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[Intervention Review]

Honey for acute cough in children

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ABSTRACT

Background

Cough causes concern for parents and is a major cause of outpatient visits. Cough can impact quality of life, cause anxiety, and affect sleep in children and their parents. Honey has been used to alleviate cough symptoms. This is an update of reviews previously published in 2014, 2012, and 2010.

Objectives

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

Search methods

We searched CENTRAL (2018, Issue 2), which includes the Cochrane Acute Respiratory Infections Group's Specialised Register, MEDLINE (2014 to 8 February 2018), Embase (2014 to 8 February 2018), CINAHL (2014 to 8 February 2018), EBSCO (2014 to 8 February 2018), Web of Science (2014 to 8 February 2018), and LILACS (2014 to 8 February 2018). We also searched ClinicalTrials.gov and the World Health Organization International Clinical Trial Registry Platform (WHO ICTRP) on 12 February 2018. The 2014 review included searches of AMED and CAB Abstracts, but these were not searched for this update due to lack of institutional access.

Selection criteria

Randomised controlled trials comparing honey alone, or in combination with antibiotics, versus no treatment, placebo, honey-based cough syrup, or other over-the-counter cough medications for children aged 12 months to 18 years for acute cough in ambulatory settings.

Data collection and analysis

We used standard methodological procedures expected by Cochrane.

Main results

We included six randomised controlled trials involving 899 children; we added three studies (331 children) in this update.

We assessed two studies as at high risk of performance and detection bias; three studies as at unclear risk of attrition bias; and three studies as at unclear risk of other bias.

Studies compared honey with dextromethorphan, diphenhydramine, salbutamol, bromelin (an enzyme from the Bromeliaceae (pineapple) family), no treatment, and placebo. Five studies used 7-point Likert scales to measure symptomatic relief of cough; one used an unclear 5-point scale. In all studies, low score indicated better cough symptom relief.

Using a 7-point Likert scale, honey probably reduces cough frequency better than no treatment or placebo (no treatment: mean difference (MD) -1.05, 95% confidence interval (CI) -1.48 to -0.62; I^2 = 0%; 2 studies; 154 children; moderate-certainty evidence; placebo: MD -1.62, 95% CI -3.02 to -0.22; I^2 = 0%; 2 studies; 402 children; moderate-certainty evidence). Honey may have a similar effect as dextromethorphan in reducing cough frequency (MD -0.07, 95% CI -1.07 to 0.94; I^2 = 87%; 2 studies; 149 children; low-certainty evidence). Honey may be better than diphenhydramine in reducing cough frequency (MD -0.57, 95% CI -0.90 to -0.24; 1 study; 80 children; low-certainty evidence).

Giving honey for up to three days is probably more effective in relieving cough symptoms compared with placebo or salbutamol. Beyond three days honey probably had no advantage over salbutamol or placebo in reducing cough severity, bothersome cough, and impact of cough on sleep for parents and children (moderate-certainty evidence). With a 5-point cough scale, there was probably little or no difference between the effects of honey and bromelin mixed with honey in reducing cough frequency and severity.

Adverse events included nervousness, insomnia, and hyperactivity, experienced by seven children (9.3%) treated with honey and two children (2.7%) treated with dextromethorphan (risk ratio (RR) 2.94, 95% CI 0.74 to 11.71; I^2 = 0%; 2 studies; 149 children; low-certainty evidence). Three children (7.5%) in the diphenhydramine group experienced somnolence (RR 0.14, 95% CI 0.01 to 2.68; 1 study; 80 children; low-certainty evidence). When honey was compared with placebo, 34 children (12%) in the honey group and 13 (11%) in the placebo group complained of gastrointestinal symptoms (RR 1.91, 95% CI 1.12 to 3.24; I^2 = 0%; 2 studies; 402 children; moderate-certainty evidence). Four children who received salbutamol had rashes compared to one child in the honey group (RR 0.19, 95% CI 0.02 to 1.63; 1 study; 100 children; moderate-certainty evidence). No adverse events were reported in the no-treatment group.

Authors' conclusions

Honey probably relieves cough symptoms to a greater extent than no treatment, diphenhydramine, and placebo, but may make little or no difference compared to dextromethorphan. Honey probably reduces cough duration better than placebo and salbutamol. There was no strong evidence for or against using honey. Most of the children received treatment for one night, which is a limitation to the results of this review. There was no difference in occurrence of adverse events between the honey and control arms.

PLAIN LANGUAGE SUMMARY

Honey for acute cough in children

Review question

Can honey reduce cough symptoms caused by bacteria and viruses in children?

Background

Cough causes concern for parents and is a major reason for outpatient visits. Honey is believed to prevent growth of germs and reduce inflammation.

Search date

We searched databases to 8 February 2018 and trial registers to 12 February 2018.

Study characteristics

We included six small trials involving 899 children aged 12 months to 18 years conducted in Iran, Israel, the USA, Brazil, and Kenya. This update included three new trials conducted between 2007 and 2016 that involved 331 children.

Study funding sources

Two studies were supported by pharmaceutical manufacturers; one by a university research centre; one by the Honey Board of Israel and non-government agencies; and one by USA National Honey Board. One study did not report funding sources.

Key results

We compared honey to over-the-counter cough preparations, bromelin (a pineapple enzyme) mixed with honey, fake treatment (placebo), and no treatment.

Honey probably reduces cough symptoms more than placebo and salbutamol (a drug that opens lung airways) when given for up to three days. Honey is probably more effective at providing cough relief and reducing the impact of cough on children's sleep at night than no treatment.

There may be little or no difference between the effects of honey and dextromethorphan (an ingredient in over-the-counter cough remedies) or honey and bromelin with honey on all cough symptoms. Honey may be better than diphenhydramine (an antihistamine) at relieving and reducing children's cough.

The parents of seven children given honey and two given dextromethorphan reported side effects in their children, such as not falling asleep easily, restlessness, and becoming overexcited. The parents of three children in the diphenhydramine group reported that their children were often sleepy. The parents of nine children given salbutamol, seven given honey, and six given placebo reported diarrhoea. The parents of four children who received salbutamol and one child given honey reported rash.

We found no evidence for or against the use of honey to relieve cough in children. Using honey for infants aged up to 12 months is not advised because of poor immunity against bacteria that may be present, which can cause paralysis. Most of the children received honey for just one night, which is a limitation to the results of this review.

Quality of the evidence

Overall, evidence quality was low to moderate. Some studies did not blind participants.

SUMMARY OF FINDINGS

Summary of findings for the main comparison. Honey compared to dextromethorphan for acute cough in children

Honey compared to dextromethorphan for acute cough in children

Patient or population: acute cough in children
Setting: ambulatory
Intervention: honey
Comparison: dextromethorphan

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with dextromethorphan	Risk with honey				
Duration of cough	-	-	-	-	-	Not assessed
Frequency of cough[1]	The mean frequency of cough (reduction in frequency of cough score) was -1.54.	MD 0.07 score lower (1.07 lower to 0.94 higher)	-	149 (2 RCTs)	⊕⊕⊖⊖ LOW [2, 3]	Follow-up: mean 1 day
Severity of cough[1]	The mean severity of cough (reduction in severity of cough score) was -1.52.	MD 0.13 score lower (1.25 lower to 0.99 higher)	-	149 (2 RCTs)	⊕⊕⊖⊖ LOW [2, 3]	Follow-up: mean 1 day
Bothersome cough[1]	The mean bothersome cough (reduction in bothersome nature of cough score) was -1.94.	MD 0.29 score higher (0.56 lower to 1.14 higher)	-	69 (1 RCT)	⊕⊕⊕⊖ MODERATE [5]	Follow-up: mean 1 day
Cough impact on children's sleep[1]	The mean cough impact on children's sleep (cough impact on children' sleep score) was -1.75.	MD 0.03 score higher (1.12 lower to 1.19 higher)	-	149 (2 RCTs)	⊕⊕⊖⊖ LOW [2, 3]	Follow-up: mean 6 days
Cough impact on parents' sleep[1]	The mean cough impact on parents' sleep (cough impact on parents' sleep score) was -1.97.	MD 0.16 score lower (0.84 lower to 0.53 higher)	-	149 (2 RCTs)	⊕⊕⊖⊖ LOW [2, 3]	Follow-up: mean 1 day
Adverse events	**Population**					
Nervousness, insomnia, hyperactivity	3 per 100	8 per 100 (2 to 32)	RR 2.94 (0.74 to 11.71)	149 (2 RCTs)	⊕⊕⊖⊖ LOW [4]	Follow-up: mean 1 day
Stomachache, nausea, and vomiting	1 per 100	7 per 100	RR 4.86 (0.24 to 97.69)	69 (1 RCT)	⊕⊕⊖⊖ LOW [5]	

		(0 to 100)			
Drowsiness	1 per 100	4 per 100 (0 to 100)	RR 2.92 (0.12 to 69.20)	69 (1 RCT)	⊕⊕⊖⊖ LOW [5]

*__The risk in the intervention group__ (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; **MD:** mean difference; **RCT:** randomised controlled trial; **RR:** risk ratio

GRADE Working Group grades of evidence
High certainty: We are very confident that the true effect lies close to that of the estimate of the effect.
Moderate certainty: We are moderately confident in the effect estimate: the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.
Low certainty: Our confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of the effect.
Very low certainty: We have very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of effect.

[1]Assessed on a 7-point Likert scale from 0 to 6; lower score is better.
[2]Downgraded by one level because of study limitations: it was unclear if Shadkam 2010 concealed allocation; there was no blinding, which could increase the risk of bias in the study outcomes.
[3]Downgraded by one level for serious heterogeneity, which could be due to difference in dextromethorphan dose. In Paul 2007, 8.5 mg/2.5 mL dextromethorphan was given compared to 7.5 mg/2.5 mL given to children aged under 5 years by Shadkam 2010.
[4]Downgraded by two levels for risk of bias, inconsistency, and imprecision; the studies were underpowered to detect differences.
[5]Downgraded by two levels for very serious imprecision. Data were available from only Paul 2007, which had a small sample size.

Summary of findings 2. Honey compared to diphenhydramine for acute cough in children

Honey compared to diphenhydramine for acute cough in children

Patient or population: acute cough in children
Setting: ambulatory
Intervention: honey
Comparison: diphenhydramine

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with diphenhydramine	Risk with honey				
Cough duration	-	-	-	-	-	Not assessed
Frequency of cough[1]	The mean frequency of cough (reduction in cough frequency score) was -1.73.	MD 0.57 lower (0.9 lower to 0.24 lower)	-	80 (1 RCT)	⊕⊕⊖⊖ LOW [2, 3]	Follow-up: mean 1 day

Severity of cough[1]	The mean severity of cough (reduction in cough severity score) was -1.83.	MD 0.6 lower (0.94 lower to 0.26 lower)	-	80 (1 RCT)	⊕⊕⊖⊖ LOW [2, 3]	Follow-up: mean 1 day
Cough impact on children's sleep[1]	The mean cough impact on children's sleep (cough impact on children' sleep score) was -1.64.	MD 0.55 score lower (0.87 lower to 0.23 lower)	-	80 (1 RCT)	⊕⊕⊖⊖ LOW [2, 3]	Follow-up: mean 6 days
Cough impact on parents' sleep[1]	The mean cough impact on parents' sleep (cough impact on parents' sleep score) was -1.89.	MD 0.48 lower (0.76 lower to 0.2 lower)	-	80 (1 RCT)	⊕⊕⊖⊖ LOW [2, 3]	Follow-up: mean 1 day
Adverse event: Somnolence	**Population** 8 per 100	1 per 100 (0 to 20)	RR 0.14 (0.01 to 2.68)	80 (1 RCT)	⊕⊕⊖⊖ LOW [2, 3]	Follow-up: mean 1 day

*__The risk in the intervention group__ (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; **MD:** mean difference; **RCT:** randomised controlled trial; **RR:** risk ratio

GRADE Working Group grades of evidence
High certainty: We are very confident that the true effect lies close to that of the estimate of the effect.
Moderate certainty: We are moderately confident in the effect estimate: the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.
Low certainty: Our confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of the effect.
Very low certainty: We have very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of effect.

[1]Assessed on a 7-point Likert scale from 0 to 6; lower score is better.
[2]Downgraded by one level because of study limitations: it was unclear if Shadkam 2010 concealed allocation; there was no blinding, which could increase the risk of bias in the study outcomes.
[3]Downgraded by one level for serious imprecision: data were from one small study (Shadkam 2010).

Summary of findings 3. Honey compared to no treatment for acute cough in children

Honey compared to no treatment for acute cough in children

Patient or population: acute cough in children
Setting: ambulatory
Intervention: honey
Comparison: 'no treatment'

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with no treatment	Risk with honey				
Cough duration	-	-	-	-	-	Not assessed
Frequency of cough[1]	The mean frequency of cough (reduction in cough frequency score) was -0.98.	MD 1.05 lower (1.48 lower to 0.62 lower)	-	154 (2 RCTs)	⊕⊕⊕⊖ MODERATE [2, 3]	Follow-up: mean 1 day
Severity of cough[1] assessed with: 7-point Likert scale Scale from 0 to 6	The mean severity of cough (reduction in severity of cough score) was -1.13.	MD 1.03 score lower (1.59 lower to 0.47 lower)	-	154 (2 RCTs)	⊕⊕⊕⊖ MODERATE [2, 3]	Follow-up: mean 1 day
Bothersome cough[1] assessed with: 7-point Likert scale Scale from 0 to 6	The mean bothersome cough (reduction in bothersome nature of cough score) was -1.30.	MD 0.93 score lower (1.98 lower to 0.12 higher)	-	74 (1 RCT)	⊕⊕⊖⊖ LOW [2, 4]	Follow-up: mean 1 day
Cough impact on children's sleep[1] assessed with: 7-point Likert scale Scale from 0 to 6	The mean cough impact on children's sleep (cough impact on children' sleep score) was -1.28.	MD 1.04 score lower (1.57 lower to 0.51 lower)	-	154 (2 RCTs)	⊕⊕⊕⊖ MODERATE [2, 3]	Follow-up: mean 6 days
Cough impact on parents' sleep[1] assessed with: 7-point Likert scale Scale from 0 to 6	The mean cough impact on parents' sleep (cough impact on parents' sleep score) was -1.46.	MD 0.88 score lower (1.23 lower to 0.52 lower)	-	154 (2 RCTs)	⊕⊕⊕⊖ MODERATE [2, 3]	Follow-up: mean 1 day
Adverse events	**Population**					
Nervousness, insomnia, hyperactivity	1 per 100	6 per 100 (1 to 33)	RR 9.40 (1.16 to 76.20)	154 (2 RCTs)	⊕⊕⊖⊖ LOW [2, 4]	Follow-up: mean 1 day
Stomachache, nausea, and vomiting	1 per 100	7 per 100 (0 to 62)	RR 5.90 (0.27 to 127.14)	74 (1 RCT)	⊕⊕⊖⊖ LOW [2, 4]	
Drowsiness	1 per 100	4 per 100 (0 to 53)	RR 3.43 (0.14 to 87.09)	74 (1 RCT)	⊕⊕⊖⊖ LOW [2, 4]	

*__The risk in the intervention group__ (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; **MD:** mean difference; **RCT:** randomised controlled trial; **RR:** risk ratio

GRADE Working Group grades of evidence
High certainty: We are very confident that the true effect lies close to that of the estimate of the effect.
Moderate certainty: We are moderately confident in the effect estimate: the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.
Low certainty: Our confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of the effect.
Very low certainty: We have very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of effect.

[1]Assessed on a 7-point Likert scale from 0 to 6; lower score is better.
[2]Downgraded by one level for risk of bias. Participants in the no-treatment arm were not blinded; knowledge of receiving no treatment may have influenced assessment of this subjective outcome (Paul 2007; Shadkam 2010).
[3]Downgraded by one level for imprecision and risk of bias.
[4]Downgraded by one level for serious imprecision: data from one small study (Paul 2007).

Summary of findings 4. Honey compared to placebo for acute cough in children

Honey compared to placebo for acute cough in children

Patient or population: acute cough in children
Setting: ambulatory
Intervention: honey
Comparison: placebo

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with placebo	Risk with honey				
Day 1						
Frequency of cough[1]	The mean frequency of cough (reduction in cough frequency score) was -0.99.	MD 1.62 score lower (3.02 lower to 0.22 lower)	-	402 (2 RCT)	⊕⊕⊕⊖ MODERATE [2]	Follow-up: mean 1 day
Severity of cough[1]	The mean severity of cough (reduction in severity of cough score) was -0.80.	MD 1.07 score lower (2.43 lower to 0.3 higher)	-	402 (2 RCT)	⊕⊕⊕⊖ MODERATE [2]	
Bothersome cough (mean	The mean bothersome cough (reduction in bothersome nature of cough) was -1.08.	MD 1.4 score lower (2.82 lower to 0.03 higher)	-	402 (2 RCTs)	⊕⊕⊕⊖ MODERATE [2]	

improvement score)[1]						
Cough impact on children's sleep[1]	The mean cough impact on children's sleep (cough impact on children' sleep score) was -1.03.	MD 1.21 score lower (2.61 lower to 0.19 higher)	-	402 (2 RCTs)	⊕⊕⊕⊖ MODERATE [2]	Follow-up: mean 6 days
Cough impact on parents' sleep[1]	The mean cough impact on parents' sleep (cough impact on parents' sleep score) was -1.44.	MD 1.29 score lower (2.71 lower to 0.13 higher)	-	402 (2 RCTs)	⊕⊕⊕⊖ MODERATE [2]	Follow-up: mean 1 day
Day 3						
Frequency of cough[1]	The mean frequency of cough (reduction in frequency of cough score) was -0.9.	MD 1.13 score lower (1.71 lower to 0.55 lower)	-	102 (1 RCT)	⊕⊕⊕⊖ MODERATE [2]	Follow-up: mean 6 days
Severity of cough[1]	The mean severity of cough (reduction in severity of cough score) was -1.08.	MD 0.85 score lower (1.41 lower to 0.29 lower)	-	102 (1 RCT)	⊕⊕⊕⊖ MODERATE [2]	
Bothersome cough[1]	The mean bothersome cough (reduction in bothersome nature of cough score) was -0.99.	MD 1.33 score lower (1.87 lower to 0.79 lower)	-	102 (1 RCT)	⊕⊕⊕⊖ MODERATE [2]	
Cough impact on children's sleep[1]	The mean cough impact on children's sleep (cough impact on children's sleep score) was -0.46.	MD 0.93 score lower (1.42 lower to 0.44 lower)	-	102 (1 RCT)	⊕⊕⊕⊖ MODERATE [2]	
Cough impact on parents' sleep[3]	The mean cough impact on parents' sleep (cough impact on parents' sleep score) was -1.04.	MD 0.88 score lower (1.38 lower to 0.38 lower)	-	102 (1 RCT)	⊕⊕⊕⊖ MODERATE [2]	
Day 5						
Cough duration	The mean cough duration was 5.18 days.	MD 0.72 days lower (1.31 lower to 0.13 lower)	-	102 (1 RCT)	⊕⊕⊕⊖ MODERATE [2]	Follow-up: mean 6 days; assessed with: 7-point Likert scale Scale from 0 to 6
Frequency of cough[1]	The mean frequency of cough (reduction in frequency of cough score) was -1.95.	MD 0.48 score lower (2.95 lower to 1.99 higher)	-	102 (1 RCT)	⊕⊕⊕⊖ MODERATE [2]	
Severity of cough[1]	The mean severity of cough (reduction in severity of cough score) was -1.96.	MD 0.43 score lower (2.21 lower to 1.35 higher)	-	102 (1 RCT)	⊕⊕⊕⊖ MODERATE [2]	

Bothersome cough[1]	The mean bothersome cough (reduction in bothersome nature of cough score) was -1.85.	MD 0.51 score lower (3.01 lower to 1.99 higher)	-	102 (1 RCT)	⊕⊕⊕⊖ MODERATE [2]	
Cough impact on children's sleep[1]	The mean cough impact on children's sleep (cough impact on children' sleep score) was -1.68.	MD 0.55 score lower (1.79 lower to 0.69 higher)	-	102 (1 RCT)	⊕⊕⊕⊖ MODERATE [2]	
Cough impact on parents' sleep	The mean cough impact on parents' sleep (cough impact on parents' sleep score) was -1.54.	MD 0.57 score lower (1.59 lower to 0.45 higher)	-	102 (1 RCT)	⊕⊕⊕⊖ MODERATE [2]	
Adverse events	**Population**					
Stomachache, nausea, and vomiting	11 per 100	21 per 100 (12 to 35)	RR 1.91 (1.12 to 3.24)	402 (2 RCTs)	⊕⊕⊕⊖ MODERATE[2]	Follow-up: mean 6 days
Diarrhoea	13 per 100	12 per 100 (4 to 34)	RR 0.92 (0.33 to 2.55)	102 (1 RCT)	⊕⊕⊖⊖ LOW [3]	
Tachycardia	2 per 100	4 per 100 (0 to 37)	RR 1.58 (0.15 to 16.86)	102 (1 RCT)	⊕⊕⊖⊖ LOW [3]	

*__The risk in the intervention group__ (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; **MD:** mean difference; **RCT:** randomised controlled trial; **RR:** risk ratio

GRADE Working Group grades of evidence
High certainty: We are very confident that the true effect lies close to that of the estimate of the effect.
Moderate certainty: We are moderately confident in the effect estimate: the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.
Low certainty: Our confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of the effect.
Very low certainty: We have very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of effect.

[1]Assessed on a 7-point Likert scale from 0 to 6; lower score is better.
[2]Downgraded by one level for serious imprecision.
[3]Downgraded by two levels for very serious imprecision: Waris 2014 was insufficiently powered to detect differences.

Summary of findings 5. Honey compared to salbutamol for acute cough in children

Honey compared to salbutamol for acute cough in children

Patient or population: acute cough in children
Setting: ambulatory
Intervention: honey
Comparison: salbutamol

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with salbutamol	Risk with honey				
Day 1						
Frequency of cough (mean improvement score)[1]	The mean frequency of cough (reduction in frequency of cough score) was -0.52.	MD 0.26 lower (3.14 lower to 2.62 higher)	-	100 (1 RCT)	⊕⊕⊕⊖ MODERATE [2]	Follow-up: mean 6 days
Severity of cough (mean improvement score)[1]	The mean severity of cough (reduction in severity of cough score) was -0.74.	MD 0.1 lower (0.39 lower to 0.19 higher)	-	100 (1 RCT)	⊕⊕⊕⊖ MODERATE [2]	
Bothersome cough (mean improvement score)[1]	The mean bothersome cough (reduction in bothersome nature of cough score) was -1.00.	MD 0.21 lower (0.9 lower to 0.48 higher)	-	100 (1 RCT)	⊕⊕⊕⊖ MODERATE [2]	
Cough impact on children's sleep[1]	The mean cough impact on children's sleep (cough impact on children' sleep score) was -1.24.	MD 0.09 higher (0.05 lower to 0.23 higher)	-	100 (1 RCT)	⊕⊕⊕⊖ MODERATE [2]	
Cough impact on parents' sleep[1]	The mean cough impact on parents' sleep (cough impact on parents' sleep score) was -1.22.	MD 0.05 higher (0.03 lower to 0.13 higher)	-	100 (1 RCT)	⊕⊕⊕⊖ MODERATE [2]	
Day 3						
Frequency of cough[1]	The mean frequency of cough (reduction in frequency of cough score) was -1.34.	MD 0.69 lower (1.13 lower to 0.25 lower)	-	100 (1 RCT)	⊕⊕⊕⊖ MODERATE [2]	Follow-up: mean 4 days
Severity of cough[1]	The mean severity of cough (reduction in severity of cough score) was -1.59.	MD 0.34 lower (0.64 lower to 0.04 lower)	-	100 (1 RCT)	⊕⊕⊕⊖ MODERATE [2]	

Bothersome cough[1]	The mean bothersome cough (reduction in bothersome nature of cough score) was -2.08.	MD 0.24 lower (0.38 lower to 0.1 lower)	-	100 (1 RCT)	⊕⊕⊕⊖ MODERATE [2]	
Cough impact on children's sleep[1]	The mean cough impact on children's sleep (cough impact on children' sleep score) was -2.25.	MD 0.31 higher (0.13 higher to 0.49 higher)	-	100 (1 RCT)	⊕⊕⊕⊖ MODERATE [2]	Follow-up: mean 6 days
C**ough impact on parents' sleep**[1]	The mean cough impact on parents' sleep (cough impact on parents' sleep score) was -2.13.	MD 0.21 higher (0.06 higher to 0.36 higher)	-	100 (1 RCT)	⊕⊕⊕⊖ MODERATE [2]	Follow-up: mean 4 days
Day 5						
Cough duration assessed (days)	The mean cough duration was 5 days.	MD 0.54 days lower (0.98 lower to 0.1 lower)	-	100 (1 RCT)	⊕⊕⊕⊖ MODERATE [2]	Follow-up: mean 6 days
Frequency of cough (mean improvement score)[1]	The mean frequency of cough (reduction in frequency of cough score) was -2.19.	MD 0.54 lower (1.03 lower to 0.05 lower)	-	100 (1 RCT)	⊕⊕⊕⊖ MODERATE [2]	
Severity of cough (mean improvement score)[1]	The mean severity of cough (reduction in severity of cough score) was -2.08.	MD 0.41 lower (0.78 lower to 0.04 lower)	-	100 (1 RCT)	⊕⊕⊕⊖ MODERATE [2]	
Bothersome cough (mean improvement score)[1]	The mean bothersome cough (reduction in bothersome nature of cough score) was -2.47.	MD 0.27 lower (0.48 lower to 0.06 lower)	-	100 (1 RCT)	⊕⊕⊕⊖ MODERATE [2]	
Cough impact on children's sleep[1]	The mean cough impact on children's sleep (cough impact on children's sleep score) was -2.47.	MD 0.15 higher (0.04 higher to 0.26 higher)	-	100 (1 RCT)	⊕⊕⊕⊖ MODERATE [2]	
Cough impact on parents' sleep[1]	The mean cough impact on parents' sleep (cough impact on parents' sleep score) was -2.33.	MD 0.04 higher (0.01 higher to 0.07 higher)	-	100 (1 RCT)	⊕⊕⊕⊖ MODERATE [2]	
Adverse events	**Population**					
Stomachache, nausea, and vomiting	30 per 100	53 per 100 (31 to 88)	RR 1.74 (1.04 to 2.92)	100 (1 RCT)	⊕⊕⊕⊖ MODERATE [2]	Follow-up: mean 6 days
Rash	9 per 100	2 per 100 (0 to 15)	RR 0.19 (0.02 to 1.63)	100 (1 RCT)	⊕⊕⊕⊖ MODERATE [2]	

Tachycardia	2 per 100	4 per 100 (0 to 39)	RR 1.51 (0.14 to 16.10)	100 (1 RCT)	⊕⊕⊖⊖ LOW [3]
Diarrhoea	21 per 100	12 per 100 (5 to 30)	RR 0.59 (0.24 to 1.45)	100 (1 RCT)	⊕⊕⊕⊖ MODERATE [2]

*__The risk in the intervention group__ (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; **MD:** mean difference; **RCT:** randomised controlled trial; **RR:** risk ratio

GRADE Working Group grades of evidence
High certainty: We are very confident that the true effect lies close to that of the estimate of the effect.
Moderate certainty: We are moderately confident in the effect estimate: the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.
Low certainty: Our confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of the effect.
Very low certainty: We have very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of effect.

[1]Assessed on a 7-point Likert scale from 0 to 6; lower score is better.
[2]Downgraded by one level for serious imprecision. Data were from one small study (Waris 2014).
[3]Downgraded by two levels for very serious imprecision. Data were from one small study (Waris 2014).

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 (Cuestas 2017). Cough can be caused by bacterial or viral infections, the presence of an irritant or allergen in the respiratory tract, or both (Ma 2017). Respiratory infections can be situated along the upper or lower respiratory tract, and the resulting cough can be either productive or unproductive of sputum. Unproductive cough is usually referred to as 'dry' cough. Children with dry cough tend to have minimal airway secretions (Chang 2005).

Cough can be classified as acute or chronic. Chronic cough lasts for more than three weeks (Smith 2016). Acute cough from upper respiratory tract infection (URTI) is a very common symptom seen in primary care settings or by general practitioners (Butler 2005; Derebery 2013). Most coughs from URTIs are caused by viral infections (Braman 2006; Butler 2005). Cough is cause for parental concern (Hay 2003), and a major reason for outpatient visits for both children and adults (Kigen 2015; Kusel 2007). Cough can impact on quality of life (French 2002), cause anxiety, and affect the sleep of children and their parents. For these reasons, immediate remedy for cough is often sought by parents and carers of children with cough.

Description of the intervention

Many people use over-the-counter (OTC) cough medications, and general practitioners in primary care settings often recommend these as first-line treatments (Kigen 2015). Although many OTC cough preparations are available, there is no good evidence regarding their efficacy (Chang 2014; Smith 2014). In children, OTC cough medications may be associated with serious adverse events such as death, altered consciousness, and arrhythmias (CDC 2007; Gunn 2001; Kelly 2004). Study findings vary in reported relief of cough symptoms, with several studies finding no effect compared with placebo (Banderali 1995; Freestone 1997; Kurth 1978; Smith 2014).

Cough mixtures contain a variety of drugs with differing modes of action, which makes them difficult to compare (Morice 1998). Over-the-counter cough medications may contain dextromethorphan hydrobromide, phenylephrine hydrochloride, chlorpheniramine maleate, and methylparaben (El-Gindy 2005).

Honey is a sweet, viscous liquid with a complex chemical composition of approximately 25 carbohydrates (Sanz 2004), free amino acids (Hermosin 2003; Suárez-Luque 2002), vitamins and trace elements (Golob 2005; Hernández 2005; Nanda 2003; Tuzen 2007; Yao 2003). Honey also contains compounds that function as antioxidants such as flavonoids and carotenoids, polyphenol, phenolic acids, vitamin C, and glucose oxydase enzymes (Khalil 2010; Nagai 2006).

How the intervention might work

Honey confers antibacterial (Lusby 2005; Mullai 2007), antiviral (Shahzad 2012; Watanabe 2014; Zeina 1996), antifungal (Ahmed 2013b; Irish 2006; Kuncic 2012), and anti-inflammatory properties (Tonks 2003). Studies of the antimicrobial effect of honey show that it has broad-spectrum antimicrobial effects on various gram-negative and gram-positive bacteria (Agbaje 2006; Katrina 2014). Honey is reported to be active against certain bacteria that have been isolated from the upper respiratory tract such as *Staphylococcus aureus*, *Enterococcus faecalis*,*Candida albicans*,*Klebsiella pneumoniae*,*Pseudomonas aeruginosa*,*Escherichia coli*, *Salmonella* spp., and *Shigella dysenteriae* (Adeleye 2003; Kousalya 2010; Mullai 2007). Honey has antiviral effects against *Varicella zoster* virus (Shahzad 2012), influenza virus (Watanabe 2014), and rubella virus (Zeina 1996). It is believed that the antibacterial activities of honey are intrinsic and not dependent on any external factors such as geographical location or its source (Katrina 2014).

