

# Prevention and treatment of the common cold: making sense of the evidence

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The common cold is an acute, self-limiting viral infection of the upper respiratory tract involving the nose, sinuses, pharynx and larynx. The virus is spread by hand contact with secretions from an infected person (direct or indirect) or aerosol of the secretions and virus.<sup>1</sup> The incubation period varies but is just under two days for rhinovirus.<sup>2</sup> Symptoms, which generally relate to the infected mucosa, typically peak at 1–3 days and last 7–10 days, although they occasionally persist for three weeks.<sup>1,3–5</sup> They include sore throat, rhinitis, rhinorrhea, cough and malaise.<sup>1,4</sup> The severity and type of symptoms will vary among individuals and with different infective agents. For example, fever is common in children but rare and mild in adults.<sup>1</sup> The incidence of the common cold declines with age.<sup>5–7</sup> Children under two years have about six infections a year, adults two to three and older people about one per year.<sup>5–9</sup> Stress<sup>10</sup> and poor sleep<sup>11</sup> may increase the risk of the common cold among adults, whereas attendance at a daycare centre<sup>12</sup> increases the risk among preschool children.

Rhinovirus accounts for 24%–52% of clinical cases or 52%–76% of infections with an identified pathogen.<sup>6–8,13</sup> No pathogen is identified in 31%–57% of upper respiratory tract infections,<sup>8,13</sup> likely because of a host of reasons, including poor collection technique, low pathogen count due to sampling late in the illness, or previously unidentified agents.<sup>1</sup> Only about 5% of clinically diagnosed cases were found to have bacterial infection (with or without viral co-infection).<sup>13</sup>

Although self-limiting, the common cold is

highly prevalent and may be debilitating. It causes declines in function and productivity at work<sup>14,15</sup> and may affect other activities such as driving.<sup>16</sup> Its impact on society and health care is large. Of individuals with an upper respiratory tract infection, 7%–17% of adults<sup>17,18</sup> and 33% of children<sup>17</sup> visit a physician. Upper respiratory tract infections result in an estimated increase of 12.5% in patient visits per month during cold and flu season.<sup>19</sup> In the United States, direct medical costs related to the common cold (physician visits, secondary infections and medications) were an estimated \$17 billion a year in 1997.<sup>17</sup> Indirect costs owing to missed work because of illness or caring for an ill child were an estimated \$25 billion a year.<sup>17</sup>

We review the evidence underpinning preventive and treatment interventions for the common cold. We do not explore the proposed biologic mechanisms for the different products, because most are not substantiated and generally represent more supposition than science. The quality of the evidence was frequently poor, with a moderate to high risk of bias. Although preventive interventions have somewhat discrete outcomes (presence of an upper respiratory tract infection), interpretation of the evidence for treatment of the common cold is challenged by the complexity of outcome reporting. The evidence used in this review is described in Box 1.

## How can the common cold be distinguished from other conditions?

The symptoms and signs of the common cold overlap with those of other conditions. Allergic rhinitis presents similarly, but it may have a seasonal component or clear allergic aggravation and is unlikely to have an accompanying sore throat. When sore throat is the primary complaint, streptococcal pharyngitis should be considered. Centor criteria<sup>20</sup> are helpful in delineating the need for throat swabs and antibiotics.

Sinusitis (acute or subacute) is a clinical diagnosis without reliable clinical scoring criteria to help differentiate it from the common cold. Groups

## KEY POINTS

- Evidence for interventions aimed at preventing and treating the common cold is frequently of poor quality, and results are inconsistent.
- The best evidence for the prevention of the common cold supports physical interventions (e.g., handwashing) and possibly the use of zinc supplements.
- The best evidence for traditional treatments supports the use of acetaminophen and nonsteroidal anti-inflammatory drugs (for pain and fever) and possibly antihistamine–decongestant combinations and intranasal ipratropium. Ibuprofen appears to be superior to acetaminophen for the treatment of fever in children.
- The best evidence for nontraditional treatments of the common cold supports the use of oral zinc supplements in adults and honey at bedtime for cough in children over one year.

reviewing the evidence for the antibiotic treatment of sinusitis recommend that symptoms be present for 7–10 days and not show signs of improvement before antibiotics are considered.<sup>21,22</sup>

Ear pain and otitis media commonly accompany or follow the common cold, particularly in children. Findings on physical examination can be helpful in diagnosing otitis media (e.g., a bulging tympanic membrane has a likelihood ratio of 51),<sup>23</sup> and there are simple rules for prescribing antibiotics or using watchful waiting in children with possible otitis media.<sup>24</sup>

People with influenza usually are sicker than those with the common cold, the former having fever, chills, headaches, myalgia and malaise. Influenza can be serious in older people and those who are immunocompromised. More serious illness should prompt consideration of meningococcal disease or septicemia.

