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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 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 FOR THE MAIN COMPARISON [Explanation]

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	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	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)	not be treated (TN); 32 may receive unnecessary antibiotics (FP)	not be treated (TN); 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., $\leq$ 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 $\leq$ 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 (rho). 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 McIsaac 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 McIsaac score greater than two as a categorical covariate in the model; we compared studies with less than 70% of patients with a McIsaac score greater than two to studies with more than 70% of patients with a McIsaac 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

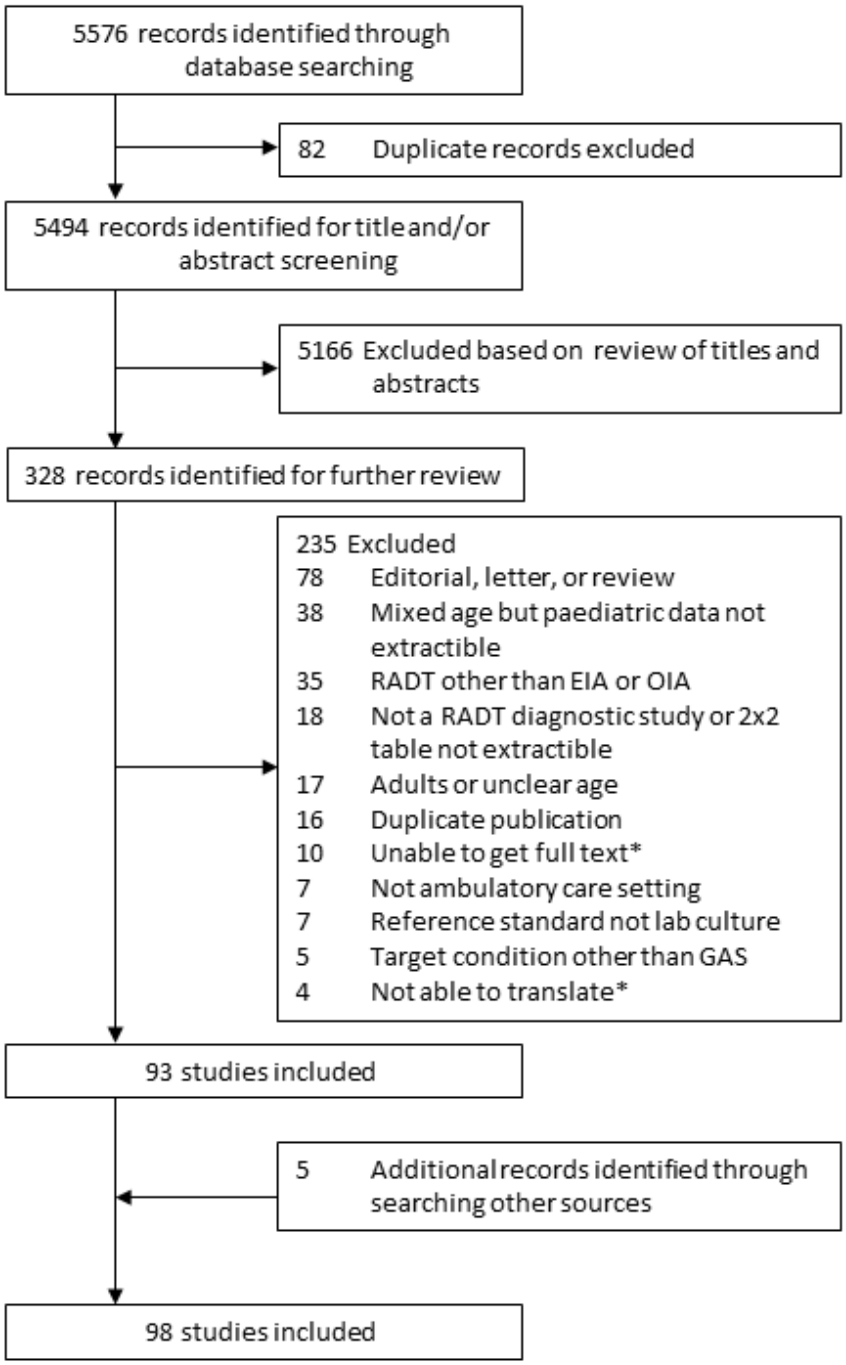
We did not try to assess reporting bias (Macaskill 2010).

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; Gieseker 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).

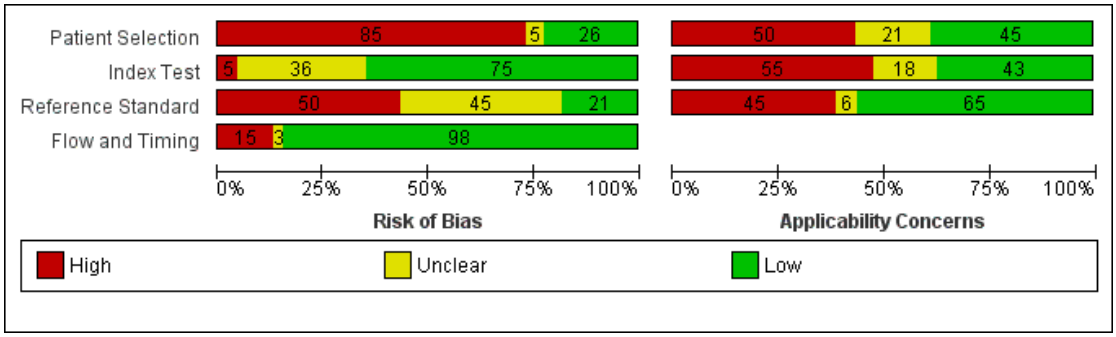
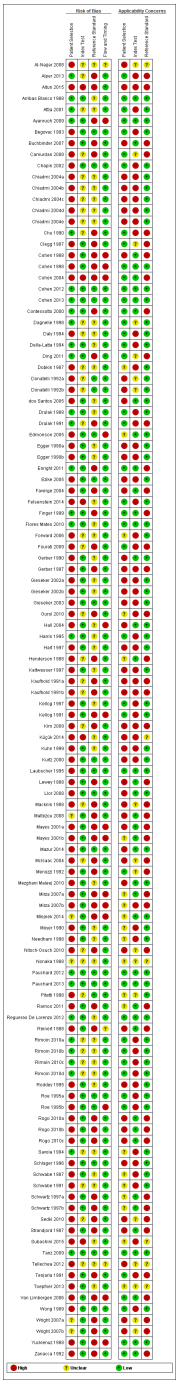


Figure 3. Risk of bias and applicability concerns summary: review authors' judgements about each domain for each included study cohort (n = 116).



