### ANHANG B

#### Evidenztabellen – Aggregierte Evidenz

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<tr>
<th>Referenz</th>
<th>Eingeschlossene Studien</th>
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<th>Ergebnisse Zusammenfassung</th>
<th>Datenqualität</th>
<th>Erläuterungen</th>
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<tr>
<td>Aalbers J, O’Brien KK, Chan WS, et al. Predicting streptococcal pharyngitis in adults in primary care: a systematic review of the diagnostic accuracy of symptoms and signs and validation of the Centor score. <em>BMC Med</em> 2011;9:67. doi:10.1186/1741-7015-9-67</td>
<td>Search: PubMed was searched from January 1966 to 26 July 2010 and EMBASE from January 1980 to 26 July 2010. Literature: A total of 21 studies incorporating 4,839 patients were included in the meta-analysis on diagnostic accuracy of signs and symptoms.</td>
<td>1</td>
<td>10 + 1 partial yes</td>
<td>As a decision rule for considering antibiotic prescribing (score ≥ 3), the Centor score has reasonable specificity (0.82, 95% CI 0.72 to 0.88) and a post-test probability of 12% to 40% based on a prior prevalence of 5% to 20% Pooled calibration shows no significant difference between the numbers of patients predicted and observed to have GABHS pharyngitis across strata of Centor score (0-1 risk ratio (RR) 0.72, 95% CI 0.49 to 1.06; 2-3 RR 0.93, 95% CI 0.73 to 1.17; 4 RR 1.14, 95% CI 0.95 to 1.37).</td>
<td>gut</td>
<td>The results were heterogeneous and suggest that individual signs and symptoms generate only small shifts in post-test probability. Individual signs and symptoms are not powerful enough to discriminate GABHS pharyngitis from other types of sore throat. The Centor score is a well calibrated clinical prediction rule for estimating the probability of GABHS pharyngitis. The Centor score can enhance appropriate prescribing of antibiotics but should be used with caution in low prevalence settings of GABHS pharyngitis such as primary care.</td>
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<td>Altamimi S, Khalil A, Khalaiwi KA, et al. Short-term late-generation antibiotics versus longer term penicillin for acute streptococcal pharyngitis in children. <em>Cochrane Database Syst Rev</em> 2012;:Cd004872. doi:10.1002/14651858.CD004872.pub3</td>
<td>Search: of Controlled Trials (CENTRAL) accessed 3 April 2012, MEDLINE to March week 3, 2012) and EMBASE to April 2012). Literature: We included 20 studies (RCTs) with 13,102 cases of acute GABHS pharyngitis.</td>
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<td>Compared to standard duration treatment, the short duration treatment studies had shorter periods of fever (mean difference (MD) -0.30 days, 95% confidence interval (CI) -0.45 to -0.14) and throat soreness (MD -0.50 days, 95% CI -0.78 to -0.22); lower risk of early clinical treatment failure (odds ratio (OR) 0.80, 95% CI 0.67 to 0.94); no significant difference in early bacteriological treatment failure (OR 1.08, 95% CI 0.97 to 1.20) or late clinical recurrence (OR 0.95, 95% CI 0.83 to 1.08). However, the overall risk of late bacteriological recurrence was worse in the short duration</td>
<td>schwach</td>
<td>A significant number of studies were at high risk for selection bias, performance bias, detection bias and attrition bias. Most studies used uncenconcled randomization methods and were not blinded. The majority of the results from one study to the other however, were consistent. Three to six days of oral antibiotics had comparable efficacy compared to the standard</td>
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<td>Study</td>
<td>Search</td>
<td>Treatment Studies (OR 1.31, 95% CI 1.16 to 1.48), although no significant differences were found when studies of low dose azithromycin (10 mg/kg) were eliminated (OR 1.06, 95% CI 0.92 to 1.22).</td>
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<td>Burton MJ, Glasziou PP, Chong LY, et al.</td>
<td>Tonsillectomy or adenotonsillectomy versus non-surgical treatment for chronic/recurrent acute tonsillitis. Cochrane Database Syst Rev 2014;:Cd001802. doi:10.1002/14651858.CD001802.pub3</td>
<td>Good information about the effectiveness of adenotonsillectomy is only available for the first year following surgery in children and for a shorter period (five to six months) in adults. Children who had an adenotonsillectomy had an average of three episodes of sore throats (of any severity) in the first postoperative year, compared to 3.6 episodes in the control group; a difference of 0.6 episodes (95% confidence interval (CI) -1 to -0.1; moderate quality evidence). Adenotonsillectomy leads to a reduction in the number of episodes of sore throat and days with sore throat in children in the first year after surgery compared to (initial) non-surgical treatment. Children who were more severely affected were more likely to benefit as they had a small reduction in moderate/severe sore throat episodes.</td>
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<td>Cohen JF, Bertille N, Cohen R, et al.</td>
<td>Rapid antigen detection test for group A streptococcus in children with pharyngitis. In: The Cochrane Collaboration, ed. Cochrane Database of Systematic Reviews.</td>
<td>In studies in which all participants underwent both RADT and throat culture (105 test evaluations; 58,244 participants; median prevalence of participants with GAS was 29.5%), RADT had a summary sensitivity of 85.6%; 95% confidence interval (CI) 83.3 to 87.6 and a summary specificity of 95.4%; 95% CI 94.5 to 96.2.</td>
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**Duration 10-day course of oral penicillin in treating children with acute GABHS pharyngitis. In areas where the prevalence of rheumatic heart disease is still high, our results must be interpreted with caution.**

| Search: | Schwach bis gut | Schwach | The overall methodological quality of included studies was poor, mainly because many studies were at high risk of bias regarding patient selection and the reference standard used (in 73% and 43% of test evaluations, respectively. |
We included 98 unique studies in the review (116 test evaluations; 101,121 participants)

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

Search: We searched the Cochrane Central Register of Controlled Trials (CENTRAL 2014, Issue 11), which includes the Cochrane Acute Respiratory Infections Group’s Specialised Register, MEDLINE (1946 to November week 3, 2014), EMBASE (2010 to December 2014) and Web of Science (1985 to December 2014).