Honey has been used in traditional medicine to treat cough (Adeleye 2003), and in modern medicine to treat infected wounds (Lusby 2005; Molan 2006); it is also an ingredient in some cough syrups (Zeina 1996). However, the use of honey in infants aged under 12 months is restricted because of babies' poor immunity against *Clostridium botulinum*, a possible contaminant in honey (Küplülü 2006; Nevas 2002).

Why it is important to do this review

Identification of ineffective preparations for cough could reduce costs for consumers and healthcare providers (Smith 2014). Cochrane Reviews have assessed the effectiveness of OTC cough medications (Chang 2014; Smith 2014), but none have studied honey for cough relief.

If effective, honey may save significant annual expenditure on OTC cough medications (Dicpinigaitis 2011). Previous versions of this review were inconclusive about the effectiveness of using honey to treat acute cough in children (Oduwole 2010; Oduwole 2012; Oduwole 2014a). The aim of this review was to examine the comparative effectiveness of honey to relieve acute cough in children.

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 children aged 12 months to 18 years with cough caused by acute viral or bacterial URTI. We excluded studies that included participants with chronic cough (lasting for more than three weeks). We also excluded studies with sample sizes of fewer than 10 per intervention.

Types of interventions

Studies that compared:

1. honey only versus:
   a. honey-based cough syrup;
   b. non-honey cough syrup;
   c. placebo; and
   d. no treatment;
2. honey plus antibiotics versus antibiotics alone; and
3. honey plus antibiotics versus non-honey cough syrups plus antibiotics

were eligible for inclusion.

Types of outcome measures

Primary outcomes

1. Duration of cough.
2. Symptomatic relief of cough (frequency of cough, reduction in severity, and less bothersome 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 (e.g. school attendance and playing).
4. Adverse effects.
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; 2018, Issue 2), part of the Cochrane Library (searched 8 February 2018), which includes the Cochrane Acute Respiratory Infections Group's Specialised Register, MEDLINE (Ovid) (October 2014 to 8 February 2018), Embase (Elsevier) (October 2014 to 8 February 2018), CINAHL (Cumulative Index to Nursing and Allied Health Literature) (EBSCO) (October 2014 to 8 February 2018), Web of Science (Clarivate Analytics) (October 2014 to 8 February 2018), and LILACS (Latin American and Caribbean Health Sciences Literature) (BIREME) (October 2014 to 8 February 2018). The 2014 version of this review included searches of AMED (Appendix 1) and CAB Abstracts (Appendix 2), but these were not searched for this update due to lack of institutional access to those databases. Details of previous searches are in Appendix 3.

We used the search strategy in Appendix 4 to search MEDLINE and CENTRAL, and modified terms to search Embase (Appendix 5), CINAHL (Appendix 6), Web of Science (Appendix 7), and LILACS (Appendix 8). We did not combine the MEDLINE search string with the Cochrane Highly Sensitive Search Strategies for identifying randomised trials in MEDLINE (Lefebvre 2011), because we found very few results. We imposed no language or publication restrictions.

Searching other resources

We searched the World Health Organization International Clinical Trials Registry Platform (WHO ICTRP) (apps.who.int/trialsearch/) and ClinicalTrials.gov (www.clinicaltrials.gov) on 12 February 2018.

We checked the reference lists of all relevant articles obtained from our search and those from previously published systematic reviews to identify additional articles. We also contacted the authors of studies added for this update for information and unpublished data (Ahmadi 2013; Paul 2007; Waris 2014).

Data collection and analysis

Selection of studies

Two review authors (OO, EU) independently screened search results using Covidence for eligible studies based on a priori inclusion criteria (Covidence). Any disagreements were resolved by consensus.

Data extraction and management

One review author (OO) independently extracted and entered data into Review Manager 5 (Review Manager 2014). Ahmadi 2013 was translated from Farsi to English for assessment. Another review author (EU) checked data extraction for accuracy and completeness. Any disagreements were resolved by consensus.

Assessment of risk of bias in included studies

Two review authors (OO, EU) assessed risk of bias of the included trials using Cochrane's 'Risk of bias' tool. We assessed random sequence generation, allocation concealment, blinding, selective reporting, and other sources of bias, and recorded the assessment in the 'Risk of bias' tables. We ranked the studies as low, unclear, or 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 (ANOVA) to compare treatment effects for cough duration, cough symptoms, and quality of sleep. We presented estimates of effects as mean differences (MD) derived from parents' subjective assessment of cough symptoms and cough impact on sleep quality using validated questions on a 7-point Likert scale (Likert 1932).

We used the mean and standard deviation (SD) to analyse pair-wise comparisons of treatment effect between honey and placebo and honey and salbutamol on cough duration. We also analysed pair-wise comparisons of other outcomes using generic inverse variance in Review Manager 5 (Review Manager 2014). We estimated MD between children's 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 and standard error (SE) for the pair-wise comparison of treatment effect between honey and dextromethorphan, honey and diphenhydramine, honey and no treatment, honey and placebo, honey and salbutamol, and honey and bromelin. We used the Mantel-Haenszel method to analyse the risk ratio (RR) for adverse events in Review Manager 5 (Review Manager 2014). We presented results for other measures of effects not presented as MD in Table 1.

Unit of analysis issues

There were no unit of analysis issues.

Dealing with missing data

We contacted the lead author of Paul 2007 and obtained the SE of the mean. We used PEPI version 3, Abramson 1999, to calculate the SE of the mean for Shadkam 2010 and Microsoft 2007 for both Cohen 2012 and Waris 2014. We also contacted the authors of Waris 2014 and Peixoto 2016 to request unpublished data. Ahmadi 2013 was translated from Farsi to English.

We performed an intention-to-treat analysis by including all randomised children in the analysis according to methods provided in the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2011). We assumed that all missing participants did not improve.

Assessment of heterogeneity

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

Assessment of reporting biases

We could not test for asymmetry using a funnel plot because we included fewer than 10 studies.

Data synthesis

We used the fixed-effect model to combine data from four included studies (Cohen 2012; Paul 2007; Shadkam 2010; Waris 2014). We used the mean and SE to analyse pair-wise comparisons of treatment effect between honey and placebo and honey and salbutamol on cough duration.

We used Review Manager 5 to perform an inverse-variance meta-analysis using a fixed-effect model for differences in mean between pre- and postintervention (Review Manager 2014). We conducted pair-wise comparisons of postintervention scores between honey and dextromethorphan, honey and diphenhydramine, honey and no treatment, honey and placebo, and honey and salbutamol. We used a random-effects model in the presence of heterogeneity.

We extracted the estimates of effects (MD) and SE of the mean for each outcome and calculated 95% confidence intervals (CIs) of the MDs using generic inverse variance. We used the Mantel-Haenszel method to analyse the RR for adverse events.

We combined the mean score of the three honey groups (eucalyptus, citrus, or Labiatae) and compared these to the placebo group in Cohen 2012.

Peixoto 2016 treated honey as a placebo and compared it to bromelin (a pineapple enzyme) mixed with honey. We presented the placebo arm as a honey intervention for Peixoto 2016. Because data for honey and bromelin were presented as medians, data were tabulated for presentation (Table 1).

We could not include Ahmadi 2013 in the meta-analyses because the results were reported as a proportion of children with reduced cough score. We presented the results in Table 1.

GRADE and 'Summary of findings' table

We created 'Summary of findings' tables for the following outcomes:

1. duration of cough;
2. symptomatic relief of cough (frequency of cough, reduction in severity, and less bothersome cough);
3. improvement in quality of sleep at night for children (cough impact on sleep score);
4. improvement in quality of sleep at night for caregivers (cough impact on sleep score); and
5. adverse effects.

We used the five GRADE considerations (study limitations, consistency of effect, imprecision, indirectness, and publication bias) to assess the quality of a body of evidence as it relates to the studies that contribute data to the meta-analyses for the prespecified outcomes (Atkins 2004). We used methods and recommendations described in Section 8.5 and Chapter 12 of the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2011), employing GRADEpro GDT software (GRADEpro GDT 2015). We justified all decisions to downgrade the quality of studies in footnotes, and made comments to aid readers' understanding of the review where necessary.

Subgroup analysis and investigation of heterogeneity

Data were available from six small studies, and investigation of sources of heterogeneity was not feasible. We used a random-effects model to investigate possible sources of heterogeneity. We performed subgroup analyses for different types of honey.

Sensitivity analysis

We did not perform a sensitivity analysis because we included only five trials in the meta-analyses.

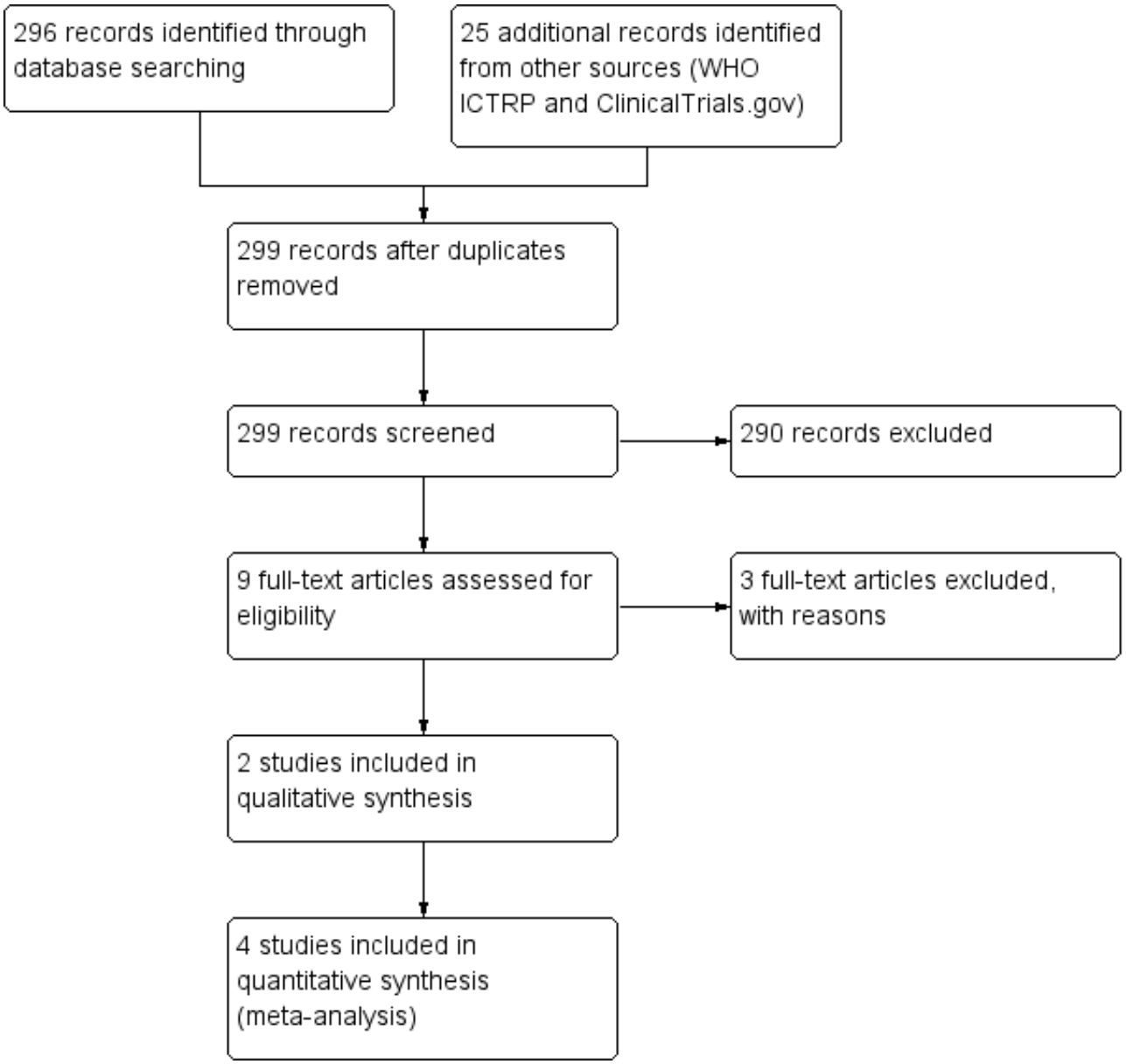
RESULTS

Description of studies

Results of the search

Our updated 2018 search yielded 321 records. After removal of duplicates, we screened 299 records by title and abstract, and excluded 290 records. We assessed nine full-text records and excluded three studies that did not meet our inclusion criteria. This update included three additional studies (Ahmadi 2013; Peixoto 2016; Waris 2014), bringing the total number of included studies to six. We included two studies in the qualitative analysis (Ahmadi 2013; Peixoto 2016), and four in the meta-analyses (Cohen 2012; Paul 2007; Shadkam 2010; Waris 2014). See Figure 1.

Figure 1. Study flow diagram (2018 update).



Included studies

We included six RCTs involving 899 children (Ahmadi 2013; Cohen 2012; Paul 2007; Peixoto 2016; Shadkam 2010; Waris 2014). Of these, three were added for this update (N = 331) (Ahmadi 2013; Peixoto 2016; Waris 2014). Ahmadi 2013 was published in Farsi and was translated for analysis. In our protocol we proposed to include children aged from 2 to 18 years. We decided to include studies with children aged 12 months to 18 years because very few clinical trials were available on honey for acute cough in children. We also think that it is best for physicians to decide whether or not to prescribe honey to children aged up to 12 months based on the available evidence.

Study populations

The age of participants ranged from 12 months to 16 years. We obtained proportions of boys and girls from available data only.

Ahmadi 2013 randomised 126 children aged from 2 to 5 years (48% boys, 52% girls) with viral URTI with cough for up to 2 days. Study duration was two years (2010 to 2012).

Cohen 2012 randomised 300 children aged 12 to 71 months (54% boys, 46% girls) with URTI who "were ill with a mean ± SD of 2.8 ± 2.0 before enrolment". Study duration was a year (January 2009 to December 2009).

Paul 2007 randomised 108 children aged 2 to 16 years (105 completed the study; 47% boys, 53% girls) with URTI "characterized by the presence of rhinorrhoea and cough for 7 or fewer days' duration. Other symptoms may have included but were not limited to congestion, fever, sore throat, myalgias, and headache". Study duration was six months (September 2005 to March 2006).

Peixoto 2016 randomised 60 children aged 2 to 15 years (43% boys, 57% girls) "with irritative cough for at least 24 hours, which led to the need for medical consultation" and no history of chronic disease. The study start date was June 2011 and the estimated completion date was March 2012, however the actual study completion date is unclear.

Shadkam 2010 randomised 160 children aged 24 to 60 months (139 completed the study; 49% boys, 51% girls) with URTI-induced cough. The study started in December 2008 and ended in May 2009.

Waris 2014 randomised 145 children aged 12 months to 12 years (51% boys, 49% girls) with uncomplicated acute upper respiratory infection. Waris 2014 enrolled participants from December 2010 to February 2012.

No studies enrolled children with comorbidities.

Study settings

Studies by Ahmadi 2013 and Shadkam 2010 were conducted in Iran; Cohen 2012 in Israel; Paul 2007 in the USA; Peixoto 2016 in Brazil; and Waris 2014 in Kenya.

Five were single-centre studies (Ahmadi 2013; Paul 2007; Peixoto 2016; Shadkam 2010; Waris 2014). Cohen 2012 enrolled participants from six study centres.

All studies recruited participants from paediatric outpatient clinics.

Interventions

- Honey mixed with distilled lukewarm water (Ahmadi 2013).
- Three different types of honey: eucalyptus (family Myrtaceae), Labiatae (family Labiatae), or citrus (family Rutaceae) honeys (Cohen 2012).
- Buckwheat honey (Paul 2007).
- Honey was placebo and compared to bromelin (*Ananas comosus,* pineapple extract) mixed with honey (Peixoto 2016).
- Natural honey from Kafi-Abad (a village in Yazd, Iran) (Shadkam 2010).
- "the darkest locally available honey" (Kenya) (Waris 2014).

Comparators

- Ahmadi 2013 compared honey and diphenhydramine. Children received interventions three times a day, the last dose one hour before bed at night.
- Cohen 2012 compared three types of honey to placebo ("Silan date extract was selected as the placebo because its structure, brown color, and taste are similar to that of honey" p. 466) ("Parents were instructed to administer 10 g of their child's treatment product within 30 minutes of the child going to sleep" p. 466). Treatment could also be given with a non-caffeinated beverage.
- Paul 2007 compared honey to dextromethorphan and no treatment. Parents were told that their child's treatment could be given with a non-caffeinated beverage administered within 30 minutes of the child going to sleep.
- Peixoto 2016 compared honey alone (labelled as placebo) to bromelin (*Ananas comosus* (pineapple)) mixed with honey. Two treatment regimens were administered: children up to 20 kg received 5 mL; those weighing > 20 kg received 1 mL for every 5 kg of additional weight.
- Shadkam 2010 compared honey to dextromethorphan, diphenhydramine, and no treatment. Treatment regimens were administered before sleep.
- Waris 2014 compared honey to salbutamol and placebo. The interventions were administered three times daily for five days.

Study funding sources

All included studies declared no conflicts of interest.

- Source of funding for Ahmadi 2013 was not declared.
- Cohen 2012 reported "This study was supported in part by a research grant from the Israel Ambulatory Pediatric Association, Materna Infant Nutrition Research Institute, and the Honey Board of Israel. The funders had no role in the study design, data collection or analysis, decision to publish, or preparation of the manuscript" (p. 465).
- Peixoto 2016 was funded by Hebron Indústrias Químicas (a pharmaceutical manufacturer) (p. 416).
- Paul 2007 reported "This work was supported by an unrestricted research grant from the National Honey Board, an industry-funded agency of the US Department of Agriculture" (p. 1145).
- Shadkam 2010 was "fully funded by the Department of Research Administration, Shahid Sadoughi University of Medical Sciences (SSUMS) in Yazd, Iran" (p. 791).
- Waris 2014 indicated that "Universal Corporation Ltd prepared all study drugs and at no cost" (p. 55).

Excluded studies

We excluded three studies after assessment for this update: Cohen 2017 compared honey-based cough syrup to non-honey-based cough syrup; Ayazi 2017 was a quasi-RCT; Baker 2016 was a commentary on our review. We had previously excluded two studies, Gilbert 2008 and Warren 2007, from our 2010 review (Oduwole 2010); and two studies, Ahmed 2013a and Miceli Sopo 2014, from the 2014 update (Oduwole 2014a).

Studies awaiting classification

We had previously identified two studies that were awaiting classification (Ahmadi 2013; Peixoto 2016), which we included in this update.

Ongoing studies

We identified two ongoing studies (NCT03218696; UMIN000020651). A study identified as ongoing in 2014 was published, but was excluded because it was a quasi-RCT (Ayazi 2017).

Risk of bias in included studies

Two review authors independently assessed the methodological quality of all included studies according to the methods described in the *Cochrane Handbook for Systematic Reviews of Interventions* (Figure 2; Figure 3) (Higgins 2011).

Figure 2. Risk of bias graph: review authors' judgements about each risk of bias item presented as percentages across all included studies.

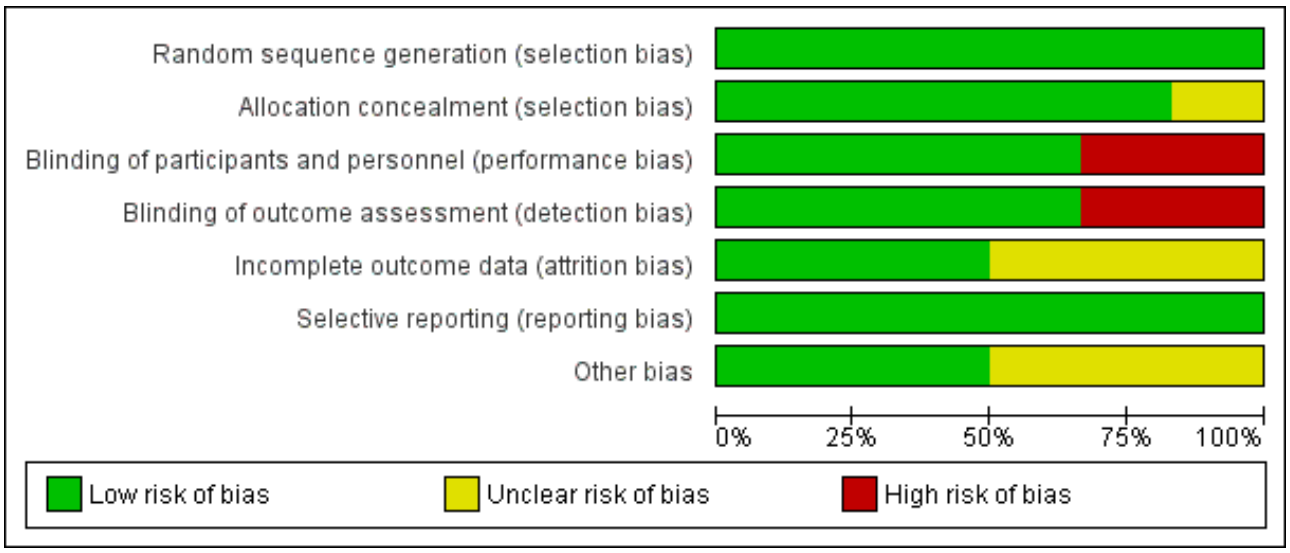
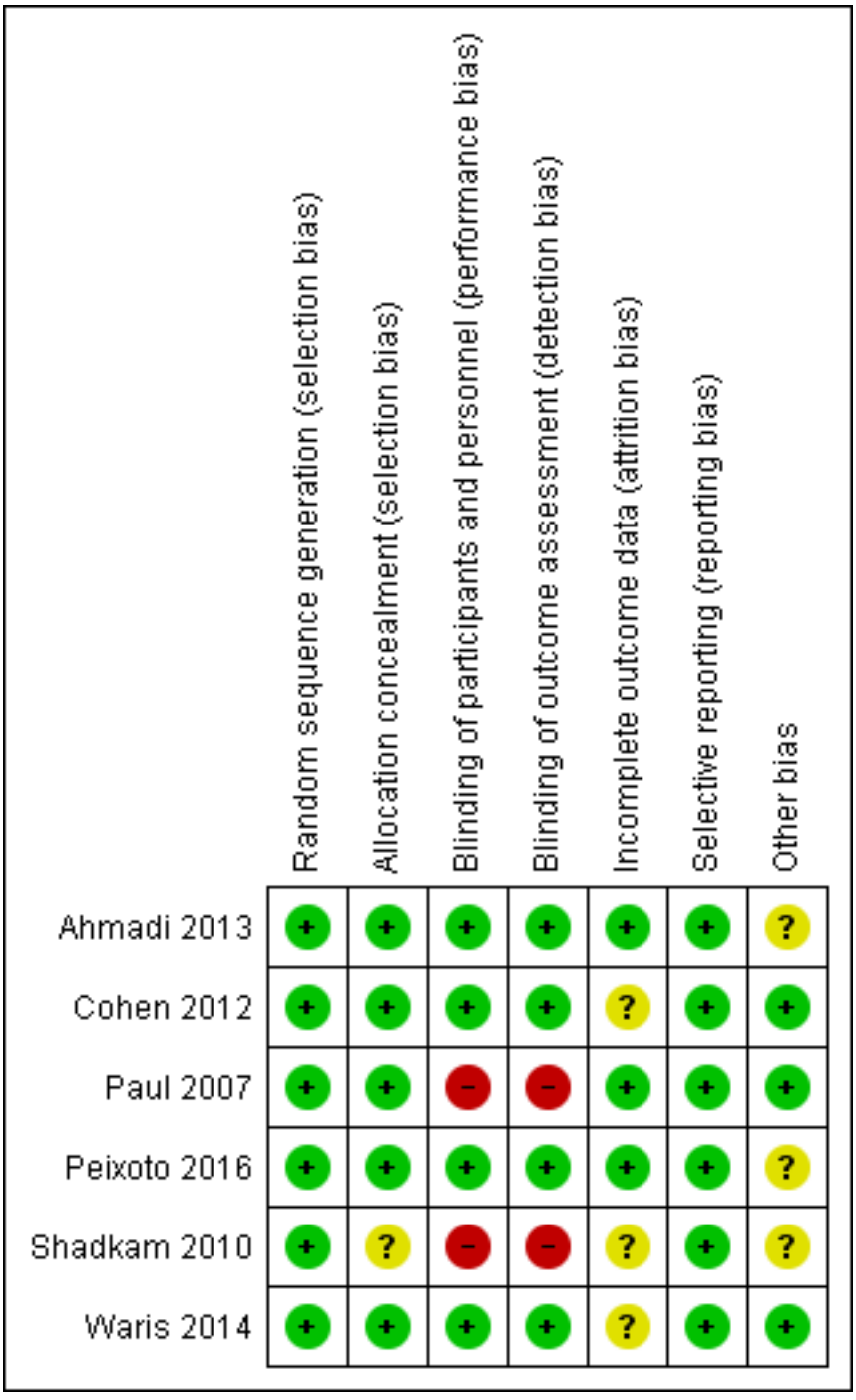


Figure 3. 'Risk of bias' summary: review authors' judgements about each risk of bias item for each included study.



Allocation

We rated all six included studies as at low risk of bias for sequence generation. We assessed five studies as at low risk for allocation concealment bias (Ahmadi 2013; Cohen 2012; Paul 2007; Peixoto 2016; Waris 2014). We rated Shadkam 2010 as at unclear risk of bias for this domain.

Blinding

We rated four studies as at low risk for performance and detection bias (Ahmadi 2013; Cohen 2012; Peixoto 2016; Waris 2014). We assessed two studies as at high risk of bias for this domain (Paul 2007; Shadkam 2010). There was partial blinding in Paul 2007; only the no-treatment group was aware of receiving no intervention. We rated Paul 2007 as at high risk of bias for this domain because all outcomes were subjective: participants knowing they received no treatment could have influenced performance and assessment of the outcomes.

Incomplete outcome data

We assessed three studies as at low risk of bias of attrition bias (Ahmadi 2013; Paul 2007; Peixoto 2016). We assessed three studies as at unclear risk of attrition bias (Cohen 2012; Shadkam 2010; Waris 2014). In Cohen 2012, attrition was significantly higher in the eucalyptus honey (19%) and citrus honey (18%) groups than Labiatae honey (3%) and placebo (5%) groups. It was unclear if reasons for attrition were related to the study. Shadkam 2010 reported that children were either lost to follow-up or were withdrawn for violating the protocol (but did not state to which group children lost to follow-up or withdrawn belonged).

Selective reporting

We rated all studies as at low risk of bias for selective reporting; all outcomes proposed in the methods sections were reported in results. We obtained protocols of two included studies (Ahmadi 2013; Peixoto 2016); both reported all outcomes proposed.

Other potential sources of bias

We assessed two studies as at low risk of bias (Cohen 2012; Paul 2007; Waris 2014), and three studies as at unclear risk of bias for this domain (Ahmadi 2013; Peixoto 2016; Shadkam 2010). In Shadkam 2010, "Some of the questions put to mothers were answered by the paediatrician because the questions were ambiguous", which could have influenced outcome assessment. Ahmadi 2013 reported results as the proportion of children with reduced cough symptoms instead of actual mean reduction in cough scores of children as reported by other studies. In addition, the study protocol was registered retrospectively after completion of the study (Ahmadi 2013). It is unclear if the authors had planned to report results as proportion of children with reduced cough score. It is also not clear if the two outcomes (cough frequency and severity) listed in the methods section of the published paper and protocol was their original intention (Ahmadi 2013). Peixoto 2016 used an unvalidated cough scale.

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** Honey compared to placebo for acute cough in children; **Summary of findings 5** Honey compared to salbutamol for acute cough in children

Primary outcomes

1. Duration of cough

Only one study assessed duration of cough in comparison to salbutamol and placebo (Waris 2014). The effect of honey on cough duration was compared to salbutamol after five days of treatment; moderate-certainty evidence indicated that cough was relieved sooner in children who received honey (mean difference (MD) -0.54, 95% confidence interval (CI) -0.98 to -0.10; 1 study, N = 100; Analysis 1.13). Compared with placebo, honey also provided faster cough relief (MD -0.72, 95% CI -1.31 to -0.13; 1 study, N = 102; Analysis 1.8; moderate-certainty evidence).

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

2.1 Frequency of cough (pre- and postintervention comparison)

Four studies used a 7-point Likert scale to report cough frequency (Ahmadi 2013; Cohen 2012; Paul 2007; Shadkam 2010; Waris 2014). Caregivers' responses to the questionnaire on cough symptoms ranged from 'extremely' (6 points) to 'not at all' (0 points) (lower score indicated better cough symptom relief). Pre- and postintervention comparison for each treatment arm showed that honey was more effective in reducing the frequency of cough in six studies. Four studies were meta-analysed (moderate-certainty evidence) (Cohen 2012; Paul 2007; Shadkam 2010; Waris 2014). Data from two studies are presented in Table 1 (moderate-certainty evidence, one study with unclear cough scales) (Ahmadi 2013; Peixoto 2016).

When the effect of honey on cough symptoms was compared after a five-day treatment to the night before the first dose of intervention (pre- and postintervention cough score) using the 7-point Likert scale, honey reduced cough frequency to a greater extent (MD -2.65, 95% CI -4.32 to -0.98; 1 study, N = 57; moderate-certainty evidence) than salbutamol (MD -2.19, 95% CI -3.55 to -0.83; 1 study, N = 43; moderate-certainty evidence) and placebo (MD -1.95, 95% CI -4.42 to 0.52; 1 study, N = 45; moderate-certainty evidence; Analysis 2.1).

When the frequency of cough on Day 1 of treatment was assessed, parents of children in the honey group rated their children's coughs to be slightly less frequent (MD -1.71, 95% CI -2.28 to -1.13; I^2 = 0%; 4 studies, N = 357; moderate-certainty evidence) compared to children who received dextromethorphan (MD -1.54, 95% CI -2.30 to -0.78; 2 studies, N = 74; moderate-certainty evidence), placebo (MD -0.99, 95% CI -1.79 to -0.18; I^2 = 0%; 2 studies, N = 120; moderate-certainty evidence), no treatment (MD -0.98, 95% CI -1.38 to -0.59; I^2 = 17%; 2 studies, N = 79; low-certainty evidence), and salbutamol (MD -0.52, 95% CI -6.28 to 5.24; 1 study, N = 43; moderate-certainty evidence), but not better than diphenhydramine (MD -1.73, 95% CI -2.72 to -0.74; 1 study, N = 40; low-certainty evidence; Analysis 2.1).

2.2 Reduction in severity

Similarly, honey reduced the severity of cough in children postintervention on a 7-point Likert scale (MD -1.65, 95% CI -2.39 to -0.91; I^2 = 0%; 4 studies, N = 357; moderate-certainty evidence) to a greater extent than dextromethorphan (MD -1.52, 95% CI -2.24 to -0.80; I^2 = 29%; 2 studies, N = 74; moderate-certainty evidence), no treatment (MD -1.13, 95% CI -1.54 to -0.72; I^2 = 2%; 2 studies, N = 79; low-certainty evidence), placebo (MD -0.80, 95% CI -1.47 to -0.13; I^2 = 0%; 2 studies, N = 120; moderate-certainty evidence), or salbutamol (MD -0.74, 95% CI -2.87 to 1.39; 1 study, N = 43; moderate-certainty evidence), but not diphenhydramine (MD -1.83, 95% CI -2.88 to -0.78; 1 study, N = 40; low-certainty evidence; Analysis 2.2).