More details regarding primary conditions whose signs and symptoms overlap with those of the common cold are available in guidelines and review articles on allergic rhinitis,<sup>25</sup> sore throat,<sup>26</sup> sinusitis,<sup>21</sup> otitis media<sup>24</sup> and influenza.<sup>27,28</sup> In addition, the National Institute for Health and Care Excellence (NICE) has released a primary care guide for prescribing antibiotics for upper respiratory tract infections.<sup>29</sup>

## What interventions are effective for preventing the common cold?

Preventive therapies are summarized in Table 1.<sup>30–50</sup>

### Physical interventions

A Cochrane systematic review examined the effectiveness of traditional physical public health interventions in preventing upper respiratory tract infections in 67 studies of various types (randomized controlled trials [RCTs], cluster RCTs, retrospective and prospective cohort studies, case-control studies and before-after studies).<sup>30</sup> The type of interventions varied considerably — handwashing, use of alcohol-based disinfectants, other disinfectants, hand-wipes, gloves, masks, gowns and various combinations. As a result, pooling of data was limited, and many of the studies had an unclear or high risk of bias. Nevertheless, the majority of results suggested that physical preventive measures such as handwashing reduced the risk of getting or spreading upper respiratory tract infections.

### Zinc

Zinc appears to be effective in reducing the number of colds per year, at least in children. A Cochrane review<sup>31</sup> of the prophylactic efficacy of orally administered zinc considered two RCTs that we

also examined individually.<sup>32,33</sup> These studies had methodologic concerns and included only children given zinc sulfate 10 mg or 15 mg daily. The mean number of colds was significantly lower in the zinc group than in the placebo group both in the pooled analysis (Table 1) and in the individual studies (mean 1.2 v. 1.7 [ $p = 0.003$ ] in one trial<sup>32</sup> and 1.7 v. 3.1 [ $p < 0.001$ ] in the other<sup>33</sup>). School absences were significantly lower in the zinc groups of each study, by an average of 0.4 days ( $p = 0.04$ )<sup>32</sup> and 0.8 days ( $p < 0.001$ ).<sup>33</sup> Antibiotic use was also significantly lower in the zinc groups of each study (5 v. 18 [ $p = 0.009$ ]<sup>32</sup> and 20 v. 47 [ $p < 0.001$ ]<sup>33</sup> respectively). In one of the studies,<sup>32</sup> the proportion of children with no colds during the study period was 33% in the zinc group versus 14% in the control group, for a number needed to treat of six.

Although the evidence for cold prevention with zinc comes from studies involving only children, there is no biological reason why zinc would work only in children and not adults.

### Probiotics

Probiotics may be helpful in preventing upper respiratory tract infections, but the interventions and evidence are inconsistent. A systematic review of 14 RCTs included 10 trials ( $n = 3451$ ) that provided sufficient data for pooling.<sup>34</sup> Pediatric and adult populations from a wide variety of countries were included. Probiotic prophylaxis reduced the number of participants who had one or more upper respiratory tract infections (odds ratio [OR] 0.58, 95% confidence interval [CI] 0.36 to 0.92) and the number of upper respiratory tract infections per person-year (rate ratio 0.88, 95% CI 0.81 to 0.96). Both outcomes had inconsistent results in the individual studies, reflected in estimates of heterogeneity ( $I^2 = 69%$  and 44%, respectively).

#### Box 1: Summary of literature review

In July and August 2012, a literature search was performed by one of us (G.M.A.) of PubMed, the Cochrane Database of Systematic Reviews, *ACP Journal Club* and *Evidence-Based Medicine*. Search terms included “common cold” and “upper respiratory tract infection.” In PubMed, the search was restricted to randomized controlled trials (RCTs), reviews, systematic reviews and meta-analyses. Individual treatments were also searched (e.g., “vitamin C”). A similar search was performed in early 2012 by B.A. for a related project. We conducted a manual search of the bibliographies of included articles. Further details of the literature search are available from the authors upon request.

We selected the highest level of evidence available for each intervention, focusing on systematic reviews (with or without a meta-analysis) and RCTs. We rated the quality of evidence for each intervention as high, moderate or low risk of bias. For systematic reviews, we considered the authors' assessment of methodologic quality (e.g., blinding) of included trials but also examined the quality of the systematic review itself (e.g., thoroughness of the literature search). For RCTs, we considered traditional validity criteria (e.g., allocation concealment) as well other limitations (e.g., funding or restricted populations). Lastly, we considered the overall volume (size and number of RCTs) and the consistency of the evidence. We used lower levels of evidence for general information such as epidemiology.

However, use of probiotics reduced antibiotic use (risk ratio 0.67, 95% CI 0.45 to 0.98). In all but two studies, the probiotics varied in types of organisms, combinations of organisms, formulations (e.g., pills, liquids) and quantity (colony-forming units). These inconsistencies limit the clinical application of the study findings.