There was substantial heterogeneity in sensitivity across studies; specificity was more stable.

Whether or not RADT can be used as a stand-alone test to rule out GAS will depend mainly on the epidemiological context. The sensitivity of EIA and OIA tests seems comparable.


There is moderate quality evidence that interventions that aim to facilitate shared decision making reduce antibiotic use for ARIs in primary care (immediately after or within six weeks of the consultation), compared with usual care, from 47% to 29%: risk ratio (RR) 0.61, 95% confidence interval (CI) 0.55 to 0.68. Reduction in antibiotic prescribing occurred without an increase in patient-initiated re-consultations (RR 0.87, 95% CI 0.74 to 1.03, moderate quality evidence) or a decrease in patient satisfaction with the consultation (OR 0.86, 95% CI 0.57 to 1.30, low quality evidence).

The main risk of bias came from participants in most studies knowing whether they had received the intervention or not, and we downgraded the rating of the quality of evidence because of this.

There is moderate quality evidence that interventions that aim to facilitate shared decision making reduce antibiotic use for ARIs in primary care.
| de Bont EG, Alink M, Falkenberg FC, et al. Patient information leaflets to reduce antibiotic use and reconsultation rates in general practice: a systematic review. *BMJ Open* 2015;5:e007612. doi:10.1136/bmjopen-2015-007612 | Search: PubMed and EMBASE bis April 2014 | 1 | 8 + 1 partial | Three of four studies presented data on antibiotic use and showed significant reductions of prescriptions in leaflet groups with a relative risk (RR) varying from 0.53 (0.40 to 0.69) to 0.96 (0.83 to 1.11). Effects on reconsultation varied widely. One large study showed lower reconsultation rates (RR 0.70 (0.53 to 0.91), two studies showed no effect, and one study showed increased reconsultation rates (RR 1.53 (1.03 to 2.27)). schwach | Studies were too heterogenic to perform a meta-analysis. We identified a high risk of bias for all studies for failing to blind participants and personnel. Results on reconsultation rates for similar symptoms vary, with a tendency toward fewer reconsultations when patients are provided with a leaflet. |
| De Paor M, O’Brien K, Fahey T, et al. Antiviral agents for infectious mononucleosis (glandular fever). *Cochrane Database Syst Rev* 2016;12:Cd011487. doi:10.1002/14651858.CD011487.pub2 | Search: Cochrane Central Register of Controlled Trials (CENTRAL) bis März 2016. MEDLINE, Embase, CINAHL, LILACS, Web of Science bis April 2016. | 1 | 10 | Benefits and side effects of antiviral treatment for patients with infectious mononucleosis vs. placebo 1) Time to clinical recovery (doctor judgement) ☒5 Tage (95%CI 8,04-1,08) weniger in der Interventionsgruppe 2) Time to clinical recovery (patient judgement) ☒6 Tage (95%CI 26,23-15,05) weniger in der Interventionsgruppe 3) Adverse events and side effects Nur narrativer Bericht in 5 RCTs, Autoren waren unsicher ob Nebenwirkungen durch Erkrankung oder Medikation 4) Duration of lymphadenopathy ☒9 Tage (95%CI 11,75-6,14) weniger in der Interventionsgruppe 5) Development of complications of infectious mononucleosis 3 Studien berichteten narrativ von Komplikationen. Kein Unterschied in der Inzidenz zwischen Kontroll- und Interventionsgruppe 6) Viral shedding Viral shedding was suppressed while on treatment, keine Quantifizierung. 7) Days missing from school / work schwach | The quality of the evidence is very low. The majority of included studies were at unclear or high risk of bias and so questions remain about the effectiveness of this intervention. The effectiveness of antiviral agents (acyclovir, valomaciclovir and valacyclovir) in acute IM is uncertain. Alongside the lack of evidence of effectiveness, decision makers need to consider the potential adverse events and possible associated costs, and antiviral resistance. |

Search: CENTRAL, MEDLINE, EMBASE, CINAHL, DARE, LILACS, AMED, PsychINFO, IRAN MedEx, Scopus bis Februar 2013

Literature: Seven reviews containing 44 relevant randomized controlled trials were included.

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<td></td>
<td>Six trials (2114 patients) assessed GI bleeding and/or abdominal pain and showed no significant differences between corticosteroids and placebo (1.5% vs. 1.8%, respectively). Various behavioural effects and hypertension/blood pressure were measured in four trials each (838 and 1617 patients, respectively), with no significant differences reported. None of the trials reported deaths in any of the treatment groups. Based on 17 trials (2056 patients), there were significantly fewer admissions at day 1 with corticosteroids (risk differences=−0.11, 95% confidence interval −0.18 to −0.05; Peto odds ratios=0.63, 95% confidence interval 0.52 to 0.78). Corticosteroids resulted in over 8 fewer hours in hospital compared with placebo (mean differences=−8.49 hours, 95% confidence interval−1.76 to−3.23). There were significantly fewer relapses leading to hospitalization with corticosteroids (Peto odds ratios 0.42, 95% confidence interval 0.23 to 0.76). We did not find any increase in hospital admission at day 1, length of stay or rehospitalization in the other acute respiratory conditions.</td>
<td>Schwach bis gut</td>
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Thus, the overall quality of the safety data available to us was less than desirable, even when the trials were considered well designed from the perspective of the primary efficacy aim. Practitioners may prescribe systemic corticosteroids in otherwise healthy children when indicated for the management of acute respiratory conditions (i.e. infections or asthma exacerbations) with minimal concern about short-term adverse effects.