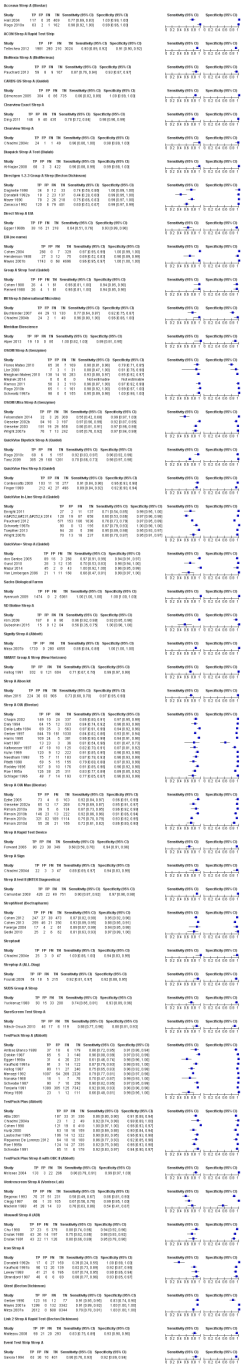
Interpretation of the results of the RADT was done with blinding of the result of throat culture in 84 of 116 cases (72%). An appropriate reference standard (i.e., laboratory throat culture on a blood agar plate during 48 hours) was used in 72 study cohorts (62%). Interpretation of the results of the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

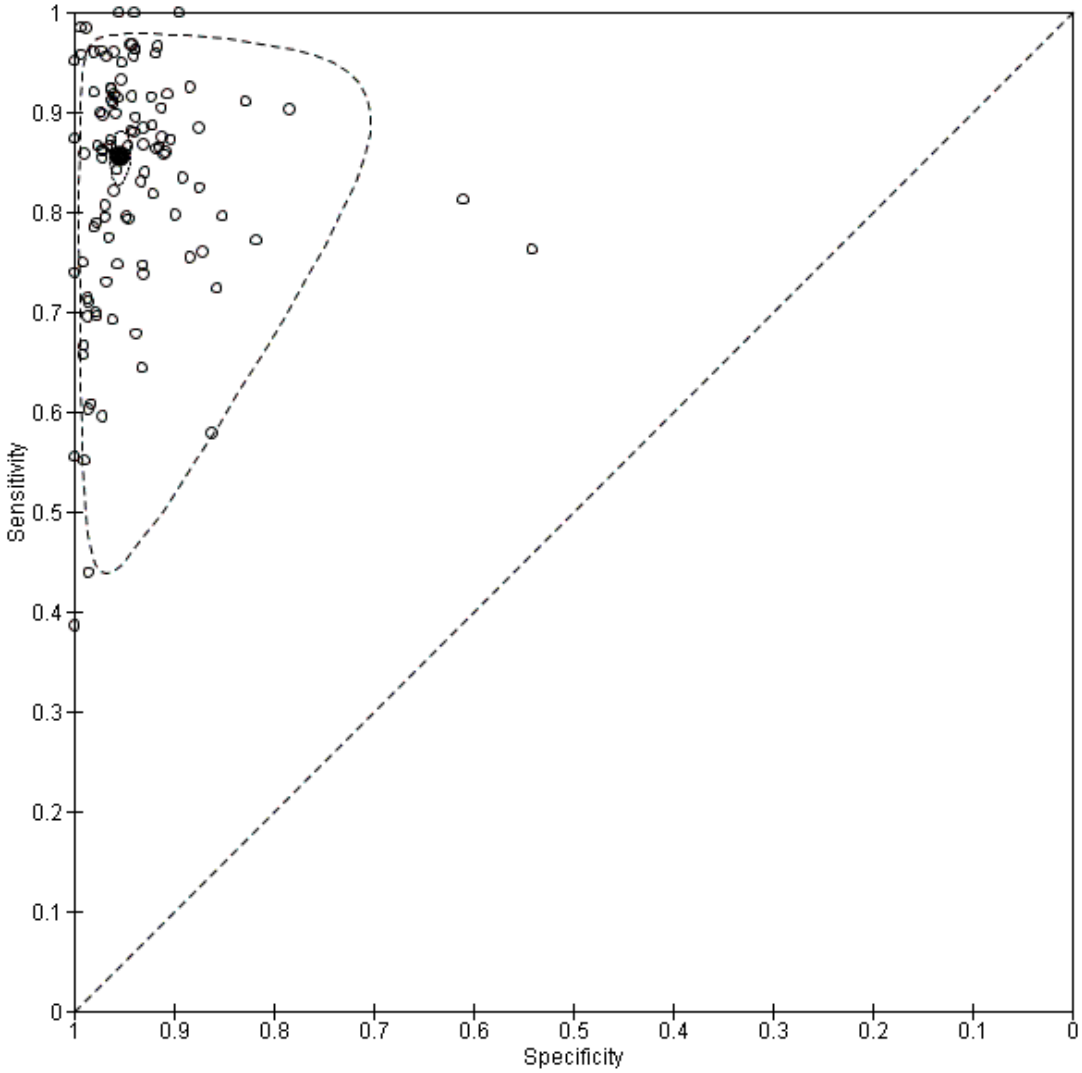
Figure 4. Forest plots of RADT sensitivity and specificity for GAS detection, ordered by commercial kit. TP = True Positive; FP = False Positive; FN = False Negative; TN = True Negative.



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).

