Sore throat

Search date September 2013

Tim Kenealy

ABSTRACT

INTRODUCTION: About 10% of people present to primary healthcare services with sore throat each year. The causative organisms of sore throat may be bacteria (most commonly Streptococcus) or viruses (typically rhinovirus), although it is difficult to distinguish bacterial from viral infections clinically.

METHODS AND OUTCOMES: We conducted a systematic review and aimed to answer the following clinical question: What are the effects of interventions to reduce symptoms of acute infective sore throat? We searched Medline, Embase, The Cochrane Library, and other important databases up to September 2013 (Clinical Evidence reviews are updated periodically; please check our website for the most up-to-date version of this review). We included harms alerts from relevant organisations such as the US Food and Drug Administration (FDA) and the UK Medicines and Healthcare products Regulatory Agency (MHRA).

RESULTS: We found 6 studies that met our inclusion criteria. We performed a GRADE evaluation of the quality of evidence for interventions.

CONCLUSIONS: In this systematic review, we present information relating to the effectiveness and safety of the following interventions: antibiotics, corticosteroids, non-steroidal anti-inflammatory drugs, and paracetamol.

QUESTIONS

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

INTERVENTIONS

<table>
<thead>
<tr>
<th>TREATING SYMPTOMS</th>
<th>Covered elsewhere in Clinical Evidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Likely to be beneficial</td>
<td></td>
</tr>
<tr>
<td>Paracetamol (acetaminophen)</td>
<td>Acute bronchitis</td>
</tr>
<tr>
<td>Corticosteroids (in people receiving antibiotics)</td>
<td>Acute otitis media</td>
</tr>
<tr>
<td>Trade off between benefits and harms</td>
<td>Acute sinusitis</td>
</tr>
<tr>
<td>NSAIDs</td>
<td>Common cold</td>
</tr>
<tr>
<td>Antibiotics</td>
<td>Tonsillitis</td>
</tr>
</tbody>
</table>

Key points

- Sore throat is an acute upper respiratory tract infection that affects the respiratory mucosa of the throat.
- About 10% of people in Australia present to primary healthcare services with sore throat each year.
  
  The causative organisms of sore throat may be bacteria (most commonly Streptococcus) or viruses (typically rhinovirus), but it is difficult to distinguish bacterial from viral infections clinically.

- Paracetamol seems to effectively reduce the pain of acute infective sore throat after regular doses over 2 days.
  
  There is a risk of rare but serious skin reactions with paracetamol (acetaminophen).

- Non-steroidal anti-inflammatory drugs (NSAIDs) may reduce the pain of sore throat at 2 to 5 days.
  
  NSAIDs are associated with gastrointestinal and renal adverse effects.

- 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 added to antibiotics may reduce the severity of pain from sore throat in people compared with antibiotics alone.
  
  Most trials used a single dose of corticosteroid. However, data from other disorders suggest that long-term use of corticosteroids is associated with serious adverse effects.

DEFINITION

Sore throat is an acute upper respiratory tract infection that affects the respiratory mucosa of the throat. Since infections can affect any part of the mucosa, it is often arbitrary whether an acute upper respiratory tract infection is called ‘sore throat’ (‘pharyngitis’ or ‘tonsillitis’), ‘common cold’, ‘sinusitis’, ‘otitis media’, or ‘bronchitis’ (see figure 1, p 9 ). Sometimes, all areas are affected (simultaneously or at different times) in one illness. In this review, we aim to cover people whose principal presenting symptom is sore throat. This may be associated with headache, fever, and general malaise. Suppurative complications include acute otitis media (most commonly), acute sinusitis, and peritonsillar abscess (quinsy). Non-suppurative complications include acute rheumatic fever and acute glomerulonephritis. This review does not include people with previous rheumatic fever or previous glomerulonephritis, who are importantly different from the general population of...
people with sore throats. It also does not include people who are clinically seriously unwell (as these people are typically not included in the primary studies).

**INCIDENCE/PREVALENCE**
There is little seasonal fluctuation in sore throat. About 10% of the Australian population present to primary healthcare services annually with an upper respiratory tract infection consisting predominantly of sore throat. This reflects about one fifth of the overall annual incidence. However, it is difficult to distinguish between the different types of upper respiratory tract infection. A Scottish mail survey found that 31% of adult respondents reported a severe sore throat in the previous year, for which 38% of these people visited a doctor.