We examined the two highest-quality studies included in the systematic review. In the first,<sup>35</sup> 638 children aged three to six years attending a community preschool or daycare were randomly assigned to receive either a drink containing the probiotic strain *Lactobacillus casei* DN-114 001 (10<sup>8</sup> colony-forming units) or a matching placebo for 90 days. Use of the probiotic resulted in a reduction of 0.6 upper respiratory tract infections per 100 person-days ( $p = 0.036$ ). In the second RCT,<sup>36</sup> 742 children more than 12 months of age who were admitted to hospital were randomly assigned to drink 100 mL of a fermented milk product containing either *Lac-*

*tobacillus rhamnosus* strain GG (10<sup>9</sup> colony-forming units) or no probiotic for the duration of their hospital stay. The incidence of upper respiratory tract infections was reduced in the probiotic group (relative risk 0.38, 95% CI 0.18 to 0.85), for a number needed to treat of 30.

**Gargling**

Frequent gargling with water may help reduce episodes of upper respiratory tract infection, but evidence is limited to a single study. The well-designed RCT involved 387 adults randomly assigned to gargling with water, gargling with a diluted povidone-iodine solution or usual care (control).<sup>37</sup> Gargling with the povidone-iodine solution had no effect, whereas gargling with water was effective in reducing the risk of an upper respiratory tract infection (30.1% v. 40.8% in the control group;  $p = 0.044$ ), for a number needed to treat of 10. The degree of gargling

**Table 1 (part 1 of 2): Interventions for the prevention of the common cold**

Intervention	Formulation and dose	Evidence	Risk of bias	Outcome	Harms	Comment
Physical intervention <sup>30</sup>	Various techniques (e.g., handwashing, use of alcohol-based hand disinfectant, gloves, masks)	Systematic review of 67 studies (various types)	High (studies had unclear risk of bias for most quality indicators)	General reduced risk with handwashing, hand disinfectant, gloves and masks	N95 masks offered no advantage over normal surgical masks, were uncomfortable and irritated the skin	Likely beneficial
Zinc supplement <sup>31-33</sup>	Zinc sulfate tablets, 10 mg and 15 mg	Meta-analysis (2 RCTs; $n = 400$ , age 5-8 yr)	High (unclear randomization, <sup>33</sup> and events censored from analysis for unclear reasons <sup>32</sup> )	Pooled analysis of 2 RCTs: significant reduction in colds (RR 0.64, 95% CI 0.47 to 0.88); about 0.5-1.4 fewer colds over 5-7 "winter" months	3 children in the intervention group in one RCT had mild gastrointestinal discomfort; no other significant differences noted	Likely beneficial
Probiotics <sup>34-36</sup>	Different organisms, combinations, formulations and quantity; <i>Lactobacillus</i> most common ( <i>rhamnosus</i> , <i>casei</i> and other species)	Systematic review and meta-analysis (10 RCTs; $n = 3451$ ), with focus on 2 RCTs of highest quality	Moderate ( $\leq 50\%$ of the trials were low risk of bias for quality indicators)	Pooled analysis of 6 RCTs: significant reduction in number with $\geq 1$ colds (OR 0.58, 95% CI 0.36 to 0.92); results of RCTs were inconsistent ( $I^2 = 69\%$ )	No difference noted	May be beneficial
Gargling <sup>37</sup>	Tap water or diluted povidone-iodine (7%) solution, 20 mL gargled for 15 s 3 times per session; repeated at least 3 times daily	RCT ( $n = 384$ )	Low (allocation concealment and blinded outcome assessment)	Significantly fewer URTIs with gargling water (RR 0.64, 95% CI 0.42 to 0.99); no significant reduction with gargling povidone-iodine (RR 0.87, 95% CI 0.58 to 1.34)	Not reported	Unclear benefit from water gargling; no benefit from gargling of iodine solution
Ginseng <sup>38-40</sup>	North American ginseng as COLD-FX brand in 5 of 6 RCTs (400 mg generally); Asian ginseng as Ginsana G115 brand	Systematic review (5 RCTs; $n = 747$ ) and single RCT ( $n = 783$ )	High (multiple variations of analysis)	Pooled analysis of 5 RCTs: no significant reduction in colds (relative risk 0.70, 95% CI 0.48 to 1.02); results of RCTs were inconsistent ( $I^2 = 68\%$ ) Analysis of single RCT: no significant difference from placebo ( $p = 0.23$ )	No consistent difference	Unclear benefit
Exercise <sup>41</sup>	45 min of moderate-intensity exercise 5 d/wk	RCT ( $n = 115$ overweight or obese postmenopausal women)	High (unclear allocation concealment and equivocal findings)	Significantly fewer self-reported colds per person-year in intervention group (0.55 v. 0.96 in control group, $p = 0.02$ ); no difference in URTIs between groups ( $p = 0.16$ )	Not reported	Unclear benefit

required was considerable (20 mL for 15 seconds repeated three times, performed three times daily). Confirmation from a second RCT would be helpful before recommending gargling.