Honey also reduced cough severity on Day 5 (MD -2.62, 95% CI -5.04 to -0.20; 1 study, N = 57; moderate-certainty evidence) better than salbutamol (MD -2.08, 95% CI -4.21 to 0.05; 1 study, N = 43; moderate-certainty evidence) or placebo (MD -1.96, 95% CI -3.74 to -0.18; 1 study, N = 45; moderate-certainty evidence; Analysis 2.2).

Peixoto 2016 expressed results as medians and showed no difference between honey and bromelin (honey + pineapple) (moderate-certainty evidence; Table 1).

2.3 Less bothersome cough

Children's cough was less bothersome in the honey group after one day of treatment (MD -2.22, 95% CI -3.24 to -1.21; I^2 = 0%; 3 studies, N = 317; moderate-certainty evidence) compared with the dextromethorphan (MD -1.94, 95% CI -3.05 to -0.83; 1 study, N = 34; moderate-certainty evidence), no treatment (MD -1.30, 95% CI -2.07 to -0.53; 1 study, N = 39; low-certainty evidence), placebo (MD -1.08, 95% CI -2.06 to -0.10; I^2 = 0%; 2 studies, N = 120; moderate-certainty evidence), and salbutamol groups (MD -1.00, 95% CI -4.28 to 2.28; 1 study, N = 43; moderate-certainty evidence; Analysis 2.3).

On Day 5, honey reduced bothersome cough to a greater extent (MD -2.74, 95% CI -5.27 to -0.21; 1 study, N = 57) than salbutamol (MD -2.47, 95% CI -4.73 to -0.21; 1 study, N = 43; moderate-certainty evidence) or placebo (MD -1.85, 95% CI -3.56 to -0.14; 1 study, N = 45; moderate-certainty evidence; Analysis 2.3).

Subgroup analysis comparing types of honey

Effect of different types of honey on cough symptoms

When we compared different types of honey in a subgroup analysis, dark honey from Kenya reduced cough frequency to a greater extent (MD -2.65, 95% CI -4.32 to -0.98; Waris 2014, N = 57; moderate-certainty evidence) than natural honey from Iran (MD -2.16, 95% CI -3.40 to -0.92; Shadkam 2010, N = 40; low-certainty evidence), citrus honey (MD -1.95, 95% CI -3.55 to -0.35; Cohen 2012, N = 75; moderate-certainty evidence), buckwheat honey (MD -1.89, 95% CI -2.96 to -0.81; Paul 2007, N = 35; moderate-certainty evidence), Labiatae honey (MD -1.82, 95% CI -3.30 to -0.34; Cohen 2012, N = 75; moderate-certainty evidence), and eucalyptus honey (MD -1.77, 95% CI -3.22 to -0.32; Cohen 2012, N = 75; moderate-certainty evidence; Analysis 2.1).

On treatment Day 1, dark honey from Kenya reduced children's cough severity to a greater extent (MD -2.62, 95% CI -5.04 to -0.20; 1 study, N = 57; moderate-certainty evidence) than natural honey from Iran (MD -2.33, 95% CI -3.67 to -0.99; 1 study, N = 40; low-certainty evidence), buckwheat honey (MD -1.80, 95% CI -2.88 to -0.72; 1 study, N = 35; moderate-certainty evidence), Labiatae honey (MD -1.94, 95% CI -3.07 to -0.81; 1 study, N = 75; moderate-certainty evidence), eucalyptus honey (MD -1.78, 95% CI -2.82 to -0.74; 1 study, N = 75; moderate-certainty evidence), and citrus honey (MD -1.77, 95% CI -2.74 to -0.80; 1 study, N = 75; moderate-certainty evidence; Analysis 2.2).

Dark honey from Kenya reduced bothersome cough to some extent (MD -2.74, 95% CI -5.27 to -0.21; 1 study, N = 57; moderate-certainty evidence) more than buckwheat honey (MD -2.23, 95% CI -3.50 to -0.96; 1 study, N = 35; moderate-certainty evidence), citrus honey (MD -2.16, 95% CI -4.20 to -0.12; 1 study, N = 75; moderate-certainty evidence), Labiatae honey (MD -2.07, 95% CI -4.03 to -0.11; 1 study, N = 75; moderate-certainty evidence), or eucalyptus honey (MD -2.00, 95% CI -3.82 to -0.18; 1 study, N = 75; moderate-certainty evidence; Analysis 2.3).

Secondary outcomes

1. Improvement in quality of sleep at night for children (cough impact on sleep score)

Caregivers' Likert scores for cough impact on children's sleep were reduced to a greater extent in the honey group (MD -2.23, 95% CI -2.87 to -1.59; I^2 = 0%; 4 studies, N = 357; moderate-certainty evidence) than in the dextromethorphan (MD -1.75, 95% CI -2.46 to -1.04; I^2 = 1%; 2 studies, N = 74; moderate-certainty evidence), diphenhydramine (MD -1.64, 95% CI -2.58 to -0.70; 1 study, N = 40; low-certainty evidence), no treatment (MD -1.28, 95% CI -1.81 to -0.76; I^2 = 60%; 2 studies, N = 79; moderate-certainty evidence), or placebo groups (MD -1.03, 95% CI -2.05 to 0.00; I^2 = 0%; 2 studies, N = 120; moderate-certainty evidence). After children received dark Kenyan honey, salbutamol, or placebo for five days, caregivers' Likert scores for cough impact on their children's sleep were reduced to a greater extent in the honey group (MD -2.32, 95% CI -3.63 to -1.01; 1 study, N = 57; moderate-certainty evidence) than in the salbutamol (MD -2.47, 95% CI -3.84 to -1.10; 1 study, N = 43; moderate-certainty evidence) and placebo groups (MD -1.68, 95% CI -2.63 to -0.73; 1 study, N = 45; moderate-certainty evidence; Analysis 2.4).

2. Improvement in quality of sleep at night for caregiver (cough impact on sleep score)

At postintervention, cough impact on parents' sleep was also improved to a greater extent by honey (measured on a 7-point Likert scale) (MD -2.25, 95% CI -2.89 to -1.61; I^2 = 0%; 4 studies, N = 357; moderate-certainty evidence) than by dextromethorphan (MD -1.97, 95% CI -2.77 to -1.17; I^2 = 0%; 2 studies, N = 74; moderate-certainty evidence), diphenhydramine (MD -1.89, 95% CI -2.97 to -0.81; 1 study, N = 40; low-certainty evidence), no treatment (MD -1.46, 95% CI -2.06 to -0.87; I^2 = 2%; 2 studies, N = 79; low-certainty evidence), or placebo (MD -1.44, 95% CI -2.28 to -0.61; I^2 = 0%; 2 studies, N = 120; moderate-certainty evidence).

On Day 5 of treatment, honey improved the quality of sleep of caregivers to a greater extent (MD -2.29, 95% CI -3.86 to -0.72; 1 study, N = 57; moderate-certainty evidence) than placebo (MD -1.54, 95% CI -2.60 to -0.48; 1 study, N = 45; moderate-certainty evidence) but not salbutamol (MD -2.33, 95% CI -3.91 to -0.75; 1 study, N = 43; moderate-certainty evidence; Analysis 2.5).

Combined improvement score

When the scores of each intervention were combined across all categories, children in the honey group had reduced cough symptoms to a greater extent (MD -10.60, 95% CI -14.43 to -6.77; I^2 = 0%; 3 studies, N = 317; moderate-certainty evidence) than those in the dextromethorphan (MD -8.39, 95% CI -10.95 to -5.84; 1 study, N = 34; low-certainty evidence), no treatment (MD -6.41, 95% CI -8.82 to -3.99; 1 study, N = 39; low-certainty evidence), or placebo groups (MD -7.11, 95% CI -10.78 to -3.44; I^2 = 0%; 2 studies, N = 132; moderate-certainty evidence). Likewise, after five days treatment with honey, salbutamol, or placebo, honey reduced cough to a greater extent (MD -12.68, 95% CI -14.06 to -11.30; 1 study, N = 57; moderate-certainty evidence) than salbutamol (MD -11.37, 95% CI -17.55 to -5.19; 1 study, N = 43; moderate-certainty evidence) or placebo (MD -8.69, 95% CI -14.17 to -3.21; 1 study, N = 45; moderate-certainty evidence; Analysis 2.6).

3. Improvement in quality of life (e.g. school attendance and playing)

None of the included studies assessed the effect of honey on children's quality of life.

4. Adverse effects

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

(stomachache, nausea, diarrhoea, and vomiting), rash, tachycardia, drowsiness, and somnolence. The difference observed in adverse events in comparisons of honey versus dextromethorphan, honey versus diphenhydramine, honey versus salbutamol, and honey versus placebo were not statistically significant. Seven children (9.3%) from the honey group compared to two (2.7%) from the dextromethorphan group experienced reactions such as nervousness, insomnia, and hyperactivity (risk ratio (RR) 2.94, 95% CI 0.74 to 11.71; I^2 = 0%; 2 studies, N = 149; low-certainty evidence; Analysis 3.1). Two children (2.7%) from the honey group had gastrointestinal symptoms compared to none from the dextromethorphan group (RR 4.86, 95% CI 0.24 to 97.69; 1 study, N = 69; low-certainty evidence; Analysis 3.1). One (1.3%) child in the honey group experienced drowsiness (RR 2.92, 95% CI 0.12 to 69.20; I^2 = 0%; 1 study, N = 69; low-certainty evidence; Analysis 3.1). Three children (7.5%) experienced somnolence in the diphenhydramine group, but this result was not significantly different from the honey group (RR 0.14, 95% CI 0.01 to 2.68; 1 study, N = 80; low-certainty evidence; Analysis 3.2). No adverse effects were reported for the no-treatment group.

A total of 34 children (12%) in the honey group compared to 13 children (11%) from the placebo group experienced gastrointestinal symptoms (RR 1.91, 95% CI 1.12 to 3.24; I^2 = 0%; 2 studies, N = 402; moderate-certainty evidence; Analysis 3.3). Similarly, more gastrointestinal symptoms probably occurred with honey than with salbutamol (RR 1.74, 95% CI 1.04 to 2.92; 1 study, N = 100; moderate-certainty evidence).

Diarrhoea was reported in the salbutamol (N = 9, 21%), honey (N = 7, 12%), and placebo (N = 6, 13%) groups. The risk of diarrhoea was similar in the honey group compared to the placebo group (RR 0.92, 95% CI 0.33 to 2.55; 1 study, N = 102; low-certainty evidence; Analysis 3.3). The risk of diarrhoea probably increased to a greater extent in the salbutamol group than in the honey group (RR 0.59, 95% CI 0.24 to 1.45; 1 study, N = 100; moderate-certainty evidence; Analysis 3.4).

The risk of rash in the salbutamol group was probably higher than in the honey group (RR 0.19, 95% CI 0.02 to 1.63; 1 study, N = 100; moderate-certainty evidence; Analysis 3.4). Two children in the honey group had tachycardia compared to one in the placebo group (RR 1.58, 95% CI 0.15 to 16.86; 1 study, N = 102; low-certainty evidence; Analysis 3.3) and one in the salbutamol group (RR 1.51, 95% CI 0.14 to 16.10; 1 study, N = 100; low-certainty evidence; Analysis 3.4).

5. Improvement in appetite

None of the included studies assessed improvement in appetite as an outcome.

6. Cost of honey alone compared with other cough syrups

None of the included studies assessed cost of treatment as an outcome.

Pair-wise comparison of honey and dextromethorphan

There was no difference between honey and dextromethorphan in reducing cough frequency (MD -0.07, 95% CI -1.07 to 0.94; I^2 = 87%; 2 studies, N = 149; low-certainty evidence), cough severity (MD -0.13, 95% CI -1.25 to 0.99; I^2 = 85%; 2 studies, N = 149; low-certainty evidence), bothersome cough (MD 0.29, 95% CI -0.56 to 1.14; 1 study, N = 69; moderate-certainty evidence), impact of cough on children's sleep (MD 0.03, 95% CI -1.12 to 1.19; I^2 = 84%; 2 studies, N = 149; low-certainty evidence), and parents' sleep (MD -0.16, 95% CI -0.84 to 0.53; I^2 = 59%; 2 studies, N = 149; low-certainty evidence; Analysis 1.1).

Pair-wise comparison of honey versus diphenhydramine

Honey may be better than diphenhydramine in reducing cough frequency (MD -0.57, 95% CI -0.90 to -0.24; 1 study, N = 80; low-certainty evidence), cough severity (MD -0.60, 95% CI -0.94 to -0.26; 1 study, N = 80; low-certainty evidence), cough impact on children's sleep (MD -0.55, 95% CI -0.87 to -0.23; 1 study, N = 80; low-certainty evidence), and cough impact on parents' sleep (MD -0.48, 95% CI -0.76 to -0.20; 1 study, N = 80; low-certainty evidence; Analysis 1.2).

Ahmadi 2013 reported that the frequency and severity of night- and daytime coughing was significantly reduced by 79.4% and 84.1% in the group receiving honey, and 58.7% and 58.7% in the group receiving diphenhydramine, quote: "P < 0.02" (Table 1).

Pair-wise comparison of honey versus no treatment

Moderate-certainty evidence showed that the effect of honey was probably better than no treatment in reducing cough frequency (MD -1.05, 95% CI -1.48 to -0.62; I^2 = 0%; 2 studies, N = 154), cough severity (MD -1.03, 95% CI -1.59 to -0.47; I^2 = 63%; 2 studies, N = 154), cough impact on children's sleep (MD -1.04, 95% CI -1.57 to -0.51; I^2 = 7%; 2 studies, N = 154), and cough impact on parents' sleep (MD -0.88, 95% CI -1.23 to -0.52; I^2 = 26%; 2 studies, N = 154). However, honey was no different than no treatment in resolving bothersome cough (MD -0.93, 95% CI -1.98 to 0.12; 1 study, N = 74; low-certainty evidence; Analysis 1.3).

Pair-wise comparison of honey versus placebo

Moderate-certainty evidence showed that honey probably reduces the duration of cough more than placebo (MD -0.72, 95% CI -1.31 to -0.13; 1 study, N = 102).

After a one-night honey intervention, the available evidence showed that honey reduced cough frequency to a greater extent than placebo (MD -1.62, 95% CI -3.02 to -0.22; I^2 = 0%; 2 studies, N = 402; moderate-certainty evidence). Honey also had a greater effect in reducing cough severity (MD -1.07, 95% CI -2.43 to 0.30; I^2 = 50%; 2 studies, N = 402; moderate-certainty evidence) and bothersome cough (MD -1.40, 95% CI -2.82 to 0.03; I^2 = 6%; 2 studies, N = 402; moderate-certainty evidence) than placebo, but the difference was not statistically significant. Caregivers reported that honey improved quality of sleep better than placebo for parents (MD -1.29, 95% CI -2.71 to 0.13; I^2 = 73%; 2 studies, N = 402; moderate-certainty evidence) and their children (MD -1.21, 95% CI -2.61 to 0.19; I^2 = 78%; 2 studies, N = 402; moderate-certainty evidence). The difference between intervention groups was not statistically significant (Analysis 1.4).

On Day 3 of honey versus placebo treatment, moderate-certainty evidence showed that honey reduced cough frequency (MD -1.13, 95% CI -1.71 to -0.55; 1 study, N = 102), cough severity (MD -0.85, 95% CI -1.41 to -0.29; 1 study, N = 102), bothersome cough (MD -1.33, 95% CI -1.87 to -0.79; 1 study, N = 102), impact of cough on children's sleep (MD -0.93, 95% CI -1.42 to -0.44; 1 study, N = 102), and impact of cough on parents' sleep to a greater extent than placebo (MD -0.88, 95% CI -1.38 to -0.38; 1 study, N = 102; Analysis 1.6).

Honey reduced cough duration to a greater extent than placebo (MD -0.72, 95% CI -1.31 to -0.13; 1 study, N = 102; moderate-certainty evidence).

On the fifth day of treatment, moderate-certainty evidence showed there was no significant difference between honey and placebo in reducing cough frequency (MD -0.48, 95% CI -2.95 to 1.99; 1 study, N = 102), cough severity (MD -0.43, 95% CI -2.21 to 1.35; 1 study, N = 102), bothersome cough (MD -0.51, 95% CI -3.01 to 1.99; 1 study, N = 102), cough impact on children's sleep (MD -0.55, 95% CI -1.79 to 0.69; 1 study, N = 102), and cough impact on parents' sleep (MD -0.57, 95% CI -1.59 to 0.45; 1 study, N = 102; Analysis 1.8).

Pair-wise comparison of honey versus salbutamol

After the first night of treatment, honey reduced cough frequency (MD -0.26, 95% CI -3.14 to 2.62; 1 study, N = 100; moderate-certainty evidence), cough severity (MD -0.10, 95% CI -0.39 to 0.19; 1 study, N = 100; moderate-certainty evidence), and bothersome cough (MD -0.21, 95% CI -0.90 to 0.48; 1 study, N = 100; moderate-certainty evidence) more than salbutamol, but the difference was not statistically significant. However, salbutamol reduced cough impact on children's sleep (MD 0.09, 95% CI -0.05 to 0.23; 1 study, N = 100; moderate-certainty evidence) and cough impact on parents' sleep (MD 0.05, 95% CI -0.03 to 0.13; 1 study, N = 100; moderate-certainty evidence) more than honey. The difference was not statistically significant (Analysis 1.9).

On Day 3 of the intervention, honey reduced cough frequency (MD -0.69, 95% CI -1.13 to -0.25; 1 study, N = 100; moderate-certainty evidence), cough severity (MD -0.34, 95% CI -0.64 to -0.04; 1 study, N = 100; moderate-certainty evidence), and bothersome cough to a greater extent than salbutamol (MD -0.24, 95% CI -0.38 to -0.10; 1 study, N = 100; moderate-certainty evidence). Salbutamol probably reduced the impact of cough on children's sleep (MD 0.31, 95% CI 0.13 to 0.49; 1 study, N = 100; moderate-certainty evidence) and impact of cough on parents' sleep (MD 0.21, 95% CI 0.06 to 0.36; 1 study, N = 100; moderate-certainty evidence; Analysis 1.11).

Moderate-certainty evidence showed that honey reduced cough duration (MD -0.54, 95% CI -0.98 to -0.10; 1 study, N = 100), cough frequency (MD -0.54, 95% CI -1.03 to -0.05; 1 study, N = 100), cough severity (MD -0.41, 95% CI -0.78 to -0.04; 1 study, N = 100), and bothersome cough more than salbutamol on Day 5 (MD -0.27, 95% CI -0.48 to -0.06; 1 study, N = 100). Salbutamol reduced cough impact on children's sleep (MD 0.15, 95% CI 0.04 to 0.26; 1 study, N = 100) and parents' sleep to a greater extent than honey (MD 0.04, 95% CI 0.01 to 0.07; 1 study, N = 100; Analysis 1.13).

Pair-wise comparison of honey versus bromelin + honey

There was no difference between the effect of honey alone and bromelin with honey on cough frequency (moderate-certainty evidence; Table 1).

DISCUSSION

Summary of main results

We included six small trials (899 children). Honey was given for one night only in four studies (Cohen 2012; Paul 2007; Peixoto 2016; Shadkam 2010). One study administered honey three times on one day (Ahmadi 2013), and one study administered honey three times daily for five days (Waris 2014). Giving honey for a day was better in relieving cough severity and bothersome cough when compared to no treatment, but the effect was not statistically significantly different from the use of other interventions. However, this evidence was derived from five small studies, two of which had a high risk of performance and detection bias.

Moderate-certainty evidence showed that honey probably reduces cough duration to a greater extent than salbutamol or placebo. Honey group participants were first to get total relief of cough compared to salbutamol or placebo.

Honey probably relieves cough symptoms and improves sleep quality for both children and parents better than no treatment. Honey may resolve bothersome cough to a greater extent than no treatment, but the difference was not statistically significant. Honey probably reduces cough frequency better than placebo when given to children for a day. Honey probably reduces cough severity, bothersome cough, and impact of cough on both children's and parents' sleep to a greater extent than placebo, but the difference was not statistically significant.

The effect estimate showed that after one night of administration honey may reduce cough symptoms and improve sleep quality of children and their parents better than diphenhydramine. Honey probably had little effect or no difference compared to dextromethorphan or salbutamol for symptomatic relief of cough, resolving bothersome cough, and improving sleep quality for both children and parents.

When we compared types of honey, dark honey from Kenya probably reduced cough frequency and cough severity to a greater extent than the other types of honey. However, dark Kenyan honey was administered three times daily compared to other types of honey that were administered once at night; this may have contributed to the effect size of the African honey.

Three days of honey administration was probably more effective than one day of treatment in relieving symptomatic cough and resolving the bothersome nature of cough when compared with salbutamol or placebo. However, salbutamol probably improved sleep quality for children and parents more than honey.

There is probably little or no difference between honey alone and bromelin (pineapple enzyme extract) mixed with honey for relieving cough symptoms.

On Day 5 of administration, there was probably little or no difference between honey versus placebo or honey versus salbutamol for symptomatic relief of cough and reduction of cough impact on the sleep quality of children and their parents.

No serious adverse events were reported in any of the treatment groups. Non-severe adverse events such as stomachache, nausea, and vomiting were probably more common in the honey groups than no-treatment and placebo groups, but comparable with dextromethorphan, diphenhydramine, and salbutamol groups. There was probably little or no difference in numbers of events in the honey, no-treatment, placebo, dextromethorphan, diphenhydramine, and salbutamol groups for other non-severe adverse events such as rash and tachycardia.

Overall completeness and applicability of evidence

The available evidence shows that honey may be better than placebo and salbutamol in reducing cough duration for children with acute cough. However, as the data for this evidence were from a small study, the applicability of this evidence is uncertain.

We also found that giving honey for three days is probably more effective in relieving symptoms of cough when compared to placebo or salbutamol. However, salbutamol was more effective in reducing the impact of cough on sleep quality of children and their parents. The administration of honey beyond three days had no advantage over salbutamol or placebo in the reduction of cough severity and bothersome cough. This evidence was generated from a small study, and as such caution is required in its application.

Overall, the direction of effect was in favour of honey compared to no treatment, placebo, dextromethorphan, diphenhydramine, and salbutamol for relieving symptomatic cough and resolving bothersome cough, but it was not better than dextromethorphan, diphenhydramine, and salbutamol at improving the quality of sleep in children and their parents. Other outcomes such as improvements in appetite, school attendance, and playing were not reported. We cannot generalise on the applicability of our findings because most children in this review received treatment for one night, even though an acute cough may last for more than one week.

Waris 2014 reported that they used the darkest honey they could find; it is believed that the darker the honey, the more the antioxidant property (Cohen 2012). However, there is insufficient evidence to support this estimate of effect.

Quality of the evidence

We included six small RCTs that we assessed as at overall low risk of bias (Figure 2). We assessed two studies as at high risk of bias relating to blinding (overall, we assessed the certainty of the evidence as low to moderate certainty for outcomes measured; Summary of findings for the main comparison; Summary of findings 2; Summary of findings 3; Summary of findings 4; Summary of findings 5). This was largely due to imprecision of the effect estimate, heterogeneity, and high risk of bias of some of the studies. We rated the certainty of the evidence as moderate to low for all outcomes for the comparisons of honey to dextromethorphan, no treatment, bromelin, and placebo. However, we rated the certainty of evidence as low for honey versus diphenhydramine on symptomatic relief of cough. We assessed two included studies as at high risk of bias of performance and detection bias (Paul 2007; Shadkam 2010). We rated Paul 2007 as at high risk for performance bias because they did not blind the no-treatment arm of their study. Shadkam 2010 did not blind participants and investigators for all treatment arms. We assessed Cohen 2012 and Waris 2014 as at low risk of bias for all domains except for attrition bias, which we judged as unclear. We rated Ahmadi 2013 as unclear risk of bias for selective reporting and other bias because results were presented as the proportion of children with reduced cough instead of the actual mean symptom scores reported by the other included studies. In addition, the scale used for measurement was not clear (a 7-point Likert-like scale was used for cough assessment), and the protocol was registered retrospectively after completion of study. African honey was administered thrice daily for five days compared to one night for other honey types; this may have been responsible for its higher effect on cough symptoms. Also, most studies measured all outcomes using a 7-point Likert scale, except Peixoto 2016, which used an unvalidated 5-point cough scale; for this reason we rated Peixoto 2016 as at unclear risk of other bias. These scales are qualitative ordinal scales; as a result, symptom scores may be subjective.

Potential biases in the review process

Due to limitations in the design and reporting of the included studies, conclusive evidence for or against the use of honey in the treatment of cough symptoms and their impact on sleep remains elusive. Data from two studies could not be meta-analysed because of the way results were presented (Ahmadi 2013; Peixoto 2016). Peixoto 2016 also used an unvalidated cough scale, and the cough scale used by Ahmadi 2013 was unclear. We were unable to conduct sensitivity analyses to determine publication bias because there were too few studies. We screened, extracted, and reported data according to the methods in the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2011). Most included studies were underpowered. The risk of bias for attrition was unclear in three studies because the studies only stated the proportion of children lost to follow-up in each treatment group, but no clear information on the reason for the loss (Cohen 2012; Shadkam 2010; Waris 2014).

We did not limit electronic searches by language or publication.

Agreements and disagreements with other studies or reviews

An overview of reviews of honey for treating cough included three reviews (Nitsche 2016). Of the three reviews included in the overview, Oduwole 2014a and Oduwole 2014b are earlier versions of this review, and Smith 2014 is a Cochrane Review that assessed over-the-counter remedies for acute cough in community settings. The conclusions reported by Nitsche 2016 were similar to the findings of this review. We also identified a related study (Mulholland 2011), but we did not think it was relevant to our review, and moreover, the review had no included studies.

AUTHORS' CONCLUSIONS

Implications for practice

We found that giving honey for up to three days is probably more effective in relieving cough symptoms compared to placebo or salbutamol. However, to an extent, salbutamol was more effective in relieving the impact of cough on the quality of sleep of children and their parents. The administration of honey beyond three days probably had no advantage over salbutamol or placebo in the reduction of cough severity and bothersome cough.

When given for one day, honey is probably more effective in reducing cough frequency, cough severity, and impact of cough on sleep for both children and parents than no treatment. Honey may also resolve bothersome cough to a greater extent than no treatment. Honey probably reduces cough frequency more effectively than placebo. Honey probably also reduces cough severity, resolves bothersome cough, and improves sleep quality for both children and their parents to a greater extent than placebo. Its effect on cough frequency, cough severity, and quality of sleep for children and their parents is also likely to be better than with diphenhydramine, an over-the-counter cough remedy. Its effect may be comparable to dextromethorphan (another over-

the-counter drug) for reducing cough frequency, cough severity, and the impact of cough on sleep quality of children and their parents. There was probably little or no difference between honey and bromelin mixed with honey for reducing cough frequency and severity. One of the included studies assessed the effect of honey on cough duration; the available evidence suggests that honey reduces cough duration to a greater extent than placebo or salbutamol. There was no difference in the occurrence of non-severe adverse events between honey and the various control arms.

These findings are from six small studies, two of which were at high risk of performance and detection bias with moderate- to low-certainty evidence, and may not be generalisable.

Implications for research

We advocate for more high-quality, large randomised controlled trials evaluating the effectiveness of honey in relieving acute cough in children. Randomised controlled trials need to look at dosage, longer treatment times, and follow-up of participants, and measure other important secondary outcomes relevant to caregivers such as cost of the intervention and quality of life of the children.

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CHARACTERISTICS OF STUDIES

Characteristics of included studies *[ordered by study ID]*

Ahmadi 2013

Methods	Study design: RCT Study duration: 2010 to November 2012

Participants	• Setting: a paediatric outpatient clinic, Shariatee Hospital, Bandar Abbas
	• Country: Iran
	• Health status: viral upper respiratory tract infection with complaints of sneezing, blocked nose, sore throat, cough, mild headache
	• Number: treatment (63); control (63)
	• Age (mean ± SD)
	  * treatment: 45.21 ± 11.39 months
	  * control: 43.98 ± 11.95 months
	• Sex (M/F): 60/66
	  * treatment (M/F): 27/36
	  * control (M/F): 33/30
	
	Exclusion criteria
	
	Onset of otitis or sinusitis symptoms; onset of symptoms of lower respiratory tract involvement; adding a bacterial infection (purulent nasal discharge, high fever, difficulty breathing, periorbital oedema, facial pain); not using recommended treatments; adding other drugs to recommended treatment; conflicting reports of the carers of the participants

Interventions	**Treatment group** • Intervention: honey (Mahram) • Dose, duration, frequency, administration: honey was placed in glasses similar to those belonging to diphenhydramine and with a similar concentration, mixed with distilled lukewarm water, administered 3 times a day, with last dose given an hour before sleeping. **Control group** • Intervention: 5 mg/kg diphenhydramine syrup • Dose, duration, frequency, administration: 5 mg/kg body weight, 3 times a day, with last dose given an hour before sleeping Honey was given in the same volume, frequency, and duration of use as diphenhydramine.
Outcomes	• Severity of cough • Frequency of cough
Notes	• Funding source: unknown • Contact with study authors for additional information: we contacted authors for additional information but received no response. • A volunteer translated the study from Farsi to English. • A 7-point Likert-like scale was used for cough assessment.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Not described but likely done. Randomisation was done by the hospital pharmacist who was not involved in the study.

Ahmadi 2013 *(Continued)*

Allocation concealment (selection bias)	Low risk	Not described but probably done. Quote: "The classification of patients was done by the hospital pharmacist"
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Honey was placed in glasses similar to those belonging to diphenhydramine and with a similar concentration, mixed with distilled lukewarm water. The honey and diphenhydramine mixtures were prepared by the pharmacist, who was not part of the study. The paediatricians and parents were unaware of the nature of the treatment each child received.
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "the treating doctor and the mother were unaware of the nature of the medication (honey or diphenhydramine)"; "In order to prevent the confounding factor of mother's anxiety or her personal situation, her reports were only accepted if they were corroborated by the reports of a third person close to the child"
Incomplete outcome data (attrition bias) All outcomes	Low risk	All children randomised to treatment arms completed the 2-day study.
Selective reporting (reporting bias)	Low risk	Both outcomes listed in the methods section were reported.
Other bias	Unclear risk	Results were presented as the proportion of children with reduced symptom cough instead of the actual mean symptom scores. Furthermore, the scale used for measurement was not clear (a 7-point Likert-like scale was used for cough assessment). The protocol was registered retrospectively after completion of the study.