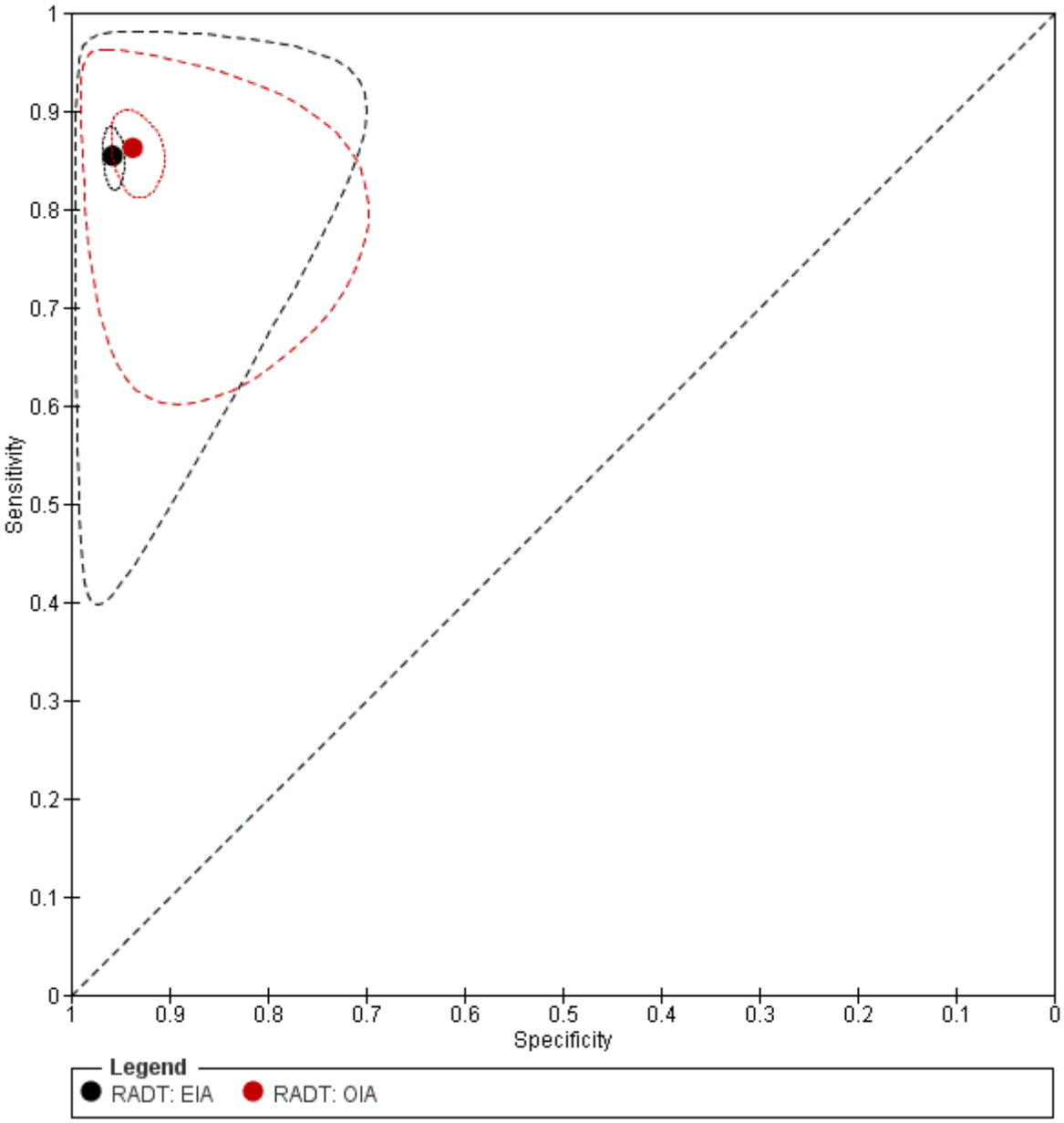
Figure 5. Summary ROC plot of RADT sensitivity and specificity for GAS detection (n = 105). Each individual study cohort is represented by an empty circle. The filled circle is the pooled summary estimate for sensitivity and specificity. The solid curve represents the 95% confidence region around the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

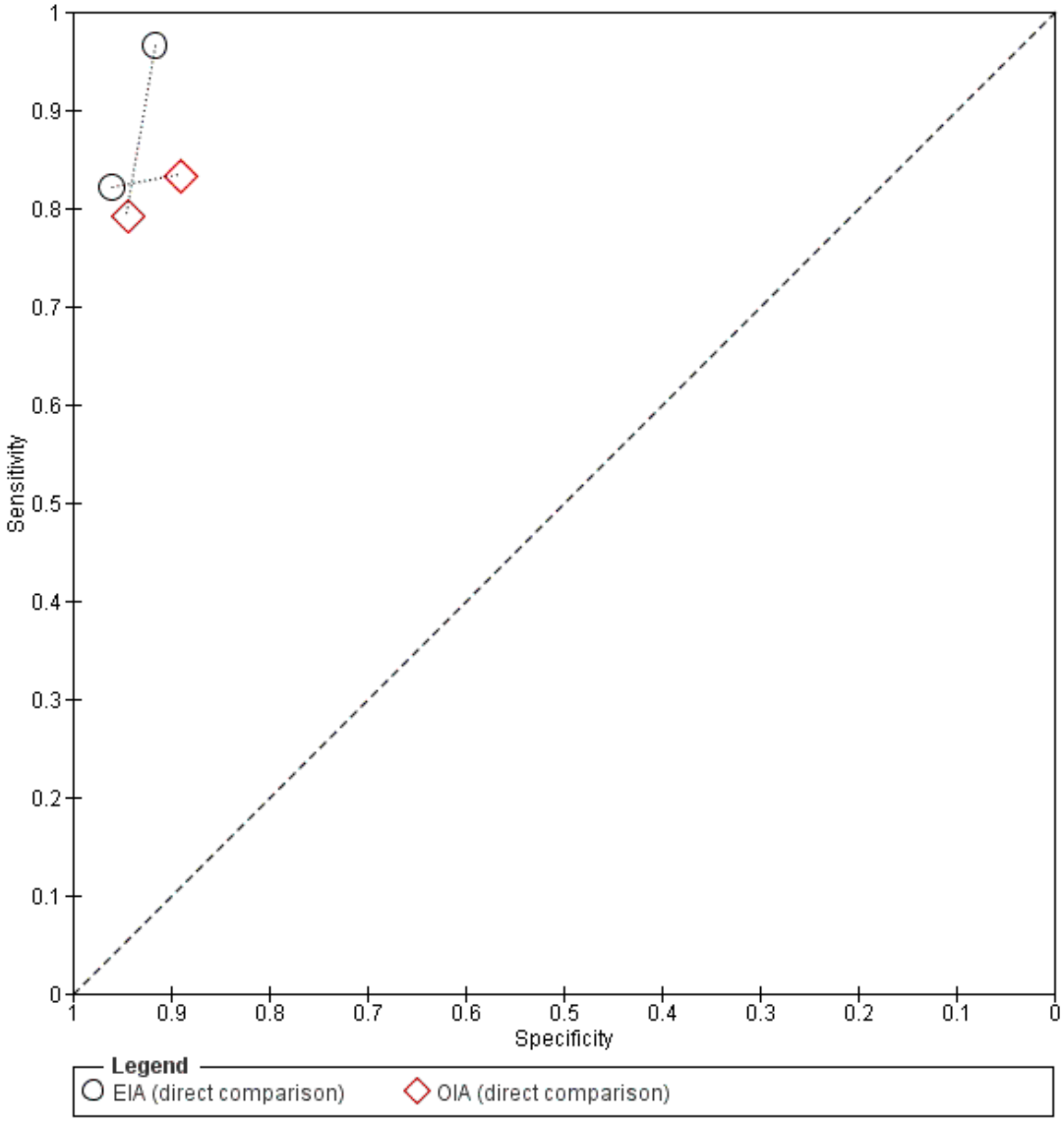
Visual inspection of the forests plots and ROC space suggested substantial heterogeneity in accuracy estimates, especially amongst estimates of sensitivity, as reflected by the wide prediction areas around summary estimates. The results of investigations of heterogeneity are summarised in Table 3.

