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Saline nasal irrigation for acute upper respiratory tract infections

David King¹, Ben Mitchell¹, Christopher P Williams², Geoffrey KP Spurling¹

¹Discipline of General Practice, School of Medicine, The University of Queensland, Brisbane, Australia. ²University of Queensland, Royal Brisbane Hospital, Brisbane, Australia

Contact address: David King, Discipline of General Practice, School of Medicine, The University of Queensland, Herston, Brisbane, Queensland, 4029, Australia. d.king@uq.edu.au. d.king@sph.uq.edu.au.

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ABSTRACT

Background

Acute upper respiratory tract infections (URTIs), including the common cold and rhinosinusitis, are common afflictions that cause discomfort and debilitation and contribute significantly to workplace absenteeism. Treatment is generally by antipyretic and decongestant drugs and sometimes antibiotics, even though most infections are viral. Nasal irrigation with saline is often employed as an adjunct treatment for URTI symptoms despite a relative lack of evidence for benefit in this clinical setting. This review is an update of the Cochrane review by Kassel et al, which found that saline was probably effective in reducing the severity of some symptoms associated with acute URTIs.

Objectives

To assess the effects of saline nasal irrigation for treating the symptoms of acute URTIs.

Search methods


Selection criteria

Randomised controlled trials (RCTs) comparing topical nasal saline treatment to other interventions in adults and children with clinically diagnosed acute URTIs.

Data collection and analysis

Two review authors (DK, BM) independently assessed trial quality with the Cochrane 'Risk of bias' tool and extracted data. We analysed all data using the Cochrane Review Manager software. Due to the large variability of outcome measures only a small number of outcomes could be pooled for statistical analysis.
Main results

We identified five RCTs that randomised 544 children (three studies) and 205 adults (exclusively from two studies). They all compared saline irrigation to routine care or other nose sprays, rather than placebo. We included two new trials in this update, which did not contribute data of sufficient size or quality to materially change the original findings. Most trials were small and we judged them to be of low quality, contributing to an unclear risk of bias. Most outcome measures differed greatly between included studies and therefore could not be pooled. Most results showed no difference between nasal saline treatment and control. However, one larger trial, conducted with children, did show a significant reduction in nasal secretion score (mean difference (MD) -0.31, 95% confidence interval (CI) -0.48 to -0.14) and nasal breathing (obstruction) score (MD -0.33, 95% CI -0.47 to -0.19) in the saline group. However, a MD of -0.33 on a four-point symptom scale may have minimal clinical significance. The trial also showed a significant reduction in the use of decongestant medication by the saline group. Minor nasal discomfort and/or irritation was the only side effect reported by a minority of participants.

Authors’ conclusions

Nasal saline irrigation possibly has benefits for relieving the symptoms of acute URTIs. However, the included trials were generally too small and had a high risk of bias, reducing confidence in the evidence supporting this. Future trials should involve larger numbers of participants and report standardised and clinically meaningful outcome measures.

PLAIN LANGUAGE SUMMARY

Nasal saline irrigation for acute upper airway infection symptoms

Review question

Does the addition of nasal saline spray or wash to usual care or placebo reduce the severity of symptoms or speed the recovery of adults and children with cold and flu symptoms that have been present for less than four weeks?

Background

Acute upper respiratory tract infections (URTIs) include colds, influenza and infections of the throat, nose or sinuses. They are usually self limiting viral infections, though sometimes symptoms may persist for many weeks beyond the clearance of the initial infection, with or without establishment of secondary bacterial infections. The aim of treatment is predominantly for relief of symptoms, though some treatments may have a role in reducing the duration of post-viral symptoms, such as cough. Saline nose spray and larger volume nasal washes have become more popular as one of many treatment options for URTIs, and they have been shown to have some effectiveness for chronic sinusitis and following nasal surgery. However, little is known about their effectiveness in the treatment of acute URTI or which symptoms they may be effective for.

Study characteristics

We identified five studies, with a total of 749 participants enrolled and 565 participants providing data, which addressed the research question and met the inclusion criteria. They all compared saline irrigation with routine care or other nose sprays. These studies covered a wide range of ages, countries, sample sizes, dosing methods and frequency, and time since onset of URTI symptoms. They were also highly variable in their design and the symptoms that were measured. This is not surprising due to the lack of consistent measures of URTI symptoms and signs. This resulted in very few common outcome measures that could be combined across these five studies. The evidence is current to August 2014.

Key results

The two additional studies included since the original systematic review have not contributed data of sufficient size or quality to materially change the original findings. Only the largest study, which studied 401 children aged 6 to 10 years, found significant reductions in a number of symptoms, including nasal secretions, sore throat, nasal breathing score and nasal obstruction, as well as reduced use of additional nasal decongestant medications. It also reported a significant improvement in the health status score. There was a reduction in the outcome of time to resolution of symptoms, which was reported in two trials on adult participants, but the difference was not clinically significant. Nasal saline is safe but may cause minor adverse effects, such as irritation or a burning sensation, particularly with products using higher flows or concentrations.

Quality of the evidence
Most studies were small and had significant shortcomings in the design or implementation of the research. Further studies, preferably larger in size and using common outcome measures, are needed to establish the potential for the role of nasal saline irrigation in reducing the severity and duration of acute URTI symptoms, secondary infections and possibly antibiotic usage.
<table>
<thead>
<tr>
<th>Outcomes</th>
<th>Illustrative comparative risks* (95% CI)</th>
<th>Relative effect (95% CI)</th>
<th>No. of participants (studies)</th>
<th>Quality of the evidence (GRADE)</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Mean days to wellness</strong></td>
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<tr>
<td>Patient reports</td>
<td>The mean days to wellness in the control groups was 9.24 days</td>
<td>The mean days to wellness in the intervention groups was 0.74 lower (2.58 lower to 1.11 higher)</td>
<td>111 (2 studies)</td>
<td>⊕⃝⃝⃝</td>
<td>very low¹,²,³</td>
</tr>
<tr>
<td><strong>Antibiotic usage</strong></td>
<td>Study population</td>
<td>OR 0.65 (0.29 to 1.46)</td>
<td>422 (2 studies)</td>
<td>⊕⃝⃝⃝</td>
<td>very low³,⁴</td>
</tr>
<tr>
<td>Patient-reported usage</td>
<td>89 per 1000</td>
<td>60 per 1000</td>
<td></td>
<td></td>
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<tr>
<td></td>
<td>(27 to 124)</td>
<td>(27 to 124)</td>
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<td></td>
<td>Moderate</td>
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<td></td>
<td>88 per 1000</td>
<td>59 per 1000</td>
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<td>(27 to 123)</td>
<td>(27 to 123)</td>
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<tr>
<td><strong>Sore throat</strong></td>
<td>The mean sore throat in the control groups was 1.23 points</td>
<td>The mean sore throat in the intervention groups was 0.14 lower</td>
<td>390 (1 study)</td>
<td>⊕⊕⊕⊕</td>
<td>low⁴</td>
</tr>
</tbody>
</table>
The basis for the assumed risk (e.g. the median control group risk across studies) is provided in footnotes. The corresponding risk (and its 95% confidence interval) is based on the assumed risk in the comparison group and the relative effect of the intervention (and its 95% CI).

CI: confidence interval; OR: odds ratio

GRADE Working Group grades of evidence

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

Moderate quality: Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.

Low quality: 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.

Very low quality: We are very uncertain about the estimate.

1 Bias is likely in the included studies as adequate blinding is not possible with this intervention.
2 There is inconsistency in treatment effects as each study showed trends on either side of the null effect line.
3 The included studies had small numbers of participants. The resulting confidence intervals around the estimated effect vary from minor to large, clinically significant effects.
4 The study was assessed as having a high risk of bias in both randomisation and blinding, with other domains unclear.
5 The mean time of follow-up was not specified. Patients were all reported to be followed up within three weeks.
**BACKGROUND**

**Description of the condition**

Acute upper respiratory tract infections (URTIs) involve the upper airways (the nose, sinuses, larynx and pharynx) and include the common cold, influenza, rhinitis, sinusitis, laryngitis, pharyngitis, tonsillitis and otitis media. Acute infections are defined as those with symptoms lasting up to 28 days (Meltzer 2006).

Acute URTIs are common, can vary in severity from mild to distressing and debilitating and are a major cause of lost days of work and schooling. The economic impact of the common cold alone on workplace absenteeism is estimated to be billions of dollars (Bramley 2002).

Usual treatments for URTIs are symptomatic. Treatment may include antipyretic and analgesic drugs, mucolytics, expectorants and decongestants (NICE 2008; Simasek 2007). While acute URTIs are mainly caused by viruses, antibiotics are often prescribed (Nash 2002). This may lead to increased antibiotic resistance and adverse outcomes, as well as being unnecessary for the patient (NICE 2008).

**Description of the intervention**

Saline can be delivered to the nose as a large-volume wash using reservoir pots and tubing, or in a small volume via spray devices that deliver a fine mist or jet of saline into the nose. The usual concentration is 'normal saline', which approximates an iso-osmolar fluid. Hypertonic saline is sometimes used to deliver a stronger concentration of fluid to the nasal cavity and sinuses.

