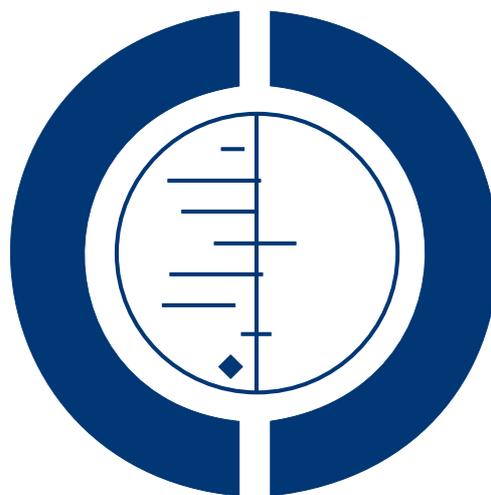


Honey for acute cough in children (Review)

Oduwole O, Meremikwu MM, Oyo-Ita A, Udoh EE



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Honey for acute cough in children (Review)

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[Intervention Review]

Honey for acute cough in children

Olabisi Oduwole¹, Martin M Meremikwu², Angela Oyo-Ita³, Ekong E Udoh²

¹Institute of Tropical Diseases Research and Prevention, University of Calabar Teaching Hospital (ITDR/P), Calabar, Nigeria.

²Department of Paediatrics, University of Calabar Teaching Hospital, Calabar, Nigeria. ³Department of Community Health, University of Calabar Teaching Hospital, Calabar, Nigeria

Contact address: Olabisi Oduwole, Institute of Tropical Diseases Research and Prevention, University of Calabar Teaching Hospital (ITDR/P), Moore Road, Calabar, Cross River State, Nigeria. olabisioduwole@yahoo.co.uk. olabisioduwole@gmail.com.

Editorial group: Cochrane Acute Respiratory Infections Group.

Publication status and date: New search for studies and content updated (no change to conclusions), published in Issue 3, 2012.

Review content assessed as up-to-date: 11 January 2012.

Citation: Oduwole O, Meremikwu MM, Oyo-Ita A, Udoh EE. Honey for acute cough in children. *Cochrane Database of Systematic Reviews* 2012, Issue 3. Art. No.: CD007094. DOI: 10.1002/14651858.CD007094.pub3.

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ABSTRACT

Background

Cough causes concern for parents and is a major cause of outpatient visits. It can impact on quality of life, cause anxiety and affect sleep in parents and children. Several remedies, including honey, have been used to alleviate cough symptoms.

Objectives

To evaluate the effectiveness of honey for acute cough in children in ambulatory settings.

Search methods

We searched the Cochrane Central Register of Controlled Trials (CENTRAL) (*The Cochrane Library* Issue 4, 2011) which contains the Cochrane Acute Respiratory Infections Group's Specialised Register; MEDLINE (1950 to December week 4, 2011); EMBASE (1990 to January 2012); CINAHL (1981 to January 2012); Web of Science (2000 to January 2012); AMED (1985 to January 2012); LILACS (1982 to January 2012); and CAB abstracts (2009 to January 2012).

Selection criteria

Randomised controlled trials (RCTs) comparing honey given alone, or in combination with antibiotics, versus nothing, placebo or other over-the-counter (OTC) cough medications to participants aged from two to 18 years for acute cough in ambulatory settings.

Data collection and analysis

Two review authors independently screened search results for eligible studies and extracted data on reported outcomes.

Main results

We included two RCTs of high risk of bias involving 265 children. The studies compared the effect of honey with dextromethorphan, diphenhydramine and 'no treatment' on symptomatic relief of cough using the 7-point Likert scale.

Honey was better than 'no treatment' in reducing frequency of cough (mean difference (MD) -1.07; 95% confidence interval (CI) -1.53 to -0.60; two studies; 154 participants). Moderate quality evidence suggests honey did not differ significantly from dextromethorphan in reducing cough frequency (MD -0.07; 95% CI -1.07 to 0.94; two studies; 149 participants). Low quality evidence suggests honey may be slightly better than diphenhydramine in reducing cough frequency (MD -0.57; 95% CI -0.90 to -0.24; one study; 80 participants).

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Adverse events included mild reactions (nervousness, insomnia and hyperactivity) experienced by seven children (9.3%) from the honey group and two (2.7%) from the dextromethorphan group; the difference was not significant (risk ratio (RR) 2.94; 95% CI 0.74 to 11.71; two studies; 149 participants). Three children (7.5%) in the diphenhydramine group experienced somnolence (RR 0.14; 95% CI 0.01 to 2.68; one study; 80 participants) but there was no significant difference between honey versus dextromethorphan or honey versus diphenhydramine. No adverse event was reported in the 'no treatment' group.

Authors' conclusions

Honey may be better than 'no treatment' and diphenhydramine in the symptomatic relief of cough but not better than dextromethorphan. There is no strong evidence for or against the use of honey.

PLAIN LANGUAGE SUMMARY

Honey for acute cough in children

Cough is a cause for concern for parents and a major cause of outpatient visits in most settings for both children and adults. Cough can impact on quality of life, cause anxiety and affect sleep for parents and children. For this reason an immediate remedy is usually sought by both the caregiver and the recipient. Cochrane reviews have assessed the effectiveness of over-the-counter (OTC) cough medications, but none have studied honey as a cough relief. A systematic review evaluating the effectiveness of honey for reducing acute cough symptoms due to upper respiratory tract infections (URTIs) in children would be useful. A review of two small randomised controlled trials (RCTs) showed that honey was moderately better than 'no treatment' for the relief of cough, reducing bothersome cough, improving quality of sleep for children and parents and reducing the severity of cough.

This review included two small trials involving 265 children, aged two to 18 years. The effects of honey and dextromethorphan on symptomatic relief of cough, bothersome cough, and quality of sleep for both child and parent did not differ. Honey may be better than diphenhydramine for symptomatic relief of cough, reducing the severity of cough, and improving sleep quality for both parent and child. Dextromethorphan and diphenhydramine are both common ingredients in cough medications. Parents of seven children given honey and two given dextromethorphan reported their children suffered mild reactions from insomnia, hyperactivity and nervousness. Parents of three children in the diphenhydramine group reported somnolence. However, as with other medications, its benefit should be considered alongside the adverse effects. The limitation of this review update is that only two small studies with high risk of bias were included.

SUMMARY OF FINDINGS FOR THE MAIN COMPARISON *[Explanation]*

Honey compared to dextromethorphan for acute cough in children						
Patient or population: children with acute cough Settings: ambulatory setting Intervention: honey Comparison: dextromethorphan						
Outcomes	Illustrative comparative risks* (95% CI)		Relative effect (95% CI)	No. of participants (studies)	Quality of the evidence (GRADE)	Comments
	Assumed risk	Corresponding risk				
	Dextromethorphan	Honey				
Fre- quency of cough (mean improvement score) 7-point Linkert scale Scale from: 0 to 6 Follow-up: mean 1 day	The mean frequency of cough (mean improvement) in the control groups was -1.44 mean improvement in symptom score	The mean frequency of cough (mean improvement) in the intervention groups was 0.07 lower (1.07 lower to 0.94 higher)		149 (2 studies)	⊕⊕⊕○ moderate ¹	
Severity of cough (mean improvement score) 7-point Linkert scale Scale from: 0 to 6 Follow-up: mean 1 day	The mean severity of cough (mean improvement) in the control groups was -1.40 mean improvement in symptom score	The mean severity of cough (mean improvement) in the intervention groups was 0.13 lower (1.25 lower to 0.99 higher)		149 (2 studies)	⊕⊕⊕○ moderate ²	
Bother- some cough (mean improvement score) 7-point Linkert scale Scale from: 0 to 6 Follow-up: mean 1 day	The mean bothersome cough (mean improvement) in the control groups was -1.94 mean improvement in symptom score	The mean bothersome cough (mean improvement) in the intervention groups was 0.29 higher (0.56 lower to 1.14 higher)		69 (1 study)	⊕⊕⊕○ moderate ³	

<p>Childrens' sleep (cough impact on childrens' sleep score) 7-point Linkert scale Scale from: 0 to 6 Follow-up: 1 day</p>	<p>The mean childrens' sleep quality (cough impact on childrens' sleep score) in the control groups was -1.77 cough impact on sleep quality score</p>	<p>The mean childrens' sleep quality (cough impact on childrens' sleep score) in the intervention groups was 0.03 higher (1.12 lower to 1.19 higher)</p>	<p>149 (2 studies)</p>	<p>⊕⊕⊕○ moderate³</p>
<p>Parents' sleep (cough impact on parent's sleep score) 7-point Linkert scale Scale from: 0 to 6 Follow-up: mean 1 day</p>	<p>The mean parents' sleep quality (cough impact on parents' sleep score) in the control groups was -1.97 cough impact on sleep quality score</p>	<p>The mean parents' sleep quality (cough impact on parents' sleep score) in the intervention groups was 0.16 lower (0.84 lower to 0.53 higher)</p>	<p>149 (2 studies)</p>	<p>⊕⊕⊕○ moderate³</p>

*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% CI) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

CI: confidence interval

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 The 'no treatment' arm was not blinded by [Paul 2007](#), while [Shadkam 2010](#) did not blind any of the treatment arms in their study.

² There was no blinding of the 'no treatment' arm.

³ No explanation was provided.

BACKGROUND

Description of the condition

Cough is a normal protective mechanism (Landau 2006) and a means by which the respiratory system rids itself of excessive secretions and foreign bodies (French 1998). Cough can be caused by bacterial or viral infections and/or the presence of an irritant or allergen in the respiratory tract (AAAI 2006; Greaves 1997). Respiratory infections can be situated along the upper or lower respiratory tract and the resulting cough can be either productive or unproductive of sputum. When cough is unproductive of sputum it is usually referred to as a 'dry' cough. Children with a dry cough tend to have minimal airway secretions (Chang 2005).

Cough can also be classified as acute or chronic. Chronic cough is a cough that lasts for more than three weeks (Meyer 1996). Acute cough from an upper respiratory tract infection (URTI) is one of the most common symptoms presenting to primary care settings or general practitioners (Britt 2002; Butler 2005; Cherry 2003). It has been reported that most coughs from acute URIs are caused by viral infections (Braman 2006; Butler 2005). Cough is a cause for concern for parents (Hay 2003) and a major cause of outpatient visits in most settings for both children and adults (Gonzales 2000; Kusel 2007). Cough can impact on quality of life (French 2002), cause anxiety and affect sleep for parents and children. For this reason an immediate remedy is usually sought by both the caregiver and the recipient.

Description of the intervention

People frequently self-prescribe over-the-counter (OTC) cough medications and many general practitioners in primary care settings recommend OTC medications to their patients as a first-line of treatment (PAGB 2000). Numerous OTC cough preparations are available but there is no conclusive evidence regarding their efficacy (Chang 2010; Smith 2010). In children, these medications may be associated with serious adverse events such as death, altered consciousness and arrhythmias (Gunn 2001; Kelly 2004; CDC 2007). In some studies, cough preparations have been shown to relieve cough symptoms, but other studies have found that they have no effect compared with a placebo (Banderali 1995; Freestone 1997; Kurth 1978; Smith 1993). It has been reported that cough mixtures contain a variety of drugs with differing modes of action, thus making them difficult to compare (Morice 1998). OTC cough medication could contain any of the following: dextromethorphan hydrobromide, phenylephrine hydrochloride, chlorpheniramine maleate and methylparaben (El-Gindy 2005).

How the intervention might work

Honey is a sweet, viscous liquid with a complex chemical composition. It is made up of a mixture of approximately 25 carbohydrates

(Sanz 2004), free amino acids (Hermosin 2003; Suárez-Luque 2002), vitamins, trace elements (Golob 2005; Hernández 2005; Nanda 2003; Tuzen 2007; Yao 2003) and flavonoids (Havsteen 2002). It also contains compounds that function as antioxidants (Nagai 2006). Honey is said to possess antibacterial (Lusby 2005; Mullai 2007) and anti-inflammatory properties (Tonks 2003). A study of the antimicrobial effect of honey showed that it has broad-spectrum antimicrobial actions, various gram-negative and gram-positive bacteria (Agbaje 2006; Garedeew 2004), and is active against common bacteria found in the upper respiratory tract such as *Staphylococcus aureus* (*S. aureus*), *Streptococcus faecalis* (*S. faecalis*), *Candida albicans* (*C. albicans*), *Klebsiella pneumoniae* (*K. pneumoniae*), *Pseudomonas aeruginosa* (*P. aeruginosa*), *Escherichia coli* (*E. coli*), *Salmonella spp* and *Shigella dysenteriae* (*S. dysenteriae*) (Adeleye 2003; Mullai 2007). In another study honey was also shown to have antiviral properties (Zeina 1996). Due to these properties, honey has been used in traditional medicine for the treatment of cough (Adeleye 2003). It is also used in modern medicines to treat infected wounds (Lusby 2005; Molan 2006) and is an ingredient in some cough syrups (Zeina 1996). However, the use of honey in infants under the age of one, is restricted because of their poor immunity against *Clostridium botulinum* (*C. botulinum*), a possible contaminant of honey (Kuplulu 2006; Nevas 2002).

