ClinicalEvidence

Common cold

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ABSTRACT

INTRODUCTION: Each year, children suffer up to 5 colds and adults have 2–3 infections, leading to time off school or work, and considerable discomfort. Most symptoms resolve within a week, but coughs often persist for longer. METHODS AND OUTCOMES: We conducted a systematic review and aimed to answer the following clinical question: What are the effects of treatments for common cold? We searched: Medline, Embase, The Cochrane Library and other important databases up to May 2007 (BMJ 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 19 systematic reviews, RCTs, or observational 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: analgesics or anti-inflammatory drugs, antibiotics, antihistamines, decongestants (norephedrine, oxymetazoline, or pseudoephedrine), decongestants plus antihistamine, echinacea, steam inhalation, vitamin C, and zinc (intranasal gel or lozenges).

QUESTIONS

INTERVENTIONS

TREATMENTS

Key points

- Transmission of common cold infections is mostly through hand-to-hand contact rather than droplet spread. Several types of virus can cause symptoms of colds.

  Each year, children suffer up to five colds and adults have two to three infections, leading to time off school or work and considerable discomfort. Most symptoms resolve within a week, but coughs often persist for longer.

- Nasal and oral decongestants reduce nasal congestion over 3–10 hours, but we don't know whether they are effective in the longer term (more than 10 hours).

- Antibiotics don't reduce symptoms overall, and can cause adverse effects and increase antibiotic resistance.

  Antibiotics may improve symptoms after 5 days compared with placebo in people with nasopharyngeal culture-positive *Haemophilus influenzae*, *Moraxella catarrhalis*, or *Streptococcus pneumoniae*, but it is difficult to identify which people may have these infections.

- Vitamin C seems unlikely to reduce the duration or severity of cold symptoms compared with placebo.

  We don't know whether zinc gel or lozenges, echinacea, steam inhalation, analgesics, or anti-inflammatory drugs reduce the duration of symptoms of colds.

- Antihistamines may slightly reduce runny nose and sneezing, but their overall effect seems small. Some antihistamines may cause sedation or arrhythmias.

- We don't know whether decongestants plus antihistamines reduce cold symptoms or cold duration.

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DEFINITION

Common colds are defined as upper respiratory tract infections that affect the predominantly nasal part of the respiratory mucosa. Because upper respiratory tract infections can affect any part of the mucosa, it is often arbitrary whether an upper respiratory tract infection is called a "cold" or "sore throat" ("pharyngitis" or "tonsillitis"), "sinusitis", "acute otitis media", or "bronchitis" (see figure 1 in review on sore throat). Sometimes all areas (simultaneously or at different times) are affected during one illness. Symptoms include sneezing, rhinorrhoea (runny nose), headache, and general malaise. In addition to nasal symptoms, half of sufferers experience sore throat, and 40% experience cough. [1] This review does not include treatments for people with acute sinusitis (see review on acute sinusitis), acute bronchitis (see review on acute bronchitis), or sore throat (see review on sore throat). One prospective US study (1246 children enrolled at birth) found that children who had frequent colds when aged 2 or 3 years were twice as likely to experience frequent colds at year 6 compared with children who had infrequent colds at 2 or 3 years (RR 2.8, 95% CI 2.1 to 3.9). [2]

INCIDENCE/ PREVALENCE

Upper respiratory tract infections, nasal congestion, throat complaints, and cough are responsible for 11% of general practice consultations in Australia. [3] Each year, children suffer about five such infections and adults two to three infections. [3] [4] [5] One cross-sectional study in Norwegian children aged 4–5 years found that 48% experienced more than two common colds annually. [6]

AETIOLOGY/ RISK FACTORS

Transmission of common cold infection is mostly through hand-to-hand contact, with subsequent passage to the nostrils or eyes — rather than, as commonly perceived, through droplets in the air. [1] Common cold infections are mainly caused by viruses (typically rhinovirus, but also coronavirus and respiratory syncytial virus, or metapneumovirus and others). For many colds, no infecting organism can be identified.

PROGNOSIS

Common colds are usually short lived, lasting a few days, with a few lingering symptoms lasting longer, especially cough. Symptoms peak within 1–3 days and generally clear by 1 week, although cough often persists. [1] Although they cause no mortality or serious morbidity, common colds are responsible for considerable discomfort, lost work, and medical costs.