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Search: Medline, the Cochrane Database of Systematic Reviews, DARE, Health Technology Assessment

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<td>8 (1 partial yes)</td>
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<td>Cold-steel tonsillectomy versus diathermy tonsillectomy: The use of diathermy in tonsillectomy in adults or children is associated with reduced rates of primary bleeding but...</td>
<td>Schwach</td>
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Low-quality evidence Further research is very likely to have an important impact on our confidence in the estimate.
Cold-steel tonsillectomy versus diathermy tonsillectomy:
5 systematic reviews of RCTs, 9 RCTs

Tonsillectomy versus no surgery in children:
three systematic reviews (search dates 1998, 2003, and 2008), [17] [18] [19] which identified seven RCTs in total. We found one subsequent RCT.

Tonsillectomy versus no surgery in adults:
One systematic review (search date 2008), [18] which identified one RCT in adults.

increased rates of secondary and overall bleeding.
• Overall, cold-steel dissection tonsillectomy seems to have the lowest rates of postoperative haemorrhage and pain, although it is associated with slightly increased intra-operative bleeding.
• Adequate training in the appropriate use of diathermy during tonsillectomy is important. In deciding which method to apply, the surgeon should consider the underlying characteristics of patients, as well as the relative importance of secondary compared with primary bleeding and intra-operative blood loss compared with postoperative pain.

Tonsillectomy versus no surgery in children:
• In children, the effectiveness of tonsillectomy has to be judged against the potential harms.
• Tonsillectomy is more beneficial in children with severe symptoms, while in populations with a low incidence of tonsillitis, the modest benefit may be outweighed by the morbidity associated with the surgery.
• Tonsillectomy is associated with intra-operative and postoperative morbidity, including haemorrhage, while antibiotics are associated with adverse effects, such as rash.

Tonsillectomy versus no surgery in adults:
• We found limited evidence from one small RCT that surgery may reduce

Search: CENTRAL bis June 2012, MEDLINE bis Mai 2012), EMBASE bis Juni 2012, DARE) and the NHS Health Economics Database bis Juni 2012.

Literature: We included eight trials involving 743 participants (369 children and 374 adults). All trials gave antibiotics to both placebo and corticosteroid groups; no trials assessed corticosteroids as standalone treatment for sore throat.

In addition to any effect of antibiotics and analgesia, corticosteroids increased the likelihood of complete resolution of pain at 24 hours by more than three times (risk ratio (RR) 3.2, 95% confidence interval (CI) 2.0 to 5.1, P < 0.001, I2 statistic 44%) and at 48 hours by 1.7 times. Fewer than four people need to be treated to prevent one person continuing to experience pain at 24 hours. Corticosteroids also reduced the mean time to onset of pain relief and the mean time to complete resolution of pain by 6 and 14 hours, respectively, although significant heterogeneity was present. At 24 hours, pain (assessed by visual analogue scores) was reduced by an additional 14% by corticosteroids. No difference in rates of recurrence, relapse or adverse events were reported for participants taking corticosteroids compared to placebo, although reporting of adverse events was poor.

Limitations of the review include the absence of any trials set in Europe and the fact that only two trials addressed the question in children. As all the included trials also gave antibiotics to all participants, we recommend that future research should examine the benefit of corticosteroids in patients who are not also taking antibiotics.

Oral or intramuscular corticosteroids, in addition to antibiotics, increase the likelihood of both resolution and improvement of pain in patients with sore throat. Further trials assessing corticosteroids in the absence of antibiotics and in children are warranted.


Clinical Evidence search and appraisal January 2010.


What are the effects of interventions to reduce symptoms of acute infective sore throat?

Analgesics versus placebo:

- Paracetamol seems to effectively reduce the pain of acute infective sore throat after a single dose, or regular doses over 2 days.
- We found no direct information from RCTs about other analgesics in the treatment of people with sore throat.

High-quality evidence for Antibiotics versus placebo concerning prevention of complications

Moderate-quality evidence for Analgesics

High-quality evidence: Further research is very unlikely to change our confidence in the estimate of effect.

Moderate-quality evidence: Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.
<table>
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<th>Interventions</th>
<th>Effects</th>
<th>Literature: What are the effects of interventions to reduce symptoms of acute infective sore throat?</th>
<th>NSAIDs versus placebo:</th>
<th>Antibiotics versus placebo:</th>
<th>Corticosteroids versus placebo in people receiving antibiotics:</th>
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<td>Analgesics versus placebo:</td>
<td>One systematic review (search date 1999, 3 RCTs, 312 people with acute moderate to severe sore throat for up to 4 days), one subsequent RCT comparing paracetamol (acetaminophen) versus placebo. No systematic review or RCTs of other analgesics in people with sore throat.</td>
<td>NSAIDs may reduce the pain of sore throat at 24 hours or less, and at 2 to 5 days. NSAIDs are associated with gastrointestinal and renal adverse effects.</td>
<td>Antibiotics can reduce the proportion of people with symptoms associated with sore throat at 3 days. Reduction in symptoms seems greater for people with positive throat swabs for Streptococcus than for people with negative swabs. Antibiotics are generally associated with adverse effects such as nausea, rash, vaginitis, and headache, and widespread use may lead to bacterial resistance.</td>
<td>Corticosteroids added to antibiotics may reduce the severity of pain from sore throat in adults compared with antibiotics alone. Effects in children are uncertain. Most trials used a single dose. However, data from use of corticosteroids in other disorders</td>
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hours or less. Six RCTs (697 people) assessed the effects of NSAIDs over >24 hours.

