Accuracy and Precision of the Signs and Symptoms of Streptococcal Pharyngitis in Children: A Systematic Review

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Objective To conduct a systematic review to determine whether clinical findings can be used to rule in or to rule out streptococcal pharyngitis in children.

Study design Two authors independently searched MEDLINE and EMBASE. We included articles if they contained data on the accuracy of symptoms or signs of streptococcal pharyngitis, individually or combined into prediction rules, in children 3-18 years of age.

Results Thirty-eight articles with data on individual symptoms and signs and 15 articles with data on prediction rules met all inclusion criteria. In children with sore throat, the presence of a scarlatiniform rash (likelihood ratio [LR], 3.91; 95% CI, 2.00-7.62), palatal petechiae (LR, 2.69; CI, 1.92-3.77), pharyngeal exudates (LR, 1.85; CI, 1.58-2.16), vomiting (LR, 1.79; CI, 1.58-2.16), and tender cervical nodes (LR, 1.72; CI, 1.54-1.93) were moderately useful in identifying those with streptococcal pharyngitis. Nevertheless, no individual symptoms or signs were effective in ruling in or ruling out streptococcal pharyngitis.

Conclusions Symptoms and signs, either individually or combined into prediction rules, cannot be used to definitively diagnose or rule out streptococcal pharyngitis. (J Pediatr 2012;160:487-93).

Pharyngitis accounts for 6%-8% of visits by children to family medicine physicians and pediatricians.1 Accurate diagnosis of children with streptococcal pharyngitis is important because untreated group A Streptococcal (GAS) pharyngitis can lead to supplicative (eg, peritonsillar abscess, retropharyngeal abscess, lymphadenitis) and nonsuppurative (eg, acute rheumatic fever) complications. A rapid test that uses antibodies to detect GAS specific carbohydrates is widely available (sensitivity, 0.85; CI, 0.84-0.87; specificity, 0.96; CI, 0.96-0.97).2 Nevertheless, indiscriminant testing of all children with sore throat will lead to antimicrobial overuse; apart from increased cost and additional discomfort, this approach is likely to result in overtreatment of carriers of GAS (defined as individuals with positive throat cultures for GAS but without an immunologic response to GAS). Accordingly, the question of whether clinical findings can be used to accurately identify high-risk children who can be treated empirically, or to identify low-risk children who could be managed without additional testing, is an important one.

Guidelines on the diagnosis of children with streptococcal pharyngitis differ in their recommendations regarding the need for microbiologic testing.3 Even though most guidelines suggest that clinical diagnosis is unreliable (and thus recommend microbiologic testing for all suspected children),4-6 other guidelines recommend using the presence or absence of key symptoms and signs to guide clinical decision making.7,8 Thus, we systematically reviewed the pediatric literature to determine whether symptoms or signs, individually or in combination, can be used to identify children who need to be tested for streptococcal pharyngitis.

Methods

We searched the medical literature to determine the accuracy of clinical examination in children suspected of having streptococcal pharyngitis. We searched MEDLINE and EMBASE for articles published in 1950 through April 2011 and 1966 through April 2011, respectively. Search terms included sore throat, pharyngitis, tonsillitis, tonsillopharyngitis, strep throat, streptococcus pyogenes, sensitivity, specificity, clinical, symptom, exam, criteria, tests, petechiae, tonsillar exudate, cervical adenopathy, fever, pharyngeal erythema, tonsillar enlargement, symptoms, signs, physical examination, and medical history taking (Appendix 1; available at www.jpeds.com). This computerized search was supplemented with a manual review of bibliographies of all articles meeting inclusion criteria. Two authors independently screened the titles and abstracts (when available) of the search results. Articles that could contain data regarding symptoms and signs of streptococcal pharyngitis were retrieved. Two authors independently reviewed, rated, and abstracted data from each article.

We applied explicit a priori inclusion and exclusion criteria. We included articles in our review if they contained original data on the accuracy of history and/or physical examination findings in the diagnosis of streptococcal pharyngitis.

