT?	Unclear		
Is the throat culture method likely to correctly identify GAS (laboratory culture on a blood agar plate during 48 hr)?	Yes		
Were the culture medium, atmosphere, duration of incubation and GAS-confirmation technique described?	Yes		
		Unclear	Low

DOMAIN 4: Flow and Timing

Was the delay between the performance of the RADT and throat culture plating less than 48 hours?	Unclear		
Did all patients receive a throat culture?	Yes		
Did patients receive the same throat culture method?	Yes		
Were undetermined/uninterpretable results reported?	No		
Were withdrawals from the study explained?	No		
		Low	

Schlager 1996
Study characteristics

Patient sampling	Cross-sectional study Prospective design Sample: unclear
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Schlager 1996 (Continued)

Direct comparison of different RADTs: no
 Direct comparison of several throat culture techniques: yes
 Person performing the throat sample: unclear

 Exclusion if recent antibiotics use before inclusion: no

 Clinical selection of patients: unclear

 Presenting signs and symptoms: pharyngitis

 Age range for inclusion: not reported

Patient characteristics and setting	Sample size: 262 Age (distribution): not reported GAS prevalence according to culture (with 95% confidence interval): 24% (95% CI not reported) Country of study: USA Sex (% of girls): not reported Clinical severity assessment: none Clinical setting: mixed (paediatric and family practice clinics in a primary care centre) Single-centre study
Index tests	Throat swab: 1 double Commercial name of the RADT: Strep A OIA Type of RADT: OIA
Target condition and reference standard(s)	Throat culture medium: standard Atmosphere of incubation: aerobic Duration of incubation: 48 hours GAS confirmation: latex test Number of plates inoculated: 1 Assessment of GAS antibody response: no Relevant details: the study compared the accuracy of different throat culture techniques. We extracted data used by the authors to calculate accuracy estimates for the rapid test ("standard culture").
Flow and timing	No follow-up
Comparative	
Type of study	Journal article
Notes	—

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient Selection			
Was a consecutive or random sample of patients enrolled?	Unclear		
Was it a cross-sectional study or a RCT?	Yes		
Were selection criteria clearly described (at least presenting signs and symptoms and age limits for inclusion)?	No		

Schlager 1996 *(Continued)*

Was clinical selection of patients avoided?	Unclear		
Were patients seen in an ambulatory care setting?	Yes		
		High	High
DOMAIN 2: Index Test All tests			
Were the RADT results interpreted with blinding of the results of culture?	Yes		
Was the type of the RADT mentioned (EIA or OIA)?	Yes		
Were RADTs conducted during consultation time?	No		
		Low	High
DOMAIN 3: Reference Standard			
Were culture results interpreted with blinding of the results of the RADT?	Yes		
Is the throat culture method likely to correctly identify GAS (laboratory culture on a blood agar plate during 48 hr)?	Yes		
Were the culture medium, atmosphere, duration of incubation and GAS-confirmation technique described?	Yes		
		Low	Low
DOMAIN 4: Flow and Timing			
Was the delay between the performance of the RADT and throat culture plating less than 48 hours?	Unclear		
Did all patients receive a throat culture?	Yes		
Did patients receive the same throat culture method?	Yes		
Were undetermined/uninterpretable results reported?	No		
Were withdrawals from the study explained?	Yes		
		Low	

Schwabe 1987
Study characteristics

Patient sampling	Cross-sectional study Prospective design Sample: unclear Direct comparison of different RADTs: no Direct comparison of several throat culture techniques: no Person performing the throat sample: unclear
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Schwabe 1987 (Continued)

Exclusion if recent antibiotics use before inclusion: yes (2 weeks before throat swab collection)

Clinical selection of patients: none

Presenting signs and symptoms: current respiratory tract infection

Age range for inclusion: unclear (but Dr. LD Schwabe confirmed that study specimens were primarily from children ≤ 21 years seen in paediatric offices)

Patient characteristics and setting	<p>Sample size: 365 Age (distribution): not reported</p> <p>GAS prevalence according to culture (with 95% confidence interval): 27.4% (95% CI not reported) Country of study: USA Sex (% of girls): not reported Clinical severity assessment: none Clinical setting: paediatric offices Single-centre study</p>
Index tests	<p>Throat swab: 1 single swab (used for culture and then for the RADT)</p> <p>Commercial name of the RADT: TestPack Strep A Type of RADT: EIA</p>
Target condition and reference standard(s)	<p>Throat culture medium: standard Atmosphere of incubation: anaerobic for the first 24 hours and then aerobic with CO₂ enrichment for the second 24 hours Duration of incubation: 48 hours GAS confirmation: latex test Number of plates inoculated: 1 Assessment of GAS antibody response: no Relevant details: -</p>
Flow and timing	No follow-up
Comparative	
Type of study	Journal article
Notes	We thank Dr. LD Schwabe for confirming that study specimens were primarily from children ≤ 21 years seen in paediatric offices

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient Selection			
Was a consecutive or random sample of patients enrolled?	Unclear		
Was it a cross-sectional study or a RCT?	Yes		

Schwabe 1987 (Continued)

Were selection criteria clearly described (at least presenting signs and symptoms and age limits for inclusion)?	No		
Was clinical selection of patients avoided?	Unclear		
Were patients seen in an ambulatory care setting?	Yes		
		High	Unclear
DOMAIN 2: Index Test All tests			
Were the RADT results interpreted with blinding of the results of culture?	Yes		
Was the type of the RADT mentioned (EIA or OIA)?	Yes		
Were RADTs conducted during consultation time?	No		
		Low	High
DOMAIN 3: Reference Standard			
Were culture results interpreted with blinding of the results of the RADT?	Unclear		
Is the throat culture method likely to correctly identify GAS (laboratory culture on a blood agar plate during 48 hr)?	Yes		
Were the culture medium, atmosphere, duration of incubation and GAS-confirmation technique described?	Yes		
		Unclear	Low
DOMAIN 4: Flow and Timing			
Was the delay between the performance of the RADT and throat culture plating less than 48 hours?	Yes		
Did all patients receive a throat culture?	Yes		
Did patients receive the same throat culture method?	Yes		
Were undetermined/uninterpretable results reported?	No		
Were withdrawals from the study explained?	Yes		
		Low	

Schwabe 1991
Study characteristics

Patient sampling	Cross-sectional study
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Schwabe 1991 (Continued)

Prospective design
 Sample: unclear
 Direct comparison of different RADTs: no
 Direct comparison of several throat culture techniques: yes
 Person performing the throat sample: mixed (physicians, nurses, technologists, other)

 Exclusion if recent antibiotics use before inclusion: yes (2 weeks prior to throat swab collection)

 Clinical selection of patients: unclear

 Presenting signs and symptoms: unclear

 Age range for inclusion: unclear from the study report (but Dr. LD Schwabe confirmed 98.6% of participants were paediatric patients)

Patient characteristics and setting	Sample size: 261 Age (distribution): not reported GAS prevalence according to culture (with 95% confidence interval): 27.1% (95 CI% not reported) Country of study: USA Sex (% of girls): not reported Clinical severity assessment: none Clinical setting: mixed (paediatric offices, a university student health centre and a general community hospital outpatient laboratory) Multi-centre study
Index tests	Throat swab: 1 single swab (culture then RADT) Commercial name of the RADT: Test Pack Plus Strep A Type of RADT: EIA
Target condition and reference standard(s)	Throat culture medium: standard Atmosphere of incubation: anaerobic for the first 24 hours and aerobic with CO ₂ enrichment for the second 24 hours Duration of incubation: 48 hours GAS confirmation: bacitracin disk and latex test Number of plates inoculated: 1 Assessment of GAS antibody response: no Relevant details: only data for culture on the nonselective medium were extracted
Flow and timing	No follow-up
Comparative	
Type of study	Journal article
Notes	We thank Dr. LD Schwabe for confirming that numbers in the published contingency table are from paediatric patients (99%)

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
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DOMAIN 1: Patient Selection

Schwabe 1991 (Continued)

Was a consecutive or random sample of patients enrolled?	Unclear		
Was it a cross-sectional study or a RCT?	Yes		
Were selection criteria clearly described (at least presenting signs and symptoms and age limits for inclusion)?	No		
Was clinical selection of patients avoided?	Unclear		
Were patients seen in an ambulatory care setting?	Yes		
		High	Unclear
DOMAIN 2: Index Test All tests			
Were the RADT results interpreted with blinding of the results of culture?	Unclear		
Was the type of the RADT mentioned (EIA or OIA)?	Yes		
Were RADTs conducted during consultation time?	No		
		Unclear	High
DOMAIN 3: Reference Standard			
Were culture results interpreted with blinding of the results of the RADT?	Unclear		
Is the throat culture method likely to correctly identify GAS (laboratory culture on a blood agar plate during 48 hr)?	Yes		
Were the culture medium, atmosphere, duration of incubation and GAS-confirmation technique described?	Yes		
		Unclear	Low
DOMAIN 4: Flow and Timing			
Was the delay between the performance of the RADT and throat culture plating less than 48 hours?	Yes		
Did all patients receive a throat culture?	Yes		
Did patients receive the same throat culture method?	Yes		
Were undetermined/uninterpretable results reported?	No		
Were withdrawals from the study explained?	Yes		
		Low	

Schwartz 1997a
Study characteristics

Patient sampling	Cross-sectional study Prospective design Sample: unclear Direct comparison of different RADTs: yes (2 different EIAs) Direct comparison of several throat culture techniques: no Person performing the throat sample: not reported Exclusion if recent antibiotics use before inclusion: no Clinical selection of patients: not reported Presenting signs and symptoms: unclear Age range for inclusion: unclear
Patient characteristics and setting	Sample size: 258 Age (distribution): not reported GAS prevalence according to culture (with 95% confidence interval): 40.0% (95% CI not reported) Country of study: USA Sex (% of girls): not reported Clinical severity assessment: none Clinical setting: office-based (paediatric clinic) Single-centre study
Index tests	Throat swab: not reported Commercial name of the RADT: OSOM Strep A (Wyntek) Type of RADT: EIA
Target condition and reference standard(s)	Throat culture medium: standard Atmosphere of incubation: aerobic Duration of incubation: 24 hours GAS confirmation: not reported Number of plates inoculated: not reported Assessment of GAS antibody response: no Relevant details: -
Flow and timing	No follow-up
Comparative	
Type of study	Journal article
Notes	—

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient Selection			
Was a consecutive or random sample of patients enrolled?	Unclear		

Schwartz 1997a (Continued)

Was it a cross-sectional study or a RCT?	Yes		
Were selection criteria clearly described (at least presenting signs and symptoms and age limits for inclusion)?	No		
Was clinical selection of patients avoided?	Unclear		
Were patients seen in an ambulatory care setting?	Yes		
		High	Unclear

DOMAIN 2: Index Test All tests

Were the RADT results interpreted with blinding of the results of culture?	Yes		
Was the type of the RADT mentioned (EIA or OIA)?	Yes		
Were RADTs conducted during consultation time?	Yes		
		Low	Low

DOMAIN 3: Reference Standard

Were culture results interpreted with blinding of the results of the RADT?	Unclear		
Is the throat culture method likely to correctly identify GAS (laboratory culture on a blood agar plate during 48 hr)?	No		
Were the culture medium, atmosphere, duration of incubation and GAS-confirmation technique described?	Yes		
		High	High

DOMAIN 4: Flow and Timing

Was the delay between the performance of the RADT and throat culture plating less than 48 hours?	Yes		
Did all patients receive a throat culture?	Yes		
Did patients receive the same throat culture method?	Yes		
Were undetermined/uninterpretable results reported?	No		
Were withdrawals from the study explained?	Yes		
		Low	

Schwartz 1997b
Study characteristics

Schwartz 1997b (Continued)

Patient sampling	See Schwartz 1997a
Patient characteristics and setting	See Schwartz 1997a
Index tests	Throat swab: not reported Commercial name of the RADT: QuickVue In-Line Strep A (Quidel) Type of RADT: EIA
Target condition and reference standard(s)	See Schwartz 1997a
Flow and timing	No follow-up
Comparative	
Type of study	Journal article
Notes	—

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient Selection			
Was a consecutive or random sample of patients enrolled?	Unclear		
Was it a cross-sectional study or a RCT?	Yes		
Were selection criteria clearly described (at least presenting signs and symptoms and age limits for inclusion)?	No		
Was clinical selection of patients avoided?	Unclear		
Were patients seen in an ambulatory care setting?	Yes		
		High	Unclear
DOMAIN 2: Index Test All tests			
Were the RADT results interpreted with blinding of the results of culture?	Yes		
Was the type of the RADT mentioned (EIA or OIA)?	Yes		
Were RADTs conducted during consultation time?	Yes		
		Low	Low
DOMAIN 3: Reference Standard			
Were culture results interpreted with blinding of the results of the RADT?	Unclear		
Is the throat culture method likely to correctly identify GAS (laboratory culture on a blood agar plate during 48 hr)?	No		

Schwartz 1997b (Continued)

Were the culture medium, atmosphere, duration of incubation and GAS-confirmation technique described? Yes

High
High
DOMAIN 4: Flow and Timing

Was the delay between the performance of the RADT and throat culture plating less than 48 hours? Yes

Did all patients receive a throat culture? Yes

Did patients receive the same throat culture method? Yes

Were undetermined/uninterpretable results reported? No

Were withdrawals from the study explained? Yes

Low
Sedki 2010
Study characteristics

Patient sampling

Cross-sectional study
 Prospective design
 Sample: unclear
 Direct comparison of different RADTs: no
 Direct comparison of several throat culture techniques: no
 Person performing the throat sample: physician

Exclusion if recent antibiotics use before inclusion: yes

Clinical selection of patients: clinical score (Centor)

Presenting signs and symptoms: pharyngitis with at least 2 Centor criteria

Age range for inclusion: 3 to 15 years

Patient characteristics and setting

Sample size: 95
 Age (distribution): median = 8.98 years (range 3.3 to 13.8)

GAS prevalence according to culture (with 95% confidence interval): 32.6% (95% CI not reported)
 Country of study: Egypt
 Sex (% of girls): 58%
 Clinical severity assessment: none
 Clinical setting: mixed (outpatient clinic of health centre or the school dispensary room)
 Multi-centre study

Index tests

Throat swab: 2 different swabs

Commercial name of the RADT: StreptAtest
 Type of RADT: EIA

Sedki 2010 (Continued)

Target condition and reference standard(s)	Throat culture medium: standard Atmosphere of incubation: aerobic with CO ₂ enrichment Duration of incubation: 24 hours GAS confirmation: other (penicillin susceptibility and gram stain microscopy) Number of plates inoculated: 1 Assessment of GAS antibody response: no Relevant details: -
Flow and timing	No follow-up
Comparative	
Type of study	Journal article
Notes	The rapid test kits were supplied by the manufacturer

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient Selection			
Was a consecutive or random sample of patients enrolled?	Unclear		
Was it a cross-sectional study or a RCT?	Yes		
Were selection criteria clearly described (at least presenting signs and symptoms and age limits for inclusion)?	Yes		
Was clinical selection of patients avoided?	No		
Were patients seen in an ambulatory care setting?	Yes		
		High	High
DOMAIN 2: Index Test All tests			
Were the RADT results interpreted with blinding of the results of culture?	Unclear		
Was the type of the RADT mentioned (EIA or OIA)?	Yes		
Were RADTs conducted during consultation time?	Unclear		
		Unclear	Unclear
DOMAIN 3: Reference Standard			
Were culture results interpreted with blinding of the results of the RADT?	Unclear		
Is the throat culture method likely to correctly identify GAS (laboratory culture on a blood agar plate during 48 hr)?	No		

Sedki 2010 (Continued)

Were the culture medium, atmosphere, duration of incubation and GAS-confirmation technique described? Yes

High
High
DOMAIN 4: Flow and Timing

Was the delay between the performance of the RADT and throat culture plating less than 48 hours? Yes

Did all patients receive a throat culture? Yes

Did patients receive the same throat culture method? Yes

Were undetermined/uninterpretable results reported? Yes

Were withdrawals from the study explained? Yes

Low
Strandjord 1987
Study characteristics

Patient sampling

Cross-sectional study
 Prospective design
 Sample: unclear
 Direct comparison of different RADTs: yes (LA versus EIA; data extracted only for EIA)
 Direct comparison of several throat culture techniques: no
 Person performing the throat sample: unclear

Exclusion if recent antibiotics use before inclusion: no

Clinical selection of patients: implicit criteria (see below)

Presenting signs and symptoms: "patients who were suspect of having GAS pharyngitis"

Age range for inclusion: 2 to 18 years

Patient characteristics and setting

Sample size: 138
 Age (distribution): not reported

GAS prevalence according to culture (with 95% confidence interval): 37.7% (95% CI not reported)
 Country of study: USA
 Sex (% of girls): not reported
 Clinical severity assessment: none
 Clinical setting: mixed (emergency department and acute care clinic)
 Single-centre study

Index tests

Throat swab: 1 double swab (1 swab for culture, 1 swab for performing the RADT)

Commercial name of the RADT: Icon Strep A (Hybritech)
 Type of RADT: EIA

Strandjord 1987 (Continued)

Target condition and reference standard(s)	Throat culture medium: standard Atmosphere of incubation: aerobic with CO ₂ enrichment Duration of incubation: 24 hours GAS confirmation: fluorescent antibody technique Number of plates inoculated: not reported Assessment of GAS antibody response: no Relevant details: -
Flow and timing	No follow-up
Comparative	
Type of study	Journal article
Notes	—

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient Selection			
Was a consecutive or random sample of patients enrolled?	Unclear		
Was it a cross-sectional study or a RCT?	Yes		
Were selection criteria clearly described (at least presenting signs and symptoms and age limits for inclusion)?	No		
Was clinical selection of patients avoided?	No		
Were patients seen in an ambulatory care setting?	Yes		
		High	High
DOMAIN 2: Index Test All tests			
Were the RADT results interpreted with blinding of the results of culture?	Yes		
Was the type of the RADT mentioned (EIA or OIA)?	Yes		
Were RADTs conducted during consultation time?	Yes		
		Low	Low
DOMAIN 3: Reference Standard			
Were culture results interpreted with blinding of the results of the RADT?	Unclear		
Is the throat culture method likely to correctly identify GAS (laboratory culture on a blood agar plate during 48 hr)?	No		
Were the culture medium, atmosphere, duration of incubation and GAS-confirmation technique described?	Yes		

Strandjord 1987 (Continued)