**Antibiotics versus placebo:**
One systematic review (search date 2008, 27 randomised or quasi-randomised trials, 12,835 people with sore throat, severity unclear) comparing antibiotics versus placebo.

**Corticosteroids versus placebo in people receiving antibiotics:**
One systematic review (search date 2008, 8 RCTs, 743 people [369 children, 374 adults] (47% had exudative sore throat and 44% were positive for group A beta-haemolytic streptococcus)
In 5 RCTs, (all participants also received antibiotics) 3 RCTs (participants received antibiotics if direct antigen testing or culture for Streptococcus was positive), 2 RCTs included only children, 3 included only adults, and 3 included both.

suggest that longterm use of corticosteroids is associated with serious adverse effects.

**Probiotics versus placebo:**
- Super-colonisation with Streptococcus isolated from healthy individuals apparently resistant to infections from Respiratory disorders (acute)
- Streptococcus may reduce recurrence of sore throat, although there is currently no evidence to suggest it may treat symptoms of acute sore throat.
- We found no direct information about other probiotics, or about the effects of probiotics on the symptoms of acute sore throat.

**What are the effects of interventions to prevent complications of acute infective sore throat?**

**Antibiotics versus placebo:**
- Antibiotics may reduce suppurative and non-suppurative complications of group A beta-haemolytic streptococcal pharyngitis, although non-suppurative complications are rare in industrialised countries.
- Antibiotics increase the risk of adverse effects, including gastrointestinal upset, rash, and vaginitis. Widespread antibiotic use may lead to bacterial resistance to antibiotics.
Probiotics versus placebo:
One systematic review [6] (search date 1999, 2 RCTs and one subsequent RCT comparing super-colonisation with Streptococcus grown from a child resistant to infections from Streptococcus versus placebo (see comment below). We found no RCTs of other probiotics.

What are the effects of interventions to prevent complications of acute infective sore throat?

Antibiotics versus placebo:
One systematic review (search date 2008, 27 randomised or quasi-randomised trials, 12,835 people with sore throat, severity unclear) comparing antibiotics versus placebo to prevent complications of sore throat infection.


Search: MEDLINE, EMBASE, Cochrane Database of Systematic Reviews bis Dezember 2008.

Literature:

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<td>All RCTs found a statistically significant faster reduction of pain or complete pain relief from steroid use compared with placebo. The trials used different steroids (dexamethasone, betamethasone, prednisone), and most participants had received antibiotics at least initially. Analgesic medication, such as</td>
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Steroids are effective in relieving pain in acute pharyngitis. Although no serious adverse effects were observed, the benefits have to be balanced with possible adverse drug effects.
| Lennon D, Kerdemelidis M, Arroll B. Meta-analysis of trials of streptococcal throat treatment programs to prevent rheumatic fever. *Pediatr Infect Dis J* 2009;28:e259–64. DOI:10.1097/INF.0b013e3181a8e12a | Our review found 8 relevant randomized controlled trials (RCTs) with a total of 806 patients. | acetaminophen, was allowed in all studies, but this factor was not always controlled. No serious adverse side effects were reported. | schwach | Many studies were poor quality. Title and available abstracts of non-English studies were checked. Our view is that in communities with high rates of RF (we suggest greater than 50 per 100,000 children per year), that school- and/or community-based programs be actively considered to prevent this potentially chronic disease with significant mortality and morbidity. |
| Li S, Yue J, Dong BR, *et al.* Acetaminophen (paracetamol) for the common cold in adults. *Cochrane Database Syst Rev* 2013;.Cd008800. doi:10.1002/14651858.CD008800.pub2 | Search: CENTRAL, MEDLINE, EMBASE, CiNAHL, LILACS bis Februar. Literature: 4 RCTs involving 758 participants: All included trials were randomised, double-blind, placebo-controlled, parallel-group | Participants treated with acetaminophen had significant improvements in nasal obstruction in two of the four studies. One study showed that acetaminophen was superior to placebo in decreasing rhinorrhoea severity but was not superior for treating sneezing and coughing. Acetaminophen did not improve sore throat or malaise in two of the four studies. Two studies showed that headache and achiness improved more in the acetaminophen group than in the placebo group, while one study | schwach | We did not pool data because of heterogeneity in study designs, outcomes and time points. The studies provided sparse information about effects longer than a few hours, as three of four included studies were short trials of only four to six hours. *Acetaminophen may help relieve nasal obstruction and rhinorrhoea* |
Two studies were conducted in the US (Ryan 1987; Sperber 2000), one study in Ukraine and Russia (Bachert 2005) and one study in Australia (Graham 1990). Two studies took place in an out-patient setting, one in a Medical University, and one did not specify the setting. Studies showed no difference between the acetaminophen and placebo group. None of the included studies reported the duration of common cold symptoms. Minor side effects (including gastrointestinal adverse events, dizziness, dry mouth, somnolence and increased sweating) in the acetaminophen group were reported in two of the four studies. One of them used a combination of pseudoephedrine and acetaminophen.