GAS Group A Streptococcal
LR Likelihood ratio

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Studies of children 3-18 years of age coming to medical attention for evaluation of sore throat or pharyngitis, in which the diagnosis was made using a throat culture, were considered for inclusion. Articles in which rapid antigen testing was used for diagnosis were included only if the specimens that were negative on the rapid test were sent for culture confirmation. We limited our search to articles written in English, French, German, Italian, and Spanish. We excluded articles that evaluated both adults and children unless separate results were reported for children. Because streptococcal pharyngitis is most prevalent in school-aged children, and because only limited data on symptoms can be obtained from preverbal children, if data for separate age groups were presented in the article, we chose the age group closest to 3-18 years of age. Studies with insufficient data to calculate likelihood ratios (LRs) were excluded.

We present data on a particular finding if data on that finding was reported in 2 or more studies. Because univariate tests for heterogeneity such as the I² statistic do not account for heterogeneity explained by differences in threshold between studies (eg, differences in how erythema was defined), we judged heterogeneity by examining the Galbraith plots for the diagnostic OR for each finding. If more than one-third of the studies fell outside the 95% CI of the Galbraith plot, we compared the results with and without these studies included. Random effects models (bivariate model if ≥4 studies, Dersimonian and Laird if <4 studies) were used to calculate the CIs for the pooled estimate. Stata 10 was used for all analyses (Stata Corp, College Station, Texas). To facilitate interpretation of results, we considered a test useful in ruling in disease if it increased the probability of streptococcal pharyngitis to at least 85% (ie, the finding performed almost as well as the rapid strep test which increases the probability of pharyngitis to 92%). Assuming that the prevalence of GAS pharyngitis among children presenting with sore throat is 37%9, a finding with a positive LR of 9.6 would be required to increase the probability of streptococcal pharyngitis to this level. Similarly, to decrease the probability of streptococcal infection to 12% (prevalence of GAS carriage among asymptomatic children),9 a finding with a negative LR of 0.25 would be needed.

Because no validated tools have been developed specifically to assess the quality of clinical examination studies, we used a modified version of the Quality Assessment of Diagnostic Accuracy Studies (QUADAS) tool.10 Of the 14 items in the QUADAS tool, only 4 were relevant to the studies being assessed. To these 4 questions, we added 3 questions that we thought could impact the results: (1) Were children receiving or recently receiving antibiotics excluded? (2) Were the data collected prospectively?; and (3) Was this a case-control study? (Appendix 2, available at www.jpeds.com.) A total quality score was not calculated. Rather, we assessed each of the study quality indicators separately.11 We explored whether the conclusions would have changed by limiting the analysis to: (1) studies in which streptococci were verified as belonging to group A using bacitracin sensitivity or latex agglutination; or (2) studies in which children had not recently received antibiotics.

We also conducted a separate search for articles on the precision of symptoms and signs of streptococcal pharyngitis in MEDLINE by using the terms pharyngitis, reproducibility of results, observer variation, kappa, and agreement (Appendix 1). Finally, using a MEDLINE filter developed by Wong,12 we conducted an electronic literature search to identify articles with data on the accuracy of prediction rules in children with sore throat (Appendix 1). Only validated rules (ie, a rule derived and validated in independent samples) were considered. Multilevel LRs were calculated when stratum-specific data were available.13

## Results

From 2334 articles identified through our search strategy, 313 could not be excluded based on the title or abstract (Figure). We retrieved and reviewed the full text of these articles. Thirty-four articles, that included 24,418 children, met all inclusion criteria (Table 1). The pooled prevalence of streptococcal pharyngitis in the included studies was 33.8% (CI, 30.4%-37.2%). The studies were published between 1953-2010 and most (n = 24) were conducted in the United States or Europe. One large study (n = 1219) included patients up to 24 years of age.14 However, because the study was conducted in a pediatric practice and because only a handful of patients were over 18 years of age, we retained this study. Several studies included children <3 years of age. Because the prevalence of streptococcal pharyngitis in children <3 years is low, we retained these studies.
Quality of the Included Studies

We included 2 case-control studies, 3 retrospective studies, and 4 studies in which patients with milder or more severe disease than commonly encountered in primary care were enrolled (Table II; available at www.jpeds.com). In 6 of the studies included, streptococci were not specifically identified as group A. We found evidence for partial or differential verification bias only infrequently. A total of 20 studies included children who had received antibiotics recently.