Why it is important to do this review

Identification of ineffective preparations could reduce costs for consumers and healthcare providers (Smith 2010). Cochrane reviews have assessed the effectiveness of OTC cough medications (Chang 2010; Smith 2010), but none have studied honey for cough relief. A systematic review evaluating the effectiveness of honey for reducing acute cough symptoms due to URIs in children would be useful. This is the first update of our review (Oduwole 2010). If honey is effective it may save billions of dollars spent annually on OTC cough medications (Dicpinigaitis 2009). Our original review had no strong evidence for or against the use of honey for treating acute cough in children because only one small trial was included. Identifying more RCTs that evaluate the effectiveness of honey for acute cough in children could answer this question.

OBJECTIVES

To evaluate the effectiveness of honey for acute cough in children in ambulatory settings.

METHODS

Criteria for considering studies for this review

Types of studies

Randomised controlled trials (RCTs).

Types of participants

We included participants aged from two to 18 years with a cough caused by an acute URTI (viral or bacterial). We excluded studies that included participants with a chronic cough (cough lasting for more than three weeks). We also excluded studies with a sample size of less than 10 per intervention.

Types of interventions

We included studies comparing the following.

1. Honey only versus:
 - i) honey-based cough syrup;
 - ii) non-honey cough syrup;
 - iii) placebo; and
 - iv) 'no treatment'.
2. Honey plus antibiotics versus antibiotics alone.
3. Honey plus antibiotics versus non-honey cough syrups plus antibiotics.

Types of outcome measures

Primary outcomes

1. Duration of cough.
2. Symptomatic relief of cough (less bothersome, reduction in severity and frequency of cough).

Secondary outcomes

1. Improvement in quality of sleep at night for children (cough impact on sleep score).
2. Improvement in quality of sleep at night for caregiver (cough impact on sleep score).
3. Improvement in quality of life (for example, school attendance and playing).
4. Adverse effects of the medications on participants.
5. Improvement in appetite.
6. Cost of honey alone compared with other cough syrups.

Search methods for identification of studies

Electronic searches

For this update we searched the Cochrane Central Register of Controlled Trials (CENTRAL) (*The Cochrane Library* 2011, Issue 4), which contains the Cochrane Acute Respiratory Infections Group's Specialised Register (www.thecochranelibrary.com - accessed 11 January 2011); MEDLINE (March 2009 to December week 4, 2011); EMBASE (March 2009 to January 2012); CINAHL (2009 to January 2012); Web of Science (2009 to January 2012); AMED (2009 to January 2012); LILACS (2009 to January 2012); and CAB abstracts (2009 to January 2012).

Previously we searched CENTRAL (*The Cochrane Library* 2009, Issue 2) which contains the Cochrane Acute Respiratory Infections Group's Specialised Register; MEDLINE (1950 to April Week 2, 2009); EMBASE (1990 to April 2009); CINAHL (1982 to April 2009); Web of Science (2000 to April 2009); AMED (1985 April 2009); and LILACS (1982 to April 2009).

We used the search strategy in [Appendix 1](#) for searching MEDLINE and CENTRAL and modified terms for searching EMBASE (see [Appendix 2](#)), CINAHL ([Appendix 3](#)), Web of Science ([Appendix 4](#)), AMED ([Appendix 5](#)), LILACS ([Appendix 6](#)) and CAB abstracts ([Appendix 7](#)). We did not combine the MEDLINE search string with the Cochrane highly sensitive search strategy for identifying randomised trials in MEDLINE ([Lefebvre 2011](#)) because we found very few results.

Searching other resources

We also searched databases of complementary and alternative medicine literature and clinical trials registers. We imposed no language or publication restrictions. We checked the reference lists of all relevant articles obtained from our search and those from previously published systematic reviews to identify other possible articles. We also contacted authors of the new included study for information on unpublished data.

Data collection and analysis

Selection of studies

Two review authors (OO, EU) independently screened search results for eligible studies based on a priori inclusion criteria. The third (AO) or fourth (MM) review author resolved disagreements regarding inclusion of studies.

Data extraction and management

Two authors (OO, AO) independently extracted data and entered it into Review Manager 5 ([RevMan 2011](#)). The same two review authors (OO, EU) resolved disagreements by consensus.

Assessment of risk of bias in included studies

Two authors (OO, AO) determined the risk of bias for the included trials by assessing random sequence generation, allocation concealment, blinding, selective reporting, and other sources of bias, and recorded the assessment in the 'Risk of bias' table. We ranked the studies as low risk, unclear risk and high risk of bias, as recommended in the *Cochrane Handbook for Systematic Reviews of Interventions* [Higgins 2011](#).

Measures of treatment effect

We used one-way analysis of variance in comparing treatment effect for cough symptoms and quality of sleep by the trial authors. We presented estimates of effects as mean differences (MDs) derived from parents' subjective assessment of cough symptoms and its impact on sleep quality through validated questions using a 7-point Likert scale ([Likert 1932](#)).

We analysed pair-wise comparisons of outcomes using generic inverse variance in [RevMan 2011](#). We estimated MDs between patients' Likert scores at baseline and postintervention for frequency of cough, bothersome cough, and cough impact on quality of sleep for child and parent. We used the MD for the pair-wise comparison of treatment effect between honey and dextromethorphan, honey and diphenhydramine, and honey and 'no treatment', using generic inverse variance in [RevMan 2011](#).

Unit of analysis issues

Not applicable.

Dealing with missing data

We obtained the standard error (SE) of the mean from the lead trial author of the [Paul 2007](#) study. We calculated the SE of the mean using PEPI version 3 ([Abramson 1999](#)) for the [Shadkam 2010](#) study. We performed an intention-to-treat (ITT) analysis by including all randomised participants in the analysis according to the *Cochrane Handbook for Systematic Reviews of Interventions* ([Higgins 2011](#)).

Assessment of heterogeneity

We considered heterogeneity statistically significant when the I^2 statistic was 50% or more. We used the random-effects model for meta-analysis when the I^2 statistic was > 50%.

Assessment of reporting biases

We could not test asymmetry with a funnel plot because the number of included studies were too few.

Data synthesis

We used the fixed-effect model for combining data from the two included studies. We used [RevMan 2011](#) to perform an inverse-variance meta-analysis using a fixed-effect method for differences in mean between pre- and postintervention Likert scores and pair-wise comparisons of postintervention mean Likert scores between honey and dextromethorphan, honey and diphenhydramine and honey and 'no treatment'. We used a random-effects model where there was heterogeneity. We extracted the estimates of effects (MDs) and SE of the mean for each outcome and calculated 95% CIs of the MDs using generic inverse variance. We used the Mantel-Haenszel method to analyse the risk ratio (RR) for adverse events.

Subgroup analysis and investigation of heterogeneity

Data were only available for two small studies; therefore investigation of heterogeneity was not feasible. We used a random-effects model instead of a fixed-effect model to address any possible heterogeneity.

Sensitivity analysis

We did not perform a sensitivity analysis because we only included two trials.

RESULTS

Description of studies

See: [Characteristics of included studies](#); [Characteristics of excluded studies](#).

Results of the search

Our updated search yielded 79 studies. Only one new study ([Shadkam 2010](#)) met our inclusion criteria. There was total agreement between the review authors on the relevance of this trial.

Included studies

We included two RCTs ([Paul 2007](#); [Shadkam 2010](#)) involving 268 participants in the review.

The first RCT in the review ([Paul 2007](#)) randomised 108 participants, but included only 105 participants in the final analysis. The median age was 5.22 years (range 2.22 to 16.92 years). These participants presented with URIs and nocturnal symptoms. The duration of illness was seven days or less. The second included study ([Shadkam 2010](#)) randomised 160 participants but only involved 139 participants in the final analysis. The mean age of the

participants was 37.75 ± 11.12 months. These participants also presented with URTIs and nocturnal symptoms. The duration of illness was five days or less. Both trials compared honey (buckwheat honey in Paul 2007 and natural honey from Kafi-Abad, a village in Yazd, Iran in Shadkam 2010) to dextromethorphan and 'no treatment'. Shadkam 2010 also included diphenhydramine in their comparison.

Excluded studies

In the first publication of our review, we excluded two studies because they were reviews of the included studies (Gilbert 2008; Warren 2007). From the updated searches, we identified 61 studies. We selected 17 studies and excluded 16 of them because they were either commentaries, non-clinical studies, or reviews relating

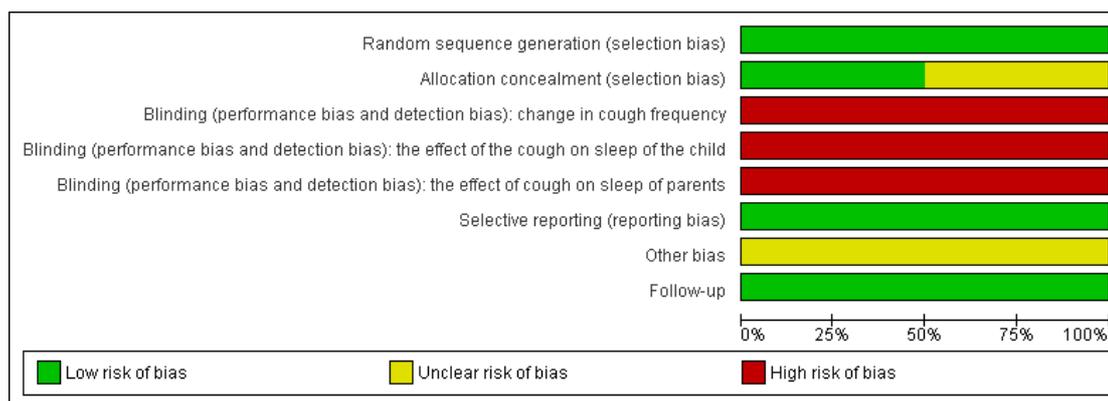
to the included studies.

Risk of bias in included studies

Allocation

The randomisation sequence in Paul 2007 was generated by a statistician not affiliated with the study. Participants were assigned to their treatment groups by the study co-ordinator according to the sequence generated by the statistician. Allocation sequence was concealed in brown envelopes. In Shadkam 2010 randomisation was achieved through the use of a random number table and it was not stated clearly if there was allocation concealment (Figure 1).

Figure 1. Risk of bias graph for included studies



Blinding

The baseline characteristics did not differ significantly between treatment groups in the included studies. In Paul 2007, the study personnel and participants were blinded to two intervention arms (dextromethorphan and honey) but it was not feasible to blind the 'no treatment' arm. This could have been a source of bias. The awareness of not receiving any treatment could have affected self-reported outcomes in the 'no treatment' arm. There was no form of blinding in Shadkam 2010 (Figure 2).

Figure 2. Risk of bias summary: review authors' judgements about each risk of bias item for each included study.

	Random sequence generation (selection bias)	Allocation concealment (selection bias)	Blinding (performance bias and detection bias): change in cough frequency	Blinding (performance bias and detection bias): the effect of the cough on sleep of the child	Blinding (performance bias and detection bias): the effect of cough on sleep of parents	Selective reporting (reporting bias)	Other bias	Follow-up
Paul 2007	+	+	-	-	-	+	?	+
Shadkam 2010	+	?	-	-	-	+	?	+

Incomplete outcome data

Attrition in the [Paul 2007](#) study was minimal. The authors accounted for all of the participants: attrition rates were 3% and 5% for the dextromethorphan and 'no treatment' groups, respectively. Two participants were lost to follow-up in the 'no treatment' group, while one was excluded from the dextromethorphan group for discontinuing the assigned intervention (see 'Risk of bias' table). There was no loss to follow-up or exclusion of participants from the honey group. Attrition in the [Shadkam 2010](#) study was relatively high. Attrition in the honey group was 17.5%, 10% in the dextromethorphan group, 15% in the diphenhydramine group and 10% in the 'no treatment' arm. All randomised participants were not included the final analysis.