### Ginseng

The role of ginseng in preventing colds is questionable. A familiar product in Canada is COLD-FX, a proprietary extract produced from the roots of North American ginseng (*Panax quinquefolius*). A meta-analysis<sup>38</sup> of five RCTs (four of COLD-FX and one of Asian ginseng [*P. ginseng*]) and one RCT<sup>39</sup> of COLD-FX have provided inconsistent results. Some of the trials showed a statistically significant reduction in laboratory-confirmed colds and influenza, whereas others found small changes in clinical, but not laboratory-confirmed, upper respiratory tract infections only.<sup>40</sup> Trials of COLD-FX were found

to have multiple problems, including dropout rates above 10% before a single dose was taken, post-hoc modification of analyses to achieve statistical significance (per-protocol analysis, combination of trials or selection of certain time frames), multiple analyses, a focus on laboratory (not clinical) outcomes and inconsistent results.<sup>40</sup>

### Other interventions

A variety of other interventions have been studied for the prevention of the common cold. Studies of exercise,<sup>41</sup> garlic<sup>42,43</sup> and homeopathy<sup>44–46</sup> showed unclear evidence of benefit, whereas those of vitamin D<sup>48,49</sup> and echinacea<sup>50</sup> showed no evidence of benefit. Vitamin C<sup>47</sup> may provide some benefit in people under physical stress (e.g., marathon runners or soldiers in subarctic environments), but no meaningful benefit has been shown for the average patient.

**Table 1 (part 2 of 2): Interventions for the prevention of the common cold**

Intervention	Formulation and dose	Evidence	Risk of bias	Outcome	Harms	Comment
Garlic supplement <sup>42,43</sup>	Allicin powder 180 mg	Meta-analysis (1 RCT; <i>n</i> = 146)	High (1 trial had unclear allocation concealment)	73 participants in each group; over 90-d period, 24 colds in intervention group v. 65 in control group ( <i>p</i> < 0.001); unclear how many had no colds	Not reported (other than 4 taking garlic and 1 taking placebo having a smell when burping)	Unclear benefit
Homeopathy <sup>44–46</sup>	Multiple different treatments	3 RCTs ( <i>n</i> = 170, 142 and 199 children, respectively, aged ≤ 10 yr)	Moderate (2 trials had 15%–23% drop out before first dose; 1 was nonblinded)	2 placebo-controlled RCTs: no significant effect; 1 RCT with wait-list control showed reduced symptoms and days ill	1 of 3 RCTs reported adverse events; 22% had mild and transient adverse effects, but control group not mentioned	Unclear (likely no) benefit
Vitamin C <sup>47</sup>	Vitamin C 0.2–3 g/d (1 g/d most common)	Meta-analysis (29 RCTs; <i>n</i> = 11 306)	Unclear (reviewers used blinding as surrogate of allocation concealment)	Community participants: no effect (RR 0.97, 95% CI 0.94 to 1.00); participants exposed to cold or heavy physical stress: fewer colds (RR 0.48, 95% CI 0.35 to 0.64). Duration shorter than with placebo (mean difference –9.1%, 95% CI –12.6% to –5.6%). Effect not better with higher dose	None reported	No benefit (no meaningful benefit in the average patient)
Vitamin D <sup>48,49</sup>	Vitamin D 400 IU daily; 200 000 IU monthly for 2 mo, then 100 000 IU monthly	2 RCTs ( <i>n</i> = 164 male military recruits, 322 health workers or students)	Moderate (high risk of bias in one trial, low risk in the other trial)	No consistent benefit	Likely none	No benefit
Echinacea <sup>50</sup>	<i>Echinacea purpurea</i> , <i>E. angustifolia</i> (pressed juice or extract in different dilutions and volumes)	Systematic review (2 RCTs; <i>n</i> = 519)	Low	3 comparisons, not pooled: none showed statistical difference from placebo in preventing colds	No significant difference from placebo	No benefit

Note: CI = confidence interval, OR = odds ratio, RCT = randomized control trial, RR = rate ratio, URTI = upper respiratory tract infection.

Summarized details of these interventions can be found in Table 1. See also Appendix 1 (available at [www.cmaj.ca/lookup/suppl/doi:10.1503/cmaj.121442/-/DC1](http://www.cmaj.ca/lookup/suppl/doi:10.1503/cmaj.121442/-/DC1)) for a more detailed discussion of each intervention.

### What medications are effective for treating the common cold?

The traditional pharmacologic treatments of the common cold are summarized in Table 2.<sup>51–66</sup>

#### Antihistamines, monotherapy

Antihistamines as monotherapy have no meaningful effect in the treatment of the common cold.<sup>51,52</sup> A recent meta-analysis showed no significant improvement in general symptoms for this intervention (Peto OR 0.97, 95% CI 0.85 to 1.12); multiple sensitivity and subgroup analyses did not alter the finding in a meaningful way.<sup>52</sup> Although statistical significance was reached for some nasal symptoms, clinical significance ( $\leq 0.3$

change on 4–5-point scale) was reached for none. An earlier meta-analysis had similar results.<sup>51</sup>

