### ANHANG B

## Evidenztabellen – Aggregierte Evidenz

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<tr>
<th>Referenz</th>
<th>Eingeschlossene Studien</th>
<th>LoE</th>
<th>AMSTAR II</th>
<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. BMC Med 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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<tr>
<td>Altamimi S, Khalil A, Khalaiwi KA, et al. Short-term late-generation antibiotics versus longer term penicillin for acute streptococcal pharyngitis in children. Cochrane Database Syst Rev 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>
<td>1</td>
<td>14</td>
<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 unconcealed 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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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).

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: Central, PubMed, EMBASE, CINAHL, LILACS, KoreaMed; IndMed; PakMediNet; CAB Abstracts; Web of Science; ISRCTN; Clinical-Trials.gov; ICTR; Google and Google Scholar. In searches prior to 2013, we also searched BIOSIS Previews 1926 to 2012.

Literature: This review includes seven trials with low to moderate risk of bias: five undertaken in children (987 participants) and two in adults (156 participants). An eighth trial in adults (40 participants) was at high risk of bias and did not provide any data for analysis.

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% CI 83.3 to 87.6 and a summary specificity of 95.4%; 95% CI 94.5 to 96.2.


Literature: 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.


Literature: The impact of surgery, as demonstrated in the included studies, is modest. Many participants in the non-surgical group improve spontaneously (although some people randomized to this group do in fact undergo surgery). The potential 'benefit' of surgery must be weighed against the risks of the procedure as adenotonsillectomy is associated with a small but significant degree of morbidity in the form of primary and secondary haemorrhage and, even with good analgesia, is particularly uncomfortable for adults.
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.

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.

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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 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.
<table>
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<tr>
<th>Publication</th>
<th>Search</th>
<th>N</th>
<th>Yes/No</th>
<th>Description</th>
</tr>
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<tbody>
<tr>
<td>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. <em>BMJ Open</em> 2015;5:e007612. doi:10.1136/bmjopen-2015-007612</td>
<td>PubMed and EMBASE bis April 2014</td>
<td>8 + 1 partial</td>
<td>Yes</td>
<td>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)).</td>
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<td>Schwach</td>
<td>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.</td>
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<td>De Paor M, O’Brien K, Fahey T, et al. Antiviral agents for infectious mononucleosis (glandular fever). <em>Cochrane Database Syst Rev</em> 2016;12:CD011487. doi:10.1002/14651858.CD011487.pub2</td>
<td>Cochrane Central Register of Controlled Trials (CENTRAL) bis März 2016. MEDLINE, Embase, CINAHL, LILACS, Web of Science bis April 2016.</td>
<td>10</td>
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<td>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 Incidenz zwischen Kontroll- und Interventionsgruppe 6) Viral shedding Viral shedding was suppressed while on treatment, keine Quantifizierung. 7) Days missing from school / work</td>
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<tr>
<td>Schwach</td>
<td>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.</td>
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1 Tage (95%CI -4.47-6.53) weniger in der Interventionsgruppe

Sechs Studien (2114 Patienten) analysierten GI-Blutung und/oder abdominale Schmerzen und zeigten keine signifikanten Unterschiede zwischen Kortison und Placebo (1.5% vs. 1.8%, jeweils). Verschiedene Verhaltenswirkungen und Hypertonie/Blutdruck wurden in vier Studien (838 und 1617 Patienten) gemessen, wobei keine signifikanten Unterschiede berichtet wurden.

Keine der Studien berichteten Todesfälle in den Behandlungsgruppen.

Basis auf 17 Studien (2056 Patienten), waren signifikant weniger Einweisungen am Tag 1 bei Kortison (Risikodifferenzen=-0.11, 95% Konfidenzintervall -0.18 bis -0.05; Peto Wirkungsquoten=0.63, 95% Konfidenzintervall 0.52 bis 0.78).

Kortison resultierte in über 8 weniger Stunden im Krankenhaus im Vergleich mit Placebo (mittlerer Unterschied=-8.49 Stunden, 95% Konfidenzintervall-1.76 bis -3.23).

