ESCMID Guideline for the Management of Acute Sore Throat

GUEST EDITOR
Mical Paul

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Guideline for the management of acute sore throat

ESCMID Sore Throat Guideline Group

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Abstract

The European Society for Clinical Microbiology and Infectious Diseases established the Sore Throat Guideline Group to write an updated guideline to diagnose and treat patients with acute sore throat. In diagnosis, Centor clinical scoring system or rapid antigen test can be helpful in targeting antibiotic use. The Centor scoring system can help to identify those patients who have higher likelihood of group A streptococcal infection. In patients with high likelihood of streptococcal infections (e.g. 3–4 Centor criteria) physicians can consider the use of rapid antigen test (RAT). If RAT is performed, throat culture is not necessary after a negative RAT for the diagnosis of group A streptococci. To treat sore throat, either ibuprofen or paracetamol are recommended for relief of acute sore throat symptoms. Zinc gluconate is not recommended to be used in sore throat. There is inconsistent evidence of herbal treatments and acupuncture as treatments for sore throat. Antibiotics should not be used in patients with less severe presentation of sore throat, e.g. 0–2 Centor criteria to relieve symptoms. Modest benefits of antibiotics, which have been observed in patients with 3–4 Centor criteria, have to be weighed against side effects, the effect of antibiotics on microbiota, increased antibacterial resistance, medicalisation and costs. The prevention of suppurative complications is not a specific indication for antibiotic therapy in sore throat. If antibiotics are indicated, penicillin V, twice or three times daily for 10 days is recommended. At the present, there is no evidence enough that indicates shorter treatment length.

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Background

Acute sore throat is a symptom often caused by an inflammatory process in the pharynx, tonsils or nasopharynx. Most of these cases are of viral origin and occur as a part of the common cold. Adults average two to four and children six to eight upper respiratory tract infections per year usually during the colder months of the year. In addition to viral pathogens, bacterial pathogens may also cause pharyngeal infections. These pathogens include *Streptococcus pyogenes* (group A β-haemolytic streptococcus), but groups C or G β-haemolytic streptococci as well as *Mycoplasma pneumoniae* and *Chlamydia pneumoniae* have also been suggested to be pathogens. Although rare today in Europe, streptococcal pharyngitis can be complicated by acute rheumatic fever or acute glomerulonephritis. Fear of these complications, or a wish to relieve pain or to satisfy patients often lead physicians to use antibiotic treatment for sore throat. Acute sore throat is itself a symptom, and pain or discomfort in the pharynx is not always caused by an
Infectious agent. Conversely, infectious agents are often found in the pharyngeal area in asymptomatic patients. There is an apparent lack of studies on sore throat with simultaneous identification of a wide spectrum of different infectious agents, both bacterial and viral, alone or mixed, in symptomatic or asymptomatic children or adults, and during different seasons.

The European Society for Clinical Microbiology and Infectious Diseases (ESCMID) established the ESCMID Sore Throat Guideline Group to write an updated guideline to diagnose and treat patients with acute sore throat. This guideline answers questions concerning the use of clinical diagnostic criteria and laboratory diagnostics to detect possible bacterial infection. In addition to diagnostic recommendations, the first-choice treatment regimen is also evaluated and recommendations are given.

The following text is a summary of the recommendations themselves and a discussion of the evidence on which the recommendations are based.

**Guideline approach**

To limit the scope of this guideline we restrict our recommendations to diagnosis and treatment of acute (duration of symptoms <14 days), uncomplicated sore throat in adults and children in Europe. The recommendations concern first-line diagnostics as well as symptomatic and antibiotic treatment.

The guideline does not cover recurrent or persistent cases of sore throat, complicated pharyngitis (peritonsillar abscesses, Lemierre disease, Vincent’s angina), severe comorbidity, immunosuppression or history of acute rheumatic fever. Moreover, special circumstances, such as sore throat after travel outside Europe, sore throat linked to sexual transmission or rare epidemics (e.g. diphtheria), are not debated.

### Methods for literature search

We retrieved the main keywords/MeSH terms from previous clinical guidelines and reviews on sore throat. We defined separate search strings according to different topics, and performed systematic literature searches in the Medline database, using PubMed, and the Cochrane Database.

As various guidelines and reviews on sore throat were published between 2000 and 2002, providing several materials that were considered in this investigation, we decided to limit our search to the period 2002–2009. More than 1000 articles were reviewed. Abstracts and unpublished studies were excluded. No studies were excluded a priori for weakness of design or data quality. Detailed search methods are described in the Appendix.

### Grading criteria of evidence

The appraisal of the available evidence was performed following the same lines of reasoning used in the previously developed guidelines for the management of adult lower respiratory tract infections [1]. Studies were evaluated according to their design as well as their potential bias or validity, to define the strength of evidence they provided. A checklist for the critical appraisal of each selected publication was used to assess the validity of selected studies, and their level of clinical evidence was summarized using criteria described in Table 1.

A few changes were made to the checklist used by Woodhead et al. [1], by including specific questions aimed at the evaluation of potential bias and flaws of randomized clinical trials, which was particularly useful for the section on treatment. The evaluated studies were included in various evidence matrices developed to answer specific questions on diagnosis, prognosis and treatment of acute sore throat. Clinical evidence was translated into recommendations using a protocol described in Table 2.

### TABLE 1. Checklist for levels of evidence in literature search

<table>
<thead>
<tr>
<th>Evidence levels</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 Systematic reviews and meta-analyses</td>
<td>Low risk of bias results; all or most of the validity criteria are met (i.e. at least four out of six flaws are unlikely, for randomized trials)</td>
</tr>
<tr>
<td>2 Randomized trials</td>
<td>Moderate risk of bias results; half of the validity criteria are met (i.e. at least three out of six flaws are unlikely, for randomized trials)</td>
</tr>
<tr>
<td>3 Prospective cohort</td>
<td>High risk of biased results; most of the validity criteria are not met (i.e. two or fewer out of six flaws are unlikely, for randomized trials)</td>
</tr>
<tr>
<td>4 Case-control, cross-sectional, retrospective cohort</td>
<td>Certain criteria are met, but the study design is not suitable for other study designs</td>
</tr>
<tr>
<td>5 Case reports</td>
<td>Consensus statements, other</td>
</tr>
<tr>
<td>6 Expert opinions</td>
<td>Evidence levels may be uncertain, but clinical validity can be assured</td>
</tr>
</tbody>
</table>

### TABLE 2. Checklist for grading recommendations

| A Consistent evidence: clear outcome |
| B Inconsistent evidence: unclear outcome |
| C Insufficient evidence: consensus |

**Suffixes**

- A Consistent evidence: clear outcome
- B Inconsistent evidence: unclear outcome
- C Insufficient evidence: consensus

### For preventive and therapeutic intervention studies (including harm of intervention)

| 1 Systematic reviews (SR) or meta-analyses (MA) of randomized controlled trials (RCT) | A Consistent evidence: clear outcome |
| 2 One RCT or more than one RCT but no SR or MA | B Inconsistent evidence: unclear outcome |
| 3 One cohort study or more than one cohort study but no SR or MA | C Insufficient evidence: consensus |
| 4 Other | Other |

### For other studies

| 1 Systematic reviews (SR) or meta-analyses (MA) of cohort studies | A Consistent evidence: clear outcome |
| 2 One cohort study or more than one cohort study but no SR or MA | B Inconsistent evidence: unclear outcome |
| 3 Other | C Insufficient evidence: consensus |

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Recommendation summary

Clinical assessment of acute sore throat
What is the role of clinical scoring in the diagnosis of group A streptococcal infections?

The Centor clinical scoring system can help to identify those patients who have a higher likelihood of group A streptococcal infection (A-3). However, its utility in children appears lower than in adults because of the different clinical presentation of sore throat in the first years of life.

Laboratory tests for sore throat
Is throat culture considered a necessary clinical instrument for diagnosis of group A streptococci?