Selective reporting

We could not ascertain whether there was selective reporting in the two included studies as we had no access to the study protocols of the trials.

Other potential sources of bias

The baseline characteristics did not differ significantly between treatment groups but [Paul 2007](#) and [Shadkam 2010](#) did not conduct an ITT analysis.

Effects of interventions

See: [Summary of findings for the main comparison Honey compared to dextromethorphan for acute cough in children](#); [Summary of findings 2 Honey compared to diphenhydramine for acute cough in children](#); [Summary of findings 3 Honey compared to 'no treatment' for acute cough in children](#); [Summary of findings 4 Adverse events](#)

Pre- and post-intervention comparison

Honey was more effective in reducing frequency of cough in the two studies (MD -1.92; 95% CI -2.35 to -1.49; two studies, 75 participants) than diphenhydramine (MD -1.73; 95% CI -2.72 to -0.74; one study, 40 participants), dextromethorphan (MD -1.44; 95% CI -1.86 to -1.02; two studies, 74 participants) and the 'no treatment' arm (MD -0.97; 95% CI -1.34 to -0.61; two studies, 79 participants) at postintervention ([Analysis 1.1](#)). Similarly, honey was better in reducing the severity of cough in children (MD -1.88; 95% CI -2.38 to -1.37; two studies, 75 participants) than dextromethorphan (MD -1.40; 95% CI -1.89 to -0.91; two studies, 74 participant), diphenhydramine (MD -1.83; 95% CI -2.88 to -0.78; one study, 40 participants) and the 'no

treatment' arm (MD -1.13; 95% CI -1.55 to -0.72; two studies, 79 participants) ([Analysis 1.2](#)). The quality of evidence was moderate.

Only [Paul 2007](#) studied the effectiveness of the interventions on bothersome cough. There was a reduction in bothersome cough in the three arms studied: honey (MD -2.23; 95% CI -2.82 to -1.63; one study, 35 participants), dextromethorphan (MD -1.94; 95% CI -2.55 to -1.33; one study, 34 participants) and 'no treatment' (MD -1.30; 95% CI -1.87 to -0.72; one study, 39 participants). However, the effect was better in honey ([Analysis 1.3](#)).

Caregivers' Likert score on cough impact on childrens' sleep was more likely reduced in honey (MD -2.44; 95% CI -2.99 to -1.89; two studies, 75 participants), than in dextromethorphan (MD -1.77; 95% CI -2.30 to -1.24; two studies, 74 participant), diphenhydramine (MD -1.64; 95% CI -2.58 to -0.70; one study, 40 participants) and in the 'no treatment' group (MD -1.37; 95% CI -1.81 to -0.93; two studies, 79 participants) ([Analysis 1.4](#)). The quality of evidence is moderate.

Cough impact on parents' sleep was more improved for honey (MD -2.33; 95% CI -2.90 to -1.76; two studies, 75 participant) than dextromethorphan (MD -1.97; 95% CI -2.53 to -1.41; two studies, 74 participants), diphenhydramine (MD -1.89; 95% CI -2.97 to -0.81; one study, 40 participants) and for 'no treatment' (MD -1.48; 95% CI 1.97 to -0.99; two studies, 79 participants.) ([Analysis 1.5](#)). The quality of evidence was moderate.

Pair-wise comparison of honey and dextromethorphan

Moderate quality evidence showed that there was no difference between honey and dextromethorphan in reducing cough frequency (MD -0.07; 95% CI -1.07 to 0.94; two studies, 149 participants), cough severity (MD -0.13; 95% CI -1.25 to 0.99; two studies, 149 participants), bothersome cough (MD 0.29; 95% CI -0.56 to 1.14; one study, 69 participants), impact of cough on childrens' sleep (MD 0.03; 95% CI -1.12 to 1.19; two studies, 149 participants) and parents' sleep (MD -0.16; 95% CI -0.84 to 0.53; two studies, 149 participants) ([Analysis 2.1](#)).

Pair-wise comparison of honey versus diphenhydramine

Honey may be better than diphenhydramine in reducing frequency of cough (MD -0.57; 95% CI -0.90 to -0.24; one study, 80 participants), severity of cough (MD -0.60; 95% CI -0.94 to -0.26; one study, 80 participants), cough impact on childrens' sleep (MD -0.55; 95% CI -0.87 to -0.23; one study, 80 participants) and cough impact on parents' sleep (MD -0.48; 95% CI -0.76 to -0.20; one study, 80 participants). The quality of evidence was low ([Analysis 2.2](#)).

Pair-wise comparison of honey versus 'no treatment'

Moderate quality evidence showed that the effect of honey was probably better than 'no treatment' in reducing cough frequency (MD -1.07; 95% CI -1.53 to -0.60; two studies, 154 participants; cough severity (MD -0.97; 95% CI -1.47 to -0.46; two studies, 154 participants); resolving bothersome cough (MD -0.93; 95% CI -1.77 to -0.09; one study, 74 participants), reduction in the impact of cough on childrens' sleep (MD -1.02; 95% CI -1.52 to -0.52; two studies, 154 participants) and reduction in the impact of cough on parents' sleep (MD -0.93; 95% CI -1.41 to -0.46; two studies, 154 participants) ([Analysis 2.3](#)).

Adverse events

Reported adverse events included mild reactions (nervousness, insomnia and hyperactivity); gastrointestinal symptoms (stomach

ache, nausea and vomiting); drowsiness and somnolence. The difference observed in the adverse events between honey versus dextromethorphan and honey versus diphenhydramine were not statistically significant. Seven children (9.3%) from the honey group compared to two (2.7%) from the dextromethorphan group experienced mild reactions such as nervousness, insomnia and hyperactivity (RR 2.94; 95% CI 0.74 to 11.71; 149 participants) ([Analysis 3.1](#)). Two (2.7%) children from the honey group had gastrointestinal symptoms (RR 4.86; 95% CI 0.24 to 97.69; 149 participants), and one (1.3%) experienced drowsiness (RR 2.92; 95% CI 0.12 to 69.20; 149 participants) ([Analysis 3.2](#)). Three children (7.5%) experienced somnolence in the diphenhydramine group but it was not significantly different from honey (RR 0.14; 95% CI 0.01 to 2.68; 80 participants). No adverse reaction was reported in the 'no treatment' arm ([Fisher 1922](#)).

ADDITIONAL SUMMARY OF FINDINGS *[Explanation]*

Honey compared to diphenhydramine for acute cough in children						
Patient or population: children with acute cough Settings: ambulatory setting Intervention: honey Comparison: diphenhydramine						
Outcomes	Illustrative comparative risks* (95% CI)		Relative effect (95% CI)	No. of participants (studies)	Quality of the evidence (GRADE)	Comments
	Assumed risk	Corresponding risk				
	Diphenhydramine	Honey				
Fre- quency of cough (mean improvement score) 7-point Linkert scale Scale from: 0 to 6 Follow-up: mean 1 day	The mean frequency of cough (mean improvement) in the control groups was -1.73 mean improvement in symptom score	The mean frequency of cough (mean improvement) in the intervention groups was 0.57 lower (0.9 to 0.24 lower)		80 (1 study)	⊕⊕○○ low	
Severity of cough (mean improvement score) 7-point Linkert scale Scale from: 0 to 6 Follow-up: mean 1 day	The mean severity of cough (mean improvement) in the control groups was -1.83 mean improvement in symptom score	The mean severity of cough (mean improvement) in the intervention groups was 0.6 lower (0.94 to 0.26 lower)		80 (1 study)	⊕⊕○○ low ¹	
Childrens' sleep (cough impact on childrens' sleep score) 7-point Linkert scale Scale from: 0 to 6 Follow-up: mean 1 day	The mean childrens' sleep quality (cough impact on childrens' sleep score) in the control groups was -1.64 cough impact on sleep quality score	The mean childrens' sleep quality (cough impact on childrens' sleep score) in the intervention groups was 0.55 lower (0.87 to 0.23 lower)		80 (1 study)	⊕⊕○○ low	

Parents' sleep (cough impact on parent's sleep score) 7-point Linkert scale Scale from: 0 to 6 Follow-up: mean 1 day	The mean parents' sleep quality (cough impact on parents' sleep score) in the control groups was -1.89 cough impact on sleep quality score	The mean parents' sleep quality (cough impact on parents' sleep score) in the intervention groups was 0.48 lower (0.76 to 0.2 lower)	80 (1 study)	 low
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*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%) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

CI: confidence interval

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 None of the treatment arms were blinded by [Shadkam 2010](#) and allocation concealment was unclear. It was the same for other outcomes.

Honey compared to 'no treatment' for acute cough in children						
Patient or population: children with acute cough Settings: ambulatory setting Intervention: honey Comparison: 'no treatment'						
Outcomes	Illustrative comparative risks* (95% CI)		Relative effect (95% CI)	No. of participants (studies)	Quality of the evidence (GRADE)	Comments
	Assumed risk	Corresponding risk				
	'No treatment'	Honey				
Fre- quency of cough (mean improvement score) 7-point Linkert scale Scale from: 0 to 6 Follow-up: mean 1 day	The mean frequency of cough (mean improvement) in the control groups was -0.97 mean improvement score	The mean frequency of cough (mean improvement) in the intervention groups was 1.07 lower (1.53 to 0.6 lower)		154 (2 studies)	⊕⊕⊕○ moderate ¹	
Severity of cough (mean improvement score) 7-point Linkert scale Scale from: 0 to 6 Follow-up: mean 1 day	The mean severity of cough (mean improvement) in the control groups was -1.13 mean improvement in symptom score	The mean severity of cough (mean improvement) in the intervention groups was 0.97 lower (1.47 to 0.46 lower)		154 (2 studies)	⊕⊕⊕○ moderate ²	
Bother- some cough (mean improvement score) 7-point Linkert scale Scale from: 0 to 6 Follow-up: mean 1 day	The mean bothersome cough (mean improvement) in the control groups was -0.93 mean improvement in symptoms core	The mean bothersome cough (mean improvement) in the intervention groups was 0.93 lower (1.77 to 0.09 lower)		74 (1 study)	⊕⊕⊕○ moderate ²	

<p>Childrens' sleep (cough impact on childrens' sleep score) 7-point Linkert scale Scale from: 0 to 6 Follow-up: mean 1 day</p>	<p>The mean childrens' sleep quality (cough impact on childrens' sleep quality score) in the control groups was -1.37 cough impact on sleep quality score</p>	<p>The mean childrens' sleep quality (cough impact on childrens' sleep quality score) in the intervention groups was 1.02 lower (1.52 to 0.52 lower)</p>	<p>154 (2 studies)</p>	<p>⊕⊕⊕○ moderate²</p>
<p>Parents' sleep (cough impact on parents' sleep score) 7-point Linkert scale Scale from: 0 to 6 Follow-up: mean 1 day</p>	<p>The mean parents' sleep quality (cough impact on parents' sleep score) in the control groups was -1.48 cough impact on sleep quality score</p>	<p>The mean parents' sleep quality (cough impact on parents' sleep score) in the intervention groups was 0.93 lower (1.41 to 0.46 lower)</p>	<p>154 (2 studies)</p>	<p>⊕⊕⊕○ moderate²</p>

*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% CI) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

CI: confidence interval

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 The 'no treatment group were not blinded by either of the studies; allocation concealment was unclear in the [Shadkam 2010](#) study.

² No explanation was provided.

Adverse events						
Patient or population: children with acute cough						
Settings: ambulatory setting						
Intervention: honey						
Outcomes	Illustrative comparative risks* (95% CI)		Relative effect (95% CI)	No. of participants (studies)	Quality of the evidence (GRADE)	Comments
	Assumed risk	Corresponding risk				
	Control	Honey				
Nervousness, insomnia, hyperactivity (honey versus dextromethorphan) Fixed-effect, Mantel-Haenszel (M-H), RR Follow-up: mean 1 day	Study population		RR 2.94 (0.74 to 11.71)	149 (2 studies)	⊕⊕⊕○ moderate	
	27 per 1000	79 per 1000 (20 to 316)				
	Medium risk population					
	29 per 1000	85 per 1000 (21 to 340)				
Stomach ache, nausea and vomiting (honey versus dextromethorphan) Fixed-effect, Mantel-Haenszel (M-H), RR Follow-up: mean 1 day	Study population		RR 4.86 (0.24 to 97.69)	149 (2 studies)	⊕⊕⊕○ moderate ¹	
	0 per 1000	0 per 1000 (0 to 0)				
	Medium risk population					
	0 per 1000	0 per 1000 (0 to 0)				

Drowsiness (honey versus dextromethorphan) Fixed-effect, Mantel-Haenszel (M-H), RR Follow-up: mean 1 day	Study population	RR 2.92 (0.12 to 69.2)	149 (2 studies)	⊕⊕⊕○ moderate ¹
	0 per 1000	0 per 1000 (0 to 0)		
	Medium risk population			
	0 per 1000	0 per 1000 (0 to 0)		
Somnolence (honey versus diphenhydramine) fixed-effect, Mantel-Haenszel (M-H), RR Follow-up: mean 1 day	Study population	RR 0.14 (0.01 to 2.68)	80 (1 study)	⊕⊕⊕○ moderate ²
	75 per 1000	10 per 1000 (1 to 201)		
	Medium risk population			
	75 per 1000	10 per 1000 (1 to 201)		

*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% CI) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

CI: confidence interval; **RR:** risk 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 No explanation was provided.