#### Antihistamines, combination therapy

Antihistamines combined with decongestants, analgesics or both appear to have a small to moderate effect on the common cold in older children and adults. A large systematic review and meta-analysis<sup>53</sup> found that the antihistamine–decongestant combination reduced global symptoms in six pooled studies (OR 0.27, 95% CI 0.15 to 0.50). The estimated number needed to treat was five. Although overall adverse events were not increased, there were significant increases in dry mouth (OR 3.77, 95% CI 1.75 to 8.14) and insomnia (OR 3.02, 95% CI 1.08 to 8.47). Fewer, and smaller, RCTs examined other combinations, and pooling was limited. For the antihistamine–analgesic combination, two of three studies reported on global symptoms and found significant improvement. For the antihistamine–decongestant–analgesic combination compared with placebo, four trials reported improve-

**Table 2 (part 1 of 2):** Pharmacologic interventions for the treatment of the common cold

Intervention	Formulation and dose	Evidence	Risk of bias	Outcome	Harms	Comment
Antihistamine, monotherapy <sup>51,52</sup>	Various antihistamines	2 meta-analyses (9 RCTs in first, $n = 1023$ adults; 32 RCTs in second, $n = 8930$ adults and children); total 22 RCTs	Moderate (some trial quality issues and conflicting results)	Overall symptoms and nasal obstruction not improved; subjective improvement in rhinorrhea and sneezing at days 2–4 statistically significant but not clinically significant (scores generally $\leq 0.3$ on scale of 4–5)	Adverse events (primarily sedation) increased with first-generation antihistamines (Peto OR 1.25, 95% CI 1.04–1.50); no increase with nonsedating antihistamines	No clinically meaningful benefit
Antihistamine, combination therapy <sup>53</sup>	Antihistamine plus decongestant or analgesic or both	Meta-analysis (27 RCTs; $n = 5117$ adults and children)	High (trial quality issues common, and conflicting results)	Best evidence for antihistamine–decongestant combination (NNT = 5 for global symptoms); other combinations had small to moderate effects in adults and older children	Some increased adverse events (insomnia and dry mouth) with antihistamine–decongestant combination; no statistically significant differences with other combinations	Likely beneficial in adults and older children; no effect in children $\leq 5$ yr
Decongestant <sup>54–57</sup>	Oral phenylephrine and topical nasal decongestant	3 meta-analyses and 1 systematic review (4–15 RCTs)	High (limited quality information available)	Oral and topical decongestants: small, statistically significant effect on nasal airway resistance, but no consistent clinical effect; no data for children	No consistent effect on heart rate or blood pressure; small increase in insomnia	Small benefit but uncertain clinical significance; no data for children
Intranasal ipratropium <sup>58</sup>	Ipratropium 42–168 $\mu\text{g}$ (1–2 sprays 3–4 times per day)	Meta-analysis (7 RCTs; $n = 2144$ adults and children $\geq 5$ yr)	Moderate (some trial quality issues)	Improved rhinorrhea but not nasal congestion; at 24 h, 87% of ipratropium group v. 73% of control group rated themselves as much better or better ( $p = 0.004$ )	Increased epistaxis, nasal dryness and mouth dryness	Probable benefit

ment in global symptoms and two found statistically significant improvement.

We found no evidence of effectiveness of antihistamines combined with decongestants, analgesics or both in younger children (age  $\leq 5$ ), and Health Canada recommends against use in this age group.<sup>67</sup> Adverse events were significantly increased with antihistamine–analgesic and antihistamine–decongestant–analgesic combinations, but pooled estimates were small and may not reflect actual clinical results.

### Decongestants

Decongestants result in small improvements of uncertain clinical significance in nasal symptoms, according to three meta-analyses<sup>54–56</sup> and a systematic review.<sup>57</sup> Oral decongestants were shown to decrease subjective nasal symptoms by 6% with a single dose and 4% with recurrent doses, but clinical relevance is uncertain.<sup>56</sup> Although phenylephrine (10–25 mg orally) was found to reduce nasal airway resistance by about 10% ( $p < 0.05$ ), the clinical meaning of this outcome is

uncertain.<sup>54,55</sup> Fourteen of 26 studies did not report significant improvement in any subjective clinical outcome.<sup>55</sup> A single RCT of nasal xylometazoline monotherapy found positive effects, but the trial may have selectively reported positive outcomes and was funded by the manufacturer.<sup>57</sup> Children were not represented in trials of topical decongestants, and Health Canada recommends against use in this age group.<sup>67</sup>

### Intranasal ipratropium

Inhaled ipratropium bromide appears to improve cold symptoms, particularly rhinorrhea, with a moderate increase in adverse events such as epistaxis and dryness of the nose and mouth. A systematic review and meta-analysis of intranasal ipratropium bromide spray did not pool data because of variability in scales, measurements and other parameters.<sup>58</sup> Four RCTs identified in the systematic review reported statistically significant improvement in rhinorrhea symptoms compared with placebo. However, four other RCTs found no improvement in nasal congestion compared with