Throat culture is not necessary for routine diagnosis of acute sore throat to detect group A streptococci (C-3).

What is the validity and accuracy of near patient diagnostic tests for group A streptococcus? Is it necessary to perform a throat culture after a negative rapid antigen test (RAT) for the diagnosis of group A streptococci?

If RAT is performed, throat culture is not necessary after a negative RAT for the diagnosis of group A streptococci in both children and adults (B-2).

Is the diagnostic value of RAT increased when tests are performed in subjects with high clinical scores for group A streptococcus, i.e. indicators that increase likelihood of strep throat, as Centor score or modified Centor score?

In patients with high likelihood of streptococcal infections (e.g. 3–4 Centor criteria) physicians can consider the use of RATs. In patients with lower likelihood of streptococcal infections (e.g. 0–2 Centor criteria) there is no need to routinely use RATs (B-3).

Is there a role for additional tests (e.g. C-reactive protein, procalcitonin measurements) in the assessment of severity of acute sore throat? Does clinical information combined with biomarker information provide better prognostic information?

It is not necessary to routinely use biomarkers in the assessment of acute sore throat (C-3).

Does improved diagnosis or the use of near patient tests improve antibiotic use?

Clinical scoring systems and rapid tests can be helpful in targeting antibiotic use (B-2).

Treatment
Are analgesics effective in sore throat?

Either ibuprofen or paracetamol are recommended for relief of acute sore throat symptoms (A-1).

What are the indications for use of glucocorticoids in sore throat?

Use of corticosteroids in conjunction with antibiotic therapy is not routinely recommended for treatment of sore throat. It can however be considered in adult patients with more severe presentations, e.g. 3–4 Centor criteria (A-1).

What are the indications for use of zinc gluconate in sore throat?

Zinc gluconate is not recommended for use in sore throat (B-2).

What are the indications for complementary treatments, e.g. herbal treatments or acupuncture, in sore throat?

There is inconsistent evidence of herbal treatments and acupuncture as treatments for sore throat (C-1 to C-3).

What is the average benefit from antibiotics and which groups of patients do benefit from antibiotic treatment?

Sore throat should not be treated with antibiotics to prevent the development of rheumatic fever and acute glomerulonephritis in low-risk patients (e.g. patients with no previous history of rheumatic fever) (A-1). The prevention of suppurative complications is not a specific indication for antibiotic therapy in sore throat (A-1). Clinicians do not need to treat most cases of acute sore throat to prevent quinsy, acute otitis media, cervical lymphadenitis, mastoiditis and acute sinusitis (A-3).

Do antibiotics relieve symptoms in sore throat?

Antibiotics should not be used in patients with less severe presentation of sore throat, e.g. 0–2 Centor criteria, to relieve symptoms (A-1). In patients with more severe presentations, e.g. 3–4 Centor criteria, physicians should consider discussion of the likely benefits with patients. Modest benefits of antibiotics, which have been observed in group A β-haemolytic streptococcus-positive patients and patients with 3–4 Centor criteria, have to be weighed against side effects, the effect of antibiotics on the microbiota, increased antibacterial resistance, medicalization and costs (A-1).

Which antimicrobial agent is the first choice in patients with acute sore throat?

If antibiotics are indicated, penicillin V, twice or three times daily for 10 days, is recommended (A-1). There is not enough evidence that indicates shorter treatment length.
Bacterial pathogens in sore throat

Group A β-haemolytic streptococcus

The role of group A β-haemolytic streptococcus as a bacterial pathogen in sore throat is evident and is not questioned. Reviews and guidelines considering the diagnosis of sore throat have therefore been focused mainly or exclusively on group A streptococci and related symptomatic presentation.

Asymptomatic carriage of β-haemolytic streptococci is frequent, especially in children. According to Tanz and Shulman [2], over 20% of asymptomatic school children may be carriers of group A streptococcal infection during the winter and spring. Several European investigations examined the carriage rates in children and adults. The highest rate was found in subjects aged 14 years or less (10.9%), whereas rates were 2.3% in patients aged 15–44 years and 0.6% in those aged 45 years or older [3].

Similar results emerged in a Swedish study [4], reporting carriage rates of 11.3% in 4-year-old children, 5.9% in school children and 0.8% in adults. In a study from Croatia [5], carriage rate of group A streptococci was 8.3% overall, with highest rates being reported for subjects aged 6–14 years. Higher rates were found in a prospective study conducted in Turkey on 351 asymptomatic primary school children, as about 26% of them were group A streptococcal infection carriers [6].

Complications of group A β-haemolytic streptococcal pharyngitis are generally rare in both children and adults (Tables 3 and 4; [7–14]). Potential adverse outcomes include both suppurative (i.e. quinsy, acute otitis media, cervical lymphadenitis, mastoiditis, acute sinusitis) and non-suppurative (i.e. acute rheumatic fever, acute glomerulonephritis) complications. In particular, acute rheumatic fever has been widely investigated during the last decades, but its incidence is very low in Europe. Prevention of acute rheumatic fever depends on effective control of group A streptococcal pharyngitis [7] and is important for patients at high risk (e.g. those who have had rheumatic fever before). Acute glomerulonephritis is another rare consequence of sore throat, following group A streptococcal pharyngitis after a latency period of a few weeks. Quinsy, a complication that occurs mainly in young adults, is a polymicrobial infection but group A streptococcus is the main organism associated with the disease (Tables 5 and 6; [7–9,11,15–17]).

Tanz and Shulman [2] conclude that pharyngeal carriers of group A streptococci show an extremely low risk of post-streptococcal complications, and their likelihood of transmitting the infection is also small.

Group C and G β-haemolytic streptococci

A number of studies are available on the symptomatic presentation of β-haemolytic streptococci other than group A streptococci. Two observational studies (one cohort study, one case–control study) supported a milder clinical presentation of group C or group G streptococcal pharyngitis than group A streptococcal pharyngitis (Table 7; [17–25]). On the other hand, five observational studies (three cohort, two case–control) and one case series investigation reported a similar clinical picture.

At least 12 original studies, mostly case series and case reports, described severe symptoms or complications following acute sore throat associated with group C and group G streptococci (Table 8; [12,25–35]). Cases of severe or recurrent pharyngitis because of group C streptococci have been reported. A case–control study of college students found that patients with group C streptococci had exudative tonsillitis and anterior cervical adenopathy more frequently than subjects negative for this infection [29]. On the other hand, there is little evidence to address the issue of whether there is an association between group G streptococci and severe or recurrent pharyngitis.

Uncommon complications of pharyngitis caused by group C or G streptococci that have been reported include reactive arthritis, subdural empyema and acute glomerulonephritis, but a causal relationship was not clearly established. In 1997, Efstratiou reported consistent results of group C and G septicaemia over a 10-year period [36].

### TABLE 3. Summary information on group A streptococci and prognosis of sore throat from papers

<table>
<thead>
<tr>
<th>First author</th>
<th>Type of study</th>
<th>Objective</th>
<th>Evidence level</th>
</tr>
</thead>
<tbody>
<tr>
<td>Talmon [8]</td>
<td>Case series</td>
<td>Describe 11 cases of acute myopericarditis complicating acute tonsillitis</td>
<td>5+</td>
</tr>
<tr>
<td>Galoto [9]</td>
<td>Review</td>
<td>To review diagnosis and treatment of peritonsillar abscess</td>
<td>6+</td>
</tr>
<tr>
<td>Abdel-Haq [10]</td>
<td>RCS</td>
<td>Identify the predisposing factors and the microbiology of RPA</td>
<td>4C</td>
</tr>
<tr>
<td>Almroth [12]</td>
<td>Case series</td>
<td>Study an epidemic of acute glomerulonephritis associated with throat infections</td>
<td>5I</td>
</tr>
<tr>
<td>Hanou [14]</td>
<td>RCS</td>
<td>To describe the epidemiology of peritonsillar abscess disease in Northern Ireland</td>
<td>4B+</td>
</tr>
</tbody>
</table>

GAS, group A streptococci; RCS, retrospective cohort study; RPA, retropharyngeal abscess.
While sore throat caused by group A streptococci is known to be rarely associated with acute rheumatic fever in developed countries, this has not been reported as a complication following group C or group G streptococcal infection [37]. There are, however, studies and expert opinions indicating that group C and group G streptococci might...
contribute to acute rheumatic fever pathogenesis in high-incidence settings [38,39].