² None of the treatment arms were blinded in [Shadkam 2010](#) or [Paul 2007](#).

DISCUSSION

Summary of main results

Honey was probably better than 'no treatment' for symptomatic relief of cough, resolving bothersome cough and improving sleep quality for both children and parents. Honey may also be better than diphenhydramine for symptomatic relief of cough and for reduction of cough impact on the sleep quality of children and their parents. Honey was likely to be no better than dextromethorphan for symptomatic relief of cough, resolving bothersome cough and improving sleep quality for both children and parents.

No serious adverse event was reported for any of the treatment groups. Non-severe adverse events were more common in the honey group than the 'no treatment' group and comparable with the dextromethorphan group and diphenhydramine group.

Overall completeness and applicability of evidence

This review included two small trials. Outcomes could have been different or more reliable if treatment and follow-up were longer than one night. Other outcomes such as improvements in appetite, school attendance and playing were not reported. We cannot generalise on the applicability of our findings.

Quality of the evidence

The two included studies were of high risk of bias due to non-blinding of the 'no treatment' arm. Also in [Shadkam 2010](#), allocation concealment was unclear and none of the study arms were blinded. Use of supportive treatment for all the study arms in the [Shadkam 2010](#) trial may have contributed to the higher effects of interventions observed in this study.

Potential biases in the review process

None.

Agreements and disagreements with other studies or reviews

No other systematic review has been conducted on honey for treating cough.

AUTHORS' CONCLUSIONS

Implications for practice

This study suggests that honey may be better than 'no treatment' for reducing cough frequency, cough severity, resolving bothersome cough and improving sleep quality for both children and parents. Its effect on cough frequency, cough severity and quality of sleep for children and parents is also likely to be better than diphenhydramine, an over-the-counter (OTC) cough remedy. Its effect is comparable to dextromethorphan (another OTC drug) for reducing cough frequency, cough severity and the impact of cough on the quality of sleep for children and parents. These findings are from two small studies of 'high risk of bias' with moderate to low quality evidence, and may not be generalised.

Implications for research

There is a need for more high quality RCTs on the use of honey in the treatment of cough in children. Future studies should include longer treatment and follow-up periods, and measure other outcomes such as improvement in appetite, level of physical activity, school attendance and cost, all of which are relevant to caregivers.

ACKNOWLEDGEMENTS

The review authors wish to thank Liz Dooley and Sarah Thorning from the Cochrane ARI Group for their contributions. Also we would like to acknowledge the comments of the following referees: Matthew Thompson, Clare Jeffrey, Peter Molan, Jenny Wilkinson, David Gregory, Teresa Neeman, Mark Jones and Lisa Baniran. Finally, we wish to thank IM Paul, J Beiler, A McMonagle, ML Shaffer, L Duda and CM Berlin, authors of one of the included studies for their prompt responses to our requests.

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* Indicates the major publication for the study

CHARACTERISTICS OF STUDIES

Characteristics of included studies [ordered by study ID]

Paul 2007

Methods	RCT
Participants	108 participants (35 allocated to honey, 34 allocated to dextromethorphan and 39 received 'no treatment'); 2 to 18 years of age with URIs, nocturnal symptoms and illness duration of 7 days or less
Interventions	A single dose of buckwheat honey, honey flavoured dextromethorphan, or 'no treatment' administered 30 minutes prior to bedtime
Outcomes	Cough frequency, cough severity, bothersome nature of cough, cough impact on sleep quality for children and parents
Notes	This study was supported by an unrestricted research grant from the National Honey Board, an industry-funded agency of the United States Department of Agriculture. It is possible that participants in the 'no treatment' group showed the least improvement because they were aware they did not receive the active treatment, which could have been a source of bias to their responses

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	The randomisation sequence was done by a statistician not affiliated with the study and was then used by the study co-ordinators to assign the treatment groups
Allocation concealment (selection bias)	Low risk	Treatment allocation was concealed in opaque brown envelopes
Blinding (performance bias and detection bias) change in cough frequency	High risk	The syringes used for all the three treatment groups were opaque and placed in a brown paper bag to conceal the treatments from the investigators. The 'no treatment' group was not blinded to their treatment but the honey and dextromethorphan arms were blinded
Blinding (performance bias and detection bias) the effect of the cough on sleep of the child	High risk	Though all participants were given syringes in brown paper bags the 'no treatment' group had empty syringes which could influence the assessment of the outcome
Blinding (performance bias and detection bias) the effect of cough on sleep of parents	High risk	The 'no treatment' group was not blinded to the intervention they received
Selective reporting (reporting bias)	Low risk	All outcomes were adequately reported

Paul 2007 (Continued)

Other bias	Unclear risk	It is unclear whether any of the 'no treatment' group revealed to any of the assessors during phone conversations that they were given 'no treatment'. Participants lost to follow-up or withdrawn were not included in the final analysis
Follow-up	Low risk	2 participants from the 'no treatment' group were lost to follow-up; 1 was withdrawn from the dextromethorphan group because the participant did not take the treatment

Shadkam 2010

Methods	RCT
Participants	160 participants (40 allocated to honey, 40 allocated to dextromethorphan, 40 allocated to diphenhydramine and 40 were in the 'no treatment' group (but received supportive treatment given to others); 2 to 5 years of age with URIs, nocturnal symptoms and illness duration of 5 days
Interventions	A single dose of natural honey from Kafi-Abad (a village in Yazd, Iran), dextromethorphan, diphenhydramine or 'no treatment' (all treatment arms were advised to take supportive treatment saline nose drops, water vapour, cleaning a blocked nose and using acetaminophen for fever, if necessary)
Outcomes	Cough frequency, cough severity, cough impact on sleep quality for children and parents
Notes	160 participants were randomised into the 4 groups but only 139 were finally analysed

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Randomisation was by random numbers table
Allocation concealment (selection bias)	Unclear risk	It was not clear whether treatment allocation was concealed
Blinding (performance bias and detection bias) change in cough frequency	High risk	Both the investigators and caregivers were not blinded to the treatment given which could greatly influence the assessment of outcome
Blinding (performance bias and detection bias) the effect of the cough on sleep of the child	High risk	Both the investigators and caregivers were not blinded to the treatment given which could greatly influence the assessment of outcome
Blinding (performance bias and detection bias) the effect of cough on sleep of parents	High risk	Investigators and caregivers were not blinded to the treatment given which could greatly influence the assessment of outcome

Shadkam 2010 (Continued)

Selective reporting (reporting bias)	Low risk	All outcomes were adequately reported
Other bias	Unclear risk	Some of the questions put to mothers were answered by the paediatrician because the questions were ambiguous, which could also be an influence on the assessment of outcomes. Since mothers were filling-in the questionnaire in the presence of the physician, this could also be a source of influence on the assessment of outcomes. No ITT analysis. Participants that were withdrawn or lost to follow-up were also not included in the final analysis which could have also made a difference in the effect of the interventions
Follow-up	Low risk	7 participants from the honey group, 4 from the dextromethorphan group, 6 from the diphenhydramine group and 4 from the control group were either lost to follow-up or withdrawn for violating protocol

ITT: intention-to-treat; RCT: randomised controlled study; URTI: upper respiratory tract infection.

Characteristics of excluded studies [ordered by study ID]

Study	Reason for exclusion
Gilbert 2008	This is a non-Cochrane review on the included study selected from www.inforpoem.com by the study authors
Warren 2007	This study is a non-Cochrane review on the included study (Paul 2007)

DATA AND ANALYSES

Comparison 1. Pre- and postintervention comparison

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Cough frequency (mean improvement)	2		Mean Difference (Random, 95% CI)	Subtotals only
1.1 Honey	2	75	Mean Difference (Random, 95% CI)	-1.92 [-2.35, -1.49]
1.2 Dextromethorphan	2	74	Mean Difference (Random, 95% CI)	-1.44 [-1.86, -1.02]
1.3 Diphenhydramine	1	40	Mean Difference (Random, 95% CI)	-1.73 [-2.72, -0.74]
1.4 No treatment	2	79	Mean Difference (Random, 95% CI)	-0.97 [-1.34, -0.61]
2 Severity of cough (mean improvement)	2		Mean Difference (Random, 95% CI)	Subtotals only
2.1 Honey	2	75	Mean Difference (Random, 95% CI)	-1.88 [-2.38, -1.37]
2.2 Dextromethorphan	2	74	Mean Difference (Random, 95% CI)	-1.40 [-1.89, -0.91]
2.3 Diphenhydramine	1	40	Mean Difference (Random, 95% CI)	-1.83 [-2.88, -0.78]
2.4 No treatment	2	79	Mean Difference (Random, 95% CI)	-1.13 [-1.55, -0.72]
3 Bothersome cough (mean improvement) reduction	1		Mean Difference (Fixed, 95% CI)	Subtotals only
3.1 Honey	1	35	Mean Difference (Fixed, 95% CI)	-2.23 [-2.82, -1.63]
3.2 Dextromethorphan	1	34	Mean Difference (Fixed, 95% CI)	-1.94 [-2.55, -1.33]
3.3 No treatment	1	39	Mean Difference (Fixed, 95% CI)	-1.30 [-1.87, -0.72]
4 Childrens' sleep (cough impact on childrens' sleep score)	2		Mean Difference (Fixed, 95% CI)	Subtotals only
4.1 Honey	2	75	Mean Difference (Fixed, 95% CI)	-2.44 [-2.99, -1.89]
4.2 Dextromethorphan	2	74	Mean Difference (Fixed, 95% CI)	-1.77 [-2.30, -1.24]
4.3 Diphenhydramine	1	40	Mean Difference (Fixed, 95% CI)	-1.64 [-2.58, -0.70]
4.4 No treatment	2	79	Mean Difference (Fixed, 95% CI)	-1.37 [-1.81, -0.93]
5 Parents' sleep (cough impact on parents' sleep score)	2		Mean Difference (Fixed, 95% CI)	Subtotals only
5.1 Honey	2	75	Mean Difference (Fixed, 95% CI)	-2.33 [-2.90, -1.76]
5.2 Dextromethorphan	2	74	Mean Difference (Fixed, 95% CI)	-1.97 [-2.53, -1.41]
5.3 Diphenhydramine	1	40	Mean Difference (Fixed, 95% CI)	-1.89 [-2.97, -0.81]
5.4 No treatment	2	79	Mean Difference (Fixed, 95% CI)	-1.48 [-1.97, -0.99]
6 Combined improvement	1		Mean Difference (Fixed, 95% CI)	Subtotals only
6.1 Honey	1	35	Mean Difference (Fixed, 95% CI)	-10.71 [-13.20, -8.23]
6.2 Dextromethorphan	1	34	Mean Difference (Fixed, 95% CI)	-8.39 [-10.95, -5.84]
6.3 No treatment	1	39	Mean Difference (Fixed, 95% CI)	-6.41 [-8.82, -3.99]