Diagnostic Accuracy of Individual Symptoms and Signs

Individual findings were not particularly useful in either ruling in or ruling out streptococcal pharyngitis (Table III). Five findings increased the probability of streptococcal pharyngitis to >50% and can thus be regarded as useful but not diagnostic. These included scarlatiniform rash (LR, 3.91; CI, 2.00-7.62), palatal petechiae (LR, 2.69; 1.92-3.77), pharyngeal exudate (LR, 1.85; CI, 1.58-2.16), vomiting (LR, 1.79; CI, 1.58-2.16), and tender cervical nodes (LR, 1.72; CI, 1.54-1.93).

Heterogeneity

There was significant heterogeneity with regard to the following 7 signs and symptoms: abdominal pain, dysphagia, lack of cough, tonsillar exudates, tonsillar and/or pharyngeal exudates, headache, and red tonsils and/or pharynx. Excluding studies that were outliers for these 7 findings did not significantly change any of the results. The results that follow represent the pooled values with all the studies included (ie, without excluding the outliers).

Sensitivity Analysis

Limiting the analysis to studies in which streptococci were specifically identified as belonging to group A using bacitracin sensitivity or latex agglutination testing did not change the conclusions. Neither did excluding case-control studies or studies in which the spectrum of children enrolled was not representative alter the results significantly. Results also were similar qualitatively when the analysis was restricted to studies that excluded children who were receiving, or who had recently received, antibiotics.

Diagnostic Accuracy of Combinations of Symptoms and Signs

There were limited data on accuracy of combinations of symptoms and signs; only 2 combinations were reported by more than 1 study. The combination of exudate plus large and tender cervical nodes had a pooled positive and negative LR of 2.52 (CI, 1.19-5.36) and 0.92 (CI, 0.87-0.96), respectively.

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Table I. Characteristics of studies with data on the accuracy of signs and symptoms of streptococcal pharyngitis