**AETIOLOGY/RISK FACTORS**
The causative organisms of sore throat may be bacteria (Streptococcus, most commonly group A beta-haemolytic, but sometimes Haemophilus influenzae, Moraxella catarrhalis, and others) or viruses (typically rhinovirus, but also coronavirus, respiratory syncytial virus, metapneumovirus, Epstein–Barr virus, and others). It is difficult to distinguish bacterial from viral infections clinically. Features suggestive of Streptococcus infection are: fever >38.5°C, exudate on the tonsils, anterior neck lymphadenopathy, and absence of cough. Sore throat can be caused by processes other than primary infections, including GORD, physical or chemical irritation (e.g., from nasogastric tubes or smoke), and occasionally hay fever. However, we consider only primary infections in this review.

**PROGNOSIS**
The untreated symptoms of sore throat disappear by 3 days in about 40% of people, and untreated fevers in about 85%. By 1 week, 85% of people are symptom-free. This natural history is similar in Streptococcus-positive, Streptococcus-negative, and untested people.

**AIMS OF INTERVENTION**
To relieve symptoms of sore throat for 48 hours or longer.

**OUTCOMES**
Symptom severity: reduction in severity and duration of symptoms (sore throat pain, general malaise, headache, and fever) assessed at 48 hours or longer; patient satisfaction; health care utilisation. Time off work or school. Adverse effects of treatment.

**METHODS**
Clinical Evidence search and appraisal September 2013. The following databases were used to identify studies for this systematic review: Medline 1966 to September 2013, Embase 1980 to September 2013, and The Cochrane Database of Systematic Reviews 2013, issue 9 (1966 to date of issue). Additional searches were carried out in the Database of Abstracts of Reviews of Effects (DARE) and the Health Technology Assessment (HTA) Database. We also searched for retractions of studies included in the review. Titles and abstracts identified by the initial search, run by an information specialist, were first assessed against predefined criteria by an evidence scanner. Full texts for potentially relevant studies were then assessed against predefined criteria by an evidence analyst. Studies selected for inclusion were discussed with an expert contributor. All data relevant to the review were then extracted by an evidence analyst. Study design criteria for inclusion in this review were published systematic reviews and RCTs. Open label trials were included where outcomes were objective; for subjective outcomes, trials were at least single-blinded and containing 20 or more individuals, of whom more than 80% were followed up. There was a minimum length of follow-up of 48 hours. We included RCT and systematic reviews of RCTs where harms of an included intervention were assessed, applying the same study design criteria for inclusion as we did for benefits. In addition, we use a regular surveillance protocol to capture harms alerts from organisations such as the FDA and the MHRA, which are added to the reviews as required. To aid readability of the numerical data in our reviews, we round many percentages to the nearest whole number. Readers should be aware of this when relating percentages to summary statistics such as relative risks (RRs) and odds ratios (ORs). We have performed a GRADE evaluation of the quality of evidence for interventions included in this review (see table, p 10). The categorisation of the quality of the evidence (high, moderate, low, or very low) reflects the quality of evidence available for our chosen outcomes in our defined populations of interest. These categorisations are not necessarily a reflection of the overall methodological quality of any individual study, because the Clinical Evidence population and outcome of choice may represent only a small subset of the total outcomes reported, and population included, in any individual trial. For further details of how we perform the GRADE evaluation and the scoring system we use, please see our website (www.clinicevidence.com).
QUESTION: What are the effects of interventions to reduce symptoms of acute infective sore throat?

OPTION: **PARACETAMOL (ACETAMINOPHEN) TO REDUCE SYMPTOMS OF ACUTE INFECTIVE SORE THROAT**

- For GRADE evaluation of interventions for Sore throat, see table, p 10.
- Paracetamol seems to effectively reduce the pain of acute infective sore throat after regular doses over 2 days.
- The FDA issued a drug safety alert on the risk of rare but serious skin reactions with paracetamol (acetaminophen) (August 2013).

**Benefits and harms**

**Paracetamol versus placebo:**

We found one systematic review (search date 1999, 3 RCTs, 312 people with acute moderate to severe sore throat for up to 4 days) comparing paracetamol (acetaminophen) versus placebo. Two RCTs (158 people) identified by the review assessed the effects of paracetamol over 24 hours or less, and so we have not reported these data further.