Group C streptococci can cause severe or recurrent pharyngitis, but there is insufficient evidence for a role of group C streptococci in other adverse outcomes. There is insufficient evidence for a role of group G streptococci in severe/recurrent pharyngitis and other adverse outcomes.

Mycoplasma pneumoniae and Chlamydia pneumoniae

Mycoplasma pneumoniae and C. pneumoniae infection has been associated with non-streptococcal acute pharyngitis in selected studies [40]. It is not clear whether pharyngitis due to these infections may have an unwanted outcome, including longer duration or recurrence of symptoms and occurrence of other complications. The available evidence is scanty and limited to paediatrics (Table 9; [40–44]). Two observational studies (one prospective cohort, one case–control) reported increased risk of recurrence of symptoms after M. pneumoniae infection. One prospective cohort study reported an increased risk of recurrence of respiratory illness after C. pneumoniae infection. Case reports and case series found a possible association between M. pneumoniae infection and Bell’s palsy or Stevens–Johnson syndrome.

Clinical assessment of acute sore throat

What is the role of clinical scoring in the diagnosis of group A streptococcal infections?

The Centor score for the diagnosis of group A streptococcal throat infections was proposed in 1981 [45]. It was based on the study of 286 adult patients with sore throat who presented to the Emergency Department at the University College of Virginia. Centor and colleagues identified four signs and symptoms to estimate the probability of acute group A streptococcal pharyngitis in adults with sore throat.

The four signs and symptoms were tonsillar exudate, swollen tender anterior cervical nodes, the lack of cough and fever. According to the Centor score [45], the risk of group A streptococcal infection depends on the number of signs and symptoms, as described in Box 1.

BOX 1.

<table>
<thead>
<tr>
<th>Number of signs and symptoms</th>
<th>Risk of group A streptococcal infection (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>4</td>
<td>56</td>
</tr>
<tr>
<td>3</td>
<td>32</td>
</tr>
<tr>
<td>2</td>
<td>15</td>
</tr>
<tr>
<td>1</td>
<td>6.5</td>
</tr>
<tr>
<td>0</td>
<td>2.5</td>
</tr>
</tbody>
</table>

This clinical decision rule was validated only in adults and not in children.

The Centor score was later modified by adding age, and was validated in about 600 adults and children (3–15 years old) in a Canadian study [46]. The modified Centor score was based on a total sore throat score that determines the likelihood of group A streptococcal pharyngitis. To determine the patient’s total sore throat score it is necessary to assign points using the criteria detailed in Box 2.

BOX 2.

<table>
<thead>
<tr>
<th>Criteria</th>
<th>Point</th>
</tr>
</thead>
<tbody>
<tr>
<td>Temperature &gt;38°C</td>
<td>1</td>
</tr>
<tr>
<td>No cough</td>
<td>1</td>
</tr>
<tr>
<td>Tender anterior cervical adenopathy</td>
<td>1</td>
</tr>
<tr>
<td>Tonsillar swelling or exudate</td>
<td>1</td>
</tr>
<tr>
<td>Age 3–14 years</td>
<td>1</td>
</tr>
<tr>
<td>Age 15–44 years</td>
<td>0</td>
</tr>
<tr>
<td>Age &gt;44 years</td>
<td>-1</td>
</tr>
</tbody>
</table>

The risk of group A streptococcal infection depends on the total sore throat score (Box 3) [46].

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**TABLE 8. Summary information on group C and group G streptococci and prognosis of sore throat**

<table>
<thead>
<tr>
<th>First author</th>
<th>Type of study</th>
<th>Objective</th>
<th>Evidence level</th>
</tr>
</thead>
<tbody>
<tr>
<td>Shah [26]</td>
<td>Case report</td>
<td>Description of a case of severe GCS pharyngitis</td>
<td>5+</td>
</tr>
<tr>
<td>Turner [27]</td>
<td>PCS</td>
<td>Association between GCS and exudative pharyngitis</td>
<td>3A+</td>
</tr>
<tr>
<td>Dudley [28]</td>
<td>Case series</td>
<td>Report of cases of tonsillitis due to non-GAS</td>
<td>5+</td>
</tr>
<tr>
<td>Turner [29]</td>
<td>PCS</td>
<td>To determine whether non-GAS is associated with endemic pharyngitis</td>
<td>4A+</td>
</tr>
<tr>
<td>Fulginiti [31]</td>
<td>Case report</td>
<td>Report of a case of recurrent GCS tonsillitis</td>
<td>5+</td>
</tr>
<tr>
<td>Jensen [32]</td>
<td>Case series</td>
<td>To investigate reactive arthritis secondary to throat infection</td>
<td>5+</td>
</tr>
<tr>
<td>Young [33]</td>
<td>Case report</td>
<td>A case of reactive arthritis after GGS pharyngitis</td>
<td>5+</td>
</tr>
<tr>
<td>Other adverse outcomes</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Almroth [12]</td>
<td>Case series</td>
<td>Study an epidemic of acute glomerulonephritis associated with throat infections</td>
<td>5?</td>
</tr>
<tr>
<td>Nazo [34]</td>
<td>Case report</td>
<td>Report of a case of streptococcal toxic shock-like syndrome caused by a GCS strain</td>
<td>5+</td>
</tr>
<tr>
<td>Gettler [35]</td>
<td>Case report</td>
<td>GCS subdural empyema after pharyngitis</td>
<td>5+</td>
</tr>
<tr>
<td>Corson [25]</td>
<td>Case report and case series</td>
<td>Review of cases of pharyngitis in relation to β-haemolytic streptococci</td>
<td>5+</td>
</tr>
</tbody>
</table>

GAS, group A streptococci; GCS, group C streptococci; GGS, group G streptococci; PCS, prospective cohort study.
**TABLE 9. Summary information from papers on Mycoplasma pneumoniae and Chlamydia trachomatis infection and prognosis of sore throat**

<table>
<thead>
<tr>
<th>First author</th>
<th>Type of study</th>
<th>Objective</th>
<th>Evidence level</th>
</tr>
</thead>
<tbody>
<tr>
<td>Esposito [40]</td>
<td>PCS</td>
<td>To evaluate the natural history of acute tonsillopharyngitis</td>
<td>3B+</td>
</tr>
<tr>
<td>Esposito [41]</td>
<td>Case-control</td>
<td>To establish the role of atypical bacteria in acute pharyngitis</td>
<td>4A+</td>
</tr>
<tr>
<td>Levy [42]</td>
<td>Case series + review of case reports</td>
<td>Analyse the relation between M. pneumoniae infection and SJS</td>
<td>5+</td>
</tr>
<tr>
<td>Klar [43]</td>
<td>Case report</td>
<td>Case report of an infant who developed bilateral facial paresis 4 weeks</td>
<td>5+</td>
</tr>
<tr>
<td>Volter [44]</td>
<td>Case series</td>
<td>Analyse the relation between Bell's palsy and M. pneumoniae infection</td>
<td>5+</td>
</tr>
</tbody>
</table>

PCS, prospective cohort study; SJS, Stevens–Johnson syndrome.