<table>
<thead>
<tr>
<th>Source, year</th>
<th>Age range or mean age, y</th>
<th>No. of patients</th>
<th>Setting</th>
<th>Country</th>
<th>Prevalence of GAS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Breese et al, 1953</td>
<td>&lt;16</td>
<td>1199</td>
<td>Clinic</td>
<td>US</td>
<td>0.45</td>
</tr>
<tr>
<td>Siegel et al, 1961</td>
<td>3-16</td>
<td>2545</td>
<td>Clinic</td>
<td>US</td>
<td>0.41</td>
</tr>
<tr>
<td>Stillerman et al, 1960</td>
<td>Children</td>
<td>1141</td>
<td>Clinic</td>
<td>US</td>
<td>0.36</td>
</tr>
<tr>
<td>Dyment et al, 1968</td>
<td>Children</td>
<td>1307</td>
<td>Clinic</td>
<td>US</td>
<td>0.30</td>
</tr>
<tr>
<td>Randolph et al, 1970</td>
<td>1-16</td>
<td>430</td>
<td>Clinic</td>
<td>US</td>
<td>0.41</td>
</tr>
<tr>
<td>Kaplan et al, 1971</td>
<td>&lt;15</td>
<td>624</td>
<td>ED</td>
<td>US</td>
<td>0.35</td>
</tr>
<tr>
<td>Margelith et al, 1971</td>
<td>2-15</td>
<td>82</td>
<td>Clinic</td>
<td>US</td>
<td>0.71</td>
</tr>
<tr>
<td>Ross et al, 1971</td>
<td>3-15</td>
<td>525</td>
<td>Clinic</td>
<td>England</td>
<td>0.37</td>
</tr>
<tr>
<td>Rowe et al, 1977</td>
<td>2-16</td>
<td>2158</td>
<td>Clinic</td>
<td>US</td>
<td>0.21</td>
</tr>
<tr>
<td>Egenberger et al, 1980</td>
<td>&gt;1</td>
<td>1116</td>
<td>Clinic</td>
<td>Switzerland</td>
<td>0.30</td>
</tr>
<tr>
<td>Schwartz et al, 1982</td>
<td>Adolescents</td>
<td>119</td>
<td>Clinic</td>
<td>US</td>
<td>0.22</td>
</tr>
<tr>
<td>Fujikawa et al, 1983</td>
<td>Children</td>
<td>271</td>
<td>ED</td>
<td>Japan</td>
<td>0.40</td>
</tr>
<tr>
<td>Reed et al, 1988</td>
<td>2-12</td>
<td>242</td>
<td>Clinic</td>
<td>US</td>
<td>*</td>
</tr>
<tr>
<td>Uncetta et al, 1988</td>
<td>0.3-14</td>
<td>662</td>
<td>Clinic</td>
<td>Spain</td>
<td>0.24</td>
</tr>
<tr>
<td>Principi et al, 1990</td>
<td>0.4-14</td>
<td>865</td>
<td>Clinic</td>
<td>Italy</td>
<td>0.27</td>
</tr>
<tr>
<td>Cohen et al, 1994</td>
<td>3-16</td>
<td>307</td>
<td>Clinic</td>
<td>France</td>
<td>0.37</td>
</tr>
<tr>
<td>Edmond et al, 1996</td>
<td>&lt;18</td>
<td>271</td>
<td>ED</td>
<td>Australia</td>
<td>*</td>
</tr>
<tr>
<td>Grimpel et al, 1996</td>
<td>2-16</td>
<td>190</td>
<td>ED</td>
<td>France</td>
<td>0.27</td>
</tr>
<tr>
<td>Altia et al, 1999</td>
<td>0.5-18</td>
<td>297</td>
<td>ED</td>
<td>US</td>
<td>0.29</td>
</tr>
<tr>
<td>De Silva et al, 1998</td>
<td>3-12</td>
<td>137</td>
<td>Clinic</td>
<td>Sri Lanka</td>
<td>0.45</td>
</tr>
<tr>
<td>Schwartz et al, 1998</td>
<td>1-18</td>
<td>192</td>
<td>Clinic</td>
<td>US</td>
<td>0.69</td>
</tr>
<tr>
<td>Ulukol et al, 2000</td>
<td>1-15</td>
<td>514</td>
<td>Clinic</td>
<td>Turkey</td>
<td>0.31</td>
</tr>
<tr>
<td>Bassili et al, 2002</td>
<td>1-15</td>
<td>578</td>
<td>Clinic</td>
<td>Egypt</td>
<td>0.17</td>
</tr>
<tr>
<td>Gieseker et al, 2003</td>
<td>Children</td>
<td>887</td>
<td>Clinic</td>
<td>US</td>
<td>0.24</td>
</tr>
<tr>
<td>Hossain et al, 2003</td>
<td>3-15</td>
<td>300</td>
<td>Clinic</td>
<td>Finland</td>
<td>*</td>
</tr>
<tr>
<td>Lin et al, 2003</td>
<td>1-15</td>
<td>1175</td>
<td>Clinic</td>
<td>Taiwan</td>
<td>0.21</td>
</tr>
<tr>
<td>Sahin et al, 2003</td>
<td>&lt;17</td>
<td>243</td>
<td>Clinic</td>
<td>Turkey</td>
<td>0.27</td>
</tr>
<tr>
<td>Hall et al, 2004</td>
<td>2-17</td>
<td>561</td>
<td>ED</td>
<td>US</td>
<td>0.27</td>
</tr>
<tr>
<td>Dos Santos et al, 2005</td>
<td>2-13</td>
<td>376</td>
<td>ED</td>
<td>Brazil</td>
<td>0.24</td>
</tr>
<tr>
<td>Edmonson et al, 2004</td>
<td>&lt;24</td>
<td>1219</td>
<td>Clinic</td>
<td>US</td>
<td>0.38</td>
</tr>
<tr>
<td>Steinhoff et al, 2005</td>
<td>2-13</td>
<td>410</td>
<td>Clinic</td>
<td>Egypt</td>
<td>0.25</td>
</tr>
<tr>
<td>Karacan et al, 2007</td>
<td>3-15</td>
<td>857</td>
<td>Clinic</td>
<td>Turkey</td>
<td>0.49</td>
</tr>
<tr>
<td>Fretzayas et al, 2009</td>
<td>4-14</td>
<td>144</td>
<td>Clinic</td>
<td>Greece</td>
<td>0.40</td>
</tr>
<tr>
<td>Rimoin et al, 2010</td>
<td>2-12</td>
<td>2472</td>
<td>Clinic</td>
<td>Brazil/Egypt/Latvia/Croatia</td>
<td>0.29</td>
</tr>
</tbody>
</table>

