

Effectiveness of honey for symptomatic relief in upper respiratory tract infections: a systematic review and meta-analysis

Hibatullah Abuelgasim ¹, Charlotte Albury,² Joseph Lee²

10.1136/bmjebm-2020-111336

► Additional material is published online only. To view please visit the journal online (<http://dx.doi.org/10.1136/bmjebm-2020-111336>).

¹Oxford University Medical School, University of Oxford, Oxford, UK

²Nuffield Department of Primary Care Health Sciences, University of Oxford, Oxford, UK

Correspondence to: **Hibatullah Abuelgasim**, Medical Sciences Divisional Offices, University of Oxford, Oxford, OX3 9DU, UK; hibatullah.abuelgasim@new.ox.ac.uk



© Author(s) (or their employer(s)) 2020. No commercial re-use. See rights and permissions. Published by BMJ.

To cite: Abuelgasim H, Albury C, Lee J. *BMJ Evidence-Based Medicine* Epub ahead of print: [please include Day Month Year]. doi:10.1136/bmjebm-2020-111336

Abstract

Background Antibiotic over prescription for upper respiratory tract infections (URTIs) in primary care exacerbates antimicrobial resistance. There is a need for effective alternatives to antibiotic prescribing. Honey is a lay remedy for URTIs, and has an emerging evidence base for its use. Honey has antimicrobial properties, and guidelines recommended honey for acute cough in children. **Objectives** To evaluate the effectiveness of honey for symptomatic relief in URTIs.

Methods A systematic review and meta-analysis. We searched Pubmed, Embase, Web of Science, AMED, Cab abstracts, Cochrane Library, LILACS, and CINAHL with a combination of keywords and MeSH terms.

Results We identified 1345 unique records, and 14 studies were included. Overall risk of bias was moderate. Compared with usual care, honey improved combined symptom score (three studies, mean difference -3.96 , 95%CI -5.42 to -2.51 , $I^2=0\%$), cough frequency (eight studies, standardised mean difference (SMD) -0.36 , 95%CI -0.50 to -0.21 , $I^2=0\%$) and cough severity (five studies, SMD -0.44 , 95%CI -0.64 to -0.25 , $I^2=20\%$). We combined two studies comparing honey with placebo for relieving combined symptoms (SMD -0.63 , 95%CI -1.44 to 0.18 , $I^2=91\%$).

Conclusions Honey was superior to usual care for the improvement of symptoms of upper respiratory tract infections. It provides a widely available and cheap alternative to antibiotics. Honey could help efforts to slow the spread of antimicrobial resistance, but further high quality, placebo controlled trials are needed.

PROSPERO registration No Study ID, CRD42017067582 on PROSPERO: International prospective register of systematic reviews (<https://www.crd.york.ac.uk/prospéro/>).

Introduction

Upper respiratory tract infections (URTIs) are the most frequent reason for antibiotic prescription.¹ Since the majority of URTIs are viral, antibiotic prescription is both ineffective^{2 3} and inappropriate.⁴ However, a lack of effective alternatives, as well as a desire to preserve the patient–doctor relationship, both contribute to antibiotic over prescription.^{5 6} Antibiotic overuse is a key driver of antimicrobial resistance,⁷ rated by the UK

Summary box

What is already known about this subject?

- Honey is a well known lay therapy for symptoms of upper respiratory tract infections (URTIs); other medications for URTIs are ineffective and can have harmful side effects
- The use of antibiotics for URTIs is a particular problem, because they are ineffective, and contribute to antimicrobial resistance
- A Cochrane systematic review found that honey can improve cough in children; honey has not been systematically reviewed for other URTI symptoms, or in other patient groups

What are the new findings?

- Honey is more effective than usual care alternatives for improving URTI symptoms, particularly cough frequency and cough severity
- Comparisons with placebo are more limited, and require more high quality, placebo controlled trials

How might it impact on clinical practice in the foreseeable future?

- There are currently very few effective options that clinicians can prescribe for URTIs
- Honey can be used as an alternative to antibiotics by clinicians who wish to offer treatment for URTIs, which may help to combat antimicrobial resistance

government as one of the top 10 risks facing Britain.⁸ Furthermore, drug resistant infections are associated with worse patient outcomes than antibiotic susceptible infections,⁹ underlining the impact of antimicrobial resistance on individual patients.