	High	High
DOMAIN 4: Flow and Timing		
Was the delay between the performance of the RADT and throat culture plating less than 48 hours?		Unclear
Did all patients receive a throat culture?		Yes
Did patients receive the same throat culture method?		Yes
Were undetermined/uninterpretable results reported?		No
Were withdrawals from the study explained?		Yes
Low		

Subashini 2015

Study characteristics	
Patient sampling	Cross-sectional study Retrospective or prospective design: unclear Sample: unclear Direct comparison of different RADTs: no Direct comparison of several throat culture techniques: no Person performing the throat sample: not reported Exclusion if recent antibiotics use before inclusion: no Clinical selection of patients: not reported Presenting signs and symptoms: pharyngitis Age range for inclusion: not reported ("children")
Patient characteristics and setting	Sample size: 111 Age (distribution): not reported GAS prevalence according to culture (with 95% confidence interval): 24.3% (95% CI not reported) Country of study: India Sex (% of girls): not reported Clinical severity assessment: none Clinical setting: outpatient clinic Single-centre study
Index tests	Throat swab (1 single, 1 double, 2 different): not reported Commercial name of the RADT: SD Bioline Strep A Type of RADT: EIA
Target condition and reference standard(s)	Throat culture medium: standard Atmosphere of incubation: aerobic with CO ₂ enrichment Duration of incubation: not reported GAS confirmation: latex test Number of plates inoculated (n): not reported

Subashini 2015 (Continued)

 Assessment of GAS antibody response: no
 Relevant details: -

Flow and timing	No follow-up
Comparative	
Type of study	Journal article
Notes	—

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient Selection			
Was a consecutive or random sample of patients enrolled?	Unclear		
Was it a cross-sectional study or a RCT?	Yes		
Were selection criteria clearly described (at least presenting signs and symptoms and age limits for inclusion)?	No		
Was clinical selection of patients avoided?	Unclear		
Were patients seen in an ambulatory care setting?	Yes		
		High	Unclear
DOMAIN 2: Index Test All tests			
Were the RADT results interpreted with blinding of the results of culture?	Yes		
Was the type of the RADT mentioned (EIA or OIA)?	Yes		
Were RADTs conducted during consultation time?	No		
		High	High
DOMAIN 3: Reference Standard			
Were culture results interpreted with blinding of the results of the RADT?	Unclear		
Is the throat culture method likely to correctly identify GAS (laboratory culture on a blood agar plate during 48 hr)?	Unclear		
Were the culture medium, atmosphere, duration of incubation and GAS-confirmation technique described?	No		
		Unclear	Unclear
DOMAIN 4: Flow and Timing			

Subashini 2015 (Continued)

Was the delay between the performance of the RADT and throat culture plating less than 48 hours?	Unclear
Did all patients receive a throat culture?	Yes
Did patients receive the same throat culture method?	Yes
Were undetermined/uninterpretable results reported?	No
Were withdrawals from the study explained?	Yes
Low	

Tanz 2009
Study characteristics

Patient sampling	<p>Cross-sectional study Prospective design Sample: consecutive Direct comparison of different RADTs: no Direct comparison of several throat culture techniques: yes (office culture versus laboratory culture) Person performing the throat sample: physician</p> <p>Exclusion if recent antibiotics use before inclusion: no</p> <p>Clinical selection of patients: none</p> <p>Presenting signs and symptoms: pharyngitis</p> <p>Age range for inclusion: 3 to 18 years</p>
Patient characteristics and setting	<p>Sample size: 1848 Age (distribution): 13% under 5 years of age (mean or median not reported)</p> <p>GAS prevalence according to culture (with 95% confidence interval): 30% (95% CI not reported) Country of study: USA Sex (% of girls): 53% Clinical severity assessment: Mclsaac score Clinical setting: office-based Multi-centre study</p>
Index tests	<p>Throat swab: 2 different swabs (swab A used first for office culture and then for performing the RADT; swab B used for laboratory culture)</p> <p>Commercial name of the RADT: QuickVue dipstick (Quidel) Type of RADT: EIA</p>
Target condition and reference standard(s)	<p>Throat culture medium: standard Atmosphere of incubation: aerobic Duration of incubation: 48 hours GAS confirmation: latex agglutination Number of plates inoculated: 1 Assessment of GAS antibody response: no</p>

Tanz 2009 (Continued)

Relevant details: swab A was streaked on a blood agar plate for office culture and then used for the RADT; data for office culture not extracted

Flow and timing	No follow-up
Comparative	
Type of study	Journal article
Notes	Last author (Dr Shulman) is on the medical advisory board of Quidel (manufacturer of the RADT)

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient Selection			
Was a consecutive or random sample of patients enrolled?	Yes		
Was it a cross-sectional study or a RCT?	Yes		
Were selection criteria clearly described (at least presenting signs and symptoms and age limits for inclusion)?	Yes		
Was clinical selection of patients avoided?	Yes		
Were patients seen in an ambulatory care setting?	Yes		
		Low	Low
DOMAIN 2: Index Test All tests			
Were the RADT results interpreted with blinding of the results of culture?	Yes		
Was the type of the RADT mentioned (EIA or OIA)?	Yes		
Were RADTs conducted during consultation time?	Yes		
		Low	Low
DOMAIN 3: Reference Standard			
Were culture results interpreted with blinding of the results of the RADT?	Yes		
Is the throat culture method likely to correctly identify GAS (laboratory culture on a blood agar plate during 48 hr)?	Yes		
Were the culture medium, atmosphere, duration of incubation and GAS-confirmation technique described?	Yes		

Tanz 2009 (Continued)

Low
Low
DOMAIN 4: Flow and Timing

Was the delay between the performance of the RADT and throat culture plating less than 48 hours? No

Did all patients receive a throat culture? Yes

Did patients receive the same throat culture method? Yes

Were undetermined/uninterpretable results reported? No

Were withdrawals from the study explained? No

Low
Tellechea 2012
Study characteristics

Patient sampling
 Cross-sectional study
 Retrospective design
 Sample: non-consecutive
 Direct comparison of different RADTs: no
 Direct comparison of several throat culture techniques: no
 Person performing the throat sample: laboratory personnel

 Exclusion if recent antibiotics use before inclusion: yes (within the previous week)

 Clinical selection of patients: implicit criteria (see below)

 Presenting signs and symptoms: symptoms compatible with GAS

 Age range for inclusion: 3 to 15 years

Patient characteristics and setting
 Sample size: 5505
 Age (distribution): not reported

 GAS prevalence according to culture (with 95% confidence interval): 39.8% (95% CI not reported)
 Country of study: Argentina
 Sex (% of girls): not reported
 Clinical severity assessment: none
 Clinical setting: paediatric emergency department
 Single-centre study

Index tests
 Throat swab: not reported

 Commercial name of the RADT: ACON Strep A Rapid Test Strip (ACON Lab)
 Type of RADT: EIA

Target condition and reference standard(s)
 Throat culture medium: standard
 Atmosphere of incubation: not reported
 Duration of incubation: not reported
 GAS confirmation: not reported

Tellechea 2012 (Continued)

 Number of plates inoculated: not reported
 Assessment of GAS antibody response: no
 Relevant details: -

Flow and timing	No follow-up
Comparative	
Type of study	Journal article (in Spanish)
Notes	—

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient Selection			
Was a consecutive or random sample of patients enrolled?	No		
Was it a cross-sectional study or a RCT?	Yes		
Were selection criteria clearly described (at least presenting signs and symptoms and age limits for inclusion)?	Yes		
Was clinical selection of patients avoided?	No		
Were patients seen in an ambulatory care setting?	Yes		
		High	High
DOMAIN 2: Index Test All tests			
Were the RADT results interpreted with blinding of the results of culture?	Yes		
Was the type of the RADT mentioned (EIA or OIA)?	Yes		
Were RADTs conducted during consultation time?	No		
		Unclear	Unclear
DOMAIN 3: Reference Standard			
Were culture results interpreted with blinding of the results of the RADT?	Unclear		
Is the throat culture method likely to correctly identify GAS (laboratory culture on a blood agar plate during 48 hr)?	Unclear		
Were the culture medium, atmosphere, duration of incubation and GAS-confirmation technique described?	No		
		Unclear	Unclear
DOMAIN 4: Flow and Timing			

Tellechea 2012 (Continued)

Was the delay between the performance of the RADT and throat culture plating less than 48 hours?	Unclear
Did all patients receive a throat culture?	Yes
Did patients receive the same throat culture method?	Unclear
Were undetermined/uninterpretable results reported?	No
Were withdrawals from the study explained?	Yes
Unclear	

Tenjarla 1991
Study characteristics

Patient sampling	Cross-sectional study Prospective design Sample: unclear Direct comparison of different RADTs: no Direct comparison of several throat culture techniques: no Person performing the throat sample: physicians and office staff Exclusion if recent antibiotics use before inclusion: no Clinical selection of patients: none Presenting signs and symptoms: clinical tonsillopharyngitis Age range for inclusion: "pediatric patients"
Patient characteristics and setting	Sample size: 9161 children (among a total of 11,088) Age (distribution): 3 months to 18 years ("pediatric population") GAS prevalence according to culture (with 95% confidence interval): 16.5% (95% CI not reported) Country of study: USA Sex (% of girls): not reported Clinical severity assessment: none Clinical setting: office-based Single- or multi-centre study: unclear
Index tests	Throat swab: 1 double swab (1 swab for culture, 1 swab for performing the RADT) Commercial name of the RADT: TestPack Strep A (Abbott) Type of RADT: EIA
Target condition and reference standard(s)	Throat culture medium: standard Atmosphere of incubation: anaerobic Duration of incubation: 16 to 42 hours GAS confirmation: TestPack Strep A used on beta-haemolytic colonies Number of plates inoculated: 1 Assessment of GAS antibody response: no Relevant details: in this study the RADT was also used as a confirmation technique to identify beta-haemolytic colonies as <i>S. pyogenes</i>

Tenjarla 1991 (Continued)

Flow and timing	No follow-up
Comparative	
Type of study	Journal article
Notes	Included adults and children; data extracted only for children

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient Selection			
Was a consecutive or random sample of patients enrolled?	Unclear		
Was it a cross-sectional study or a RCT?	Yes		
Were selection criteria clearly described (at least presenting signs and symptoms and age limits for inclusion)?	No		
Was clinical selection of patients avoided?	Yes		
Were patients seen in an ambulatory care setting?	Yes		
		High	Low
DOMAIN 2: Index Test All tests			
Were the RADT results interpreted with blinding of the results of culture?	Yes		
Was the type of the RADT mentioned (EIA or OIA)?	Yes		
Were RADTs conducted during consultation time?	No		
		Low	High
DOMAIN 3: Reference Standard			
Were culture results interpreted with blinding of the results of the RADT?	Unclear		
Is the throat culture method likely to correctly identify GAS (laboratory culture on a blood agar plate during 48 hr)?	No		
Were the culture medium, atmosphere, duration of incubation and GAS-confirmation technique described?	Yes		
		High	High
DOMAIN 4: Flow and Timing			

Tenjarla 1991 *(Continued)*

Was the delay between the performance of the RADT and throat culture plating less than 48 hours?	Yes
Did all patients receive a throat culture?	Yes
Did patients receive the same throat culture method?	Yes
Were undetermined/uninterpretable results reported?	No
Were withdrawals from the study explained?	Yes
Low	

Toepfner 2013
Study characteristics

Patient sampling	Cross-sectional study Prospective design Sample: unclear Direct comparison of different RADTs: yes Direct comparison of several throat culture techniques: no Person performing the throat sample: unclear Exclusion if recent antibiotics use before inclusion: no Clinical selection of patients: none Presenting signs and symptoms: tonsillopharyngitis Age range for inclusion: not reported
Patient characteristics and setting	Sample size: 517 (324 in 2009 and 193 in 2010) Age (distribution): not reported GAS prevalence according to culture (with 95% confidence interval): 17.6% (95% CI not reported) Country of study: Germany Sex (% of girls): not reported Clinical severity assessment: none Clinical setting: unclear Single- or multi-centre study: unclear
Index tests	Throat swab: 1 single swab (used for culture and then for the RADT) Commercial name of the RADT: QuickVue In-Line Strep A Type of RADT: EIA
Target condition and reference standard(s)	Throat culture medium: standard Atmosphere of incubation: not reported Duration of incubation: not reported GAS confirmation: not reported Number of plates inoculated: not reported Assessment of GAS antibody response: no Relevant details: -
Flow and timing	No follow-up

Toepfner 2013 (Continued)

Comparative

Type of study	Journal article
Notes	<p>In this study, the accuracy of the rapid test was compared between physicians and laboratory technicians. Our review focused on the accuracy of RADT with laboratory culture as the reference standard, therefore we extracted data only for laboratory technicians. The study also comprised 2 phases: before (2009) and after (2010) training of physicians by laboratory technicians. We extracted data only for laboratory technicians, therefore we pooled the data from 2009 and 2010.</p> <p>We thank Dr. M Hufnagel for confirming that numbers in the published contingency table are from paediatric patients.</p>

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient Selection			
Was a consecutive or random sample of patients enrolled?	Unclear		
Was it a cross-sectional study or a RCT?	Yes		
Were selection criteria clearly described (at least presenting signs and symptoms and age limits for inclusion)?	No		
Was clinical selection of patients avoided?	Unclear		
Were patients seen in an ambulatory care setting?	Yes		
		High	Unclear
DOMAIN 2: Index Test All tests			
Were the RADT results interpreted with blinding of the results of culture?	Yes		
Was the type of the RADT mentioned (EIA or OIA)?	Yes		
Were RADTs conducted during consultation time?	Unclear		
		Low	Unclear
DOMAIN 3: Reference Standard			
Were culture results interpreted with blinding of the results of the RADT?	Unclear		
Is the throat culture method likely to correctly identify GAS (laboratory culture on a blood agar plate during 48 hr)?	Unclear		

Toepfner 2013 (Continued)

Were the culture medium, atmosphere, duration of incubation and GAS-confirmation technique described? No

Unclear

Unclear

DOMAIN 4: Flow and Timing

Was the delay between the performance of the RADT and throat culture plating less than 48 hours? Unclear

Did all patients receive a throat culture? Yes

Did patients receive the same throat culture method? Yes

Were undetermined/uninterpretable results reported? No

Were withdrawals from the study explained? Yes

Low

Van Limbergen 2006
Study characteristics

Patient sampling

Cross-sectional study
 Prospective design
 Sample: consecutive
 Direct comparison of different RADTs: no
 Direct comparison of several throat culture techniques: no
 Person performing the throat sample: nursing staff

Exclusion if recent antibiotics use before inclusion: no

Clinical selection of patients: none

Presenting signs and symptoms: clinical diagnosis of pharyngitis

Age range for inclusion: not reported ("children")

Patient characteristics and setting

Sample size: 201
 Age (distribution): mean (SD) = 3.85 (3.15) years

GAS prevalence according to culture (with 95% confidence interval): 15.9% (95% CI not reported)
 Country of study: Scotland
 Sex (% of girls): 48.4%
 Clinical severity assessment: none
 Clinical setting: emergency department
 Single-centre study

Index tests

Throat swab: unclear

Commercial name of the RADT: QuickVue Plus Strep A (Quidel)

Van Limbergen 2006 (Continued)

Type of RADT: EIA

Target condition and reference standard(s)	Throat culture medium: not reported Atmosphere of incubation: not reported Duration of incubation: not reported GAS confirmation: not reported Number of plates inoculated: not reported Assessment of GAS antibody response: no Relevant details: throat culture technique not described
Flow and timing	No follow-up
Comparative	
Type of study	Journal article
Notes	The test kits were provided by Quidel (manufacturer of the RADT) Throat culture performed only for children with negative RADT results (partial verification)

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient Selection			
Was a consecutive or random sample of patients enrolled?	Yes		
Was it a cross-sectional study or a RCT?	Yes		
Were selection criteria clearly described (at least presenting signs and symptoms and age limits for inclusion)?	No		
Was clinical selection of patients avoided?	Yes		
Were patients seen in an ambulatory care setting?	Yes		
		High	Low
DOMAIN 2: Index Test All tests			
Were the RADT results interpreted with blinding of the results of culture?	Yes		
Was the type of the RADT mentioned (EIA or OIA)?	Yes		
Were RADTs conducted during consultation time?	Yes		
		Low	Low
DOMAIN 3: Reference Standard			
Were culture results interpreted with blinding of the results of the RADT?	No		

Van Limbergen 2006 *(Continued)*

Is the throat culture method likely to correctly identify GAS (laboratory culture on a blood agar plate during 48 hr)?	Unclear
Were the culture medium, atmosphere, duration of incubation and GAS-confirmation technique described?	No
	High
DOMAIN 4: Flow and Timing	
Was the delay between the performance of the RADT and throat culture plating less than 48 hours?	Unclear
Did all patients receive a throat culture?	No
Did patients receive the same throat culture method?	Yes
Were undetermined/uninterpretable results reported?	Yes
Were withdrawals from the study explained?	Yes
	High

Wong 1989
Study characteristics

Patient sampling	Cross-sectional study Prospective design Sample: convenience Direct comparison of different RADTs: no Direct comparison of several throat culture techniques: no Person performing the throat sample: unclear Exclusion if recent antibiotics use before inclusion: no Clinical selection of patients: none Presenting signs and symptoms: symptoms of viral or streptococcal pharyngitis Age range for inclusion: < 18 years (data for adults not extracted)
Patient characteristics and setting	Sample size: 147 children (data for 151 adults not extracted) Age (distribution): not reported GAS prevalence according to culture (with 95% confidence interval): 23.8% (95% CI not reported) Country of study: Canada Sex (% of girls): not reported Clinical severity assessment: none Clinical setting: walk-in clinic Single-centre study
Index tests	Throat swab: 2 different swabs

Wong 1989 (Continued)

 Commercial name of the RADT: TestPack Strep A
 Type of RADT: EIA

Target condition and reference standard(s)	Throat culture medium: standard Atmosphere of incubation: aerobic with CO ₂ enrichment Duration of incubation: 48 hours GAS confirmation: latex test Number of plates inoculated: 1 Assessment of GAS antibody response: no Relevant details: -
Flow and timing	No follow-up
Comparative	
Type of study	Journal article
Notes	—