ED, emergency department.
*Case-control study; cannot calculate prevalence.
respective.\(^\text{15,16}\) The combination of tender or large cervical node was associated with a pooled positive and negative LR of 1.60 (CI, 1.25-2.04) and 0.98 (CI, 0.97-1.00), respectively.\(^\text{17,18}\)

**Diagnostic Accuracy of Prediction Rules**

Fifteen studies provided data on accuracy of 5 prediction rules in the diagnosis of streptococcal pharyngitis in children (Table IV). None of the prediction rules had an LR (probability of GAS >85%) that could be used to rule in streptococcal pharyngitis. A score of 0 on the prediction rule developed by Attia had an LR of 0.21 (CI, 0.05-0.92). Thus, a child with moderate to severe coryza who does not have moderate to severe tonsillar swelling, moderate to severe enlarge cervical nodes, or a scarlatiniform rash has an 11% (CI, 2.9-35) probability of having streptococcal pharyngitis (moderate to severe not further defined in the original studies). However, the CI around this estimate is wide.

**Precision of Symptoms and Signs**

The limited data available suggest that precision of the symptoms and signs of streptococcal pharyngitis is fair to moderate. Attia reported an overall agreement of 70% to 98% on 4 clinical characteristics (tonsillar swelling, cervical lymphadenopathy, scarlatiniform rash, and lack of coryza) between the 2 independent observers; however, kappa values were not used to evaluate agreement beyond chance.\(^\text{15}\) Jensen reported moderate agreement (κ: 0.41-0.60), among pairs of physicians, for the presence of palatal petechiae, scarlatiniform rash, tonsillar exudate, and tonsillar enlargement.\(^\text{20}\) Fair agreement (κ: 0.2-0.4)\(^\text{21}\) was reported for the following findings: coryza, tonsillar erythema, and cervical adenopathy.\(^\text{20}\)

## Discussion

In children with sore throat, certain symptoms and signs (scarlatiniform rash, palatal petechiae, pharyngeal exudate, vomiting, and tender cervical nodes) increase the probability of streptococcal pharyngitis to >50%. However, no finding in isolation has a sufficiently high LR to permit a definitive diagnosis (defined here as a probability of >85%). Prediction rules were also not accurate enough to allow for a definitive diagnosis of streptococcal pharyngitis. Accordingly, empiric treatment based on symptoms and signs would no doubt lead to overuse of antibiotics.

Similarly, in a child with sore throat, individual symptoms and signs cannot be used to exclude streptococcal pharyngitis. One prediction rule (moderate to severe coryza without moderate to severe tonsillar swelling or moderate to severe enlarge cervical nodes or a scarlatiniform rash) appeared in one study to be useful in identifying low-risk children who
could be managed without further testing. However, further study is required to confirm the accuracy of this combination. Accordingly, in children with sore throat, foregoing testing could lead to missing children with bona fide streptococcal pharyngitis.