AIMS OF INTERVENTION

To relieve symptoms, shorten the illness, or reduce complications; to reduce infectivity to others, with minimal adverse effects from treatments.

OUTCOMES

Cure rate; duration of symptoms; time away from work or school; incidence of complications; adverse effects of treatment.

METHODS

BMJ Clinical Evidence search and appraisal May 2007. The following databases were used to identify studies for this systematic review: Medline 1966 to May 2007, Embase 1980 to May 2007, and The Cochrane Database of Systematic Reviews and Cochrane Central Register of Controlled Clinical Trials 2007, Issue 2. Additional searches were carried out using these websites: NHS Centre for Reviews and Dissemination (CRD) — for Database of Abstracts of Reviews of Effects (DARE) and Health Technology Assessment (HTA), Turning Research into Practice (TRIP), and NICE. We also searched for retractions of studies included in the review. Abstracts of the studies retrieved from the initial search were assessed by an information specialist. Selected studies were then sent to the author for additional assessment, using pre-determined criteria to identify relevant studies. Study design criteria for inclusion in this review were: published systematic reviews and RCTs in any language, at least single blinded, and containing more than 20 individuals of whom more than 80% were followed up. The minimum length of follow-up required to include studies was 7 days. We excluded all studies described as "open", "open label", or not blinded for subjective outcomes (unwell) but did not for objective outcomes (fever). We use a regular surveillance protocol to capture harms alerts from organisations such as the FDA and the UK Medicines and Healthcare products Regulatory Agency (MHRA), which are added to the reviews as required. Where possible, we have excluded RCTs undertaken solely in people with experimentally induced colds, although meta-analyses in some systematic reviews do include such RCTs. We have also excluded RCTs that only assessed the outcome of bacteriological clearance. We performed a broad search for RCTs of any decongestant, analgesic, or anti-inflammatory in people with common cold, and included any RCTs of sufficient quality. We have performed a GRADE evaluation of the quality of evidence for interventions included in this review (see table, p 10).

QUESTION What are the effects of treatments for common cold?

OPTION ANTIHISTAMINES

Symptom relief

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Compared with placebo Antihistamines may be no more effective at relieving symptoms of common cold (very low-quality evidence).

For GRADE evaluation of interventions for common cold, see table, p 10 .

Benefits:

Antihistamines versus placebo:
We found two systematic reviews [7] [8] and one subsequent RCT. [9] The first review (search date not reported, 9 RCTs, 1757 adults; 7 RCTs in adults with naturally acquired colds, 2 RCTs in adults with experimentally induced colds) included previously unpublished individual patient data comparing antihistamines (chlorpheniramine or doxylamine) versus placebo. [7] The review found that, compared with placebo, antihistamines reduced the symptoms of runny nose and sneezing for the first 2 days of colds. However, the effects were small. On a severity scale ranging from 0 (no symptoms) to 3 or 4 (severe symptoms), antihistamines reduced the score by about 0.25 (95% CI 0.10 to 0.40; results presented graphically) for runny nose on days 1 and 2, 0.15 (95% CI 0 to 0.30) for sneezing on day 1, and 0.30 (95% CI 0.15 to 0.45) for sneezing on day 2. The second review (search date 2003, 32 RCTs, 8228 adults and children with naturally acquired colds, 702 with experimentally induced colds) compared antihistamines alone or antihistamines in combination with another treatment, usually decongestants, versus placebo (see comment below). [8] The review found no significant difference in overall symptoms at 1–10 days between antihistamines alone and placebo (proportion recovered at 1–2 days, 5 RCTs: 998/1825 [55%] with antihistamines alone *v* 892/1667 [54%] with placebo; RR 0.99, 95% CI 0.93 to 1.05; at 3–5 days, 3 RCTs: RR 1.03, 95% CI 0.92 to 1.16; at 8–10 days, 4 RCTs: RR 0.95, 95% CI 0.83 to 1.09). The subsequent RCT (37 children aged 6–18 years with nocturnal cough due to upper respiratory infection) compared three interventions: an antihistamine (diphenhydramine, single bedtime dose, based on label recommendations for age, 12 children), an antitussive (dextromethorphan, single bedtime dose, based on label recommendations for age, 12 children), and placebo (13 children). [9] The RCT assessed the antitussive in comparison with the antihistamine and placebo and found no significant difference in cough frequency between groups (measured on a 7-point Likert scale, comparing one night without treatment to a second night with treatment, Likert point improvement 1.75 with dextromethorphan *v* 1.58 with diphenhydramine *v* 1.38 with placebo; P = 0.85 for dextromethorpan *v* either other treatment). However the study was small and outcomes were measured in one night.