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient Selection			
Was a consecutive or random sample of patients enrolled?	No		
Was it a cross-sectional study or a RCT?	Yes		
Were selection criteria clearly described (at least presenting signs and symptoms and age limits for inclusion)?	No		
Was clinical selection of patients avoided?	Yes		
Were patients seen in an ambulatory care setting?	Yes		
		High	Low
DOMAIN 2: Index Test All tests			
Were the RADT results interpreted with blinding of the results of culture?	Yes		
Was the type of the RADT mentioned (EIA or OIA)?	Yes		
Were RADTs conducted during consultation time?	No		
		Low	High
DOMAIN 3: Reference Standard			
Were culture results interpreted with blinding of the results of the RADT?	Yes		
Is the throat culture method likely to correctly identify GAS (laboratory culture on a blood agar plate during 48 hr)?	Yes		

Wong 1989 (Continued)

Were the culture medium, atmosphere, duration of incubation and GAS-confirmation technique described? Yes

Low
Low
DOMAIN 4: Flow and Timing

Was the delay between the performance of the RADT and throat culture plating less than 48 hours? Yes

Did all patients receive a throat culture? Yes

Did patients receive the same throat culture method? Yes

Were undetermined/uninterpretable results reported? No

Were withdrawals from the study explained? Yes

Low
Wright 2007a
Study characteristics

Patient sampling

Cross-sectional study
 Prospective design
 Sample: unclear
 Direct comparison of different RADTs: yes (2 EIAs)
 Direct comparison of several throat culture techniques: no
 Person performing the throat sample: other ("medical technician")

Exclusion if recent antibiotics use before inclusion: no

Clinical selection of patients: explicit criteria but not a score (see below)

Presenting signs and symptoms: "Criteria for throat swab included sore throat, erythematous tonsils or pharynx, cervical lymphadenopathy, and exudates"

Age range for inclusion: 0 to 18 years

Patient characteristics and setting

Sample size: 338
 Age (distribution): not reported

GAS prevalence according to culture (with 95% confidence interval): 26.0% (95% CI not reported)
 Country of study: USA
 Sex (% of girls): not reported
 Clinical severity assessment: none
 Clinical setting: military air force base
 Single-centre study

Index tests

Throat swab: 1 double swab (each swab used for antigen detection and culture)

Commercial name of the RADT: OSOM Ultra Strep A
 Type of RADT: EIA

Wright 2007a (Continued)

Target condition and reference standard(s)	Throat culture medium: standard Atmosphere of incubation: aerobic Duration of incubation: 48 hours GAS confirmation: not reported Number of plates inoculated: not reported Assessment of GAS antibody response: no Relevant details: unclear if the reference standard was a single-plate culture or a composite of both plates.		
Flow and timing	No follow-up		
Comparative			
Type of study	Journal article		
Notes	—		
Methodological quality			
Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient Selection			
Was a consecutive or random sample of patients enrolled?	Unclear		
Was it a cross-sectional study or a RCT?	Yes		
Were selection criteria clearly described (at least presenting signs and symptoms and age limits for inclusion)?	Yes		
Was clinical selection of patients avoided?	Unclear		
Were patients seen in an ambulatory care setting?	No		
		Unclear	High
DOMAIN 2: Index Test All tests			
Were the RADT results interpreted with blinding of the results of culture?	Yes		
Was the type of the RADT mentioned (EIA or OIA)?	Yes		
Were RADTs conducted during consultation time?	Unclear		
		Low	Unclear
DOMAIN 3: Reference Standard			
Were culture results interpreted with blinding of the results of the RADT?	Yes		

Wright 2007a (Continued)

Is the throat culture method likely to correctly identify GAS (laboratory culture on a blood agar plate during 48 hr)?	Yes		
Were the culture medium, atmosphere, duration of incubation and GAS-confirmation technique described?	No		
		High	High
DOMAIN 4: Flow and Timing			
Was the delay between the performance of the RADT and throat culture plating less than 48 hours?	Unclear		
Did all patients receive a throat culture?	Yes		
Did patients receive the same throat culture method?	Yes		
Were undetermined/uninterpretable results reported?	No		
Were withdrawals from the study explained?	Yes		
		Low	

Wright 2007b

Study characteristics			
Patient sampling	See Wright 2007a		
Patient characteristics and setting	See Wright 2007a		
Index tests	Throat swab: 1 double swab Commercial name of the RADT: QuickVue In-Line Strep A (Quidel) Type of RADT: EIA		
Target condition and reference standard(s)	See Wright 2007a		
Flow and timing	No follow-up		
Comparative			
Type of study	Journal article		
Notes	—		
Methodological quality			
Item	Authors' judgement	Risk of bias	Applicability concerns

DOMAIN 1: Patient Selection

Was a consecutive or random sample of patients enrolled?	Unclear		
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Wright 2007b (Continued)

Was it a cross-sectional study or a RCT?	Yes		
Were selection criteria clearly described (at least presenting signs and symptoms and age limits for inclusion)?	Yes		
Was clinical selection of patients avoided?	Unclear		
Were patients seen in an ambulatory care setting?	No		
		Unclear	High

DOMAIN 2: Index Test All tests

Were the RADT results interpreted with blinding of the results of culture?	Yes		
Was the type of the RADT mentioned (EIA or OIA)?	Yes		
Were RADTs conducted during consultation time?	Unclear		
		Low	Unclear

DOMAIN 3: Reference Standard

Were culture results interpreted with blinding of the results of the RADT?	Yes		
Is the throat culture method likely to correctly identify GAS (laboratory culture on a blood agar plate during 48 hr)?	Yes		
Were the culture medium, atmosphere, duration of incubation and GAS-confirmation technique described?	No		
		High	High

DOMAIN 4: Flow and Timing

Was the delay between the performance of the RADT and throat culture plating less than 48 hours?	Unclear		
Did all patients receive a throat culture?	Yes		
Did patients receive the same throat culture method?	Yes		
Were undetermined/uninterpretable results reported?	No		
Were withdrawals from the study explained?	Yes		
		Low	

Yuckienuz 1988
Study characteristics

Patient sampling	Cross-sectional study
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Yuckienuz 1988 (Continued)

	Prospective design Sample: unclear Direct comparison of different RADTs: no Direct comparison of several throat culture techniques: yes (office culture versus laboratory culture) Person performing the throat sample: physicians Exclusion if recent antibiotics use before inclusion: no Clinical selection of patients: none Presenting signs and symptoms: pharyngitis Age range for inclusion: not reported ("children")
Patient characteristics and setting	Sample size: 341 Age (distribution): not reported GAS prevalence according to culture (with 95% confidence interval): 37.0% (95% CI not reported) Country of study: USA Sex (% of girls): not reported Clinical severity assessment: none Clinical setting: office-based Single-centre study
Index tests	Throat swab: 1 double swab (1 swab for culture, 1 swab for performing the RADT) Commercial name of the RADT: SUDS Group A Strep (Murex) Type of RADT: EIA
Target condition and reference standard(s)	Throat culture medium: standard Atmosphere of incubation: aerobic during 24 hours (office culture) and then anaerobic during 24 hours (laboratory) Duration of incubation: 48 hours GAS confirmation: bacitracin disk and latex test Number of plates inoculated: 1 plate initially inoculated in the office but several subcultures performed in the laboratory Assessment of GAS antibody response: no Relevant details: 1 swab was used for office culture (aerobic 24-hour incubation) and the plates were then transferred to the laboratory for further exploration (anaerobic 24-hour reincubation +/- subcultures of suspect colonies)
Flow and timing	No follow-up
Comparative	
Type of study	Journal article
Notes	The manufacturer of the RADT (Murex) financially supported the study and provided the test kits

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient Selection			

Yuckienuz 1988 (Continued)

Was a consecutive or random sample of patients enrolled?	Unclear		
Was it a cross-sectional study or a RCT?	Yes		
Were selection criteria clearly described (at least presenting signs and symptoms and age limits for inclusion)?	No		
Was clinical selection of patients avoided?	Yes		
Were patients seen in an ambulatory care setting?	Yes		
		High	Low
DOMAIN 2: Index Test All tests			
Were the RADT results interpreted with blinding of the results of culture?	Yes		
Was the type of the RADT mentioned (EIA or OIA)?	Yes		
Were RADTs conducted during consultation time?	Yes		
		Low	Low
DOMAIN 3: Reference Standard			
Were culture results interpreted with blinding of the results of the RADT?	No		
Is the throat culture method likely to correctly identify GAS (laboratory culture on a blood agar plate during 48 hr)?	Yes		
Were the culture medium, atmosphere, duration of incubation and GAS-confirmation technique described?	Yes		
		High	Low
DOMAIN 4: Flow and Timing			
Was the delay between the performance of the RADT and throat culture plating less than 48 hours?	Yes		
Did all patients receive a throat culture?	Yes		
Did patients receive the same throat culture method?	No		
Were undetermined/uninterpretable results reported?	No		
Were withdrawals from the study explained?	Yes		
		High	

Zanacca 1992
Study characteristics

Patient sampling	Cross-sectional study Prospective design Sample: unclear Direct comparison of different RADTs: no Direct comparison of several throat culture techniques: no Person performing the throat sample: not reported Exclusion if recent antibiotics use before inclusion: no Clinical selection of patients: none Presenting signs and symptoms: symptoms of pharyngitis Age range for inclusion: not reported ("patients from the pediatric outpatients departments")		
Patient characteristics and setting	Sample size: 606 Age (distribution): not reported GAS prevalence according to culture (with 95% confidence interval): 32.8% (95% CI not reported) Country of study: Italy Sex (% of girls): not reported Clinical severity assessment: none Clinical setting: walk-in clinic Multi-centre study		
Index tests	Throat swab: 2 different swabs (1 swab for culture, 1 swab for performing the RADT) Commercial name of the RADT: Directgen 1-2-3 Group A Strep (Becton Dickinson) Type of RADT: EIA (liposomal test)		
Target condition and reference standard(s)	Throat culture medium: inhibitory Atmosphere of incubation: not reported Duration of incubation: not reported GAS confirmation: not reported Number of plates inoculated: not reported Assessment of GAS antibody response: no Relevant details:-		
Flow and timing	No follow-up		
Comparative			
Type of study	Conference abstract		
Notes	—		
Methodological quality			
Item	Authors' judgement	Risk of bias	Applicability concerns

Zanacca 1992 (Continued)

DOMAIN 1: Patient Selection

Was a consecutive or random sample of patients enrolled?	Unclear
Was it a cross-sectional study or a RCT?	Yes
Were selection criteria clearly described (at least presenting signs and symptoms and age limits for inclusion)?	No
Was clinical selection of patients avoided?	Yes
Were patients seen in an ambulatory care setting?	Yes

High
Low
DOMAIN 2: Index Test All tests

Were the RADT results interpreted with blinding of the results of culture?	Yes
Was the type of the RADT mentioned (EIA or OIA)?	Yes
Were RADTs conducted during consultation time?	Yes

Low
Low
DOMAIN 3: Reference Standard

Were culture results interpreted with blinding of the results of the RADT?	Unclear
Is the throat culture method likely to correctly identify GAS (laboratory culture on a blood agar plate during 48 hr)?	Unclear
Were the culture medium, atmosphere, duration of incubation and GAS-confirmation technique described?	No

High
High
DOMAIN 4: Flow and Timing

Was the delay between the performance of the RADT and throat culture plating less than 48 hours?	Unclear
Did all patients receive a throat culture?	Yes
Did patients receive the same throat culture method?	Yes
Were undetermined/uninterpretable results reported?	No
Were withdrawals from the study explained?	No

Low

CI: confidence interval

EIA: enzyme immunoassay

FISH: fluorescence in situ hybridisation

GAS: group A streptococcus

LA: latex agglutination

n/a: not applicable

OIA: optical immunoassay

PCR: polymerase chain reaction

PYR: pyrrolidonyl peptidase

RADT: rapid antigen detection test

SD: standard deviation

USAID: United States Agency for International Development

WHO: World Health Organization

Characteristics of excluded studies *[ordered by study ID]*

Study	Reason for exclusion
Abu-Sabaah 2006	Not ambulatory care setting
Andersen 1994	Mixed age but no paediatric data
Andersen 2003a	Duplicate publication
Andersen 2003b	Not ambulatory care setting
Anhalt 1992	Mixed age but no paediatric data
Anonymous 1985a	Editorial, letter or review
Anonymous 1985b	Duplicate publication
Anonymous 1985c	Duplicate publication
Anonymous 1986	Editorial, letter or review
Anonymous 1991	Editorial, letter or review
Anonymous 1992	Editorial, letter or review
Araj 1986	RADT other than EIA or OIA
Araujo 2005	Adults or unclear age
Armengol 2004a	Reference standard not laboratory culture
Armengol 2004b	Reference standard not laboratory culture
Arya 1993	Editorial, letter or review
Atlas 2005	Adults or unclear age
Ausina 1987	Editorial, letter or review
Ba-Saddik 2014	RADT other than EIA or OIA
Badgett 1996	Editorial, letter or review
Baker 1995	Mixed age but no paediatric data

Study	Reason for exclusion
Baselski 1988	Adults or unclear age
Berger-Jekic 1987	RADT other than EIA or OIA
Berke 1989	Editorial, letter or review
Betriu 1988	Not a RADT diagnostic study or 2 x 2 table not extractable
Betriu 1989	Adults or unclear age
Bischoff 2007	Editorial, letter or review
Bjerrum 2013	Editorial, letter or review
Blade 1991	Mixed age but no paediatric data
Blanco 1988	Duplicate publication
Boccazzi 2011	Not a RADT diagnostic study or 2 x 2 table not extractable
Bodino 1987	RADT other than EIA or OIA
Boss 1992	Editorial, letter or review
Bourbeau 1993	Mixed age but no paediatric data
Brahmadathan 1986	Not a RADT diagnostic study or 2 x 2 table not extractable
Burke 1988	Mixed age but no paediatric data
Calvino 2015	Adults or unclear age
Cardoso 2013	Not a RADT diagnostic study or 2 x 2 table not extractable
Carey 1991	Mixed age but no paediatric data
Centor 1984	RADT other than EIA or OIA
Centor 1985	RADT other than EIA or OIA
Chen 2000	Editorial, letter or review
Chessman 1998	Editorial, letter or review
Choi 1995	Adults or unclear age
Coban 2013	Not ambulatory care setting
Cohen 1993	Editorial, letter or review
Cohen 2000	Editorial, letter or review
Cohen 2012a	Duplicate publication
Cohen 2013a	Duplicate publication

Study	Reason for exclusion
Corneli 2001	Editorial, letter or review
Dale 1994	Adults or unclear age
Dale 1997	Editorial, letter or review
De Lorenzo 2012	Duplicate publication
Demeyere 1992	Mixed age but no paediatric data
Diaz-Berenguer 1992	Mixed age but no paediatric data
Dimatteo 2001	Adults or unclear age
Dingle 2014	Mixed age but paediatric data not extractable
DiNicola 1986	RADT other than EIA or OIA
DuBois 1986	RADT other than EIA or OIA
DuBose 1996	Editorial, letter or review
Eaton 1987	Editorial, letter or review
Edmonson 2003	Duplicate publication
Edouard 2014	Editorial, letter or review
Ehrlich 1993	Reference standard not laboratory culture
Enright 2009	Duplicate publication
Esteban 2004	Editorial, letter or review
Fellah 1988	RADT other than EIA or OIA
Figura 1981	Not a RADT diagnostic study or 2 x 2 table not extractable
Fischer 1992	Editorial, letter or review
Foong 1992	Mixed age but no paediatric data
Fox 2006a	Reference standard not laboratory culture
Fox 2006b	Reference standard not laboratory culture
Frei 1991	Editorial, letter or review
Fries 1995	Reference standard not laboratory culture
Gaustad 1991	Editorial, letter or review
Gerber 1986a	RADT other than EIA or OIA
Gerber 1989	Editorial, letter or review

Study	Reason for exclusion
Gerber 1990a	RADT other than EIA or OIA
Gerber 1997a	Editorial, letter or review
Gerber 1997b	Editorial, letter or review
Gerber 1998	Editorial, letter or review
Ghanassia 1996	Editorial, letter or review
Gnehm 1987	RADT other than EIA or OIA
Gonsu 2015	Not ambulatory care setting
Greiver 1999	Editorial, letter or review
Gupta 1992	Target condition other than GAS
Gupta 1997	Adults or unclear age
Gutman 1996	Editorial, letter or review
Hadfield 1987	RADT other than EIA or OIA
Hallander 1988	Editorial, letter or review
Handrick 2006	Editorial, letter or review
Hansen 1992a	RADT other than EIA or OIA
Hansen 1992b	Editorial, letter or review
Harbeck 1993	Mixed age but no paediatric data
Harbeck 1995	Editorial, letter or review
Hasin 1989	Mixed age but no paediatric data
Haym 1986	Not a RADT diagnostic study or 2 x 2 table not extractable
Hedges 1991	Adults or unclear age
Heiter 1993	Mixed age but no paediatric data
Heiter 1995	Mixed age but no paediatric data
Hinfey 2010	Mixed age but no paediatric data
Hodgins 1988	Not a RADT diagnostic study or 2 x 2 table not extractable
Hoffmann 1987	Editorial, letter or review
Hoffmann 1990	Mixed age but no paediatric data
Holbrook 1998	Editorial, letter or review

Study	Reason for exclusion
Hufnagel 2010	Duplicate publication
Humair 2006	Editorial, letter or review
Issa 2014	Editorial, letter or review
Johansson 2003	Mixed age but no paediatric data
Johnson 1995	Editorial, letter or review
Joslyn 1995	Mixed age but no paediatric data
Joubaud 2003	Mixed age but no paediatric data
Kawakami 2003	Mixed age but no paediatric data
Kayaba 1996	Not a RADT diagnostic study or 2 x 2 table not extractable
Keahey 2002	RADT other than EIA or OIA
Kechrid 1988	RADT other than EIA or OIA
Kellogg 1986a	Not a RADT diagnostic study or 2 x 2 table not extractable
Kellogg 1986b	Editorial, letter or review
Kellogg 1987	Mixed age but no paediatric data
Kellogg 1988	Mixed age but no paediatric data
Kellogg 1990	Editorial, letter or review
Klein 1986	Adults or unclear age
Kljakovic 2009	Editorial, letter or review
Kojima 2002	Not a RADT diagnostic study or 2 x 2 table not extractable
Kramer 1980	Editorial, letter or review
Kurtz 1999	Duplicate publication
Larkin 2001	Editorial, letter or review
Laubscher 1994	Editorial, letter or review
Lind 1988	Editorial, letter or review
Lindbaek 2004	Mixed age but no paediatric data
Lindsay 1985	Editorial, letter or review
Llor 2009a	Editorial, letter or review
Llor 2009b	Mixed age but no paediatric data