Honey is a well known traditional therapy for URTI symptoms. Guidelines recommend it for acute cough in children¹⁰ but the evidence base for honey use for other URTI symptoms and populations has not been evaluated. We therefore systematically reviewed the use of honey for the

resolution of symptoms associated with URTIs, in patients of all ages, in any setting.

Methods

The protocol for this systematic review was prospectively published on <https://www.crd.york.ac.uk/prospetro/> (study ID CRD42017067582).

Information sources and search

We searched Pubmed, Embase, Web of Science, AMED, Cab abstracts, Cochrane Library, LILACS and CINAHL with a combination of keywords and MeSH terms (online supplementary material, extended methods). The search was updated on 18 March 2019. The search strategy was developed with an information specialist, and experts reviewed the search terms. No language or date restrictions were applied. We also hand searched the bibliographies of included studies for relevant studies. The search strategy included atopic conditions, but we present here findings for URTIs only. The results for atopic conditions will be published separately.

Study selection

Studies eligible for inclusion had to meet the following criteria:

1. Randomised clinical trials or in vivo observational studies.
2. Patients of any age and gender, in any setting, with clinically or laboratory diagnosed infectious and atopic upper respiratory tract (URT) conditions.
3. Comparing honey (of any type, administered in any way, alone or in conjunction with other treatments) with at least one other group (no treatment, placebo or usual therapy) for the treatment of URT symptoms.

We excluded in vitro studies, animal studies, protocol only publications, case reports, case series and studies without an appropriate comparator. We defined URTIs as acute infections of the respiratory tract, including acute cough, colds and influenza-like illness, but excluding bronchitis or other infections of the lower respiratory tract. We also excluded ear infections without other URTI symptoms, and infections following surgical or medical interventions. We included any commonly used treatments under 'usual care'.

Two reviewers (HA and either JL or CA) screened each citation at the title and abstract, and full text. We discussed discrepancies, and if unresolved, the remaining reviewer (JL or CA) adjudicated.

Data extraction and risk of bias assessment

Data were extracted by HA and checked by a second reviewer. Where studies were not published in English, native speakers of the appropriate language translated them. If studies did not report the required details, we requested data from the study authors, and where possible, estimated from published data; full methods for estimation can be found in the online supplementary material, table 1. Two reviewers (HA and JL) assessed the risk of bias with the Cochrane risk of bias tool. Each study was assessed with regard to the following bias domains: selection, performance, detection, attrition, reporting and other. Other was defined in the Cochrane Handbook as "bias due to problems not covered elsewhere" in the bias domains.¹¹ We planned to use funnel plots and Eggers test to examine the risk of publication bias if there were sufficient studies.

Statistical methods

We used RevMan 5.3 software¹² to undertake random effects meta-analysis. Where studies used the same outcome measure, such as a validated questionnaire, we estimated mean differences (MDs)

in symptom scores before and after the intervention, with 95% confidence intervals (CIs). We estimated standard mean difference (SMD) with 95% CIs for studies that used different scales. We used odds ratios (OR) with 95% CIs for binary outcomes. The I^2 statistic was our measure of statistical heterogeneity.

We compared honey with usual care and undertook subgroup analyses of the different types of usual care. There are no effective active treatments for URTIs, but many commonly used remedies. We therefore combined ineffective remedies as 'usual care' but also undertook sensitivity analyses of the different substances to support this approach.

We undertook sensitivity analyses excluding studies where MDs had to be estimated using extra calculations or assumptions (online supplementary table 1).

Patient and public involvement

This research was conducted without patient involvement.

Results

Study selection

The search identified 1345 unique records and we excluded 1241 records at the titles and abstracts stage (figure 1). After full text screening, a further 84 studies were excluded. The reasons for exclusion are given in online supplementary table 2. Here, we report results for the 14 studies of URTIs.