Harms:

Harms were not actively looked for in the RCTs identified by the first review. [7] The second review found that antihistamines were associated with sedation, dizziness, dry mouth, and headache. [8] It found that first-generation antihistamines significantly increased the proportion of people who had one or more adverse effect, particularly sedation (9 RCTs: RR 1.20, 95% CI 1.03 to 1.40). It found no significant difference in the proportion of people who had one or more adverse effect between non-sedating antihistamines and placebo (3 RCTs: RR 1.10, 95% CI 0.55 to 2.18). The subsequent RCT gave no information on adverse effects. [9] Some non-sedating antihistamines are associated with arrhythmias and adverse interactions with other drugs. The FDA has recently released a warning that respiratory depression, leading to death in some cases, has been reported when promethazine hydrochloride was given to children aged less than 2 years. [10] The FDA recommends not using promethazine hydrochloride in children aged under 2 years, and that parents and caregivers seek a doctor's advice about giving promethazine hydrochloride in any form to children aged 2 years and older.

Comment:

The RCTs identified by the second review assessed a wide variety of antihistamines, including cetirizine, chlorpheniramine, clemastine, doxylamine succinate, loratadine, promethazine hydrochloride, and terfenadine. [8] Decongestants used in combination with antihistamines included phenylpropanolamine and pseudoephedrine.

OPTION DECONGESTANTS FOR SHORT-TERM RELIEF

Symptom relief
Compared with placebo A single dose of a decongestant (oral norephedrine, topical oxymetazoline, or oral pseudoephedrine) seems to be moderately more effective at reducing nasal congestion over 3–10 hours, and at reducing objective airways resistance in adults with common cold (moderate-quality evidence).

Note
Phenylpropanolamine has been associated with an increased risk of haemorrhagic stroke.

For GRADE evaluation of interventions for common cold, see table, p 10 .

Benefits:

We found one systematic review (search date 2006, 6 RCTs, 246 adults with naturally acquired colds). [11] The review found that, compared with placebo, a single dose of decongestant (oral norephedrine, topical oxymetazoline, or oral pseudoephedrine) moderately but significantly reduced nasal congestion over 3–10 hours (6 RCTs, 643 adults; congestion measured on a scale from 0–1:

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WMD –0.06, 95% CI –0.19 to –0.3). The authors concluded that there was a small but statistically significant (6%) decrease in subjective symptoms after a single dose of decongestant compared with placebo. This was supported by a significant decrease in objective nasal airways resistance (6 RCTs, 606 adults; SMD –0.24, 95% CI –0.4 to –0.08).

Harms: Two of the RCTs within the review reported data on adverse events, which included insomnia, headache and hypertension. The systematic review found that rates of combined adverse events were not significantly different between groups (25/226 [11%] for treatment *v* 18/222 [8%] for control; OR 1.43, 95% CI 0.75 to 2.72). [11] One case control study compared the use of cold preparations containing phenylpropanolamine in 702 people with a history of haemorrhagic stroke versus 1376 control people with no history of stroke. [12] The study found a non-significant trend towards increased haemorrhagic stroke with phenylpropanolamine (RR 1.50, 95% CI 0.85 to 2.65). [12] However, the study was too small to draw definitive conclusions. Formulations containing phenylpropanolamine have mostly been reformulated or withdrawn by manufacturers in the UK.

Comment: The review found no RCTs in children. [11]

OPTION DECONGESTANTS FOR LONG-TERM RELIEF

Symptom relief
Compared with placebo Multiple doses of nasal decongestants may be more effective at 3–5 days at decreasing nasal congestion in adults with a cold (low-quality evidence).

For GRADE evaluation of interventions for common cold, see table, p 10 .