**BOX 3.**

<table>
<thead>
<tr>
<th>Total score</th>
<th>Risk of group A streptococcal infection (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>4</td>
<td>38–63</td>
</tr>
<tr>
<td>3</td>
<td>27–28</td>
</tr>
<tr>
<td>2</td>
<td>10–12</td>
</tr>
<tr>
<td>1</td>
<td>4–6</td>
</tr>
<tr>
<td>0</td>
<td>2–3</td>
</tr>
</tbody>
</table>

The modified Centor score was further adapted in 2004 [47]. Although the criteria remained the same, the estimated risk of group A streptococcal infection was updated as follows (Box 4):

**BOX 4.**

<table>
<thead>
<tr>
<th>Total score</th>
<th>Risk of group A streptococcal infection (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>≥4</td>
<td>51–53</td>
</tr>
<tr>
<td>3</td>
<td>28–35</td>
</tr>
<tr>
<td>2</td>
<td>11–17</td>
</tr>
<tr>
<td>1</td>
<td>5–10</td>
</tr>
<tr>
<td>&lt;0</td>
<td>1–2.5</td>
</tr>
</tbody>
</table>

Children with acute sore throat have a higher rate of asymptomatic carriage of group A streptococci than adults and commonly present with a temperature >38°C, tender anterior cervical adenopathy and tonsillar swelling (e.g. modified Centor score 3); it is difficult to differentiate children with streptococcal pharyngitis on the basis of these scores.

The Centor clinical scoring system can help to identify those patients who have higher likelihood of group A streptococcal infection (A-3). However, its utility in children appears lower than in adults because of the different clinical presentation of sore throat in the first years of life.

**Laboratory tests for sore throat**

Is throat culture considered a necessary clinical instrument for diagnosis of group A streptococci?

The major disadvantage of throat culture in clinical practice is the delay in obtaining the results (18–24 h or longer). Further, there is debate as to whether negative cultures should be re-examined after an additional day to increase the sensitivity of the test (Tables 10 and 11 [48,49]). Most of the reviews and guidelines considered do not support throat culture as a necessary clinical instrument for routine diagnosis of group A streptococci (Tables 12 and 13; [37,49–53]).

**Throat culture is not necessary for routine diagnosis of acute sore throat to detect group A streptococci (C-3).**

**What is the validity and accuracy of near patient diagnostic tests for group A streptococcus? Is it necessary to perform a throat culture after a negative RAT for the diagnosis of group A streptococci?**

A wide variety of RATs are available for diagnosing group A streptococcal pharyngitis, with different diagnostic properties [37,55].

The great majority of RATs have a high specificity (≥95%) compared with culturing a throat swab on a sheep blood agar plate culture [37]. The negative predictive values of the

**TABLE 10. Summary information from papers analysing the optimal duration of incubation of throat cultures**

<table>
<thead>
<tr>
<th>First author</th>
<th>Type of study</th>
<th>Objective</th>
<th>Evidence level</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kocoglu [48]</td>
<td>PCS</td>
<td>Evaluation of accuracy of throat culture at 24, 48 and 72 h of incubation</td>
<td>3A+</td>
</tr>
<tr>
<td>Shulman [49]</td>
<td>Review</td>
<td>Diagnosis and treatment of acute streptococcal pharyngitis</td>
<td>6+</td>
</tr>
</tbody>
</table>

PCS, prospective cohort study.

**TABLE 11. Summary information from guidelines analysing the optimal duration of incubation of throat cultures**

<table>
<thead>
<tr>
<th>Guideline</th>
<th>Country</th>
<th>Conclusions</th>
<th>Age group</th>
<th>Evidence level</th>
</tr>
</thead>
<tbody>
<tr>
<td>Infectious Diseases Society of America (IDSA)</td>
<td>USA</td>
<td>It is advisable to examine plates that yield negative results at 24 h again at 48 h</td>
<td>All</td>
<td>6+</td>
</tr>
</tbody>
</table>
RATs are high, ranging between 93% [52] and 97% [53], and generally being around 95% [54]. The sensitivity of most RATs is around 90% (ranging between 86% and 94.8% [37]) compared with culturing a throat swab on sheep blood agar plate cultures. As reported in several diagnostic accuracy studies on a specific RAT, the RATs are less sensitive than declared by the manufacturer [52,55,56]. The positive predictive values of the RATs ranged between 77% [52] and 97% [57], generally being around 90% [58].

However, the performance of RATs for group A streptococci is influenced by the skill, experience and expertise of the individual obtaining the throat swab and performing the RAT. The performance is also a function of the clinical characteristics of the illness of the patients selected for testing. As a result of this bias, often called 'spectrum bias', the performance of RAT is not an absolute feature of a given test [37,59]. To improve the accuracy of RAT, the RAT should be performed by trained staff [60] and performed in the posterior pharyngeal wall and both tonsils (Tables 14 and 15; [49,61,62]).

### Table 12. Summary information from papers evaluating the optimal sites where throat culture should be performed

<table>
<thead>
<tr>
<th>First author</th>
<th>Type of study</th>
<th>Objective</th>
<th>Evidence level</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fox [61]</td>
<td>PCS</td>
<td>Comparison between testing throat swab in mouth and throat culture</td>
<td>3A+</td>
</tr>
<tr>
<td>van der Veen [62]</td>
<td>PCS</td>
<td>Comparison between testing throat swab on the tonsillar surface and posterior pharyngeal wall</td>
<td>3A+</td>
</tr>
<tr>
<td>Shulman [49]</td>
<td>Review</td>
<td>Diagnosis and treatment of acute streptococcal pharyngitis</td>
<td>6+</td>
</tr>
</tbody>
</table>

PCS, prospective cohort study.

As already asserted for the first generation of RAT [63], the new generation of RAT may have an additional value for the management of sore throat. In children, eight observational studies (five prospective cohort, three retrospective cohort) and two guidelines supported the need for confirmation by a throat culture after a negative RAT. One clinical trial, two observational studies (both were prospective cohorts) and one guideline did not consider confirmation by a throat culture necessary (Tables 16 and 17; [47,50,52,56,57,64–70]). In adults, except for one prospective study, the observational study and two guidelines did not support the need to perform a throat culture after a negative RAT.

If RAT is performed, throat culture is not necessary after a negative RAT for the diagnosis of group A streptococci in both children and adults (B-2).

Is the diagnostic value of RAT increased when tests are performed in subjects with high clinical scores for group A streptococci, i.e. indicators that increase the likelihood of strep throat, as Centor score or modified Centor score? In children and adults, all the observational studies and the guidelines considered supported higher accuracy of RATs when these were performed in patients with a high probability of strep throat (Tables 18 and 19; [54,55,64,66,67,71]). In conclusion, accuracy of RAT increases in patients with clinical criteria for group A streptococci, in both children and adults.

### Table 13. Summary information from guidelines evaluating the use of throat culture in diagnosis of group A streptococcal sore throat

<table>
<thead>
<tr>
<th>Guideline</th>
<th>Country</th>
<th>Conclusions</th>
<th>Age group</th>
<th>Evidence level</th>
</tr>
</thead>
<tbody>
<tr>
<td>Agence Française de Sécurité Sanitaire des Produits de Santé (AFSSAPS)</td>
<td>France</td>
<td>Use of throat culture is not recommended</td>
<td>Adults</td>
<td>6–</td>
</tr>
<tr>
<td>NHS Clinical Knowledge Summaries (CKS)</td>
<td>UK</td>
<td>Throat swabs have poor sensitivity and results take up to 48 h to be reported</td>
<td>All</td>
<td>6–</td>
</tr>
<tr>
<td>Scottish Intercollegiate Guidelines Network (SIGN)</td>
<td>UK</td>
<td>Throat swabs should not be carried out routinely in sore throat</td>
<td>All</td>
<td>6–</td>
</tr>
<tr>
<td>Centers for Disease Control and Prevention (CDC)</td>
<td>USA</td>
<td>The use of throat culture for clinical decision making is not included in the recommendations</td>
<td>Adults</td>
<td>6–</td>
</tr>
<tr>
<td>Infectious Diseases Society of America (IDSA)</td>
<td>USA</td>
<td>Culture of a throat swab remains the standard and if done correctly, has a high sensitivity</td>
<td>All</td>
<td>6+</td>
</tr>
<tr>
<td>The Swedish Strategic Programme for the Rational Use of Antimicrobial Agents (STRAMA)</td>
<td>Sweden</td>
<td>Throat cultures provide support to a suspected clinical diagnosis of group A streptococci</td>
<td>All</td>
<td>6+</td>
</tr>
</tbody>
</table>
In patients with a high likelihood of streptococcal infections (e.g., 3–4 Centor criteria) physicians can consider the use of RATs. In patients with lower likelihood of streptococcal infections (e.g., 0–2 Centor criteria) there is no need to routinely use RATs (B-3).