Study characteristics

We included 14 studies in the qualitative analysis, all of which were randomised controlled trials.^{13–26} Study characteristics are summarised in table 1. Nine studies were paediatric only. There was considerable diversity of 'usual care' interventions (table 1 and online supplementary table 3), and while nine studies used pure honey, two used Grintuss syrup^{19 21} (a cough suppressant syrup containing honey and plant complexes) and one used Honitus syrup (an Ayeverdric honey based syrup containing herb extracts).²² Additionally, two combined honey with coffee,^{15 26} and one with milk.¹⁸ We evaluated all of these as 'honey' interventions. Twelve studies could be combined in meta-analyses.^{13–16 18–24 26} Outcome measures were diverse (table 1). The most common were measures of cough. Six studies measured cough with validated scores,^{13 15 16 23–25} three used modified or unvalidated scores,^{14 17 19} and three used questionnaires.^{12 21 22} Apart from cough symptoms, studies also included outcomes for sleep difficulty,¹³ overall subjective symptoms¹⁸ and duration of a combination of rhinitis, myalgia, congestion and cough assessed by investigators.²⁰ Full study characteristics are in the supplementary material (online supplementary table 4).

Risk of bias within studies

Figure 2 and table 2 summarise our risk of bias assessments for the included studies. Few studies made mention of specific attempts to minimise other forms of bias. Due to the small numbers of studies, we were unable to use funnel plots to assess publication bias. Table 3 shows the pooled results of the meta-analyses.

Honey versus placebo

Two studies^{19 20} compared honey with placebo for cough, on validated Likert scales, and could be combined. Both had a low risk of bias and included a total of 372 patients. Honey was not superior to placebo in improving combined symptoms, and heterogeneity was considerable (table 3 and online supplementary figure 1). We therefore considered these studies separately. Cohen²⁰ estimated