Benefits: We found one systematic review (search date 2006, 7 RCTs, 734 adults with naturally acquired colds). [11] The review found a borderline significant effect on nasal congestion for nasal decongestants (multiple doses) compared with placebo, after last treatment dose (2 RCTs, 443 people, WMD –0.03, CI –0.07 to 0.00). The review found that, compared with placebo, nasal decongestants (multiple doses) produced a small but statistically significant decrease in objective nasal airways resistance, measured at 3–5 days (2 RCTs, 432 people, WMD –0.04, 95% CI –0.06 to –0.01). The RCTs did not specify the method of randomisation.

Harms: See harms of decongestants for short-term relief, p 3 .

Comment: See comment on decongestants for short-term relief, p 3 .

OPTION DECONGESTANTS PLUS ANTIHISTAMINES New

We found no direct information about decongestants plus antihistamines in the treatment of people with common cold.

For GRADE evaluation of interventions for common cold, see table, p 10 .

Benefits: We found no systematic review or RCTs of decongestants plus antihistamines in people with common cold.

Harms: We found no RCTs.

Comment: None.

OPTION ANALGESICS OR ANTI-INFLAMMATORY DRUGS

We found no direct information about analgesics or anti-inflammatory drugs in the treatment of people with common cold.

For GRADE evaluation of interventions for common cold, see table, p 10 .

Benefits: We found no systematic review or RCTs of analgesics or anti-inflammatory drugs in people with common cold.

Harms: We found no RCTs.

Comment: None.

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OPTION ECHINACEA

Symptom duration
Compared with placebo We don't know whether echinacea is more effective at reducing the duration of symptoms of the common cold (moderate-quality evidence).

For GRADE evaluation of interventions for common cold, see table, p 10 .

Benefits:

Echinacea versus placebo:
We found one systematic review (search date 2005), which included 14 placebo-controlled RCTs of echinacea (16 comparisons), of which five assessed cold duration, seven cold incidence, and two, both outcomes. These RCTs found differing results. [13] Two RCTs reported data on symptom duration. One found that echinacea significantly reduced symptom duration compared with placebo (160 people, mean 9.30 days *v* 12.90 days; SMD –1.83 days, 95% CI –2.20 to –1.46). However, the second RCT found no significant reduction in symptom duration compared with placebo (142 people, mean 6.27 days *v* 5.75 days; SMD 0.22 days, 95% CI –0.11 to 0.55). One RCT found that echinacea was significantly more effective than placebo for improving combined measures of the severity and duration of cold, whereas five RCTs found no significant difference between echinacea and placebo for this outcome. However, the groups in one of these RCTs may not have been balanced at baseline. Two RCTs found that echinacea significantly reduced overall symptom score at 2–4 days compared with placebo, whereas four RCTs found no significant difference. Five RCTs found that echinacea significantly reduced overall symptom score at 5–10 days compared with placebo, whereas five RCTs found no significant difference. Two RCTs found that echinacea significantly reduced nasal symptoms at 2–4 days compared with placebo, whereas four RCTs found no significant difference. Three RCTs found that echinacea significantly reduced nasal symptoms at 5–10 days compared with placebo, whereas seven RCTs found no significant difference. One RCT found that echinacea significantly reduced the duration of colds compared with placebo, whereas another RCT found no significant difference. Two RCTs included in the review assessed early treatment in people with prodromal symptoms. One of these RCTs found that, compared with placebo, echinacea significantly reduced the proportion of people developing a full-blown cold (24/60 [40%] with echinacea *v* 36/60 [60%] with placebo; RR 0.67, 95% CI 0.46 to 0.97), whereas the other found a trend towards reduction that did not quite reach significance (35/41[83%] with echinacea *v* 38/39 [97%] with placebo; RR 0.88, 95% CI 0.76 to 1.00).