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) (Gieseker 2002a; Roe 1995a); data were too limited to perform additional statistical analysis. In Gieseker 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 McIsaac score. The median proportion of severe patients (patients with a McIsaac 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 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
Notes	-

Al-Najjar 2008 (*Continued*)

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		

Al-Najjar 2008 (*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?	Unclear		
Were undetermined/uninterpretable results reported?	No		
Were withdrawals from the study explained?	No		
		Unclear	

Alper 2013

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 (within 3 days before inclusion) Clinical selection of patients: none Presenting signs and symptoms: patients with a chief complaint of sore throat Age range for inclusion: 7 to 15 years
Patient characteristics and setting	Sample size: 114 Age (distribution): mean (SD) = 10.0 (0.24) years GAS prevalence according to culture (with 95% confidence interval): 16.7% (95% CI not reported) Country of study: Turkey Sex (% of girls): not reported

Alper 2013 (*Continued*)

	Clinical severity assessment: Centor score Clinical setting: walk-in clinic (family practice centre) Single-centre study		
Index tests	Throat swab: unclear Commercial name of the RADT: only the name of the manufacturer was reported (Meridian Bioscience) 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: bacitracin disk 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	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**

Alper 2013 (*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)?	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		

Alper 2013 (*Continued*)

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		

Altun 2015 (*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?	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	

Arribas Blanco 1988

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 (most of the time) or nurse (sometimes) Exclusion if recent antibiotics use before inclusion: no Clinical selection of patients: none Presenting signs and symptoms: acute pharyngo-tonsillitis Age range for inclusion: < 21 years
Patient characteristics and setting	Sample size: 240 Age (distribution): not reported GAS prevalence according to culture (with 95% confidence interval): 18.9% (95% CI not reported) Country of study: Spain Sex (% of girls): not reported

Arribas Blanco 1988 (*Continued*)

	Clinical severity assessment: none Clinical setting: walk-in clinic Single-centre study		
Index tests	Throat swab: 2 different swabs 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: aerobic Duration of incubation: 48 hours GAS confirmation: bacitracin disk 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	We thank Dr JM Arribas Blanco 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?	Yes		
Were patients seen in an ambulatory care setting?	Yes		
		Low	**Low**

Arribas Blanco 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?	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	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: yes (within 5 days of enrollment) Clinical selection of patients: none Presenting signs and symptoms: patients with signs and symptoms of acute pharyngitis Age range for inclusion: 1 to 18 years
Patient characteristics and setting	Sample size: 587 Age (distribution): mean (SD) = 6.7 (3.9) years 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
Index tests	Throat swab: 2 different swabs (1 swab for culture, 1 swab for the RADT) Commercial name of the RADT: TestPack Plus (Abbott) 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	Funded by a grant from the Nemours Research Programmes

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		

Attia 2001 (*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?	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	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 Exclusion if recent antibiotics use before inclusion: yes (within 14 days of presentation) Clinical selection of patients: none Presenting signs and symptoms: patients with clinical signs of pharyngitis Age range for inclusion: 3 to 18 years
Patient characteristics and setting	Sample size: 6557 Age (distribution): not reported 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
Index tests	Throat swab: not reported Commercial name of the RADT: only the name of the manufacturer was reported (Sacks Biological Farms) 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: 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?	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		

Ayanruoh 2009 (*Continued*)

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

Begovac 1993 (*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?	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		

Begovac 1993 (*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		
		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 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")

Buchbinder 2007 (*Continued*)

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		
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 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	

Camurdan 2008 (*Continued*)

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?	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		

Camurdan 2008 (*Continued*)

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 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")

Chapin 2002 (*Continued*)

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		
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		

Chapin 2002 (*Continued*)

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

Chiadmi 2004a

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: yes (within 7 days before inclusion) Clinical selection of patients: explicit criteria but not a score (see below) Presenting signs and symptoms: signs and symptoms of pharyngitis or pharyngo-tonsillitis (fever, sore throat, inflammation of pharynx) Age range for inclusion: 8 to 14 years
Patient characteristics and setting	Sample size: 75 Age (distribution): not reported 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
Index tests	Throat swab (1 single, 1 double, 2 different): unclear Commercial name of the RADT: Test Pack Plus (Abbott) Type of RADT: EIA
Target condition and reference standard(s)	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: -

Chiadmi 2004a (*Continued*)

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**

Chiadmi 2004a (*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	

Chiadmi 2004b

Study characteristics	
Patient sampling	See Chiadmi 2004a
Patient characteristics and setting	See Chiadmi 2004a

Chiadmi 2004b (*Continued*)

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			
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**
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			
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		

Chiadmi 2004d (*Continued*)

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**
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	Yes		

signs and symptoms and age limits for inclusion)?			
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		

Chiadmi 2004e (*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	

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

Chu 1990 (*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?	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**

Chu 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)?	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

Clegg 1987 (*Continued*)

	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			
Was a consecutive or random sample of patients enrolled?	Unclear		
Was it a cross-sectional study or a RCT?	Yes		

Clegg 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?	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			