Comparison 2. Pair-wise comparison

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Honey versus dextromethorphan	2		Mean Difference (Random, 95% CI)	Subtotals only
1.1 Frequency of cough (mean improvement)	2	149	Mean Difference (Random, 95% CI)	-0.07 [-1.07, 0.94]
1.2 Severity of cough (mean improvement)	2	149	Mean Difference (Random, 95% CI)	-0.13 [-1.25, 0.99]
1.3 Bothersome cough (mean improvement)	1	69	Mean Difference (Random, 95% CI)	0.29 [-0.56, 1.14]
1.4 Childrens' sleep (cough impact on childrens' sleep score)	2	149	Mean Difference (Random, 95% CI)	0.03 [-1.12, 1.19]
1.5 Parents' sleep (cough impact on parents' sleep score)	2	149	Mean Difference (Random, 95% CI)	-0.16 [-0.84, 0.53]
1.6 Combined mean improvement	1	69	Mean Difference (Random, 95% CI)	2.32 [-1.24, 5.88]
2 Honey versus diphenhydramine	1		Mean Difference (Random, 95% CI)	Subtotals only
2.1 Frequency of cough (mean improvement)	1	80	Mean Difference (Random, 95% CI)	-0.57 [-0.90, -0.24]
2.2 Severity of cough (mean improvement)	1	80	Mean Difference (Random, 95% CI)	-0.6 [-0.94, -0.26]
2.3 Childrens' sleep (cough impact on childrens' sleep score)	1	80	Mean Difference (Random, 95% CI)	-0.55 [-0.87, -0.23]
2.4 Parents' sleep (cough impact on parents' sleep score)	1	80	Mean Difference (Random, 95% CI)	-0.48 [-0.76, -0.20]
3 Honey versus 'no treatment'	2		Mean Difference (Random, 95% CI)	Subtotals only
3.1 Frequency of cough (mean improvement score)	2	154	Mean Difference (Random, 95% CI)	-1.07 [-1.53, -0.60]
3.2 Severity of cough (mean improvement)	2	154	Mean Difference (Random, 95% CI)	-0.97 [-1.47, -0.46]
3.3 Bothersome cough (mean improvement)	1	74	Mean Difference (Random, 95% CI)	-0.93 [-1.77, -0.09]
3.4 Childrens' sleep (cough impact on childrens' sleep score)	2	154	Mean Difference (Random, 95% CI)	-1.02 [-1.52, -0.52]
3.5 Parents' sleep (cough impact on parents' sleep score)	2	154	Mean Difference (Random, 95% CI)	-0.93 [-1.41, -0.46]
3.6 Combined mean improvement	1	74	Mean Difference (Random, 95% CI)	-4.31 [-7.77, -0.85]

Comparison 3. Adverse events

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Nervousness, insomnia, hyperactivity	2	149	Risk Ratio (M-H, Fixed, 95% CI)	2.94 [0.74, 11.71]
2 Stomach ache, nausea and vomiting	2	149	Risk Ratio (M-H, Fixed, 95% CI)	4.86 [0.24, 97.69]
3 Drowsiness	2	149	Risk Ratio (M-H, Fixed, 95% CI)	2.92 [0.12, 69.20]
4 Somnolence	1	80	Risk Ratio (M-H, Fixed, 95% CI)	0.14 [0.01, 2.68]

Analysis 1.1. Comparison 1 Pre- and postintervention comparison, Outcome 1 Cough frequency (mean improvement).

Review: Honey for acute cough in children

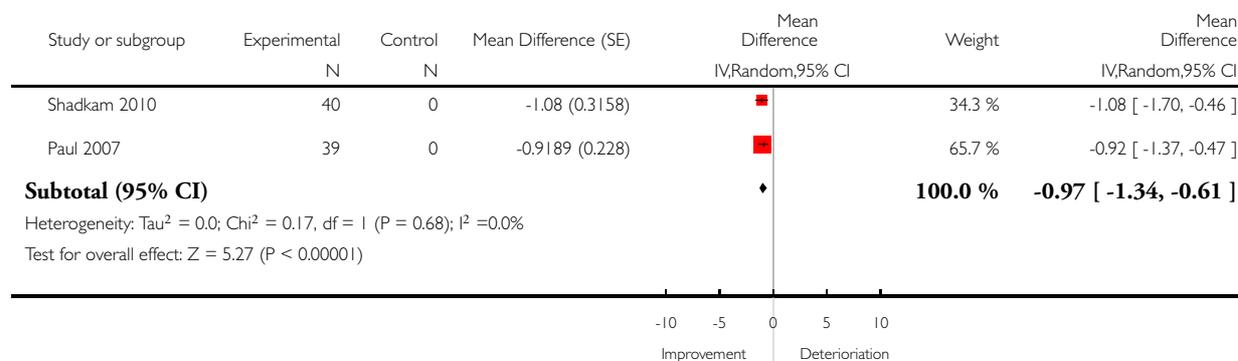
Comparison: 1 Pre- and postintervention comparison

Outcome: 1 Cough frequency (mean improvement)

Study or subgroup	Experimental N	Control N	Mean Difference (SE)	Mean Difference IV,Random,95% CI	Weight	Mean Difference IV,Random,95% CI
1 Honey						
Shadkam 2010	40	0	-2.16 (0.6316)		12.1 %	-2.16 [-3.40, -0.92]
Paul 2007	35	0	-1.8857 (0.2344)		87.9 %	-1.89 [-2.35, -1.43]
Subtotal (95% CI)					100.0 %	-1.92 [-2.35, -1.49]
Heterogeneity: Tau ² = 0.0; Chi ² = 0.17, df = 1 (P = 0.68); I ² = 0.0%						
Test for overall effect: Z = 8.73 (P < 0.00001)						
2 Dextromethorphan						
Shadkam 2010	40	0	-1.61 (0.4708)		20.8 %	-1.61 [-2.53, -0.69]
Paul 2007	34	0	-1.3939 (0.2414)		79.2 %	-1.39 [-1.87, -0.92]
Subtotal (95% CI)					100.0 %	-1.44 [-1.86, -1.02]
Heterogeneity: Tau ² = 0.0; Chi ² = 0.17, df = 1 (P = 0.68); I ² = 0.0%						
Test for overall effect: Z = 6.70 (P < 0.00001)						
3 Diphenhydramine						
Shadkam 2010	40	0	-1.73 (0.5059)		100.0 %	-1.73 [-2.72, -0.74]
Subtotal (95% CI)					100.0 %	-1.73 [-2.72, -0.74]
Heterogeneity: not applicable						
Test for overall effect: Z = 3.42 (P = 0.00063)						
4 No treatment						

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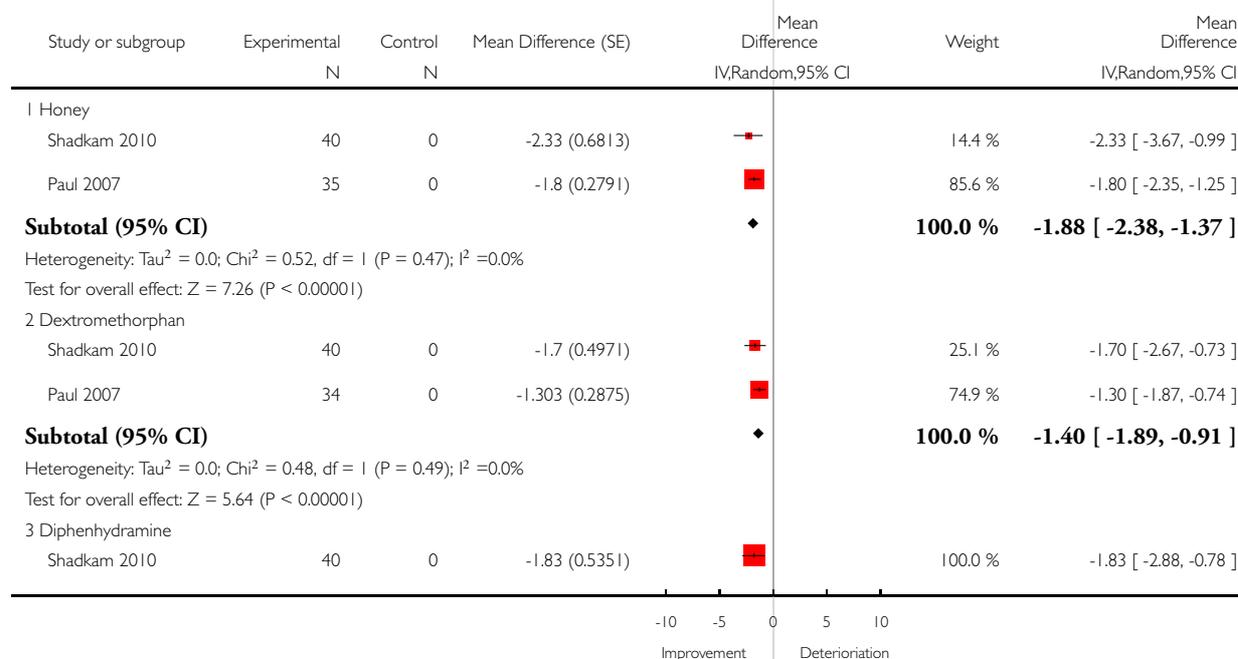


Analysis 1.2. Comparison 1 Pre- and postintervention comparison, Outcome 2 Severity of cough (mean improvement).

Review: Honey for acute cough in children

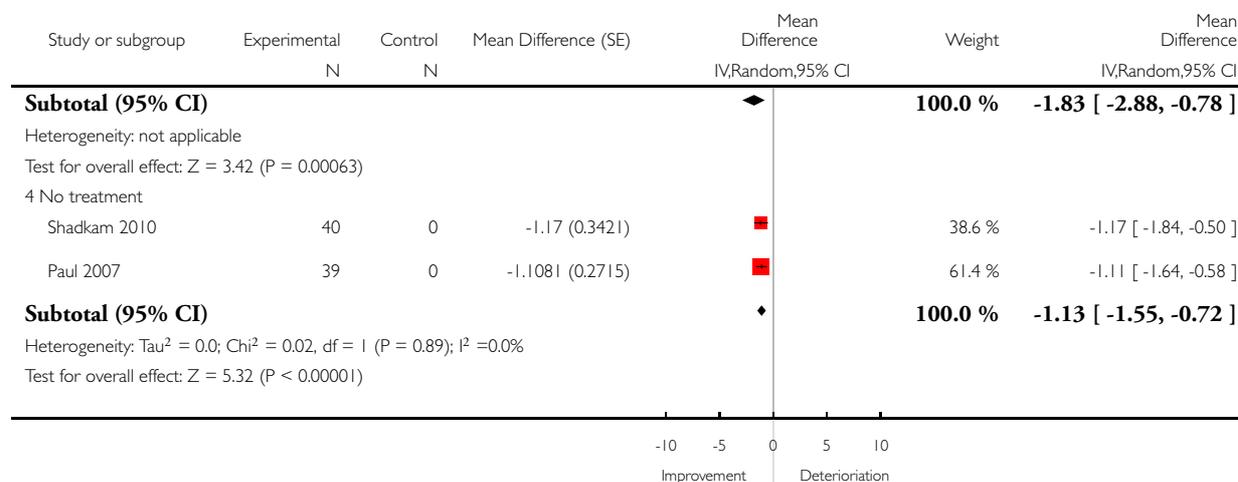
Comparison: 1 Pre- and postintervention comparison

Outcome: 2 Severity of cough (mean improvement)



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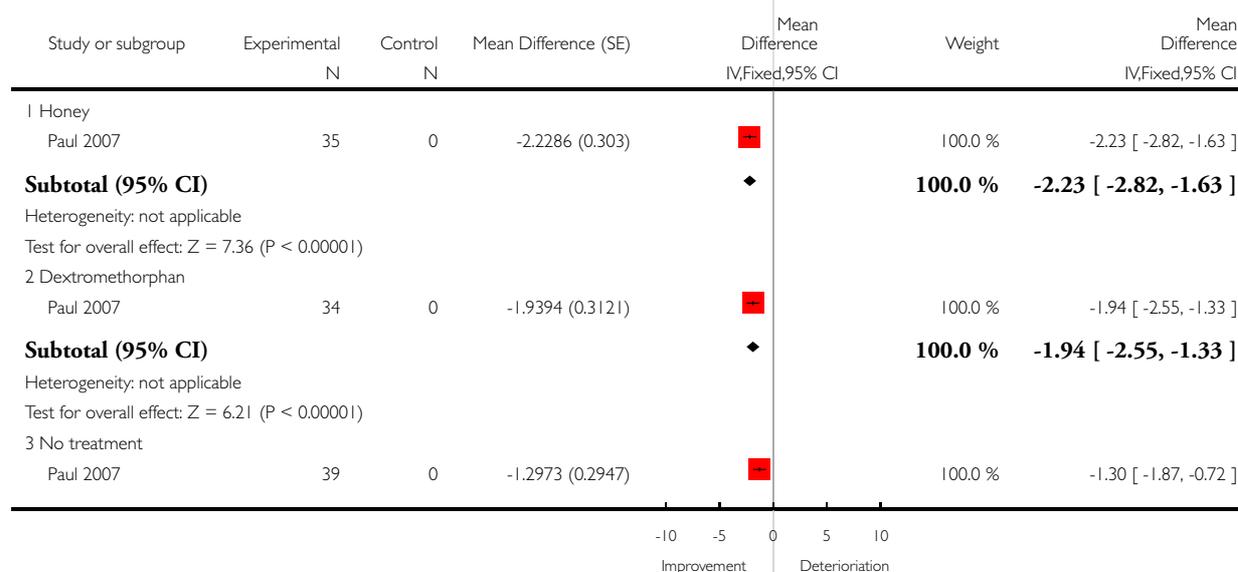


Analysis 1.3. Comparison 1 Pre- and postintervention comparison, Outcome 3 Bothersome cough (mean improvement) reduction.