Harms:

Echinacea versus placebo:
Six RCTs included in the systematic review reported on adverse events; none of these RCTs found any significant difference between echinacea and placebo (results not pooled owing to heterogeneity). [13] Two RCTs found no significant difference between echinacea and placebo in withdrawals caused by adverse effects (first RCT: 1/41 [2%] with echinacea *v* 0/39 [0%] with placebo; RR 2.86, 95% CI 0.12 to 68.10; second RCT: 6/215 [3%] with echinacea *v* 1/221 [0%] with placebo; RR 6.17, 95% CI 0.75 to 50.80). [13] One RCT included in the review found that echinacea significantly increased the proportion of children who had rash compared with placebo (7% with echinacea *v* 3% with placebo; P = 0.008). [14] Outside the trials, isolated cases of anaphylaxis have been reported in people taking echinacea. [15] [16]

Comment:

Echinacea is not a single product. There are more than 200 different preparations based on different plants, different parts of the plant (roots, herbs, whole plant), and different methods of extraction. The weakness of trial methods and differences in interventions make it difficult to draw conclusions about effectiveness. Large RCTs may be difficult because echinacea is not patentable, and each producer controls a small share of the market. The authors of the systematic review received personal information about several unpublished studies that they were not able to include.

OPTION STEAM INHALATION

Symptom relief
Compared with sham inhalation We don't know whether steam inhalation is more effective at reducing the proportion of people with symptoms of common cold after treatment (very low-quality evidence).

For GRADE evaluation of interventions for common cold, see table, p 10 .

Benefits:

Steam inhalation versus sham inhalation:
We found one systematic review (search date 2005), which compared steam inhalation at 40–47 °C versus sham inhalation (air at 30 °C or higher). [17] The review (6 RCTs, 319 people: 4 RCTs in people with naturally acquired colds, 2 in people with experimentally induced colds) could not perform a meta-analysis of all of the RCTs because of heterogeneity in populations, methods used to assess symptoms, and poor reporting in some of the RCTs (see comment below). Pooling of

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data from two RCTs that used similar methods of assessing symptoms found limited evidence that, compared with sham inhalation, steam inhalation significantly reduced the proportion of people with symptoms immediately after steam inhalation in one RCT, and at 4 days in the other (146 people with naturally acquired or experimentally induced colds; AR for symptoms: 29/77 [38%] with steam *v* 46/69 [67%] with sham; RR 0.56, 95% CI 0.40 to 0.79; see comment below). Another RCT identified by the review, which used a different method of assessing symptoms, found no significant difference between steam and sham inhalation in the proportion of people with improved symptoms at the end of treatment (20 people with experimentally induced colds; no improvement in symptom score: 23/45 [51%] with steam *v* 26/39 [67%] with sham; RR 0.77, 95% CI 0.53 to 1.10), but may have been too small to detect a clinically important difference. [17]

Harms: The RCTs identified by the review found no evidence of adverse effects. [17] There may be a danger from spilling hot water and from nosocomial infections related to humidifier units.

Comment: The review stated that the RCTs used different symptom score indices, but did not specify which indices were used. [17] It is unclear whether sham inhalation is a valid control.

OPTION ZINC

Symptom duration

Zinc lozenges compared with placebo We don't know whether zinc gluconate or acetate lozenges are more effective at reducing the duration of cold symptoms at 7 days (very low-quality evidence).

Intranasal zinc compared with placebo High doses of zinc intranasal gel seem more effective at reducing the mean duration of cold symptoms (high-quality evidence).

For GRADE evaluation of interventions for common cold, see table, p 10 .

Benefits:

Zinc lozenges versus placebo:

We found three systematic reviews (search date 1997; [18] search date 1998; [19] search date 2003 [20]), which compared zinc lozenges (gluconate or acetate) versus placebo for the treatment of naturally acquired colds. The reviews had different inclusion and exclusion criteria. The first two reviews found that symptoms were unchanged at 3 and 5 days. The first review (7 RCTs, including 2 RCTs excluded from the second review because they were in people with experimentally induced colds; 681 people with naturally acquired colds, 73 people with experimentally induced colds) found that zinc lozenges significantly reduced continuing symptoms at 7 days compared with placebo (random effects model: 14/93 [15%] with zinc *v* 46/94 [49%] with placebo; RR 0.31, 95% CI 0.18 to 0.52). [18] However, the second review (8 RCTs, including 5 RCTs included in the first review and 1 RCT excluded from the first review owing to poor methods, all in people with naturally acquired colds) found no significant difference between zinc lozenges and placebo in continuing symptoms at 7 days (OR 0.52, 95% CI 0.25 to 1.20; absolute results presented graphically). [19] The results at 7 days were statistically heterogeneous, which may be because the RCTs retrieved by the reviews used different zinc formulations, were undertaken in people with different types of virus, or because of other unknown factors. The third review was narrative in character and did not pool data. [20] It found 10 RCTs that were included in the other two reviews (including all of the RCTs identified by both earlier reviews and 1 RCT excluded by the first review owing to poor methods, and 2 RCTs excluded by the second review because they involved people with experimentally induced colds). In addition, it included two RCTs carried out subsequent to the earlier reviews. Of these two RCTs, the first found that zinc lozenges significantly reduced the mean duration of cold compared with placebo (48 people with naturally acquired colds; mean duration: 4.5 days with zinc lozenges *v* 8.1 days with placebo; P less than 0.01). [20] The second RCT (281 people with naturally acquired colds) found no significant difference between zinc lozenges and placebo in the duration or severity of symptoms (median duration of symptoms: 7 days with zinc lozenges *v* 7 days with placebo; P = 0.45). [20]