Clegg 1987 (*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	

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

Cohen 1988 (*Continued*)

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		
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		

Cohen 1988 (*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)?	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 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 7 days before inclusion) Clinical selection of patients: implicit criteria (see below) Presenting signs and symptoms: acute pharyngitis or tonsillitis with dysphagia or fever Age range for inclusion: 4 to 15 years		
Patient characteristics and setting	Sample size: 563 Age (distribution): not reported 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		
Index tests	Throat swab: 2 different (first one for the RADT, second one only if RADT+) Commercial name of the RADT: TestPack Plus Strep A (Abbott) Type of RADT: EIA		
Target condition and reference standard(s)	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: -		
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			

Cohen 1998 (*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)?	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		

Cohen 1998 (*Continued*)

		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 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: McIsaac score and Wald score Clinical setting: mixed (office-based and emergency department) Multi-centre study

Cohen 2004 (*Continued*)

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		
Was clinical selection of patients avoided?	Yes		
Were patients seen in an ambulatory care setting?	Yes		
		High	**Low**
DOMAIN 2: Index Test All tests			

Cohen 2004 (*Continued*)

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 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: McIsaac 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

Cohen 2012 (*Continued*)

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		

Cohen 2012 (*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?	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 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

Cohen 2013 (*Continued*)

	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		
Were patients seen in an ambulatory care setting?	Yes		

Cohen 2013 (*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?	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 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	-

Contessotto 2000 (*Continued*)

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)?	Yes		

Contessotto 2000 (*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	

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 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

Dagnelie 1998 (*Continued*)

	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**

Dagnelie 1998 (*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?	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		

Dagnelie 1998 (*Continued*)

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")
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

Daly 1994 (*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?	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		
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		

Daly 1994 (*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?	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

Della-Latta 1994 (*Continued*)

Patient characteristics and setting	Sample size: 690 Age (distribution): not reported 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		

Della-Latta 1994 (*Continued*)

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		

Della-Latta 1994 (*Continued*)

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% 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: -

Ding 2011 (*Continued*)

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**
DOMAIN 3: Reference Standard			

Ding 2011 (*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)?	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

Dobkin 1987 (*Continued*)

	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 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	No		

Dobkin 1987 (*Continued*)

limits for inclusion)?			
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			
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		

Dobkin 1987 (*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	

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) 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

Donatelli 1992a (*Continued*)

	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

Donatelli 1992b (*Continued*)

	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 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		

Donatelli 1992b (*Continued*)

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**
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			

Donatelli 1992b (*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	

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 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

dos Santos 2005 (*Continued*)

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		
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 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: Visuwell 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 (Visuwell, 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**
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	Yes		

Drulak 1988 (*Continued*)

technique described?			
		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 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

Drulak 1991 (*Continued*)

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**
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		

Drulak 1991 (*Continued*)

		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 diagnotic test to detect GAS 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)

Edmonson 2005 (*Continued*)

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		
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		

Edmonson 2005 (*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?	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 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

Egger 1990a (*Continued*)

	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**

Egger 1990a (*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?	No		
Did all patients receive a throat culture?	Yes		
Did patients receive the same throat culture method?	Yes		
Were undetermined/uninterpretable results reported?	Yes		

Egger 1990a (*Continued*)

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		
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		

Egger 1990b (*Continued*)

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		
Did all patients receive a throat culture?	Yes		

Egger 1990b (*Continued*)

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

Enright 2011 (*Continued*)

Flow and timing	No follow-up		
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			

Enright 2011 (*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?	Yes		
Were withdrawals from the study explained?	Yes		
		Low	

Ezike 2005

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: physician Exclusion if recent antibiotics use before inclusion: yes

Ezike 2005 (*Continued*)

	Clinical selection of patients: explicit criteria but not a score (see below) Presenting signs and symptoms: acute pharyngitis without rhinorrhoea or conjunctivitis (considered suggestive of viral infection) Age range for inclusion: 5 to 18 years
Patient characteristics and setting	Sample size: 186 (group 2) Age (distribution): mean (SD) = 9.9 (3.7) years 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
Index tests	Throat swab: 2 different swabs Commercial name of the RADT: Strep A OIA MAX Type of RADT: OIA
Target condition and reference standard(s)	Throat culture medium: enrichment 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	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			

Ezike 2005 (*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?	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

Faverge 2004 (*Continued*)

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

Felsenstein 2014

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: nurse Exclusion if recent antibiotics use before inclusion: no Clinical selection of patients: none Presenting signs and symptoms: pharyngitis, fever of unknown origin, upper respiratory tract symptoms, or subjective complaints of throat pain or discomfort on swallowing Age range for inclusion: not reported ("paediatric patients")		
Patient characteristics and setting	Sample size: 361 Age (distribution): mean (SD) = 7.4 (4.2) years 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		
Index tests	Throat swab: 2 different swabs Commercial name of the RADT: OSOM Ultra Strep A 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: -		
Flow and timing	No follow-up		
Comparative			
Type of study	Journal article		
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	Yes		

Felsenstein 2014 (*Continued*)

technique described?			
		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	

Finger 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: no Person performing the throat sample: unclear Exclusion if recent antibiotics use before inclusion: no Clinical selection of patients: none 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) Age range for inclusion: 3 to 16 years
Patient characteristics and setting	Sample size: 777 Age (distribution): not reported GAS prevalence according to culture (with 95% confidence interval): 30.8% (95% CI not reported) Country of study: Vietnam Sex (% of girls): not reported Clinical severity assessment: none Clinical setting: mixed (emergency department and outpatient clinics) Multi-centre study

Finger 1999 (*Continued*)

Index tests	Throat swab: 2 different swabs (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: not reported Duration of incubation: 48 hours GAS confirmation: bacitracin disk Number of plates inoculated: 1 Assessment of GAS antibody response: no Relevant details: during the first half of the study, the laboratory investigators read cultures with knowledge of the result of the RADT		
Flow and timing	No follow-up		
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			

Finger 1999 (*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?	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			
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		

Finger 1999 (*Continued*)