**How the intervention might work**

Saline irrigation of the nose, which is a popular treatment for sinonasal conditions, is believed to alleviate URTI symptoms by clearing excess mucus, reducing congestion and improving breathing (Tomooka 2000). It is thought to improve mucociliary clearance by increasing the ciliary beat frequency (Talbot 1997). As well as relieving sinonasal symptoms, saline irrigation may remove infectious material from the sinuses and reduce cough associated with postnasal drip (Kaliner 1998). There is evidence for the effectiveness of nasal saline irrigation for chronic sinusitis (Rabago 2002) and allergic rhinitis (Garavello 2003). It has been used as monotherapy or as an adjunct to other treatments, such as oral antihistamines. It is available commercially in various concentrations and formulations of salt and water combinations and is usually delivered by atomised spray or in larger volumes for lavage.

**Why it is important to do this review**

Nasal saline treatment may reduce the burden of disease and workplace absenteeism and reduce the over-prescription of antibiotics for acute URTIs. One non-systematic review of the existing literature found that most trials of nasal saline in acute URTIs were very small, with some being uncontrolled experiments, and concluded that the evidence in favour of nasal saline was “fair” (Papsin 2003).

A Cochrane Review assessed nasal saline irrigation as a treatment for chronic rhinosinusitis and found that it may be useful in providing symptomatic relief, without significant side effects (Harvey 2007).

This systematic review evaluates the efficacy of saline irrigation in the treatment of acute URTIs, to determine whether saline nasal irrigation improves respiratory symptoms of acute URTIs.

**OBJECTIVES**

To assess the effects of saline nasal irrigation for treating the symptoms of acute URTIs.

**METHODS**

**Criteria for considering studies for this review**

**Types of studies**

Randomised controlled trials (RCTs) comparing topical nasal saline treatment (liquid, drops or spray) with at least one other intervention or placebo. We excluded studies trialing another therapy where saline irrigation was used as a control treatment. We excluded non-RCTs or non-comparative studies.

**Types of participants**

Adults and children diagnosed with acute URTIs featuring nasal and/or sinus symptoms for less than four weeks. (Types of acute URTIs include rhinosinusitis, pharyngitis, otitis media, tonsillitis, common cold and influenza).

We excluded studies involving patients with allergic respiratory symptoms, chronic respiratory infections or chronic diseases with respiratory features, such as cystic fibrosis, or those recovering from sinus surgery. We also excluded studies that examined the prevention of developing URTIs from regular use of saline irrigation.
Types of interventions

We proposed to include the following interventions.
1. Nasal lavage, irrigation or similar topical nasal liquid saline treatment, compared with a placebo.
2. Nasal lavage, irrigation or similar topical nasal liquid saline treatment, compared with other standard treatment.
3. Nasal saline plus standard treatment compared with standard treatment alone.

We included studies using atomised sprays or irrigation with larger volumes of saline solutions and all types of commercially available saline preparations and concentrations, including isotonic and hypertonic solutions.

Types of outcome measures

Primary outcomes
1. Change in severity of acute URTI-related symptoms (for example, nasal discharge, congestion, sneezing, headache, sore throat) over periods up to 28 days.
2. Time to resolution of symptomatic illness.

Secondary outcomes
1. Adverse events associated with treatment.
2. Days off work or school.
3. Antibiotic and URTI medication use.

Search methods for identification of studies

Electronic searches
For this update we searched the Cochrane Central Register of Controlled Trials (CENTRAL 2014, Issue 7) (accessed 13 August 2014), which contains the Acute Respiratory Infections (ARI) Group’s Specialised Register, MEDLINE (May 2009 to July week 5, 2014), EMBASE (May 2009 to August 2014), CINAHL (May 2009 to August 2014), AMED (May 2009 to August 2014) and LILACS (May 2009 to August 2014). Details of the previous search strategy are in Appendix 1.

We used the search terms described in Appendix 2 to search MEDLINE and CENTRAL. We combined the MEDLINE search with the Cochrane Highly Sensitive Search Strategy for identifying randomised trials in MEDLINE; sensitivity- and precision-maximising version (2008 revision); Ovid format (Lefebvre 2011).

We modified the search terms to search EMBASE (Appendix 3), CINAHL (Appendix 4), AMED (Appendix 5) and LILACS (Appendix 6). There were no language or publication restrictions.

Searching other resources


We made and handsearched a list of relevant journals. This included: Archives of Otolaryngology, Laryngoscope, Archives of Family Medicine, Journal of Family Practice, Clinical Otolaryngology and American Journal of Otolaryngology.

We also identified studies by checking the bibliographies of all studies retrieved. We contacted authors of relevant trials regarding any recent unpublished work.

Data collection and analysis

We considered, processed and reported data from the included trials in close consultation with the Cochrane Handbook for Systematic Reviews of Interventions version 5.1.0 (Higgins 2011).

Selection of studies

In this 2014 update, two review authors (DK, CW) independently screened the titles and abstracts to exclude studies that were clearly irrelevant. We compared the full texts of the potentially relevant studies to the eligibility criteria. In the original search, one review author (JK) selected the studies. Two review authors (DK, GS) checked the results.

Data extraction and management

Two review authors (DK, BM) independently extracted and summarised details of the studies using a data extraction sheet. Data extracted included year and country of study, study population, methodological quality, type of saline solution used, any adverse events and outcomes. We contacted trial authors for missing information where possible. However, the authors of one paper in the updated search replied to questions about methodology but provided no further information (Wang 2009). We managed and analysed data using Review Manager software, version 5.3 (RevMan 2014).

Assessment of risk of bias in included studies

We assessed trials for risk of bias and appropriateness for inclusion as per the Cochrane Handbook for Systematic Reviews of Interventions version 5.1.0 (Higgins 2011). We undertook ‘Risk of bias’
assessment by evaluating the following components for each included study.

1. The method of generation of the randomisation sequence - if it delivered a known chance allocation to each given group, but individual allocation could not be anticipated.
2. The method of allocation concealment - considered 'adequate' when the assignment could not be foreseen.
3. Who was masked or unmasked to the intervention (participants, clinicians, outcome assessors).
4. Participants lost to follow-up in each arm of the study (split into post-randomisation exclusions and later losses if possible) and whether participants were analysed in the groups to which they were originally randomised (intention-to-treat).

In addition, we collated aspects related to follow-up, participants lost to follow-up, protocol violations and sample size determinations. We recorded the information in the 'Risk of bias' tables and gave a description of the quality of each study, based on a summary of these components.

**Measures of treatment effect**
We measured treatment effects using odds ratio for categorical outcomes and mean difference for continuous measures such as days of illness and symptom scores. Where continuous outcomes were measuring the same outcome, such as symptom score, but using different scales we used standardised mean difference to assess the potential to combine such studies in a meta-analysis.

**Unit of analysis issues**
The unit of analysis was the individual patient who was randomised in each RCT, which allowed standard analysis techniques. Cluster-randomisation did not occur in the included studies.

**Dealing with missing data**
Where missing data were present, we intended to contact the original investigators to request the missing data. We assumed that missing data were missing at random. Where studies were missing more than 40% of their data, we intended to conduct sensitivity analysis to explore the nature of the missing data, where the data were available to do this.

**Assessment of heterogeneity**
We assessed heterogeneity for results measuring similar outcomes. Firstly, we assessed heterogeneity by the degree of overlap in confidence intervals. Where there was little or no overlap, we assumed significant heterogeneity. Secondly, we looked at the Chi² test and assumed that for results with a P value greater than 0.1, significant heterogeneity was likely. Thirdly, we looked at the I² statistic and assumed that results greater than 40% indicated concern about heterogeneity. Where we suspected significant heterogeneity, we did not report totals.

**Assessment of reporting biases**
We attempted to retrieve all the collected data from all included studies (published and unpublished). We intended to compare the results of studies funded by manufacturers of nasal saline delivery products versus those that were funded independently. We also intended to compare the results of published and unpublished studies. We compared the outcomes reported in the trial against the protocol for the studies, whenever possible, to assess for reporting bias.

**Data synthesis**
We undertook meta-analysis for outcomes where there were sufficient comparable data using random-effects methods and heterogeneity did not preclude pooling of results. We conducted narrative synthesis of results where it was not possible to pool outcome data.

**Subgroup analysis and investigation of heterogeneity**
We intended to analyse by subgroups in the event of multiple outcome measures with significant heterogeneity. Groupings that may have been relevant to this study include gender, geographical location, age of participants and type of intervention. This was not relevant to this review as there were insufficient studies to pool data.

**Sensitivity analysis**
We intended to consider sensitivity analysis to investigate the effects of published versus unpublished studies, the quality of included studies and the different types of nasal saline delivery. However, these analyses were not required in this review owing to the small number of outcomes for a small number of included studies.

**GRADE and 'Summary of findings' table**
In this update, we used the GRADE approach to interpret the main findings and report outcome-specific information and the overall quality of evidence from the included studies in each comparison (GRADE 2009). We used the GRADE profiler (GRADEpro 2014) software to import data from Review Manager 5.3 (RevMan 2014) to create a 'Summary of findings' table. We downgraded the evidence from 'high quality' by one level (two if severe) for study limitations that are likely to have a serious impact on the results, including bias for blinding, inconsistency in treatment effects and imprecision (studies with small numbers had confidence intervals that included minor to very large effect sizes).

**RESULTS**
Description of studies

Results of the search

The initial (2009) search yielded the following results: 146 articles in MEDLINE, 68 in EMBASE, 49 in CENTRAL, 22 in CINAHL and none in AMED or LILACS. Of the total 285 trials retrieved, we excluded 280 based on a review of titles and abstracts. Of the five remaining trials, we assessed three as meeting the inclusion criteria and excluded two as not meeting the minimum quality criteria.