Zinc intranasal gel versus placebo:

We found one systematic review (search date 2003), [20] which included three RCTs comparing intranasal zinc versus placebo in people with naturally acquired colds. [21] [22] [23] The review was narrative in character and did not pool data. Two higher-dose RCTs found a benefit, whereas one lower-dose RCT did not. The first RCT found that intranasal zinc (daily dose 2.1 mg) significantly reduced overall symptom duration compared with placebo (213 people with naturally acquired colds of less than 24 hours' duration; mean duration: 2.3 days with intranasal zinc *v* 9.0 days with placebo; P less than 0.05). [21] The second RCT also found that intranasal zinc (daily dose 2.1 mg) significantly reduced the duration of cold symptoms compared with placebo (80 people with naturally acquired colds; median duration of symptoms: 4.3 days with intranasal zinc *v* 6.0 days with placebo; P = 0.002). [22] The third RCT found no significant difference in overall symptom duration

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between intranasal zinc (daily dose 0.044 mg) and placebo (160 people with naturally acquired colds of less than 24 hours' duration; mean duration: 7 days for each group; P = 0.45). [23]

Harms:

Zinc lozenges versus placebo:
The first review stated that, in some of the RCTs, a higher proportion of people had nausea, altered taste, dry mouth, abdominal pain, and headache with zinc lozenges compared with placebo, but did not state whether the difference was significant. [18] The second review gave no information on adverse effects. [19]

Zinc intranasal gel versus placebo:
The first RCT identified by the review found that a similar proportion of people experienced a tingling or burning sensation with zinc intranasal gel compared with placebo (45/108 [42%] with zinc *v* 39/105 [37%] with placebo; CI not reported). [21] The second RCT found no significant difference between zinc intranasal gel and placebo in the proportion of people who had one or more adverse effect, although almost twice as many people taking zinc had one or more adverse effect (12/40 [30%] with intranasal gel *v* 5/38 [13%] with placebo; P = 0.10). [22] The RCT reported that nasal stinging or burning sensation was the most common adverse effect reported in both groups. [22] The third RCT found a similar proportion of people with adverse effects (including nausea, mouth or nasal irritation, abdominal pain, or headache) with zinc intranasal gel compared with placebo (any adverse effect: 41/81 [51%] with zinc *v* 40/78 [51%] with placebo). [23]

Comment:

Since our search was performed the first systematic review has been withdrawn because data was out of date. [18]

OPTION VITAMIN C

Symptom relief
Compared with placebo Vitamin C is no more effective at reducing the severity of colds (high-quality evidence).

Symptom duration
Compared with placebo Vitamin C taken at the onset of cold symptoms is no more effective at reducing the duration of cold (high-quality evidence).

For GRADE evaluation of interventions for common cold, see table, p 10 .

Benefits:

Vitamin C versus placebo:
We found one systematic review. [17] The review included any RCT using vitamin C (200 mg or more daily) compared with placebo in people with the common cold. [17] The review found no significant difference in the duration of colds between vitamin C and placebo, commenced after cold symptoms had begun (search date 2004, 7 RCTs, 11 different trial arms; 3294 cold episodes in adults; mean symptom days per episode standardised against control group: WMD –2.54 days, 95% CI –10.09 days to +5.02 days). [17] The RCTs included in the analysis used a variety of therapeutic protocols, ranging from a single dose at the onset of cold symptoms to continued treatment for 4 days using differing regimens. The review noted that RCTs in which vitamin C was used in doses up to 4 g daily as treatment did not demonstrate any benefit, but one large RCT reported an “equivocal” benefit from the use of a very high 8 g therapeutic dose at the onset of symptoms. [17] The review also found no significant difference in the severity of colds between vitamin C and placebo (4 RCTs, 8 different trial arms; 2753 adults; severity measured by mean days indoors or off work or by mean symptom severity score: SMD –0.070, 95% CI –0.016 to +0.020). [17] Again, the included RCTs used a variety of different vitamin C regimens.