| Morad A, Sathe NA, Francis DO, et al. Tonsillectomy Versus Watchful Waiting for Recurrent Throat Infection: A Systematic Review. *Pediatrics* 2017;139. doi:10.1542/peds.2016-3490 | Search: MEDLINE, Embase, Cochrane Library bis Juni 2016. Literature: Seven studies including children with ≥3 infections in the previous 1 to 3 years were included | 1 | 8 + 1 partial yes | In studies reporting baseline data, number of infections/sore throats decreased from baseline in both groups, with greater decreases in sore throat days, clinician contacts, diagnosed group A streptococcal infections, and school absences in tonsillecromized children in the short term (<12 months). Quality of life was not markedly different between groups at any time point. | Schwach bis gut | Compared with no surgery, tonsillectomy reduced utilization (clinician contacts) and missed school/work in the short term. We have low confidence in this conclusion (low strength of evidence). Throat infections, utilization, and school absences improved in the first postsurgical year in tonsillecromized children versus children not receiving surgery. Benefits did not persist over time; longer-term outcomes are limited. |

| Reveiz L, Cardona Andrès F. Antibiotics for acute laryngitis in adults. *Cochrane Database Syst Rev* Published Online First: 2015. doi:10.1002/14651858.CD004783.pub5 | Search: CENTRAL bis December 2014), MEDLINE bis November 2014), EMBASE bis December 2014, LILACS bis December 2014, BIOSIS bis December. Literature: | 1 | 13 | In one study of acute laryngitis in adults, 100 participants were randomised to receive penicillin V (800 mg twice daily for five days) or an identical placebo. A recording of each patient reading a standardised text was made at the first visit, during re-examination after one and two weeks, and at follow-up after two to six months. No significant differences were found between the groups. The trial also measured symptoms | schwach | The quality of the evidence was very low for all outcomes. We downgraded the studies because of limitations in study design or execution (risk of bias), imprecision and inconsistency of results. |
| We included three RCTs (351 participants) that had moderate to high risk of bias. | reported by participants and found no significant differences. One study investigated erythromycin for acute laryngitis in 106 adults. The mean objective voice scores measured at the first visit, at re-examination after one and two weeks, and at follow-up after two to six months did not significantly differ between the groups. At one week there were significant beneficial differences in the severity of reported vocal symptoms (slight, moderate and severe) as judged by participants (P value = 0.042). However, the rates of participants having improved voice disturbance (subjective symptoms) at one and two weeks were not significantly different among groups. Comparing erythromycin and placebo groups on the rate of persistence of cough at two weeks, the risk ratio (RR) was 0.38 (95% confidence interval (CI) 0.15 to 0.97, P value = 0.04) and the number needed to treat for an additional beneficial outcome (NNTB) was 5.87 (95% CI 3.09 to 65.55). We calculated a RR of 0.64 (95% CI 0.46 to 0.90, P value = 0.034) and a NNTB of 3.76 (95% CI 2.27 to 13.52; P value = 0.01) for the subjective voice scores at one week. A third trial from Russia included 145 patients with acute laryngitis symptoms. Participants were randomised to three treatment groups: Group 1: seven-day course of fusafungine (six times a day by inhalation); Group 2: seven-day course of fusafungine (six times a day by inhalation) plus clarithromycin (250 mg twice daily for seven days); Group 3: no treatment. Clinical cure rates were measured at days 5 ± 1, 8 ± 1 and 28 ± 2. The authors reported significant differences in the rates of clinical cure at day 5 ± 1 favouring fusafungine (one trial; 93 participants; RR 1.50, 95% CI 1.02 to 2.20; P value = 0.04) and fusafungine plus clarithromycin. | Antibiotics do not appear to be effective in treating acute laryngitis when assessing objective outcomes. They appear to be beneficial for some subjective outcomes. Erythromycin could reduce voice disturbance at one week and cough at two weeks when measured subjectively. Fusafungine could increase the cure rate at day five. |


**Literature:** 24 studies were included.

1 11, 3 partial yes The meta-analysis determined an overall sensitivity of 0.85 [95% CI, 0.84–0.87], specificity was 0.96 [95% CI, 0.96–0.97], likelihood ratio (+) 22.21 [95% CI, 15.12–32.63], and likelihood ratio (−) 0.15 [95% CI, 0.13–0.18]. The rapid antigen-detection test demonstrated a good diagnostic performance. The sensitivity ranged between 65.6% and 96.4%; specificity from 68.7%–99.3%; the positive predictive value was between 59.4%–97.4%; and the negative predictive value from 87.8%–98%.


Search: Medline, Embase, Cochrane Central Register of Controlled Trials (CENTRAL), trial registries up to May 2017.

**Literature:** 10 eligible trials enrolled 1426 individuals.

1 14 Patients who received single low dose corticosteroids (the most common: oral dexamethasone with a maximum dose of 10 mg) were twice as likely to experience pain relief after 24 hours (relative risk 2.2, 95% confidence interval 1.2 to 4.3; risk difference 12.4%; moderate quality evidence) and 1.5 times more likely to have no pain at 48 hours (1.5, 1.3 to 1.8; risk difference 18.3%; high quality). The mean time to onset of pain relief in patients treated with corticosteroids was 4.8 hours earlier (95% confidence interval −1.9 to −7.8; moderate quality) and the mean time to complete resolution of pain was 11.1 hours earlier (−0.4 to −21.8; low quality) than in those treated with placebo. The absolute pain reduction at 24 hours (visual analogue scale 0-10) was greater in patients treated with corticosteroids (mean gut Moderate to high (Complete resolution of pain at 48 hours)

The quality of included studies was measured according to Quadas’s criteria.

Rapid tests offer good accuracy for use as diagnostic method, however, these devices have to be complemented with the microbiological culture, because there are false positive and negative results.

Moderate to high quality evidence suggests the addition of one (or two) dose(s) of corticosteroids reduces the intensity and duration of pain in patients with sore throat with no increase in serious adverse effects.