**Table 2 (part 2 of 2):** Pharmacologic interventions for the treatment of the common cold

Intervention	Formulation and dose	Evidence	Risk of bias	Outcome	Harms	Comment
Over-the-counter cough treatments <sup>58</sup>	Antitussives, antihistamines, mucolytics, expectorants, alone or in combination*	Meta-analysis (8 RCTs, $n = 616$ children; 18 RCTs, $n = 3421$ adults)	High (multiple trial quality issues and conflicting results)	Children: no benefit Adults: some inconsistent benefit with some combinations and dextromethorphan	Inconsistently reported	No benefit in children; benefit unclear (but likely small) in adults
Vapour rub <sup>59</sup>	5–10 mL rubbed on chest and neck one night	RCT ( $n = 138$ children, age 2–11 yr)	Moderate (poorly described randomization, blinding limited, single study)	No improvement in cough or rhinorrhea but small improvement in sleep for child and parent compared with placebo	Significant increase in adverse events (burning of skin, eyes and nose)	Unclear benefit, but harms present
NSAID <sup>60</sup>	7 different NSAIDs used (ibuprofen most common)	Meta-analysis (9 RCTs; $n = 1069$ adults)	Moderate (main limitation was missing information on randomization)	No improvement in duration of cold, overall symptoms or most respiratory symptoms; improvement in some pain areas (ear, muscles, headache) but not sore throat	Nonsignificant trend to increased adverse events (risk ratio 2.94, 95% CI 0.51 to 17.03)	Likely beneficial for pain; no benefit for other symptoms
Acetaminophen (paracetamol) <sup>61–64</sup>	1000 mg 4 times daily in adults or 15 mg/kg in children	2 RCTs ( $n = 90$ children, 392 adults), plus 2 meta-analyses focused on fever	Moderate (few trials with limited randomization and allocation information)	Overall, acetaminophen was more effective than placebo in reducing fever and providing mild analgesia; it was less effective than ibuprofen in fever control (in children)	Adverse events higher with 1000 mg acetaminophen v. (25% v. 5%, $p < 0.001$ ); all events were mild or moderate (e.g., sweating)	Likely effective for fever and analgesia v. placebo; inferior to ibuprofen for fever control
Antibiotic <sup>65</sup>	Various antibiotics	Meta-analysis (6 RCTs; $n = 1047$ adults and children)	Moderate (some trial quality concerns and inconsistent results)	No effect on reduction of persistent symptoms (risk ratio 0.95, 95% CI 0.59 to 1.51)	Adverse events increased (relative risk 1.8, 95% CI 1.01 to 3.21)	No benefit, and harms present

Note: CI = confidence interval, NNT = number needed to treat, NSAIDs = nonsteroidal anti-inflammatory drugs, OR = odds ratio, RCT = randomized control trial.  
\*Includes dextromethorphan, codeine, letosteine, brompheniramine–phenylpropanolamine, guaifenesin, pseudoephedrine, diphenhydramine, chlorpheniramine, clemastine and combinations.

placebo. Two RCTs found a statistically significant improvement in the global assessment of symptoms, with 10%–15% more patients in the ipratropium group reporting themselves as “good or better” or “much better or better” on day 1 or 2 (e.g., in one study, 74% of patients using ipratropium and 61% of those using placebo rated themselves “much better or better” [ $p = 0.02$ ]). Pooled data on adverse events (from up to six RCTs) showed significantly increased epistaxis (OR 3.21, 95% CI 1.68 to 6.13), nasal dryness (OR 2.55, 95% CI 1.50 to 4.33) and dry mouth (OR 3.59, 95% CI 1.38 to 9.38).

### Over-the-counter cough suppressants

Over-the-counter cough suppressants are of no benefit for children, and Health Canada recommends against their use in children under the age of six years.<sup>67</sup> For adults, the benefit is unclear but likely small. A systematic review<sup>59</sup> evaluated a variety of outcomes such as cough and global improvement scores in children (age two to seven years), but statistically significant improvements were infrequent and inconsistent and of doubtful clinical significance.<sup>59,68</sup> In addition, a Canadian review of codeine for acute cough in children found no benefit when compared with placebo.<sup>69</sup> In adults, antihistamines and codeine had no effect on cough.<sup>59</sup> One study of guaifenesin found no benefit; in another, 75% of participants reported that guaifenesin was helpful for their cough, compared with 31% given placebo ( $p < 0.01$ ).<sup>59</sup> Dextromethorphan had mixed results, with two positive trials showing a 12%–36% improvement in cough scores ( $p < 0.05$ ).<sup>59</sup> Combination products seemed to have some benefit, but there is little consistency in outcomes and it is not clear whether all negative outcomes were reported. Poor trial quality, varying reported outcomes and inconsistent results limit interpretation.<sup>59</sup>

### Vapour rub

Vapour rub containing camphor, menthol and eucalyptus oil is applied to the neck and chest. In the one RCT<sup>60</sup> we found that assessed its efficacy, harms appeared to outweigh benefits. No effect was found on rhinorrhea. Scores for cough frequency and severity were improved compared with no treatment ( $p = 0.006$  or better) but not compared with petrolatum (placebo). Scores for child and parental sleep were both significantly improved with vapour rub versus petrolatum ( $p = 0.008$  or better). For the combination of all scales (range 6–42), vapour rub had an improved score of about 4 higher than petrolatum ( $p = 0.03$ ). However, significantly increased adverse events over placebo included burning sensation to the skin (28%), nose (14%) and eyes (16%) ( $p < 0.001$  each). Rash and redness of skin each

occurred in 5% of patients using vapour rub, compared with none using petrolatum.