Cohen 2012

Methods	Study design: RCT Study duration: January 2009 to December 2009

Participants	• Setting: 6 paediatric community clinics
	• Country: Israel
	• Health status: children with upper respiratory infection who "were ill with a mean ± SD of 2.8 ± 2.0 days before enrolment". Upper respiratory infection was "defined by the presence of cough and rhinorrhea of #7 days' duration".
	• Number (total = 300):
	  * treatment 1, eucalyptus honey (N = 75)
	  * treatment 2, citrus honey (N = 75)
	  * treatment 3, Labiatae honey (N = 75)
	  * control, placebo (N = 75)
	• Age: median age of children who completed the study was 29 months (range 12 to 71 months).
	  * treatment:
	  ☐ eucalyptus honey: mean 27.5 months ± 13.9
	  ☐ citrus honey: mean age 29 months ± 13.5
	  ☐ Labiatae honey: mean age 30 months ± 16.6
	  * control: mean age 29 months ± 14.9
	• Sex: unclear
	Exclusion criteria

Cohen 2012 *(Continued)*

	Quote: "children were excluded if they had signs or symptoms of asthma, pneumonia, laryngotracheobronchitis, sinusitis, and/or allergic rhinitis. Children were also excluded if they had used any cough or cold medication or honey on the night before entering the study"
Interventions	**Treatment group** • Intervention: eucalyptus honey, citrus honey, or Labiatae honey (3 intervention arms) • Dose, duration, frequency, administration: single 10 g dose administered 30 minutes before bedtime **Control group** • Intervention: silan (date) extract (similar structure, colour, and taste to honey) • Dose, duration, frequency, administration: single 10 g dose administered 30 minutes before bedtime
Outcomes	• Cough frequency • Cough severity • Bothersome nature of cough • Child and parent sleep quality • The combined score of these 4 measures
Notes	• Funding source: quote: "Supported in part by a research grant from Israel Ambulatory Paediatric Association, Maternal Infant Nutrition Research Institute and the Honey Board of Israel" • Contact with study authors for additional information: we contacted the authors to confirm the proportion of boys to girls of the 300 children randomised. Authors did not respond to our query.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Randomisation was in blocks of 4.
Allocation concealment (selection bias)	Low risk	The envelopes containing the codes for the study preparations were stored at the office of the Ministry of Agriculture, Extension service, Beekeeping Department and were not opened until after the statistical analysis was completed.
Blinding of participants and personnel (performance bias) All outcomes	Low risk	The 3 honeys and the placebo were prepared by someone not involved in the study; interventions were packed in small plastic containers marked A, B, C, and D and distributed to the paediatric community clinics. Silan date extract was used as a placebo because its structure, brown colour, and taste are similar to that of honey. The parents, physicians, and investigators did not know the content of the preparation that was dispensed.
Blinding of outcome assessment (detection bias) All outcomes	Low risk	The parents, physicians, and investigators did not know the content of the preparation that was dispensed. Interventions were packed in small plastic containers marked A, B, C, and D and distributed to the paediatric community clinics. Silan date extract was used as a placebo because its structure, brown colour, and taste are similar to that of honey.
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	14 (19%), 13 (18%), 2 (3%), and 4 (5%) children were lost to follow-up in the eucalyptus honey, citrus honey, Labiatae honey, and placebo groups, respectively. The authors stated that the reasons for loss to follow-up were unknown. However, attrition was significantly high in the eucalyptus honey and citrus honey groups. It is unclear if the reasons for attrition in the treatment groups were related to the study or not and if the reasons were similar.
Selective reporting (reporting bias)	Low risk	All outcomes listed in the protocol were reported.

Cohen 2012 *(Continued)*

Other bias	Low risk	Not detected

Paul 2007

Methods	RCT

Participants	• Setting: a single outpatient general paediatric practice
	• Country: USA
	• Health status: "The URIs were characterized by the presence of rhinorrhea and cough for 7 or fewer days' duration. Other symptoms may have included but were not limited to congestion, fever, sore throat, myalgias, and headache" (p. 1141)
	• Number (total = 108):
	  * honey (N = 35)
	  * control:
	  ☐ dextromethorphan (N = 34)
	  ☐ no treatment (N = 39)
	• Age: 2 to 18 years; median age of the 105 children completing the study was 5.22 years (range 2.22 to 16.92 years)
	  * treatment (median ± interquartile range, years): honey = 5.43 ± 3.81
	  * control (median ± interquartile range, years):
	  ☐ dextromethorphan = 4.42 ± 3.83
	  ☐ no treatment = 5.22 ± 4.33
	• Sex: unclear
	
	Exclusion criteria
	
	Quote: "patients were excluded if they had signs or symptoms of a more treatable disease (e.g., asthma, pneumonia, laryngotracheobronchitis, sinusitis, allergic rhinitis). They were also ineligible when they had a history of reactive airways disease, asthma, or chronic lung disease or were using a drug known to inhibit the metabolism of dextromethorphan, such as selective serotonin reuptake inhibitors. Subjects were also excluded if on the prior evening they had taken a medication that included an antihistamine or dextromethorphan hydrobromide within 6 hours of bedtime or dextromethorphan polistirex within 12 hours of bedtime on the evening prior to or on the day of enrolment" (p. 1141)

Interventions	**Treatment group** • Intervention: buckwheat honey • Dose, duration, frequency, administration: "For the honey group, the volume of honey dispensed was equivalent to the age-driven volume dispensed for DM [dextromethorphan]" **Control group** • Intervention: "artificially honey-flavoured DM [dextromethorphan], (17 mg/5 mL prepared using DM hydrobromide powder [100% pure United States Pharmacopeia grade], artificial honey flavoring, coloring, stevia liquid extract, methocel, and simple syrup [Professional Compounding Centers of America, Houston, Texas])", no treatment = empty syringe • Dose, duration, frequency, administration: "dosage for DM [dextromethorphan] approximated typical OTC label recommendations, with children aged 2 to 5 years receiving 8.5 mg/dose (1/2 teaspoon), children aged 6 to 11 years receiving 17 mg/dose (1 teaspoon), and children aged 12 to 18 years receiving 34 mg/dose (2 teaspoons). Of note, these concentrations slightly exceed typical OTC products, which contain 15 mg/5 mL, and were the result of the compounding process but may be more likely to achieve a beneficial effect based on our previous analyses" Parents were instructed that their child's treatment could be given with a non-caffeinated beverage and should be administered within 30 minutes of the child going to sleep. Intervention and control were in a 10-millilitre opaque syringe and kept in brown paper bags.

Paul 2007 *(Continued)*

Outcomes	• Cough frequency • Cough severity • Bothersome nature of cough • Cough impact on sleep quality for child and parent • The combined score of these 4 measures
Notes	• Funding source: "this study was supported by an unrestricted research grant from the National Honey Board, an industry-funded agency of the USA Department of Agriculture" • Contact with study authors for additional information: we contacted the lead author for additional information on the proportion of boys to girls of the 108 children randomised and other missing data. Authors responded that they could not provide the information because they no longer have the data.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Not described but probably done. Quote: "The randomisation sequence was constructed by a statistician not affiliated with the study and was then used by the study coordinators to assign treatment group"
Allocation concealment (selection bias)	Low risk	Not described but probably done. Treatment allocation was concealed in 10-millilitre opaque syringe and kept in brown paper bags.
Blinding of participants and personnel (performance bias) All outcomes	High risk	The syringes used for all 3 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 of outcome assessment (detection bias) All outcomes	High risk	Although all participants were given syringes in brown paper bags, the no-treatment group had empty syringes, which could influence the assessment of the outcome.
Incomplete outcome data (attrition bias) All outcomes	Low risk	2 children 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.
Selective reporting (reporting bias)	Low risk	All outcomes were adequately reported.
Other bias	Low 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. Children lost to follow-up or withdrawn were not included in the final analysis.

Peixoto 2016

Methods	RCT
Participants	• Setting: a paediatric service of Clinica Amaury Coutinho, linked to Recife City Hall • Country: Brazil • Health status: "irritative cough for at least 24 hours, which led to the need for medical consultation, participated in the study. Patients should have acute cough due to viral upper airway infection, thus considered due to the presence of mild fever or fever associated with hyaline or catarrhal rhinorrhea, lasting less than 72 hours, without clinical manifestations of associated bronchospasm"

Peixoto 2016 *(Continued)*

- Number (total = 60):
  - treatment: honey (N = 29)
  - control: bromelin (N = 31)
- Age: age in years, mean (25 to 75 percentiles):
  - treatment: honey: mean 5.6 years (2.0 to 7.5 years)
  - control: bromelin: mean 5.3 years (3.0 to 7.5 years)
- Sex of children who completed study (M/F):
  - treatment: honey (13/16)
  - control: bromelin (13/18)

Exclusion criteria

Children with history of obstructive pulmonary disease, cystic fibrosis, neuropathies, heart disease, diabetes, or identifiable primary or secondary immunodeficiencies

Interventions	**Treatment group** • Intervention: honey • Dose, duration, frequency, administration: children up to 20 kg received 5 mL; for those weighing > 20 kg, 1 mL was administered for every 5 kg additional weight. **Control group** • Intervention: the combination of honey and *Ananas comosus* extract HBS19820501 (rich in bromelin) as syrup formulation • Dose, duration, frequency, administration: children up to 20 kg received 5 mL; for those weighing > 20 kg, 1 mL was administered for every 5 kg additional weight. Quote: "the quality of the honey was certified in both groups and approved by the regulatory agencies and the National Health Surveillance Agency (Anvisa) for sale; the honey had been recently produced and underwent strict bacteriological control"
Outcomes	• Cough frequency • Reduction in cough severity
Notes	• Funding source: Hebron Indústrias Químicas

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Randomisation was carried out according to a table generated in Microsoft Excel.
Allocation concealment (selection bias)	Low risk	Not described but very likely. Treatments were labelled A and B. Quote: "Neither the investigator nor the patient, nor the family knew which product was used"; "The treatment groups were revealed only after the analysis of the study results"
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "neither the investigator nor the patient, nor the family knew which product was used. The treatment groups were revealed only after the analysis of the study results"
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "neither the investigator nor the patient, nor the family knew which product was used. The treatment groups were revealed only after the analysis of the study results"

Peixoto 2016 *(Continued)*

Incomplete outcome data (attrition bias) All outcomes	Low risk	All participants randomised were included in the final analysis.
Selective reporting (reporting bias)	Low risk	All outcomes listed in the study protocol and methods section were reported.
Other bias	Unclear risk	Used an unvalidated 5-point cough scale that differed from the cough scale used by the other included studies

Shadkam 2010

Methods	RCT

Participants	• Setting: 6 paediatric community clinics
	• Country: Iran
	• Health status: "2 to 5 years of age with URTIs, nocturnal symptoms and illness duration of 5 days. All or some of these children were suffering from symptoms such as rhinorrhoea, sneeze, sore throat, and stuffed nose. Their coughing had lasted 5 days"
	• Number (total = 160):
	  * treatment: honey (N = 40)
	  * control:
	  ☐ dextromethorphan (N = 40)
	  ☐ diphenhydramine (N = 40)
	  ☐ no treatment (N = 40)
	• Age (children who completed the study): 37.75 ± 11.12 months
	  * treatment: honey: mean age 37 ± 11.4 months
	  * control:
	  ☐ dextromethorphan: mean age 37 ± 11.1 months
	  ☐ diphenhydramine: mean age 38 ± 11.4 months
	  ☐ no treatment: mean age 37.8 ± 10.9 months
	• Sex: not reported
	
	Exclusion criteria
	
	"asthma, pneumonia, laryngotracheobronchitis, sinusitis, allergic rhinitis, chronic lung disease, congenital heart disease, malignancy, and diabetes were not included in the study. antihistamine, diphenhydramine, or dextromethorphan 4 hours before sleep or had consumed cytochrome P450 inhibitors simultaneously (i.e. serotonin-reabsorption selective inhibitors) were also excluded from the study. Parents were also excluded if they were using a drug and herbal that had an effect on sleeping, such as sedatives"

Interventions	**Treatment group** • Intervention: a single dose of natural honey from Kafi-Abad (a village in Yazd, Iran) • Dose, duration, frequency, administration: received 2.5 mL of natural honey before sleep **Control group** • Intervention: dextromethorphan, diphenhydramine, or no treatment (received supportive treatment recommended for other groups as well) • Dose, duration, frequency, administration: the second (dextromethorphan) and third (diphenhydramine) groups received 2.5 mL of dextromethorphan syrup (7.5 mg, Pour-Sina drug manufacturing company in Tehran, Registered No. 1228051241) and 2.5 mL of diphenhydramine syrup (6.25 mg, RamooFarmon drug manufacturing company, Registered No. 1228056772), respectively, before sleep.

Shadkam 2010 *(Continued)*

	• All treatment arms were advised to take supportive treatment with saline nose drops, water vapour, cleaning of a blocked nose, and use of paracetamol for fever, if necessary. All mothers were offered the same standard on the disease and how to use liquids, nose drops, and humidifier by a paediatrician.
Outcomes	• Cough frequency • Cough severity • Child sleep score • Parents' sleep quality
Notes	• Funding source: Department of Research Administration, Shahid Sadoughi University of Medical Sciences (SSUMS) in Yazd, Iran

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 of participants and personnel (performance bias) All outcomes	High risk	Neither the investigators nor caregivers were blinded to treatments given, which could greatly influence the assessment of outcome.
Blinding of outcome assessment (detection bias) All outcomes	High risk	Neither the investigators nor caregivers were blinded to treatments given, which could greatly influence the assessment of outcome.
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	7 participants from the honey group, 4 from the dextromethorphan group, 6 from the diphenhydramine group, and 4 from the no-treatment group were either lost to follow-up or withdrawn for violating the protocol. Attrition was high for the honey and diphenhydramine groups. Participants were excluded from analysis for not visiting the physician as scheduled or using the drugs inappropriately. The proportion of children who did not visit physician as scheduled or violated protocol per group was unclear.
Selective reporting (reporting bias)	Low risk	All outcomes listed in the protocol were 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 have influenced the assessment of outcomes. Since mothers were filling in the questionnaire in the presence of the physician, it is unclear if this could have influenced the assessment of outcomes (p. 788)

Waris 2014

Methods	RCT
Participants	• Setting: the paediatric casualty of the Aga Khan University Hospital Nairobi. This is a national tertiary referral and teaching hospital serving the middle- and upper-income society in Nairobi and its environment. • Country: Kenya

Waris 2014 *(Continued)*

- Health status: an uncomplicated acute upper respiratory infection (authors did not define acute upper respiratory infection)
- Number (total = 145):
  - treatment: honey (N = 57)
  - control:
    - salbutamol (N = 43)
    - placebo (N = 45)
- Age: 1 to 12 years
  - treatment: not clear
  - control: not clear
- Sex of children who completed study (M/F):
  - honey (30/24)
  - control:
    - salbutamol (unclear)
    - placebo: (unclear)

Exclusion criteria

Prior use (48 hours) of any cough mixture, study agents, oral antihistamines, nasal decongestants, steroids, or antibiotics. Other exclusions were any past history of atopy, asthma, or any chronic lung disease as well as hospitalisation for lower respiratory tract infection in the past 6 months.

Interventions	**Treatment group**
	• Intervention: the darkest locally available honey was used.
	• Dose, duration, frequency, administration: 2.5 mL (age 1 to 2 years), 5 mL (age 2 to 6 years), 7.5 mL (age 6 to 12 years); all were administered 3 times daily for 5 days
	Control group
	• Intervention:
	  * salbutamol has 2 mg of active ingredient per 5 mL.
	  * placebo was a brown-coloured sugar and alcohol-free syrup with an inert thickening agent whose ingredients included sodium citrate, citric acid monohydrate hypromellose, sodium benzoate, saccharin sodium, sodium chloride, caramel colour, and water.
	• Dose, duration, frequency, administration: 2.5 mL (age 1 to 2 years), 5 mL (age 2 to 6 years), 7.5 mL (age 6 to 12 years); all were administered 3 times daily for 5 days

Outcomes	• Cough frequency • Cough severity • Bothersome cough • Cough effect on children's sleep • Cough effect on parents' sleep • Combined symptom score
Notes	• Funding source: Universal Corporation Ltd prepared all study drugs at no cost. • Contact with study authors for additional information: we contacted the authors for additional information on cough scores and mean age of children randomised. • It is unclear if the salbutamol was oral or inhaled. It was most likely oral because parents were given all study drugs to administer to their children at home.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Dispensing study drugs was undertaken following a random order previously generated by a statistician not involved in care of study participants.

Waris 2014 *(Continued)*

Allocation concealment (selection bias)	Low risk	Not described, but risk of bias unlikely. All 3 study drugs were prepared, bottled, packaged, and labelled as Study Drug A, B, and C by Universal Corporation Ltd, who also held the code until after statistical analysis was completed.
Blinding of participants and personnel (performance bias) All outcomes	Low risk	All 3 study drugs were prepared, bottled, packaged, and labelled as Study Drug A, B, and C by Universal Corporation Ltd, who also held the code until after statistical analysis was completed.
Blinding of outcome assessment (detection bias) All outcomes	Low risk	All 3 study drugs were prepared, bottled, packaged, and labelled as Study Drug A, B, and C by Universal Corporation Ltd, who also held the code until after statistical analysis was completed.
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	13%, 7%, and 5% of children in the placebo, honey, and salbutamol groups, respectively, were lost to follow-up or were in violation of study protocol. It is unclear if the reasons for not completing the study were the same across study groups. It is possible that more participants in the placebo group left because their condition worsened.
Selective reporting (reporting bias)	Low risk	Not detected
Other bias	Low risk	Unlikely

ITT: intention-to-treat; OTC: over-the-counter; RCT: randomised controlled trial; SD: standard deviation; URTI: upper respiratory tract infection

Characteristics of excluded studies *[ordered by study ID]*

Study	Reason for exclusion
Ahmed 2013a	Not an RCT; this was a feasibility study of honey for the treatment of cough in children
Ayazi 2017	Quasi-RCT
Baker 2016	Not an RCT; commentary on a previous version of this review (Oduwole 2014a)
Cohen 2017	Wrong intervention: compared polysaccharide-resin-honey to carbocysteine syrup. The study examined honey-based cough syrup (polysaccharide-resin-honey) versus a non-honey-based cough syrup (carbocysteine syrup). We would have included this study if the comparisons had been polysaccharide-resin-honey versus honey alone/polysaccharide-resin alone or carbocysteine syrup + honey versus carbocysteine syrup alone.
Gilbert 2008	Not an RCT
Miceli Sopo 2014	Wrong intervention: compared honey and milk versus dextromethorphan and honey and milk versus levodropropizine
Warren 2007	Not an RCT

RCT: randomised controlled trial

Characteristics of studies awaiting assessment [ordered by year of study]

IRCT20140908190 37N1

Methods	Randomised clinical trial
Participants	Children aged 2 to 12 years
Interventions	2 types of honey versus diphenhydramine
Outcomes	Cough frequency, bothersome nature of cough, and severity
Notes	Completed

Characteristics of ongoing studies [author-defined order]

NCT03218696

Trial name or title	Comparison of a protective cough syrup against placebo on night cough in children 1 to 5 years coughing since 1 to 2 days due to common cold
Methods	Randomised controlled trial
Participants	Children aged 1 to 5 years (i.e. 1 day before the 6th birthday, males and females) Inclusion criteria: cough attributed to infection of the upper respiratory tract present in the child for not more than 2 days
Interventions	Cough syrup containing specific plant extracts (Poliflav MA) and honey versus placebo
Outcomes	Primary • night cough frequency score reduction Secondary • night cough bothersome score reduction • night cough intensity score reduction • reduction of influence of cough on child sleep score • reduction of influence of cough on combined night score • reduction of influence of cough on parent sleep score (Time frame: First and only night of treatment)
Starting date	September 2017
Contact information	Prof Herman A Cohen Email: hermanc@clalit.org.il Affiliation: Clalit Health Services
Notes	This study is not yet open for participant recruitment (November 2017).

UMIN000020651

Trial name or title	Effectiveness of honey and expectorant for nocturnal cough in children with acute upper respiratory infection: a prospective interventional study

UMIN000020651 *(Continued)*

Methods	Parallel randomised
Participants	Children aged 2 to 16 years Inclusion criteria: • Patient diagnosed with acute upper respiratory infection with cough for 7 or fewer days duration • Nocturnal cough score 3 or more (using a 7-point Likert scale)
Interventions	Honey (5 g for those age 2 to 5 years, 10 g for those aged 6 years and above) orally before bedtime for a week versus carbocysteine (30 mg/kg/day) and ambroxol (0.9 mg/kg/day) orally for a week
Outcomes	Primary outcome: change in frequency of nocturnal cough on the next day when honey or expectorant had been given prior to bedtime compared to that on the first day of presentation when no medication had been given Secondary outcomes: Change in severity of nocturnal cough, bothersome cough, appetite, and quality of sleep at night on the next day when honey or expectorant had been given prior to bedtime compared to that on the first day of presentation when no medication had been given. Improvement of nocturnal cough 1 week after honey or expectorant had been given prior to bedtime compared to that on the first day of presentation when no medication had been given
Starting date	25 January 2016
Contact information	Name: Kazushi Agata; Shun Kishibe Address: 1163 Tatemachi, Hachioji, Tokyo, Japan; 2-8-29 Musashidai, Fuchu-shi, Tokyo, Japan Email: tokyoseki2016@gmail.com; jemstone625@gmail.com Affiliation: Tokyo Medical University Hachioji Medical Center Pediatrics; Tokyo Metropolitan Children's Medical Center Pediatric Emergency Medicine
Notes	

DATA AND ANALYSES

Comparison 1. 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 reduction in cough frequency)	2	149	Mean Difference (Random, 95% CI)	-0.07 [-1.07, 0.94]
1.2 Severity of cough (mean reduction in severity of cough)	2	149	Mean Difference (Random, 95% CI)	-0.13 [-1.25, 0.99]

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1.3 Bothersome cough (mean reduction in bothersome cough)	1	69	Mean Difference (Random, 95% CI)	0.29 [-0.56, 1.14]
1.4 Children's sleep (mean reduction in cough impact on sleep score)	2	149	Mean Difference (Random, 95% CI)	0.03 [-1.12, 1.19]
1.5 Parents' sleep (mean reduction in cough impact on sleep score)	2	149	Mean Difference (Random, 95% CI)	-0.16 [-0.84, 0.53]
1.6 Combined cough score (reduction in combined cough score)	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 reduction in cough frequency)	1	80	Mean Difference (Random, 95% CI)	-0.57 [-0.90, -0.24]
2.2 Severity of cough (mean reduction in severity of cough)	1	80	Mean Difference (Random, 95% CI)	-0.6 [-0.94, -0.26]
2.3 Children's sleep (mean reduction in cough impact on sleep score)	1	80	Mean Difference (Random, 95% CI)	-0.55 [-0.87, -0.23]
2.4 Parents' sleep (mean reduction in cough impact on 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 reduction in frequency of cough)	2	154	Mean Difference (Random, 95% CI)	-1.05 [-1.48, -0.62]
3.2 Severity of cough (mean reduction in severity of cough)	2	154	Mean Difference (Random, 95% CI)	-1.03 [-1.59, -0.47]
3.3 Bothersome cough (mean reduction in bothersome cough)	1	74	Mean Difference (Random, 95% CI)	-0.93 [-1.98, 0.12]
3.4 Children's sleep (mean reduction in cough impact on sleep score)	2	154	Mean Difference (Random, 95% CI)	-1.04 [-1.57, -0.51]
3.5 Parents' sleep (mean reduction in cough impact on sleep score)	2	154	Mean Difference (Random, 95% CI)	-0.88 [-1.23, -0.52]
3.6 Combined reduction in symptoms score	1	74	Mean Difference (Random, 95% CI)	-4.31 [-6.77, -1.85]
4 Honey versus placebo (Day 1)	2		Mean Difference (Random, 95% CI)	Subtotals only
4.1 Frequency of cough (mean reduction in frequency of cough)	2	402	Mean Difference (Random, 95% CI)	-1.62 [-3.02, -0.22]

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
4.2 Severity of cough (mean reduction in severity of cough)	2	402	Mean Difference (Random, 95% CI)	-1.07 [-2.43, 0.30]
4.3 Bothersome cough (mean reduction in bothersome cough)	2	402	Mean Difference (Random, 95% CI)	-1.40 [-2.82, 0.03]
4.4 Children's sleep (mean reduction in cough impact on sleep score)	2	402	Mean Difference (Random, 95% CI)	-1.21 [-2.61, 0.19]
4.5 Parents' sleep (mean reduction in cough impact on sleep score)	2	402	Mean Difference (Random, 95% CI)	-1.29 [-2.71, 0.13]
5 Honey versus placebo (Day 2)	1		Mean Difference (Random, 95% CI)	Subtotals only
5.1 Frequency of cough (mean reduction in frequency of cough)	1	102	Mean Difference (Random, 95% CI)	-0.71 [-1.22, -0.20]
5.2 Severity of cough (mean reduction in severity of cough)	1	102	Mean Difference (Random, 95% CI)	-0.63 [-1.36, 0.10]
5.3 Bothersome cough (mean reduction in bothersome cough)	1	102	Mean Difference (Random, 95% CI)	-1.11 [-1.79, -0.43]
5.4 Children's sleep (mean reduction in cough impact on sleep score)	1	102	Mean Difference (Random, 95% CI)	-0.69 [-1.43, 0.05]
5.5 Parents' sleep (mean reduction in cough impact on sleep score)	1	102	Mean Difference (Random, 95% CI)	-0.87 [-1.59, -0.15]
6 Honey versus placebo (Day 3)	1		Mean Difference (Random, 95% CI)	Subtotals only
6.1 Frequency of cough (mean reduction in frequency of cough)	1	102	Mean Difference (Random, 95% CI)	-1.13 [-1.71, -0.55]
6.2 Severity of cough (mean reduction in severity of cough)	1	102	Mean Difference (Random, 95% CI)	-0.85 [-1.41, -0.29]
6.3 Bothersome cough (mean reduction in bothersome cough)	1	102	Mean Difference (Random, 95% CI)	-1.33 [-1.87, -0.79]
6.4 Children's sleep (mean reduction in cough impact on sleep score)	1	102	Mean Difference (Random, 95% CI)	-0.93 [-1.42, -0.44]
6.5 Parents' sleep (mean reduction in cough impact on sleep score)	1	102	Mean Difference (Random, 95% CI)	-0.88 [-1.38, -0.38]
7 Honey versus placebo (Day 4)	1		Mean Difference (Random, 95% CI)	Subtotals only
7.1 Frequency of cough (mean reduction in frequency of cough)	1	102	Mean Difference (Random, 95% CI)	-1.16 [-1.83, -0.49]

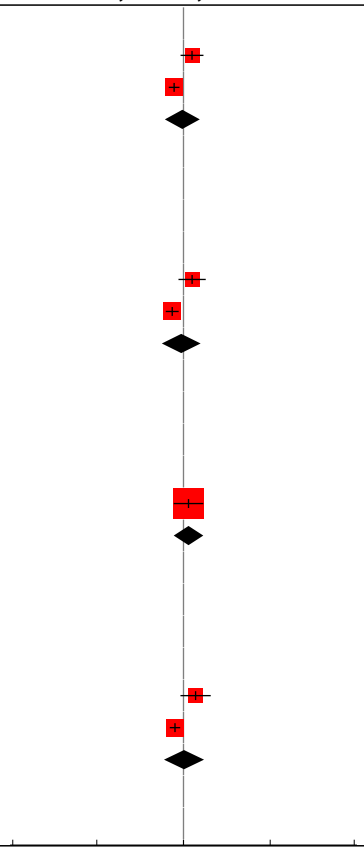
Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
7.2 Severity of cough (mean reduction in severity of cough)	1	102	Mean Difference (Random, 95% CI)	-0.88 [-1.59, -0.17]
7.3 Bothersome cough (mean reduction in bothersome cough)	1	102	Mean Difference (Random, 95% CI)	-0.90 [-1.76, -0.04]
7.4 Children's sleep (mean reduction in cough impact on sleep score)	1	102	Mean Difference (Random, 95% CI)	-0.7 [-1.25, -0.15]
7.5 Parents' sleep (mean reduction in cough impact on sleep score)	1	102	Mean Difference (Random, 95% CI)	-0.90 [-1.51, -0.29]
8 Honey versus placebo (Day 5)	1		Mean Difference (Random, 95% CI)	Subtotals only
8.1 Cough duration (mean number of days)	1	102	Mean Difference (Random, 95% CI)	-0.72 [-1.31, -0.13]
8.2 Frequency of cough (mean reduction in frequency of cough)	1	102	Mean Difference (Random, 95% CI)	-0.48 [-2.95, 1.99]
8.3 Severity of cough (mean reduction in severity of cough)	1	102	Mean Difference (Random, 95% CI)	-0.43 [-2.21, 1.35]
8.4 Bothersome cough (mean reduction in bothersome cough)	1	102	Mean Difference (Random, 95% CI)	-0.51 [-3.01, 1.99]
8.5 Children's sleep (mean reduction in cough impact on sleep score)	1	102	Mean Difference (Random, 95% CI)	-0.55 [-1.79, 0.69]
8.6 Parents' sleep (mean reduction in cough impact on sleep score)	1	102	Mean Difference (Random, 95% CI)	-0.57 [-1.59, 0.45]
9 Honey versus salbutamol (Day 1)	1		Mean Difference (Random, 95% CI)	Subtotals only
9.1 Frequency of cough (mean reduction in frequency of cough)	1	100	Mean Difference (Random, 95% CI)	-0.26 [-3.14, 2.62]
9.2 Severity of cough (mean reduction in severity of cough)	1	100	Mean Difference (Random, 95% CI)	-0.1 [-0.39, 0.19]
9.3 Bothersome cough (mean reduction in bothersome cough)	1	100	Mean Difference (Random, 95% CI)	-0.21 [-0.90, 0.48]
9.4 Children's sleep (mean reduction in cough impact on sleep score)	1	100	Mean Difference (Random, 95% CI)	0.09 [-0.05, 0.23]
9.5 Parents' sleep (mean reduction in cough impact on sleep score)	1	100	Mean Difference (Random, 95% CI)	0.05 [-0.03, 0.13]
10 Honey versus salbutamol (Day 2)	1		Mean Difference (Random, 95% CI)	Subtotals only