**Search:** MEDLINE, EMBASE, Capus, BIOSIS, CABA, AGRICOLA, TOXCENTER, SCISEARCH, NAHL, and NAPRALET.

**Literature:**
Six clinical studies with a total of 2458 participants were included in the meta-analysis.

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<th>Study</th>
<th>Search</th>
<th>N</th>
<th>Total</th>
<th>Use of echinacea extracts was associated with reduced risk of recurrent respiratory infections (RR 0.649, 95% CI 0.545–0.774; P &lt; 0.0001).</th>
</tr>
</thead>
<tbody>
<tr>
<td>Schapowal A, Klein P, Johnston SL.</td>
<td>MEDLINE, EMBASE, Capus, BIOSIS, CABA, AGRICOLA, TOXCENTER, SCISEARCH, NAHL, and NAPRALET were searched for clinical trials that studied recurrent respiratory infections and complications on treatment with echinacea extracts in a generally healthy population.</td>
<td>1</td>
<td>10</td>
<td>schwach</td>
</tr>
</tbody>
</table>


**Search:** Medline bis November 2008.

**Literature:**
Six clinical studies with a total of 19 + 1 partial yes were included in the meta-analysis.

<table>
<thead>
<tr>
<th>Study</th>
<th>Search</th>
<th>N</th>
<th>Total</th>
<th>Use of echinacea extracts was associated with reduced risk of recurrent respiratory infections (RR 0.649, 95% CI 0.545–0.774; P &lt; 0.0001).</th>
</tr>
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<tr>
<td>Shaikh N, Leonard E, Martin JM.</td>
<td>Medline bis November 2008.</td>
<td>1</td>
<td>9 + 1 partial yes</td>
<td>schwach</td>
</tr>
</tbody>
</table>


**Use of echinacea extracts was associated with reduced risk of recurrent respiratory infections (RR 0.649, 95% CI 0.545–0.774; P < 0.0001).**

*Only high-quality studies with a total Jadad Score of C4 were selected for analysis to control the risk of bias.*

*Use of echinacea extracts was associated with reduced risk of recurrent respiratory infections.*
Of the 266 articles retrieved, 29 met all inclusion criteria. The prevalence of GAS carriage among well children with no signs or symptoms of pharyngitis was 12% (95% CI: 9%–14%).


Search: MEDLINE and EMBASE bis April 2011. Literature: 38 articles with data on individual symptoms and signs and 15 articles with data on prediction rules met all inclusion criteria. 9 + 1 partial yes

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.

Unklar (keine RCTs)

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. A total quality score was not calculated. Rather, we assessed each of the study quality indicators separately.

**Symptoms and signs, either individually or combined into prediction rules, cannot be used to definitively diagnose or rule out streptococcal pharyngitis.**


Search: CENTRAL, MEDLINE, EMBASE bis Juli 2013. Literature: 27 RCTs with 12,835 cases of sore throat. 10

1. **Symptoms**
   Throat soreness and fever were reduced by about half by using antibiotics. The greatest difference was seen at day three. The number needed to treat to benefit (NNTB) to prevent one sore throat at day three was less than six; at week one it was 21.

2. **Non-suppurative complications**
   The trend was antibiotics protecting against acute glomerulonephritis but there were too few cases to be sure. Several studies found antibiotics reduced acute rheumatic fever by more than two-thirds within one month (risk ratio (RR) 0.27; 95% confidence interval (CI) 0.12 to 0.60). Antibiotics reduced the incidence of acute otitis media within 14 days (RR 0.30; 95% CI 0.15 to 0.58); acute sinusitis within 14 days

Gut (moderate to high according to GRADE)

The quality of the included studies was moderate to high. However, there were very few recent trials included in the review (only three since 2000), hence it is unclear if changes in bacterial resistance in the community may have affected the effectiveness of antibiotics.

**Antibiotics confer relative benefits in the treatment of sore throat. However, the absolute benefits are modest. Protecting sore throat sufferers against suppurative and non-suppurative complications in high-income countries requires treating many with antibiotics for**
4. Subgroup analyses of symptom reduction

Antibiotics were more effective against symptoms at day three (RR 0.58; 95% CI 0.48 to 0.71) if throat swabs were positive for *Streptococcus*, compared to RR 0.78; 95% CI 0.63 to 0.97 if negative. Similarly at week one the RR was 0.29 (95% CI 0.12 to 0.70) for positive and 0.73 (95% CI 0.50 to 1.07) for negative *Streptococcus* swabs.

Gut (Moderate according to GRADE).

The results for clinical outcomes were based on moderate-quality evidence according to GRADE assessment.

There were no differences between immediate, delayed, and no antibiotics for many symptoms including fever, pain, feeling unwell, cough, and runny nose. The only differences were small and favoured immediate antibiotics for relieving pain, fever, and runny nose.

Compared to no antibiotics, delayed antibiotics led to a small reduction in how long pain, fever, and cough persisted in people with colds. There was little difference in antibiotic adverse effects, and no significant difference in complications.


doi:10.1002/14651858.CD004417.pub5


Literature: This review included 11 RCTs with a total of 3555 participants.

Delayed antibiotics resulted in a significant reduction in antibiotic use compared to immediate antibiotics prescription (odds ratio (OR) 0.04, 95% confidence interval (CI) 0.03 to 0.05). However, a delayed antibiotic was more likely to result in reported antibiotic use than no antibiotics (OR 2.55, 95% CI 1.59 to 4.08) (moderate quality evidence - GRADE assessment).

Patient satisfaction favoured delayed over no antibiotics (OR 1.49, 95% CI 1.08 to 2.06). There was no significant difference in patient satisfaction between delayed antibiotics and immediate antibiotics (OR 0.65, 95% CI 0.39 to 1.10).