### Other interventions

Nonsteroidal anti-inflammatory drugs and acetaminophen appear to be effective in relieving pain and fever in people with upper respiratory tract infection but not in relieving other symptoms.<sup>61–63</sup> Ibuprofen has been shown to be superior to acetaminophen in fever control, whereas the safety of these drugs, at least in pediatric populations, is equivalent.<sup>64,65</sup> Antibiotics have no beneficial effect on the common cold but do increase adverse events.<sup>66</sup> Because many symptoms of bacterial upper respiratory tract infections overlap with cold symptoms, clinicians may be tempted to prescribe antibiotics. Although prescribing should be minimized, issuing a delayed prescription for an antibiotic at times of uncertainty has been shown to reduce antibiotic use from 93% to 32%.<sup>70</sup>

Summarized details of these interventions can be found in Table 2. See also Appendix 1 for a more detailed discussion of each intervention.

## What alternative and nonpharmacologic treatments of the common cold are effective?

Alternative and nonpharmacologic treatments of the common cold are summarized in Table 3.<sup>47,50,71–80</sup>

### Honey

Consistent findings of three RCTs involving children suggest that a single night-time dose of honey can have a small effect on cough and sleep in children over 12 months old.<sup>71–73</sup> Multiple methodologic issues were present in one or more of the trials, including inadequate description of randomization and allocation, no blinding, exclusion of patients who deviated from the protocol, substitution of clinician ratings in place of parent or child ratings, funding by the Honey Board and uncertain clinical significance.<sup>68,71–73</sup> There was no consistency in adverse events between the trials. Honey should not be given to children younger than 12 months.

### Zinc, oral or intranasal

Inconsistent evidence from a meta-analysis suggests that orally administered zinc reduces the duration and severity of the common cold in adults.<sup>74</sup> A 23-mg zinc gluconate lozenge every two hours was the most commonly studied regimen, although there was considerable variability across studies in dose (4.5 to 23.7 mg), frequency (twice daily to 10 times daily) and formulations (gluconate, sulfate or acetate).<sup>74</sup> Zinc shortened the course of colds significantly (mean difference  $-1.65$  d, 95% CI  $-2.5$  to

–0.8, compared with placebo),<sup>74</sup> a finding similar to but somewhat better than the Cochrane review<sup>31</sup> (standardized mean difference –0.97 d, 95% CI –1.56 to –0.38). However, zinc was found to have no significant effect on the duration of colds in children (mean difference –0.26, 95% CI –0.78 to 0.25), but the effect was significant in adults (mean difference –2.63, 95% CI –3.69 to –1.58).<sup>74</sup> Higher doses appeared to be more effective than lower doses. Zinc did not significantly affect symptom severity in children (standard mean difference –0.05, 95% CI –0.27 to 0.17) but did reduce severity in adults (standard mean difference –0.64, 95% CI –1.05 to –0.24).<sup>74</sup> Although the data were posi-

tive for adults, heterogeneity was consistently high in all results ( $P = 55\%$  to  $95\%$ ), which reflected a high level of inconsistency, even in subgroup testing.<sup>74</sup> Use of oral zinc supplements was associated with an increased risk of adverse events such as bad taste and nausea (risk ratio 1.24, 95% CI 1.05 to 1.46).<sup>74</sup> It is unclear why oral zinc treatment seems to benefit adults more than children.

The evidence to support intranasal use of zinc is weak, and important risks exist.<sup>79</sup> We found only three RCTs of zinc used intranasally, 0.044 mg to 2.1 mg daily in four doses.<sup>79</sup> There was no significant difference in any persisting symptoms at day 3 for all pooled studies, and again the het-