Es gab signifikant weniger Relapsen, die zu einem Aufenthalt in der Klinik führten (Peto Wirkungsquoten 0.42, 95% Konfidenzintervall 0.23 bis 0.76).

Wir fanden keine Zunahme der Klinikbehandlung am Tag 1, Länge des Aufenthalts oder eines Rehospitalisierungs bei den anderen akuten respiratorischen bedingten Zuständen.

Die Qualität der verfügbaren Sicherheitstaten war weniger als erwünscht, selbst wenn die Studien als gut entworfen aus der Perspektive der primären Effizienz angesehen wurden.

Praktizierende können systemische Kortikosteroide bei sonst gesunden Kindern, wenn angezeigt, für die Behandlung akuter respiratorischer Zustände (z.B. Infektionen oder Asthma-Exazerbationen) verwenden, mit minimalem Kurzfristigem Nebenwirkungsrisiko.
HTA Database bis April 2014

**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.

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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

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*Very low-quality evidence* Any estimate of effect is very uncertain.

- Sehr starke Heterogenität der Studien bezüglich Studiendesign, Outcomes und time point, keine Metaanalyse möglich. Insgesamt sehr schwache Datenqualität
<table>
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<tr>
<th>Reference</th>
<th>Search: CENTRAL bis June 2012, MEDLINE bis Mai 2012, EMBASE bis Juni 2012, DARE and the NHS Health Economics Database bis Juni 2012.</th>
<th>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.</th>
<th>1</th>
<th>12 + 1 partial yes</th>
<th>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 &lt; 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.</th>
<th>gut</th>
<th>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.</th>
</tr>
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<tbody>
<tr>
<td>Kenealy T. Sore throat. BMJ Clin Evid 2014.</td>
<td>Clinical Evidence search and appraisal January 2010.</td>
<td>Search: Medline 1966 to January 2010, Embase 1980 to January 2010, The Cochrane Database of Systematic Reviews 2009, Issue 4 (1966 to date of issue), Database of Abstracts of Reviews of</td>
<td>1</td>
<td>8 (2 partial yes)</td>
<td>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.</td>
<td>High-quality evidence for Antibiotics versus placebo concerning prevention of complications Moderate-quality evidence for Analgesics</td>
<td>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.</td>
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Effects (DARE), the Health Technology Assessment (HTA) database.

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

**Analgesics versus placebo:**
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.

**NSAIDs versus placebo:**
One systematic review (search date 1999, 12 RCTs, 1189 people with acute sore throat for up to 5 days, severity unclear) comparing NSAIDs versus placebo. (no meta-analysis). Seven RCTs (492 people) assessed the effects of NSAIDs (including 1 RCT of oral aspirin and 1 RCT of aspirin gum) over 24 hours.

- The FDA issued a drug safety alert on the risk of rare but serious skin reactions with paracetamol (acetaminophen) (August 2013).

**NSAIDs versus placebo:**
- 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.

**Antibiotics versus placebo:**
- 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.

**Corticosteroids versus placebo in people receiving antibiotics:**
- 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 versus placebo, NSAIDs versus placebo, Antibiotics versus placebo, Corticosteroids versus placebo in people receiving antibiotics, Probiotics versus placebo concerning prevention of symptoms.
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: 1 8

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 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.
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.