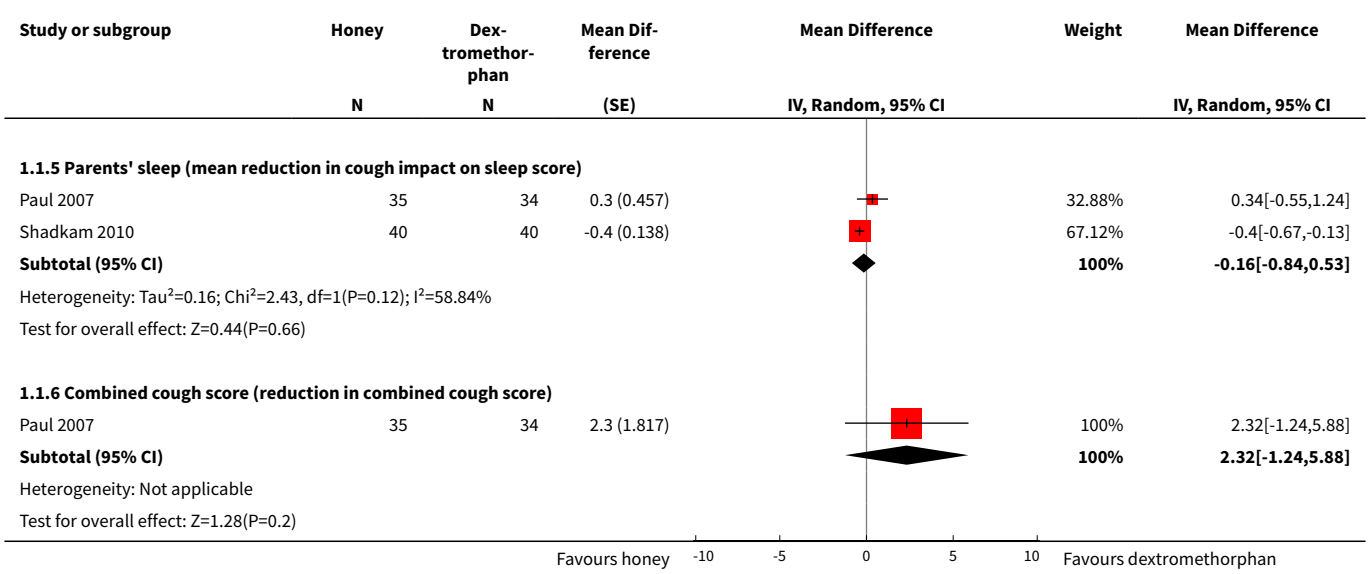
Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
10.1 Frequency of cough (mean reduction in frequency of cough)	1	100	Mean Difference (Random, 95% CI)	-0.67 [-1.35, 0.01]
10.2 Severity of cough (mean reduction in severity of cough)	1	100	Mean Difference (Random, 95% CI)	-0.42 [-1.16, 0.32]
10.3 Bothersome cough (mean reduction in bothersome cough)	1	100	Mean Difference (Random, 95% CI)	-0.27 [-0.52, -0.02]
10.4 Children's sleep (mean reduction in cough impact on sleep score)	1	100	Mean Difference (Random, 95% CI)	0.17 [-0.04, 0.38]
10.5 Parents' sleep (mean reduction in cough impact on sleep score)	1	100	Mean Difference (Random, 95% CI)	0.03 [-0.00, 0.06]
11 Honey versus salbutamol (Day 3)	1		Mean Difference (Random, 95% CI)	Subtotals only
11.1 Frequency of cough (mean reduction in frequency of cough)	1	100	Mean Difference (Random, 95% CI)	-0.69 [-1.13, -0.25]
11.2 Severity of cough (mean reduction in severity of cough)	1	100	Mean Difference (Random, 95% CI)	-0.34 [-0.64, -0.04]
11.3 Bothersome cough (mean reduction in bothersome cough)	1	100	Mean Difference (Random, 95% CI)	-0.24 [-0.38, -0.10]
11.4 Children's sleep (mean reduction in cough impact on sleep score)	1	100	Mean Difference (Random, 95% CI)	0.31 [0.13, 0.49]
11.5 Parents' sleep (mean reduction in cough impact on sleep score)	1	100	Mean Difference (Random, 95% CI)	0.21 [0.06, 0.36]
12 Honey versus salbutamol (Day 4)	1		Mean Difference (Random, 95% CI)	Subtotals only
12.1 Frequency of cough (mean reduction in frequency of cough)	1	100	Mean Difference (Random, 95% CI)	-0.61 [-0.96, -0.26]
12.2 Severity of cough (mean reduction in severity of cough)	1	100	Mean Difference (Random, 95% CI)	-0.43 [-0.78, -0.08]
12.3 Bothersome cough (mean reduction in bothersome cough)	1	100	Mean Difference (Random, 95% CI)	-0.3 [-0.59, -0.01]
12.4 Children's sleep (mean reduction in cough impact on sleep score)	1	100	Mean Difference (Random, 95% CI)	0.22 [0.05, 0.39]
12.5 Parents' sleep (mean reduction in cough impact on sleep score)	1	100	Mean Difference (Random, 95% CI)	0.15 [0.04, 0.26]
13 Honey versus salbutamol (Day 5)	1		Mean Difference (Random, 95% CI)	Subtotals only

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
13.1 Cough duration (mean number of days)	1	100	Mean Difference (Random, 95% CI)	-0.54 [-0.98, -0.10]
13.2 Frequency of cough (mean reduction in frequency of cough)	1	100	Mean Difference (Random, 95% CI)	-0.54 [-1.03, -0.05]
13.3 Severity of cough (mean reduction in severity of cough)	1	100	Mean Difference (Random, 95% CI)	-0.41 [-0.78, -0.04]
13.4 Bothersome cough (mean reduction in bothersome cough)	1	100	Mean Difference (Random, 95% CI)	-0.27 [-0.48, -0.06]
13.5 Children's sleep (mean reduction in cough impact on sleep score)	1	100	Mean Difference (Random, 95% CI)	0.15 [0.04, 0.26]
13.6 Parents' sleep (mean reduction in cough impact on sleep score)	1	100	Mean Difference (Random, 95% CI)	0.04 [0.01, 0.07]

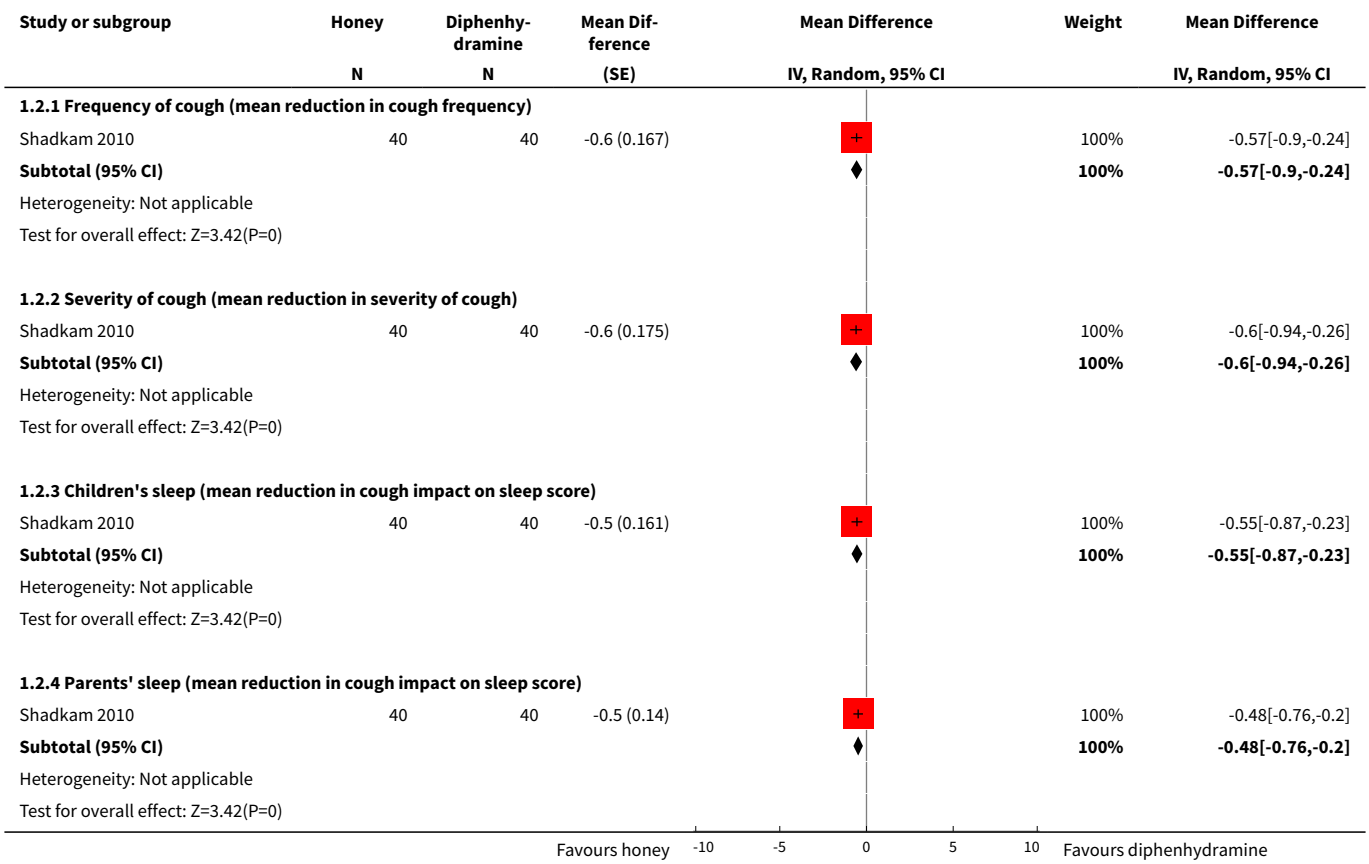
Analysis 1.1. Comparison 1 Pair-wise comparison, Outcome 1 Honey versus dextromethorphan.

Study or subgroup	Honey N	Dextromethorphan N	Mean Difference (SE)	Mean Difference IV, Random, 95% CI	Weight	Mean Difference IV, Random, 95% CI
1.1.1 Frequency of cough (mean reduction in cough frequency)						
Paul 2007	35	34	0.5 (0.337)		45.85%	0.49[-0.17,1.15]
Shadkam 2010	40	40	-0.5 (0.158)		54.15%	-0.54[-0.85,-0.23]
Subtotal (95% CI)					**100%**	**-0.07[-1.07,0.94]**
Heterogeneity: Tau^2=0.46; Chi^2=7.71, df=1(P=0.01); I^2=87.02%						
Test for overall effect: Z=0.13(P=0.9)						
1.1.2 Severity of cough (mean reduction in severity of cough)						
Paul 2007	35	34	0.5 (0.401)		45.27%	0.5[-0.29,1.28]
Shadkam 2010	40	40	-0.6 (0.19)		54.73%	-0.65[-1.02,-0.28]
Subtotal (95% CI)					**100%**	**-0.13[-1.25,0.99]**
Heterogeneity: Tau^2=0.56; Chi^2=6.69, df=1(P=0.01); I^2=85.05%						
Test for overall effect: Z=0.23(P=0.82)						
1.1.3 Bothersome cough (mean reduction in bothersome cough)						
Paul 2007	35	34	0.3 (0.435)		100%	0.29[-0.56,1.14]
Subtotal (95% CI)					**100%**	**0.29[-0.56,1.14]**
Heterogeneity: Not applicable						
Test for overall effect: Z=0.66(P=0.51)						
1.1.4 Children's sleep (mean reduction in cough impact on sleep score)						
Paul 2007	35	34	0.7 (0.445)		43.81%	0.7[-0.17,1.57]
Shadkam 2010	40	40	-0.5 (0.153)		56.19%	-0.49[-0.79,-0.19]
Subtotal (95% CI)					**100%**	**0.03[-1.12,1.19]**
Heterogeneity: Tau^2=0.59; Chi^2=6.37, df=1(P=0.01); I^2=84.29%						
Test for overall effect: Z=0.05(P=0.96)						



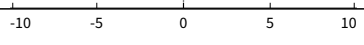


Analysis 1.2. Comparison 1 Pair-wise comparison, Outcome 2 Honey versus diphenhydramine.



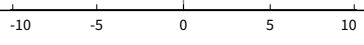
Analysis 1.3. Comparison 1 Pair-wise comparison, Outcome 3 Honey versus no treatment.

Study or subgroup	Honey N	No treatment N	Mean Difference (SE)	Mean Difference IV, Random, 95% CI	Weight	Mean Difference IV, Random, 95% CI
1.3.1 Frequency of cough (mean reduction in frequency of cough)						
Paul 2007	35	39	-1 (0.282)		59.98%	-0.97[-1.52,-0.41]
Shadkam 2010	40	40	-1.2 (0.345)		40.02%	-1.18[-1.86,-0.5]
Subtotal (95% CI)					**100%**	**-1.05[-1.48,-0.62]**
Heterogeneity: Tau²=0; Chi²=0.23, df=1(P=0.63); I²=0%						
Test for overall effect: Z=4.82(P<0.0001)						
1.3.2 Severity of cough (mean reduction in severity of cough)						
Paul 2007	35	39	-0.7 (0.511)		31.31%	-0.69[-1.69,0.31]
Shadkam 2010	40	40	-1.2 (0.345)		68.69%	-1.18[-1.86,-0.5]
Subtotal (95% CI)					**100%**	**-1.03[-1.59,-0.47]**
Heterogeneity: Tau²=0; Chi²=0.63, df=1(P=0.43); I²=0%						
Test for overall effect: Z=3.59(P=0)						
1.3.3 Bothersome cough (mean reduction in bothersome cough)						
Paul 2007	35	39	-0.9 (0.534)		100%	-0.93[-1.98,0.12]
Subtotal (95% CI)					**100%**	**-0.93[-1.98,0.12]**
Heterogeneity: Not applicable						
Test for overall effect: Z=1.74(P=0.08)						
1.3.4 Children's sleep (mean reduction in cough impact on sleep score)						
Paul 2007	35	39	-0.9 (0.534)		25.89%	-0.92[-1.97,0.13]
Shadkam 2010	40	40	-1.1 (0.316)		74.11%	-1.08[-1.7,-0.46]
Subtotal (95% CI)					**100%**	**-1.04[-1.57,-0.51]**
Heterogeneity: Tau²=0; Chi²=0.07, df=1(P=0.79); I²=0%						
Test for overall effect: Z=3.82(P=0)						
1.3.5 Parents' sleep (mean reduction in cough impact on sleep score)						
Paul 2007	35	39	-0.8 (0.233)		60.6%	-0.8[-1.26,-0.34]
Shadkam 2010	40	40	-1 (0.29)		39.4%	-0.99[-1.56,-0.42]
Subtotal (95% CI)					**100%**	**-0.88[-1.23,-0.52]**
Heterogeneity: Tau²=0; Chi²=0.26, df=1(P=0.61); I²=0%						
Test for overall effect: Z=4.82(P<0.0001)						
1.3.6 Combined reduction in symptoms score						
Paul 2007	35	39	-4.3 (1.256)		100%	-4.31[-6.77,-1.85]
Subtotal (95% CI)					**100%**	**-4.31[-6.77,-1.85]**
Heterogeneity: Not applicable						
Test for overall effect: Z=3.43(P=0)						

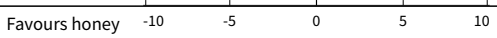


Analysis 1.4. Comparison 1 Pair-wise comparison, Outcome 4 Honey versus placebo (Day 1).

Study or subgroup	Honey N	Placebo N	Mean Difference (SE)	Mean Difference IV, Random, 95% CI	Weight	Mean Difference IV, Random, 95% CI
1.4.1 Frequency of cough (mean reduction in frequency of cough)						

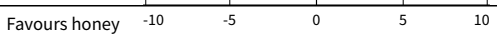


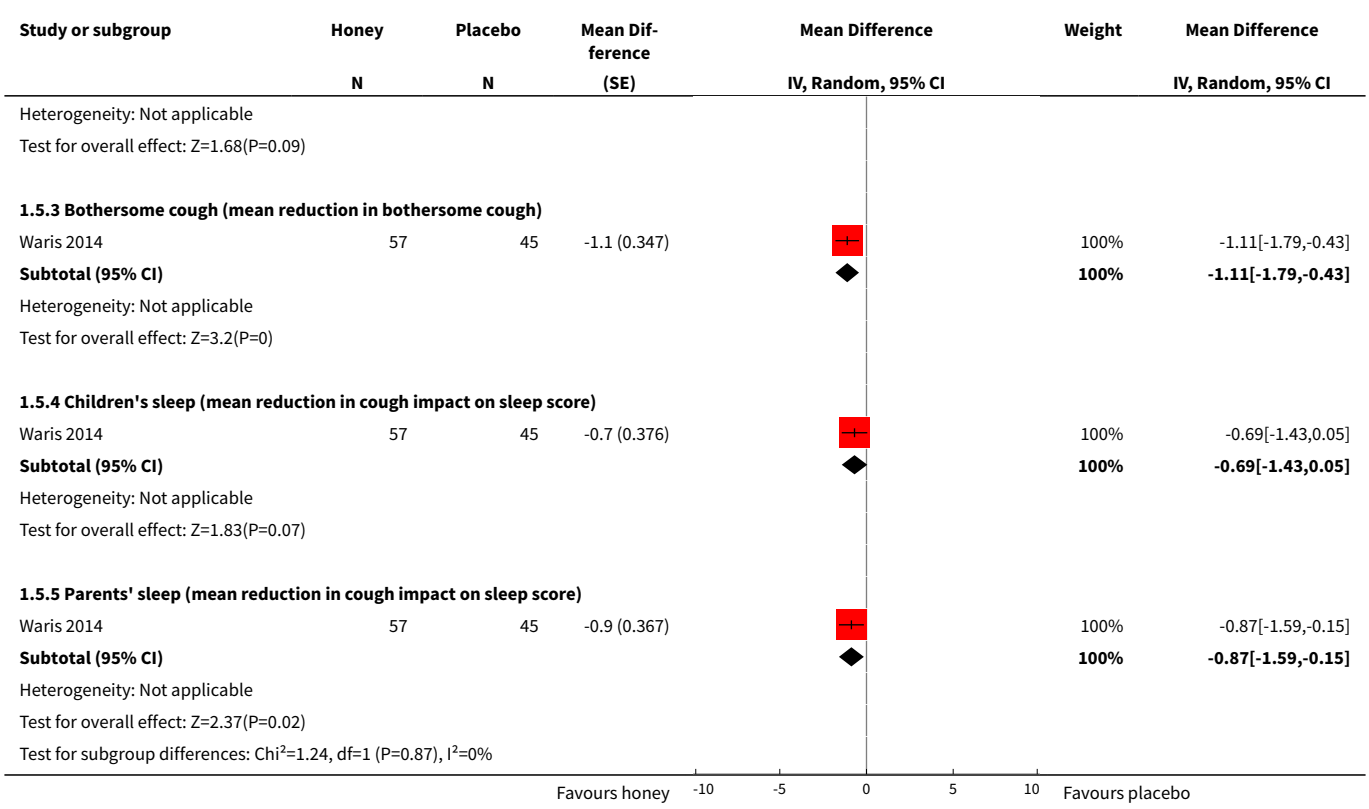
Study or subgroup	Honey N	Placebo N	Mean Difference (SE)	Mean Difference IV, Random, 95% CI	Weight	Mean Difference IV, Random, 95% CI
Cohen 2012	225	75	-1.8 (0.773)		85.36%	-1.85[-3.36,-0.33]
Waris 2014	57	45	-0.3 (1.866)		14.64%	-0.33[-3.99,3.33]
Subtotal (95% CI)					**100%**	**-1.62[-3.02,-0.22]**
Heterogeneity: Tau^2=0; Chi^2=0.56, df=1(P=0.45); I^2=0%						
Test for overall effect: Z=2.27(P=0.02)						
1.4.2 Severity of cough (mean reduction in severity of cough)						
Cohen 2012	225	75	-1.8 (0.761)		45.37%	-1.83[-3.32,-0.34]
Waris 2014	57	45	-0.4 (0.631)		54.63%	-0.43[-1.67,0.81]
Subtotal (95% CI)					**100%**	**-1.07[-2.43,0.3]**
Heterogeneity: Tau^2=0.49; Chi^2=2.01, df=1(P=0.16); I^2=50.14%						
Test for overall effect: Z=1.53(P=0.13)						
1.4.3 Bothersome cough (mean reduction in bothersome cough)						
Cohen 2012	225	75	-2.1 (0.965)		53.34%	-2.08[-3.97,-0.19]
Waris 2014	57	45	-0.6 (1.036)		46.66%	-0.62[-2.65,1.41]
Subtotal (95% CI)					**100%**	**-1.4[-2.82,0.03]**
Heterogeneity: Tau^2=0.06; Chi^2=1.06, df=1(P=0.3); I^2=5.52%						
Test for overall effect: Z=1.92(P=0.05)						
1.4.4 Children's sleep (mean reduction in cough impact on sleep score)						
Cohen 2012	225	75	-1.9 (0.492)		49.04%	-1.94[-2.9,-0.97]
Waris 2014	57	45	-0.5 (0.45)		50.96%	-0.51[-1.39,0.37]
Subtotal (95% CI)					**100%**	**-1.21[-2.61,0.19]**
Heterogeneity: Tau^2=0.8; Chi^2=4.58, df=1(P=0.03); I^2=78.17%						
Test for overall effect: Z=1.7(P=0.09)						
1.4.5 Parents' sleep (mean reduction in cough impact on sleep score)						
Cohen 2012	225	75	-2.1 (0.583)		47.39%	-2.05[-3.2,-0.91]
Waris 2014	57	45	-0.6 (0.479)		52.61%	-0.6[-1.54,0.34]
Subtotal (95% CI)					**100%**	**-1.29[-2.71,0.13]**
Heterogeneity: Tau^2=0.77; Chi^2=3.71, df=1(P=0.05); I^2=73.08%						
Test for overall effect: Z=1.78(P=0.08)						



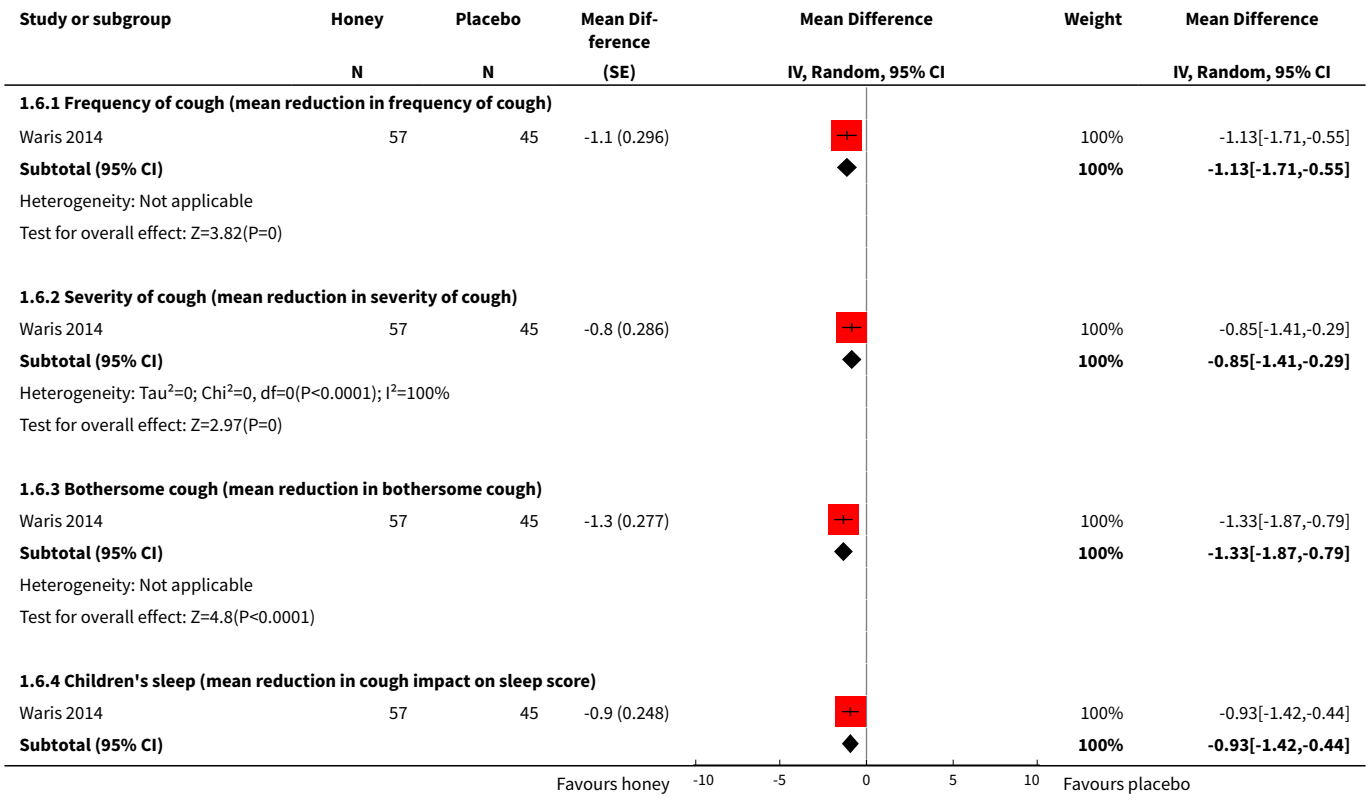
Analysis 1.5. Comparison 1 Pair-wise comparison, Outcome 5 Honey versus placebo (Day 2).

Study or subgroup	Honey N	Placebo N	Mean Difference (SE)	Mean Difference IV, Random, 95% CI	Weight	Mean Difference IV, Random, 95% CI
1.5.1 Frequency of cough (mean reduction in frequency of cough)						
Waris 2014	57	45	-0.7 (0.26)		100%	-0.71[-1.22,-0.2]
Subtotal (95% CI)					**100%**	**-0.71[-1.22,-0.2]**
Heterogeneity: Not applicable						
Test for overall effect: Z=2.73(P=0.01)						
1.5.2 Severity of cough (mean reduction in severity of cough)						
Waris 2014	57	45	-0.6 (0.374)		100%	-0.63[-1.36,0.1]
Subtotal (95% CI)					**100%**	**-0.63[-1.36,0.1]**





Analysis 1.6. Comparison 1 Pair-wise comparison, Outcome 6 Honey versus placebo (Day 3).



Study or subgroup	Honey N	Placebo N	Mean Difference (SE)	Mean Difference IV, Random, 95% CI	Weight	Mean Difference IV, Random, 95% CI
Heterogeneity: Not applicable						
Test for overall effect: Z=3.75(P=0)						
1.6.5 Parents' sleep (mean reduction in cough impact on sleep score)						
Waris 2014	57	45	-0.9 (0.253)		100%	-0.88[-1.38,-0.38]
Subtotal (95% CI)					**100%**	**-0.88[-1.38,-0.38]**
Heterogeneity: Not applicable						
Test for overall effect: Z=3.48(P=0)						
Test for subgroup differences: Chi^2=2.18, df=1 (P=0.7), I^2=0%						

Favours honey -10 -5 0 5 10 Favours placebo

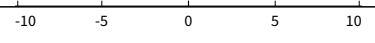
Analysis 1.7. Comparison 1 Pair-wise comparison, Outcome 7 Honey versus placebo (Day 4).

Study or subgroup	Honey N	Placebo N	Mean Difference (SE)	Mean Difference IV, Random, 95% CI	Weight	Mean Difference IV, Random, 95% CI
1.7.1 Frequency of cough (mean reduction in frequency of cough)						
Waris 2014	57	45	-1.2 (0.342)		100%	-1.16[-1.83,-0.49]
Subtotal (95% CI)					**100%**	**-1.16[-1.83,-0.49]**
Heterogeneity: Not applicable						
Test for overall effect: Z=3.39(P=0)						
1.7.2 Severity of cough (mean reduction in severity of cough)						
Waris 2014	57	45	-0.9 (0.363)		100%	-0.88[-1.59,-0.17]
Subtotal (95% CI)					**100%**	**-0.88[-1.59,-0.17]**
Heterogeneity: Not applicable						
Test for overall effect: Z=2.43(P=0.02)						
1.7.3 Bothersome cough (mean reduction in bothersome cough)						
Waris 2014	57	45	-0.9 (0.441)		100%	-0.9[-1.76,-0.04]
Subtotal (95% CI)					**100%**	**-0.9[-1.76,-0.04]**
Heterogeneity: Tau^2=0; Chi^2=0, df=0(P<0.0001); I^2=100%						
Test for overall effect: Z=2.04(P=0.04)						
1.7.4 Children's sleep (mean reduction in cough impact on sleep score)						
Waris 2014	57	45	-0.7 (0.283)		100%	-0.7[-1.25,-0.15]
Subtotal (95% CI)					**100%**	**-0.7[-1.25,-0.15]**
Heterogeneity: Not applicable						
Test for overall effect: Z=2.48(P=0.01)						
1.7.5 Parents' sleep (mean reduction in cough impact on sleep score)						
Waris 2014	57	45	-0.9 (0.314)		100%	-0.9[-1.51,-0.29]
Subtotal (95% CI)					**100%**	**-0.9[-1.51,-0.29]**
Heterogeneity: Tau^2=0; Chi^2=0, df=0(P<0.0001); I^2=100%						
Test for overall effect: Z=2.87(P=0)						
Test for subgroup differences: Chi^2=1.08, df=1 (P=0.9), I^2=0%						

Favours honey -10 -5 0 5 10 Favours placebo

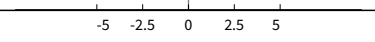
Analysis 1.8. Comparison 1 Pair-wise comparison, Outcome 8 Honey versus placebo (Day 5).

Study or subgroup	Honey N	Placebo N	Mean Difference (SE)	Mean Difference IV, Random, 95% CI	Weight	Mean Difference IV, Random, 95% CI
1.8.1 Cough duration (mean number of days)						
Waris 2014	57	45	-0.7 (0.302)		100%	-0.72[-1.31,-0.13]
Subtotal (95% CI)					**100%**	**-0.72[-1.31,-0.13]**
Heterogeneity: Not applicable						
Test for overall effect: Z=2.38(P=0.02)						
1.8.2 Frequency of cough (mean reduction in frequency of cough)						
Waris 2014	57	45	-0.5 (1.26)		100%	-0.48[-2.95,1.99]
Subtotal (95% CI)					**100%**	**-0.48[-2.95,1.99]**
Heterogeneity: Not applicable						
Test for overall effect: Z=0.38(P=0.7)						
1.8.3 Severity of cough (mean reduction in severity of cough)						
Waris 2014	57	45	-0.4 (0.907)		100%	-0.43[-2.21,1.35]
Subtotal (95% CI)					**100%**	**-0.43[-2.21,1.35]**
Heterogeneity: Not applicable						
Test for overall effect: Z=0.47(P=0.64)						
1.8.4 Bothersome cough (mean reduction in bothersome cough)						
Waris 2014	57	45	-0.5 (1.275)		100%	-0.51[-3.01,1.99]
Subtotal (95% CI)					**100%**	**-0.51[-3.01,1.99]**
Heterogeneity: Not applicable						
Test for overall effect: Z=0.4(P=0.69)						
1.8.5 Children's sleep (mean reduction in cough impact on sleep score)						
Waris 2014	57	45	-0.5 (0.631)		100%	-0.55[-1.79,0.69]
Subtotal (95% CI)					**100%**	**-0.55[-1.79,0.69]**
Heterogeneity: Not applicable						
Test for overall effect: Z=0.87(P=0.38)						
1.8.6 Parents' sleep (mean reduction in cough impact on sleep score)						
Waris 2014	57	45	-0.6 (0.523)		100%	-0.57[-1.59,0.45]
Subtotal (95% CI)					**100%**	**-0.57[-1.59,0.45]**
Heterogeneity: Not applicable						
Test for overall effect: Z=1.09(P=0.28)						
Test for subgroup differences: Chi^2=0.19, df=1 (P=1), I^2=0%						

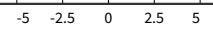


Analysis 1.9. Comparison 1 Pair-wise comparison, Outcome 9 Honey versus salbutamol (Day 1).