		Low	

Flores Mateo 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: physicians Exclusion if recent antibiotics use before inclusion: yes (within 15 days before enrollment) Clinical selection of patients: none Presenting signs and symptoms: sore throat for less than 5 days Age range for inclusion: 1 to 14 years
Patient characteristics and setting	Sample size: 211 Age (distribution): mean (SD) = 6.6 (3.8) years 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
Index tests	Throat swab: 2 different swabs (1 swab for the RADT, 1 swab for culture) Commercial name of the RADT: OSOM Strep A (Gemzyme) 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: 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 (in Spanish)
Notes	-
Methodological quality	

Flores Mateo 2010 (*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	

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

Forward 2006 (*Continued*)

	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: -		
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**

Forward 2006 (*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)?	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	

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	
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		

Fourati 2009 (*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?	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	

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

Gerber 1990 (*Continued*)

	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		
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**

Gerber 1990 (*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?	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	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 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 ("children")
Patient characteristics and setting	Sample size: 2113 Age (distribution): not reported 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
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 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)
Flow and timing	No follow-up
Comparative	

Gerber 1997 (*Continued*)

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?	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		

Gerber 1997 (*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		
		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	

Gieseker 2002a

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 Person performing the throat sample: unclear Exclusion if recent antibiotics use before inclusion: no Clinical selection of patients: implicit criteria ("children suspected of having S. pyogenes pharyngitis") Presenting signs and symptoms: not reported Age range for inclusion: not reported ("children")

Gieseker 2002a (*Continued*)

Patient characteristics and setting	Sample size: 302 Age (distribution): not reported 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
Index tests	Throat swab: 2 different swabs Commercial name of the RADTs: Strep A OIA Max (Biostar) Type of RADTs: OIA
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: 4 Assessment of GAS antibody response: no 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
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		
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		

Gieseker 2002a (*Continued*)

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

Gieseker 2002b

Study characteristics			
Patient sampling	See Gieseker 2002a		
Patient characteristics and setting	See Gieseker 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 Gieseker 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		
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			

Gieseker 2002b (*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	

Gieseker 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 Clinical selection of patients: implicit criteria (see below) Presenting signs and symptoms: patients suspected of having *S. pyogenes* pharyngitis Age range for inclusion: not reported
Patient characteristics and setting	Sample size: 887 Age (distribution): not reported GAS prevalence according to culture (with 95% confidence interval): 23.7% (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: OSOM Ultra Strep A Type of RADT: EIA

Gieseker 2003 (*Continued*)

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: 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		
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		
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 Exclusion if recent antibiotics use before inclusion: no Clinical selection of patients: patients for whom RADT and culture were requested Presenting signs and symptoms: not reported Age range for inclusion: not reported ("all patients", i.e., adults and children; data extractable for children 0 to 9 years of age)		
Patient characteristics and setting	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) 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		
Index tests	Throat swab: unclear 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: not reported 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	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		
Methodological quality			
Item	**Authors' judgement**	**Risk of bias**	**Applicability concerns**

Gurol 2010 (*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?	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	No		

Gurol 2010 (*Continued*)

technique described?			
		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	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 Exclusion if recent antibiotics use before inclusion: no Clinical selection of patients: implicit criteria ("all children with suspected GAS pharyngitis") Presenting signs and symptoms: unclear (see above) Age range for inclusion: 2 to 17 years
Patient characteristics and setting	Sample size: 561 Age (distribution): median age = 9 years 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		
Index tests	Throat swab: 2 different swabs (1 swab for culture, 1 swab for the RADT) Commercial name of the RADT: Acceava Strep A (Biostar) Type of RADT: EIA		
Target condition and reference standard(s)	Throat culture medium: standard (plate 1) and inhibitory (plate 2) Atmosphere of incubation: aerobic (plate 1) and aerobic with CO_2 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: -		
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**
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	

Harris 1995 (*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?	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		

Harris 1995 (*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?	Yes		
		Low	

Hart 1997

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: nurses Exclusion if recent antibiotics use before inclusion: no Clinical selection of patients: none Presenting signs and symptoms: patients presenting with pharyngitis Age range for inclusion: not reported ("adults" and "children"; data extractable for patients $\leq$ 18 years)
Patient characteristics and setting	Sample size: total sample 263, paediatric sample 75 Age (distribution): not reported 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
Index tests	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) 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 (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
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			
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		

Hart 1997 (*Continued*)

Were undetermined/uninterpretable results reported?	Yes		
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	

Henderson 1988 (*Continued*)

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 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			

Henderson 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?	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	

Kaltwasser 1997

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 (and culture versus PCR) Person performing the throat sample: other ("emergency department personnel") Exclusion if recent antibiotics use before inclusion: no

Kaltwasser 1997 (*Continued*)

	Clinical selection of patients: implicit criteria (enrollment if "the medical staff evaluating the patient determined that detection of GAS was needed") Presenting signs and symptoms: pharyngitis Age range for inclusion: not reported ("children")
Patient characteristics and setting	Sample size: 200 Age (distribution): not reported 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
Index tests	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) 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 with CO_2 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)
Flow and timing	No follow-up
Comparative	
Type of study	Journal article
Notes	The study compared the RADT to 2 types of culture and to PCR. We extracted data regarding OIA versus simple agar plating Study supported in part by an unrestricted 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)?	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			

Kaltwasser 1997 (*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?	Yes		
Were withdrawals from the study explained?	No		
		Low	

Kaufhold 1991a

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: not reported Exclusion if recent antibiotics use before inclusion: data not extracted Clinical selection of patients: none Presenting signs and symptoms: suspicion of streptococcal pharyngitis Age range for inclusion: 0 to 16 years
Patient characteristics and setting	Sample size: 230 Age (distribution): not reported 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
Index tests	Throat swab: 1 double swab Commercial name of the RADT: TestPack Strep A Type of RADT: EIA

Kaufhold 1991a (*Continued*)

Target condition and reference standard(s)	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: -		
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			
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	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 Exclusion if recent antibiotics use before inclusion: data not extracted Clinical selection of patients: none Presenting signs and symptoms: suspicion of streptococcal pharyngitis Age range for inclusion: 0 to 16 years		
Patient characteristics and setting	Sample size: 261 Age (distribution): not reported 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		
Index tests	Throat swab: 1 double swab Commercial name of the RADT: Tandem Icon Strep A Type of RADT: EIA		
Target condition and reference standard(s)	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: -		
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			

Kaufhold 1991b (*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?	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		

Kaufhold 1991b (*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?	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

Kellog 1987 (*Continued*)

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 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		

Kellog 1987 (*Continued*)

		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		
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		

Kellog 1987 (*Continued*)

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
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.