<table>
<thead>
<tr>
<th>Study</th>
<th>Search</th>
<th>Design</th>
<th>N</th>
<th>Partial yes</th>
<th>Notes</th>
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<tbody>
<tr>
<td>Lennon D, Kerdemelidis M, Arroll B. Meta-analysis of trials of streptococcal throat treatment programs to prevent rheumatic fever. <em>Pediatr Infect Dis J</em> 2009;28:e259–64. DOI:10.1097/INF.0b013e3181a8e12a</td>
<td>Search: Medline, Old Medline, the Cochrane Library, DARE, CENTRAL, NHS, EED, NICE, NRMC, Clinical Evidence, CDC. Literature: Six studies which met the criteria and could be pooled were included. RCTs or trials of before/after design examining treatment of sore throats in schools or communities with RF as an outcome where data were able to be pooled for analysis.</td>
<td>12 + 1 partial yes</td>
<td>1</td>
<td>Meta-analysis of these trials for RF control produced a relative risk of 0.41 (95% CI: 0.23–0.70). There was statistical heterogeneity (I² 70.5%). Hence a random effects analysis was conducted. schwach</td>
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<td>Li S, Yue J, Dong BR, et al. Acetaminophen (paracetamol) for the common cold in adults. <em>Cochrane Database Syst Rev</em> 2013;:Cd008800. doi:10.1002/14651858.CD008800.pub2</td>
<td>Search: CENTRAL, MEDLINE, EMBASE, CIINAHL, LILACS bis Februar. Literature: 4 RCTs involving 758 participants: All included trials were randomised, double-blind, placebo-controlled, parallel-group</td>
<td>1</td>
<td>10</td>
<td>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</td>
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There are safe and effective over-the-counter medications to relieve throat pain. Most patients received concomitant antibiotics; however, reducing the prescription of antibiotics for generally benign upper respiratory tract infection is a public health goal.

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.

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 outpatient setting, one in a Medical University, and one did not specify the setting. Two 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.

**Sehr starke Heterogenität der Studien bezüglich Studiendesign, Outcomes und time point, keine Metaanalyse möglich.**

**Insgesamt sehr schwache Datenqualität**

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<tr>
<td>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.</td>
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<td>1</td>
<td>8 + 1 partial yes</td>
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<td>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 tonsillecctomized children in the short term (&lt;12 months). Quality of life was not markedly different between groups at any time point.</td>
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<td>Schwach bis gut</td>
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**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 tonsillecctomized children versus children not receiving surgery. Benefits did not persist over time; longer-term outcomes are limited.**

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<tr>
<td>Search: CENTRAL bis December 2014, MEDLINE bis November 2014), EMBASE bis December 2014, LILACS bis December 2014, BIOSIS bis December. Literature:</td>
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<td>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.</td>
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**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.
<table>
<thead>
<tr>
<th>Study</th>
<th>Search</th>
<th>Literature</th>
<th>Total</th>
<th>Partial Yes</th>
<th>Summary</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ruiz-Aragon J, Rodríguez Lopez R, Molina Linde JM. Evaluation of rapid methods for detecting Streptococcus pyogenes. Systematic review and meta-analysis. <em>An Pediatr</em> 2010;72:391–402.</td>
<td>Search: MedLine, Embase, Cochrane Library, Cinahl, CRD, ECRI, Hayes and HTA's agencies.</td>
<td>24 studies were included.</td>
<td>1</td>
<td>11, 3 partial yes</td>
<td>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%.</td>
</tr>
<tr>
<td>Sadeghirad B, Siemieniuk RAC, Brignardello-Petersen R, et al. Corticosteroids for treatment of sore throat: systematic review and meta-analysis of randomised trials. <em>Bmj</em> 2017;358:j3887. doi:10.1136/bmj.j3887</td>
<td>Search: Medline, Embase, Cochrane Central Register of Controlled Trials (CENTRAL), trial registries up to May 2017.</td>
<td>10 eligible trials enrolled 1426 individuals.</td>
<td>1</td>
<td>14</td>
<td>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</td>
</tr>
</tbody>
</table>
Single low dose corticosteroids can provide pain relief in patients with sore throat, with no increase in serious adverse effects. Included trials did not assess the potential risks of larger cumulative doses in patients with recurrent episodes of acute sore throat.

| Schapowal A, Klein P, Johnston SL. | Echinacea reduces the risk of recurrent respiratory tract infections and complications: a meta-analysis of randomized controlled trials. *Adv Ther* 2015;32:187–200. doi:10.1007/s12325-015-0194-4 | 1 | 10 | 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). schwach | 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. |

| Shaikh N, Leonard E, Martin JM. | Prevalence of streptococcal pharyngitis and streptococcal carriage in children: a meta-analysis. | 1 | 9 + 1 partial yes | Among children of all ages who present with sore throat, the pooled prevalence of GAS was 37% (95% confidence interval [CI]: 32%–43%). Children who were younger than 5 years had a lower prevalence of GAS (24% [95% CI: 21%–26%]). Unklar (keine RCTs) | We adapted a quality assessment system for prevalence articles. Prevalence rates of GAS disease and carriage varied by age; children who were younger than |
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%).