Study or subgroup	Honey N	Salbutamol N	Mean Difference (SE)	Mean Difference IV, Random, 95% CI	Weight	Mean Difference IV, Random, 95% CI
1.9.1 Frequency of cough (mean reduction in frequency of cough)						
Waris 2014	57	43	-0.3 (1.47)		100%	-0.26[-3.14,2.62]
Subtotal (95% CI)					**100%**	**-0.26[-3.14,2.62]**
Heterogeneity: Not applicable						



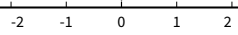
Study or subgroup	Honey N	Salbutamol N	Mean Difference (SE)	Mean Difference IV, Random, 95% CI	Weight	Mean Difference IV, Random, 95% CI
Test for overall effect: Z=0.18(P=0.86)						
1.9.2 Severity of cough (mean reduction in severity of cough)						
Waris 2014	57	43	-0.1 (0.147)		100%	-0.1[-0.39,0.19]
Subtotal (95% CI)					**100%**	**-0.1[-0.39,0.19]**
Heterogeneity: Not applicable						
Test for overall effect: Z=0.68(P=0.5)						
1.9.3 Bothersome cough (mean reduction in bothersome cough)						
Waris 2014	57	43	-0.2 (0.351)		100%	-0.21[-0.9,0.48]
Subtotal (95% CI)					**100%**	**-0.21[-0.9,0.48]**
Heterogeneity: Not applicable						
Test for overall effect: Z=0.6(P=0.55)						
1.9.4 Children's sleep (mean reduction in cough impact on sleep score)						
Waris 2014	57	43	0.1 (0.072)		100%	0.09[-0.05,0.23]
Subtotal (95% CI)					**100%**	**0.09[-0.05,0.23]**
Heterogeneity: Tau^2=0; Chi^2=0, df=0(P<0.0001); I^2=100%						
Test for overall effect: Z=1.24(P=0.21)						
1.9.5 Parents' sleep (mean reduction in cough impact on sleep score)						
Waris 2014	57	43	0.1 (0.04)		100%	0.05[-0.03,0.13]
Subtotal (95% CI)					**100%**	**0.05[-0.03,0.13]**
Heterogeneity: Not applicable						
Test for overall effect: Z=1.25(P=0.21)						
Test for subgroup differences: Chi^2=1.94, df=1 (P=0.75), I^2=0%						



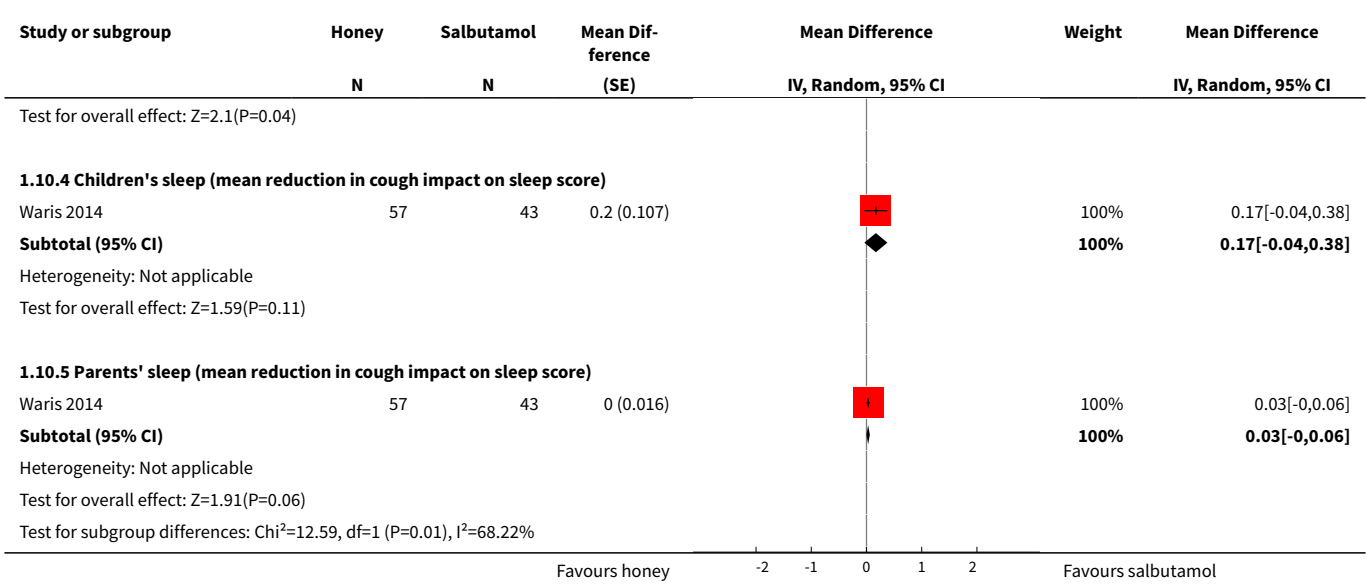
Favours honey | Favours salbutamol

Analysis 1.10. Comparison 1 Pair-wise comparison, Outcome 10 Honey versus salbutamol (Day 2).

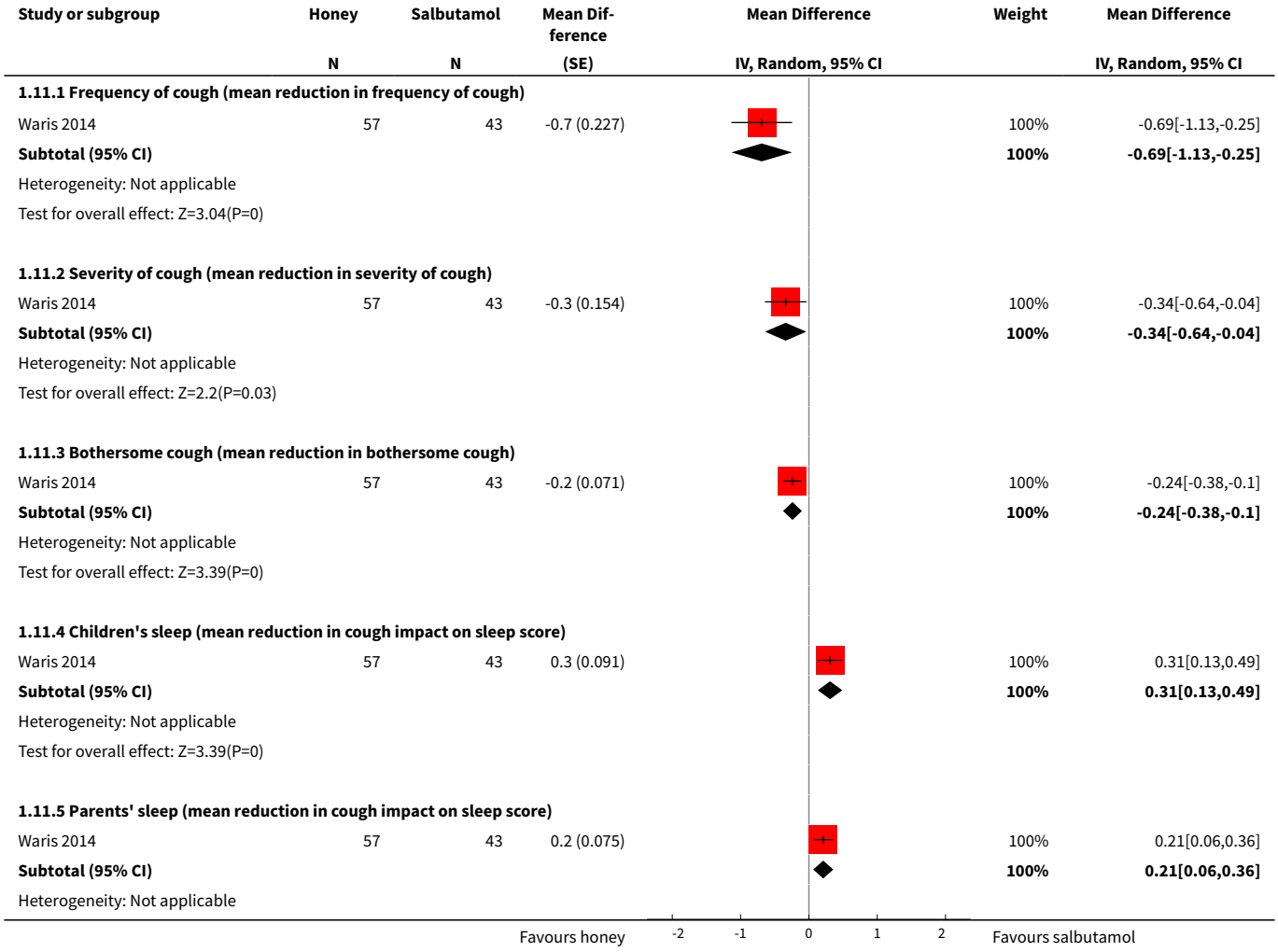
Study or subgroup	Honey N	Salbutamol N	Mean Difference (SE)	Mean Difference IV, Random, 95% CI	Weight	Mean Difference IV, Random, 95% CI
1.10.1 Frequency of cough (mean reduction in frequency of cough)						
Waris 2014	57	43	-0.7 (0.348)		100%	-0.67[-1.35,0.01]
Subtotal (95% CI)					**100%**	**-0.67[-1.35,0.01]**
Heterogeneity: Not applicable						
Test for overall effect: Z=1.93(P=0.05)						
1.10.2 Severity of cough (mean reduction in severity of cough)						
Waris 2014	57	43	-0.4 (0.379)		100%	-0.42[-1.16,0.32]
Subtotal (95% CI)					**100%**	**-0.42[-1.16,0.32]**
Heterogeneity: Tau^2=0; Chi^2=0, df=0(P<0.0001); I^2=100%						
Test for overall effect: Z=1.11(P=0.27)						
1.10.3 Bothersome cough (mean reduction in bothersome cough)						
Waris 2014	57	43	-0.3 (0.128)		100%	-0.27[-0.52,-0.02]
Subtotal (95% CI)					**100%**	**-0.27[-0.52,-0.02]**
Heterogeneity: Not applicable						

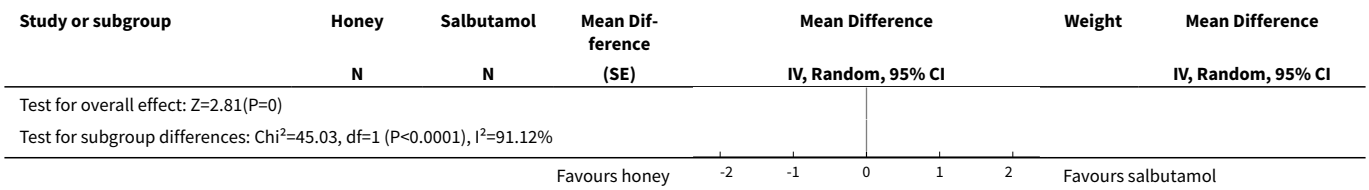


Favours honey | Favours salbutamol

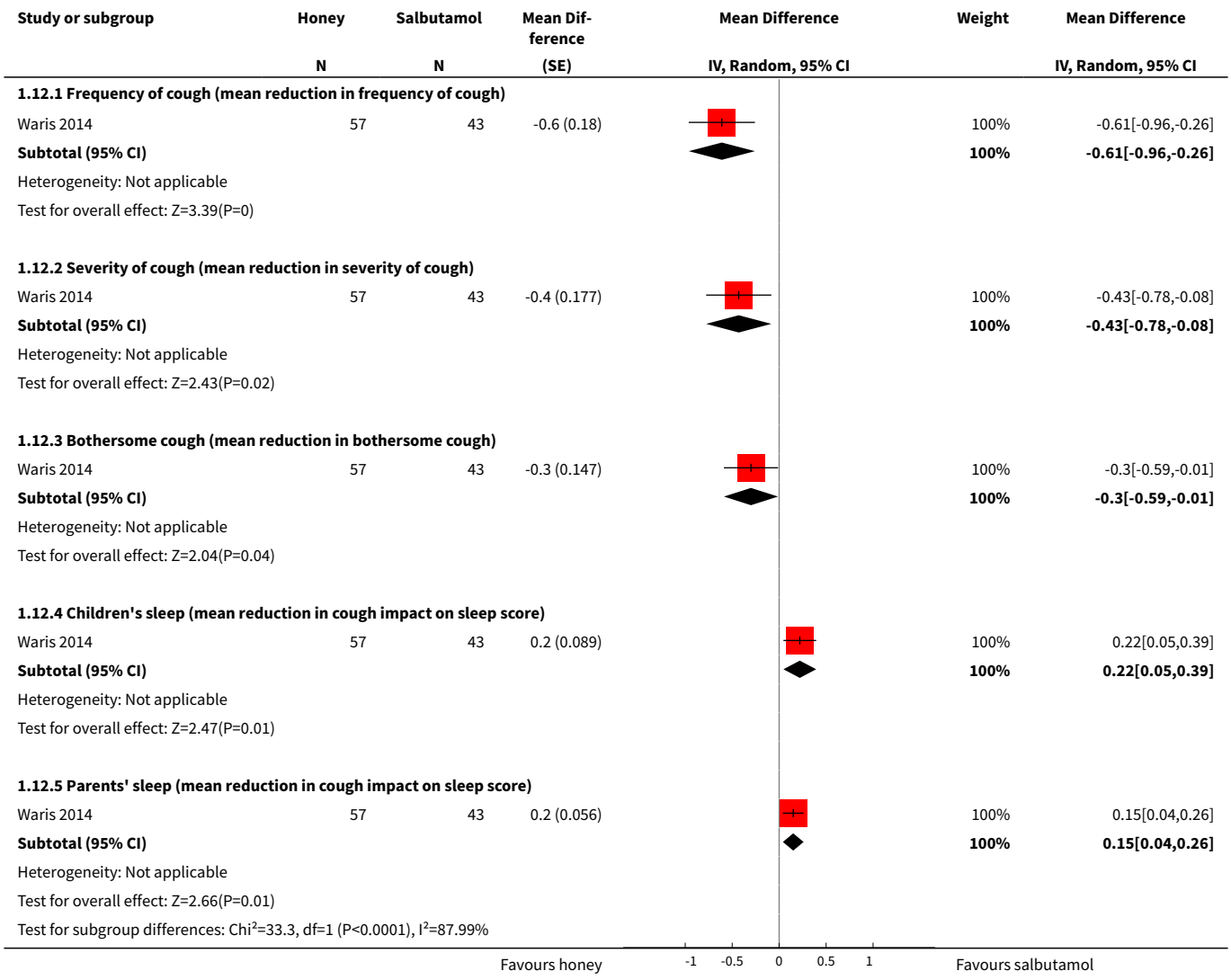


Analysis 1.11. Comparison 1 Pair-wise comparison, Outcome 11 Honey versus salbutamol (Day 3).

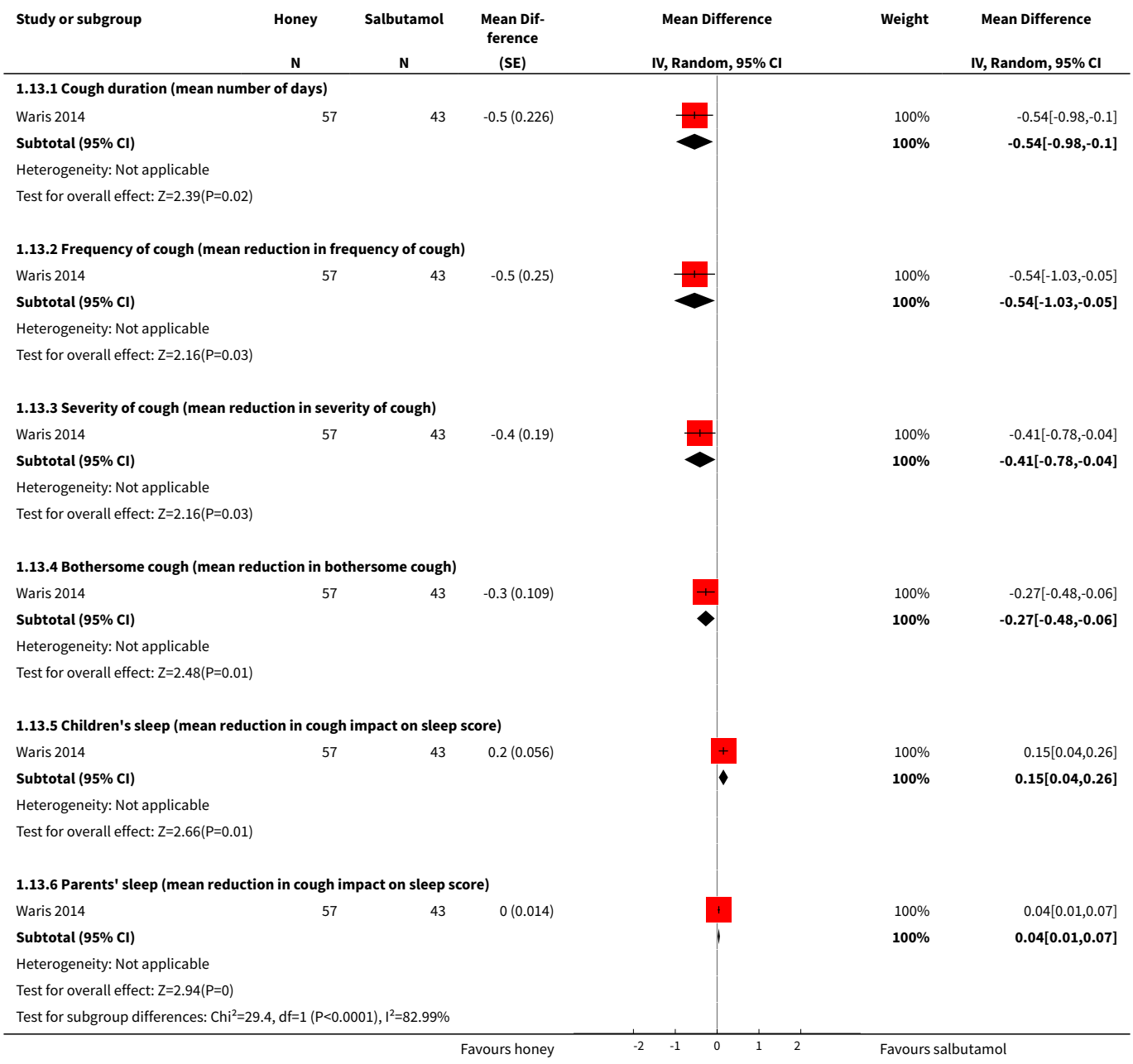




Analysis 1.12. Comparison 1 Pair-wise comparison, Outcome 12 Honey versus salbutamol (Day 4).



Analysis 1.13. Comparison 1 Pair-wise comparison, Outcome 13 Honey versus salbutamol (Day 5).



Comparison 2. Pre- and postintervention comparison

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Cough frequency (mean reduction in frequency)	4		Mean Difference (Fixed, 95% CI)	Subtotals only
1.1 Honey	4	357	Mean Difference (Fixed, 95% CI)	-1.71 [-2.28, -1.13]

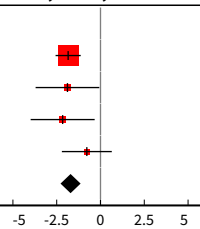
Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1.2 Dextromethorphan	2	74	Mean Difference (Fixed, 95% CI)	-1.54 [-2.30, -0.78]
1.3 Diphenhydramine	1	40	Mean Difference (Fixed, 95% CI)	-1.73 [-2.72, -0.74]
1.4 Placebo	2	120	Mean Difference (Fixed, 95% CI)	-0.99 [-1.79, -0.18]
1.5 Salbutamol Day 1	1	43	Mean Difference (Fixed, 95% CI)	-0.52 [-6.28, 5.24]
1.6 No treatment	2	79	Mean Difference (Fixed, 95% CI)	-0.98 [-1.38, -0.59]
1.7 Buckwheat honey	1	35	Mean Difference (Fixed, 95% CI)	-1.89 [-2.96, -0.81]
1.8 Natural honey from Kafi-Abad (Iran)	1	40	Mean Difference (Fixed, 95% CI)	-2.16 [-3.40, -0.92]
1.9 Eucalyptus honey	1	75	Mean Difference (Fixed, 95% CI)	-1.77 [-3.22, -0.32]
1.10 Labiatae honey	1	75	Mean Difference (Fixed, 95% CI)	-1.82 [-3.30, -0.34]
1.11 Citrus honey	1	75	Mean Difference (Fixed, 95% CI)	-1.95 [-3.55, -0.35]
1.12 Salbutamol Day 5	1	43	Mean Difference (Fixed, 95% CI)	-2.19 [-3.55, -0.83]
1.13 African honey Day 5	1	57	Mean Difference (Fixed, 95% CI)	-2.65 [-4.32, -0.98]
1.14 Placebo Day 5	1	45	Mean Difference (Fixed, 95% CI)	-1.95 [-4.42, 0.52]
2 Severity of cough (mean reduction in severity)	4		Mean Difference (Fixed, 95% CI)	Subtotals only
2.1 Honey	4	357	Mean Difference (Fixed, 95% CI)	-1.65 [-2.39, -0.91]
2.2 Dextromethorphan	2	74	Mean Difference (Fixed, 95% CI)	-1.52 [-2.24, -0.80]
2.3 Diphenhydramine	1	40	Mean Difference (Fixed, 95% CI)	-1.83 [-2.88, -0.78]
2.4 Salbutamol Day 1	1	43	Mean Difference (Fixed, 95% CI)	-0.74 [-2.87, 1.39]
2.5 No treatment	2	79	Mean Difference (Fixed, 95% CI)	-1.13 [-1.54, -0.72]
2.6 Placebo	2	120	Mean Difference (Fixed, 95% CI)	-0.80 [-1.47, -0.13]
2.7 Buckwheat honey	1	35	Mean Difference (Fixed, 95% CI)	-1.80 [-2.88, -0.72]
2.8 Natural honey from Kafi-Abad (Iran)	1	40	Mean Difference (Fixed, 95% CI)	-2.33 [-3.67, -0.99]
2.9 Eucalyptus honey	1	75	Mean Difference (Fixed, 95% CI)	-1.78 [-2.82, -0.74]
2.10 Labiatae honey	1	75	Mean Difference (Fixed, 95% CI)	-1.94 [-3.07, -0.81]
2.11 Citrus honey	1	75	Mean Difference (Fixed, 95% CI)	-1.77 [-2.74, -0.80]

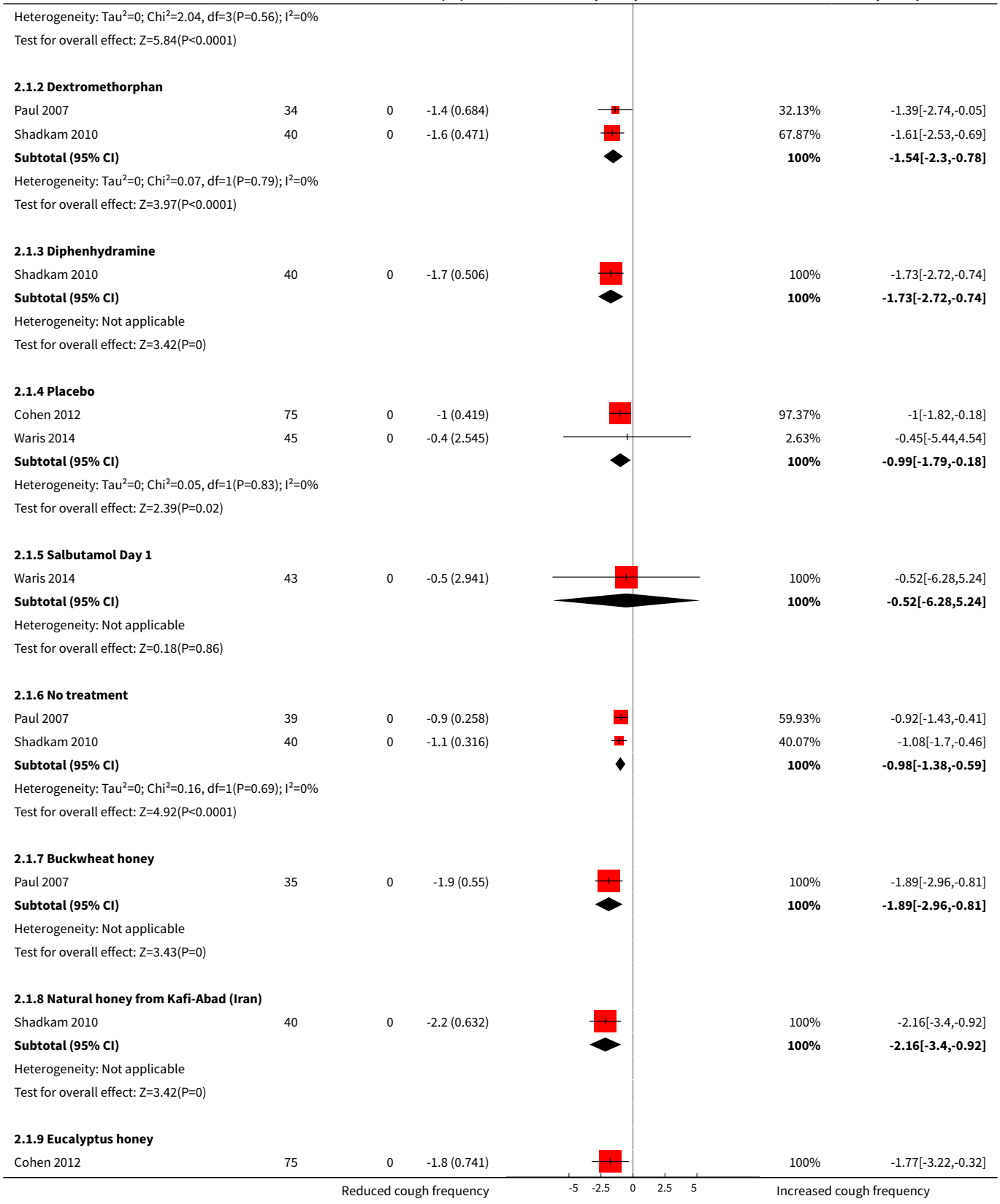
Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
2.12 Salbutamol Day 5	1	43	Mean Difference (Fixed, 95% CI)	-2.08 [-4.21, 0.05]
2.13 African honey Day 5	1	57	Mean Difference (Fixed, 95% CI)	-2.62 [-5.04, -0.20]
2.14 Placebo Day 5	1	45	Mean Difference (Fixed, 95% CI)	-1.96 [-3.74, -0.18]
3 Bothersome cough (mean reduction in bothersome cough)	3		Mean Difference (Fixed, 95% CI)	Subtotals only
3.1 Honey	3	317	Mean Difference (Fixed, 95% CI)	-2.22 [-3.24, -1.21]
3.2 Dextromethorphan	1	34	Mean Difference (Fixed, 95% CI)	-1.94 [-3.05, -0.83]
3.3 Salbutamol Day 1	1	43	Mean Difference (Fixed, 95% CI)	-1.0 [-4.28, 2.28]
3.4 No treatment	1	39	Mean Difference (Fixed, 95% CI)	-1.30 [-2.07, -0.53]
3.5 Placebo	2	120	Mean Difference (Fixed, 95% CI)	-1.08 [-2.06, -0.10]
3.6 Buckwheat honey	1	35	Mean Difference (Fixed, 95% CI)	-2.23 [-3.50, -0.96]
3.7 Eucalyptus honey	1	75	Mean Difference (Fixed, 95% CI)	-2.0 [-3.82, -0.18]
3.8 Labiatae honey	1	75	Mean Difference (Fixed, 95% CI)	-2.07 [-4.03, -0.11]
3.9 Citrus honey	1	75	Mean Difference (Fixed, 95% CI)	-2.16 [-4.20, -0.12]
3.10 Salbutamol Day 5	1	43	Mean Difference (Fixed, 95% CI)	-2.47 [-4.73, -0.21]
3.11 African honey Day 5	1	57	Mean Difference (Fixed, 95% CI)	-2.74 [-5.27, -0.21]
3.12 Placebo Day 5	1	45	Mean Difference (Fixed, 95% CI)	-1.85 [-3.56, -0.14]
4 Children's sleep (mean reduction in cough impact on sleep score)	4		Mean Difference (Random, 95% CI)	Subtotals only
4.1 Honey	4	357	Mean Difference (Random, 95% CI)	-2.23 [-2.87, -1.59]
4.2 Dextromethorphan	2	74	Mean Difference (Random, 95% CI)	-1.75 [-2.46, -1.04]
4.3 Diphenhydramine	1	40	Mean Difference (Random, 95% CI)	-1.64 [-2.58, -0.70]
4.4 No treatment	2	79	Mean Difference (Random, 95% CI)	-1.28 [-1.81, -0.76]
4.5 Placebo	2	120	Mean Difference (Random, 95% CI)	-1.03 [-2.05, 0.00]
4.6 Salbutamol Day 5	1	43	Mean Difference (Random, 95% CI)	-2.47 [-3.84, -1.10]
4.7 African honey Day 5	1	57	Mean Difference (Random, 95% CI)	-2.32 [-3.63, -1.01]
4.8 Placebo Day 5	1	45	Mean Difference (Random, 95% CI)	-1.68 [-2.63, -0.73]

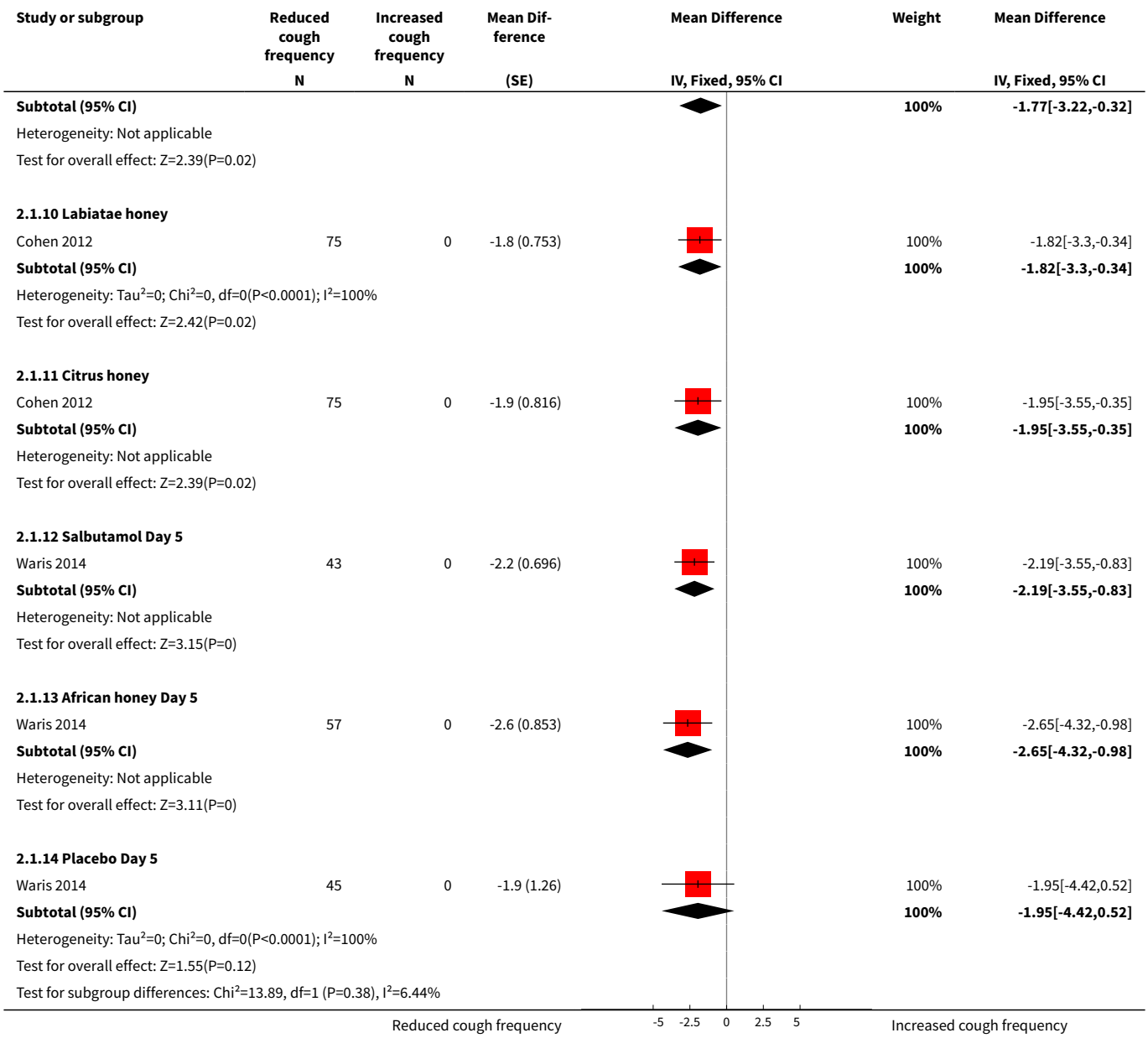
Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
5 Parents' sleep (mean reduction in cough impact on sleep score)	4		Mean Difference (Fixed, 95% CI)	Subtotals only
5.1 Honey	4	357	Mean Difference (Fixed, 95% CI)	-2.25 [-2.89, -1.61]
5.2 Dextromethorphan	2	74	Mean Difference (Fixed, 95% CI)	-1.97 [-2.77, -1.17]
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)	-1.46 [-2.06, -0.87]
5.5 Placebo	2	120	Mean Difference (Fixed, 95% CI)	-1.44 [-2.28, -0.61]
5.6 Salbutamol Day 5	1	43	Mean Difference (Fixed, 95% CI)	-2.33 [-3.91, -0.75]
5.7 African honey Day 5	1	57	Mean Difference (Fixed, 95% CI)	-2.29 [-3.86, -0.72]
5.8 Placebo Day 5	1	45	Mean Difference (Fixed, 95% CI)	-1.54 [-2.60, -0.48]
6 Combined reduction in symptoms score	3		Mean Difference (Fixed, 95% CI)	Subtotals only
6.1 Honey	3	317	Mean Difference (Fixed, 95% CI)	-10.60 [-14.43, -6.77]
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]
6.4 Placebo	2	132	Mean Difference (Fixed, 95% CI)	-7.11 [-10.78, -3.44]
6.5 Honey Day 5	1	57	Mean Difference (Fixed, 95% CI)	-12.68 [-14.06, -11.30]
6.6 Placebo Day 5	1	45	Mean Difference (Fixed, 95% CI)	-8.69 [-14.17, -3.21]
6.7 Salbutamol Day 5	1	43	Mean Difference (Fixed, 95% CI)	-11.37 [-17.55, -5.19]

Analysis 2.1. Comparison 2 Pre- and postintervention comparison, Outcome 1 Cough frequency (mean reduction in frequency).