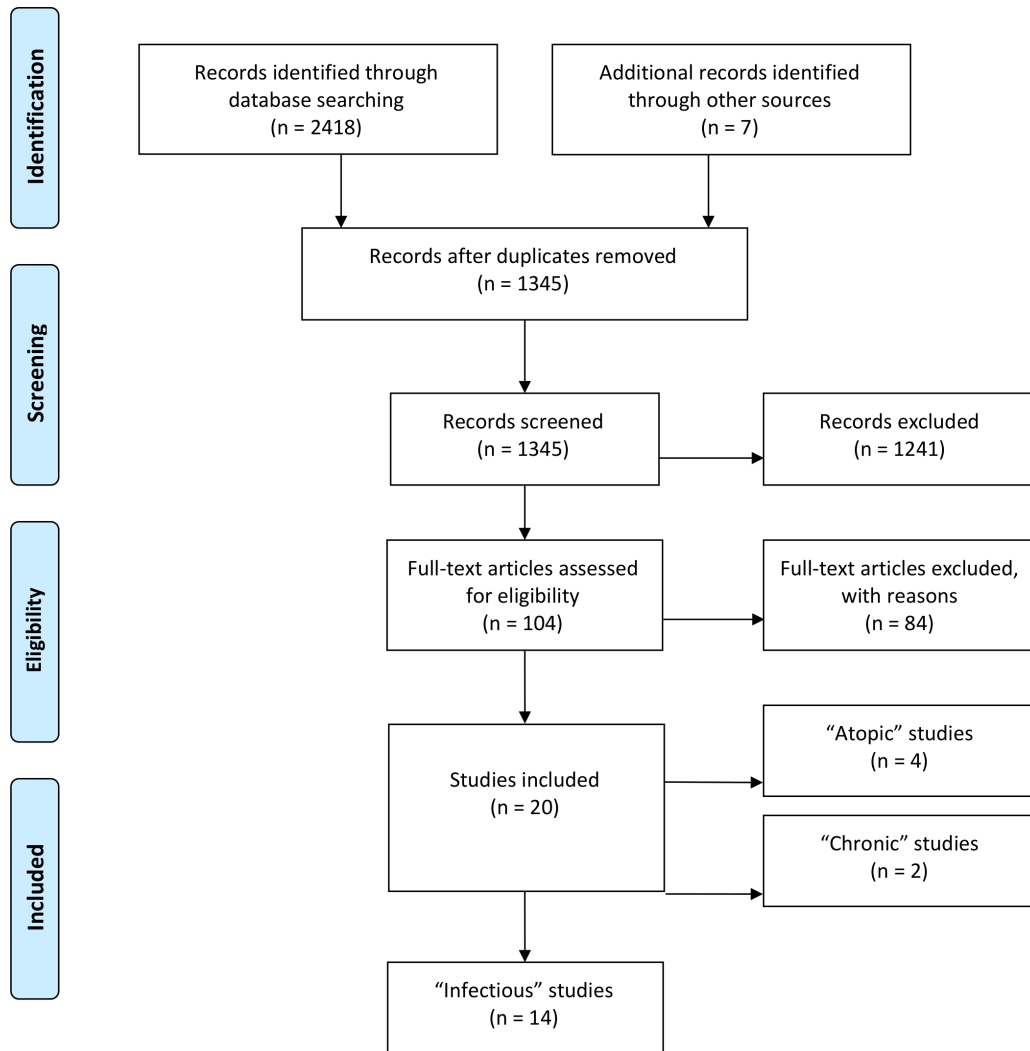


Figure 1 Preferred reporting items for systematic reviews and meta-analyses (PRISMA) flow diagram outlining the process of study selection.

a beneficial effect (SMD -1.03 , 95% CI -1.32 to -0.75) and Canciani¹⁹ did not (SMD -0.20 , 95% CI -0.59 to 0.19). A further study, Waris¹⁷, could not be included in the meta-analysis but reported that honey reduced combined symptom score significantly more than placebo by the final day of the study (mean difference = 3.99 , $p=0.003$).

Honey versus usual care

Combined symptom scores were obtainable from three studies of children^{14 21 24} with considerable risk of bias. Cough frequency and cough severity were obtainable from eight^{13-16 21 22 24 26} and five studies,^{13 14 16 21 24} respectively, of variable risk of bias. All three of these symptoms improved significantly more for patients taking honey than usual care, with low statistical heterogeneity (table 3, figure 3). Estimates were consistent with comparisons with placebo. Two studies^{18 23} with a high risk of bias, including 334 patients, could be combined into the binary outcome measure 'improvement'. There was moderate heterogeneity and honey was not significantly different to usual care (table 3 and online supplementary figure 2).

One study could not be included in the meta-analyses; Pourahmad²⁵ was excluded because mean differences in symptom scores were not reported. Instead, the duration of signs and symptoms of the common cold (which were not detailed) were given.

The symptoms of patients who received honey lasted 1–2 days shorter than those who received usual care. No confidence intervals or p values were reported. The usual care group was split into subgroups comparing honey with dextromethorphan and diphenhydramine.

Honey versus dextromethorphan

Two studies^{16 24} were combinable, including a total of 137 patients. Only one reported combined symptom score,²⁴ but both reported cough frequency and cough severity. Both studies had a relatively high risk of bias. Honey was not significantly better than dextromethorphan for improvement of combined symptoms (MD -2.32 , 95% CI -5.88 to 1.24), cough frequency (MD -0.52 , 95% CI -1.51 to 0.46 , $I^2=0\%$) or cough severity (MD -0.56 , 95% CI -1.65 to 0.53 , $I^2=0\%$) but the results were consistent with overall usual care (table 3 and online supplementary figure 3).

Honey versus diphenhydramine

Four studies^{13 14 16 22} were combinable, including a total of 385 patients. Only one reported combined symptom score,¹⁴ but all three reported cough frequency, and two reported cough severity. One study¹³ had a low risk of bias; the other three had a moderate²² or relatively high^{14 16} risk of bias. Honey was significantly better than diphenhydramine for improvement of all three