Is there role for additional tests (e.g., C-reactive protein, procalcitonin measurements) in the assessment of severity of
acute sore throat? Does clinical information combined with biomarker information provide better prognostic information? There is no evidence that C-reactive protein levels are helpful in the diagnosis of acute group A streptococcal sore throat [72,73]. Anti-DNase B provides useful evidence of invasive disease but because serial tests are needed, they cannot be recommended for routine diagnosis in sore throat [74]. We could find only one review, focused on complications of group A streptococcal pharyngitis, concluding that laboratory testing (e.g. erythrocyte sedimentation rate and C-reactive protein) might be indicated for suspected post-streptococcal adverse outcomes [75] (Table 20). Further, we found no evidence of whether clinical information combined with biomarker data provides better prognostic information for sore throat.

It is not necessary, based on current evidence, to routinely use biomarkers in the assessment of acute sore throat (C-3). Does improved diagnosis or the use of near patient tests improve antibiotic use? One of the major points of disagreement between international guidelines on the management of acute pharyngitis is related to indications of the use of rapid tests [74]. In particular, from the available guidelines, it is still not clear whether a clinical decision alone, the use of rapid tests, or a combination of clinical score with rapid tests, should drive the decision on the use of antibiotics in patients presenting in the primary-care setting with acute pharyngitis. Hence, physicians in the USA, France and Finland will generally adopt a diagnostic test to decide on treatment, while in the UK and the Netherlands the decision will be driven by the severity of the disease [74]. In the UK and the Netherlands no diagnostic tests are used at all.

A number of studies have been published on the issue since 2002. As most investigations provided results stratified according to age group, we were able to separate the available data for children (Table 21; [47,49,64]) and adults (Table 22; [47,54,71,76]). When this was not possible, studies were considered apart (Table 23; [58,78,79]). Findings in children and adults were similar. Overall, four studies indicated that the use of rapid tests (alone) could reduce antibiotic use, whereas three studies indicated that a
strategy involving a combination of clinical score and rapid test use could reduce antibiotic use.

In conclusion, there is inconsistent evidence on which diagnostic strategy is best to reduce (unnecessary) antibiotic use. A strategy based on the use of clinical scores alone may be associated with higher antibiotic use as compared with either (i) a combination of clinical score and rapid tests use; or (ii) use of rapid tests alone.

**Clinical scoring systems and rapid tests can be helpful in targeting antibiotic use (B-2).**

**Treatment**

*Are analgesics effective in sore throat?*

A systematic review [80] and six randomized-controlled trials (RCTs) [16,80–85] found that non-steroidal anti-inflammatory drugs and paracetamol are more effective than placebo for reducing acute sore throat symptoms in adults. Ibuprofen and diclofenac are slightly more effective than paracetamol for pain relief (Table 24; [4,16,80–113]).

Paracetamol and ibuprofen were the safest. In a large RCT, ibuprofen, when used in accordance with the usual contraindications, was as well tolerated as paracetamol for the short-term treatment of the pain of cold and flu symptoms and of sore throat in adults [94,95]. No trials were found comparing ibuprofen and diclofenac. A systematic review showed that ibuprofen and paracetamol are more effective than placebo for reducing acute sore throat symptoms in children [80]. Another systematic review assessed the efficacy and safety of single doses of ibuprofen and paracetamol for short-term treatment of children’s pain or fever [96]. The results did not indicate any difference between the drugs in analgesic efficacy or safety.
**TABLE 24. Evidence table for studies on treatment of acute sore throat**