This 2014 update identified 75 additional records from searches covering April 2009 to August 2014, with the following results: 18 articles in MEDLINE, 32 in EMBASE, 14 in CENTRAL, 10 in CINAHL, none in AMED and one in LILACS. Of the articles found in these searches, we excluded 46 based on a review of titles and abstracts as not meeting the inclusion criteria. We only selected one study as meeting the inclusion criteria after reading the full text and included it in the updated review (Wang 2009).

We included one further study in this updated review (King 2012, unpublished). This unpublished trial was brought to the attention of the review team by one of the authors (DK). His role in the trial was as a supervisor and clinician. The 'Risk of bias' assessment and data extraction were undertaken by an independent author (BM) who had no role in this trial.

A flowchart of study selection is attached (Figure 1).
Figure 1. Study flow diagram.

- 403 records identified through database searching
- 1 additional record identified through other sources

392 records after duplicates removed

392 records screened

- 357 records excluded
- 35 full-text articles assessed for eligibility

- 30 full-text articles excluded for not meeting the inclusion criteria

5 studies included in qualitative synthesis

2 studies included in quantitative synthesis (meta-analysis)
Included studies
See Characteristics of included studies.
Adam 1998 randomised 143 adults in the USA with clinically diagnosed acute rhinosinusitis or common cold to one of three groups: hypertonic nasal saline irrigation, normal saline irrigation or no treatment (control). One hundred and nineteen adults completed follow-up and contributed data for analysis.
Bollag 1984 studied 74 children in the USA with clinically diagnosed acute URTIs that were randomised to treatment with normal saline drops, phenylephrine drops or no treatment. Forty-six participants were analysed (28 were lost to follow-up).
Slapak 2008 studied 401 children in the Czech Republic with clinically diagnosed common cold or influenza that were randomised to receive standard treatment with or without adjunct nasal irrigation with isotonic saline. Three hundred and ninety contributed data for analysis. The intervention group was further subdivided into three subgroups using different delivery strengths: fine spray, medium jet flow and fine spray eye and nose wash. Each subgroup used the same solution of commercial isotonic seawater. Results were reported for each subgroup and for the saline group as a whole; this review considers the results for the saline group as a whole. Data were reported as mean scores at entry into the study and at a second visit (up to three weeks) with standard deviations. Findings were reported as significant with a P value less than 0.05. Data on symptom scores at earlier time points prior to three weeks were not available, so could not be combined with other studies that all reported outcomes at earlier time points, therefore we have reported the findings descriptively in the text.
Wang 2009 randomised 69 children aged three to 12 years, diagnosed with acute sinusitis and who had symptoms for more than seven days, to either usual care (which included systemic antibiotics, mucolytics and nasal decongestants) or usual care plus nasal saline irrigation. Sixty-seven contributed data for analysis. Participants completed symptoms diaries (averaged over seven days) and these results were considered in this review. Participants also completed a sinus X-ray (Water's projection), a nasal smear, quality of life scores and nasal peak expiratory flow rates, but no raw data were presented. These data were also not available from the trial authors and therefore not included in this review.
King 2012 met the inclusion criteria as it randomised 62 adults with clinically diagnosed acute URTIs to receive standard treatment (analgesia, lozenges and cold and flu medications), or standard treatment plus isotonic saline nasal spray. Results were reported using symptom diaries and included first day of wellness; daily symptom scores measured on a four-point scale; days off work or school; return visits to general practice and use of antibiotics. Only 33 participants contributed data for analysis (see Risk of bias in included studies).

Excluded studies
Two trials were excluded from the original review after evaluation (Inanli 2002; Passali 2005). The main reasons for exclusion were lack of description of randomisation, unblinded studies and inadequate data analysis. Mucociliary clearance, the only outcome measure used by Inanli 2002, was further assessed to be an unsuitable measure for acute URTI symptoms. Passali 2005 was excluded due to doubt as to proper randomisation of the study. For details, see Characteristics of excluded studies table. We also excluded these trials from the 2014 review, but on the grounds of not meeting the inclusion criteria, rather than high risk of bias.

Risk of bias in included studies
A summary of the risk of bias is displayed in Figure 2 and Figure 3. Most studies had some degree of bias as outlined below. For further details, see the Characteristics of included studies table.
Figure 2. 'Risk of bias' summary: review authors' judgements about each risk of bias item for each included study.

<table>
<thead>
<tr>
<th></th>
<th>Random sequence generation (selection bias)</th>
<th>Allocation concealment (selection bias)</th>
<th>Blinding (performance bias and detection bias)</th>
<th>Incomplete outcome data (attrition bias)</th>
<th>Selective reporting (reporting bias)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adam 1998</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>?</td>
<td>+</td>
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<tr>
<td>Bollag 1984</td>
<td>+</td>
<td>?</td>
<td>?</td>
<td>-</td>
<td>+</td>
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<tr>
<td>King 2012</td>
<td>+</td>
<td>+</td>
<td>?</td>
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<tr>
<td>Slapak 2008</td>
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<td>?</td>
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<td>+</td>
<td>?</td>
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<tr>
<td>Wang 2009</td>
<td>?</td>
<td>?</td>
<td>-</td>
<td>+</td>
<td>-</td>
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</tbody>
</table>
**Allocation**

Only King 2012 used computer-generated randomisation to allocate participants to study groups (low risk of bias). Two trials used random number tables (Adam 1998; Bollag 1984). The remaining trials stated that allocation was random but did not describe the method (unclear risk of bias).

Only King 2012 described the method of allocation concealment. An opaque envelope that had been pre-packaged was used to conceal allocation (low risk of bias). The other included trials did not describe the method of allocation concealment (unclear risk of bias).

**Blinding**

Each included trial was only partially blinded (patients, clinicians or outcome assessors; sometimes two, but not all three), suggesting some risk of biased results.

In particular, the design of Slapak 2008 made patient blinding largely impossible as each participant either used the saline spray or did not. The outcome assessors were blinded only to the type of saline spray delivery used and not blinded as to whether or not participants were using the saline treatment (unclear risk of bias).

In King 2012, patient blinding was not achievable as the control group did not use a nose spray as placebo. The outcome measures were reported and extracted from a symptom diary so removing the role of any potential for detection bias (unclear risk of bias).

Wang 2009 did not blind participants to the nasal spray. For the unreported outcomes of sinus X-ray and nasal smear cytology, both of the outcome assessors were blinded to treatment allocation. Blinding was not described for other outcome measures (high risk of bias).

Participants and clinicians were blinded in Adam 1998, but blinding of outcome assessors was not discussed (low risk of bias). Conversely, the outcome assessors in Bollag 1984 were blinded to patient treatment group but blinding of participants (and parents) was not discussed (unclear risk of bias).

**Incomplete outcome data**

Adam 1998 reported 24 of 143 participants lost to follow-up, although a further 35 of the completers failed to submit a complete symptom checklist. Intention-to-treat analysis was performed (unclear risk of bias).

Bollag 1984 reports that 28 of 74 participants were lost to follow-up, though evenly distributed between trial groups (high risk of bias).

King 2012 adequately discussed patients lost to follow-up, however there was a significant difference in numbers lost to follow-up between the treatment and control groups (high risk of bias).

In Wang 2009 there was no loss to follow-up. However, there are missing data for two participants for the symptoms scores used in this review. There is one other participant with missing data for
an outcome not included in this review (low risk of bias). Slapak 2008 adequately discussed drop-outs and losses to follow-up, which numbered only 11 out of the initial 401 participants enrolled in the trial (low risk of bias).

Selective reporting
Wang 2009 reported statistically significant nasal peak expiratory flow rates but presented no data for this outcome. The authors were unable to provide this. Wang 2009 also reported significantly improved quality of life scores in the nasal saline group but again no data were presented or available to the review authors for inclusion in this review (high risk of bias).

Other potential sources of bias
The Wang 2009 paper also had methodological weaknesses. Patients recorded daily symptoms in a symptom diary, but the baseline score for individual and total symptom score (TSS) was calculated as a mean of daily scores during the baseline period of seven days, rather than on the day of entry to the trial. We also noted that there was a statistically significant difference between the two treatment groups at baseline (which included week one of treatment) as well as at two and three weeks after treatment. This could mean that there was a problem with randomisation or that nasal saline caused the difference within the first week, as these baseline data are averaged over the first seven days. We also noted incorrect data in the tables presented in the Wang 2009 paper. We contacted the trial authors who confirmed this error but stated that the results presented in the text and Table 2 of the paper were correct (high risk of bias). Other potential sources of bias were not identified in the other included studies (low risk of bias).

Bollag 1984 provided incomplete data that were not suitable for pooling, instead reporting only mean scores for each group at baseline and follow-up two days later, with baseline scores varying considerably. We could calculate the difference in mean improvement across the groups from the data given but standard deviations were not available and we were not able to access original raw data.

Effects of interventions
See: Summary of findings for the main comparison

Normal saline plus standard treatment compared to standard treatment alone for acute upper respiratory tract infections

The clinical measures used in the included studies were so heterogeneous as to only allow minimal pooling of data. Other than time to symptom resolution (assessed both by King 2012 and Adam 1998) and antibiotic usage (King 2012; Slapak 2008), the results from each study must be presented individually. Although nasal symptom score was measured by a few studies, differences in methods of data collection make pooling of data impossible or misleading. For example, Adam 1998 reported a nasal symptoms score that was a composite of both nasal and non-nasal symptoms (cough, headache), which precluded pooling of data. Wang 2009 also measured nasal symptoms scores. However, the data were averaged over a week-long cycle, without reporting the baseline score at trial entry, and could not be combined.