Study	Reason for exclusion
Llor 2010	Editorial, letter or review
Luebbert 1989	Editorial, letter or review
Lutticken 1991	Editorial, letter or review
Manasse 1989	Adults or unclear age
Mateo 2010	Duplicate publication
Mathur 1992	Editorial, letter or review
Matthys 2006	Editorial, letter or review
Mayefsky 1985	Editorial, letter or review
McCusker 1984	RADT other than EIA or OIA
Meier 1990	RADT other than EIA or OIA
Messina 2010	Not a RADT diagnostic study or 2 x 2 table not extractable
Morandi 2003	Not a RADT diagnostic study or 2 x 2 table not extractable
Morandi 2010	Not a RADT diagnostic study or 2 x 2 table not extractable
Morlan 1988	RADT other than EIA or OIA
Nahata 1986	Editorial, letter or review
Nerbrand 2002	Mixed age but no paediatric data
Nissinen 2009	Not a RADT diagnostic study or 2 x 2 table not extractable
Noorbakhsh 2011	Not a RADT diagnostic study or 2 x 2 table not extractable
Norris 1993	Editorial, letter or review
Omurzakova 2008	Target condition other than GAS
Omurzakova 2009	Target condition other than GAS
Omurzakova 2010	Target condition other than GAS
Patel 1987	Mixed age but no paediatric data
Penalba Citores 2007	Not a RADT diagnostic study or 2 x 2 table not extractable
Petts 1985	RADT other than EIA or OIA
Petts 1988	RADT other than EIA or OIA
Pichichero 1992	Editorial, letter or review
Portier 2003	Editorial, letter or review

Study	Reason for exclusion
Prakash 1985	Editorial, letter or review
Preston 1987	Editorial, letter or review
Putto 1987	RADT other than EIA or OIA
Radetsky 1985	Editorial, letter or review
Radetsky 1987	Editorial, letter or review
Raich 1990	Mixed age but no paediatric data
Rasaiah 1986	Editorial, letter or review
Raz 1987	Editorial, letter or review
Razongles 1993	RADT other than EIA or OIA
Redd 1988	RADT other than EIA or OIA
Reed 1990	Mixed age but no paediatric data
Reichardt 2009	Not a RADT diagnostic study or 2 x 2 table not extractable
Rimoin 2004	Duplicate publication
Roosevelt 2001	Reference standard not laboratory culture
Santos 2003	Not ambulatory care setting
Sarikaya 2010	Adults or unclear age
Savoia 1992	Not a RADT diagnostic study or 2 x 2 table not extractable
Schafer 1995	Editorial, letter or review
Schmuziger 1996	Mixed age but no paediatric data
Schmuziger 2003	Mixed age but no paediatric data
Schwartz 1985	RADT other than EIA or OIA
Seaberg 1997	Mixed age but no paediatric data
Seecamp 1993	Adults or unclear age
Seguido 1987	RADT other than EIA or OIA
Seki 1986	RADT other than EIA or OIA
Serra 1989	Not ambulatory care setting
Shaughnessy 2015	Editorial, letter or review
Sheeler 2002	Adults or unclear age

Study	Reason for exclusion
Shekelle 1992	Editorial, letter or review
Shriner 1985	Editorial, letter or review
Shulman 1994	Editorial, letter or review
Shulman 1995	Editorial, letter or review
Skellern 1993	Adults or unclear age
Smith 1989	RADT other than EIA or OIA
Smith 1995	Mixed age but no paediatric data
Solé 2009	Editorial, letter or review
Stillstrom 1991	Mixed age but no paediatric data
Stingu 2009	Not ambulatory care setting
Supon 1998	Mixed age but no paediatric data
Syriopoulou 2011	RADT other than EIA or OIA
Taeron 2006	Editorial, letter or review
Tagami 1997	Target condition other than GAS
Tenjarla 1990	Duplicate publication
Tocks 1992	Editorial, letter or review
Todd 1987	Editorial, letter or review
True 1986	RADT other than EIA or OIA
Uhl 2003	Mixed age but no paediatric data
Vakkila 2015	RADT other than EIA or OIA
Waagepetersen 2009	Editorial, letter or review
Wagener 1985	RADT other than EIA or OIA
Warner 1985	Editorial, letter or review
Waseem 2009	Duplicate publication
Wegner 1992	Mixed age but no paediatric data
Wegner 1996	Editorial, letter or review
White 1986	RADT other than EIA or OIA
Wolinsky 1986	RADT other than EIA or OIA

Study	Reason for exclusion
Wong 2002	Mixed age but no paediatric data
Woodburn 2007	Mixed age but no paediatric data
Wright 1987	RADT other than EIA or OIA
Yu 1988	Adults or unclear age

EIA: enzyme immunoassay
 GAS: group A streptococcus
 OIA: optical immunoassay
 RADT: rapid antigen detection test

Characteristics of studies awaiting classification *[ordered by study ID]*

Briko 1997

Study characteristics	
Patient sampling	—
Patient characteristics and setting	—
Index tests	—
Target condition and reference standard(s)	—
Flow and timing	—
Comparative	—
Notes	Unable to obtain full text

Gajos 1997

Study characteristics	
Patient sampling	—
Patient characteristics and setting	—
Index tests	—
Target condition and reference standard(s)	—
Flow and timing	—
Comparative	—
Notes	In Polish

Gnehm 1986
Study characteristics

Patient sampling	—
Patient characteristics and setting	—
Index tests	—
Target condition and reference standard(s)	—
Flow and timing	—
Comparative	—
Notes	Unable to obtain full text

Grevnina 1992
Study characteristics

Patient sampling	—
Patient characteristics and setting	—
Index tests	—
Target condition and reference standard(s)	—
Flow and timing	—
Comparative	—
Notes	Unable to obtain full text

Herranz 2007
Study characteristics

Patient sampling	—
Patient characteristics and setting	—
Index tests	—
Target condition and reference standard(s)	—
Flow and timing	—
Comparative	—
Notes	Unable to obtain full text

Mirjat 2012a
Study characteristics

Patient sampling	—
Patient characteristics and setting	—
Index tests	—
Target condition and reference standard(s)	—
Flow and timing	—
Comparative	—
Notes	Unable to obtain full text

Mirjat 2012b
Study characteristics

Patient sampling	—
Patient characteristics and setting	—
Index tests	—
Target condition and reference standard(s)	—
Flow and timing	—
Comparative	—
Notes	Unable to obtain full text

Nestorovic 2004
Study characteristics

Patient sampling	—
Patient characteristics and setting	—
Index tests	—
Target condition and reference standard(s)	—
Flow and timing	—
Comparative	—

Nestorovic 2004 *(Continued)*

Notes	Unable to obtain full text
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Sanz Moreno 2010
Study characteristics

Patient sampling	—
Patient characteristics and setting	—
Index tests	—
Target condition and reference standard(s)	—
Flow and timing	—
Comparative	—
Notes	Unable to obtain full text

Shikhman 1988
Study characteristics

Patient sampling	—
Patient characteristics and setting	—
Index tests	—
Target condition and reference standard(s)	—
Flow and timing	—
Comparative	—
Notes	Unable to obtain full text

Soyletir 1988
Study characteristics

Patient sampling	—
Patient characteristics and setting	—
Index tests	—
Target condition and reference standard(s)	—

Soyletir 1988 *(Continued)*

Flow and timing	—
Comparative	—
Notes	In Turkish

Sramek 1992
Study characteristics

Patient sampling	—
Patient characteristics and setting	—
Index tests	—
Target condition and reference standard(s)	—
Flow and timing	—
Comparative	—
Notes	In Czech

Vylegzhanina 1994
Study characteristics

Patient sampling	—
Patient characteristics and setting	—
Index tests	—
Target condition and reference standard(s)	—
Flow and timing	—
Comparative	—
Notes	Unable to obtain full text

Yilmaz 2008
Study characteristics

Patient sampling	—
Patient characteristics and setting	—

Yilmaz 2008 (Continued)

Index tests	—
Target condition and reference standard(s)	—
Flow and timing	—
Comparative	—
Notes	In Turkish

DATA

Presented below are all the data for all of the tests entered into the review.

Table Tests. Data tables by test

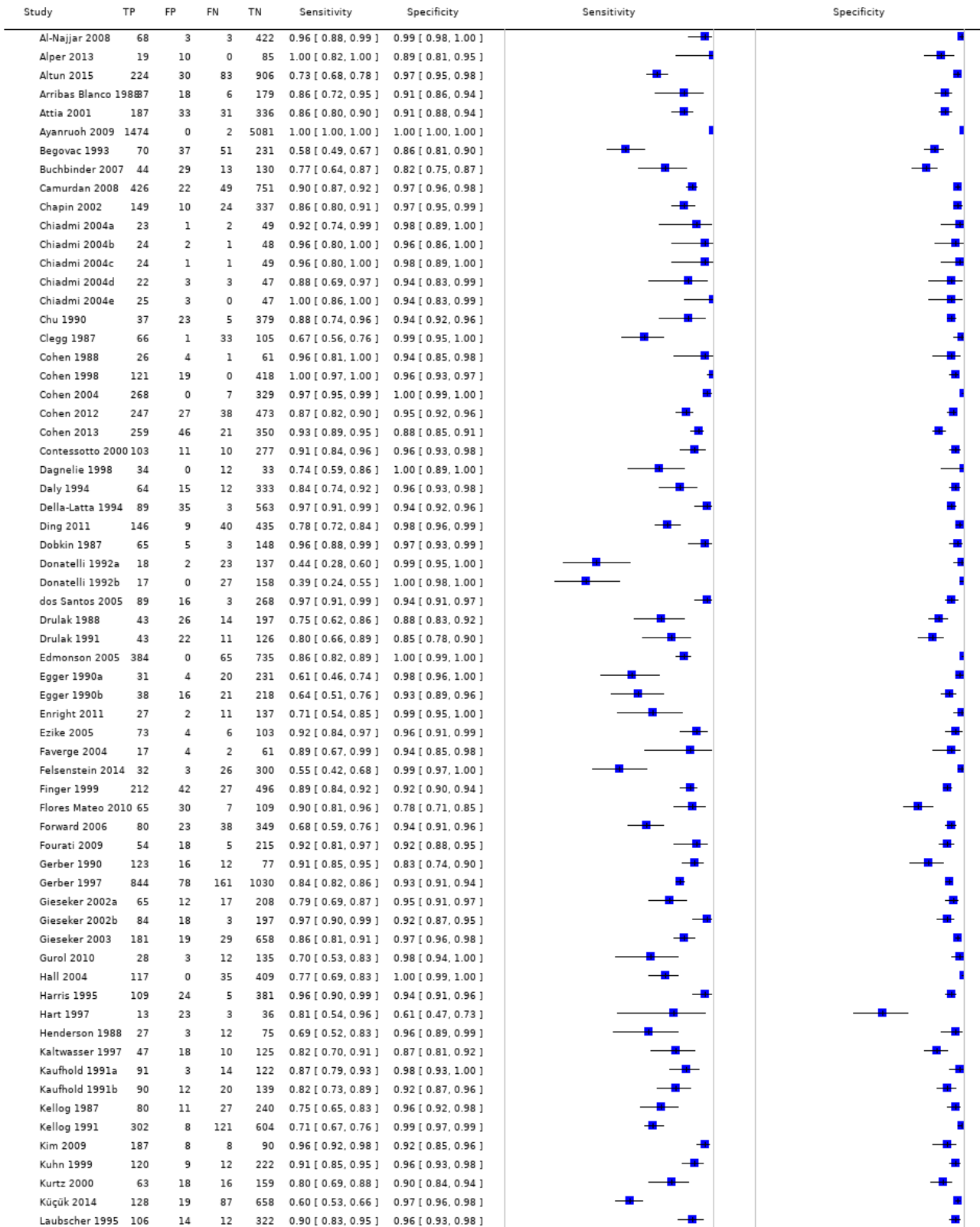
Test	No. of studies	No. of participants
1 All studies (n = 116)	116	101121
2 Complete verification (n = 105)	105	58244
3 EIA (direct comparison)	2	802
4 OIA (direct comparison)	2	802
5 Acceava Strep A (Biostar)	2	789
6 ACON Strep A Rapid Test Strip	1	5505
7 BioNexia Strep A (BioMerieux)	1	183
8 CARDS QS Strep A (Quidel)	1	1184
9 Clearview Exact Strep A	1	630
10 Clearview Strep A	1	75
11 Diaquick Strep A Test (Dialab)	1	496
12 Directgen 1-2-3 Group A Strep (Becton Dickinson)	4	1189
13 Direct Strep A EIA	1	293
14 EIA (no name)	3	7228
15 Group A Strep Test (Quidel)	2	184
16 IM Strep A (International Microbio)	2	291
17 Meridian Bioscience	1	114

Test	No. of studies	No. of participants
18 OSOM Strep A (Genzyme)	7	1349
19 OSOM Ultra Strep A (Genzyme)	4	1888
20 QuickVue Dipstick Strep A (Quidel)	2	2071
21 QuickVue Flex Strep A (Quidel)	2	1178
22 QuickVue In-Line Strep A (Quidel)	6	4122
23 QuickVue+ Strep A (Quidel)	4	845
24 Sacks Biological Farms	1	6557
25 SD Bionline Strep A	2	404
26 Signify Strep A (Abbott)	1	6865
27 SMART Group A Strep (New Horizons)	1	1035
28 Strep A Abon kit	1	1243
29 Strep A OIA (Biostar)	13	6476
30 Strep A OIA Max (Biostar)	6	2960
31 Strep A Rapid Test Device	1	490
32 Strep A Sign	1	75
33 Strep A test II (INTEX Diagnostica)	1	1248
34 StreptAtest (Dectrapharm)	4	1640
35 Streptavit	1	75
36 Streptop A (ALL-Diag)	1	292
37 SUDS Group A Strep	1	341
38 SureScreen Test Strep A	1	188
39 TestPack Strep A (Abbott)	10	14766
40 TestPack Plus (Abbott)	8	2883
41 TestPack Plus Strep A with OBC II (Abbott)	1	454
42 Ventrescreen Strep A (Ventrex Lab)	3	714
43 Visuwell Strep A (ADI)	3	926
44 Icon Strep A	4	865
45 Qtest (Becton Dickinson)	3	16645

Test	No. of studies	No. of participants
46 Link 2 Strep A Rapid Test (Becton Dickinson)	1	432
47 Event Test Strip Strep A	1	510

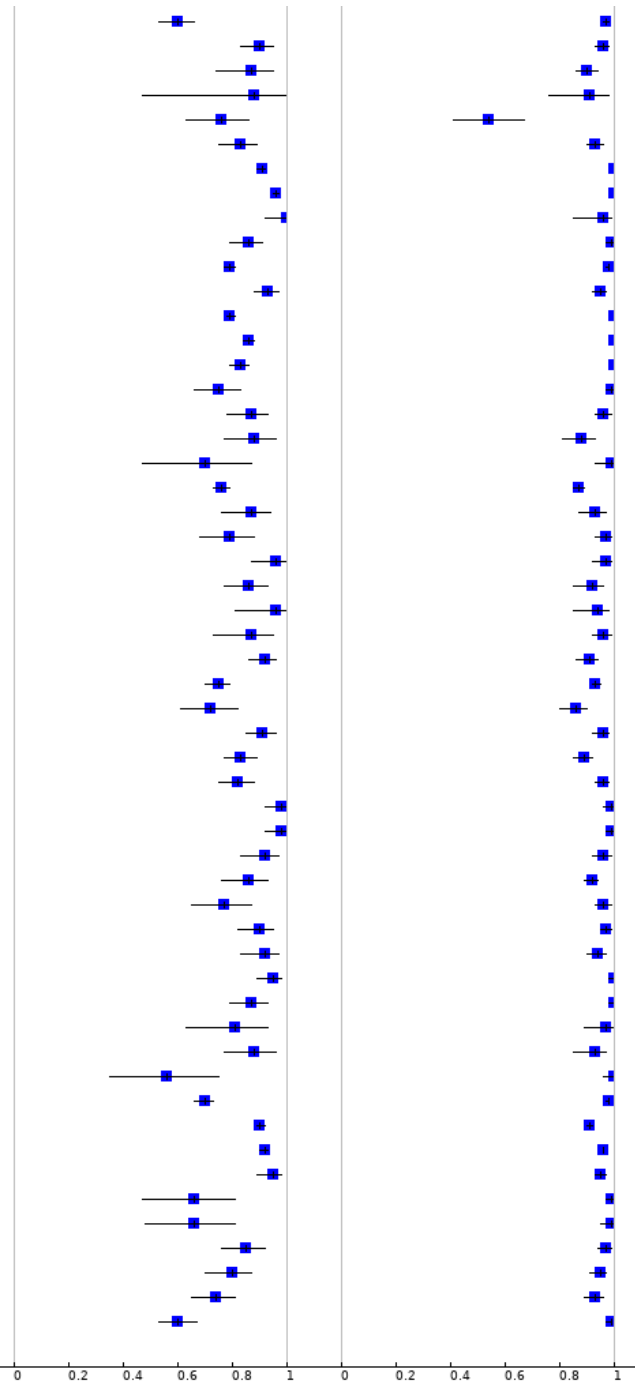
Test 1. All studies (n = 116).