**Symptom severity**

*Paracetamol compared with placebo* Paracetamol seems more effective than placebo at reducing sore throat pain at 2 days (low-quality evidence).

<table>
<thead>
<tr>
<th>Ref (type)</th>
<th>Population</th>
<th>Outcome, Interventions</th>
<th>Results and statistical analysis</th>
<th>Effect size</th>
<th>Favours</th>
</tr>
</thead>
<tbody>
<tr>
<td>[6] Systematic review</td>
<td>154 children Data from 1 RCT</td>
<td>Sore throat pain, 2 days with paracetamol 3 times daily with placebo Absolute results not reported</td>
<td>34% greater reduction with paracetamol than with placebo P &lt;0.01</td>
<td>🌟🌟🌟</td>
<td>paracetamol 3 times daily</td>
</tr>
</tbody>
</table>

**Adverse effects**

No data from the following reference on this outcome. [6]

**Further information on studies**

**Comment:** *Drug safety alert*

**August 2013, paracetamol (acetaminophen)** The Food and Drug Administration (FDA) has issued a drug safety alert on the risk of rare but serious skin reactions with paracetamol (acetaminophen). These skin reactions, known as Stevens-Johnson Syndrome (SJS), toxic epidermal necrolysis (TEN), and acute generalised exanthematous pustulosis (AGEP), can be fatal.[www.fda.gov/]

OPTION: **NSAIDS TO REDUCE SYMPTOMS OF ACUTE INFECTIVE SORE THROAT**

- For GRADE evaluation of interventions for Sore throat, see table, p 10.
- NSAIDs may reduce the pain of sore throat at 2 to 5 days.
- NSAIDs are associated with gastrointestinal and renal adverse effects.
**Benefits and harms**

**NSAIDs versus placebo:**
We found one systematic review (search date 1999, 12 RCTs, 1189 people with acute sore throat for up to 5 days, severity unclear) [6] and one subsequent RCT [7] comparing NSAIDs versus placebo. The review did not perform a meta-analysis. Seven RCTs (492 people) identified by the review assessed the effects of NSAIDs (including 1 RCT of oral aspirin and 1 RCT of aspirin gum) over 24 hours or less, and so we have not reported these data further. Six RCTs (697 people) identified by the review assessed the effects of NSAIDs over 24 hours and above.

**Symptom severity**

NSAIDs compared with placebo NSAIDs may be more effective than placebo at reducing sore throat symptoms at 2 to 5 days (low-quality evidence).

<table>
<thead>
<tr>
<th>Ref (type)</th>
<th>Population</th>
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<th>Results and statistical analysis</th>
<th>Effect size</th>
<th>Favours</th>
</tr>
</thead>
<tbody>
<tr>
<td>[6] Systematic review</td>
<td>697 people 6 RCTs in this analysis</td>
<td><strong>Symptom severity, primarily throat pain, 2 to 5 days</strong> with NSAIDs with placebo Absolute results not reported Pain was assessed using a variety of visual analogue and scoring systems</td>
<td>All the RCTs found that NSAIDs significantly reduced symptoms (primarily throat pain) compared with placebo The range of significant improvements in symptoms compared with placebo ranged from 33% to 93% <em>P &lt;0.05</em> in all RCTs</td>
<td>○○○</td>
<td>NSAIDs</td>
</tr>
<tr>
<td>[7] RCT</td>
<td>373 adults aged 18 to 75 years with recent-onset sore throat (4 days or less)</td>
<td><strong>Reduction in difficulty swallowing, at day 2</strong> with flurbiprofen (n = 186) with placebo (n = 187) Absolute results not reported Both groups had paracetamol for the home management of pain during these 2 days</td>
<td><em>P = 0.016</em></td>
<td>○○○</td>
<td>flurbiprofen</td>
</tr>
<tr>
<td>[7] RCT</td>
<td>373 adults aged 18 to 75 years with recent-onset sore throat (4 days or less)</td>
<td><strong>Reduction in difficulty swallowing, at day 3</strong> with flurbiprofen (n = 186) with placebo (n = 187) Absolute results not reported Both groups had paracetamol for the home management of pain during these 2 days</td>
<td><em>P = 0.032</em></td>
<td>○○○</td>
<td>flurbiprofen</td>
</tr>
<tr>
<td>[7] RCT</td>
<td>373 adults aged 18 to 75 years with recent-onset sore throat (4 days or less)</td>
<td><strong>Patient satisfaction (felt less distracted, felt less frustrated, felt happier), at day 3</strong> with flurbiprofen (n = 186) with placebo (n = 187) Absolute results not reported Both groups had paracetamol for the home management of pain during these 2 days</td>
<td><em>P &lt;0.05</em></td>
<td>○○○</td>
<td>flurbiprofen</td>
</tr>
</tbody>
</table>