Stewart EH, Davis B, Clemans-Taylor BL, et al. *Rapid antigen group A streptococcus test to diagnose pharyngitis: a Gut* (In 48 (81.4%) studies partial verification bias was avoided, in 47 (79.7%) studies differential verification bias was avoided, and in 47 (79.7%) studies incorporation
<table>
<thead>
<tr>
<th>Study Title</th>
<th>Search</th>
<th>Literature</th>
<th>Patients</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Systematic Review and Meta-analysis. PLoS One 2014;9:e111727. doi:10.1371/journal.pone.011727</strong></td>
<td>SciELO, CINAHL, guidelines 2000 bis 2012.</td>
<td>Literature: 59 studies were included: encompassing 55,766 patients. 43 studies (18,464 patients) fulfilled the higher quality definition.</td>
<td></td>
<td>The pooled sensitivity was 86% (95% CI, 79–92%) and the pooled specificity was 92% (95% CI, 88–95%). For the higher quality immunochromatographic methods in the adult population (1,216 patients), the pooled sensitivity was 91% (95% CI, 87 to 94%) and the pooled specificity was 93% (95% CI, 92 to 95%); however, heterogeneity was modest for sensitivity (I² 61%) and specificity (I² 72%). For enzyme immunoassay in the adult population (333 patients), the pooled sensitivity was 86% (95% CI, 81–91%) and the pooled specificity was 97% (95% CI, 96 to 99%); however, heterogeneity was high for sensitivity and specificity (both, I² 88%).</td>
</tr>
<tr>
<td>Thai TN, Dale AP, Ebell MH. Signs and symptoms of Group A versus Non-Group A strept throat: A meta-analysis. Fam Pr Published Online First: 13 October 2017. doi:10.1093/fampra/cmx072</td>
<td>Search: MEDLINE bis März 2016.</td>
<td>Literature: 8 studies met the inclusion criteria: 4 studies only children, one enrolled only adults and three enrolled both children and adults. Settings: hospital emergency department, outpatient department, general practice or a healthcare centre. All eight studies used a prospective cohort design with throat culture as the reference standard.</td>
<td>10</td>
<td>Eight studies met our inclusion criteria. Tonsillar exudate had the highest LR+ for both GAS and non-GAS pharyngitis (1.53 versus 1.71). The confidence intervals of sensitivity, LR+, LR–, and DOR for all signs, symptoms, and the Centor score between two groups overlapped, with the relative difference between sensitivities within 15% for arthralgia or myalgia, fever, injected throat, tonsillar enlargement, and tonsillar exudate. Larger differences in sensitivities were observed for sore throat, cervical adenopathy, and lack of a cough, although the difference for lack of a cough largely due to a single outlier.</td>
</tr>
<tr>
<td>Thompson M, Vodicka TA, Blair PS, et al. Duration of symptoms of respiratory tract infections in children: systematic review. BMJ</td>
<td>Search: PubMed, DARE, and CINAHL bis Juli 2012.</td>
<td>Literature:</td>
<td>19</td>
<td>In 90% of children, earache was resolved by seven to eight days, sore throat between two and seven days, croup by two days, bronchiolitis by 21 days, acute cough by 25 days, common cold by 15 days, and non-specific respiratory tract infections symptoms by 16 days.</td>
</tr>
</tbody>
</table>

**Bias was avoided. The funnel plot was asymmetric and the regression line was not vertical, suggesting the presence of publication bias.**

**RAST immunochromatographic methods appear to be very sensitive and highly specific to diagnose group A streptococcal pharyngitis among adults but not in children.**

**There are several limitations in this review. Only high quality studies reporting signs, symptoms, or the Centor score for both GAS and non-GAS pharyngitis were selected, which improved validity but limited the number of studies included in our review.**

**Signs and symptoms of patients with GAS and non-GAS pharyngitis are generally similar. No signs or symptoms clearly distinguish GAS from non-GAS infection. Further work is needed to determine whether Group C streptococcus is a pathogen that should be treated.**

**The included studies were inevitably clinically heterogeneous in many aspects. The definition of the respiratory tract infection syndromes differed (or were poorly defined) in some studies,**
Of 22,182 identified references, 23 trials and 25 observational studies met inclusion criteria. The durations of earache and common colds are considerably longer than current guidance given to parents in the United Kingdom and the United States; for other symptoms such as sore throat, acute cough, bronchiolitis, and croup the current guidance is consistent with our findings. Problem der Datenvermischung von Kindern und Erwachsenen berücksichtigt, ebenso des Zusammenhangs von sozioökonomischen Status und Inzidenz von Komplikationen bei Halsschmerzen.

| Tonkin-Crine Sarah KG, Tan Pui S, van Hecke O, et al. | Search: Cochrane Database of Systematic Reviews, DARE, MEDLINE, Embase, CINAHL, PsycINFO, and Science Citation Index to June 2016. Pre-publication search in May 2017. | Literature: 5 Cochrane Reviews (33 included trials) and 3 non-Cochrane reviews (11 included trials). | 1 | Moderate-quality evidence indicated that C-reactive protein (CRP) point-of-care testing (risk ratio (RR) 0.78, 95% confidence interval (CI) 0.66 to 0.92, 3284 participants, 6 trials), shared decision making (odds ratio (OR) 0.44, 95% CI 0.26 to 0.75, 3274 participants, 3 trials; RR 0.64, 95% CI 0.49 to 0.84, 4623 participants, 2 trials; risk difference -18.44, 95% CI -27.24 to -9.65, 481,807 participants, 4 trials), and procalcitonin-guided management (adjusted OR 0.10, 95% CI 0.07 to 0.14, 1008 participants, 2 trials) probably reduce antibiotic prescribing in general practice. We found moderate-quality evidence that procalcitonin-guided management probably reduces antibiotic prescribing in emergency departments (adjusted OR 0.34, 95% CI 0.28 to 0.43, 2605 participants, 7 trials). The overall Gut (moderate) | 113 | Three reviews (all Cochrane Reviews) scored low risk across all the ROBIS domains in Phase 2 and low risk of bias overall. The remaining five reviews scored high risk on Domain 4 of Phase 2. Three reviews (all Cochrane Reviews) scored low risk across all the ROBIS domains in Phase 2 and low risk of bias overall. The remaining five reviews scored high risk on Domain 4 of Phase 2. We found evidence that CRP testing, shared decision making, and procalcitonin-guided management reduce antibiotic prescribing for patients with ARIs which could affect less discrete conditions (such as the common cold) more than others (such as croup).
The effect of these interventions was small (few achieving greater than 50% reduction in antibiotic prescribing, most about a quarter or less), but likely to be clinically important.