Review: Rapid antigen detection test for group A streptococcus in children with pharyngitis
Test: 1 All studies (n = 116)



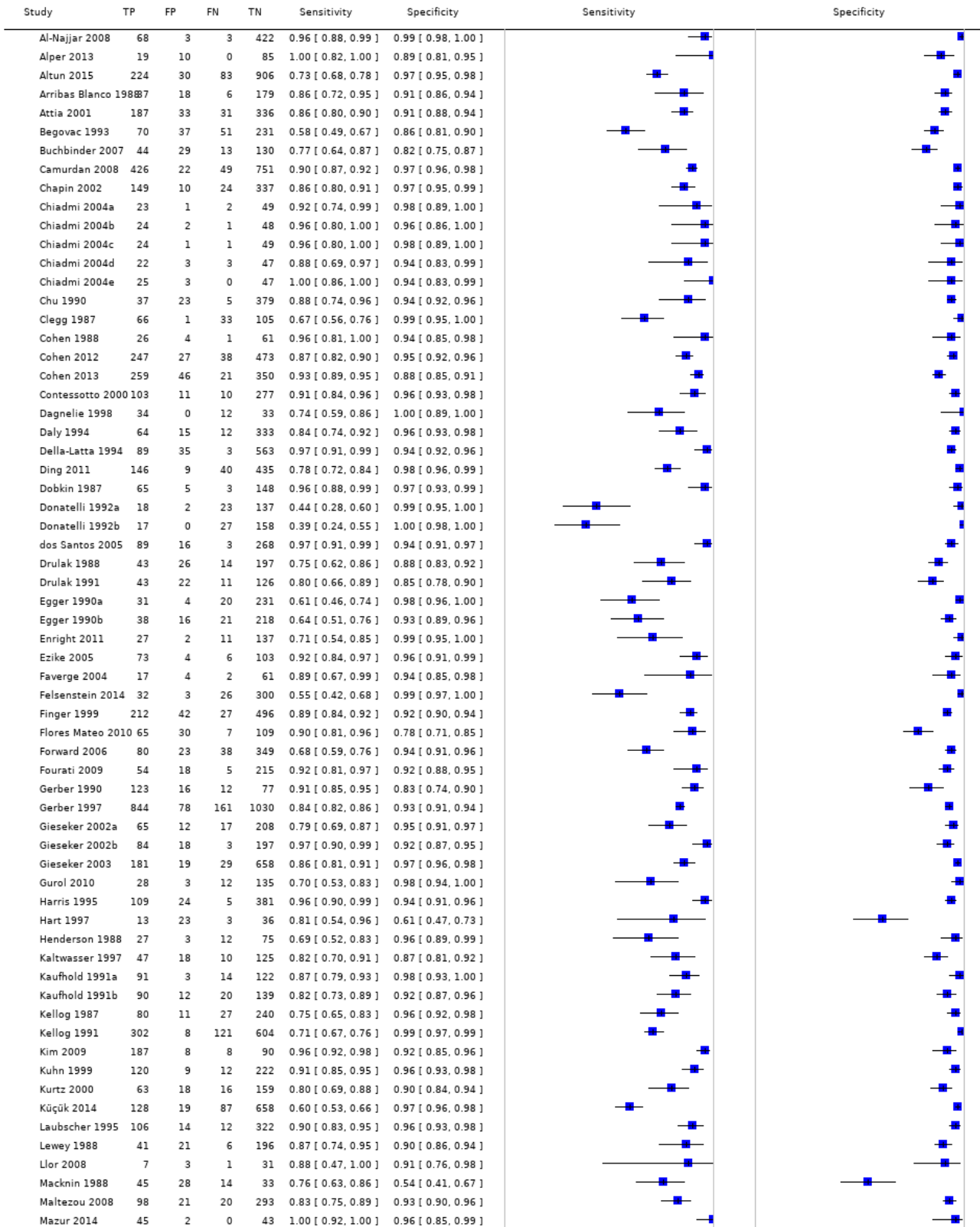
Test 1. (Continued)

Kügük 2014	128	19	87	658	0.60 [0.53, 0.66]	0.97 [0.96, 0.98]
Laubscher 1995	106	14	12	322	0.90 [0.83, 0.95]	0.96 [0.93, 0.98]
Lewey 1988	41	21	6	196	0.87 [0.74, 0.95]	0.90 [0.86, 0.94]
Llor 2008	7	3	1	31	0.88 [0.47, 1.00]	0.91 [0.76, 0.98]
Macknin 1988	45	28	14	33	0.76 [0.63, 0.86]	0.54 [0.41, 0.67]
Maltezou 2008	98	21	20	293	0.83 [0.75, 0.89]	0.93 [0.90, 0.96]
Mayes 2001a	1299	0	132	3342	0.91 [0.89, 0.92]	1.00 [1.00, 1.00]
Mayes 2001b	1743	0	68	4696	0.96 [0.95, 0.97]	1.00 [1.00, 1.00]
Mazur 2014	45	2	0	43	1.00 [0.92, 1.00]	0.96 [0.85, 0.99]
Mclsaac 2004	133	3	22	296	0.86 [0.79, 0.91]	0.99 [0.97, 1.00]
Menozzi 1992	1007	54	269	2328	0.79 [0.77, 0.81]	0.98 [0.97, 0.98]
Mezghani Maleej 2000	14	10	10	283	0.93 [0.88, 0.97]	0.95 [0.92, 0.97]
Mirza 2007a	2612	0	688	8344	0.79 [0.78, 0.81]	1.00 [1.00, 1.00]
Mirza 2007b	1730	0	280	4855	0.86 [0.84, 0.88]	1.00 [1.00, 1.00]
Mlejnek 2014	476	0	99	2848	0.83 [0.79, 0.86]	1.00 [1.00, 1.00]
Moyer 1990	78	2	26	218	0.75 [0.66, 0.83]	0.99 [0.97, 1.00]
Needham 1998	75	7	11	183	0.87 [0.78, 0.93]	0.96 [0.93, 0.99]
Nitsch-Osusch 2010	46	17	6	119	0.88 [0.77, 0.96]	0.88 [0.81, 0.93]
Nonaka 1988	16	1	7	76	0.70 [0.47, 0.87]	0.99 [0.93, 1.00]
Pauchard 2012	571	153	180	1036	0.76 [0.73, 0.79]	0.87 [0.85, 0.89]
Pauchard 2013	59	8	9	107	0.87 [0.76, 0.94]	0.93 [0.87, 0.97]
Pitetti 1998	58	5	15	155	0.79 [0.68, 0.88]	0.97 [0.93, 0.99]
Ramos 2011	50	3	2	110	0.96 [0.87, 1.00]	0.97 [0.92, 0.99]
Regueras De Lorenza 2012	10	10	10	108	0.86 [0.77, 0.93]	0.92 [0.85, 0.96]
Reinert 1988	26	4	1	61	0.96 [0.81, 1.00]	0.94 [0.85, 0.98]
Rimoin 2010a	39	5	6	134	0.87 [0.73, 0.95]	0.96 [0.92, 0.99]
Rimoin 2010b	146	23	13	222	0.92 [0.86, 0.96]	0.91 [0.86, 0.94]
Rimoin 2010c	321	82	109	1114	0.75 [0.70, 0.79]	0.93 [0.92, 0.95]
Rimoin 2010d	55	26	21	156	0.72 [0.61, 0.82]	0.86 [0.80, 0.90]
Roddey 1995	107	8	10	176	0.91 [0.85, 0.96]	0.96 [0.92, 0.98]
Roe 1995a	126	38	25	311	0.83 [0.77, 0.89]	0.89 [0.85, 0.92]
Roe 1995b	124	14	27	335	0.82 [0.75, 0.88]	0.96 [0.93, 0.98]
Rogo 2010a	63	2	1	162	0.98 [0.92, 1.00]	0.99 [0.96, 1.00]
Rogo 2010b	65	1	1	161	0.98 [0.92, 1.00]	0.99 [0.97, 1.00]
Rogo 2010c	60	6	5	157	0.92 [0.83, 0.97]	0.96 [0.92, 0.99]
Savoia 1994	63	36	10	401	0.86 [0.76, 0.93]	0.92 [0.89, 0.94]
Schlager 1996	48	7	14	193	0.77 [0.65, 0.87]	0.97 [0.93, 0.99]
Schwabe 1987	90	7	10	258	0.90 [0.82, 0.95]	0.97 [0.95, 0.99]
Schwabe 1991	65	11	6	179	0.92 [0.83, 0.97]	0.94 [0.90, 0.97]
Schwartz 1997a	98	0	5	155	0.95 [0.89, 0.98]	1.00 [0.98, 1.00]
Schwartz 1997b	90	0	13	155	0.87 [0.79, 0.93]	1.00 [0.98, 1.00]
Sedki 2010	25	2	6	62	0.81 [0.63, 0.93]	0.97 [0.89, 1.00]
Strandjord 1987	46	6	6	80	0.88 [0.77, 0.96]	0.93 [0.85, 0.97]
Subashini 2015	15	0	12	84	0.56 [0.35, 0.75]	1.00 [0.96, 1.00]
Tanz 2009	385	29	168	1261	0.70 [0.66, 0.73]	0.98 [0.97, 0.98]
Tellechea 2012	1981	290	210	3024	0.90 [0.89, 0.92]	0.91 [0.90, 0.92]
Tenjarla 1991	1389	305	125	7342	0.92 [0.90, 0.93]	0.96 [0.96, 0.96]
Toepfner 2013	94	20	5	398	0.95 [0.89, 0.98]	0.95 [0.93, 0.97]
Van Limbergen 2008	1	11	168	0.66 [0.47, 0.81]	0.99 [0.97, 1.00]	
Wong 1989	23	1	12	111	0.66 [0.48, 0.81]	0.99 [0.95, 1.00]
Wright 2007a	76	7	13	242	0.85 [0.76, 0.92]	0.97 [0.94, 0.99]
Wright 2007b	70	13	18	237	0.80 [0.70, 0.87]	0.95 [0.91, 0.97]
Yuckienuz 1988	93	15	33	200	0.74 [0.65, 0.81]	0.93 [0.89, 0.96]
Zanacca 1992	120	6	79	401	0.60 [0.53, 0.67]	0.99 [0.97, 0.99]



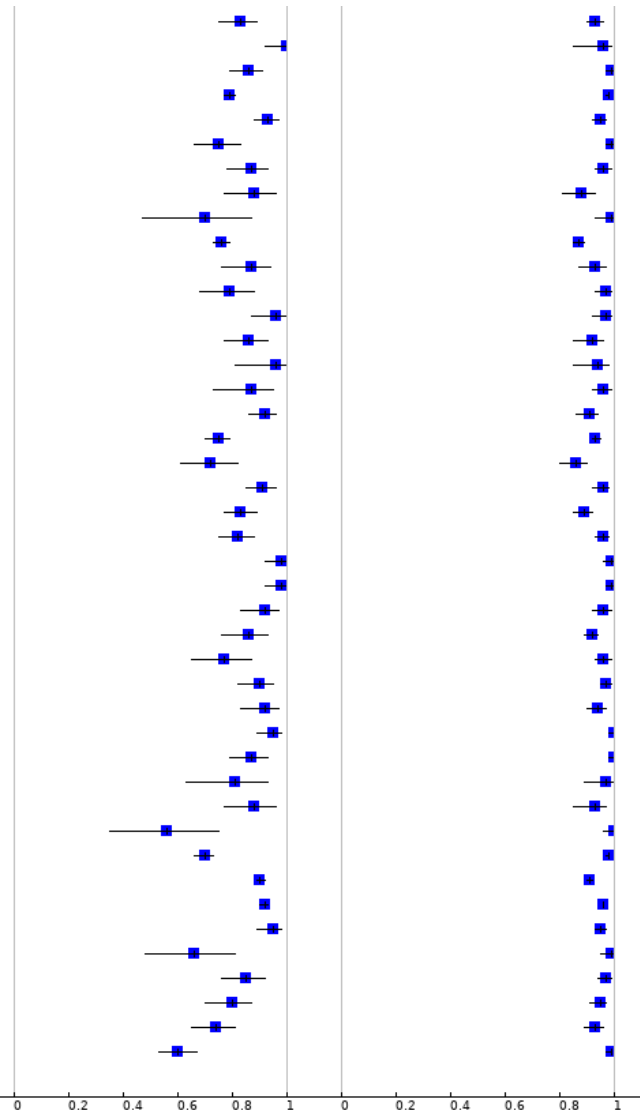
Test 2. Complete verification (n = 105).

Review: Rapid antigen detection test for group A streptococcus in children with pharyngitis
Test: 2 Complete verification (n = 105)



Test 2. (Continued)

Maltezou 2008	98	21	20	293	0.83 [0.75, 0.89]	0.93 [0.90, 0.96]
Mazur 2014	45	2	0	43	1.00 [0.92, 1.00]	0.96 [0.85, 0.99]
Mclsaac 2004	133	3	22	296	0.86 [0.79, 0.91]	0.99 [0.97, 1.00]
Menozzi 1992	1007	54	269	2328	0.79 [0.77, 0.81]	0.98 [0.97, 0.98]
Mezghani Maleej 2000	14	10	10	283	0.93 [0.88, 0.97]	0.95 [0.92, 0.97]
Moyer 1990	78	2	26	218	0.75 [0.66, 0.83]	0.99 [0.97, 1.00]
Needham 1998	75	7	11	183	0.87 [0.78, 0.93]	0.96 [0.93, 0.99]
Nitsch-Osuch 2010	46	17	6	119	0.88 [0.77, 0.96]	0.88 [0.81, 0.93]
Nonaka 1988	16	1	7	76	0.70 [0.47, 0.87]	0.99 [0.93, 1.00]
Pauchard 2012	571	153	180	1036	0.76 [0.73, 0.79]	0.87 [0.85, 0.89]
Pauchard 2013	59	8	9	107	0.87 [0.76, 0.94]	0.93 [0.87, 0.97]
Pitetti 1998	58	5	15	155	0.79 [0.68, 0.88]	0.97 [0.93, 0.99]
Ramos 2011	50	3	2	110	0.96 [0.87, 1.00]	0.97 [0.92, 0.99]
Regueras De Lorenza 2012	10	10	10	108	0.86 [0.77, 0.93]	0.92 [0.85, 0.96]
Reinert 1988	26	4	1	61	0.96 [0.81, 1.00]	0.94 [0.85, 0.98]
Rimoin 2010a	39	5	6	134	0.87 [0.73, 0.95]	0.96 [0.92, 0.99]
Rimoin 2010b	146	23	13	222	0.92 [0.86, 0.96]	0.91 [0.86, 0.94]
Rimoin 2010c	321	82	109	1114	0.75 [0.70, 0.79]	0.93 [0.92, 0.95]
Rimoin 2010d	55	26	21	156	0.72 [0.61, 0.82]	0.86 [0.80, 0.90]
Roddey 1995	107	8	10	176	0.91 [0.85, 0.96]	0.96 [0.92, 0.98]
Roe 1995a	126	38	25	311	0.83 [0.77, 0.89]	0.89 [0.85, 0.92]
Roe 1995b	124	14	27	335	0.82 [0.75, 0.88]	0.96 [0.93, 0.98]
Rogo 2010a	63	2	1	162	0.98 [0.92, 1.00]	0.99 [0.96, 1.00]
Rogo 2010b	65	1	1	161	0.98 [0.92, 1.00]	0.99 [0.97, 1.00]
Rogo 2010c	60	6	5	157	0.92 [0.83, 0.97]	0.96 [0.92, 0.99]
Savoia 1994	63	36	10	401	0.86 [0.76, 0.93]	0.92 [0.89, 0.94]
Schlager 1996	48	7	14	193	0.77 [0.65, 0.87]	0.97 [0.93, 0.99]
Schwabe 1987	90	7	10	258	0.90 [0.82, 0.95]	0.97 [0.95, 0.99]
Schwabe 1991	65	11	6	179	0.92 [0.83, 0.97]	0.94 [0.90, 0.97]
Schwartz 1997a	98	0	5	155	0.95 [0.89, 0.98]	1.00 [0.98, 1.00]
Schwartz 1997b	90	0	13	155	0.87 [0.79, 0.93]	1.00 [0.98, 1.00]
Sedki 2010	25	2	6	62	0.81 [0.63, 0.93]	0.97 [0.89, 1.00]
Strandjord 1987	46	6	6	80	0.88 [0.77, 0.96]	0.93 [0.85, 0.97]
Subashini 2015	15	0	12	84	0.56 [0.35, 0.75]	1.00 [0.96, 1.00]
Tanz 2009	385	29	168	1261	0.70 [0.66, 0.73]	0.98 [0.97, 0.98]
Tellechea 2012	1981	290	210	3024	0.90 [0.89, 0.92]	0.91 [0.90, 0.92]
Tenjarla 1991	1389	305	125	7342	0.92 [0.90, 0.93]	0.96 [0.96, 0.96]
Toepfner 2013	94	20	5	398	0.95 [0.89, 0.98]	0.95 [0.93, 0.97]
Wong 1989	23	1	12	111	0.66 [0.48, 0.81]	0.99 [0.95, 1.00]
Wright 2007a	76	7	13	242	0.85 [0.76, 0.92]	0.97 [0.94, 0.99]
Wright 2007b	70	13	18	237	0.80 [0.70, 0.87]	0.95 [0.91, 0.97]
Yuckienuz 1988	93	15	33	200	0.74 [0.65, 0.81]	0.93 [0.89, 0.96]
Zanacca 1992	120	6	79	401	0.60 [0.53, 0.67]	0.99 [0.97, 0.99]



Test 3. EIA (direct comparison).

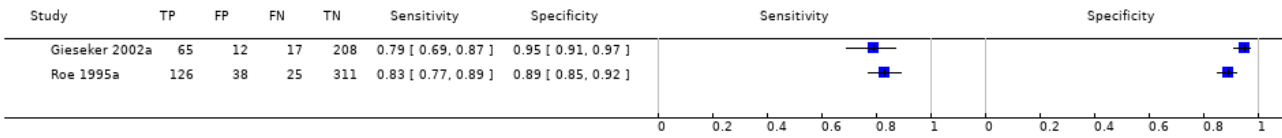
Review: Rapid antigen detection test for group A streptococcus in children with pharyngitis
Test: 3 EIA (direct comparison)

Study	TP	FP	FN	TN	Sensitivity	Specificity	Sensitivity	Specificity
Gieseke 2002a	84	18	3	197	0.97 [0.90, 0.99]	0.92 [0.87, 0.95]		
Roe 1995a	124	14	27	335	0.82 [0.75, 0.88]	0.96 [0.93, 0.98]		



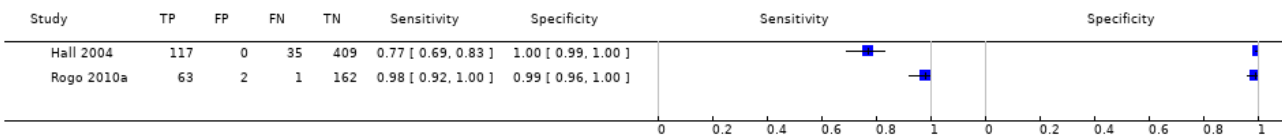
Test 4. OIA (direct comparison).

Review: Rapid antigen detection test for group A streptococcus in children with pharyngitis
Test: 4 OIA (direct comparison)



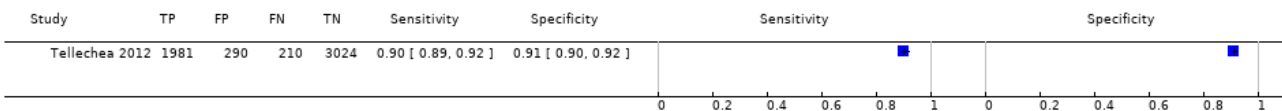
Test 5. Acceava Strep A (Biostar).