**Adverse effects**
### Adverse effects

<table>
<thead>
<tr>
<th>Ref (type)</th>
<th>Population</th>
<th>Outcome, Interventions</th>
<th>Results and statistical analysis</th>
<th>Effect size</th>
<th>Favours</th>
</tr>
</thead>
<tbody>
<tr>
<td>RCT [7]</td>
<td>373 adults aged 18 to 75 years with recent-onset sore throat (less-than or equal to 4 days)</td>
<td>Serious adverse events, at day 3 0/186 (0%) with flurbiprofen 0/187 (0%) with placebo</td>
<td>Significance assessment not reported</td>
<td></td>
<td></td>
</tr>
<tr>
<td>RCT [7]</td>
<td>373 adults aged 18 to 75 years with recent-onset sore throat (less-than or equal to 4 days)</td>
<td>Gastrointestinal adverse events, at day 3 9/186 (4.8%) with flurbiprofen 8/187 (4.3%) with placebo</td>
<td>Significance assessment not reported</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

No data from the following reference on this outcome. [8]

Further information on studies

[6] The review gave no information on adverse effects. However, data from systematic reviews in people with other disorders suggest that NSAIDs are associated with gastrointestinal and renal adverse effects (see review on NSAIDs).

Comment: Clinical guide: NSAIDs seem effective, but have potential for adverse effects. Aspirin is best avoided in children <15 years of age owing to the rare risk of Reye’s syndrome.

### OPTION

**ANTIBIOTICS TO REDUCE SYMPTOMS OF ACUTE INFECTIVE SORE THROAT**

- For GRADE evaluation of interventions for Sore throat, see table, p 10.
- 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.

### Benefits and harms

**Antibiotics versus placebo:**

We found one systematic review (search date 2008, 27 randomised or quasi-randomised trials, 12,835 people with sore throat, severity unclear) comparing antibiotics versus placebo. [5]

### Symptom severity

**Antibiotics compared with placebo** Antibiotics are more effective than placebo at reducing sore throat and headache at 3 days, particularly in people with positive throat swabs for *Streptococcus* (moderate-quality evidence).
<table>
<thead>
<tr>
<th>Ref (type)</th>
<th>Population</th>
<th>Outcome, Interventions</th>
<th>Results and statistical analysis</th>
<th>Effect size</th>
<th>Favours</th>
</tr>
</thead>
<tbody>
<tr>
<td>[5] Systematic review</td>
<td>2974 people 13 RCTs in this analysis</td>
<td>Sore throat, 6 to 8 days 246/1839 (13%) with antibiotics 206/1135 (18%) with placebo</td>
<td>RR 0.49 95% CI 0.32 to 0.76 The review estimated that this represents an average shortening of symptoms of sore throat by about 16 hours for the first week</td>
<td></td>
<td>antibiotics</td>
</tr>
<tr>
<td>[5] Systematic review</td>
<td>1334 people 7 RCTs in this analysis</td>
<td>Fever, 3 days with antibiotics with placebo Absolute results not reported</td>
<td>RR 0.71 95% CI 0.45 to 1.10</td>
<td></td>
<td>Not significant</td>
</tr>
<tr>
<td>[5] Systematic review</td>
<td>911 people 3 RCTs in this analysis</td>
<td>Headache, 3 days 122/552 (22%) with antibiotics 147/359 (41%) with placebo</td>
<td>RR 0.47 95% CI 0.38 to 0.58</td>
<td></td>
<td>antibiotics</td>
</tr>
</tbody>
</table>

**Adverse effects**

No data from the following reference on this outcome. [5]

**Further information on studies**

[5] Severely unwell people were not included in the RCTs included in the systematic review. Consequently, these findings may not apply to those people.