Table 1 Summary of characteristics of included studies

Study	Design	Age range (years)	Intervention	Comparator	Outcome measure
Ahmadi <i>et al</i> ¹³	RCT double blind	2–5	Honey	Diphenhydramine	Day time and night time cough frequency and severity (we converted this to a 3 point Likert scale)
Ayazi <i>et al</i> ¹⁴	RCT no blinding	1–12	Honey 1; honey 2	Diphenhydramine	Nocturnal cough and sleep difficulty score (validated 5 item, 7 point Likert scale ²⁴)
Canciani <i>et al</i> ¹⁹	RCT double blind	3–6	Grintuss syrup	Placebo	Day time and night time cough severity (modified from validated questionnaire ²⁵)
Cohen <i>et al</i> ²⁰	RCT double blind	1–5	Eucalyptus honey; citrus honey; labiatae honey	Placebo (silan date extract)	Cough score (validated 5 item, 7 point Likert scale ²⁴), effect on sleep and combination
Cohen <i>et al</i> ²¹	RCT single blind	2–5	Grintuss syrup	Carbocysteine syrup	Cough score (validated 5 item, 7 point Likert scale ²⁴)
Gupta <i>et al</i> ²²	RCT double blind	18–65	Honitus cough syrup	Marketed cough syrup, containing diphenhydramine	Day time and night time cough frequency score (6 point Likert scale), throat irritation
Miceli Sopo <i>et al</i> ¹⁸	RCT no blinding	2–14	Wildflower honey+milk	Dextromethorphan; levodropropizine	Cough score (validated 5 item, 7 point Likert scale ²⁴)
Nanda <i>et al</i> ²³	RCT blinding unclear	>18	Honey+supportive treatments	Supportive treatments only (regarded as placebo)	Subjective symptom score, throat pain recovery, fever recovery
Paul <i>et al</i> ²⁴	RCT partially double blind	2–18	Buckwheat honey	Dextromethorphan; no treatment	Cough score (5 item, 7 point Likert scale)
Pourahmad and Sobhanian ²⁵	Single blinded trial	intervention group mean (SD) 24.4 (7.4) comparator group mean (SD) 27.4 (6.2)	Honey+paracetamol, naproxen and chlorpheniramine	Paracetamol, naproxen and chlorpheniramine	Duration of signs and symptoms: rhinitis, muscle pain, fever, throat congestion, cough and sneezing, assessed by investigators
Raeessi <i>et al</i> ²⁶	RCT double blind	21–65	Honey; honey+coffee	Coffee	Cough frequency (questionnaire)
Raeessi <i>et al</i> ¹⁵	RCT double blind	21–65	Honey+coffee	Prednisolone; guaifenesin (regarded as placebo)	Cough frequency (questionnaire)
Shadkam <i>et al</i> ¹⁶	Four arm RCT no blinding	24–60 months	Honey	Dextromethorphan; diphenhydramine; supportive treatments also suggested to the other groups, including saline nasal drops and paracetamol	Cough score (validated 5 item, 7 point Likert scale ²⁴)
Waris <i>et al</i> ¹⁷	RCT double blind	21–1	Honey	Salbutamol syrup; placebo (brown coloured sugar syrup)	Cough score (validated 5 item, 7 point Likert scale ²⁴)

RCT, randomised controlled trial.

	Random sequence generation (selection bias)	Allocation concealment (selection bias)	Blinding of participants and personnel (performance bias)	Blinding of outcome assessment (detection bias)	Incomplete outcome data (attrition bias)	Selective reporting (reporting bias)	Other bias
Ahmadi 2013	?	+	+	+	+	+	+
Ayazi 2017	?	-	-	?	+	+	+
Canciani 2014	+	+	+	+	+	?	+
Cohen 2012	+	+	?	+	+	+	+
Cohen 2017	-	-	-	-	+	?	-
Gupta 2016	+	+	+	+	?	?	-
Miceli Sopo 2015	+	-	-	-	-	?	+
Nanda 2017	-	-	-	-	-	?	+
Paul 2007	+	-	?	?	-	+	+
Pourahmad 2009	-	-	?	+	+	?	+
Raessi 2011	+	?	+	+	+	+	+
Raessi 2013	+	+	+	+	-	+	+
Shadkam 2010	+	+	-	-	-	?	+
Waris 2014	+	+	+	+	?	?	+

Figure 2 Summary of risk of bias assessment for included studies.

outcomes (combined symptom score MD -5.31, 95%CI -7.96 to -2.67, cough frequency MD -0.29, 95%CI -0.58 to -0.01, I²=46%, cough severity MD -0.50, 95%CI -0.88 to -0.13, I²=53%) (table 3 and online supplementary figure 4).