Review: Rapid antigen detection test for group A streptococcus in children with pharyngitis
Test: 5 Acceava Strep A (Biostar)



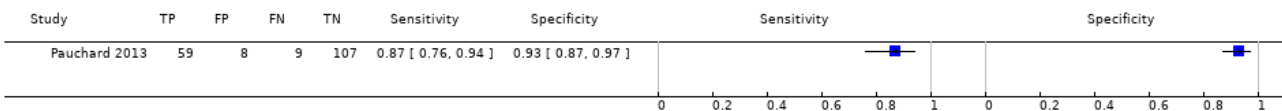
Test 6. ACON Strep A Rapid Test Strip.

Review: Rapid antigen detection test for group A streptococcus in children with pharyngitis
Test: 6 ACON Strep A Rapid Test Strip



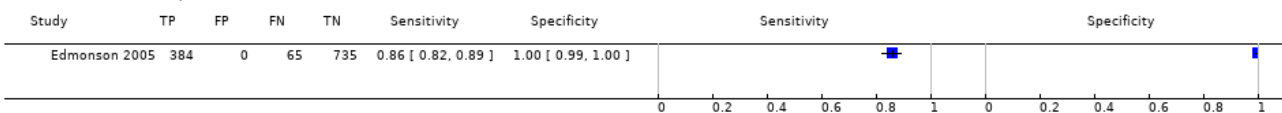
Test 7. BioNexia Strep A (BioMerieux).

Review: Rapid antigen detection test for group A streptococcus in children with pharyngitis
Test: 7 BioNexia Strep A (BioMerieux)



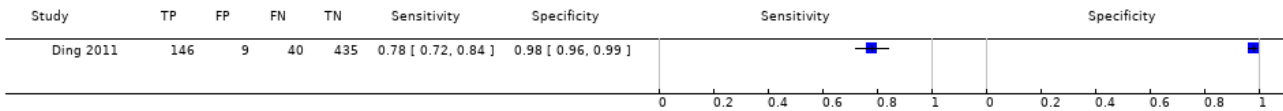
Test 8. CARDS QS Strep A (Quidel).

Review: Rapid antigen detection test for group A streptococcus in children with pharyngitis
Test: 8 CARDS QS Strep A (Quidel)



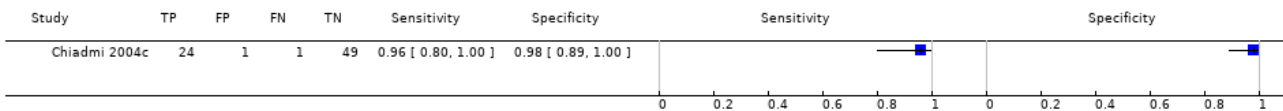
Test 9. Clearview Exact Strep A.

Review: Rapid antigen detection test for group A streptococcus in children with pharyngitis
Test: 9 Clearview Exact Strep A



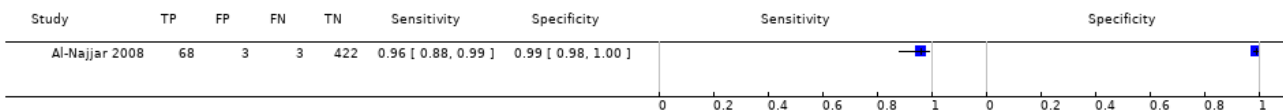
Test 10. Clearview Strep A.

Review: Rapid antigen detection test for group A streptococcus in children with pharyngitis
Test: 10 Clearview Strep A



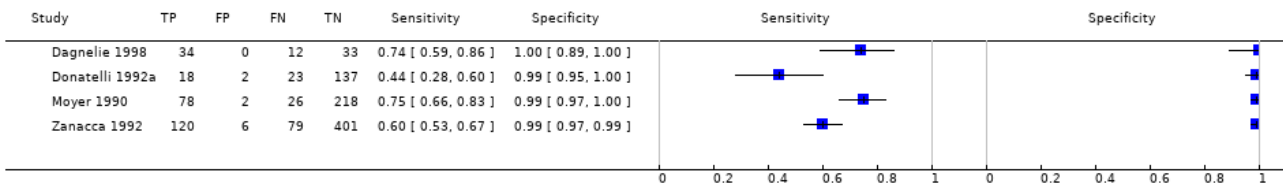
Test 11. Diaquick Strep A Test (Dialab).

Review: Rapid antigen detection test for group A streptococcus in children with pharyngitis
Test: 11 Diaquick Strep A Test (Dialab)



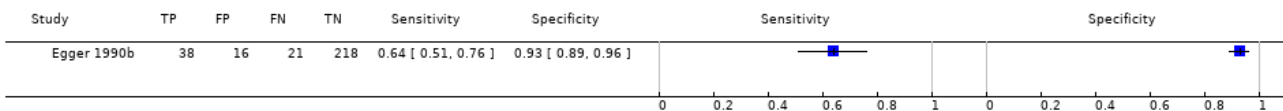
Test 12. Directgen 1-2-3 Group A Strep (Becton Dickinson).

Review: Rapid antigen detection test for group A streptococcus in children with pharyngitis
Test: 12 Directgen 1-2-3 Group A Strep (Becton Dickinson)



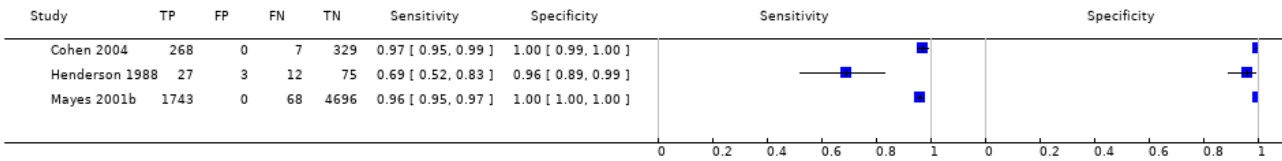
Test 13. Direct Strep A EIA.

Review: Rapid antigen detection test for group A streptococcus in children with pharyngitis
Test: 13 Direct Strep A EIA



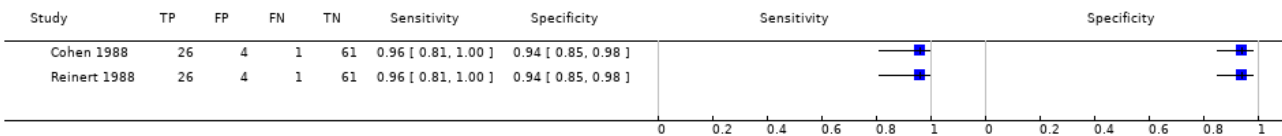
Test 14. EIA (no name).

Review: Rapid antigen detection test for group A streptococcus in children with pharyngitis
Test: 14 EIA (no name)



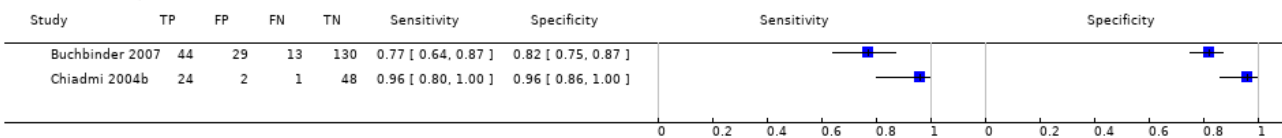
Test 15. Group A Strep Test (Quidel).

Review: Rapid antigen detection test for group A streptococcus in children with pharyngitis
Test: 15 Group A Strep Test (Quidel)



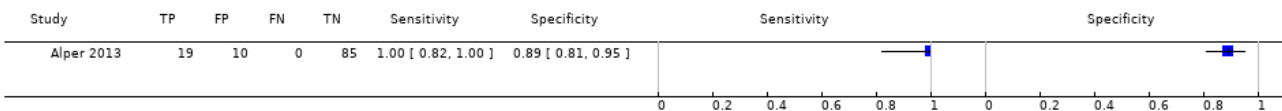
Test 16. IM Strep A (International Microbio).

Review: Rapid antigen detection test for group A streptococcus in children with pharyngitis
Test: 16 IM Strep A (International Microbio)



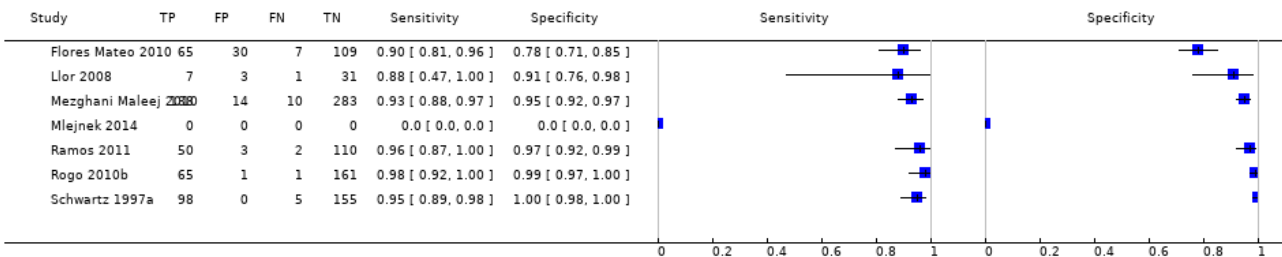
Test 17. Meridian Bioscience.

Review: Rapid antigen detection test for group A streptococcus in children with pharyngitis
Test: 17 Meridian Bioscience



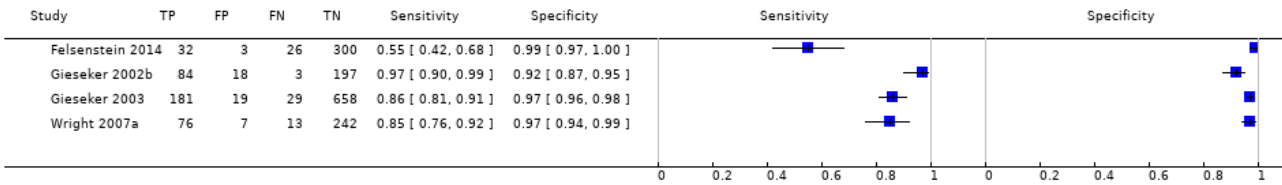
Test 18. OSOM Strep A (Genzyme).

Review: Rapid antigen detection test for group A streptococcus in children with pharyngitis
Test: 18 OSOM Strep A (Genzyme)



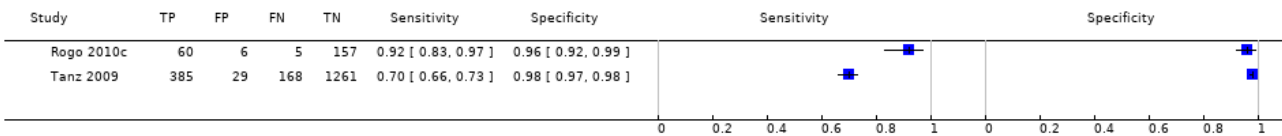
Test 19. OSOM Ultra Strep A (Genzyme).

Review: Rapid antigen detection test for group A streptococcus in children with pharyngitis
Test: 19 OSOM Ultra Strep A (Genzyme)



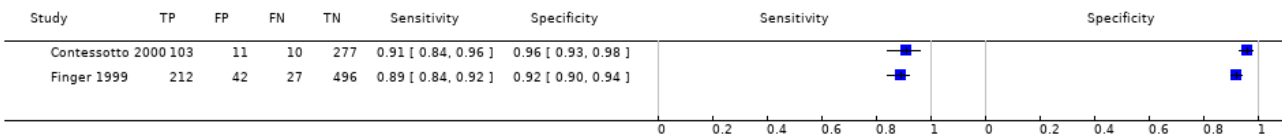
Test 20. QuickVue Dipstick Strep A (Quidel).

Review: Rapid antigen detection test for group A streptococcus in children with pharyngitis
Test: 20 QuickVue Dipstick Strep A (Quidel)



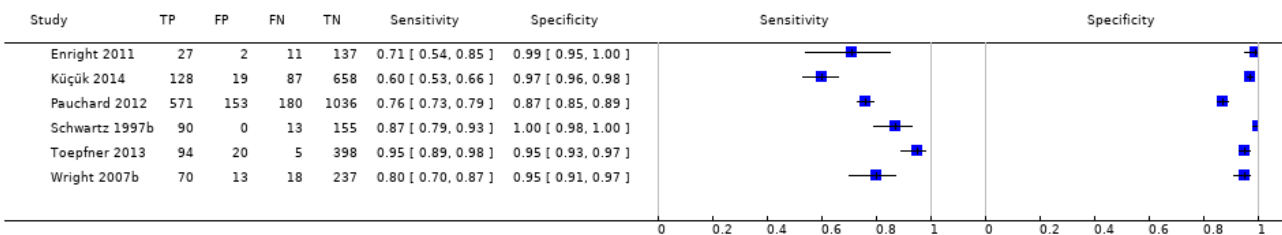
Test 21. QuickVue Flex Strep A (Quidel).

Review: Rapid antigen detection test for group A streptococcus in children with pharyngitis
Test: 21 QuickVue Flex Strep A (Quidel)



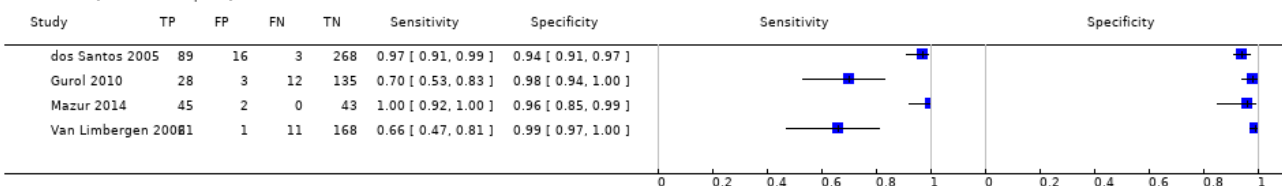
Test 22. QuickVue In-Line Strep A (Quidel).

Review: Rapid antigen detection test for group A streptococcus in children with pharyngitis
Test: 22 QuickVue In-Line Strep A (Quidel)



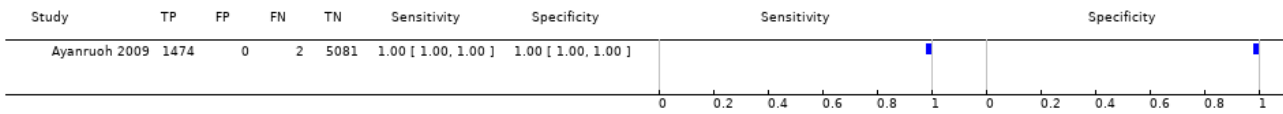
Test 23. QuickVue+ Strep A (Quidel).

Review: Rapid antigen detection test for group A streptococcus in children with pharyngitis
Test: 23 QuickVue+ Strep A (Quidel)



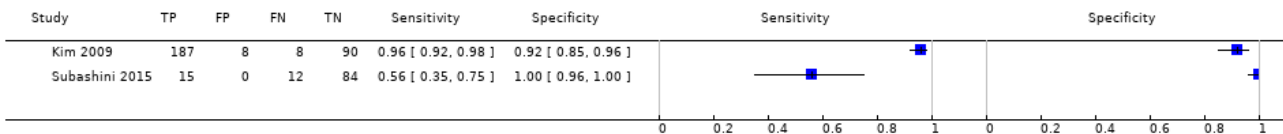
Test 24. Sacks Biological Farms.

Review: Rapid antigen detection test for group A streptococcus in children with pharyngitis
Test: 24 Sacks Biological Farms



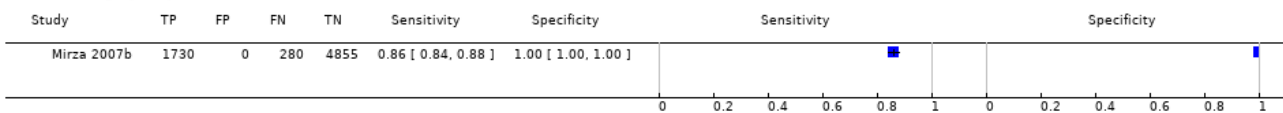
Test 25. SD Bioline Strep A.

Review: Rapid antigen detection test for group A streptococcus in children with pharyngitis
Test: 25 SD Bioline Strep A



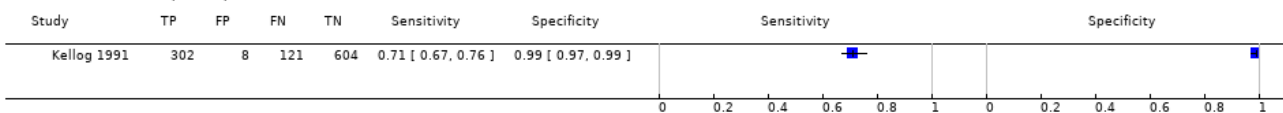
Test 26. Signify Strep A (Abbott).

Review: Rapid antigen detection test for group A streptococcus in children with pharyngitis
Test: 26 Signify Strep A (Abbott)



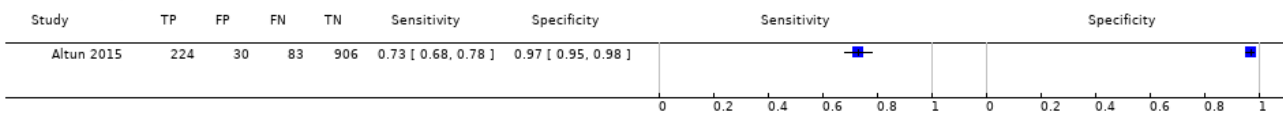
Test 27. SMART Group A Strep (New Horizons).