One reason why symptoms and signs are not particularly useful in the diagnosis of streptococcal pharyngitis may be related to how children with streptococcal pharyngitis are identified. Only children with significant symptoms and signs are likely brought in for evaluation. Accordingly, it likely that the diagnostic value of findings is “used up” by the time the child sees a clinician for streptococcal pharyngitis.²²,²³

It is important to note that the approach above is predicated on the relatively high prevalence of streptococcal pharyngitis in children 3-18 years of age with a sore throat. A different approach is required in subgroups of children with substantially lower prevalence of streptococcal pharyngitis. Most children with an upper respiratory infection do not have sore throat.²⁴ These children have a very low probability (4%, CI, 3.37%-4.78%)²⁴ of having streptococcal pharyngitis and therefore do not require testing. Likewise, routine testing is not required in children <24 months of age—in whom the prevalence of streptococcal pharyngitis is approximately 6% (CI, 1.6%-10.5%)

²⁵-²⁷—or in asymptomatic siblings of children with streptococcal pharyngitis, because it is likely to result in the overtreatment of carriers.

The approach described here also presupposes the easy availability of rapid tests and throat cultures. In low-resource settings where these tests are not available, a lower threshold for treatment (ie, lower than the 85% used in this article) may be acceptable. Our approach also is predicated on the relatively low incidence of suppurative (approximately 2% develop peritonsillar abscess)²⁸ and nonsuppurative (approximately 2% develop acute rheumatic fever)²⁸ complications following an episode of streptococcal pharyngitis that is not treated with an effective antibiotic. In settings in which rapid testing is not available or in which the incidence of complications is high, symptoms and signs (ie, the presence of a scarlatiniform rash in a child with sore throat) might be used to guide treatment decisions.

The data synthesized here support the current strategy suggested by the American Academy of Pediatrics, the American Heart Association, and the Infectious Disease Society of America, all of which recommend testing (rapid test or a throat culture) in suspected cases and avoidance of testing in children with symptoms clearly consistent with a viral upper respiratory tract infection. Of note, the use of the Centor score to identify children who require testing or treatment, which is the recommended approach in several European national guidelines, is not supported by our data.

Several guidelines on the management of streptococcal pharyngitis in adults recommend that symptoms and signs can be used to stratify patients into risk categories.²⁹ Aside from the data presented, there may be several theoretical reasons why this approach does not appear to be generalizable to children. First, because of the higher prevalence of streptococcal pharyngitis (37%³⁰ vs 10%³¹) and streptococcal carriage (12%³² vs 1%³³,³⁴) in children, a different approach is likely required. Second, because of the higher incidence of viral upper respiratory infections among children,³³ and because symptoms and signs of these infections overlap with those of streptococcal pharyngitis, the accuracy of clinical findings may be different in children than in adults (eg, given the high prevalence of Epstein-Barr virus pharyngitis, pharyngeal exudate may be a less specific finding).

A first limitation to our study is the lack of specificity regarding how signs and symptoms were defined or elicited.

### Table IV. Clinical prediction rules for streptococcal pharyngitis in children with sore throat*

<table>
<thead>
<tr>
<th>Prediction rule</th>
<th>Description</th>
<th>Score</th>
<th>LR² (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Breese score¹⁸,³⁴,⁶³</td>
<td>9-category scoring system</td>
<td>&gt;30</td>
<td>2.58 (2.15-3.09)</td>
</tr>
<tr>
<td>One point for each of the following findings:</td>
<td>0</td>
<td>0.57 (0.44-0.74)</td>
<td></td>
</tr>
<tr>
<td>History of fever, exudate, absence of cough, tender nodes</td>
<td>1</td>
<td>0.47 (0.40-0.55)</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>1.23 (0.76-1.98)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3 or 4</td>
<td>1.73 (1.28-2.35)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>McIsaac score¹⁴,⁶³,⁶⁶-⁶⁹</td>
<td>One point for each of the following findings:</td>
<td>1</td>
<td>0.38 (0.21-0.69)</td>
</tr>
<tr>
<td>Temperature =38°C, no cough, tonsillar swelling or exudate, tender nodes, age &lt;15 y</td>
<td>2</td>
<td>0.54 (0.35-0.85)</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>1.03 (0.89-1.19)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>1.48 (1.09-2.02)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>2.52 (1.13-5.59)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Wald score⁶²,⁶⁶,⁷⁰</td>
<td>One point for each of the following findings:</td>
<td>1</td>
<td>0.34 (0.13-0.85)</td>
</tr>
<tr>
<td>Age 5-15 y, November to May, Temperature &gt;38.3°C, adenopathy, pharyngitis, absence of upper respiratory tract symptoms</td>
<td>2</td>
<td>0.56 (0.41-0.78)</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>0.61 (0.40-0.94)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>0.94 (0.59-1.49)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>1.39 (1.13-1.72)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>2.53 (1.61-3.98)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Attia score¹⁹,⁵¹</td>
<td>Moderate to severe tonsillar swelling (1 point),</td>
<td>0</td>
<td>0.21 (0.05-0.92)</td>
</tr>
<tr>
<td>moderate to severe large cervical nodes (1 point), scarlatiniform rash (2 points),</td>
<td>1 to 3</td>
<td>0.88 (0.82-0.95)</td>
<td></td>
</tr>
<tr>
<td>absence of moderate to severe coryza (1 point)</td>
<td>4 or 5</td>
<td>5.90 (3.00-11.8)</td>
<td></td>
</tr>
</tbody>
</table>