Harms:

The review did not report adverse effects for RCTs using vitamin C as treatment. [17] However, the review did include RCTs using vitamin C as prophylaxis. Seven RCTs included in the review provided data on adverse effects. In these RCTs, 2490 people took more than 1 g daily of vitamin C during prophylaxis compared with 2066 people taking placebo. The review stated that no serious symptoms were reported. [17] It found that 5.8% of people taking vitamin C reported symptoms which they attributed to the medication, compared with 6.0% taking placebo (no further details reported). [17]

Comment:

None.

OPTION ANTIBIOTICS

Cure rates
Compared with placebo Antibiotics seem no more effective at 5–14 days at increasing cure rates in people with colds (moderate-quality evidence).

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For GRADE evaluation of interventions for common cold, see table, p 10 .

Benefits:

Antibiotics versus placebo:
We found three systematic reviews. [24] [25] [26] The first review found no significant difference in general improvement or cure at 7 days between antibiotics and placebo (search date 2005; 6 RCTs, 1147 people: 168/664 [25%] with antibiotics *v* 170/483 [35%] with placebo; RR 0.89, 95% CI 0.77 to 1.04). [24] The second review (search date not reported; 12 RCTs, including 4 RCTs identified by the first review and 8 RCTs excluded from the first review owing to poor methods; 1699 children with naturally acquired colds who had symptoms in the previous 2 weeks) found no significant difference in the proportion of children with worse or unchanged clinical outcome at 6–14 days between antibiotics and placebo (6 RCTs with adequate data: 309/835 [37%] with antibiotics *v* 280/647 [43%] with placebo; RR 1.01, 95% CI 0.90 to 1.13; figures reported from table in paper; see comment below), or with complications or progression (5 RCTs: 38/549 [7%] with antibiotics *v* 28/293 [10%] with placebo; RR 0.71, 95% CI 0.45 to 1.12). [25] One RCT identified by the first review (314 adults with naturally acquired colds for 1–30 days; less than 7 days in 85% of people) comparing amoxicillin/clavulanic acid (co-amoxiclav; 375 mg 3 times daily) versus placebo found no overall difference in "cure" rates at 5 days (P value not reported). [27] However, in a predefined subgroup analysis, it found that in the 61 people (20%) found to have positive nasopharyngeal cultures for *H influenzae*, *M catarrhalis*, or *S pneumoniae*, there was a significant difference in recovery at 5 days (27% with co-amoxiclav *v* 4% with placebo; P = 0.001). If such people could be identified at first consultation, then treating four of these people with antibiotic rather than placebo would result in an average of one more recovery at 5 days (NNT 4, CI not reported). However, we currently have no means of easily identifying these people at first consultation. The third systematic review (6 RCTs, 5 of which were included in one or both of the earlier reviews), examined the effect of antibiotics on acute purulent rhinitis associated with an upper respiratory tract infection. [26] It found that antibiotics significantly increased the proportion of people with clearance of purulent rhinitis at 5–8 days compared with placebo (4 RCTs, 254/355 [72%] with antibiotics *v* 154/263 [59%] with placebo; RR 1.18 95% CI 1.05 to 1.33). One RCT was excluded from the analysis as the antibiotic was topical and the placebo was a locally active agent. A second RCT was excluded as it was not clear whether the rhinitis was purulent or clear. [26]

Harms:

Two reviews found that adverse effects such as nausea, vomiting, headache, rash, or vaginitis occured more often with antibiotics than with placebo. [24] [25] We found no evidence of the size of the risk of antibiotic resistance or pseudomembranous colitis. The third review found that antibiotics significantly increased the proportion of people with adverse effects compared with placebo (4 RCTs, RR 1.46 95% CI 1.10 to 1.94; absolute numbers not reported). [26] Reported adverse effects were mainly gastrointestinal, along with a small number of rashes.