Review: Rapid antigen detection test for group A streptococcus in children with pharyngitis
Test: 27 SMART Group A Strep (New Horizons)



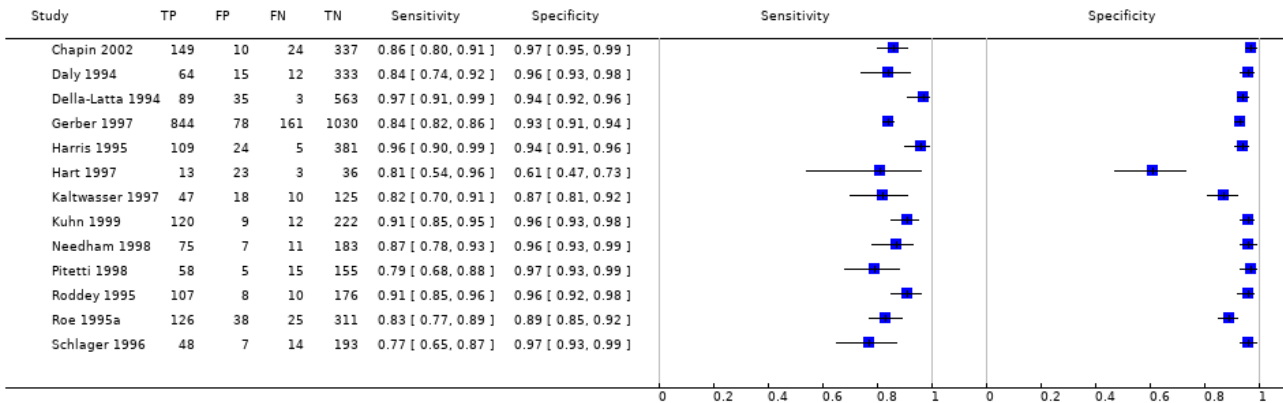
Test 28. Strep A Abon kit.

Review: Rapid antigen detection test for group A streptococcus in children with pharyngitis
Test: 28 Strep A Abon kit



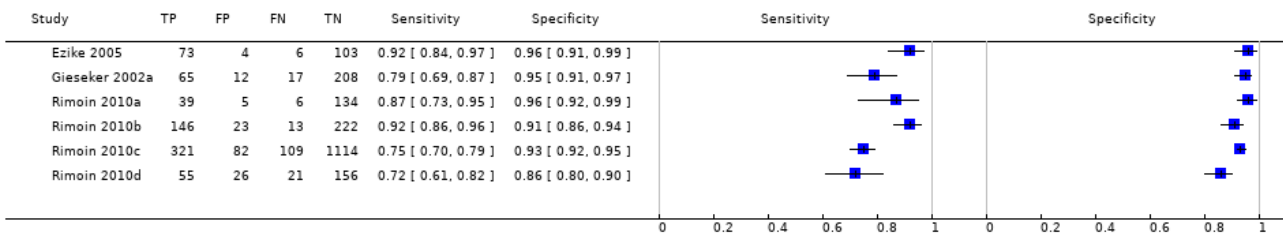
Test 29. Strep A OIA (Biostar).

Review: Rapid antigen detection test for group A streptococcus in children with pharyngitis
Test: 29 Strep A OIA (Biostar)



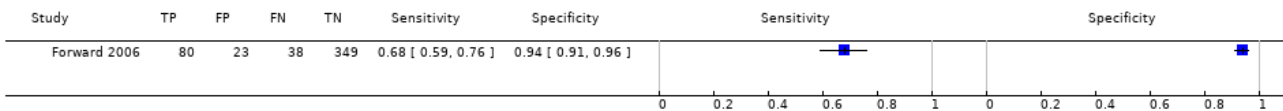
Test 30. Strep A OIA Max (Biostar).

Review: Rapid antigen detection test for group A streptococcus in children with pharyngitis
Test: 30 Strep A OIA Max (Biostar)



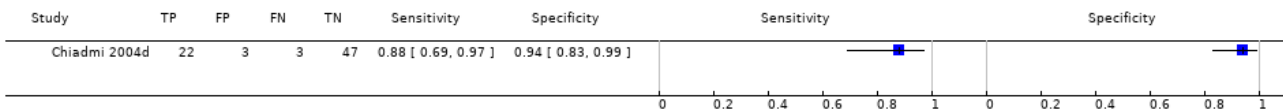
Test 31. Strep A Rapid Test Device.

Review: Rapid antigen detection test for group A streptococcus in children with pharyngitis
Test: 31 Strep A Rapid Test Device



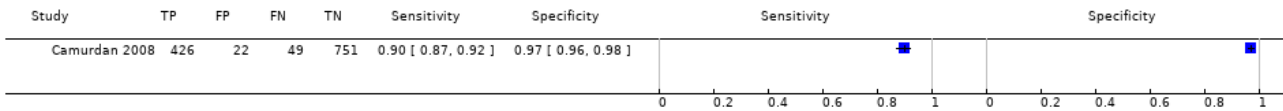
Test 32. Strep A Sign.

Review: Rapid antigen detection test for group A streptococcus in children with pharyngitis
Test: 32 Strep A Sign



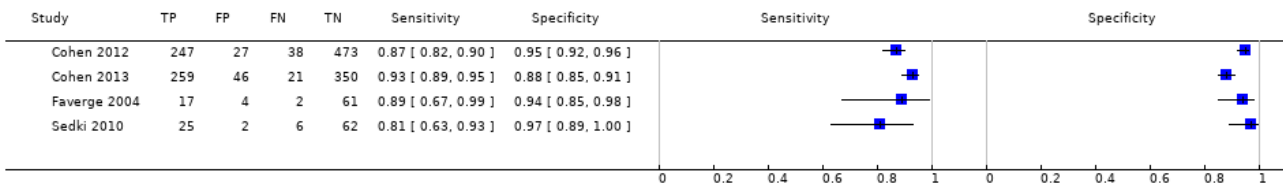
Test 33. Strep A test II (INTEX Diagnostica).

Review: Rapid antigen detection test for group A streptococcus in children with pharyngitis
Test: 33 Strep A test II (INTEX Diagnostica)



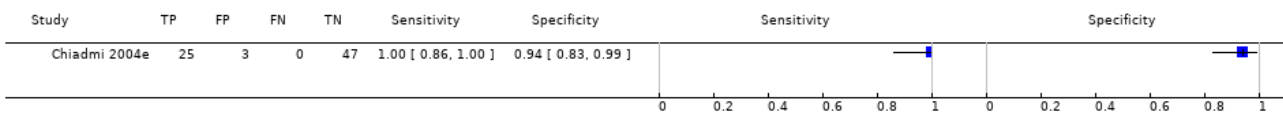
Test 34. StreptAtest (Dectrapharm).

Review: Rapid antigen detection test for group A streptococcus in children with pharyngitis
Test: 34 StreptAtest (Dectrapharm)



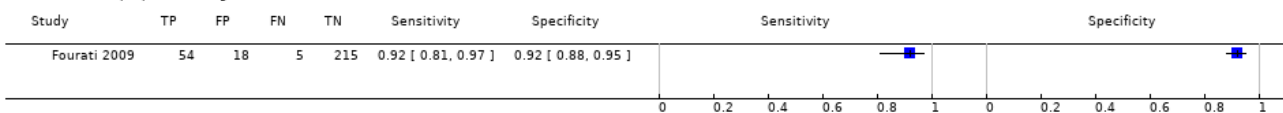
Test 35. Streptavit.

Review: Rapid antigen detection test for group A streptococcus in children with pharyngitis
Test: 35 Streptavit



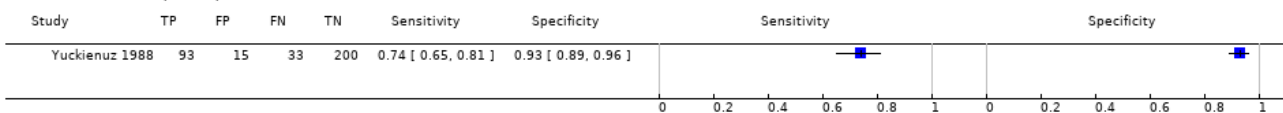
Test 36. Streptop A (ALL-Diag).

Review: Rapid antigen detection test for group A streptococcus in children with pharyngitis
Test: 36 Streptop A (ALL-Diag)



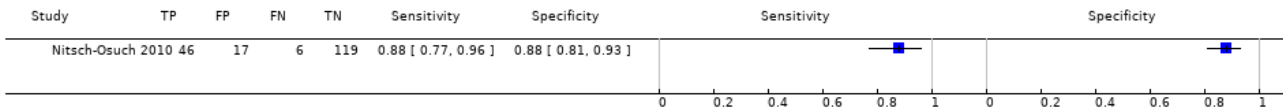
Test 37. SUDS Group A Strep.

Review: Rapid antigen detection test for group A streptococcus in children with pharyngitis
Test: 37 SUDS Group A Strep



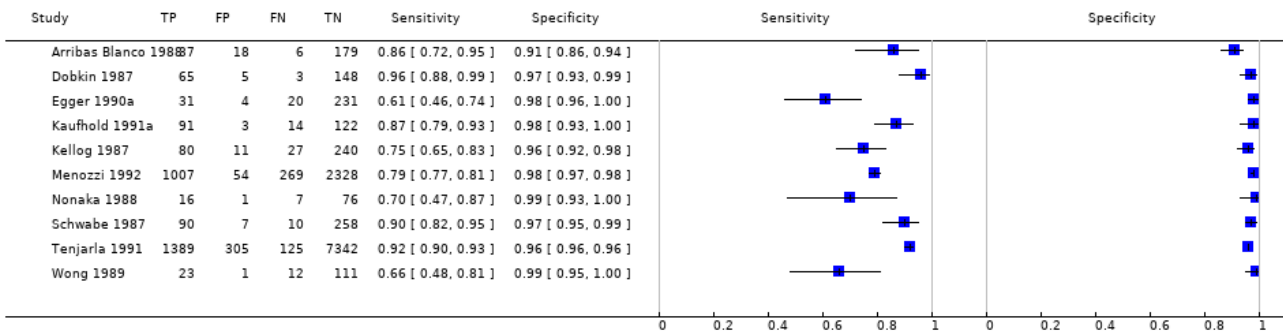
Test 38. SureScreen Test Strep A.

Review: Rapid antigen detection test for group A streptococcus in children with pharyngitis
Test: 38 SureScreen Test Strep A



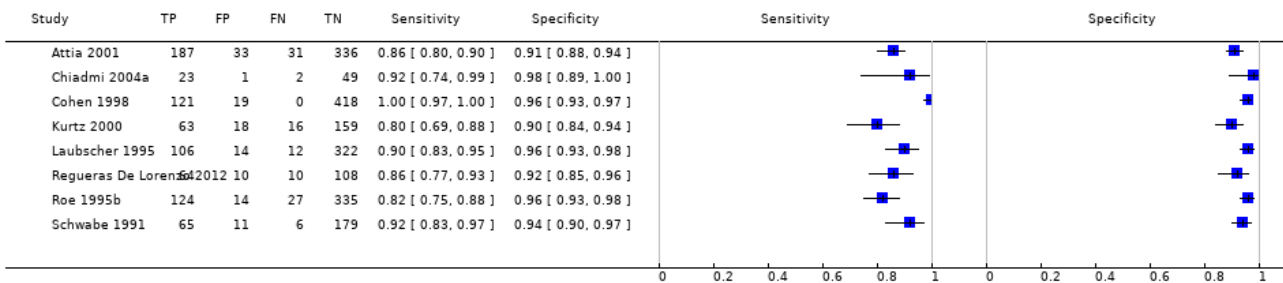
Test 39. TestPack Strep A (Abbott).

Review: Rapid antigen detection test for group A streptococcus in children with pharyngitis
Test: 39 TestPack Strep A (Abbott)



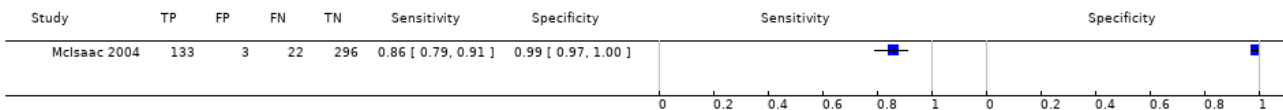
Test 40. TestPack Plus (Abbott).

Review: Rapid antigen detection test for group A streptococcus in children with pharyngitis
Test: 40 TestPack Plus (Abbott)



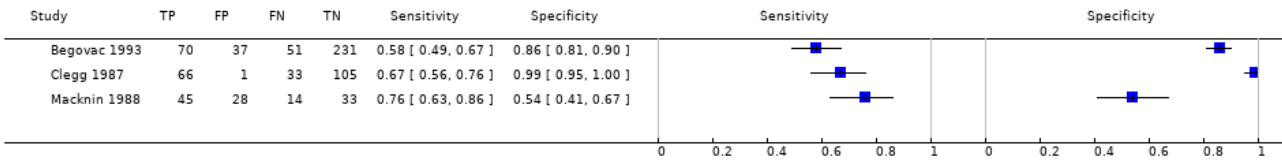
Test 41. TestPack Plus Strep A with OBC II (Abbott).

Review: Rapid antigen detection test for group A streptococcus in children with pharyngitis
Test: 41 TestPack Plus Strep A with OBC II (Abbott)



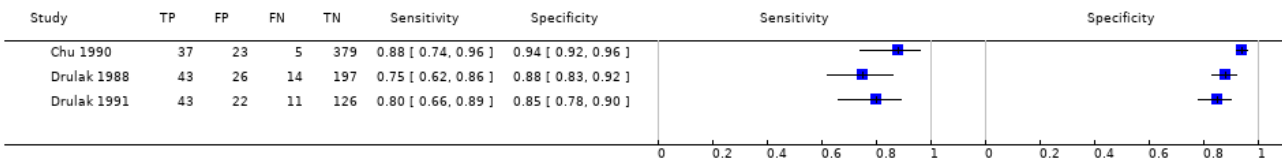
Test 42. Ventrescreen Strep A (Ventrex Lab).

Review: Rapid antigen detection test for group A streptococcus in children with pharyngitis
Test: 42 Ventrescreen Strep A (Ventrex Lab)



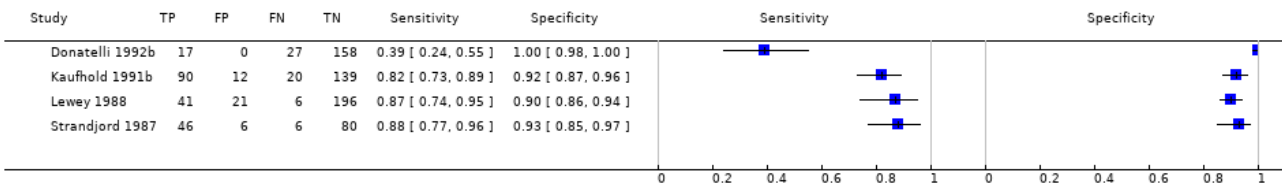
Test 43. Visuwell Strep A (ADI).

Review: Rapid antigen detection test for group A streptococcus in children with pharyngitis
Test: 43 Visuwell Strep A (ADI)



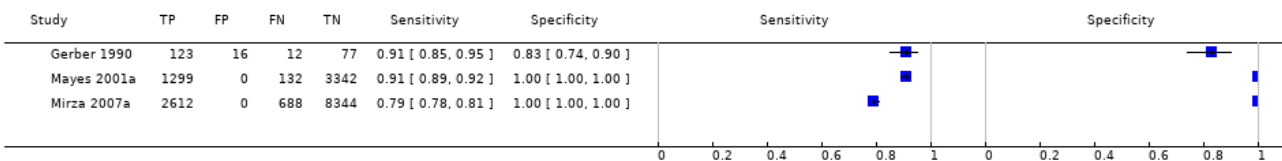
Test 44. Icon Strep A.

Review: Rapid antigen detection test for group A streptococcus in children with pharyngitis
Test: 44 Icon Strep A



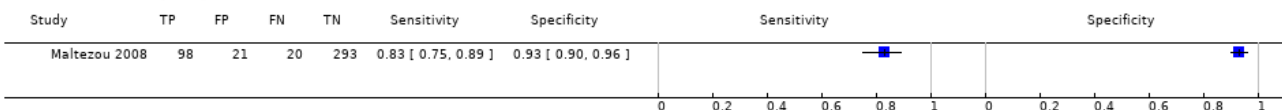
Test 45. Qtest (Becton Dickinson).

Review: Rapid antigen detection test for group A streptococcus in children with pharyngitis
Test: 45 Qtest (Becton Dickinson)



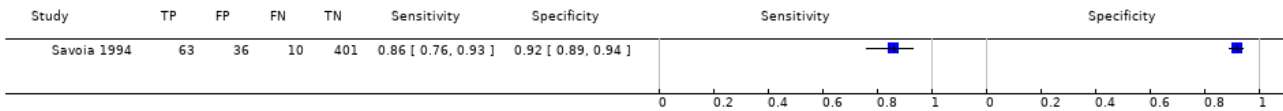
Test 46. Link 2 Strep A Rapid Test (Becton Dickinson).

Review: Rapid antigen detection test for group A streptococcus in children with pharyngitis
Test: 46 Link 2 Strep A Rapid Test (Becton Dickinson)



Test 47. Event Test Strip Strep A.