<table>
<thead>
<tr>
<th>First author</th>
<th>Objective</th>
<th>Type of study</th>
<th>Evidence level</th>
</tr>
</thead>
<tbody>
<tr>
<td>Timmer [87]</td>
<td>To assess the efficacy and safety of Pelargonium sidoides for the treatment of acute respiratory infections in children and adults</td>
<td>MA</td>
<td>1A+</td>
</tr>
<tr>
<td>Shi [86]</td>
<td>To assess the efficacy and safety of Chinese herbal medicines for patients with sore throat</td>
<td>SR</td>
<td>1A+</td>
</tr>
<tr>
<td>Brickeimann [89]</td>
<td>To investigate the safety and efficacy of Throat Coat, a traditional demulcent herbal tea, in comparison with a placebo tea in the symptomatic treatment of acute pharyngitis</td>
<td>RCT</td>
<td>2A+</td>
</tr>
<tr>
<td>Gunsberger [90]</td>
<td>To examine the value of acupuncture in the treatment of such common childhood illnesses as pharyngitis, tonsillitis, and upper respiratory infections</td>
<td>ICS</td>
<td>3C–</td>
</tr>
<tr>
<td>Hubbert [91]</td>
<td>To compare the efficacy and tolerability of spray (containing a Salvia officinalis fluid extract) against placebo in the treatment of patients with acute viral pharyngitis</td>
<td>RCT</td>
<td>2B+</td>
</tr>
<tr>
<td>Rau [92]</td>
<td>To study the effectiveness of the herbal preparation (combination of Capsicum annum, Guajacum officinale and Phytolacca americana)</td>
<td>OS</td>
<td>3C+</td>
</tr>
<tr>
<td>Wiesnauer [93]</td>
<td>To study the efficacy of three plants (combination of Capsicum annum, Guajacum officinale and Phytolacca americana) used in homeopathy</td>
<td>ICS</td>
<td>3C–</td>
</tr>
<tr>
<td>Thomas [80]</td>
<td>To estimate the benefits of treatments other than antibiotics for acute sore throat, and the differences between non-antibiotic interventions and controls in patient-perceived pain of sore throat</td>
<td>SR</td>
<td>1A+</td>
</tr>
<tr>
<td>Burnett [82]</td>
<td>To determine the time to onset of pain relief from a single dose of a tablet formulation of paracetamol containing sodium bicarbonate</td>
<td>RCT</td>
<td>2A+</td>
</tr>
<tr>
<td>Gehanno [84]</td>
<td>To compare the anti-pyretic and analgesic effects of a single oral dose of dclofenac potassium 6.25, 12.5 or 25 mg with paracetamol 1000 mg and placebo in patients with fever resulting from acute febrile sore throat</td>
<td>RCT</td>
<td>2A+</td>
</tr>
<tr>
<td>Eccles [83]</td>
<td>To investigate the efficacy and safety of acetaminol (ASA) for the treatment of sore throat pain associated with upper respiratory infections</td>
<td>RCT</td>
<td>2A+</td>
</tr>
<tr>
<td>Schachtel [85]</td>
<td>To identify and compare the analgesic activity of a single flurbiprofen lozenge (2.5, 5.0 and 12.5 mg) with placebo in patients with sore throats</td>
<td>RCT</td>
<td>2A+</td>
</tr>
<tr>
<td>Watson [16]</td>
<td>To study the efficacy of flurbiprofen lozenges compared with placebo</td>
<td>RCT</td>
<td>2A+</td>
</tr>
<tr>
<td>Benrimoj [81]</td>
<td>To determine the single dose efficacy of flurbiprofen 8.75 mg lozenges in comparison with placebo, over 6 h in patients with sore throat</td>
<td>RCT</td>
<td>2A+</td>
</tr>
<tr>
<td>Bourre [86]</td>
<td>To validate a slightly modified sore throat pain model by comparing the analgesic efficacy of ibuprofen with that of paracetamol</td>
<td>RCT</td>
<td>2A+</td>
</tr>
<tr>
<td>Moore [94]</td>
<td>To identify and quantify factors associated with the occurrence of adverse events in users of analgesic drugs</td>
<td>RCT</td>
<td>2A+</td>
</tr>
<tr>
<td>Moore [95]</td>
<td>To study the tolerability of ibuprofen, aspirin and paracetamol in patients suffering from cold/flu or sore throat</td>
<td>RCT</td>
<td>2A+</td>
</tr>
<tr>
<td>Perrott [96]</td>
<td>To summarize studies testing the efficacy and safety of single-dose acetaminophen and ibuprofen for treating children’s pain or fever</td>
<td>MA</td>
<td>1A+</td>
</tr>
<tr>
<td>Hayward [97]</td>
<td>To evaluate whether systemic corticosteroids improve symptoms of sore throat in adults and children</td>
<td>MA</td>
<td>1A+</td>
</tr>
<tr>
<td>Mossad [98]</td>
<td>To test the efficacy of zinc gluconate lozenges in reducing the duration of symptoms caused by the common cold</td>
<td>RCT</td>
<td>2A+</td>
</tr>
<tr>
<td>Macknin [99]</td>
<td>To determine the efficacy of zinc gluconate lozenges treatment of colds in children and adolescents</td>
<td>RCT</td>
<td>2A+</td>
</tr>
<tr>
<td>Spinks [100]</td>
<td>To assess the benefits of antibiotics for sore throat</td>
<td>MA</td>
<td>1A+</td>
</tr>
<tr>
<td>Cooper [101]</td>
<td>To examine the available evidence regarding the diagnosis and treatment of acute GABHS pharyngitis in adult patients</td>
<td>SR</td>
<td>1A+</td>
</tr>
<tr>
<td>Sparling [102]</td>
<td>To evaluate clinical outcomes, adverse effects, antibiotic use and patient satisfaction associated with delayed antibiotic prescribing compared with immediate prescribing or no antibiotics for acute respiratory infections</td>
<td>SR</td>
<td>1A+</td>
</tr>
<tr>
<td>Altamini [103]</td>
<td>To summarize the evidence regarding the effect of 2-6 days of oral antibiotics in treating children with acute streptococcal pharyngitis, compared with a 10-day course of oral penicillin, on duration of symptoms, eradication of the organism, and recurrence and complication rates</td>
<td>MA</td>
<td>1A+</td>
</tr>
<tr>
<td>Casey [104]</td>
<td>To compare the relative efficacy of cephalosporins with that of penicillin in the treatment of GABHS tonsillopharyngitis in adults in all available RCTs</td>
<td>MA</td>
<td>1A+</td>
</tr>
<tr>
<td>Casey [105]</td>
<td>To compare the relative efficacy of cefadroxil and penicillin treatment of GABHS tonsillopharyngitis in children in all available RCTs</td>
<td>MA</td>
<td>1A+</td>
</tr>
<tr>
<td>Casey [106]</td>
<td>To compare the relative efficacy of short-course antibiotic treatment with standard 10-day treatment courses for GAS tonsillopharyngitis</td>
<td>MA</td>
<td>1A+</td>
</tr>
<tr>
<td>Ioannidis [107]</td>
<td>To compare azithromycin with other antibiotics that typically require longer treatment courses</td>
<td>MA</td>
<td>1A+</td>
</tr>
<tr>
<td>Esposito [108]</td>
<td>To evaluate the efficacy and safety of short-course cefaclor therapy in paediatric GABHS pharyngitis by comparing 5 days of treatment with a cefaclor suspension and 10 days of treatment with an amoxicillin suspension</td>
<td>RCT</td>
<td>2A+</td>
</tr>
<tr>
<td>Sakata [109]</td>
<td>To compare a 5-day course of cefadroxil-pivoxil with a 10-day course of amoxicillin and a 10-day course of cefcapene-pivoxil for the treatment of GAS pharyngitis in children</td>
<td>RCT</td>
<td>2B+</td>
</tr>
<tr>
<td>Pichichero [110]</td>
<td>To compare the amoxicillin sprinkles administered daily for 7 days with penicillin VK four times a day for 10 days in children with tonsillopharyngitis secondary to Streptococcus pyogenes</td>
<td>RCT</td>
<td>2A+</td>
</tr>
<tr>
<td>Gerber [111]</td>
<td>To compare the effectiveness of a short (5-day) course of penicillin V potassium with the conventional 10-day oral administration of this antibiotic</td>
<td>RCT</td>
<td>2B+</td>
</tr>
<tr>
<td>Schwartz [112]</td>
<td>To evaluate the effect of duration of orally administered penicillin V potassium on the bacteriological and clinical cure of GAS pharyngitis</td>
<td>RCT</td>
<td>2A+</td>
</tr>
<tr>
<td>Stromberg [4]</td>
<td>To investigate the possibility of decreasing the length of treatment of GAS pharyngotonsillitis by comparing the bacteriological and clinical outcomes of a 5-day course of penicillin V with those of a 10-day course</td>
<td>RCT</td>
<td>2A+</td>
</tr>
<tr>
<td>Zwart [113]</td>
<td>To assess whether treatment with penicillin for 3 days and the traditional treatment for 7 days were equally as effective at accelerating resolution of symptoms in patients with sore throat compared with placebo</td>
<td>RCT</td>
<td>2A+</td>
</tr>
</tbody>
</table>

GABHS, group A β-haemolytic streptococcus; GAS, group A streptococcus; ICS, interventional cohort study; MA, meta-analysis; OS, observational study; RCT, randomized controlled trial; SR, systematic review.

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Either ibuprofen or paracetamol are recommended for relief of acute sore throat symptoms (A-1).

What are the indications for use of glucocorticoids in sore throat?

A systematic review and meta-analysis including eight trials showed that adults with severe or high Centor scoring sore throat would benefit from a single dose of corticosteroids in conjunction with antibiotic therapy [97]. No evidence of significant benefit was found in children. However, studies included in the systematic review were not sufficiently powered to detect adverse effects of short courses of oral corticosteroids. In addition, steroids might have a considerably smaller effect in a typical primary-care population, where most patients do not have severe or high Centor scoring sore throat [97,114]. The effect of steroids was also smaller when administered by oral route (Table 24).

Use of corticosteroids in conjunction with antibiotic therapy is not routinely recommended for treatment of sore throat. It can, however, be considered in adult patients with severe presentations, e.g. 3–4 Centor criteria (A-1).

What are the indications for use of zinc gluconate in the treatment of sore throat?

The trials on the effectiveness of zinc gluconate provided conflicting results [98,99]. In both trials patients in the zinc group had more adverse effects (Table 24). According to the Cochrane review zinc administered within 24 h of onset of symptoms reduces the duration and severity of the common cold in healthy people. However, it is difficult to make firm recommendations about the dose, formulation and duration that should be used [115].

Zinc gluconate is not recommended to be used in the treatment of sore throat (B-2).

What are the indications for complementary treatments, e.g. herbal treatments or acupuncture in sore throat?

There are no reliable data on the efficacy of alternative treatment (herbal treatment and acupuncture) on sore throat [87–93]. In a Cochrane systematic review, the efficacy of Pelargonium sidoides for the treatment of acute respiratory tract infections has been studied in two trials on sore throat [87]. However, both were excluded because of high risk of bias (Table 24).

Another systematic review on the efficacy of Chinese herbal medicine for treating sore throat included seven trials [88]. All trials were of methodologically poor quality. In particular, it was highly likely that there was selection bias or detection bias, or both, in all of the included trials [88].

One RCT looking at the effectiveness of Throat Coat, a demulcent herbal tea, in comparison with a placebo tea was carried out in a small number of patients [89]. Throat Coat was found to be more effective than placebo for short-term relief of pain in patients with acute pharyngitis. However, total pain relief over the first 30 min was not different between the two groups.