Primary outcomes

1. Change in severity of acute upper respiratory tract infection (URTI)-related symptoms over periods up to 28 days

Nasal symptom score

Three studies reported nasal symptoms at day three. All showed no difference between the saline nasal irrigation group and the observation only group (Adam 1998; Bollag 1984; King 2012). King 2012 rated symptoms on a four-point symptom scale, from zero (no symptoms) to three (severe symptoms). Bollag 1984 used a similar scale but reversed, with one representing severe symptoms and four indicating no symptoms. Both of these studies failed to adjust for baseline difference, while Adam 1998 used multivariate linear regression to adjust for baseline severity. Adam 1998 claimed to use a four-point symptom scale similar to King 2012, but their results were presented as mean scores up to a maximum of five. Two studies also reported nasal symptom scores at day seven, again neither reporting statistical differences between the treatment groups (Adam 1998; King 2012). Wang 2009 compared the baseline mean score from the first week to the second and third week score for four nasal and four non-nasal symptoms, and reported no statistical difference in symptoms scores, with the exception of daytime rhinorrhea and nocturnal nasal congestion (P value < 0.05).

Slapak 2008 reported a significant reduction nasal secretion score at visit two (up to three weeks after enrolment) for all nasal saline groups compared to control as a mean difference (MD) of -0.31 (95% confidence interval (CI) -0.48 to -0.14) on a four-point scale.

Nasal secretion type

Participants studied by Slapak 2008 were assessed at the first and second visits (up to three weeks from study entry) for type of nasal secretions and the qualitative assessment (absent, serous, seropurulent or purulent) was translated to a numerical score for grouping of results. For this comparison of the saline wash and control groups at the second visit on a four-point scale the MD was -0.34 (95% CI -0.50 to -0.18), indicating a small improvement with nasal saline irrigation.
Nasal patency

Slapak 2008 evaluated the degree of difficulty of nasal breathing as a four-point “breathing score” for each patient at the first and second visits. The difference for the saline wash group compared with the control group at the second visit was MD -0.33 (95% CI -0.47 to -0.19).

Wang 2009 recorded nasal peak expiratory flow rate at three intervals during their study period. The authors reported a statistically significant mean improvement in nasal peak expiratory flow rate for the normal saline group at an undisclosed medium time point and end of study time point. However, no raw data were available and therefore we cannot report the size of this difference nor comment on the clinical significance. Baseline differences were also not reported.

Respiratory symptom score

Only one included study, examining infants and children up to 24 months of age, provided respiratory symptom scores for each group of patients (Bollag 1984). This score included cough and difficulty in breathing. At day three, there was no significant difference in respiratory symptom score between any of the compared treatment or control groups based on a direct comparison to group scores on day three. However, the saline group improved by 0.91 from baseline compared to 0.26 for the phenylephrine group and 0.80 for the control group on a four-point scale.

Activity symptom score

This is a score reflecting the child’s degree of wellness in terms of behaviours such as feeding, playing and sleeping. Analysis of the data for activity symptom score at day three showed no difference, statistical or otherwise, between any of the compared treatment or control groups (Bollag 1984).

Overall health status

Slapak 2008 included health status scores, indicating the degree of symptomatic improvement based on patient reports (Table 1). Scores were given on a scale of one to four, with a health status score of one indicating cure and a score of four representing no change. The mean health status score at the follow-up examination for the group treated with normal saline irrigation, 11 out of 36 (30.5%) complained of dry nose and four out of 31 (12.9%) reported pain or irritation from the treatment (P value = 0.05 for nasal irritation).

As none of the trials discussed patient withdrawal in detail, it is possible that some may have left the studies for reasons related to adverse effects or discomfort from treatment.

1. Adverse events associated with treatment

Three studies reported adverse effects from treatment with nasal saline, or difficulty with patient toleration of treatment. The study using infant patients reported that six out of 15 participants (40.0%) did not tolerate treatment with saline nasal drops, while seven out of 16 (43.7%) did not tolerate treatment with phenylephrine drops (Bollag 1984). While the group numbers are small, the similar proportions suggest that the infants may not have tolerated the delivery of nasal drops, rather than the saline itself.

In the study using adult patients with the common cold or rhinosinusitis, in the group using hypertonic saline irrigation seven out of 33 participants (21.2%) complained of dry nose and 11 out of 33 (33.3%) reported pain or irritation (Adam 1998). Among the group treated with normal saline irrigation, 11 out of 36 (30.5%) complained of dry nose and four out of 31 (12.9%) reported pain or irritation from the treatment (P value = 0.05 for nasal irritation).

The third study, using children, found an overall rate of adverse events of 8.7%, most of which were reported by participants in the medium jet group and associated with the higher flow rate (Slapak 2008). The rates of adverse effects were not reported for the control group, only the reporting of rates for all the saline intervention groups. The trial authors did not specify further the type of complaints but mention that three participants experienced nosebleeds.

2. Days off work or school

Only King 2012 reported days off work with no significant difference between groups (1.3 days for the control group versus 1.9 for the saline group).
3. Antibiotic and URTI medication use

King 2012 and Slapak 2008 compared the use of antibiotics in saline groups versus controls and found a trend to reduced antibiotic use in the nasal saline group, though this did not reach statistical significance (Analysis 2.1). Slapak 2008 did report statistically significant reductions in nasal decongestant and mucolytic medication used for symptomatic relief in the saline groups (P value < 0.5) (Table 3).

DISCUSSION

Summary of main results

The five included randomised controlled trials (RCTs) of saline nasal irrigation provide limited evidence that treatment is effective for symptoms of acute upper respiratory tract infections (URTs). Nasal symptom scores, combined from a complex of different symptoms in different trials, were statistically similar between treatment and control groups. There was a reduction in the outcome of time to resolution of symptoms, which was reported in two trials, but the difference was not clinically significant. The largest trial, which also had a high risk of bias, reported a number of statistically significant outcomes for the nasal saline group at follow-up, including reduction of sore throat, nasal secretion and secretion type and nasal breathing score (Slapak 2008). It also reported a significant improvement in the health status score. There was a trend towards reduced antibiotic use in one study with saline nasal irrigation and this study also demonstrated a statistically significant reduction in the use of adjunct nasal decongestant treatment with nasal saline irrigation compared to control (Slapak 2008). One study, reported a significant difference in quality of life and peak nasal expiratory flow (Wang 2009). However, there were significant methodological and reporting flaws that limit the interpretation of these data.

No serious adverse effects occurred in the included trials, although three children in one study experienced nosebleeds (Slapak 2008). Minor adverse events were not uncommon and 40% to 44% of babies were shown to have difficulty with nasal drops. Discomfort in one study was associated with higher application pressures rather than the nasal saline solution itself (Slapak 2008).

Overall completeness and applicability of evidence

This review focused on RCTs of saline nasal irrigation for the symptomatic treatment of acute URTIs. The nature of saline nasal irrigation makes double-blinding difficult and an appropriate placebo difficult to find. There were a limited number of RCTs available and all of these studies were small in size. Of the five included trials, only two main outcomes could be combined for pooled analysis due to the differences in the clinical measures used. The two additional studies included since the original systematic review have not contributed data of sufficient size or quality to materially change the original findings (King 2012; Wang 2009). Each trial reviewed used different strengths of saline solution, again limiting the possibilities for data comparison. In particular, Slapak 2008 used a commercial isotonic seawater product containing zinc and other elements that may be a factor in the effects of the product.

Only one of the included papers examined the effect of saline irrigation on other symptoms, such as anosmia (loss of the sense of smell) and cough associated with acute URTIs (Slapak 2008). This is a potential clinical application of the treatment but we located no other papers addressing the topic.

The clinical outcomes measured by each study were largely subjective, focusing on patient-reported symptoms, which increases risk of bias in the results. Furthermore, Bollag 1984 and Wang 2009 relied on interpretation and reporting of infant patients’ symptoms by parents, contributing to potential bias and this is a limitation in the interpretation of the results of these studies. Two excluded studies, although excluded for not meeting the inclusion criteria, provided some corroborating evidence to support the need for future research that is better structured and controlled to investigate nasal saline irrigation as a treatment for acute URTIs (Inanli 2002; Passali 2005). The measure of mucociliary clearance (measured by Inanli 2002) is not clinically relevant and data relating to symptom relief and duration of illness would be more useful.

Quality of the evidence

The summary of the evidence is presented in the Summary of findings for the main comparison. For nasal saline versus a standard therapy or observation, we judged the evidence for a reduction in nasal symptoms or time to wellness to be of very low or low quality, meaning that we cannot have a high degree of confidence in this result. The studies are generally at unclear risk of bias and the sample sizes are small (most with fewer than 100 participants overall) and the possibility of chance findings and publication bias is high. Most of the data come from one or two trials. Further research is very likely to have an important impact on our confidence in the estimate of effect.

Potential biases in the review process

We included one unpublished study in this updated review (King 2012). This unpublished trial was supervised by one of the authors (DK), whose role in the trial was as a supervisor and clinician. The ‘Risk of bias’ assessment and data extraction were undertaken by independent authors (BM, CW), who had no role in this trial.
AUTHORS’ CONCLUSIONS

Implications for practice

Limited data from five randomised controlled trials (RCTs) suggest that saline nasal irrigation may have some benefit in patients with acute upper respiratory tract infections (URTIs). While some participants experienced minor discomfort, no serious side effects were identified. Nasal irrigation with saline is a safe treatment that may be mildly beneficial to some patients, though the existing evidence is too limited to support recommendations for or against its role as a standard intervention.