Review: Honey for acute cough in children

Comparison: 1 Pre- and postintervention comparison

Outcome: 3 Bothersome cough (mean improvement) reduction



(Continued ...)

(... Continued)

Study or subgroup	Experimental N	Control N	Mean Difference (SE)	Mean Difference IV,Fixed,95% CI	Weight	Mean Difference IV,Fixed,95% CI
Subtotal (95% CI)				◆	100.0 %	-1.30 [-1.87, -0.72]
Heterogeneity: not applicable						
Test for overall effect: Z = 4.40 (P = 0.000011)						

-10 -5 0 5 10
Improvement Deterioration

Analysis 1.4. Comparison 1 Pre- and postintervention comparison, Outcome 4 Childrens' sleep (cough impact on childrens' sleep score).

Review: Honey for acute cough in children

Comparison: 1 Pre- and postintervention comparison

Outcome: 4 Childrens' sleep (cough impact on childrens' sleep score)

Study or subgroup	Experimental N	Control N	Mean Difference (SE)	Mean Difference IV,Fixed,95% CI	Weight	Mean Difference IV,Fixed,95% CI
1 Honey						
Paul 2007	35	0	-2.4857 (0.3101)	■	81.7 %	-2.49 [-3.09, -1.88]
Shadkam 2010	40	0	-2.24 (0.655)	■	18.3 %	-2.24 [-3.52, -0.96]
Subtotal (95% CI)				◆	100.0 %	-2.44 [-2.99, -1.89]
Heterogeneity: Chi ² = 0.11, df = 1 (P = 0.73); I ² = 0.0%						
Test for overall effect: Z = 8.71 (P < 0.00001)						
2 Dextromethorphan						
Paul 2007	34	0	-1.7879 (0.3194)	■	71.3 %	-1.79 [-2.41, -1.16]
Shadkam 2010	40	0	-1.72 (0.5029)	■	28.7 %	-1.72 [-2.71, -0.73]
Subtotal (95% CI)				◆	100.0 %	-1.77 [-2.30, -1.24]
Heterogeneity: Chi ² = 0.01, df = 1 (P = 0.91); I ² = 0.0%						
Test for overall effect: Z = 6.56 (P < 0.00001)						
3 Diphenhydramine						
Shadkam 2010	40	0	-1.64 (0.4795)	■	100.0 %	-1.64 [-2.58, -0.70]
Subtotal (95% CI)				◆	100.0 %	-1.64 [-2.58, -0.70]
Heterogeneity: not applicable						
Test for overall effect: Z = 3.42 (P = 0.00063)						

-10 -5 0 5 10
Improvement Deterioration

(Continued ...)

(... Continued)

Study or subgroup	Experimental N	Control N	Mean Difference (SE)	Mean Difference IV,Fixed,95% CI	Weight	Mean Difference IV,Fixed,95% CI
4 No treatment						
Paul 2007	39	0	-1.5676 (0.3016)	■	54.5 %	-1.57 [-2.16, -0.98]
Shadkam 2010	40	0	-1.13 (0.3304)	■	45.5 %	-1.13 [-1.78, -0.48]
Subtotal (95% CI)				◆	100.0 %	-1.37 [-1.81, -0.93]
Heterogeneity: Chi ² = 0.96, df = 1 (P = 0.33); I ² = 0.0%						
Test for overall effect: Z = 6.14 (P < 0.00001)						
				-10 -5 0 5 10		
				Improvement	Deterioration	

Analysis 1.5. Comparison 1 Pre- and postintervention comparison, Outcome 5 Parents' sleep (cough impact on parents' sleep score).

Review: Honey for acute cough in children

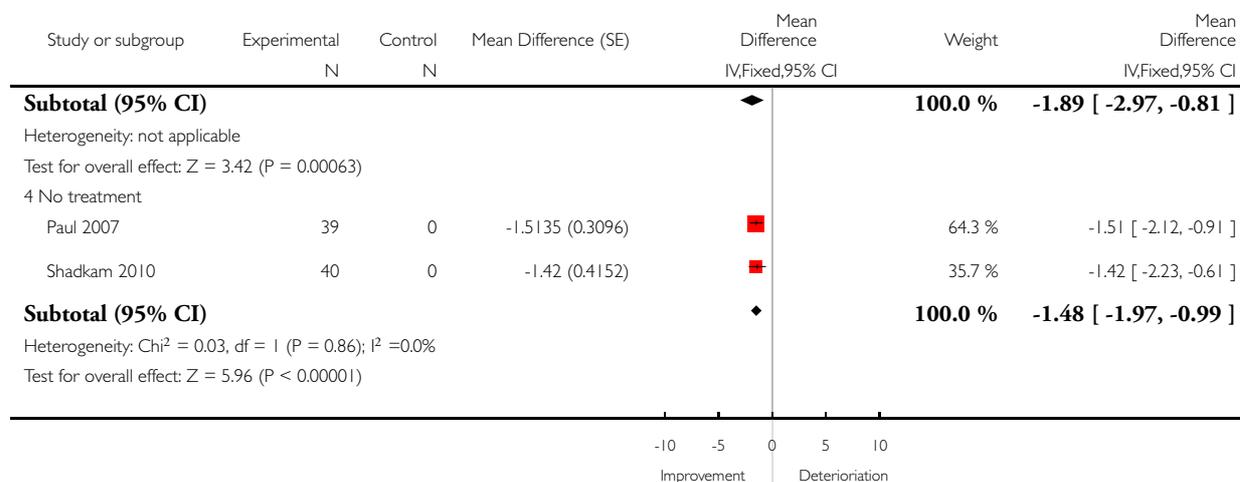
Comparison: 1 Pre- and postintervention comparison

Outcome: 5 Parents' sleep (cough impact on parents' sleep score)

Study or subgroup	Experimental N	Control N	Mean Difference (SE)	Mean Difference IV,Fixed,95% CI	Weight	Mean Difference IV,Fixed,95% CI
1 Honey						
Paul 2007	35	0	-2.3143 (0.3183)	■	82.8 %	-2.31 [-2.94, -1.69]
Shadkam 2010	40	0	-2.39 (0.6988)	■	17.2 %	-2.39 [-3.76, -1.02]
Subtotal (95% CI)				◆	100.0 %	-2.33 [-2.90, -1.76]
Heterogeneity: Chi ² = 0.01, df = 1 (P = 0.92); I ² = 0.0%						
Test for overall effect: Z = 8.03 (P < 0.00001)						
2 Dextromethorphan						
Paul 2007	34	0	-1.9697 (0.3278)	■	75.5 %	-1.97 [-2.61, -1.33]
Shadkam 2010	40	0	-1.97 (0.576)	■	24.5 %	-1.97 [-3.10, -0.84]
Subtotal (95% CI)				◆	100.0 %	-1.97 [-2.53, -1.41]
Heterogeneity: Chi ² = 0.00, df = 1 (P = 1.00); I ² = 0.0%						
Test for overall effect: Z = 6.91 (P < 0.00001)						
3 Diphenhydramine						
Shadkam 2010	40	0	-1.89 (0.5526)	■	100.0 %	-1.89 [-2.97, -0.81]
				-10 -5 0 5 10		
				Improvement	Deterioration	

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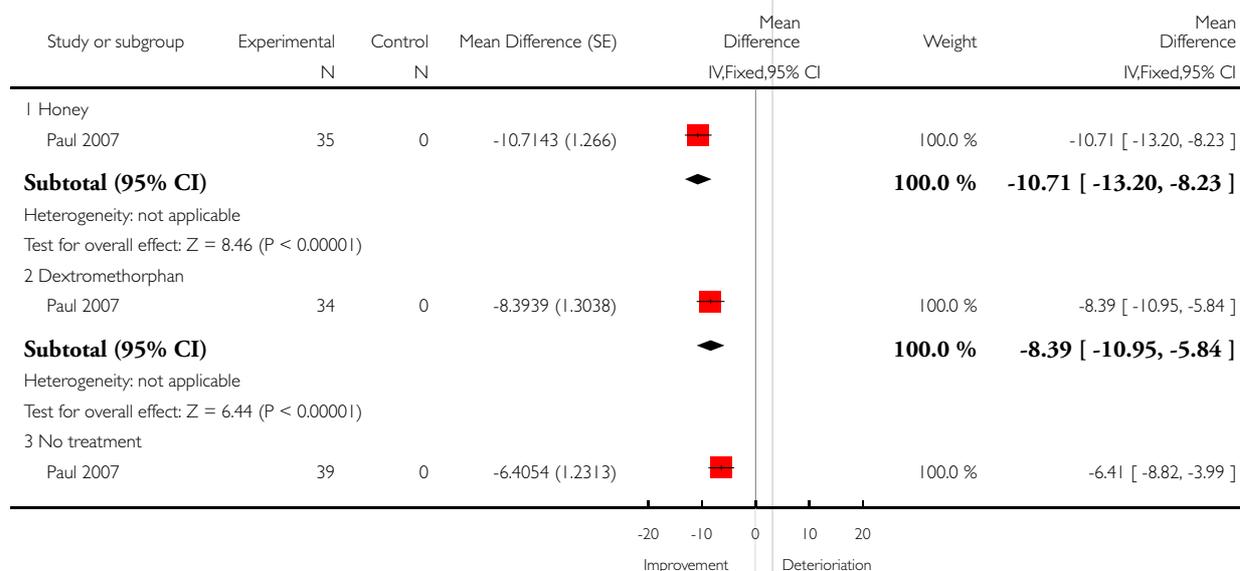


Analysis 1.6. Comparison 1 Pre- and postintervention comparison, Outcome 6 Combined improvement.

Review: Honey for acute cough in children

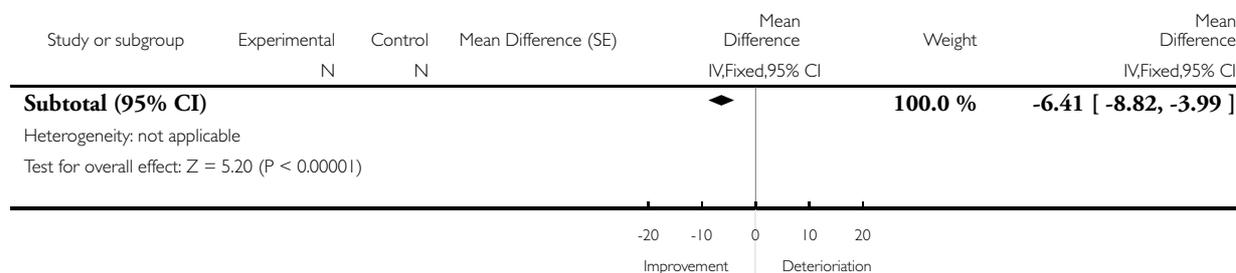
Comparison: 1 Pre- and postintervention comparison