Kellog 1991 (*Continued*)

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

Kellog 1991 (*Continued*)

		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) 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			
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		

Kim 2009 (*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?	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 Age range for inclusion: 2 to 18 years
Patient characteristics and setting	Sample size: 363 throat swabs from 248 children (multiple visits allowed) Age (distribution): median 6.6 years (range 2.2 to 15.9 years) 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

Kuhn 1999 (*Continued*)

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

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**

Kuhn 1999 (*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?	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	
Patient sampling	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 Exclusion if recent antibiotics use before inclusion: yes (previous 7 days) Clinical selection of patients: explicit criteria but not a score (see below) Presenting signs and symptoms: children with clinical signs of *S. pyogenes* pharyngitis ("fever, sore throat, and/or cervical adenitis and the absence of cough, rhinorrhea, lower respiratory infection, and otitis media") Age range for inclusion: 4 to 15 years
Patient characteristics and setting	Sample size: 256 Age (distribution): not reported 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
Index tests	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) Commercial name of the RADT: Test Pack Plus (Abbott) Type of RADT: EIA
Target condition and reference standard(s)	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

Kurtz 2000 (*Continued*)

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			
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		

Kurtz 2000 (*Continued*)

		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?	Yes		
Were withdrawals from the study explained?	Yes		
		Low	

Küçük 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: yes (without precision) Clinical selection of patients: explicit criteria but not a score Presenting signs and symptoms: acute sore throat, fever and acutely inflamed throat/tonsils with or without exudates Age range for inclusion: 0 to 17 years
Patient characteristics and setting	Sample size: 892 Age (distribution): mean = 5.3 years 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
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: not reported 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	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			

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	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: yes (within the last 5 days) Clinical selection of patients: none Presenting signs and symptoms: all patients with a clinical diagnosis of pharyngitis Age range for inclusion: not reported ("pediatric patients")
Patient characteristics and setting	Sample size: 454 Age (distribution): not reported 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
Index tests	Throat swab: 2 different swabs (1 swab for culture, 1 swab for performing the RADT) Commercial name of the RADT: Test Pack Strep A Plus (Abbott) Type of RADT: EIA

Laubscher 1995 (*Continued*)

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: 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 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**
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 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	

Lewey 1988 (*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?	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 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		
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
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	-

Macknin 1988 (*Continued*)

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		

Macknin 1988 (*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?	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	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 (within the previous week) Clinical selection of patients: clinical score (Centor) 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) Age range for inclusion: 2 to 14 years
Patient characteristics and setting	Sample size: 432 Age (distribution): mean = 6.8 years (calculated from data in table 1) 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		
Index tests	Throat swab: 2 different swabs (1 swab for culture, 1 swab for performing the RADT) Commercial name of the RADT: Link 2 Strep A Rapid Test (Becton Dickinson) 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: 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		
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) 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	

Mayes 2001a (*Continued*)

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**
DOMAIN 3: Reference Standard			

Mayes 2001a (*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?	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

Mayes 2001b (*Continued*)

	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 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 Acceava (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**
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		

Mayes 2001b (*Continued*)

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 (McIsaac) Presenting signs and symptoms: clinical and epidemiological signs of acute pharyngitis suggesting GAS aetiology and McIsaac score $\geq$ 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: McIsaac score 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

Mazur 2014 (*Continued*)

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	

McIsaac 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: McIsaac score Clinical setting: walk-in clinic Single-centre study
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			
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			

McIsaac 2004 (*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	

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
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

Menozzi 1992 (*Continued*)

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		

Menozzi 1992 (*Continued*)

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		
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: McIsaac score Clinical setting: walk-in clinic Single-centre study		
Index tests	Throat swab: 2 different swabs 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			

Mezghani Maleej 2010 (*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?	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		

Mezghani Maleej 2010 (*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?	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

Mirza 2007a (*Continued*)

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

Mirza 2007a (*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?	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		

Mirza 2007a (*Continued*)

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 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

Mirza 2007b (*Continued*)

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			
Were culture results interpreted with blinding of the results of the RADT?	No		

Mirza 2007b (*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?	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
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			
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 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

Moyer 1990 (*Continued*)

	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)

Needham 1998 (*Continued*)

	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) 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		
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			

Needham 1998 (*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	

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
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		
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 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			

Nonaka 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)?	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**
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		

Nonaka 1988 (*Continued*)

		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: McIsaac score Clinical setting: emergency department Single-centre study

Pauchard 2012 (*Continued*)

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**
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: McIsaac 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

Pauchard 2013 (*Continued*)

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		

Pauchard 2013 (*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?	Yes		
Were withdrawals from the study explained?	Yes		
		Low	

Pitetti 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: not reported Exclusion if recent antibiotics use before inclusion: yes (within one week before presentation) Clinical selection of patients: explicit criteria but not a score (see below) 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 Age range for inclusion: 1 to 18 years
Patient characteristics and setting	Sample size: 233 Age (distribution): mean = 8.6 years (range 1.5 to 18.9 years) GAS prevalence according to culture (with 95% confidence interval): 31.3% (95% CI not reported)

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		

Pitetti 1998 (*Continued*)

		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		
		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		

Pitetti 1998 (*Continued*)

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 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

Ramos 2011 (*Continued*)

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		
		Low	**Low**
DOMAIN 3: Reference Standard			
Were culture results interpreted with blinding of the results of the RADT?	Unclear		

Ramos 2011 (*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	

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 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**
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 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	

Reinert 1988 (*Continued*)

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

Reinert 1988 (*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?	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	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: yes (oral use in the 3 days prior to screening or parenteral use in the 28 days before screening) Clinical selection of patients: none Presenting signs and symptoms: sore throat Age range for inclusion: 2 to 12 years

Rimoin 2010a (*Continued*)

Patient characteristics and setting	Sample size: 184 Age (distribution): mean (SD) = 5.8 (0.21) years 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 Multi-centre study (see Rimoin 2010b-d)
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**
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		

Rimoin 2010a (*Continued*)

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		
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 2010b (*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	

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	

Rimoin 2010c (*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?	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		

Rimoin 2010c (*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?	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
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			

Rimoin 2010d (*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	

Roddey 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: yes (standard versus enriched culture) Person performing the throat sample: unclear Exclusion if recent antibiotics use before inclusion: yes (during the precedent week)