*Some articles appear here but not in Table II because the article contained no data regarding individual signs and symptoms.
†All LRs (except for Breese score ≥30) represent multilevel LRs.
‡Breese score of ≥30 had a negative LR of 0.41 CI, 0.16-1.08.
§Breese score of 0.⁄C14
$≥30 2.58 (2.15-3.09)
$≥0.57 (0.44-0.74)
$≥1.23 (0.76-1.98)
$≥1.73 (1.28-2.35)
$≥0.38 (0.21-0.69)
$≥0.54 (0.35-0.85)
$≥1.03 (0.89-1.19)
$≥1.48 (1.09-2.02)
$≥2.52 (1.13-5.59)
$≥0.34 (0.13-0.85)
$≥0.56 (0.41-0.78)
$≥0.61 (0.40-0.94)
$≥0.94 (0.59-1.49)
$≥1.39 (1.13-1.72)
$≥2.53 (1.61-3.98)
$≥0.21 (0.05-0.92)
$≥0.88 (0.82-0.95)
$≥5.90 (3.00-11.8)
in some of the original articles. A second limitation is the dearth of data regarding the accuracy of the various combinations of symptoms and signs. Third, rather than using paired acute and convalescent anti-streptococcal serology as the reference standard, we chose to use the results of the throat culture as the reference standard. The decision to use a less stringent but more practical reference standard was in part due to the small number of studies in which serological confirmation was conducted. Unlike serologic testing, throat culture is unable to differentiate true infection from the carrier state; thus, we are likely to have underestimated the accuracy of signs and symptoms (the true-positive LR is probably higher and the true-negative LR is probably lower than presented here). Nevertheless, it is unlikely this would alter any of our conclusions. Finally, heterogeneity among studies is present in all systematic reviews. We addressed heterogeneity in 2 ways. First, we used random effects pooled estimates; the CIs presented include adjustments for between-study variances. Second, we tested the robustness of our conclusions by performing sensitivity analysis with regard to clinically important variables.

In contrast to adults, determination of the risk of streptococcal pharyngitis in children 3-18 years of age with sore throat requires the use of confirmatory testing using a rapid strep test or a throat culture.

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References

Accuracy and Precision of the Signs and Symptoms of Streptococcal Pharyngitis in Children: A Systematic Review


Appendix 1

Detail of the Search Strategies Used (Ovid Syntax)