Implications for research

The two new studies added to this review have not changed the findings from the last published review. However, further well-designed, sufficiently large and well-conducted RCTs are warranted to establish the place of nasal saline irrigation in acute URTIs. Further research should include clinically relevant respiratory symptoms as outcome measures, including cough. Given the range of different available topical saline treatments, future studies could include comparisons of liquid washes to sprays in the treatment of URTIs.

ACKNOWLEDGEMENTS

The authors wish to thank Mieke van Driel for her advice and support.

REFERENCES

References to studies included in this review

Adam 1998  {published data only}

Bollag 1984  {published data only}

King 2012  {unpublished data only}

Slapak 2008  {published data only}

Wang 2009  {published data only}

References to studies excluded from this review

Inanli 2002  {published data only}

Passali 2005  {published data only}
Passali D, Damian V, Passali FM, Passali GC, Bellussi L. Atomised nasal douche vs nasal lavage in acute viral rhinitis.


Additional references

Bramley 2002

Garavello 2003

GRADE 2009

GRADEpro 2014
McMaster University. GRADEpro. 3.6. Hamilton: McMaster University, 2014.

Harvey 2007

Higgins 2011

Kaliner 1998
References to other published versions of this review

Kassel 2007

Kassel 2010

* Indicates the major publication for the study
Characteristics of included studies  

Adam 1998

<table>
<thead>
<tr>
<th>Methods</th>
<th>Randomised controlled trial. 1 year duration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Participants</td>
<td>143 adults with common cold or acute rhinosinusitis, with symptoms for less than 3 weeks duration, were randomised. Conducted in Minnesota, USA. 119 participants contributed data for analysis</td>
</tr>
</tbody>
</table>
| Interventions | Hypertonic saline spray, 2 squirts in each nostril 3 times a day  
Normal saline spray, 2 squirts in each nostril 3 times a day  
No treatment, observation only  
Treatment continued until resolution of symptoms |
| Outcomes | Nasal symptom score on day 3  
Time to symptom resolution (day of well-being)  
Additional OTC treatment required |

Notes: -

Risk of bias

<table>
<thead>
<tr>
<th>Bias</th>
<th>Authors’ judgement</th>
<th>Support for judgement</th>
</tr>
</thead>
<tbody>
<tr>
<td>Random sequence generation (selection bias)</td>
<td>Low risk</td>
<td>Random numbers table used</td>
</tr>
<tr>
<td>Allocation concealment (selection bias)</td>
<td>Unclear risk</td>
<td>Not mentioned in paper</td>
</tr>
<tr>
<td>Blinding (performance bias and detection bias) All outcomes</td>
<td>Low risk</td>
<td>Patients and clinicians blinded; outcome assessors not discussed</td>
</tr>
<tr>
<td>Incomplete outcome data (attrition bias) All outcomes</td>
<td>Unclear risk</td>
<td>Drop-out and losses to follow-up not discussed. 24 participants (16%) were lost to follow-up</td>
</tr>
<tr>
<td>Selective reporting (reporting bias)</td>
<td>Unclear risk</td>
<td>Intention-to-treat analysis performed; original study protocol not available</td>
</tr>
<tr>
<td>Other bias</td>
<td>Low risk</td>
<td>No other potential sources of bias identified</td>
</tr>
</tbody>
</table>
### Bollag 1984

<table>
<thead>
<tr>
<th>Methods</th>
<th>Randomised controlled trial. November and December 1980</th>
</tr>
</thead>
<tbody>
<tr>
<td>Participants</td>
<td>74 children were randomised, from 3 weeks to 2 years of age, with unspecified acute upper respiratory infections. Los Angeles, California, USA. 46 children contributed data for analysis</td>
</tr>
<tr>
<td>Interventions</td>
<td>Saline nose drops, 0.9%, 4 drops in each nostril every 2 hours as needed Phenylephrine nose drops, 0.25% solution, 4 drops 4 times a day for no more than 3 days No treatment</td>
</tr>
<tr>
<td>Outcomes</td>
<td>Measured at 2 days after first visit Nasal symptom score Respiratory symptom severity Activity signs</td>
</tr>
</tbody>
</table>

#### Risk of bias

<table>
<thead>
<tr>
<th>Bias</th>
<th>Authors' judgement</th>
<th>Support for judgement</th>
</tr>
</thead>
<tbody>
<tr>
<td>Random sequence generation (selection bias)</td>
<td>Low risk</td>
<td>Random numbers table used</td>
</tr>
<tr>
<td>Allocation concealment (selection bias)</td>
<td>Unclear risk</td>
<td>Not mentioned in paper</td>
</tr>
<tr>
<td>Blinding (performance bias and detection bias) All outcomes</td>
<td>Unclear risk</td>
<td>Outcome assessors blinded; others (including patients/parents) not blinded, control group had no comparable intervention to the intervention groups</td>
</tr>
<tr>
<td>Incomplete outcome data (attrition bias) All outcomes</td>
<td>High risk</td>
<td>Drop-outs and losses to follow-up adequately discussed; 28 out of 74 participants dropped out, equal in all 3 groups</td>
</tr>
<tr>
<td>Selective reporting (reporting bias)</td>
<td>Unclear risk</td>
<td>Intention-to-treat analysis not performed; original study protocol not available</td>
</tr>
<tr>
<td>Other bias</td>
<td>Low risk</td>
<td>No other potential sources of bias identified</td>
</tr>
</tbody>
</table>

### King 2012

<table>
<thead>
<tr>
<th>Methods</th>
<th>Randomised controlled trial. 2010 to 2012</th>
</tr>
</thead>
<tbody>
<tr>
<td>Participants</td>
<td>62 adults with common cold or URTI diagnosed clinically, Brisbane, Australia. 33 participants contributed data for analysis</td>
</tr>
</tbody>
</table>
King 2012  *(Continued)*

<table>
<thead>
<tr>
<th>Interventions</th>
<th>Saline nasal spray, plus usual treatment. Normal saline, instructed to use 2 to 3 sprays in each nostril at least 4 times daily Control group - usual treatment apart from any other medication delivered by nose spray</th>
</tr>
</thead>
<tbody>
<tr>
<td>Outcomes</td>
<td>Day to wellness Symptom score</td>
</tr>
<tr>
<td>Notes</td>
<td>-</td>
</tr>
</tbody>
</table>

**Risk of bias**

<table>
<thead>
<tr>
<th>Bias</th>
<th>Authors' judgement</th>
<th>Support for judgement</th>
</tr>
</thead>
<tbody>
<tr>
<td>Random sequence generation (selection bias)</td>
<td>Low risk</td>
<td>Computer-generated blocks of 10 for randomisation</td>
</tr>
<tr>
<td>Allocation concealment (selection bias)</td>
<td>Low risk</td>
<td>Allocation done using opaque envelopes that were pre-packaged</td>
</tr>
<tr>
<td>Blinding (performance bias and detection bias)</td>
<td>Unclear risk</td>
<td>Participants know which allocation they have received by the nature of their treatment Outcome assessed by patient reporting via symptom diary only</td>
</tr>
<tr>
<td>All outcomes</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Incomplete outcome data (attrition bias)</td>
<td>High risk</td>
<td>Adequately described but many more participants lost to follow-up in the treatment group compared with placebo. Only 33 of 62 enrolled completed follow-up</td>
</tr>
<tr>
<td>All outcomes</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Selective reporting (reporting bias)</td>
<td>Low risk</td>
<td>All reported on adequately as pre-described; original study protocol was available</td>
</tr>
<tr>
<td>Other bias</td>
<td>Low risk</td>
<td>Recruited from attending GPs who may have biased more serious infections - unlikely to have affected outcome</td>
</tr>
</tbody>
</table>

Slapak 2008

<table>
<thead>
<tr>
<th>Methods</th>
<th>Randomised controlled trial. Multicentre, open-label. January to April 2006</th>
</tr>
</thead>
<tbody>
<tr>
<td>Participants</td>
<td>401 children aged 6 to 10 years, with common cold or influenza. Czech Republic. 390 contributed study data</td>
</tr>
<tr>
<td>Interventions</td>
<td>3 groups randomised to receive different delivery methods of isotonic saline (sea water), delivered 6 times per day, plus standard treatments</td>
</tr>
</tbody>
</table>
### Slapak 2008 (Continued)

| Outcomes                                    | Group 1 - medium jet flow  
|                                           | Group 2 - fine spray  
|                                           | Group 3 - eye and nose wash with a fine spray  
|                                           | The 4th group received standard treatments only (control group)  
| Notes                                      |  
| Risk of bias                               |  