**Table 3:** Alternative and nonpharmacologic interventions for the treatment of the common cold

Intervention	Formulation and dose	Evidence	Risk of bias	Outcome	Harms	Comment
Honey <sup>71-73</sup>	2.5–10 mg, one dose at bedtime	3 RCTs ( $n = 105$ , 139 and 300 children, respectively); most aged 1–5 yr	Moderate (multiple trial quality issues, but results highly consistent)	Evidence of benefit over placebo and dextromethorphan	No consistent adverse events	Small benefit for cough in children (age > 1 yr); no data for adults
Zinc, oral <sup>74</sup>	Different formulations, doses, frequency; zinc gluconate 23-mg lozenge every 2 h most common	Meta-analysis (17 RCTs, $n = 2121$ )	Moderate (high or moderate risk of bias in many studies)	Pooled analysis of 8 RCTs: reduced duration of cold (mean difference –1.65 d, 95% CI –2.5 to –0.8)	Increased adverse events (bad taste and nausea)	Probable benefit in adults, but harms present; no benefit in children
Nasal irrigation <sup>75</sup>	Generally, saline drops (children) or irrigation	Systematic review and meta-analysis (3 RCTs, $n = 618$ )	High (multiple outcomes, most nonsignificant, and quality issues in RCTs)	Pooled analysis of 2 RCTs: no difference in nasal symptom score; other results inconsistent	13% nasal irritation, 30% dry nose, 40% of infants intolerant of nasal drops	Unclear benefit
Humidified air <sup>76</sup>	Heated water (42°C–47°C), vapourized	Systematic review and meta-analysis (6 RCTs, $n = 394$ )	Moderate (unclear allocation concealment and mixed results)	Pooled analysis of 2 RCTs: fewer participants with persistent symptoms (Peto OR 0.31, 95% CI 0.16 to 0.60); very inconsistent results ( $P = 89\%$ )	Increased harms, including mask discomfort and increased nasal congestion	Unclear benefit
Echinacea <sup>50</sup>	Variable formulations and dosing; <i>E. purpurea</i> most common	Systematic review (14 RCTs, $n = 2090$ )	Moderate (some trial quality issues, and inconsistent formulations, cold definitions and results)	Inconsistent results (not pooled); for example, 1 of 6 studies showed improved duration and severity of symptoms	No evidence of harms	Unclear benefit
Chinese medicinal herbs <sup>77</sup>	Various formulations	Systematic review (17 RCTs, $n = 3212$ )	High (poor trial quality)	Data not pooled; 1 of 17 RCTs showed improved severity of symptoms	Not reported	Unclear (likely no) benefit
Ginseng <sup>78</sup>	North American ginseng extract in standard dose (26 mg/kg on day 1, 17 mg/kg on day 2, 9 mg/kg on day 3) v. low dose (half the amounts on each day) v. placebo	1 RCT ( $n = 46$ children aged 3–12 yr)	Low (high-quality trial)	No effects reported	No increase in adverse events	Unclear benefit
Vitamin C <sup>47</sup>	1.5–4 g for 1–5 d	Meta-analysis (7 trials, $n = 3294$ colds)	Moderate (reviewers used blinding as a surrogate of allocation concealment)	Pooled analysis of 7 RCTs: no effect on duration	No evidence of harms	No benefit
Zinc, intranasal <sup>79,80</sup>	Zinc nasal spray 33 mmol/L, each nostril 4 times daily (2.1 mg total) in 2 of 3 studies	Meta-analysis (3 studies, $n = 453$ )	Moderate (high heterogeneity, possible nonblinding and poor description of randomization)	Pooled analysis of 3 RCTs: no significant effect on presence of symptoms at day 3	Nasal burning and stinging; unresolved concern of permanent loss of smell	Do not use (unclear benefit and possible serious harm may exist)

Note: CI = confidence interval, OR = odds ratio, RCT = randomized control trial, RR = rate ratio.

erogeneity was very high ( $I^2 = 99\%$ ). Adverse events such as nasal stinging and burning were more common with zinc used intranasally than with placebo. In addition, anosmia was described in a case series,<sup>80</sup> and a US manufacturer settled legal claims for anosmia.<sup>79</sup>

### Other interventions

Although seven trials with more than 3000 patients examined vitamin C for the treatment of the common cold, no clear benefit was shown.<sup>47</sup> It is not possible to determine whether benefit exists for most other alternative therapies. Studies of nasal irrigation,<sup>75</sup> humidified air,<sup>76</sup> Chinese herbal medicines<sup>77</sup> and echinacea<sup>50</sup> all showed inconsistent results. A single clinical trial of ginseng did not report efficacy outcomes.<sup>78</sup> We did not identify any high-level evidence for garlic or probiotics in the treatment of the common cold.

Summarized details of these interventions can be found in Table 3. See also Appendix 1 for a more detailed discussion of each intervention.

### Unanswered questions

In 1931, the author of a *CMAJ* article on the common cold said, “The common cold is so common that we are apt to pass it by with a contemptuous gesture, unless, of course, we are the sufferers ourselves.”<sup>81</sup>

Much more evidence now exists in this area, but many uncertainties remain regarding interventions to prevent and treat the common cold. We focused on RCTs and systematic reviews and meta-analyses of RCTs for therapy, but few of the studies had a low risk of bias. However, many of the results were inconsistent and had small effects (e.g., vitamin C), which arouses suspicion that any noted benefit may represent bias rather than a true effect.<sup>82</sup> We encourage researchers to perform well-designed RCTs on promising treatments or on preventive methods with limited evidence (i.e., gargling or garlic). Further work to help clinicians clearly distinguish the common cold from other upper respiratory tract infections would also be useful.

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