Diagnostic Accuracy of Individual Signs and Symptoms
A. Pharyngitis terms
1. Pharyngitis/
2. Tonsillitis/
3. sore throat.mp
4. pharyngitis.mp
5. tonsillopharyngitis.mp
6. tonsillitis.mp
7. strep throat.mp
8. or/1-7
B. Streptococcal terms
9. Streptococcus pyogenes/
10. Streptococcus infections/
11. Strep pyogenes.mp
12. Group A Strep.mp
13. Streptococc*.mp
14. or/9-13
C. Pediatric terms
15. Child/
16. Child*.mp
17. Schoolchild*.mp
18. School age*.mp
19. Preschool*.mp
20. Kid*.mp
21. Toddler*.mp
22. Adolescent/
23. Adoles*.mp
24. Teen*.mp
25. Boy*.mp
26. Girl*.mp
27. Minors/
28. Minors*.mp
29. Puberty/
30. Pubert*.mp
31. Pubescen*.mp
32. Prepubescen*.mp
33. Pediatrics/
34. Paediatric*.mp
35. Paediatric*.mp
36. Peadiatric*.mp
37. Schools/
38. Kindergar*.mp
39. Primary school*.mp
40. Secondary school*.mp
41. Elementary school*.mp
42. High school*.mp
43. Highschool*.mp
44. or/15-43
D. Diagnosis terms or specific signs and symptoms of interest
45. exp “Sensitivity and Specificity”/
46. di.fs
47. du.fs
48. sensitivity.tw
49. specificity.tw
50. (clinical* or symptom* or exam* or criteria or tests or test).fs,hw,tw
51. exudate.mp
52. erythema.mp
53. petechiae.mp
54. lymphadenopathy.mp
55. tonsillar enlargement.mp
56. tonsillar hypertrophy.mp
57. fever.mp
58. cough.mp
59. coryza.mp
60. myalgia*.mp
61. temperature.mp
62. nausea.mp
63. rhinorrhea.mp
64. headache.mp
65. abdominal pain.mp
66. or/45-65
E. Limits
67. English, French, German, Italian, Spanish, Human
F. Combine A-E above
68. 8 and 14 and 44 and 66 and 67

Diagnostic Accuracy of Prediction Rules
1. 8 and 14 and 44
2. (Predict$ or Validat$ or Rule$).mp or Predictive Value of Tests/
3. 1 and 2

Precision of Signs and Symptoms
1. Reproducibility of results/
2. Observer variation/
3. Kappa.mp
4. Agreement.mp
5. or/1-4
6. Pharyngitis/
Appendix 2

Criteria Used to Assess Quality of the Included Studies (Modified from QUADAS)

1. Was the spectrum of patients representative of the patients who will receive the test in practice?

If the spectrum of patients was similar to a representative sample of self-referred patients who would receive the test in an acute care setting (primary care office or emergency department), then score “yes.” If the sample included many children with more or less severe presentations of streptococcal pharyngitis, or if there is insufficient information to make a judgment, then score “no.” For case-control studies, score “yes” if the cases were representative.

2. Is the reference standard likely to correctly classify the target condition?

If GAS was identified using bacitracin sensitivity or latex agglutination, then this item should be scored “yes.” If GAS was not specifically identified (results reported as beta-hemolytic Streptococcus or Streptococcus), or if there is insufficient information to make a judgment, then this item should be scored as “no.”

3. Did the whole sample receive verification using a reference standard?

If it is clear that all patients, or a random selection of patients, who received the index test went on to receive verification of their disease status using a throat culture or a rapid antigen test, then this item should be scored as “yes.” If some patients received verification using only a rapid streptococcal test, or if this information is not reported by the study, this item should be scored as “no.”

4. Did patients receive the same reference standard regardless of the index test result?

If it is clear that all patients received verification of their true disease status using a throat culture, then this item should be scored as “yes.” If some patients received verification using only a rapid streptococcal test, or if this information is not reported by the study, this item should be scored as “no.”

5. Were children on antibiotics (or who were recently antibiotics) excluded?

If children currently on antibiotics, or recently on antibiotics (within 2 weeks) were excluded from the study, then this item should be scored as “yes.” If these children were not specifically excluded, score as “no.”

6. Were the data collected prospectively?

If the study was prospective, then score as “yes.” If retrospective, score as “no.”

7. Was this a case-control study?

If the study used a case-control design, then score as “yes.” If cross-sectional or cohort design, score as “no.”
<table>
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<th>Source, year</th>
<th>Spectrum of patients representative</th>
<th>Reference standard ideal</th>
<th>All cases verified using reference standard</th>
<th>All cases verified using same reference standard</th>
<th>Children on or recently on antibiotics excluded</th>
<th>Prospective design</th>
<th>Case-control design</th>
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*A quality assessment tool developed for diagnostic accuracy studies. See Appendix 2 online for explanation of how items were defined for this review.