Review: Rapid antigen detection test for group A streptococcus in children with pharyngitis
Test: 47 Event Test Strip Strep A



ADDITIONAL TABLES

Table 1. Data extracted from each study

Study ID	First author, year of publication
Type of study	Journal article or conference abstract
Clinical features and settings	Presenting signs and symptoms
	Clinical selection of patients (none, clinical score, explicit criteria but not a score, implicit criteria)
	Exclusion if antibiotics use before inclusion (yes/no)
	Clinical setting (office-based, emergency department, walk-in clinic, mixed, other)
	Single- or multi-centre study
	Age range for inclusion
Participants	Sample size (n)
	Age (distribution)
	GAS prevalence according to culture (with 95% confidence interval)
	Country of study
	Sex (% of girls)
	Clinical severity assessment (Centor score, Mclsaac score, other, none)
Study design	Cross-sectional study or RCT
	Retrospective or prospective design
	Sample (consecutive, random or unclear)
	Direct comparison of different RADTs (yes/no)
	Direct comparison of several throat culture techniques (yes/no)
	Throat swab (1 single, 1 double, 2 different)
	Person performing the throat sample (physician, nurse, laboratory personnel, other)
Reference standard(s)	Throat culture medium (standard, enrichment, inhibitory)

Table 1. Data extracted from each study (Continued)

	Atmosphere of incubation (aerobic, aerobic with CO ₂ enrichment, anaerobic)
	Duration of incubation (≤ 24, 24 to 48, ≥ 48 hours)
	GAS confirmation (bacitracin disk, latex test, other, none)
	Number of plates inoculated (n)
	Assessment of GAS antibody response (yes/no)
	Relevant details
Index tests	Commercial name of the RADT
	Type of RADT (EIA, OIA)
Data	Number of true positives, false positives, true negatives, false negatives and undetermined/uninterpretable results
Notes	Source of funding (whether any of the authors is affiliated with the manufacturer of the RADT, the study was directly funded by the manufacturer, authors reported conflicts of interests related to the manufacturer or other funding sources)
	Anything else of relevance

RADT: rapid antigen detection test

EIA: enzyme immunoassay

OIA: optical immunoassay

 CO₂: carbon dioxide

Table 2. Methodological quality assessment table for each study

Domain 1: Patient selection	
Was a consecutive or random sample of patients enrolled?	Yes, No or Unclear
Was it a cross-sectional study or a RCT?	Yes, No or Unclear
Were selection criteria clearly described (at least presenting signs and symptoms and age limits for inclusion)?	Yes, No or Unclear
Were patients seen in an ambulatory care setting?	Yes, No or Unclear
Was clinical selection of patients avoided?	Yes, No or Unclear
Could the selection of patients have introduced bias?	Risk: Low, High or Unclear
Is there concern that the included patients do not match the review question?	Concern: Low, High or Unclear
Domain 2: RADT (index test)	
Were RADTs conducted during consultation time?	Yes, No or Unclear
Were the RADT results interpreted with blinding of the results of culture?	Yes, No or Unclear

Table 2. Methodological quality assessment table for each study (Continued)

Was the type of the RADT mentioned (EIA or OIA)?	Yes, No or Unclear
Could the conduct or interpretation of the RADT have introduced bias?	Risk: Low, High or Unclear
Is there concern that the RADT, its conduct or interpretation differ from the review question?	Concern: Low, High or Unclear
Domain 3: Throat culture (reference standard)	
Were culture results interpreted with blinding of the results of the RADT?	Yes, No or Unclear
Is the throat culture method likely to correctly identify GAS (laboratory culture on a blood agar plate during ≥ 48 hr)?	Yes, No or Unclear
Were the culture medium, atmosphere, duration of incubation and GAS-confirmation technique described?	Yes, No or Unclear
Could the throat culture, its conduct or its interpretation have introduced bias?	Risk: Low, High or Unclear
Is there concern that the target condition as defined by the reference standard does not match the review question?	Concern: Low, High or Unclear
Domain 4: Flow and timing	
Was the delay between the performance of the RADT and throat culture plating ≤ 48 hours?	Yes, No or Unclear
Did all patients receive a throat culture?	Yes, No or Unclear
Did patients receive the same throat culture method?	Yes, No or Unclear
Were undetermined/uninterpretable results reported?	Yes, No or Unclear
Were withdrawals from the study explained?	Yes, No or Unclear
Could the patient flow have introduced bias?	Risk: Low, High or Unclear

Table 3. Results of investigations of heterogeneity

Study-level covariate	Studies (n)	Sensitivity (95% CI)	Specificity (95% CI)	Interpretation
Test type ^a				
Enzyme immuno-assay	86	85.4 (82.7 to 87.8)	95.8 (94.8 to 96.6)	Accuracy does not seem influenced by test type (P value = 0.23)
Optical immuno-assay	19	86.2 (82.7 to 89.2)	93.7 (91.5 to 95.4)	
Throat culture				
Without enrichment broth	88	85.5 (82.8 to 87.8)	95.6 (94.8 to 96.3)	Accuracy does not seem influenced by whether an enrichment broth was used (P value = 0.15)

Table 3. Results of investigations of heterogeneity (Continued)

With enrichment broth	10	86.3 (83.3 to 88.7)	92.7 (87.9 to 95.7)	
Mean age of participants ^b				
Below the median	16	87.1 (81.7 to 91.1)	93.2 (90.5 to 95.2)	No evidence of association with age (P value = 0.39)
Above the median	13	83.7 (78.5 to 87.9)	95.0 (92.7 to 96.6)	
% of patients with Mclsaac score > 2				
≤ 70%	4	81.3 (69.8 to 89.1)	94.9 (91.1 to 97.2)	No evidence of association with clinical severity (P value = 0.35)
> 70%	8	88.8 (82.9 to 92.9)	94.2 (89.4 to 96.9)	
Prevalence of group A streptococcus ^c				
Below the median	54	84.9 (81.1 to 88.1)	95.5 (94.2 to 96.4)	Accuracy does not seem influenced by the prevalence of group A streptococcus (P value = 0.70)
Above the median	51	86.2 (83.5 to 88.5)	95.4 (94.0 to 96.5)	

^aResults based on indirect comparisons; ^bthe median of mean age was 6.6 years; ^cthe median of group A streptococcus prevalence using throat culture as the reference standard was 29.5%.

CI: confidence interval

Table 4. Results of sensitivity analyses

Concerns	Domain	Studies at low risk (n)	Sensitivity (95% CI)	Specificity (95% CI)
Risk of bias	Patient selection	25	85.7 (82.1 to 88.6)	93.0 (91.1 to 94.5)
	Index test	65	86.6 (84.0 to 88.8)	95.2 (94.1 to 96.1)
	Reference standard	20	81.0 (74.1 to 86.5)	95.5 (93.4 to 96.9)
	Flow and timing	98	85.4 (83.0 to 87.5)	95.3 (94.4 to 96.1)
	≥ 3 domains with low risk of bias	20	84.0 (79.4 to 87.8)	95.0 (93.1 to 96.4)
Applicability				
	Patient selection	41	83.1 (79.7 to 86.0)	94.9 (93.4 to 96.0)
	Index test	33	89.1 (85.7 to 91.8)	95.0 (93.2 to 96.4)
	Reference standard	60	84.9 (81.6 to 87.6)	94.7 (93.5 to 95.7)

CI: confidence interval

Table 5. Comparison between previous systematic reviews on the diagnostic accuracy of RADTs for streptococcal pharyngitis and the present one

	Ruiz-Aragon 2010 ^a	Lean 2014	Stewart 2014	Present review
Study participants	Adults and children	Adults and children	Adults and children	Children
Timeframe for searches	2000 to 2009	1996 to 2013	2000 to 2012	1980 to 2015
Number of studies included	24	60 ^b	58 ^c	105 ^b
Number of participants included	14,936	29,934	55,766	58,244
Summary estimate of sensitivity (95% CI)	85% (84 to 87)	86% (83 to 88)	84% (83 to 85) ^d	86% (83 to 88)
Summary estimate of specificity (95% CI)	96% (96 to 97)	96% (94 to 97)	95% (94 to 95) ^d	95% (95 to 96)
Investigations of heterogeneity	None performed	No evidence of significant variation in accuracy by test type (EIA versus OIA), and by age (children versus adults)	Did not identify sources of variability ^d	Did not identify sources of variability

^aIn Spanish; ^bpairs of sensitivity and specificity; ^c59 study cohorts; ^damongst high-quality studies. CI: confidence interval

APPENDICES

Appendix 1. MEDLINE (Ovid) search strategy

- 1 Pharyngitis/ (6583)
- 2 pharyngitis.tw. (3961)
- 3 Tonsillitis/ (6246)
- 4 tonsillitis.tw. (3954)
- 5 (tonsillopharyngitis or pharyngotonsillitis).tw. (515)
- 6 sore throat*.tw. (3152)
- 7 ((throat* or pharyn* or tonsil*) adj5 (infect* or inflam*)).tw. (3411)
- 8 Pharynx/mi [Microbiology] (3411)
- 9 Streptococcal Infections/ (27643)
- 10 (strep* adj5 (throat* or pharyn* or tonsil*)).tw. (2750)
- 11 ("group a" adj5 streptococc*).tw. (7943)
- 12 gabhs.tw. (333)
- 13 (beta-hemoly* or beta-haemoly*).tw. (4341)
- 14 lancefield group a.tw. (110)
- 15 Streptococcus pyogenes/ (11396)
- 16 (streptococcus pyogenes or "s. pyogenes" or "s.pyogenes").tw. (6096)
- 17 or/1-16 (54426)
- 18 Immunoassay/ (22034)
- 19 exp Immunoenzyme Techniques/ (183964)
- 20 (enzyme adj2 (immunoassay* or immuno-assay* or immunosorbent)).tw. (80381)
- 21 Immunochromatography/ (203)
- 22 immunochromatograph*.tw. (1623)
- 23 Immunosorbent Techniques/ (6331)
- 24 exp Enzyme-Linked Immunosorbent Assay/ (123418)
- 25 (elisa or elisas or eia or eias).tw. (112952)
- 26 (sandwich* adj2 assay*).tw. (1053)

- 27 (lateral flow adj2 assay).tw. (126)
 28 (optical adj2 (immunoassay* or immuno-assay*)).tw. (93)
 29 (oia or oias).tw. (127)
 30 Antigens, Bacterial/ (39874)
 31 Reagent Kits, Diagnostic/ (14838)
 32 Point-of-Care Systems/ (6609)
 33 ((rapid or "point of care" or "near patient" or poc or poct or bedside) adj5 (test or tests or testing or detect* or diagnos* or screen* or kit or kits or assay*)).tw. (57892)
 34 (radt or radts or rdt or rdts).tw. (803)
 35 (antigen* adj3 detect*).tw. (22067)
 36 test pack strep a.tw. (5)
 37 icon strep a.tw. (4)
 38 link 2 strep a rapid test.tw. (1)
 39 acceava strep a.tw. (2)
 40 osom strep a.tw. (3)
 41 poly stat strep a.tw. (0)
 42 quickvue strep a.tw. (5)
 43 or/18-42 (395969)
 44 17 and 43 (4273)
 45 limit 44 to yr="1980 -Current" (3809)
 46 exp animals/ not humans/ (3903550)
 47 45 not 46 (3194)

Appendix 2. Embase (Elsevier) search strategy

- #39 #35 NOT #382310
 #38 #37 NOT #365030292
 #37 [animals]/lim5557209
 #36 'human'/exp AND [embase]/lim9108195
 #35 #34 AND [embase]/lim AND [1-1-1980]/sd NOT [23-5-2013]/sd2579
 #34 #17 AND #332757
 #33 #18 OR #19 OR #20 OR #21 OR #22 OR #23 OR #24 OR #25 OR #26 OR #27 OR
 #28 OR #29 OR #30 OR #31 OR #32321374
 #32 'test pack strep a':ab,ti OR 'icon strep a':ab,ti OR 'link 2 strep a rapid test':ab,ti OR 'acceava strep a':ab,ti OR 'poly stat strep a':ab,ti OR
 'quickvue strep a':ab,ti OR 'osom strep a':ab,ti AND [embase]/lim11
 #31 (antigen* NEAR/3 detect*):ab,ti AND [embase]/lim19264
 #30 radt:ab,ti OR radts:ab,ti OR rdt:ab,ti OR rdts:ab,ti AND [embase]/lim972
 #29 ((rapid OR 'point of care' OR 'near patient' OR poc OR poct OR bedside) NEAR/5 (test OR tests OR testing OR detect* OR diagnos* OR
 screen* OR kit OR kits OR assay*)):ab,ti AND [embase]/lim56547
 #28 'point of care testing'/de AND [embase]/lim3626
 #27 'streptococcus group a rapid test'/de OR 'rapid test'/de OR 'elisa kit'/de AND [embase]/lim446
 #26 'bacterial antigen'/de OR 'streptococcus antigen'/de AND [embase]/lim12962
 #25 oia:ab,ti OR oias:ab,ti AND [embase]/lim112
 #24 (optical NEAR/2 (immunoassay OR 'immuno-assay')):ab,ti AND [embase]/lim76
 #23 ((sandwich* OR 'lateral flow') NEAR/2 assay*):ab,ti AND [embase]/lim1180
 #22 elisa:ab,ti OR elisas:ab,ti OR eia:ab,ti OR eias:ab,ti AND [embase]/lim124297
 #21 immunochromatograph*:ab,ti AND [embase]/lim1576
 #20 'immunoaffinity chromatography'/de AND [embase]/lim2788
 #19 (enzyme NEAR/2 (immunoassay OR 'immuno-assay' OR immunosorben*)):ab,ti AND [embase]/lim70295
 #18 'immunoassay'/de OR 'enzyme linked immunosorbent assay'/de OR 'enzyme immunoassay'/de AND [embase]/lim212276
 #17 #1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8 OR #9 OR #10 OR #11 OR
 #12 OR #13 OR #14 OR #15 OR #1655997
 #16 'streptococcus pyogenes':ab,ti OR 's. pyogenes':ab,ti OR 's.pyogenes':ab,ti AND [embase]/lim5883
 #15 'streptococcus pyogenes'/de AND [embase]/lim8434
 #14 'streptococcal pharyngitis'/de AND [embase]/lim442
 #13 'lancefield group a':ab,ti AND [embase]/lim100
 #12 (beta NEXT/1 hemoly*):ab,ti OR (beta NEXT/1 haemoly*):ab,ti AND [embase]/lim1830
 #11 gabhs:ab,ti AND [embase]/lim372
 #10 ('group a' NEAR/5 streptococc*):ab,ti AND [embase]/lim6931
 #9 (strep* NEAR/5 (throat* OR pharyn* OR tonsil*)):ab,ti AND [embase]/lim2573
 #8 'streptococcus infection'/de OR 'group a streptococcal infection'/exp AND [embase]/lim16432
 #7 ((throat* OR pharyn* OR tonsil*) NEAR/5 (infect* OR inflam*)):ab,ti AND [embase]/lim3363

#6 'sore throat'/de AND [embase]/lim8235
 #5 tonsillopharyngitis:ab,ti OR pharyngotonsillitis:ab,ti AND [embase]/lim633
 #4 tonsillit*:ab,ti AND [embase]/lim3362
 #3 'tonsillitis'/exp AND [embase]/lim7295
 #2 pharyngit*:ab,ti AND [embase]/lim4095
 #1 'pharyngitis'/exp AND [embase]/lim16213

Appendix 3. Web of Science (Thomson ISI) search strategy

# 3	1,235
# 2	253,763
# 1	26,550

Appendix 4. Trip database search strategy

(gabhs or group a streptococ* or strep throat) and (rapid test or immunoassay or radt or rapid antigen)

Appendix 5. Medion search strategy

Each term searched individually in the abstract field.

(pharyngitis, sore throat, gabhs, beta-haemolytic, beta-hemolytic, lancefield, streptococcal, streptococcus)

CONTRIBUTIONS OF AUTHORS

MC and JFC had the original idea for the review and wrote the first draft of the protocol. RC edited the protocol. JFC and NB selected studies and extracted data. JFC performed the statistical analysis. JFC and MC interpreted the results and drafted the manuscript. All authors provided critical revisions to the manuscript. The study was supervised by MC.

DECLARATIONS OF INTEREST

Jérémie F Cohen: None known.

Robert Cohen: My relevant financial activities are only in the field of vaccines.

Martin Chalumeau: No financial competing interest. Potential academic competing interest (as any expert in the field).

Nathalie Bertille: I am supported by educational grants from Laboratoires Guigoz - Société Française de Pédiatrie - Groupe de Pédiatrie Générale - Groupe de Recherches Epidémiologiques en Pédiatrie and Ecole Doctorale 393 (Sorbonne Universités, UPMC Univ Paris 06) and I have no patents, products in development or marketed products to declare.

JFC, RC and MC have been involved in studies that were included in the review.

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External sources

- Laboratoires Guigoz - Société Française de Pédiatrie - Groupe de Pédiatrie Générale - Groupe de Recherches Epidémiologiques en Pédiatrie, France.

Educational Grant to JFC (2010)

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Educational Grant to JFC (2011)

- French Ministry of Health, France.
Research grant PHRC régional AOR 12089 (2012)
- Association Française de Pédiatrie Ambulatoire, France.
Research grant to JFC (2014)

DIFFERENCES BETWEEN PROTOCOL AND REVIEW

Authors: One author (NB) contributed to the review but not to the protocol.

Search methods for identification of studies: We intended to search the Cochrane Register of Diagnostic Test Accuracy Studies but did not do so. We searched the Cochrane Central Register of Controlled Trials (CENTRAL) but this was not initially planned. In the protocol, we stated that we would search Science Citation Index for reports that cited included articles, and OpenSIGLE and OAISTER databases for grey literature; due to the number of citations returned by our search (more than 5000) and the number of included studies (n = 98), we judged that these searches were not required.

Data collection and analysis: Two review authors independently excluded studies that were not related to pharyngitis or RADT on the basis of the titles and abstracts, instead of one. We did not use ReSyWeb, an online tool, for study selection. We initially planned to extract all study-level data in duplicate; due to the number of included studies (n = 98), independent double data extraction was restricted to signalling questions used for study quality assessment and data used for statistical analysis (data from 2 x 2 tables and covariates used for investigating heterogeneity); other descriptive data were extracted by one review author (JFC). In the protocol we stated that we would not present results in groups according to commercial test name but we finally did so because we found this grouping informative for readers.

Investigation of heterogeneity and sensitivity analyses: We intended to assess the effect of the following characteristics of the reference standard: culture medium, atmosphere of incubation, duration of incubation, use of an enrichment broth before plating, group A identification technique and number of plates inoculated; to contain the risk of false positive findings we finally decided to assess the effect of only one of such parameters (i.e. whether an enrichment broth was used before plating); we took this decision before analysing the data. We intended to investigate the effect of age of participants as a 4-class categorical covariate; in almost all studies in which mean age was reported, mean age was in one of our pre-specified age categories; we finally used a median split. We intended to investigate the effect of disease severity by using the proportion of participants with a Mclsaac score greater than two as a continuous covariate; because we lack routines to investigate the effect of continuous covariates in the bivariate model in Stata, we dichotomised this variable using an arbitrary cut-off of 70%.

Sensitivity analyses: In the protocol, we intended to carry out sensitivity analyses on the following groups: studies for which patient selection was avoided, studies for which patients were excluded on the basis of antibiotics use within seven days before inclusion, studies for which GAS antibody response was used as the reference test, and studies of high quality according to QUADAS-2; we finally decided to explore only groups based on QUADAS-2, as such criteria are explicitly meant to identify studies at low risk of bias and concerns about applicability; this decision was taken before analysing the data. We had the intention to study the effect of partial verification in a sensitivity analysis, but after discussion within the review team, we decided to exclude studies with partial verification from the meta-analysis of sensitivity and specificity estimates but to include them in a separate additional meta-analysis of the negative predictive value of RADTs.

INDEX TERMS

Medical Subject Headings (MeSH)

Antigens, Bacterial [*analysis]; Immunoenzyme Techniques [*standards] [statistics & numerical data]; Pharyngitis [*microbiology]; Reference Standards; Sensitivity and Specificity; Streptococcal Infections [*diagnosis]; Streptococcus pyogenes [*immunology]

MeSH check words

Adolescent; Child; Humans