Compared to usual care, shared decision making probably makes little or no difference to reconsultation for the same illness (RR 0.87, 95% CI 0.74 to 1.03, 1860 participants, 4 trials, moderate-quality evidence), and may make little or no difference to patient satisfaction (RR 0.86, 95% CI 0.57 to 1.30, 1110 participants, 2 trials, low-quality evidence).


Literature: We included 19 trials (18 publications) that involved 5835 people.

There was a difference in symptom resolution in favour of cephalosporins compared with penicillin (evaluable patients analysis odds ratio (OR) for absence of resolution of symptoms 0.51, 95% CI 0.27 to 0.97; number needed to treat to benefit (NNTB) 20, N = 5, n = 1660; very low quality evidence). However, this was not statistically significant in the ITT analysis (OR 0.79, 95% CI 0.55 to 1.12; N = 5, n = 2018; low quality evidence). Clinical relapse was lower for cephalosporins compared with penicillin (OR 0.55, 95% CI 0.30 to 0.99; NNTB 50, N = 4, n = 1386; low quality evidence), but this was found only in adults (OR 0.42, 95% CI 0.20 to 0.88; NNTB 33, N = 2, n = 770). There were no differences between macrolides and penicillin for any of the outcomes. One unpublished trial in children found a better cure rate for azithromycin in a single dose compared to amoxicillin for 10 days (OR 0.29, 95% CI 0.11 to 0.73; NNTB 18, N = 1, n = 482), but there was no difference between the groups in ITT analysis (OR 0.76, 95% CI 0.55 to 1.05; N = 1, n = 673) or at long-term follow-up (evaluable patients analysis OR 0.88, 95% CI 0.43 to 1.82; N = 1, n = 422). Children experienced more adverse events with azithromycin compared to amoxicillin (OR

Schwach (Low or very low)

The overall quality of the evidence assessed using the GRADE tool was low for the outcome ‘resolution of symptoms’ in the intention-to-treat (ITT) analysis and very low for the outcomes ‘resolution of symptoms’ of evaluable participants and for adverse events.

There were no clinically relevant differences in symptom resolution when comparing cephalosporins and macrolides with penicillin in the treatment of GABHS tonsillopharyngitis.
Compared with penicillin carbacephem showed better symptom resolution post-treatment in adults and children combined (ITT analysis OR 0.70, 95% CI 0.49 to 0.99; NNTB 14, N = 3, n = 795), and in the subgroup analysis of children (OR 0.57, 95% CI 0.33 to 0.99; NNTB 8, N = 1, n = 233), but not in the subgroup analysis of adults (OR 0.75, 95% CI 0.46 to 1.22, N = 2, n = 562). Children experienced more adverse events with macrolides compared with penicillin (OR 2.33, 95% CI 1.06 to 5.15; N = 1, n = 489). Studies did not report on long-term complications so it was unclear if any class of antibiotics was better in preventing serious but rare complications.


Literature: 3 of which met the inclusion criteria. AMC/DCBA lozenges (0.6 mg Amylmetacresol, 1.2 mg 2, 4-Dichlorobenzylalcohol) were compared with unflavoured, non-medicated lozenges. The AMC/DCBA formulation additionally contained lidocaine in one and flavouring additives in another trial. A total of 660 adults participated in the included trials. Fixed effects meta-analysis resulted in a standardised mean difference in pain intensity of −0.6 (−0.75; −0.45) on an 11-point ordinal rating scale, favouring the AMC/DCBA lozenges. Secondary outcomes were sore throat relief, difficulty swallowing and throat numbness. No serious side effects were reported, whereas mild side effects like headache, cough, nasal congestion and irritation of the oral cavity, were reported in up to 16% of subjects in both groups. Risk of bias was generally low in all trials. Lozenges with AMC/DCBA can be a safe treatment option to relieve pain in patients with uncomplicated sore throat looking for local treatment options and valuing the modest additional effect compared with non-medicated lozenges.

Wing A, Villa-Roel C, Yeh B, et al. Effectiveness of corticosteroid treatment in *Gut* 113

Search: Cochrane Library, MEDLINE, EMBASE, Biosis

When compared to placebo, corticosteroids reduced the time to clinically meaningful pain relief (WMD = 4.54 hours; 95%CI = 7.19 to 1.89); Overall, the quality of eight of the 10 studies was high according to the Jadad scale.

**Literature:**
From 272 potentially relevant citations, 10 RCTs met the inclusion criteria.

However, they provided only a small reduction in pain scores at 24 hours (WMD = 0.90 on a 0-10 visual analog scale; 95%CI =1.5 to 0.3).

Significant heterogeneity in the pooled results.

Corticosteroid administration for acute pharyngitis was associated with a relatively small effect in time to clinically meaningful pain relief (4.5-hour reduction) and in pain relief at 24 hours (0.9-point reduction).

Decision-making should be individualized to determine the risks and benefits; however, corticosteroids should not be used as routine treatment for acute pharyngitis.

Bemerkungen:
Rezidive oder Nebenwirkungen des Interventionsarms unterberichtet.
Praktisch alle Probanden erhielten Antibiotikum, was aber die Studienergebnisse (nach Meinung der Autoren) nicht verfälscht, da eben alle Halsschmerzpatienten Antibiotikum erhielten, ebenso wurde wohl auch zusätzliche (zu
Antibiotikum und Corticosteroid) eingenommene NSAR nicht erfasst.