Outcome: 6 Combined improvement



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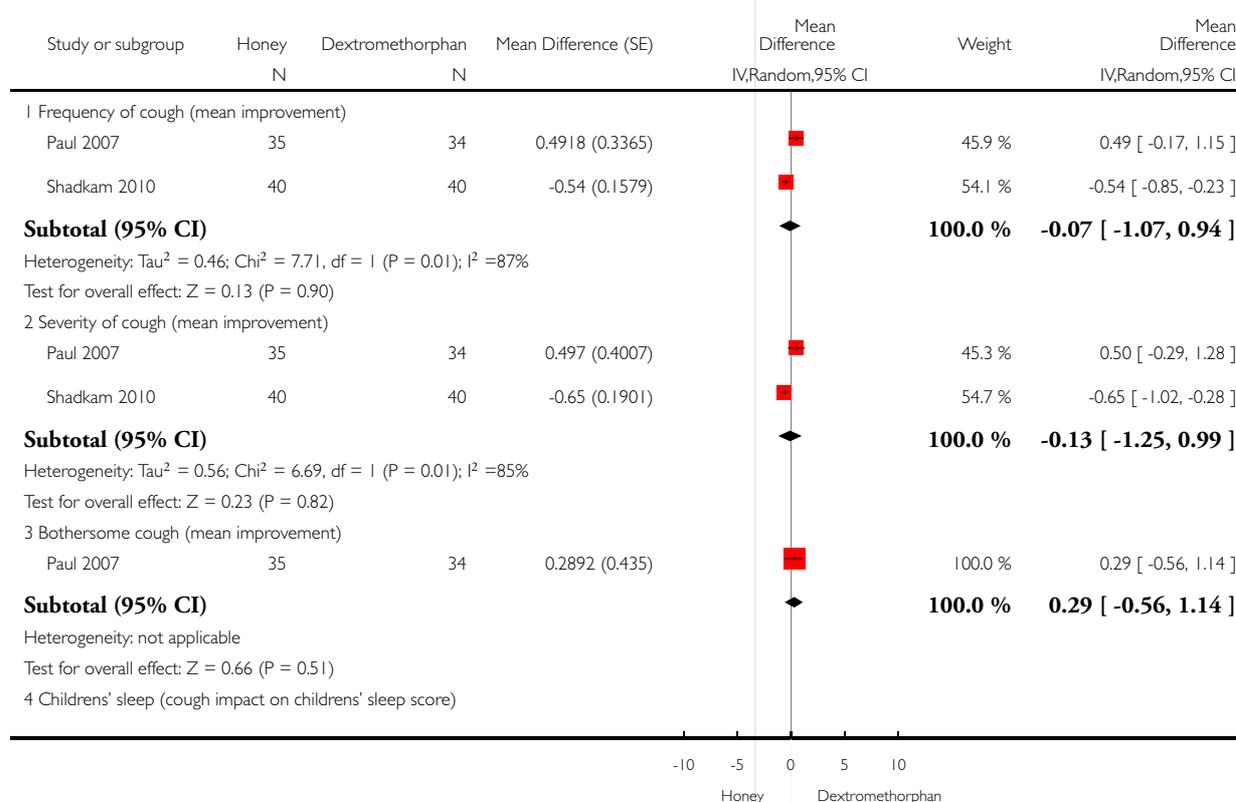


Analysis 2.1. Comparison 2 Pair-wise comparison, Outcome 1 Honey versus dextromethorphan.

Review: Honey for acute cough in children

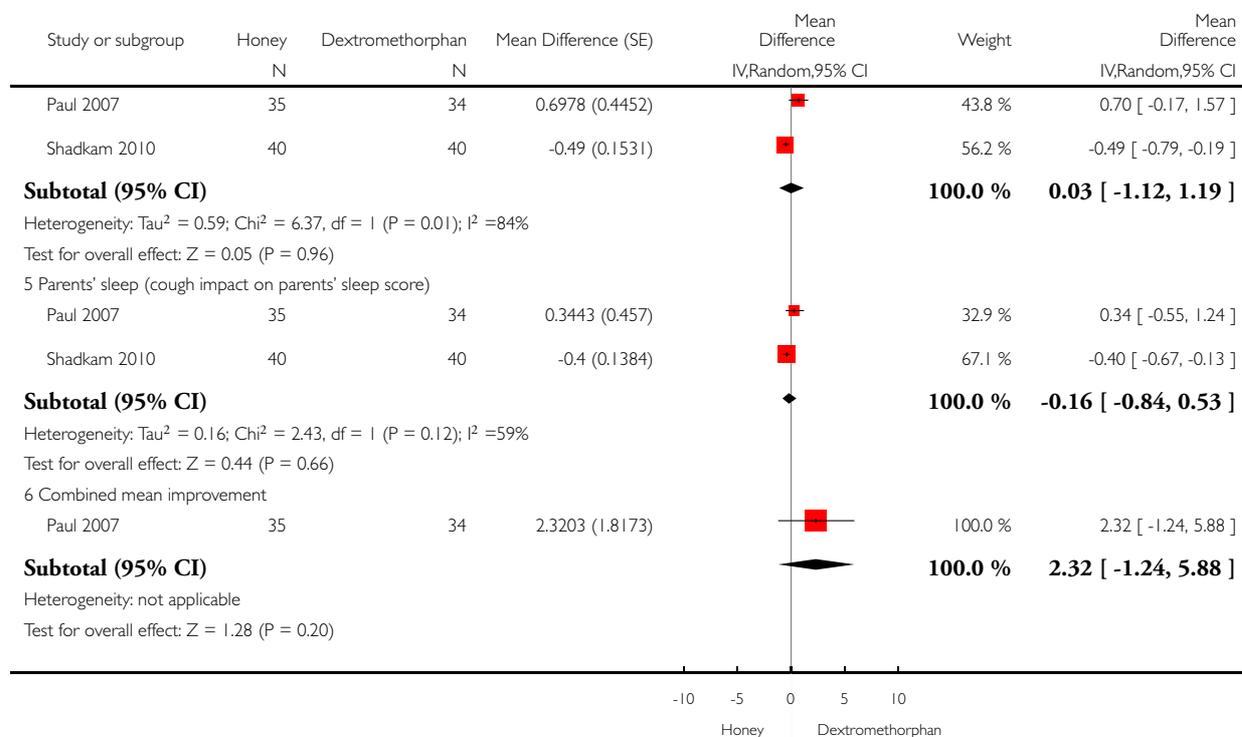
Comparison: 2 Pair-wise comparison

Outcome: 1 Honey versus dextromethorphan



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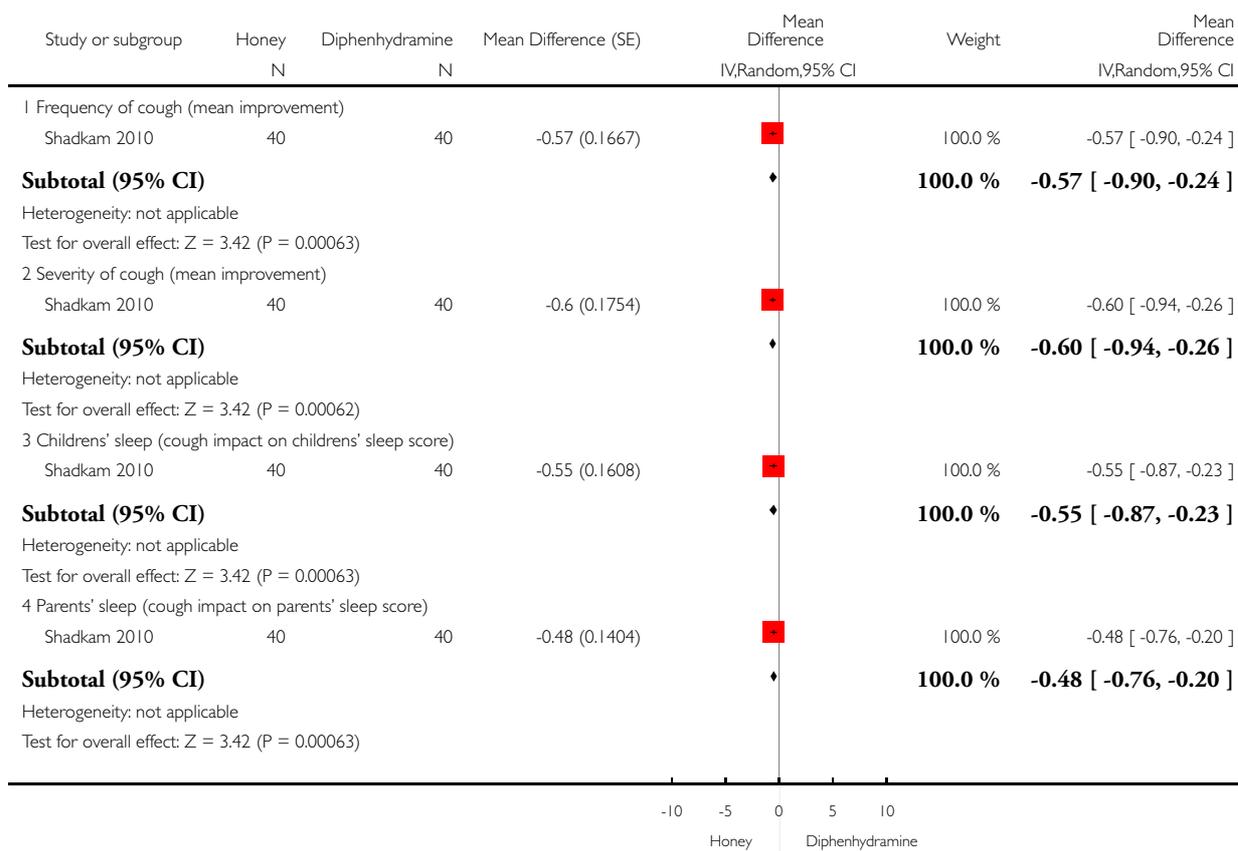


Analysis 2.2. Comparison 2 Pair-wise comparison, Outcome 2 Honey versus diphenhydramine.

Review: Honey for acute cough in children

Comparison: 2 Pair-wise comparison

Outcome: 2 Honey versus diphenhydramine

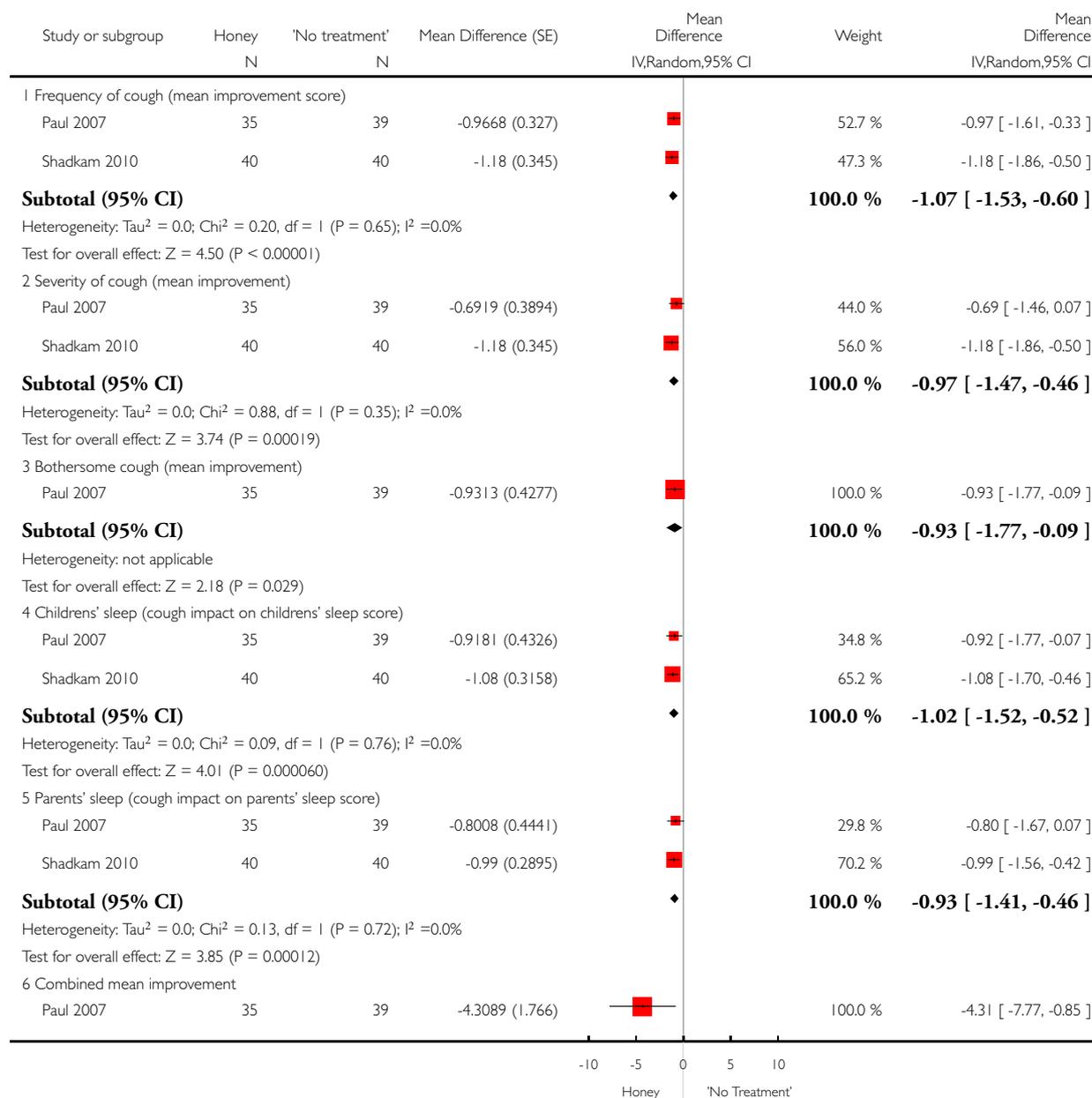


Analysis 2.3. Comparison 2 Pair-wise comparison, Outcome 3 Honey versus 'no treatment'.