Comment:

The relative risk (RR 1.01, 95% CI 0.90 to 1.13) surrounding clinical outcome reported by the second review does not match the absolute results reported; we have quoted it directly from the paper. [25]

Clinical guide:
Because most common colds are viral, the potential benefit from antibiotics is limited. Until rapid identification of those people likely to benefit is possible, the modest effects seen in trials must be weighed against the adverse effects of antibiotics, costs, and potential for inducing antibiotic resistance.

GLOSSARY

High-quality evidence Further research is very unlikely to change our confidence in the estimate of effect
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.
Very low-quality evidence Any estimate of effect is very uncertain.

SUBSTANTIVE CHANGES

Decongestants plus antihistamines New option added for which we found no systematic reviews or RCTs. Categorised as Unknown effectiveness.
Antibiotics One systematic review added, benefits and harms data enhanced; [26] categorisation unchanged (Likely to be ineffective or harmful).
Antihistamines One RCT added, benefits and harms data enhanced; [9] categorisation unchanged (Likely to be beneficial).
Decongestants for long-term relief One already-included systematic review updated, benefits and harms data enhanced; [11] categorisation unchanged (Unknown effectiveness).

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Decongestants for short-term relief One already-included systematic review updated, benefits and harms data enhanced; [11] categorisation unchanged (Likely to be beneficial).
Echinacea One already-included systematic review updated, benefits data enhanced; [13] categorisation unchanged (Unknown effectiveness).
Steam inhalation One already-included systematic review updated, no new evidence added; [17] categorisation unchanged (Unknown effectiveness).

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TABLE **GRADE evaluation of interventions for common cold**

Important outcomes	**Cure rates, symptom severity, time away from work/school, adverse effects**								
Number of studies (participants)	**Outcome**	**Comparison**	**Type of evidence**	**Quality**	**Consis-tency**	**Direct-ness**	**Effect size**	**GRADE**	**Comment**
What are the effects of treatments?									
15 (5286) [7] [8] [9]	Symptom relief	Antihistamines *v* placebo	4	−1	0	−2	0	Very low	Quality point deducted for incomplete reporting of results. Directness points deducted for inclusion of RCTs of experimentally induced colds and for inclusion of other interventions
12 (1249) [11]	Symptom relief	Decongestants (short-term relief) *v* placebo	4	−1	0	0	0	Moderate	Quality point deducted for subjective assessment of outcome
2 (432) [11]	Symptom relief	Decongestants (long-term relief) *v* placebo	4	−2	0	0	0	Low	Quality points deducted for uncertainly about method of randomisation and subjective assessment of outcome
2 (302) [13]	Symptom duration	Echinacea *v* placebo	4	0	−1	0	0	Moderate	Consistency point deducted for conflicting results
3 (230) [17]	Symptom relief	Steam inhalation *v* sham inhalation	4	−2	−1	−1	0	Very low	Quality points deducted for poor methodologies and reporting of results, and uncertainty about validity of control. Consistency point deducted for conflicting results. Directness point deducted for inclusion of RCTs of experimentally induced colds
13 (at least 516 people) [18] [19] [20]	Symptom duration	Zinc lozenges *v* placebo	4	−1	−1	−2	0	Very low	Quality point deducted for incomplete reporting of results. Consistency point deducted for conflicting results. Directness points deducted for comparing different formulations and in people infected with different viruses
3 (453) [21] [22] [23]	Symptom duration	Zinc intranasal gel *v* placebo	4	0	0	0	0	High	
4 (2753) [28]	Symptom relief	Vitamin C *v* placebo	4	0	0	0	0	High	
7 (3294 cold episodes) [17]	Symptom duration	Vitamin C *v* placebo	4	0	0	0	0	High	
2 (2179) [24] [25] [27]	Cure rates	Antibiotics *v* placebo	4	0	−1	0	0	Moderate	Consistency point deducted for different results on sub analysis

Type of evidence: 4 = RCT; 2 = Observational; 1 = Non-analytical/expert opinion
Consistency: similarity of results across studies
Directness: generalisability of population or outcomes
Effect size: based on relative risk or odds ratio

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