	Clinical selection of patients: none Presenting signs and symptoms: acute pharyngitis Age range for inclusion: not reported
Patient characteristics and setting	Sample size: 301 Age (distribution): not reported 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
Index tests	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 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 (data extracted only for standard culture) Atmosphere of incubation: aerobic 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	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		
		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

Roe 1995a (*Continued*)

Target condition and reference standard(s)	Throat culture medium: inhibitory and enrichment Atmosphere of incubation: aerobic Duration of incubation: 48 hours 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 re-	Yes		

sults of culture?			
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		
		Low	

Roe 1995b

Study characteristics			
Patient sampling	See Roe 1995a		
Patient characteristics and setting	See Roe 1995a		
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		
Target condition and reference standard(s)	See Roe 1995a		
Flow and timing	No follow-up		
Comparative			
Type of study	Journal article		
Notes	See Roe 1995a		
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		
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		

Roe 1995b (*Continued*)

		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	

Rogo 2010a (*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	**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		

Rogo 2010a (*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	

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	

Rogo 2010b (*Continued*)

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

Rogo 2010b (*Continued*)

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

Rogo 2010c (*Continued*)

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		

Rogo 2010c (*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)?	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

Savoia 1994 (*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: 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			

Savoia 1994 (*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	

Schlager 1996

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: 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

Schlager 1996 (*Continued*)

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		
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		

Schlager 1996 (*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?	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 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	Sample size: 365 Age (distribution): not reported 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		
Index tests	Throat swab: 1 single swab (used for culture and then for the RADT) 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: anaerobic for the first 24 hours and then aerobic with CO_2 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: -		
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**

Schwabe 1987 (*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?	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	Yes		

Schwabe 1987 (*Continued*)

technique described?			
		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 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)

Schwabe 1991 (*Continued*)

	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**
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**

Schwabe 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)?	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		

Schwabe 1991 (*Continued*)

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	-

Schwartz 1997a (*Continued*)

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 1997a (*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	

Schwartz 1997b

Study characteristics	
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	

Schwartz 1997b (*Continued*)

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		

Schwartz 1997b (*Continued*)

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	

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

Sedki 2010 (*Continued*)

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
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		
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		

Sedki 2010 (*Continued*)

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
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	

Strandjord 1987 (*Continued*)

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		

Strandjord 1987 (*Continued*)

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	

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")

Subashini 2015 (*Continued*)

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 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			
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		

Subashini 2015 (*Continued*)

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

Tanz 2009

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 (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: pharyngitis Age range for inclusion: 3 to 18 years
Patient characteristics and setting	Sample size: 1848 Age (distribution): 13% under 5 years of age (mean or median not reported) 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: McIsaac score Clinical setting: office-based Multi-centre study
Index tests	Throat swab: 2 different swabs (swab A used first for office culture and then for performing the RADT; swab B used for laboratory culture) Commercial name of the RADT: QuickVue dipstick (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: latex agglutination Number of plates inoculated: 1 Assessment of GAS antibody response: no 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			

Tanz 2009 (*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?	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?	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 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			
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		

Tellechea 2012 (*Continued*)

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 *S. pyogenes*

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			

Tenjarla 1991 (*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?	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	

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

Toepfner 2013 (*Continued*)

	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
Comparative	
Type of study	Journal article
Notes	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 We thank Dr. M Hufnagel for confirming that numbers in the published contingency table are from paediatric patients

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		
Were the culture medium, atmosphere, duration of incubation and GAS-confirmation technique described?	No		
		Unclear	**Unclear**
DOMAIN 4: Flow and Timing			

Toepfner 2013 (*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	

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) 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		
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?	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 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			

Wong 1989 (*Continued*)

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

Wong 1989 (*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?	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

Wright 2007a (*Continued*)

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		
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			

Wright 2007a (*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?	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	

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		
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		

Wright 2007b (*Continued*)

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

Yuckienuz 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: 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)

Yuckienuz 1988 (*Continued*)

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			
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			

Yuckienuz 1988 (*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?	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

Zanacca 1992 (*Continued*)

	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**
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

(*Continued*)

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
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

(*Continued*)

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
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

(*Continued*)

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
Gerber 1990a	RADT other than EIA or OIA
Gerber 1997a	Editorial, letter or review
Gerber 1997b	Editorial, letter or review

(*Continued*)

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

(*Continued*)

Holbrook 1998	Editorial, letter or review
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

(*Continued*)

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
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

(*Continued*)

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
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

(*Continued*)

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
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

(*Continued*)

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
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	-

Herranz 2007 (*Continued*)

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	-

Mirjat 2012b (*Continued*)

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	-
Notes	Unable to obtain full text

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)	-
Flow and timing	-
Comparative	-
Notes	In Turkish

Sramek 1992

Study characteristics	
Patient sampling	-
Patient characteristics and setting	-

Sramek 1992 (*Continued*)

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	-
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.

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
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 Bioline 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
46 Link 2 Strep A Rapid Test (Becton Dickinson)	1	432
47 Event Test Strip Strep A	1	510

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, McIsaac score, other, none)

Table 1. Data extracted from each study (*Continued*)

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)
	Atmosphere of incubation (aerobic, aerobic with CO_2 enrichment, anaerobic)
	Duration of incubation ($\leq$ 24, 24 to 48, $\geq$ 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
CO_2: 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
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 $\geq$ 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**

Table 2. Methodological quality assessment table for each study (*Continued*)

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 immunoassay	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 immunoassay	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)
	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 McIsaac score > 2					

Table 3. Results of investigations of heterogeneity (*Continued*)

	≤ 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)	

[a] Results based on indirect comparisons; [b] the median of mean age was 6.6 years; [c] the 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

[a] In Spanish; [b] pairs of sensitivity and specificity; [c] 59 study cohorts; [d] amongst high-quality studies.
CI: confidence interval

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.

SOURCES OF SUPPORT

Internal sources

- No sources of support supplied

External sources

- Laboratoires Guigoz - Société Française de Pédiatrie - Groupe de Pédiatrie Générale - Groupe de Recherches Epidémiologiques en Pédiatrie, France.

Educational Grant to JFC (2010)

- Agence Régionale de Santé d'Ile-de-France, France.

Educational Grant to JFC (2011)

- French Ministry of Health, France.

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- 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 McIsaac 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