Sensitivity analyses

In order to assess the evidence for effects in adults, we performed further analyses restricted to the four studies with an adult population (online supplementary table 5).^{15 22 23 26} Only one pooled

Table 2 Summary of risk of bias assessment

Type of bias	Low risk	Unclear risk	High risk
Selection (random sequence generation)	9/14	2/14	3/14
Performance	6/14	3/14	5/14
Detection	8/14	2/14	4/14
Attrition	7/14	2/14	5/14
Reporting	6/14	8/14	0/14
Other bias	12/14	0/14	2/14

comparison of three studies could be made, honey versus usual care for cough frequency (SMD -0.19, 95%CI -0.47 to 0.09, I²=4%). There was also evidence from single studies. Nanda²³ estimated that at 5 days there was no difference in throat congestion (OR 0.73, 95%CI 0.42 to 1.27), throat pain (OR 0.75, 95%CI 0.43 to 1.32) or complete satisfaction (which was linked to throat pain, OR 1.44, 95%CI 0.72 to 2.86) but more people had recovered from fever (OR 2.58, 95%CI 1.22 to 5.46). In addition, Pourahmad and Sobhanian included adults, and reported a statistically shorter time to clinical recovery from the common cold.²⁵ Gupta²² included adults, and reported an increased proportion of patients with at least a 75% improvement in throat irritation at day 4 (OR for failure 0.22, 95%CI 0.08 to 0.59).

We performed sensitivity analyses excluding studies where we had to estimate elements of the results (Canciani 2014¹⁹, Ahmadi 2013¹³, Raessi 2011²⁶, Raessi 2013¹⁵). For the comparison with placebo, the one remaining study²⁰ found that honey was significantly better than placebo (SMD -1.03, 95%CI -1.32 to -0.75, low risk of bias).

In the comparison with usual care, the reductions in cough frequency and cough severity remained statistically significant: cough frequency SMD -0.30 (95%CI -0.47 to -0.12), I²=0%; cough severity SMD -0.43 (-0.69 to -0.17), I² = 38%. In the subgroup comparison with diphenhydramine, SMD for cough frequency was -0.16 (-0.42 to 0.10) and I² decreased from 17% to 3%. For cough severity, SMD decreased to -0.51 (-1.24 to 0.22) while I² increased to 77%.

We performed further sensitivity analyses excluding studies with interventions combining honey with other ingredients not included in the comparator arm (Cohen 2017²¹, Gupta 2016²², Miceli Sopo 2015¹⁸, Canciani 2014¹⁹, table 3). This made little difference to the estimates. For the comparison with usual care, combined symptom score was reduced in the honey arms of the two remaining studies (MD -4.47 95%CI -6.47 to -2.48, I²=0%). Removing the study by Miceli Sopo¹⁸ from the overall 'improvement' category left only the study by Nanda²³, which also estimated no effect (OR 0.73 95%CI 0.42 to 1.27). Removing the studies by Cohen²¹ and Gupta²² from the assessment of cough frequency gave an SMD of -0.40 (95%CI -0.58 to -0.21, I²=0%). Removing the study by Cohen²¹ from the cough severity outcome analysis had no impact on the point estimate (SMD -0.44, 95%CI -0.70 to -0.17, I²=40%). In the subgroup analysis of diphenhydramine versus honey, with the outcome of cough frequency, the point estimate and confidence intervals moved further from the line of no effect, with reduced heterogeneity (SMD -0.41, 95%CI -0.69 to -0.14, I²=17%)

Discussion

Assessing all the available literature, we found evidence that honey appeared to improve URTI symptoms more effectively than usual care, but comparisons with placebo were limited. We