<table>
<thead>
<tr>
<th>Bias</th>
<th>Authors’ judgement</th>
<th>Support for judgement</th>
</tr>
</thead>
<tbody>
<tr>
<td>Random sequence generation (selection bias)</td>
<td>High risk</td>
<td>Sequence of clinic arrival used for allocation</td>
</tr>
<tr>
<td>Allocation concealment (selection bias)</td>
<td>Unclear risk</td>
<td>Not mentioned in paper</td>
</tr>
<tr>
<td>Blinding (performance bias and detection bias)</td>
<td>Unclear risk</td>
<td>No patient blinding possible due to study design; outcome assessors blinded to saline delivery method but not to intervention versus control</td>
</tr>
<tr>
<td>All outcomes</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Incomplete outcome data (attrition bias)</td>
<td>Low risk</td>
<td>Drop-out and losses to follow-up small and adequately discussed. 390 of 401 completed the study (11 lost to follow-up)</td>
</tr>
<tr>
<td>All outcomes</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Selective reporting (reporting bias)</td>
<td>Unclear risk</td>
<td>Intention-to-treat analysis not performed; original study protocol not available</td>
</tr>
<tr>
<td>Other bias</td>
<td>Low risk</td>
<td>No other potential sources of bias identified</td>
</tr>
</tbody>
</table>

### Wang 2009

<table>
<thead>
<tr>
<th>Methods</th>
<th>Randomised controlled trial. December 2006 to June 2008</th>
</tr>
</thead>
<tbody>
<tr>
<td>Participants</td>
<td>69 children, aged 3 to 12 years, with acute sinusitis. Taiwan. 2 evidently lost to follow-up</td>
</tr>
<tr>
<td>Interventions</td>
<td>Normal saline nasal irrigation, with 15 to 20 ml each nostril, 1 to 3 times a day and standard treatments Standard treatments only</td>
</tr>
</tbody>
</table>
| Outcomes                                     | Nasal symptom score  
|                                              | Paediatric Rhinoconjunctivitis Quality of Life Score  
|                                              | Nasal peak expiratory flow rate                         |
Wang 2009  
*(Continued)*

<table>
<thead>
<tr>
<th>Nasal smear</th>
<th>Sinus X-ray</th>
</tr>
</thead>
<tbody>
<tr>
<td>Notes</td>
<td>-</td>
</tr>
</tbody>
</table>

### Risk of bias

<table>
<thead>
<tr>
<th>Bias</th>
<th>Authors' judgement</th>
<th>Support for judgement</th>
</tr>
</thead>
<tbody>
<tr>
<td>Random sequence generation (selection bias)</td>
<td>Unclear risk</td>
<td>Correspondence from authors confirmed randomisation but no detail on method</td>
</tr>
<tr>
<td>Allocation concealment (selection bias)</td>
<td>Unclear risk</td>
<td>Not described in paper, nor obtained from authors. 30 participants assigned to intervention and 39 to placebo group. Significant differences between groups at baseline, particularly in rhinorrhoea score</td>
</tr>
<tr>
<td>Blinding (performance bias and detection bias)</td>
<td>High risk</td>
<td>Poorly described. Most outcome measures were not blinded to participants or researchers. Some outcomes were objective measures, less vulnerable to bias</td>
</tr>
<tr>
<td>Incomplete outcome data (attrition bias)</td>
<td>Low risk</td>
<td>There is a comparatively small loss of participant data (2 out of 69 not included) but no explanation in the paper</td>
</tr>
</tbody>
</table>
| Selective reporting (reporting bias)           | High risk          | Not all of the study’s pre-specified primary outcomes have been reported; some outcomes of interest in the review are reported incompletely  
|                                                |                    | In addition, there are errors in the reported tabulated data. We clarified with the authors which data are correct before including data in our review |
| Other bias                                     | High risk          | In addition to the above, there are some methodological flaws, mainly the averaging of symptoms over a week, especially over the first week that included a baseline measurement. We noted that from the data we cannot conclude that the groups were equal at baseline, nor that the improvement was due to an early treatment effect. We asked the authors to address this issue, with no reply |

OTC = over the counter
Characteristics of excluded studies  [ordered by study ID]

<table>
<thead>
<tr>
<th>Study</th>
<th>Reason for exclusion</th>
</tr>
</thead>
</table>
| Inanli 2002 | Failed to meet the inclusion criteria, as no clinically relevant outcomes measured  
Method of allocation concealment not described  
No blinding  
Selection bias not controlled |
| Passali 2005 | Failed to meet the inclusion criteria, as no comparison group as a control; both groups in the trial received nasal saline via different delivery methods  
Methods of randomisation and allocation concealment not described  
Doubt as to randomisation used  
No blinding  
Intention-to-treat analysis not performed |
### Comparison 1. Time to symptom resolution

<table>
<thead>
<tr>
<th>Outcome or subgroup title</th>
<th>No. of studies</th>
<th>No. of participants</th>
<th>Statistical method</th>
<th>Effect size</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 Mean days to wellness (normal saline plus standard therapy versus standard therapy)</td>
<td>2</td>
<td>111</td>
<td>Mean Difference (IV, Random, 95% CI)</td>
<td>-0.79 [-4.72, 3.14]</td>
</tr>
</tbody>
</table>

**Analysis 1.1. Comparison 1 Time to symptom resolution, Outcome 1 Mean days to wellness (normal saline plus standard therapy versus standard therapy).**

- **Review:** Saline nasal irrigation for acute upper respiratory tract infections
- **Comparison:** 1 Time to symptom resolution
- **Outcome:** 1 Mean days to wellness (normal saline plus standard therapy versus standard therapy)

<table>
<thead>
<tr>
<th>Study or subgroup</th>
<th>Normal saline</th>
<th>Standard therapy</th>
<th>Mean Difference</th>
<th>Weight</th>
<th>Mean Difference</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N</td>
<td>Mean(SD)[Days]</td>
<td>N</td>
<td>Mean(SD)[Days]</td>
<td></td>
</tr>
<tr>
<td>Adam 1998</td>
<td>43</td>
<td>9.2 (7.4735)</td>
<td>35</td>
<td>8 (3.7844)</td>
<td>50.4 %</td>
</tr>
<tr>
<td>King 2012</td>
<td>10</td>
<td>7.67 (3.57)</td>
<td>23</td>
<td>10.48 (3.57)</td>
<td>49.6 %</td>
</tr>
<tr>
<td><strong>Total (95% CI)</strong></td>
<td><strong>53</strong></td>
<td><strong>58</strong></td>
<td></td>
<td></td>
<td>100.0 %</td>
</tr>
</tbody>
</table>

Heterogeneity: $\tau^2 = 6.27$; $\chi^2 = 4.55$, df = 1 ($p = 0.03$); $I^2 = 78\%$

Test for overall effect: $Z = 0.39$ ($p = 0.69$)

Test for subgroup differences: Not applicable

---

### Comparison 2. Antibiotic use

<table>
<thead>
<tr>
<th>Outcome or subgroup title</th>
<th>No. of studies</th>
<th>No. of participants</th>
<th>Statistical method</th>
<th>Effect size</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 Antibiotic usage (normal saline plus standard therapy versus standard therapy)</td>
<td>2</td>
<td>422</td>
<td>Odds Ratio (M-H, Random, 95% CI)</td>
<td>0.64 [0.29, 1.44]</td>
</tr>
</tbody>
</table>

---

**Saline nasal irrigation for acute upper respiratory tract infections (Review)**

Copyright © 2015 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.
Analysis 2.1. Comparison 2 Antibiotic use, Outcome 1 Antibiotic usage (normal saline plus standard therapy versus standard therapy).

Review: Saline nasal irrigation for acute upper respiratory tract infections

Comparison: 2 Antibiotic use

Outcome: 1 Antibiotic usage (normal saline plus standard therapy versus standard therapy)

<table>
<thead>
<tr>
<th>Study or subgroup</th>
<th>Normal saline</th>
<th>Standard therapy</th>
<th>Odds Ratio M-H, Random, 95% CI</th>
<th>Weight</th>
<th>Odds Ratio M-H, Random, 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>King 2012</td>
<td>1/10</td>
<td>2/23</td>
<td></td>
<td>10.2 %</td>
<td>1.17 [0.09, 14.56]</td>
</tr>
<tr>
<td>Slapak 2008</td>
<td>16/288</td>
<td>9/101</td>
<td></td>
<td>89.8 %</td>
<td>0.60 [0.26, 1.41]</td>
</tr>
<tr>
<td><strong>Total (95% CI)</strong></td>
<td><strong>298</strong></td>
<td><strong>124</strong></td>
<td></td>
<td><strong>100.0 %</strong></td>
<td>0.64 [0.29, 1.44]</td>
</tr>
</tbody>
</table>

Total events: 17 (Normal saline), 11 (Standard therapy)
Heterogeneity: Tau² = 0.0; Chi² = 0.24, df = 1 (P = 0.63); I² = 0.0%
Test for overall effect: Z = 1.07 (P = 0.28)
Test for subgroup differences: Not applicable

ADDITIONAL TABLES

Table 1. Patient-reported health status score following acute phase (Slapak 2008)

<table>
<thead>
<tr>
<th>Treatment group</th>
<th>Health status score</th>
</tr>
</thead>
</table>
| Symptomatic improvement compared to beginning of illness - Normal treatment only | 2.60 (SD 1.02) - cold  
2.00 (SD 0.91) - flu |
| Symptomatic improvement compared to beginning of illness - Normal treatment plus isotonic saline | 1.87 (SD 0.84) - cold  
1.59 (SD 0.74) - flu |

Reported as significant findings (see Results section). Insufficient data to calculate confidence intervals.