Other studies on the efficacy of herbal treatment and acupuncture included restricted samples of patients [91] or were of methodologically poor quality. These three studies [90,92,93] did not randomize patients between treatment arms, failing to minimize the effects of selection bias on study results. In the study by Rau, liquid or tablet formulation of a herbal compound of Phytolacca, Guajacum and Capsicum were compared. In the study by Wiesenauer, combination of three plant substances (Phytolacca americana, Guajacum officinale, Capsicum annuum) was used in either solid (tablet) or liquid (drop) formulation. Efficacy is hard to judge from these studies as they were not placebo-controlled.

There is inconsistent evidence of herbal treatments and acupuncture as treatments for sore throat (C-1 to C-3).

What is the average benefit from antibiotics and which groups of patients benefit from antibiotic treatment?

A Cochrane systematic review and meta-analysis included 27 RCTs assessing the benefits of antibiotics in the management of sore throat [100]. There was a beneficial effect of antibiotics in reducing the incidence of rheumatic fever and acute glomerulonephritis following an episode of sore throat. However, this effect was present only in trials conducted in the 1950s and 1960s, during which time the rates of these complications (especially acute rheumatic fever) were much higher than now. The absolute risk of developing these complications following sore throat is extremely small in the Western world in the first decade of the twenty-first century and although antibiotic treatment of higher-risk patients is justified (those with previous rheumatic fever) antibiotic treatment of lower-risk patients to prevent non-suppurative complications is not justified [101] (Table 24).

Antibiotics reduced the incidence of acute otitis media and quinsy (peritonsillar abscess), but did not reduce the incidence of acute sinusitis in the Cochrane meta-analysis. However, the relative benefit exaggerates the absolute benefit because the event rates of suppurative complications are low. The number needed to treat to benefit was 27 or higher to prevent one case of quinsy [100,101]. In modern primary-care settings the number needed to treat to benefit is between 50 and 200 [113,114].

Sore throat should not be treated with antibiotics to prevent the development of rheumatic fever and acute glomerulonephritis in low-risk patients (A-1). The prevention
of suppurative complications is not a specific indication for antibiotic therapy in sore throat (A-1). Clinicians do not need to treat most cases of acute sore throat to prevent quinsy, acute otitis media, cervical lymphadenitis, mastoiditis or acute sinusitis (A-3).

Do antibiotics relieve symptoms in sore throat? Antibiotics have a modest beneficial effect over placebo in reducing the symptoms of sore throat [100]. In the Cochrane meta-analysis, antibiotics reduced symptoms of sore throat on day 3 (pooled Relative Risk 0.72, 95% CI 0.68–0.76) [54]. However, at 1 week, only the group A β-haemolytic streptococcus-positive subgroup showed a beneficial effect of antibiotics over placebo (Table 24). In trials where the Centor criteria were used there was a modest benefit of antibiotics (1–2 days) [113].

In a systematic review on appropriate antibiotic use for acute pharyngitis in adults, treatment of antibiotics within 2–3 days of symptom onset hastened symptomatic improvement by 1–2 days in patients with group A β-haemolytic streptococcal pharyngitis [101]. In the recommendations, the working group combined this information with our statement that the Centor criteria are helpful in assessing the presence of a bacterial pharyngitis. It is not necessary to start antibiotics immediately. A Cochrane review including ten RCTs compared delayed antibiotics (more than 48 h after the initial consultation) with antibiotics used immediately or no antibiotics for acute respiratory tract infections [102]. No significant differences were found in complication rates for the three prescribing strategies. In children, only one RCT of sufficient size and quality was performed, showing no relevant effects [116]. Antibiotics should not be used in patients with less severe presentation of sore throat, e.g. 0–2 Centor criteria, to relieve symptoms (A-1). In patients with more severe presentations, e.g. 3–4 Centor criteria, physicians should consider discussion with patients. Modest benefits of antibiotics (1–2 days), which have been observed in group A β-haemolytic streptococcus-positive patients and in patients with 3–4 Centor criteria, have to be weighed against side effects, the effect of antibiotics on the microbiota, increased antibacterial resistance, medicalization and costs (A-1). Using delayed prescribing of antibiotics is a valid option (A-1).

Which antimicrobial agent is the first choice in patients with acute sore throat? Penicillin has been the treatment of choice for group A β-haemolytic streptococcal pharyngitis for five decades and is recommended by North American and many European guidelines as first choice for acute sore throat [74]. Penicillin is chosen because of its proven efficacy, safety, narrow spectrum and low cost. Amoxicillin is often used in younger children in place of penicillin V because of taste considerations and its availability as syrup or suspension in some countries, but in older children amoxicillin is a poor first choice because of the risk of severe rash among patients with Epstein–Barr virus infection. Group A β-haemolytic streptococci have not developed resistance to any of the penicillins or shown an increase in penicillin minimal inhibitory concentrations over at least five decades [117] (Table 24). Although newer antibiotics seem to be more effective than penicillin in reducing sore throat symptoms, the differences in efficacy are not clinically important. Five systematic reviews addressed the question of whether penicillin should remain the treatment of choice. In adults, a meta-analysis of nine RCTs (2113 patients) comparing cephalosporins with penicillin (10 days) was performed [104]. The likelihood of bacteriological and clinical failure in the treatment of group A β-haemolytic streptococcal tonsillopharyngitis was two times higher for oral penicillin than for oral cephalosporins; the OR for clinical cure rate was 2.29 (95% CI 1.61–3.28) favouring cephalosporin treatment. In children, 35 trials including 7125 patients were included in a meta-analysis [105]. The OR for clinical cure rate was 2.34 (95% CI 1.84–2.97) favouring cephalosporins. Although clinical cure rates favoured cephalosporins, the magnitude of the differences in both meta-analyses was small and not clinically relevant. Major flaws of these reviews were discussed by Shulman and Gerber [118] and Bisno [119]. Another meta-analysis by the same authors [118,119] compared bacterial and clinical cure rates in children and adults with group A streptococcal tonsillopharyngitis treated with oral β-lactam or macrolide (other than azithromycin) antibiotics [106]. Twenty-two trials with 7470 patients were included in four separate analyses. Four or 5 days of cephalosporin therapy was superior to 10 days of penicillin therapy in terms of bacterial cure rate: OR 1.47 (95% CI 1.06–2.03). The overall clinical cure rate, however, was 1.35 (95% CI 0.90–2.03) and it was even lower in the studies of good quality.

A systematic review comparing efficacy and safety of azithromycin against other antibiotics for acute pharyngitis in adults and children found no evidence of differing efficacy between azithromycin and comparator agents [107]. Comparator drugs were penicillin (n = 7), clarithromycin (n = 3), cefaclor (n = 3), erythromycin (n = 1), roxithromycin (n = 1) and co-amoxiclav (n = 1), all typically prescribed for 10 days.

Apart from the aforementioned reviews, two RCTs compared efficacy of cephalosporins and amoxicillin in
children [108,109]. No significant differences in clinical cure rate were found in both trials. Another RCT compared the efficacy of amoxicillin and penicillin in children with acute streptococcal tonsillopharyngitis [110]. The clinical cure rates for amoxicillin and penicillin were 86% and 92%, respectively, confirming that amoxicillin could be an alternative regimen for the treatment of streptococcal tonsillopharyngitis in children. Penicillin and amoxicillin are also supported by their sufficient antibacterial spectrum and lower cost. Traditionally, a regimen of penicillin for 10 days was recommended for the treatment of sore throat to maximize eradication of bacteria. In western countries in 2011, penicillin is prescribed primarily to shorten the course of the sore throat and not to prevent complications. If shorter duration therapy is as effective as 10-day treatment, shortening the duration could improve compliance and reduce adverse effects. The aforementioned review by Casey and Pichichero [104] also reviewed trials comparing 5-day courses of penicillin with 10-day courses of penicillin and saw small clinical differences in outcome favouring 10 days of treatment. Another RCT assessed the clinical and bacteriological effects of a 3-day and a 7-day regimen of penicillin V in adult patients with sore throat, selected by clinical criteria [113]. Penicillin treatment for 7 days was superior to treatment for 3 days or placebo in resolving the symptoms of sore throat.