Table 3 Summary of results of meta-analyses

Comparator	Outcome	Studies (n)	Pooled effect estimate including all studies	Studies (n)	Pooled estimates excluding studies with ingredients other than honey*
Placebo	Combined symptom score	2 (372)	SMD -0.63, 95% CI -1.44 to 0.18, I ² =91%	1 (270)	SMD -1.03, 95% CI -1.32 to -0.75
Usual care	Combined symptom score	3 (333)	MD -3.96, 95% CI -5.42 to -2.51, I ² =0%	2 (192)	MD -4.47, 95% CI -6.47 to -2.48, I ² =0%
	Cough frequency	8 (832)	SMD -0.36, 95% CI -0.50 to -0.21, I ² =0%	6 (586)	SMD -0.40, 95% CI -0.58 to -0.21, I ² =0%
	Cough severity	5 (598)	SMD -0.44, 95% CI -0.64, to -0.25, I ² =20%	4 (457)	SMD -0.44, 95% CI -0.70 to -0.17, I ² =40%
	Improvement	2 (334)	OR 1.01, 95% CI 0.45 to 2.27, I ² =56%	1 (200)	OR 0.73, 95% CI 0.42 to 1.27
	Throat pain recovery by day 5	1 (200)	OR 0.75, 95% CI 0.43 to 1.32		No change
	Fever recovery by day 5	1 (200)	OR 2.58, 95% CI 1.22 to 5.46		No change
Dextromethorphan†	Combined symptom score	1 (68)	MD -2.32, 95% CI -5.88 to 1.24		NA
	Cough frequency	2 (137)	MD -0.52, 95% CI -1.51 to 0.46, I ² =0%		NA
	Cough severity	2 (137)	MD -0.56, 95% CI -1.65 to 0.53, I ² =0%		NA
Diphenhydramine†	Combined symptom score	1 (87)	MD -5.31, 95% CI -7.96 to -2.67		NA
	Cough frequency	4 (385)	SMD -0.29, 95% CI -0.58 to -0.01, I ² =46%	3 (280)	SMD -0.41, 95% CI -0.69 to -0.14, I ² =17%
	Cough severity	3 (280)	SMD -0.50, 95% CI -0.88 to -0.13, I ² =53%		NA

Pooled results compare honey to comparator, meta-analysed with Mantel-Haenszel random effects models. Studies=number of included studies reporting outcome.

*Results excluding Cohen 2017,²¹ Gupta 2016,²² Miceli Sopo 2015¹⁸ and Canciani 2014¹⁹.

†Subgroup of usual care.

MD, mean difference; n, total number of participants; NA, not applicable, as these studies were not in the primary analysis so results are unchanged; SMD, standard mean difference.

could combine only two placebo controlled studies in the meta-analysis, and these used honey and a honey containing syrup. The pooled result had considerable heterogeneity (91%). This may represent differences between the interventions. A sensitivity analysis excluding the syrup indicated a beneficial effect of honey on cough, but this was based on a single study. Two of the three studies comparing honey with placebo indicated a beneficial effect of honey, but overall we do not have a strong evidence base from comparisons of honey against matched placebo.

In comparison with usual care, honey was associated with a significantly greater reduction in combined symptom score, cough frequency and cough severity (table 3). The low heterogeneity in these comparisons (I²=0% for combined symptoms and cough frequency, 20% for cough severity) suggested that despite the variety of usual care treatments used by these studies, all were similarly ineffective. These estimates were consistent with estimates from comparison with placebo. The persistence of the effect size in the sensitivity analyses, despite a reduction in statistical power, implied that the effect size was robust, strengthening the evidence in favour of honey and supported our analysis strategies.

The apparent effect of honey was further supported by subgroup analyses. The results with diphenhydramine (online supplementary figure 4) were consistent with dextromethorphan (online supplementary figure 3) for improvement of all three outcomes. The dextromethorphan comparison was not significant, but included only two studies,^{16 24} with one reporting combined symptoms. Similarly, in the dichotomous outcome, 'improvement', honey was not significantly better than usual care (table 3). As well as a loss of statistical power in dichotomising outcomes, an explanation for this could be that it was the wrong question to ask. The self-limiting nature of URTIs results in a general trend of improvement in symptoms, even in the control groups. The difference, therefore, between control and intervention groups is likely to be in the degree of recovery.

Previous reviews have included children and focused on cough. Our broader inclusion criteria have allowed us to identify the more limited data for adults, both in terms of numbers of studies and effectiveness, and for symptoms such as sore throat.