[6] The review found limited evidence from indirect comparisons that, in people with throat swabs positive for *Streptococcus*, the absolute and relative reduction in the proportion of people with sore throat symptoms at 3 days was greater than in people with negative swabs (positive swabs: 11 trials, 471/1073 [44%] with antibiotics v 544/766 [71%] with placebo, RR 0.58, 95% CI 0.48 to 0.71; negative swabs: 6 trials, 262/458 [57%] with antibiotics v 202/278 [73%] with placebo, RR 0.78, 95% CI 0.63 to 0.97).

[5] The review gave no information about the adverse effects associated with antibiotic use. [5] However, data from systematic reviews in people with other disorders suggested that antibiotics were associated with nausea, vomiting, headache, skin rash, and vaginitis (see reviews on Acute bronchitis and Acute otitis media in children).

**Comment:** Clinical guide:
Widespread antibiotic use may lead to bacterial resistance to antibiotics (see review on Acute bronchitis).

**OPTION** CORTICOSTEROIDS TO REDUCE SYMPTOMS OF ACUTE INFECTIVE SORE THROAT

- For GRADE evaluation of interventions for Sore throat, see table, p 10.
- Corticosteroids added to antibiotics may reduce the severity of pain from sore throat in people compared with antibiotics alone. There is insufficient evidence to report separately on children.
- Most trials used a single dose. However, data from use of corticosteroids in other disorders suggest that long-term use of corticosteroids is associated with serious adverse effects.
Benefits and harms

Corticosteroids versus placebo in people receiving antibiotics:

We found one systematic review (search date 2012, 8 RCTs, 743 people [369 children, 374 adults], of whom 47% had exudative sore throat and 44% were positive for group A beta-haemolytic streptococcus) comparing corticosteroids versus placebo. In seven RCTs, all participants also received antibiotics; in one RCT, participants received antibiotics if direct antigen testing for *Streptococcus* was positive. The corticosteroids used were dexamethasone orally or intramuscularly (single dose, 6 RCTs), betamethasone intramuscularly (single dose, 1 RCT), or prednisone orally (1–2 days, 1 RCT). Two RCTs included only children, two included only adults, and four included both. The systematic review pooled the data on adults and children and did not present the results separately by age. Four RCTs (286 adults and children) identified by the review assessed the effects of corticosteroids at 24 hours, and so we have not reported these data further.

Symptom severity

Corticosteroids compared with placebo in people receiving antibiotics Dexamethasone, betamethasone, or prednisone (single dose or for 1–2 days), with concurrent antibiotic, are more effective than placebo at complete resolution of pain in people with sore throat at 48 hours (moderate-quality evidence).

<table>
<thead>
<tr>
<th>Ref (type)</th>
<th>Population</th>
<th>Outcome, Interventions</th>
<th>Results and statistical analysis</th>
<th>Effect size</th>
<th>Favours</th>
</tr>
</thead>
<tbody>
<tr>
<td>[8] Systematic review</td>
<td>209 adults and children</td>
<td>Complete resolution of pain, 48 hours</td>
<td>RR 1.65 95% CI 1.32 to 2.06 95% CI 2 to 6</td>
<td>corticosteroids</td>
<td></td>
</tr>
</tbody>
</table>

Time off work or school

Corticosteroids compared with placebo in people receiving antibiotics We don’t know whether corticosteroids are more effective than placebo at reducing time off work or school (low-quality evidence).

<table>
<thead>
<tr>
<th>Ref (type)</th>
<th>Population</th>
<th>Outcome, Interventions</th>
<th>Results and statistical analysis</th>
<th>Effect size</th>
<th>Favours</th>
</tr>
</thead>
<tbody>
<tr>
<td>[8] Systematic review</td>
<td>92 people Data from 1 RCT</td>
<td>Number of days off work or school, mean</td>
<td>MD −0.3 95% CI −0.87 to +0.27</td>
<td>Not significant</td>
<td></td>
</tr>
</tbody>
</table>

Adverse effects

<table>
<thead>
<tr>
<th>Ref (type)</th>
<th>Population</th>
<th>Outcome, Interventions</th>
<th>Results and statistical analysis</th>
<th>Effect size</th>
<th>Favours</th>
</tr>
</thead>
<tbody>
<tr>
<td>[8] Systematic review</td>
<td>At least 125 participants 4 RCTs in this analysis</td>
<td>Adverse effects with</td>
<td>See Further information on studies</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Further information on studies

[8] The SR noted that adverse events were reported in detail by only one RCT of 125 participants, in which five participants (three corticosteroid and two placebo) were hospitalised for fluid rehydration and three participants...
(one corticosteroid and two placebo) developed peritonsillar abscesses. One RCT reported no side effects attributable to dexamethasone; another did not identify any complications of Group A beta-haemolytic streptococcus infections in either group; and, in a third RCT, there were no participants with additional complaints or requiring additional medications.