SD: standard deviation
Table 2. Day of well-being (Adam 1998)

<table>
<thead>
<tr>
<th>Treatment group</th>
<th>Day of well-being</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypertonic saline irrigation</td>
<td>8.3 days (95% CI 6.9 to 9.7)</td>
</tr>
<tr>
<td>Normal saline irrigation</td>
<td>8.3 days (95% CI 6.82 to 9.78)</td>
</tr>
<tr>
<td>Observation only</td>
<td>8.0 days (95% CI 6.7 to 9.3)</td>
</tr>
</tbody>
</table>

CI: confidence interval

Table 3. Use of additional medications (Slapak 2008)

<table>
<thead>
<tr>
<th>Medication type</th>
<th>Use before study (%)</th>
<th>Use at follow-up (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Antipyretics</td>
<td>23.8 (control)</td>
<td>12.9 (control)</td>
</tr>
<tr>
<td></td>
<td>23.5 (saline wash)</td>
<td>7.6 (saline wash)</td>
</tr>
<tr>
<td>Decongestants</td>
<td>40.0 (control)</td>
<td>35.6 (control)</td>
</tr>
<tr>
<td></td>
<td>29.4 (saline wash)</td>
<td>15.9 (saline wash)</td>
</tr>
<tr>
<td>Mucolytics</td>
<td>20.0 (control)</td>
<td>31.7 (control)</td>
</tr>
<tr>
<td></td>
<td>15.6 (saline wash)</td>
<td>17.3 (saline wash)</td>
</tr>
<tr>
<td>Systemic antibiotics</td>
<td>5.0 (control)</td>
<td>8.9 (control)</td>
</tr>
<tr>
<td></td>
<td>3.1 (saline wash)</td>
<td>5.5 (saline wash)</td>
</tr>
</tbody>
</table>

APPENDICES

Appendix 1. Previous search strategy

We searched the Cochrane Central Register of Controlled Trials (CENTRAL) (*The Cochrane Library* 2009, issue 2), which contains the Acute Respiratory Infections (ARI) Group's Specialised Register, MEDLINE (1966 to May 2009), EMBASE (1974 to May 2009), CINAHL (1982 to May 2009), AMED (1985 to 2009) and LILACS (May 2009). The following search terms were used to search MEDLINE and CENTRAL. The MEDLINE search was combined with the Cochrane Highly Sensitive Search Strategy for identifying randomised trials in MEDLINE; sensitivity-maximising version (2008 revision); Ovid format (*Lefebvre 2011*). The search terms were modified to search other databases. See Appendix 2 for the EMBASE search strategy.

MEDLINE (Ovid)
1 exp Respiratory Tract Infections/
2 (respiratory tract infection* or upper respiratory infection*).tw.
3 urti.tw.
4 Rhinitis/
Saline nasal irrigation for acute upper respiratory tract infections (Review)

Embase.com

1. 'respiratory tract infection'/de OR 'upper respiratory tract infection'/de OR 'rhinitis'/de OR 'common cold'/de OR 'pharyngitis'/de OR 'tonsillitis'/de OR 'sore throat'/de OR 'sinusitis'/de OR 'laryngitis'/de OR 'rhinosinusitis'/de OR 'influenza'/de
2. 'respiratory tract infection':ti,ab OR 'respiratory tract infections':ti,ab OR 'upper respiratory infection':ti,ab OR 'upper respiratory tract infections':ti,ab OR 'urti':ti,ab OR 'rhinitis':ti,ab OR 'common cold':ti,ab OR 'common colds':ti,ab OR 'pharyngitis':ti,ab OR 'sore throat':ti,ab OR 'sore throats':ti,ab OR 'tonsillitis':ti,ab OR 'sinusitis':ti,ab OR 'laryngitis':ti,ab OR 'rhinosinusitis':ti,ab OR 'rhinorrhea':ti,ab OR 'rhinorrhoea':ti,ab OR 'runny nose':ti,ab OR 'runny noses':ti,ab OR 'flu':ti,ab OR 'influenza':ti,ab
3. #1 OR #2
4. 'nose'/de
5. nasal*:ti,ab OR nose*:ti,ab
6. #4 OR #5
7. lavage*:ti,ab OR wash*:ti,ab OR irrigat*:ti,ab OR rins*:ti,ab OR douch*:ti,ab OR atomis*:ti,ab OR atomiz*:ti,ab
8. #6 AND #7
9. 'sodium chloride'/de
10. saline*:ti,ab OR 'sodium chloride':ti,ab OR saline*:ti,ab
11. #9 OR #10
12. #8 AND #11
13. #3 AND #12
14. random*:ti,ab OR placebo*:ti,ab,de OR 'double blind':ti,ab
15. #13 AND #14

Appendix 2. MEDLINE (Ovid) search strategy

1 exp Respiratory Tract Infections/
2 (infect* adj3 upper respiratory).tw.
3 urti.tw.
4 Rhinitis/
5 rhinit*.tw.
6 Common Cold/
7 common cold*.tw.
8 exp Pharyngitis/
9 pharyngit*.tw.
10 sore throat*.tw.
11 Tonsillitis/
12 tonsillit*.tw.
13 exp Sinusitis/
14 sinus*.tw.
15 exp Laryngitis/
16 laryngit*.tw.
17 (rhinosinusit* or nasosinusit*).tw.
18 Influenza, Human/
19flu*.tw.
20 (rhinorrhoea* or rhinorrhea*).tw.
21 ((nasal or nose*) adj2 (congest* or discharg* or blocked or runny or running or stuffy or stuffed)).tw.
22 (infect* adj3 (nose* or throat* or sinus* or sinonasal or sino-nasal or pharyn* or laryn*)).tw.
23 or/1-22
24 Therapeutic Irrigation/
25 Nose/
26 (nasal or nose*).tw.
27 25 or 26
28 24 and 27
29 ((nasal or nose*) adj5 (irrigat* or lavage* or wash* or rins* or douch* or atomis* or atomiz*)).tw.
30 Nasal Lavage/
31 or/28-30
32 Sodium Chloride/
33 (saline or salt* or sodium chloride*).tw,nm.
34 or/32-33
35 31 and 34
36 23 and 35
Appendix 3. Embase.com search strategy

#38. #34 AND #37
#37. #35 OR #36
#36. random*:ab,ti OR placebo*:ab,ti OR crossover*:ab,ti OR cross over*:ab,ti OR cross-over*:ab,ti OR factorial*:ab,ti OR volunteer*:ab,ti OR assign*:ab,ti OR allocat*:ab,ti OR (singl* OR doubl* ) NEAR/1 (blind* OR mask*)):ab,ti
#35. 'randomized controlled trial'/exp OR 'single blind procedure'/exp OR 'double blind procedure'/exp OR 'crossover procedure'/exp OR 'cross over':ab,ti OR 'cross-over':ab,ti OR factorial*:ab,ti OR volunteer*:ab,ti OR assign*:ab,ti OR allocat*:ab,ti OR (singl* OR doubl* ) NEAR/1
#34. #31 AND #33
#33. #19 OR #32
#32. 'nose congestion'/de
#31. #22 AND #30
#30. #27 OR #28 OR #29
#29. ((nasal OR nose*) NEAR/5 (irrigat* OR lavage* OR wash* OR rins* OR douch* OR atomis* OR atomiz*)):ab,ti
#28. 'nasal lavage'/de
#27. #23 AND #26
#26. #24 OR #25 79,351
#25. nose*:ab,ti OR nasal:ab,ti
#24. 'nose'/de
#23. 'lavage'/de
#22. #20 OR #21 249,100
#21. saline:ab,ti OR salt*:ab,ti OR sodium chloride':ab,ti
#20. 'sodium chloride'/de
#19. #1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8 OR #9 OR #10 OR #11 OR #12 OR #13 OR #14 OR #15 OR #16 OR #17 OR #18
#18. influenz*:ab,ti OR flu:ab,ti
#17. 'influenza'/exp
#16. (infect* NEAR/3 (nose* OR throat* OR sinus* OR sinonasal OR sino-nasal OR pharyn* OR laryng*)):ab,ti
#15. ((nasal OR nose*) NEAR/2 (congest* OR discharg* OR blocked* OR runny OR running OR stuffy OR stuffed)):ab,ti
#14. rhinorrhoea:ab,ti OR rhinorrhea:ab,ti
#13. 'rhinorrhea'/de
#12. laryngit*:ab,ti
#11. 'laryngitis'/de OR 'laryngotracheobronchitis'/de
#10. tonsillit*:ab,ti
#9. 'tonsillitis'/de
#8. 'sore throat':ab,ti OR 'sore throats':ab,ti
#7. pharyngit*:ab,ti
#6. 'pharyngitis'/de OR 'viral pharyngitis'/de
#5. rhinit*:ab,ti OR 'common cold':ab,ti OR 'common colds':ab,ti OR rhinosinusit*:ab,ti OR nasosinusit*:ab,ti OR rhinopharyngit*:ab,ti OR nasopharyngit*:ab,ti
#4. 'rhinitis'/de OR 'common cold'/de OR 'rhinopharyngitis'/de OR 'rhinosinusitis'/de
#3. urti:ab,ti
#2. (infect* NEAR/3 'upper respiratory'):ab,ti
#1. 'upper respiratory tract infection'/exp
S42 S32 and S41
S41 S33 or S34 or S35 or S36 or S37 or S38 or S39 or S40
S40 (MH "Quantitative Studies")
S39 TI placebo* or AB placebo*
S38 (MH "Placebos")
S37 TI random* or AB random*
S36 TI (singl* blind* or doubl* blind* or tripl* blind* or trebl* blind* or singl* mask* or doubl* mask* or trebl* mask* or tripl* mask*) or AB (singl* blind* or doubl* blind* or tripl* blind* or trebl* blind* or singl* mask* or doubl* mask* or trebl* mask* or tripl* mask*)
S35 TI clinic* trial* or AB clinic* trial*
S34 PT
S33 (MH "Clinical Trials")
S32 S21 and S31
S31 S24 and S27 and S30
S30 S28 or S29
S29 TI (nose* or nasal) or AB (nose* or nasal)
S28 (MH "Nose")
S27 S25 or S26
S26 TI (irrigat* or lavage* or wash* or rins* or douch* or atomis* or atomiz*) or AB (irrigat* or lavage* or wash* or rins* or douch* or atomis* or atomiz*)
S25 (MH "Irrigation")
S24 S22 or S23
S23 TI (saline or salt* or sodium chloride) or AB (saline or salt* or sodium chloride)
S22 (MH "Sodium Chloride")
S21 S1 or S2 or S3 or S4 or S5 or S6 or S7 or S8 or S9 or S10 or S11 or S12 or S13 or S14 or S15 or S16 or S17 or S18 or S19 or S20
S20 TI (influenza* or flu) or AB (influenza* or flu)
S19 (MH "Influenza, Human")
S18 TI (infect* N3 nose* or infect* N3 throat* or infect* N3 sinus* or infect* N3 sino-nasal* or infect* N3 pharyn* or infect* N3 laryn*) or AB (infect* N3 nose* or infect* N3 throat* or infect* N3 sinus* or infect* N3 sino-nasal* or infect* N3 pharyn* or infect* N3 laryn*)
S17 TI (nose* N2 congest* or nose* N2 discharg* or nose* N2 blocked or nose* N2 runny or nose* N2 running or nose* N2 stuffy or nose* N2 stuffed) or AB (nose* N2 congest* or nose* N2 discharg* or nose* N2 blocked or nose* N2 runny or nose* N2 running or nose* N2 stuffy or nose* N2 stuffed)
S16 TI (nasal N2 congest* or nasal N2 discharg* or nasal N2 blocked or nasal N2 runny or nasal N2 running or nasal N2 stuffy or nasal N2 stuffed) or AB (nasal N2 congest* or nasal N2 discharg* or nasal N2 blocked or nasal N2 runny or nasal N2 running or nasal N2 stuffy or nasal N2 stuffed)
S15 TI (rhinorrhoea or rhinorrhea) or AB (rhinorrhoea or rhinorrhea)
S14 TI laryngit* or AB laryngit*
S13 TI sinusit* or AB sinusit*
S12 (MH "Sinusitis")
S11 TI tonsillit* or AB tonsillit*
S10 (MH "Tonsillitis")
S9 TI sore throat* or AB sore throat*
S8 TI pharyngit* or AB pharyngit*
S7 (MH "Pharyngitis")
S6 TI common cold* or AB common cold*
S5 (MH "Common Cold")
S4 TI (rhinit* or rhinosinusit* or nasosinusit*) or AB (rhinit* or rhinosinusit* or nasosinusit*)
S3 (MH "Rhinitis") OR (MH "Rhinosinusitis")
S2 TI (upper respiratory infect* or upper respiratory tract infect* or urti) or AB (upper respiratory infect* or upper respiratory tract infect* or urti)
S1 (MH "Respiratory Tract Diseases")
Appendix 5. AMED (Ovid) search strategy