5 years had lower rates of throat cultures that were positive for GAS.

Search: MEDLINE and EMBASE bis April 2011.

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

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.


**Search:** CENTRAL, Ovid EMBASE, EBSCO CINAHL, Web of Science bis Mai 2017. WHO International Clinical Trials Registry Platform, ClinicalTrials.gov bis September 2017.

**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).

**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.

**Stewart EH, Davis B, Clemans-Taylor BL, et al.** *Rapid antigen group A streptococcus test to diagnose pharyngitis: a* Search: MEDLINE, Cochrane Reviews, Centre for Reviews and Dissemination, Scopus, 1 13

For the higher quality immunochromatographic methods in children (10,325 patients), heterogeneity was high for sensitivity (inconsistency [I²] 88%) and specificity (I² 86%). For enzyme immunoassay in children (342 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</th>
<th>Search</th>
<th>Patients</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>Heterogeneity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Thai TN, Dale AP, Ebell MH</td>
<td>MEDLINE bis März 2016.</td>
<td></td>
<td>86% (95% CI, 79–92%)</td>
<td>92% (95% CI, 88–95%)</td>
<td>I² 61%</td>
</tr>
<tr>
<td>Thompson M, Vodicka TA, Blair PS, et al.</td>
<td>PubMed, DARE, and CINAHL bis Juli 2012.</td>
<td></td>
<td>91% (95% CI, 87 to 94%)</td>
<td>93% (95% CI, 92 to 95%)</td>
<td>I² 61%</td>
</tr>
</tbody>
</table>
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.


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).

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)

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).

These interventions may therefore reduce overall antibiotic consumption and consequently antibiotic resistance. There do not appear to be negative effects of these interventions on the outcomes of patient satisfaction and reconsultation, although there was limited measurement of these outcomes in the trials.


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 1.51, 95% CI 1.04 to 2.18; NNTB 8, N = 1, n = 422).

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.
<table>
<thead>
<tr>
<th>Study</th>
<th>Search</th>
<th>Weight</th>
<th>Outcomes</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Weckmann G, Hauptmann-Voss A, Baumeister SE, et al. <em>Efficacy of AMC/DCBA lozenges for sore throat: A systematic review and meta-analysis.</em> Int J Clin Pr 2017;71. doi:10.1111/ijcp.13002</td>
<td>Search: MEDLINE (PubMed), EMBASE and Cochrane (CENTRAL) bis September 2016. 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.</td>
<td>1</td>
<td>15 + 1 partial yes</td>
<td>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. Gut</td>
</tr>
<tr>
<td>Wing A, Villa-Roel C, Yeh B, et al. <em>Effectiveness of corticosteroid treatment in.</em> Search: Cochrane Library, MEDLINE, EMBASE, Biosis</td>
<td>1</td>
<td>13</td>
<td>When compared to placebo, corticosteroids reduced the time to clinically meaningful pain relief (WMD = 4.54 hours; 95%CI = 7.19 to 1.89); Gut</td>
<td>Overall, the quality of eight of the 10 studies was high according to the Jadad scale.</td>
</tr>
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</table>

Previews, Scopus, and Web of Science bis Juni 2009. controlled trial registration websites, conference proceedings, study references, experts in the field, and correspondence with authors.

**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.
Streptokokken-Schnelltests wurden 2010 in den eingeschlossenen Studien eher selten angewandt. Abstrich und Kultur auf B-Streptokokken (GABHS-positive Patienten hatten am eindeutigsten von Corticosteroid profitiert) ist in ED, wo die Patienten lediglich Stunden verweilen, unpraktikabel. 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 Corticosteroi | eingennommene NSAR nicht erfasst. |