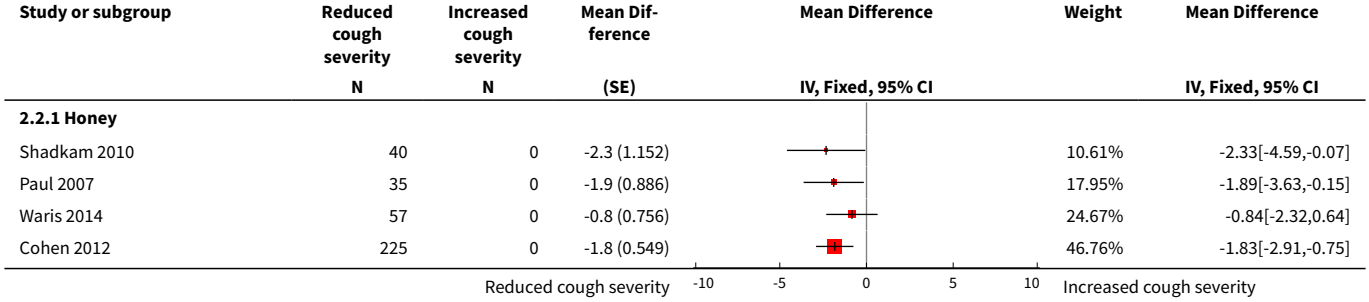
Study or subgroup	Reduced cough frequency N	Increased cough frequency N	Mean Difference (SE)	Mean Difference IV, Fixed, 95% CI	Weight	Mean Difference IV, Fixed, 95% CI
2.1.1 Honey						
Cohen 2012	225	0	-1.8 (0.366)		63.98%	-1.85[-2.56,-1.13]
Paul 2007	35	0	-1.9 (0.928)		9.95%	-1.89[-3.7,-0.07]
Shadkam 2010	40	0	-2.2 (0.932)		9.86%	-2.16[-3.99,-0.33]
Waris 2014	57	0	-0.8 (0.727)		16.21%	-0.78[-2.21,0.65]
Subtotal (95% CI)					**100%**	**-1.71[-2.28,-1.13]**



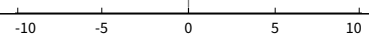




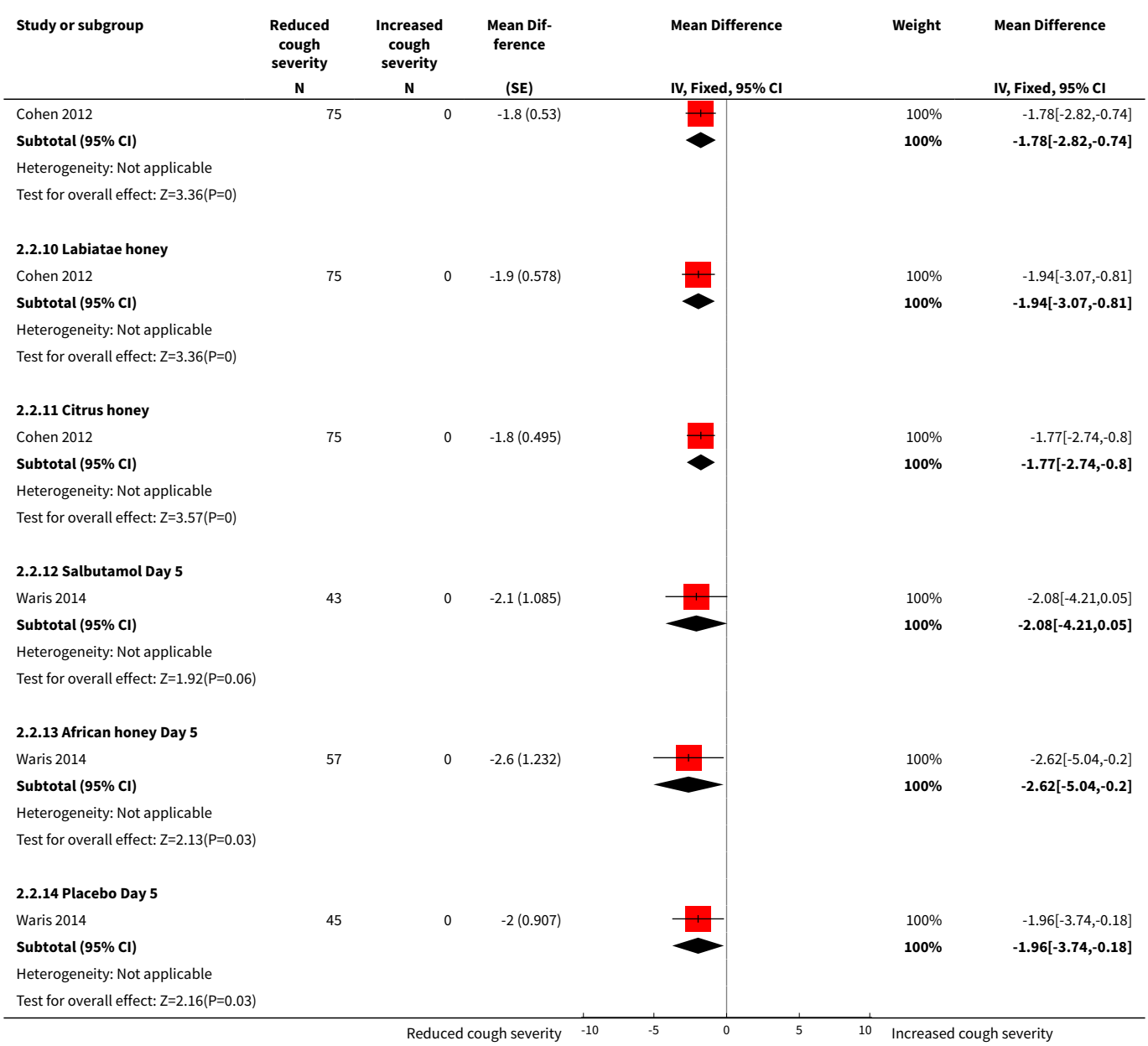
Analysis 2.2. Comparison 2 Pre- and postintervention comparison, Outcome 2 Severity of cough (mean reduction in severity).



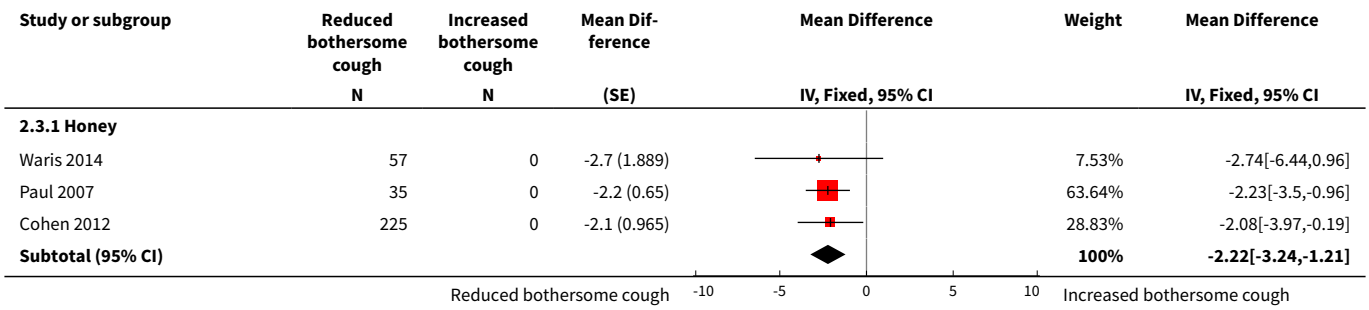
Study or subgroup	Reduced cough severity N	Increased cough severity N	Mean Difference (SE)	Mean Difference IV, Fixed, 95% CI	Weight	Mean Difference IV, Fixed, 95% CI
Subtotal (95% CI)					**100%**	**-1.65[-2.39,-0.91]**
Heterogeneity: Tau²=0; Chi²=1.68, df=3(P=0.64); I²=0%						
Test for overall effect: Z=4.4(P<0.0001)						
2.2.2 Dextromethorphan						
Paul 2007	34	0	-1.3 (0.549)		45.02%	-1.3[-2.38,-0.23]
Shadkam 2010	40	0	-1.7 (0.497)		54.98%	-1.7[-2.67,-0.73]
Subtotal (95% CI)					**100%**	**-1.52[-2.24,-0.8]**
Heterogeneity: Tau²=0; Chi²=0.29, df=1(P=0.59); I²=0%						
Test for overall effect: Z=4.13(P<0.0001)						
2.2.3 Diphenhydramine						
Shadkam 2010	40	0	-1.8 (0.535)		100%	-1.83[-2.88,-0.78]
Subtotal (95% CI)					**100%**	**-1.83[-2.88,-0.78]**
Heterogeneity: Not applicable						
Test for overall effect: Z=3.42(P=0)						
2.2.4 Salbutamol Day 1						
Waris 2014	43	0	-0.7 (1.085)		100%	-0.74[-2.87,1.39]
Subtotal (95% CI)					**100%**	**-0.74[-2.87,1.39]**
Heterogeneity: Not applicable						
Test for overall effect: Z=0.68(P=0.5)						
2.2.5 No treatment						
Shadkam 2010	40	0	-1.2 (0.342)		38%	-1.17[-1.84,-0.5]
Paul 2007	39	0	-1.1 (0.268)		62%	-1.11[-1.63,-0.58]
Subtotal (95% CI)					**100%**	**-1.13[-1.54,-0.72]**
Heterogeneity: Tau²=0; Chi²=0.02, df=1(P=0.89); I²=0%						
Test for overall effect: Z=5.37(P<0.0001)						
2.2.6 Placebo						
Waris 2014	45	0	-0.4 (0.601)		32.63%	-0.41[-1.59,0.77]
Cohen 2012	75	0	-1 (0.419)		67.37%	-0.99[-1.81,-0.17]
Subtotal (95% CI)					**100%**	**-0.8[-1.47,-0.13]**
Heterogeneity: Tau²=0; Chi²=0.63, df=1(P=0.43); I²=0%						
Test for overall effect: Z=2.33(P=0.02)						
2.2.7 Buckwheat honey						
Paul 2007	35	0	-1.8 (0.55)		100%	-1.8[-2.88,-0.72]
Subtotal (95% CI)					**100%**	**-1.8[-2.88,-0.72]**
Heterogeneity: Tau²=0; Chi²=0, df=0(P<0.0001); I²=100%						
Test for overall effect: Z=3.27(P=0)						
2.2.8 Natural honey from Kafi-Abad (Iran)						
Shadkam 2010	40	0	-2.3 (0.681)		100%	-2.33[-3.67,-0.99]
Subtotal (95% CI)					**100%**	**-2.33[-3.67,-0.99]**
Heterogeneity: Not applicable						
Test for overall effect: Z=3.42(P=0)						
2.2.9 Eucalyptus honey						

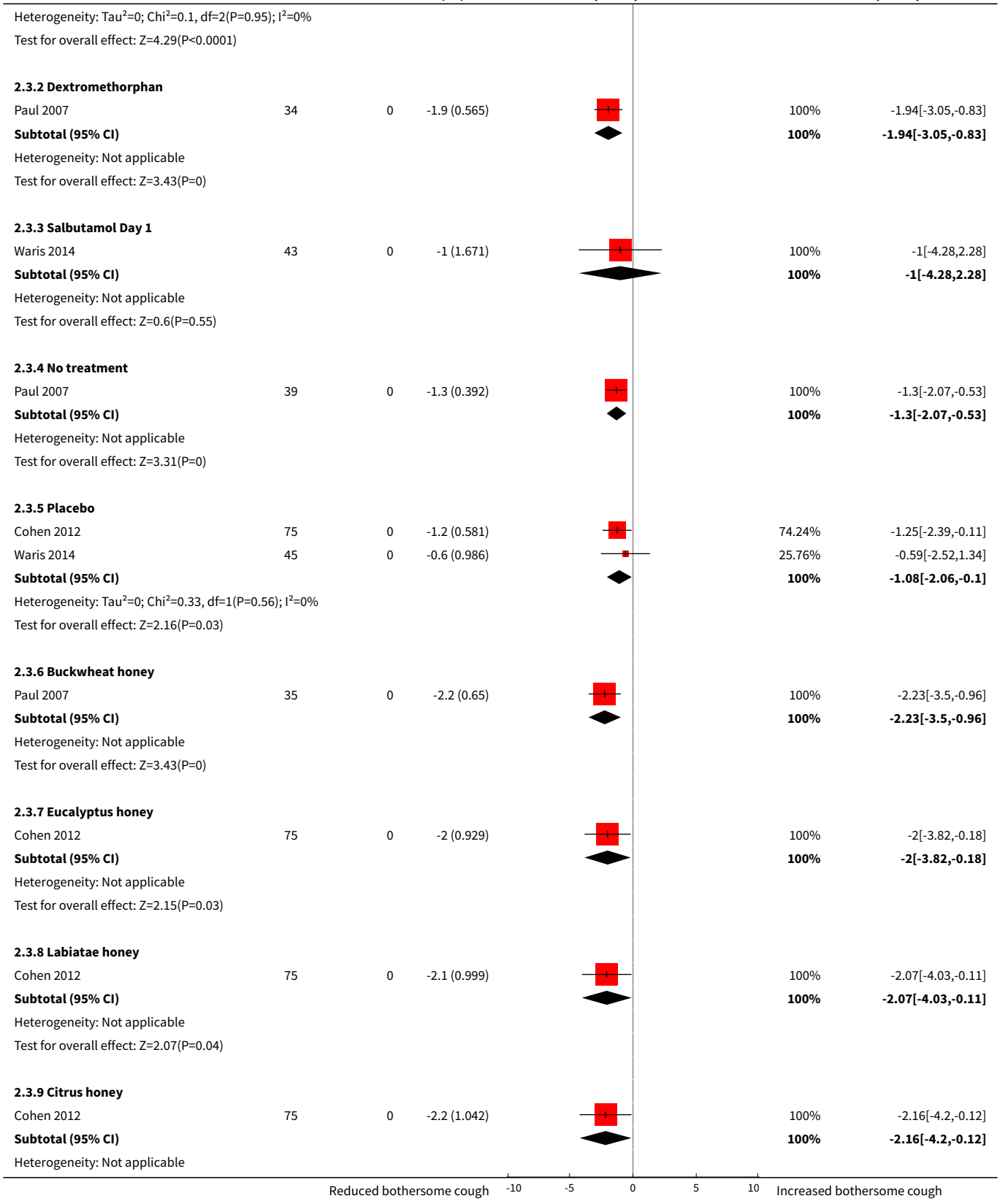


Reduced cough severity — Increased cough severity

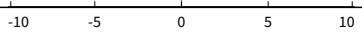


Analysis 2.3. Comparison 2 Pre- and postintervention comparison, Outcome 3 Bothersome cough (mean reduction in bothersome cough).



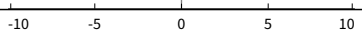


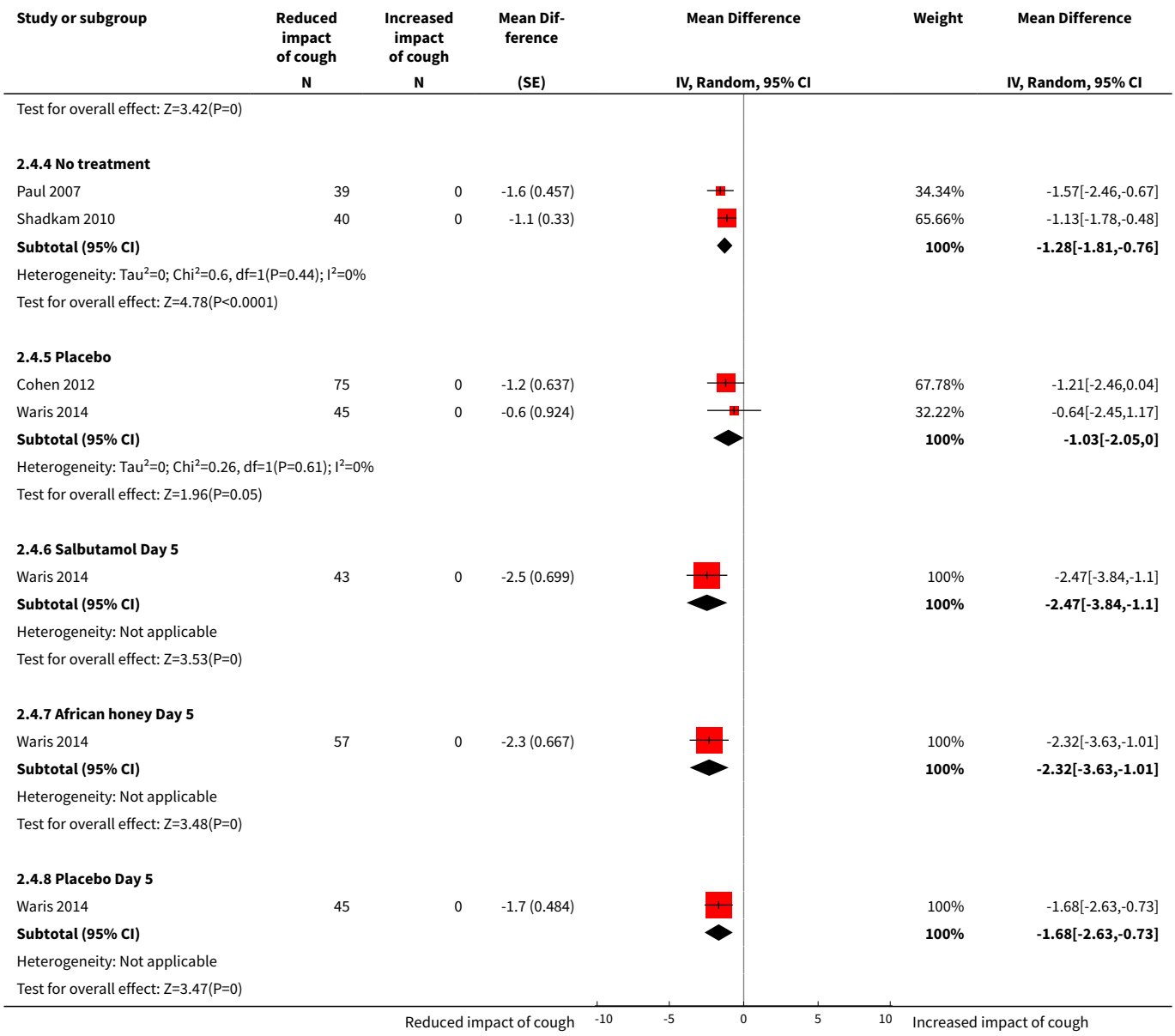
Study or subgroup	Reduced bothersome cough N	Increased bothersome cough N	Mean Difference (SE)	Mean Difference IV, Fixed, 95% CI	Weight	Mean Difference IV, Fixed, 95% CI
Test for overall effect: Z=2.07(P=0.04)						
2.3.10 Salbutamol Day 5						
Waris 2014	43	0	-2.5 (1.154)		100%	-2.47[-4.73,-0.21]
Subtotal (95% CI)					**100%**	**-2.47[-4.73,-0.21]**
Heterogeneity: Not applicable						
Test for overall effect: Z=2.14(P=0.03)						
2.3.11 African honey Day 5						
Waris 2014	57	0	-2.7 (1.289)		100%	-2.74[-5.27,-0.21]
Subtotal (95% CI)					**100%**	**-2.74[-5.27,-0.21]**
Heterogeneity: Not applicable						
Test for overall effect: Z=2.13(P=0.03)						
2.3.12 Placebo Day 5						
Waris 2014	45	0	-1.8 (0.871)		100%	-1.85[-3.56,-0.14]
Subtotal (95% CI)					**100%**	**-1.85[-3.56,-0.14]**
Heterogeneity: Not applicable						
Test for overall effect: Z=2.12(P=0.03)						



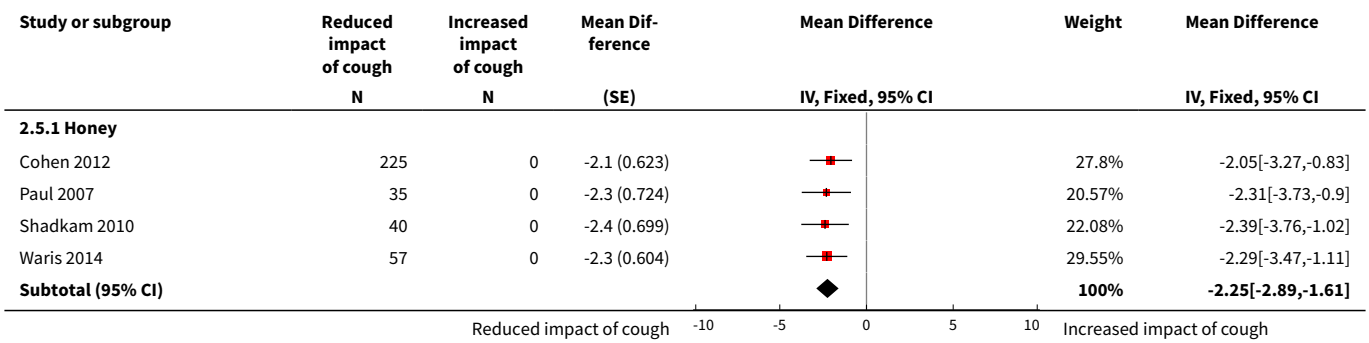
Analysis 2.4. Comparison 2 Pre- and postintervention comparison, Outcome 4 Children's sleep (mean reduction in cough impact on sleep score).

Study or subgroup	Reduced impact of cough N	Increased impact of cough N	Mean Difference (SE)	Mean Difference IV, Random, 95% CI	Weight	Mean Difference IV, Random, 95% CI
2.4.1 Honey						
Paul 2007	35	0	-2.5 (0.724)		20.14%	-2.49[-3.9,-1.07]
Waris 2014	57	0	-2.3 (0.604)		28.94%	-2.32[-3.5,-1.14]
Shadkam 2010	40	0	-2.2 (0.667)		23.71%	-2.24[-3.55,-0.93]
Cohen 2012	225	0	-1.9 (0.623)		27.22%	-1.94[-3.16,-0.72]
Subtotal (95% CI)					**100%**	**-2.23[-2.87,-1.59]**
Heterogeneity: Tau^2=0; Chi^2=0.37, df=3(P=0.95); I^2=0%						
Test for overall effect: Z=6.86(P<0.0001)						
2.4.2 Dextromethorphan						
Paul 2007	34	0	-1.8 (0.521)		48.25%	-1.79[-2.81,-0.77]
Shadkam 2010	40	0	-1.7 (0.503)		51.75%	-1.72[-2.71,-0.73]
Subtotal (95% CI)					**100%**	**-1.75[-2.46,-1.04]**
Heterogeneity: Tau^2=0; Chi^2=0.01, df=1(P=0.93); I^2=0%						
Test for overall effect: Z=4.85(P<0.0001)						
2.4.3 Diphenhydramine						
Shadkam 2010	40	0	-1.6 (0.48)		100%	-1.64[-2.58,-0.7]
Subtotal (95% CI)					**100%**	**-1.64[-2.58,-0.7]**
Heterogeneity: Not applicable						

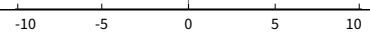




Analysis 2.5. Comparison 2 Pre- and postintervention comparison, Outcome 5 Parents' sleep (mean reduction in cough impact on sleep score).

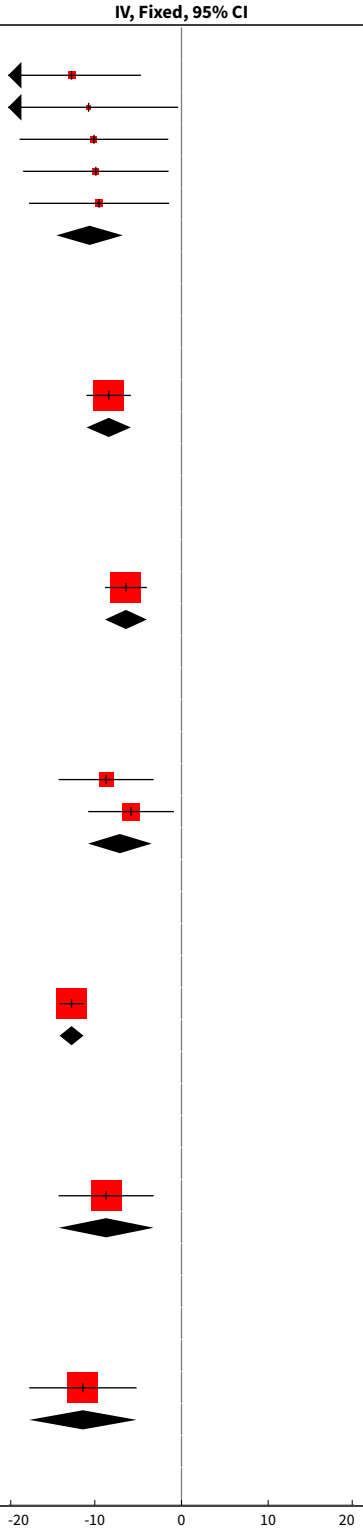


Study or subgroup	Reduced impact of cough N	Increased impact of cough N	Mean Difference (SE)	Mean Difference IV, Fixed, 95% CI	Weight	Mean Difference IV, Fixed, 95% CI
Heterogeneity: Tau²=0; Chi²=0.15, df=3(P=0.98); I²=0%						
Test for overall effect: Z=6.86(P<0.0001)						
2.5.2 Dextromethorphan						
Paul 2007	34	0	-2 (0.574)		50.19%	-1.97[-3.09,-0.85]
Shadkam 2010	40	0	-2 (0.576)		49.81%	-1.97[-3.1,-0.84]
Subtotal (95% CI)					**100%**	**-1.97[-2.77,-1.17]**
Heterogeneity: Tau²=0; Chi²=0, df=1(P=1); I²=0%						
Test for overall effect: Z=4.85(P<0.0001)						
2.5.3 Diphenhydramine						
Shadkam 2010	40	0	-1.9 (0.553)		100%	-1.89[-2.97,-0.81]
Subtotal (95% CI)					**100%**	**-1.89[-2.97,-0.81]**
Heterogeneity: Not applicable						
Test for overall effect: Z=3.42(P=0)						
2.5.4 No treatment						
Paul 2007	39	0	-1.5 (0.441)		46.97%	-1.51[-2.38,-0.65]
Shadkam 2010	40	0	-1.4 (0.415)		53.03%	-1.42[-2.23,-0.61]
Subtotal (95% CI)					**100%**	**-1.46[-2.06,-0.87]**
Heterogeneity: Tau²=0; Chi²=0.02, df=1(P=0.88); I²=0%						
Test for overall effect: Z=4.84(P<0.0001)						
2.5.5 Placebo						
Cohen 2012	75	0	-1.3 (0.694)		37.66%	-1.28[-2.64,0.08]
Waris 2014	45	0	-1.5 (0.539)		62.34%	-1.54[-2.6,-0.48]
Subtotal (95% CI)					**100%**	**-1.44[-2.28,-0.61]**
Heterogeneity: Tau²=0; Chi²=0.09, df=1(P=0.77); I²=0%						
Test for overall effect: Z=3.39(P=0)						
2.5.6 Salbutamol Day 5						
Waris 2014	43	0	-2.3 (0.806)		100%	-2.33[-3.91,-0.75]
Subtotal (95% CI)					**100%**	**-2.33[-3.91,-0.75]**
Heterogeneity: Not applicable						
Test for overall effect: Z=2.89(P=0)						
2.5.7 African honey Day 5						
Waris 2014	57	0	-2.3 (0.801)		100%	-2.29[-3.86,-0.72]
Subtotal (95% CI)					**100%**	**-2.29[-3.86,-0.72]**
Heterogeneity: Not applicable						
Test for overall effect: Z=2.86(P=0)						
2.5.8 Placebo Day 5						
Waris 2014	45	0	-1.5 (0.539)		100%	-1.54[-2.6,-0.48]
Subtotal (95% CI)					**100%**	**-1.54[-2.6,-0.48]**
Heterogeneity: Not applicable						
Test for overall effect: Z=2.85(P=0)						



Analysis 2.6. Comparison 2 Pre- and postintervention comparison, Outcome 6 Combined reduction in symptoms score.