**Comment:**

Clinical guide:

A single dose of corticosteroid seems to reduce pain earlier than placebo in people with or without evidence of streptococcal infection. There is insufficient evidence to report separately on children.

**GLOSSARY**

Low-quality evidence Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.

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.

**SUBSTANTIVE CHANGES**

**Corticosteroids to reduce symptoms of acute infective sore throat**

Existing review updated. [8] Existing evidence re-assessed. Categorisation unchanged (likely to be beneficial).

**NSAIDs to reduce symptoms of acute infective sore throat**


**Paracetamol (acetaminophen) to reduce symptoms of acute infective sore throat**

Evidence re-assessed. One RCT deleted, as it no longer fits the new stricter inclusion criteria for this Clinical Evidence review. Categorisation unchanged (likely to be beneficial).

**REFERENCES**


Tim Kenealy

Associate Professor

Department of General Practice and Primary Health Care

University of Auckland

Auckland

New Zealand

Competing interests: TK declares that he has no competing interests.

We would like to acknowledge the previous contributors for this review, including Chris Del Mar and Paul Glasziou.
FIGURE 1  Confusion and overlap in the classification of acute respiratory infections.

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# GRADE Evaluation of interventions for Sore throat.

<table>
<thead>
<tr>
<th>Important outcomes</th>
<th>Outcome</th>
<th>Comparison</th>
<th>Type of evidence</th>
<th>Quality</th>
<th>Consistency</th>
<th>Directness</th>
<th>Effect size</th>
<th>GRADE</th>
<th>Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Studies (Participants)</td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>What are the effects of interventions to reduce symptoms of acute infective sore throat?</td>
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<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>1 (154) [6]</td>
<td>Symptom severity</td>
<td>Paracetamol versus placebo</td>
<td>4</td>
<td>-2</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>Low</td>
<td>Quality points deducted for incomplete reporting of results and sparse data</td>
</tr>
<tr>
<td>7 (1070) [6] [7]</td>
<td>Symptom severity</td>
<td>NSAIDs versus placebo</td>
<td>4</td>
<td>-1</td>
<td>0</td>
<td>-1</td>
<td>0</td>
<td>Low</td>
<td>Quality point deducted for incomplete reporting of results; directness point deducted for inclusion of a co-intervention</td>
</tr>
<tr>
<td>27 (12,835) [5]</td>
<td>Symptom severity</td>
<td>Antibiotics versus placebo</td>
<td>4</td>
<td>0</td>
<td>0</td>
<td>-1</td>
<td>0</td>
<td>Moderate</td>
<td>Directness point deducted for narrow inclusion criteria</td>
</tr>
<tr>
<td>3 (209) [6]</td>
<td>Symptom severity</td>
<td>Corticosteroids versus placebo in people receiving antibiotics</td>
<td>4</td>
<td>0</td>
<td>0</td>
<td>-1</td>
<td>0</td>
<td>Moderate</td>
<td>Directness point deducted for population differences between studies</td>
</tr>
<tr>
<td>1 (92) [6]</td>
<td>Time off work or school</td>
<td>Corticosteroids versus placebo in people receiving antibiotics</td>
<td>4</td>
<td>-2</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>Low</td>
<td>Quality points deducted for sparse data and incomplete results</td>
</tr>
</tbody>
</table>

We initially allocate 4 points to evidence from RCTs, and 2 points to evidence from observational studies. To attain the final GRADE score for a given comparison, points are deducted or added from this initial score based on preset criteria relating to the categories of quality, directness, consistency, and effect size. Quality: based on issues affecting methodological rigour (e.g., incomplete reporting of results, quasi-randomisation, sparse data [<200 people in the analysis]). Consistency: based on similarity of results across studies. Directness: based on generalisability of population or outcomes. Effect size: based on magnitude of effect as measured by statistics such as relative risk, odds ratio, or hazard ratio.