1 exp respiratory tract infections/
2 (infect* adj3 upper respiratory).tw.
3 urti.tw.
4 rhinitis/
5 rhinit*.tw.
6 common cold*.tw.
7 common cold/
8 pharyngitis/
9 pharyngit*.tw.
10 sore throat*.tw.
11 tonsillitis/
12 tonsillit*.tw.
13 sinusitis/
14 sinusit*.tw.
15 laryngit*.tw.
16 (rhinosinusit* or nasosinusit*).tw.
17 (rhinorrhea or rhinorrhoea).tw.
18 influenza/
19 (influenza* or flu).tw.
20 (nasal or nose*).tw (congest* or discharg* or blocked or runny or running or stuffy or stuffed)).tw.
21 (infect* adj3 (nose* or throat* or sinus* or sinonasal* or sino-nasal* or pharyn* or laryn*)).tw.
22 or/1-21
23 salts/
24 (salt* or saline* or sodium chloride*).tw.
25 23 or 24
26 irrigation/
27 (irrigat* or lavage* or wash* or rins* or douch* or atomis* or atomiz*).tw.
28 26 or 27
29 25 and 28
30 22 and 29

Appendix 6. LILACS (BIREME) search strategy

> Search > (MH: "Respiratory Tract Infections" OR "Infecciones del Sistema Respiratorio" OR "Infecções Respiratórias" OR MH: C01.539.739$ OR MH:C08.730$ OR "upper respiratory infection" OR "upper respiratory tract infections" OR "upper respiratory infections" OR "upper respiratory tract infection" OR MH:rhinitis OR Rinitis OR Rinite OR MH:C08.460.799 OR MH:C08.730.674 OR MH:C09.603.799 OR rhinit$ OR "Common Cold" OR "common cold" OR "common colds" OR "Resfriado Común" OR "Resfriado Comum" OR coryza OR MH:C02.782.687.207 OR MH:C08.730.162 OR MH:pharyngitis OR Faringitis OR Faringite OR "sore throat" OR "sore throats" OR pharyngit$ OR MH:C07.550.781$ OR MH:C08.730.561$ OR MH:C09.775.649$ OR MH: Tonsillitis OR Tonsilitis OR Tonsilite OR MH:Sinusitis OR sinusit$ OR MH:C08.460.692.752$ OR MH:C08.730.749$ OR MH: C09.603.692.752$ OR MH:Laryngitis OR Laringitis OR Laringite OR MH:C08.360.535$ OR C08.730.368$ OR C09.400.535$ OR rhinosinusit$ OR nasosinusit$ OR MH:"Influenza, Human" OR "Gripe Humana" OR "Influenza Humana" OR Grippe OR flu* OR rhinorrhoea OR rhinorrhea) AND (MH: "Therapeutic Irrigation" OR "Irrigación Terapéutica" OR "Irrigação Terapêutica" OR douch$ OR lavage OR wash$ OR rins$ OR irrigat$ OR atomis$ OR atomiz$ OR MH: E02.533.500 OR E05.927 OR MH: "nasal lavage" OR "Lavado Nasal" OR "Lavagem Nasal" OR MH:E05.927.573) AND (MH: "sodium chloride" OR "Cloruro de Sódio" OR "Cloro de Sódio" OR "MH:D01.857.650$ OR MH:D01.210.450.150.875 OR MH: SP4.011.097.039.729.735 OR salt$ OR salin$ OR "sodium chloride") > clinical trials
**WHAT'S NEW**

Last assessed as up-to-date: 13 August 2014.

<table>
<thead>
<tr>
<th>Date</th>
<th>Event</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>13 August 2014</td>
<td>New search has been performed</td>
<td>Two new studies are included in this update (<em>King 2012</em>; <em>Wang 2009</em>).</td>
</tr>
<tr>
<td>13 August 2014</td>
<td>New citation required but conclusions have not changed</td>
<td>Our conclusions remain unchanged. We added a 'Risk of bias' assessment table, with some changes in the classification of the quality of the evidence from the included trials.</td>
</tr>
</tbody>
</table>

**HISTORY**


Review first published: Issue 3, 2010

<table>
<thead>
<tr>
<th>Date</th>
<th>Event</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>16 August 2013</td>
<td>New citation required but conclusions have not changed</td>
<td>Review update in progress.</td>
</tr>
<tr>
<td>16 August 2008</td>
<td>Amended</td>
<td>Converted to new review format.</td>
</tr>
</tbody>
</table>

**CONTRIBUTIONS OF AUTHORS**

David King (DK), Ben Mitchell (BM) and Chris Williams (CW) reviewed the search results, performed 'Risk of bias' assessments, managed data and drafted the final review. Geoffrey Spurling (GS) gave advice on performing the review and assisted with 'Risk of bias' assessment.

**DECLARATIONS OF INTEREST**

David King: supervisor and enrolling clinician for the unpublished *King 2012* study. This study is currently being prepared for submission for publication.

Ben Mitchell: none known.

Christopher P Williams: none known.

Geoffrey KP Spurling: none known.
DIFFERENCES BETWEEN PROTOCOL AND REVIEW

We undertook 'Risk of bias' assessment of all new and previously included studies following the new Cochrane recommendations. Some changes in reporting and interpretation of the data from studies included in the original review have occurred. These include changing the status of two studies from exclusion due to high risk of bias to exclusion due to not meeting the inclusion criteria for this review (Inanli 2002; Passali 2005). We changed the primary and secondary outcome measures to avoid duplication; for example, duration of symptoms was a primary outcome in the original review while time to resolution of symptoms was a secondary outcome. Also, we noted the inclusion of the outcome 'time off work or school' from Slapak 2008 in the original review to be based on follow-up periods outside of the specifications for acute URTIs as specified in the protocol, so we omitted this from inclusion in this 2014 update.

INDEX TERMS

Medical Subject Headings (MeSH)

Acute Disease; Common Cold [therapy]; Laryngitis [therapy]; Nasal Lavage [adverse effects; *methods]; Pharyngitis [therapy]; Randomized Controlled Trials as Topic; Respiratory Tract Infections [*therapy]; Rhinitis [therapy]; Sinusitis [therapy]; Sodium Chloride [adverse effects; *therapeutic use]

MeSH check words

Adult; Child; Humans