A Cochrane review and meta-analysis [103] summarized the evidence regarding the efficacy of short-duration newer antibiotics (2–6 days) compared with 10 days of oral penicillin in treating children with acute group A β-haemolytic streptococcal pharyngitis. Twenty studies were included with 13 102 cases of acute group A β-haemolytic streptococcal pharyngitis. The short-duration treatment showed slightly better clinical outcome: shorter periods of fever (mean difference −0.30 days, 95% CI −0.45 to −0.14) and throat soreness (mean difference −0.50 days, 95% CI −0.78 to −0.22); lower risk of early clinical treatment failure (OR 0.80, 95% CI 0.67–0.94), no significant difference in early bacteriological treatment failure (OR 1.08, 95% CI 0.97–1.20) or late clinical recurrence (OR 0.95, 95% CI 0.83–1.08). More side effects were seen in the short-duration treatment group (OR 1.85, 95% CI 1.55–2.21). Most of the events involved the gastrointestinal system (diarrhoea, vomiting and abdominal pain) in both treatment groups. The two lengths of treatment were difficult to compare because different types of antibiotics were compared in most trials and differences found in clinical outcomes were small.

If antibiotics are indicated, penicillin V, twice or three times daily for 10 days, is recommended (A-1). There is not enough evidence that indicates shorter treatment length.

Author contribution

Claudio Pelucchi, Larissa Grigoryan and Carlotta Galeone contributed to systematic literature review and interpretation. Susanna Esposito is expert in paediatrics. Pentti Huovinen is expert in clinical microbiology and chair of the Guideline Group. Paul Little and Theo Verheij are expert in general practice.

Transparency declaration

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Appendix: Search methods

Diagnosis

We searched the scientific literature, with restrictions according to year of publication and language, as follows:

(sore throat OR pharyngitis OR tonsillitis OR pharyngotonsillitis OR tonsillitis) AND (rapid antigen OR rapid tests OR swab OR swabs OR throat culture) AND (streptococcus OR streptococcal OR strep) AND ((English[lang]) AND (’2002’[PDat]: ’2010’[PDat]))

On 15 April 2009, we retrieved 182 papers (including 14 reviews) using PubMed. Potentially relevant articles were assessed by one reviewer, who excluded those that were not in the scope for this topic of the guideline (e.g. studies on antibiotic use, investigations focused on prognosis or on diseases other than those of the upper respiratory tract, studies that were clearly not conducted in the primary-care setting, those from developing countries, etc.) on the basis of title, abstract (when available), and keywords (MeSH...
terms). From the first selection, 113 papers were eliminated. Sixty-nine papers were selected for further consideration. Two other papers of interest were found in the Cochrane Database, and two were found by looking at the reference list of the selected papers, for a total of 73 articles (see Appendix for the full list). All of these papers were carefully considered for the development of guideline indications, though not all provided relevant information.

Prognosis—streptococci

We searched the scientific literature, with restrictions according to year of publication and language, as follows:

(“prognosis OR complication” * OR “outcome” * OR “rheumatic fever”) AND (“sore throat OR pharyngitis OR tonsillitis OR pharyngotonsillitis OR tonsillopharyngitis”) AND (“streptococcus OR streptococcal OR strep”) AND (“English[lang]”) AND (“(‘2002’[PDat]: ‘2010’[PDat])”).

On 15 September 2009, we retrieved 372 papers (including 71 reviews). Potentially relevant articles were assessed by one reviewer, who excluded those that were not in the scope for this topic of the guideline (e.g., those not focused on upper respiratory tract infections, studies on treatment or diagnosis, investigations from developing countries, studies on socio-economic costs, etc.) on the basis of title, abstract (when available), and keywords (MeSH terms). From the first selection, 327 papers were eliminated. Forty-five papers were selected for further consideration. Two further articles were retrieved by looking at reference lists of the papers selected for consideration (see Appendix for the full list). All of these papers were carefully considered for the development of guideline indications, though not all provided relevant information.

Prognosis—Mycoplasma pneumoniae or Chlamydia pneumoniae

We searched the scientific literature with a specific string for M. pneumoniae or C. pneumoniae infections, with restrictions according to language but not year of publication, as follows:

(“prognosis OR complication” * OR “outcome” * OR “rheumatic fever”) AND (“sore throat OR pharyngitis OR tonsillitis OR pharyngotonsillitis OR tonsillopharyngitis”) AND (“M. pneumoniae OR C. pneumoniae”) AND (“English[lang]”).

On 15 September 2009, we retrieved 295 papers (including 71 reviews). Potentially relevant articles were assessed by one reviewer, who excluded those that were not in the scope for this topic of the guideline (e.g., those focused on other agents involved in upper respiratory tract infections, studies on treatment or diagnostic tests, studies on socio-economic costs, reports of outbreaks, etc.) on the basis of title, abstract (when available), and keywords (MeSH terms). From the first selection, 24 papers were eliminated. Nineteen papers were selected for further consideration (see Appendix for the full list). All of these papers were carefully considered for the development of guideline indications, though not all provided relevant information.

Infection with group C or group G streptococci

We searched the scientific literature, with restrictions according to language and year of publication (limited to studies published from 1980 onwards), as follows:

(“sore throat OR pharyngitis OR tonsillitis OR pharyngotonsillitis OR tonsillopharyngitis”) AND (“(C) OR (G)”) AND (“group”) AND (“streptococcus OR streptococcal OR strep”) AND (“English[lang]”).

On 15 September 2009, we retrieved 295 papers (including 27 reviews). Potentially relevant articles were assessed by one reviewer, who excluded those that were not in the scope for this topic of the guideline (mostly, those investigating group A streptococci, studies not focused on upper respiratory tract infections, studies on treatment, molecular and mechanistic studies) on the basis of title, abstract (when available), and keywords (MeSH terms). From the first selection, 233 papers were eliminated, and 62 papers were selected for further consideration (see Appendix for the full list). All of these papers were carefully considered for the development of guideline indications, though not all provided relevant information.

Treatment

We searched the scientific literature for studies conducted in the primary-care setting, with restrictions according to language (English), and excluding studies conducted in developing countries, using the following search strategy (combined MeSH and text word search) and abstract appraisal criteria:

#1 sore throat
#2 pharyngitis
#3 tonsillitis
#4 pharyngotonsillitis
#5 tonsillopharyngitis
#6 nasopharyngitis
#7 #1 OR #2 OR #3 OR #4 OR #5 OR #6
#8 complementary treatment OR complementary therapies OR complementary medicine
#9 alternative treatment OR alternative treatments OR alternative medicine OR traditional medicine
#10 phytotherapy OR herbal OR herb OR herbs
#11 medicinal plant OR medicinal plants
Appendix – List of selected references

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70. McIsaac WJ, Goel V, To T, Permaul JA, Low DE. Effect on antibiotic prescribing of repeated clinical prompts to use a sore throat score: lessons from a failed community intervention study. Year: 2002 – from Cochrane Database.
71. Goldfarb J. What is the best way to diagnose streptococcal pharyngitis? (Brief record) Centre for Reviews and Dissemination. Year: 2002 – from Cochrane Database.

Prognosis – streptococci


**Prognosis – atypical bacteria**


**Infection with group C or group G streptococci**


4. Amess JA, O’Neill W, Giorlariabhagh CN, Dytrich JK. A six-month audit of the isolation of *Fusobacterium necrophorum* from patients

**Treatment**

68. Thomas M, Del MC, Glasziou P. How effective are treatments other than antibiotics for acute sore throat? Br J Gen Pract 2000; 50: 817–820.