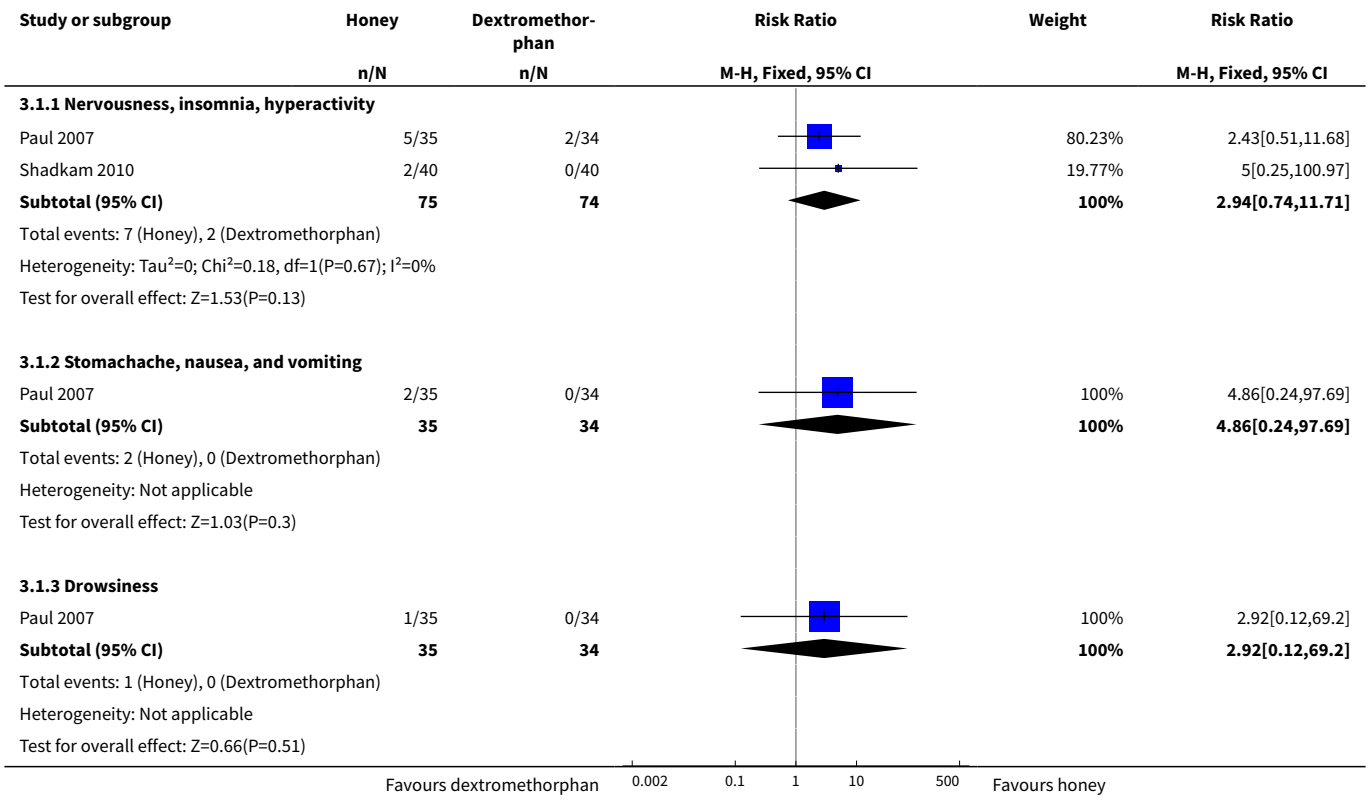
Study or subgroup	Reduced cough score N	Increased cough score N	Mean Difference (SE)	Mean Difference IV, Fixed, 95% CI	Weight	Mean Difference IV, Fixed, 95% CI
2.6.1 Honey						
Waris 2014	57	0	-12.7 (4.083)		22.91%	-12.68[-20.68,-4.68]
Paul 2007	35	0	-10.7 (5.27)		13.75%	-10.71[-21.04,-0.38]
Cohen 2012	75	0	-10.1 (4.375)		19.96%	-10.1[-18.67,-1.53]
Cohen 2012	75	0	-9.9 (4.279)		20.86%	-9.88[-18.27,-1.49]
Cohen 2012	75	0	-9.5 (4.119)		22.51%	-9.51[-17.58,-1.44]
Subtotal (95% CI)					**100%**	**-10.6[-14.43,-6.77]**
Heterogeneity: Tau²=0; Chi²=0.37, df=4(P=0.98); I²=0%						
Test for overall effect: Z=5.42(P<0.0001)						
2.6.2 Dextromethorphan						
Paul 2007	34	0	-8.4 (1.304)		100%	-8.39[-10.95,-5.84]
Subtotal (95% CI)					**100%**	**-8.39[-10.95,-5.84]**
Heterogeneity: Not applicable						
Test for overall effect: Z=6.44(P<0.0001)						
2.6.3 No treatment						
Paul 2007	39	0	-6.4 (1.231)		100%	-6.41[-8.82,-3.99]
Subtotal (95% CI)					**100%**	**-6.41[-8.82,-3.99]**
Heterogeneity: Tau²=0; Chi²=0, df=0(P<0.0001); I²=100%						
Test for overall effect: Z=5.2(P<0.0001)						
2.6.4 Placebo						
Waris 2014	57	0	-8.7 (2.798)		44.8%	-8.69[-14.17,-3.21]
Cohen 2012	75	0	-5.8 (2.521)		55.2%	-5.82[-10.76,-0.88]
Subtotal (95% CI)					**100%**	**-7.11[-10.78,-3.44]**
Heterogeneity: Tau²=0; Chi²=0.58, df=1(P=0.45); I²=0%						
Test for overall effect: Z=3.79(P=0)						
2.6.5 Honey Day 5						
Waris 2014	57	0	-12.7 (0.702)		100%	-12.68[-14.06,-11.3]
Subtotal (95% CI)					**100%**	**-12.68[-14.06,-11.3]**
Heterogeneity: Not applicable						
Test for overall effect: Z=18.07(P<0.0001)						
2.6.6 Placebo Day 5						
Waris 2014	45	0	-8.7 (2.798)		100%	-8.69[-14.17,-3.21]
Subtotal (95% CI)					**100%**	**-8.69[-14.17,-3.21]**
Heterogeneity: Not applicable						
Test for overall effect: Z=3.11(P=0)						
2.6.7 Salbutamol Day 5						
Waris 2014	43	0	-11.4 (3.155)		100%	-11.37[-17.55,-5.19]
Subtotal (95% CI)					**100%**	**-11.37[-17.55,-5.19]**
Heterogeneity: Not applicable						
Test for overall effect: Z=3.6(P=0)						



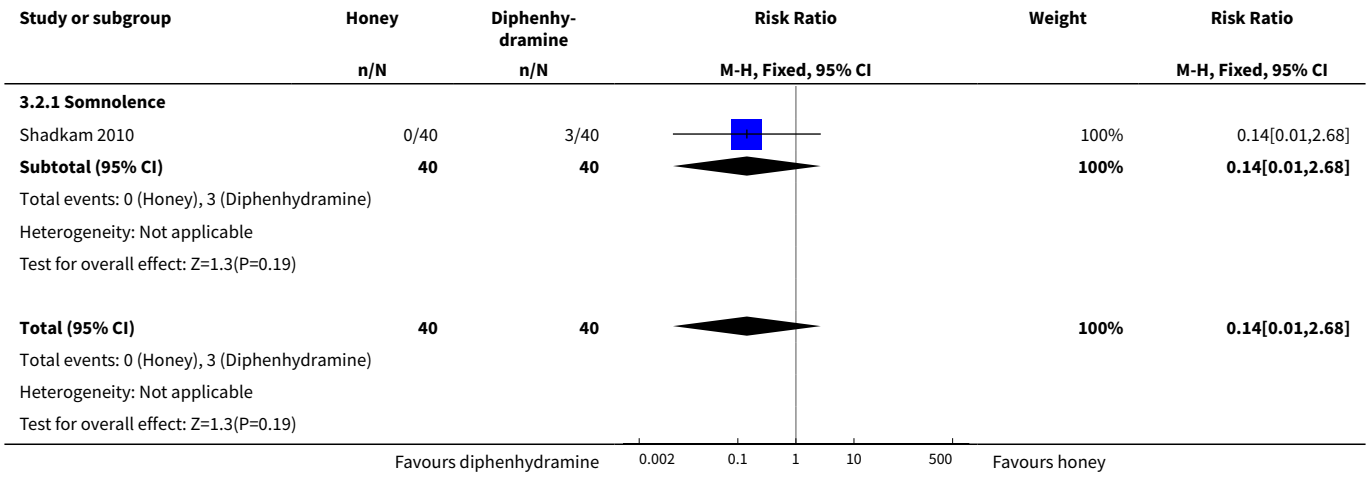
Comparison 3. Adverse events

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Honey versus dextromethorphan	2		Risk Ratio (M-H, Fixed, 95% CI)	Subtotals only
1.1 Nervousness, insomnia, hyperactivity	2	149	Risk Ratio (M-H, Fixed, 95% CI)	2.94 [0.74, 11.71]
1.2 Stomachache, nausea, and vomiting	1	69	Risk Ratio (M-H, Fixed, 95% CI)	4.86 [0.24, 97.69]
1.3 Drowsiness	1	69	Risk Ratio (M-H, Fixed, 95% CI)	2.92 [0.12, 69.20]
2 Honey versus diphenhydramine	1	80	Risk Ratio (M-H, Fixed, 95% CI)	0.14 [0.01, 2.68]
2.1 Somnolence	1	80	Risk Ratio (M-H, Fixed, 95% CI)	0.14 [0.01, 2.68]
3 Honey versus placebo	2		Risk Ratio (M-H, Fixed, 95% CI)	Subtotals only
3.1 Stomachache, nausea, and vomiting	2	402	Risk Ratio (M-H, Fixed, 95% CI)	1.91 [1.12, 3.24]
3.2 Diarrhoea	1	102	Risk Ratio (M-H, Fixed, 95% CI)	0.92 [0.33, 2.55]
3.3 Tachycardia	1	102	Risk Ratio (M-H, Fixed, 95% CI)	1.58 [0.15, 16.86]
4 Honey versus salbutamol	1		Risk Ratio (M-H, Random, 95% CI)	Subtotals only
4.1 Stomachache, nausea, and vomiting	1	100	Risk Ratio (M-H, Random, 95% CI)	1.74 [1.04, 2.92]
4.2 Rash	1	100	Risk Ratio (M-H, Random, 95% CI)	0.19 [0.02, 1.63]
4.3 Tachycardia	1	100	Risk Ratio (M-H, Random, 95% CI)	1.51 [0.14, 16.10]
4.4 Diarrhoea	1	100	Risk Ratio (M-H, Random, 95% CI)	0.59 [0.24, 1.45]
5 Honey versus no treatment	2	302	Odds Ratio (M-H, Fixed, 95% CI)	6.99 [1.55, 31.58]
5.1 Nervousness, insomnia, hyperactivity	2	154	Odds Ratio (M-H, Fixed, 95% CI)	9.40 [1.16, 76.20]
5.2 Stomachache, nausea, and vomiting	1	74	Odds Ratio (M-H, Fixed, 95% CI)	5.90 [0.27, 127.14]
5.3 Drowsiness	1	74	Odds Ratio (M-H, Fixed, 95% CI)	3.43 [0.14, 87.09]

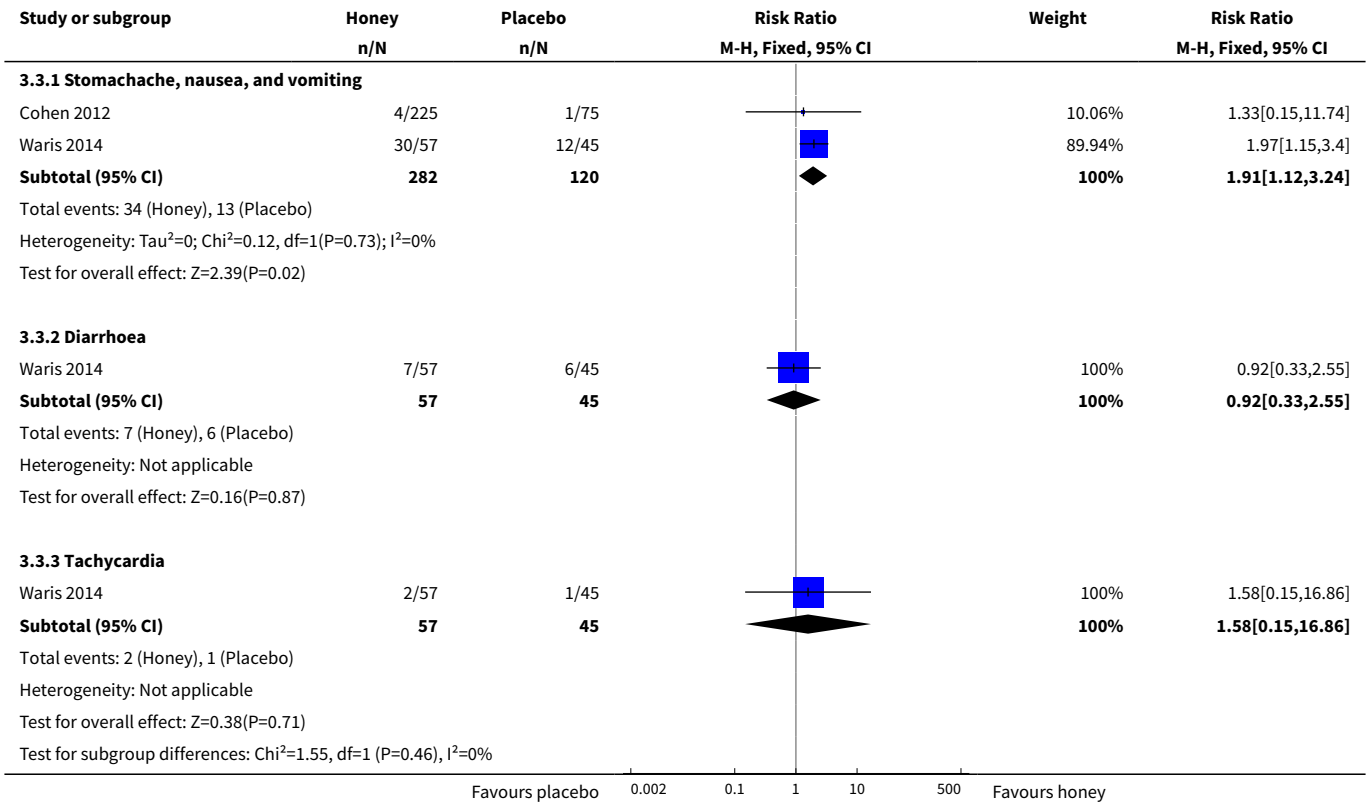
Analysis 3.1. Comparison 3 Adverse events, Outcome 1 Honey versus dextromethorphan.



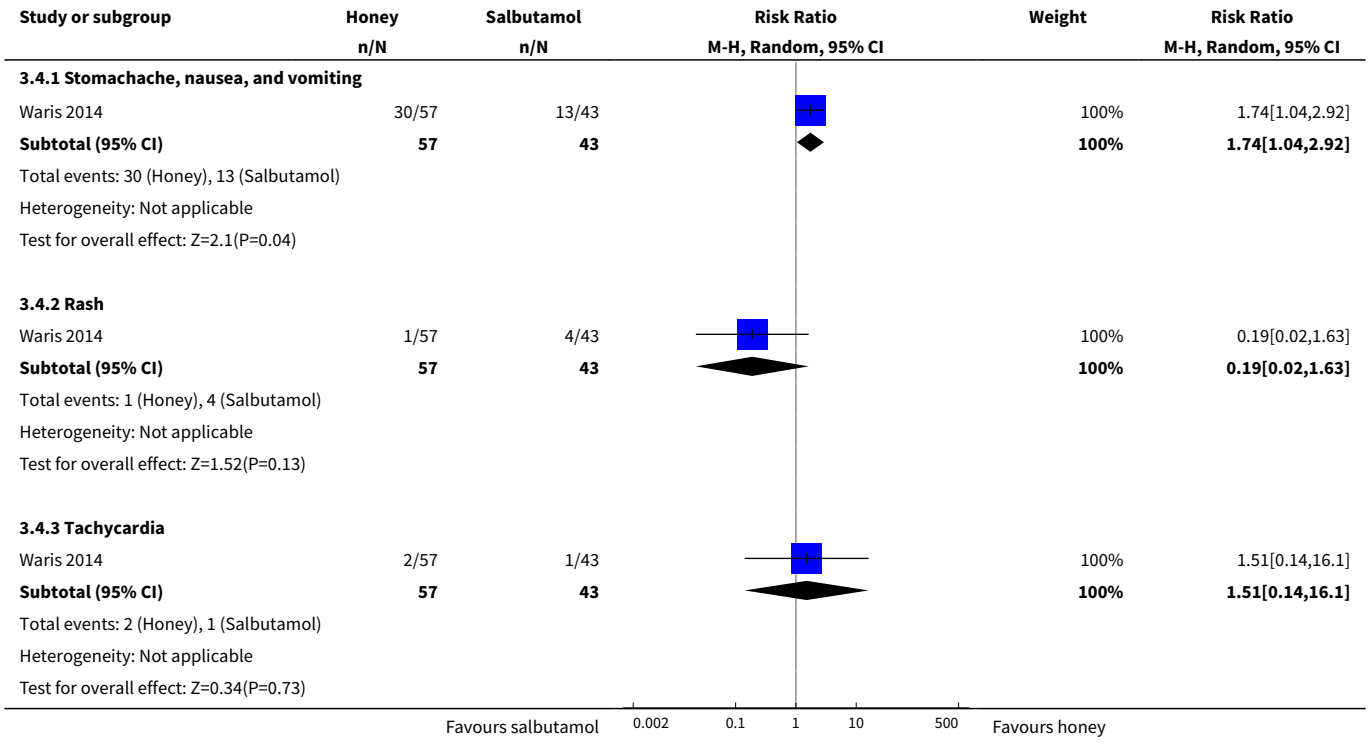
Analysis 3.2. Comparison 3 Adverse events, Outcome 2 Honey versus diphenhydramine.

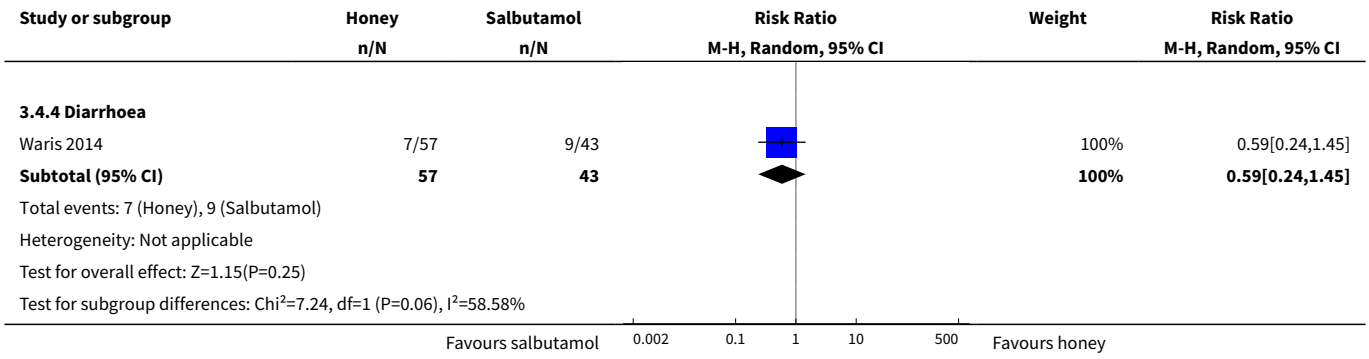


Analysis 3.3. Comparison 3 Adverse events, Outcome 3 Honey versus placebo.

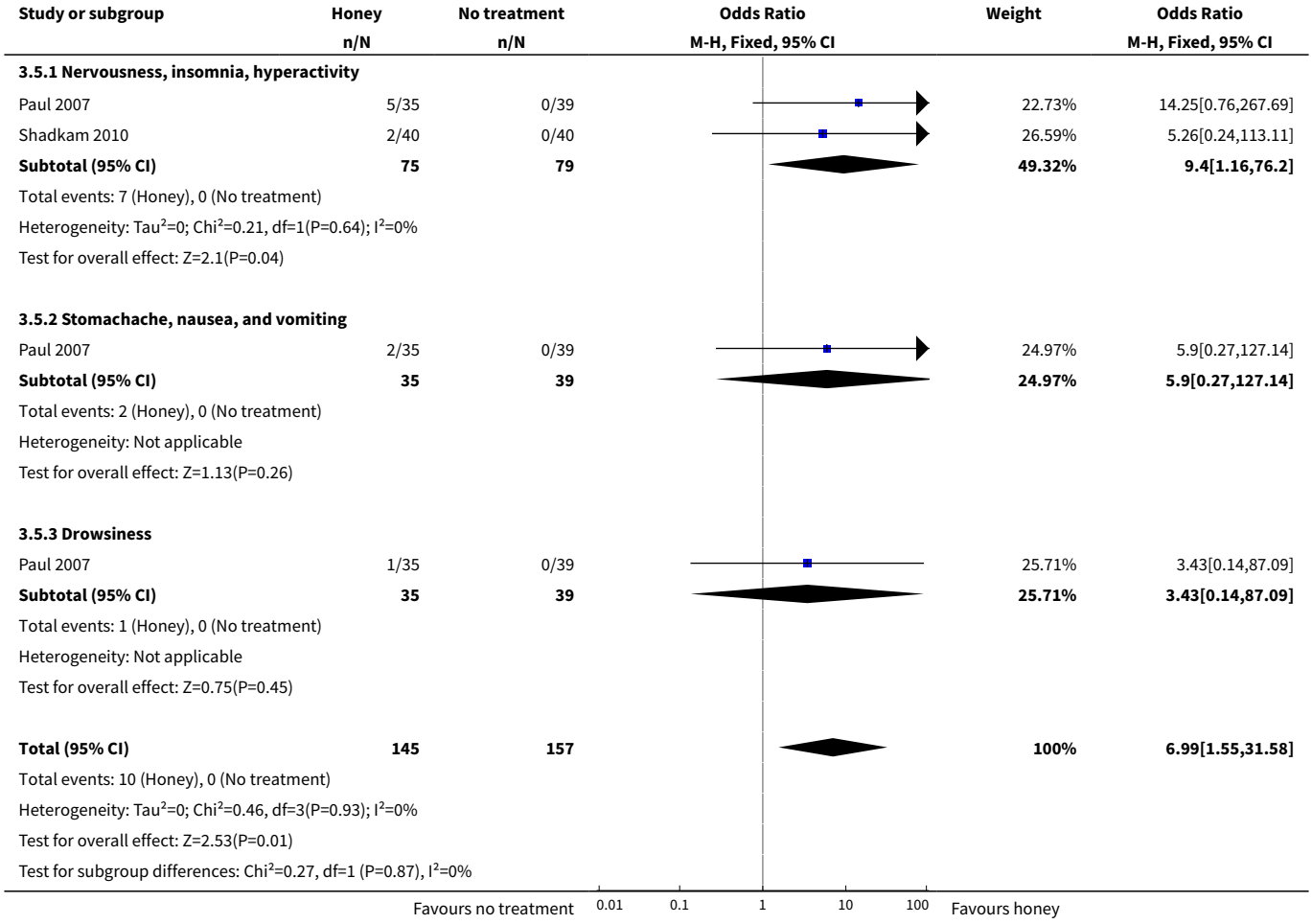


Analysis 3.4. Comparison 3 Adverse events, Outcome 4 Honey versus salbutamol.





Analysis 3.5. Comparison 3 Adverse events, Outcome 5 Honey versus no treatment.



ADDITIONAL TABLES

Table 1. Pre- and postintervention comparison of honey on cough frequency and severity expressed as medians

Study ID	Cough	Honey (N = 29)	Bromelin (pineapple extract) + honey (N = 31)	P value	Certainty of the evidence
Peixoto 2016	**Frequency of cough[1]**				
	Before, median (P25 to P75)	3 (2 to 4)	3 (2 to 3)	0.83[2]	⊕⊕⊕⊖ MODERATE [4]
	After, median (P25 to P75)	1 (1 to 1)	1 (1 to 1)	0.94[3]	
	Mean ± SD	1.76 ± 0.87	1.71 ± 0.78		
	Severity of cough[1]				
	Mean ± SD assessed with: unvalidated 5-point cough scale from 0 to 4	-0.86 ± 0.45	-0.97 ± 0.62	0.32[2] 0.22[3]	⊕⊕⊕⊖ MODERATE [4]
		Honey (N = 63)	**Diphenhydramine (N = 63)**		
Ahmadi 2013	Proportion of children with reduction in frequency and severity of daytime cough[5]	84.1% (N = 53)	58.7% (N = 37)	"< 0.02"	⊕⊕⊕⊖ MODERATE [4]
	Proportion of children with reduction in frequency and severity of nighttime cough[5]	79.4% (N = 50)	58.7% (N = 37)	"< 0.02"	⊕⊕⊕⊖ MODERATE [4]

SD: standard deviation
P: percentile
[1]Assessed on an unvalidated 5-point cough scale from 0 to 4; lower score is better.
[2]Student's t test.
[3]Chi².
[4]Downgraded by one level for risk of bias and imprecision.
[5]Assessed on a 7-point Likert scale from 0 to 6; lower score is better.

APPENDICES

Appendix 1. AMED (Ovid) 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. CAB Abstracts (Thomson Reuters) search strategy

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

Appendix 3. Previous searches

For the 2014 update we searched the Cochrane Central Register of Controlled Trials (CENTRAL) (2014, Issue 10), which contains the Cochrane Acute Respiratory Infections Group's Specialised Register, MEDLINE (January 2012 to October week 4, 2014), EMBASE (January 2012 to October 2014), CINAHL (January 2012 to October 2014), Web of Science (2011 to October 2014), AMED (2011 to October 2014), LILACS (2011 to October 2014) and CAB abstracts (2011 to January 2014).

Our initial 2009 search covered CENTRAL (*The Cochrane Library* 2009, Issue 2), 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). The search was then updated in January 2012 to cover the period April 2009 to January 2012.

Appendix 4. CENTRAL and MEDLINE (Ovid) search strategy

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

Appendix 5. Embase (Elsevier) search strategy

#7. #3 AND #6
#6. #4 OR #5
#5. honey*:ab,ti
#4. 'honey'/de
#3. #1 OR #2
#2. cough*:ab,ti
#1. 'coughing'/exp

Appendix 6. 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 7. Web of Science (Clarivate Analytics) search strategy

Topic=(cough*) AND Topic=(honey*)

Appendix 8. LILACS (BIREME) search strategy

(mh:cough OR cough* OR tos OR tosse) AND (mh:honey OR honey* OR miel OR mel) AND db:("LILACS")

WHAT'S NEW

Date	Event	Description
17 December 2018	Amended	Amendment made to Summary of findings 4. The superscripts 'moderate certainty evidence' were corrected for Day 3 and Day 5.

HISTORY

Protocol first published: Issue 2, 2008
Review first published: Issue 1, 2010

Date	Event	Description
8 February 2018	New citation required but conclusions have not changed	Our conclusions remain unchanged.
8 February 2018	New search has been performed	Searches updated. We included three new trials (Ahmadi 2013; Peixoto 2016; Waris 2014), and excluded three new trials (Ayazi 2017; Baker 2016; Cohen 2017). One study is awaiting classification (IRCT2014090819037N1), and two studies are ongoing (NCT03218696; UMIN000020651).
4 November 2014	New citation required and minor changes	Our conclusions remain unchanged.
4 November 2014	New search has been performed	Searches updated. We included one new trial (Cohen 2012), and excluded two new trials (Ahmed 2013a; Miceli Sopo 2014). Two studies are awaiting classification (IRCT201110247882N1; NCT01356693), and one study is ongoing (IRCT2014090819037N1).
11 January 2012	New search has been performed	Searches updated. We included one new trial (Shadkam 2010).
11 January 2012	New citation required but conclusions have not changed	Our conclusions remain unchanged.

CONTRIBUTIONS OF AUTHORS

Dr Olabisi Oduwole (OO) prepared the main text of this update and wrote the methods section of the update based on a template developed by the Cochrane Acute Respiratory Infections Group.
OO and Dr Ekong Udoh (EU) selected studies and extracted data.
Prof Martin Meremikwu (MM), OO, Prof Angela Oyo-Ita (AO), and EU revised the text.
All review authors contributed to this update and read and agreed upon the final version.

DECLARATIONS OF INTEREST

Olabisi Oduwole: none known.
Ekong E Udoh: none known.
Angela Oyo-Ita: none known.
Martin M Meremikwu: none known.

DIFFERENCES BETWEEN PROTOCOL AND REVIEW

An inclusion criterion in our protocol was the inclusion of children aged from two to 18 years because of safety concerns for infants less than two years (Oduwole 2008). However, we included participants aged from 12 months because most included studies enrolled children aged from 12 months and over. Studies have reported that only infants aged less than 12 months are at risk when given honey due to poor immunity against *Clostridium botulinum* (Küplülü 2006), thus our safety concern was no longer valid. Including children aged less than two years did not change the conclusions of subsequent review updates (Oduwole 2012; Oduwole 2014a), from the first publication (Oduwole 2010).

We were unable to assess the effect of honey on children's quality of life, improvement in appetite, and cost of honey alone compared with other cough syrups because none of the included studies reported these outcomes.

INDEX TERMS

Medical Subject Headings (MeSH)

Albuterol [therapeutic use]; Antitussive Agents [adverse effects] [*therapeutic use]; Apitherapy [adverse effects] [*methods]; Bromelains [therapeutic use]; Bronchodilator Agents [therapeutic use]; Cough [*therapy]; Dextromethorphan [adverse effects]

[*therapeutic use]; Diphenhydramine [adverse effects] [*therapeutic use]; Honey [adverse effects]; Placebos [therapeutic use]; Randomized Controlled Trials as Topic

MeSH check words

Adolescent; Child; Child, Preschool; Humans; Infant