Review: Honey for acute cough in children

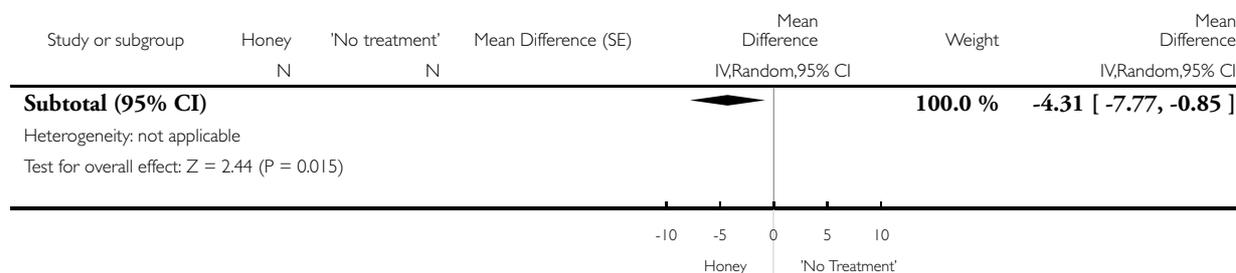
Comparison: 2 Pair-wise comparison

Outcome: 3 Honey versus 'no treatment'



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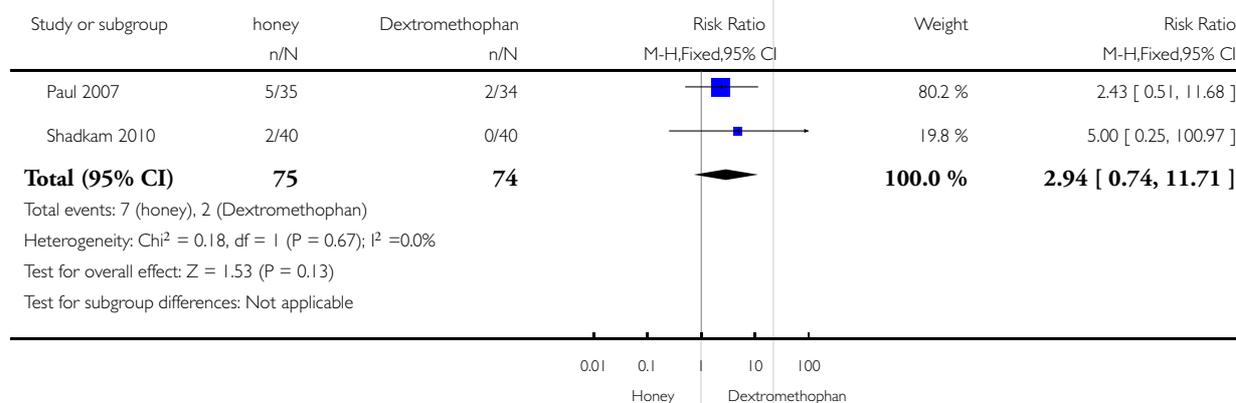


Analysis 3.1. Comparison 3 Adverse events, Outcome 1 Nervousness, insomnia, hyperactivity.

Review: Honey for acute cough in children

Comparison: 3 Adverse events

Outcome: 1 Nervousness, insomnia, hyperactivity

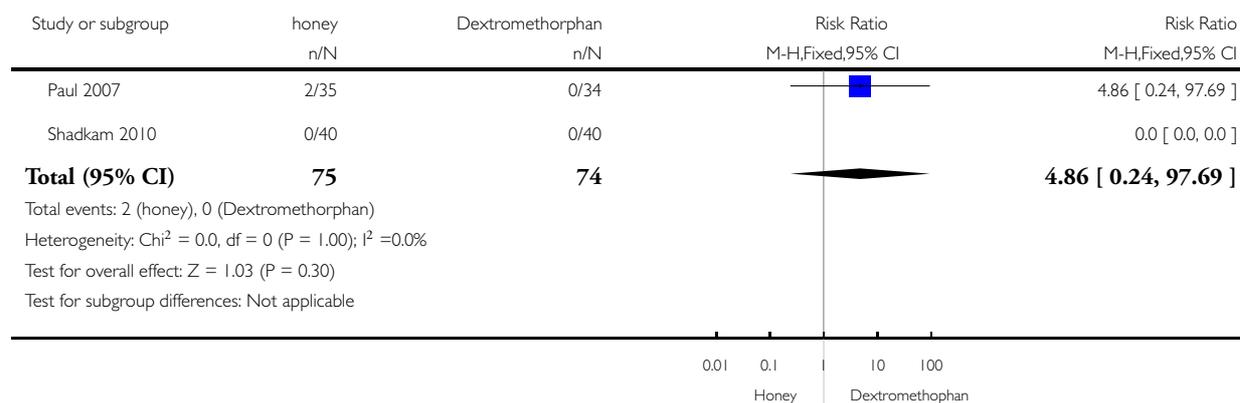


Analysis 3.2. Comparison 3 Adverse events, Outcome 2 Stomach ache, nausea and vomiting.

Review: Honey for acute cough in children

Comparison: 3 Adverse events

Outcome: 2 Stomach ache, nausea and vomiting

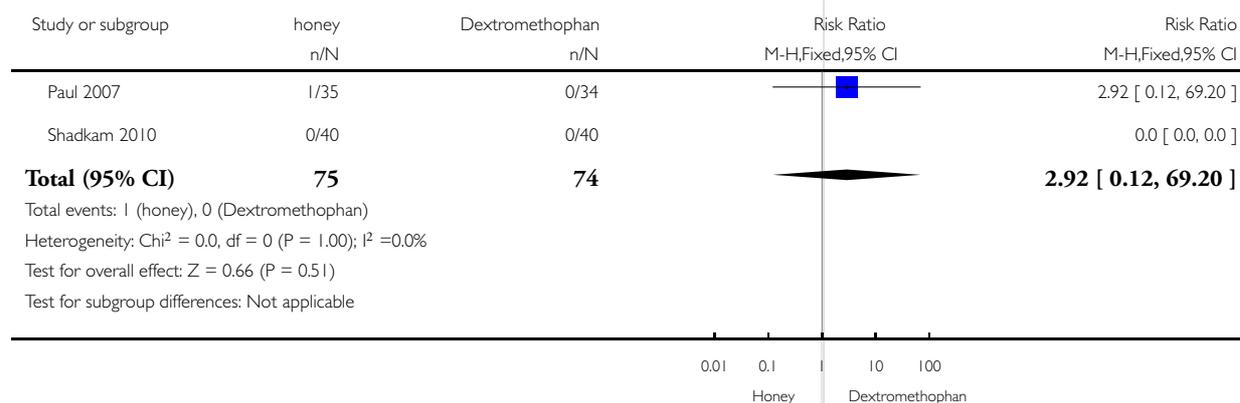


Analysis 3.3. Comparison 3 Adverse events, Outcome 3 Drowsiness.

Review: Honey for acute cough in children

Comparison: 3 Adverse events

Outcome: 3 Drowsiness

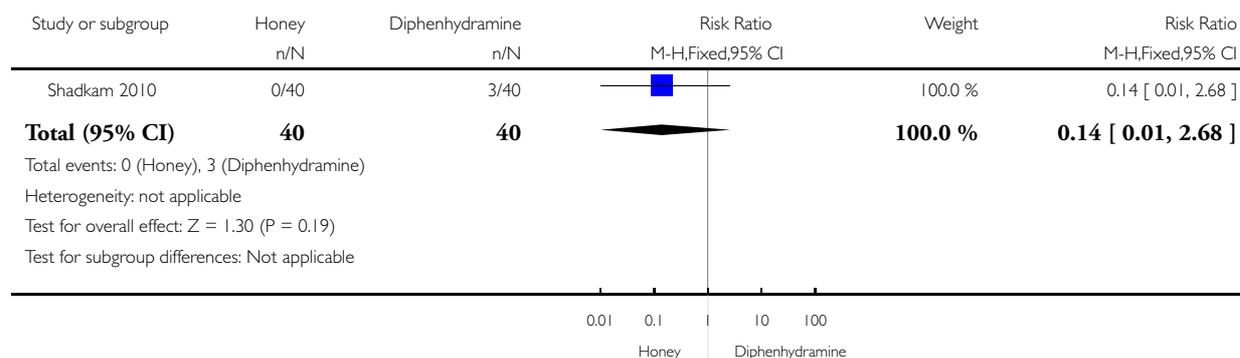


Analysis 3.4. Comparison 3 Adverse events, Outcome 4 Somnolence.

Review: Honey for acute cough in children

Comparison: 3 Adverse events

Outcome: 4 Somnolence



APPENDICES

Appendix 1. CENTRAL and MEDLINE search strategy

- 1 Cough/
- 2 cough*.tw
- 3 1 or 2
- 4 Honey/
- 5 honey*.tw.
- 6 4 or 5
- 7 3 and 6

Appendix 2. EMBASE search strategy

- #7. #3 AND #6 104 10 May 2011
- #6. #4 OR #5 7,415 10 May 2011
- #5. honey*:ab,ti AND [embase]/lim 7,150 10 May 2011
- #4. 'honey'/de AND [embase]/lim 1,674 10 May 2011
- #3. #1 OR #2 51,209 10 May 2011
- #2. cough*:ab,ti AND [embase]/lim 27,771 10 May 2011
- #1. 'coughing'/exp AND [embase]/lim 41,563 10 May 2011

Appendix 3. CINAHL (Ebsco) search strategy

S7 S3 and S6
S6 S4 or S5
S5 TI honey* or AB honey*
S4 (MH "Honey")
S3 S1 or S2
S2 TI cough* or AB cough*
S1 (MH "Cough")

Appendix 4. Web of Science search strategy

Topic=(cough*) AND Topic=(honey*)Timespan=2009-2011. Databases=SCI-EXPANDED, CPCI-S.

Appendix 5. AMED (Ovid)

1 cough/ (167)
2 cough*.tw. (532)
3 1 or 2 (532)
4 honey/ (76)
5 honey*.tw. (143)
6 4 or 5 (143)
7 3 and 6 (3)

Appendix 6. LILACS search strategy

Mh honey OR Tw honey\$ OR Tw miel OR Tw mel [Words] and Mh cough OR Tw cough\$ OR Tw tos OR Tw tosse [Words]

Appendix 7. CAB (ISI Thomson) Abstracts search strategy

Topic=(cough*) AND Topic=(honey*)Timespan=2009-2011. Databases=CAB Abstracts.

WHAT'S NEW

Last assessed as up-to-date: 11 January 2012.

Date	Event	Description
11 January 2012	New search has been performed	Searches updated. One new trial was included (Shadkam 2010)
11 January 2012	New citation required but conclusions have not changed	Our conclusions remain unchanged

HISTORY

Protocol first published: Issue 2, 2008

Review first published: Issue 1, 2010

CONTRIBUTIONS OF AUTHORS

Mrs Olabisi Oduwole (OO) prepared the main text of this update.

Dr Angela Oyo-ita (AO) and OO wrote the methods section of the update.

Prof. Martin Meremikwu (MM), OO, AO and EU revised the text. Selection of studies was carried out by OO and Dr. Ekong Udoh (EU).

Data extraction was carried out by OO and AO.

All the review authors contributed to this update, and read and agreed the final version.

DECLARATIONS OF INTEREST

None known.

SOURCES OF SUPPORT

Internal sources

- No sources of support supplied

External sources

- New Source of support, Not specified.

DIFFERENCES BETWEEN PROTOCOL AND REVIEW

None Known.

INDEX TERMS

Medical Subject Headings (MeSH)

*Apitherapy; Antitussive Agents [therapeutic use]; Cough [*therapy]; Dextromethorphan [therapeutic use]; Sleep Disorders [therapy]

MeSH check words

Child; Humans