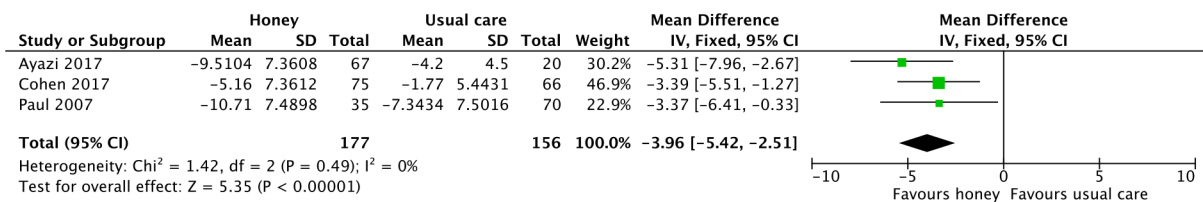
Strengths and limitations

A strength of this review was our comprehensive search strategy, which means we are unlikely to have missed any relevant studies. To our knowledge, this is the most comprehensive systematic review evaluating honey for the improvement of a range of URTI symptoms.

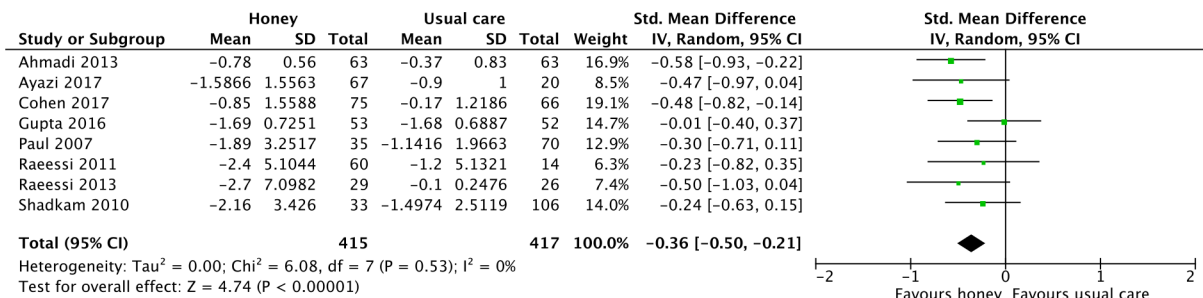
A limitation was the risk of bias in the included studies. The risk of bias was variable, and we did not assess study quality in other ways. There was limited information on how patients in the placebo arms were asked not to take honey, and how their adherence was measured. This is a weakness, and if honey were effective this would bias the effect towards the null. There were also missing data but we estimated missing values where it was possible and appropriate, allowing the pooling of studies that could not otherwise have been synthesised. We did this to include as much as possible but the weaknesses of this approach are a loss of data and including studies which tended to be smaller and at a higher risk of bias. This may explain why the dichotomised outcome, 'improvement', showed no effect compared with usual care, whereas using the combined symptom score detected a statistically significant effect.

The broad nature of our inclusion criteria, while necessary to maximise the scope of eligible studies, also resulted in considerable variability in interventions. Most studies included in the meta-analyses did evaluate pure honey, but Grintuss syrup,^{19 21} Honitus syrup,²² and honey combined with milk¹⁸ and coffee^{15 26} were also used, and we evaluated these as 'honey' interventions. A disadvantage of including these studies is the difficulty in knowing how much of any effect is due to honey, and how much

Combined symptom score:



Cough frequency:



Cough severity:

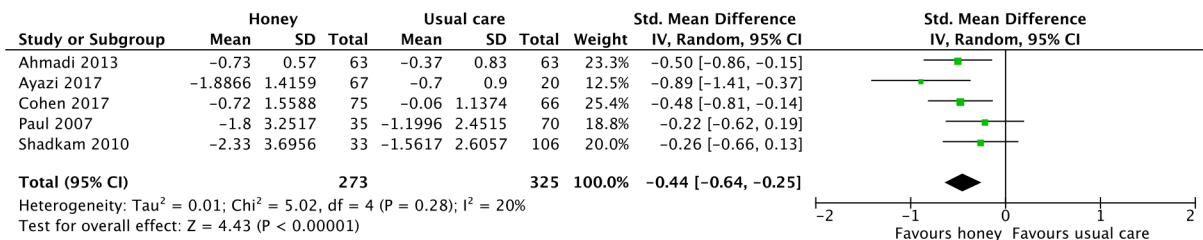


Figure 3 Forest plots for changes in combined symptoms score, cough frequency and cough severity when patients were treated with honey versus usual care.

might it be due to the other ingredients. We included these studies because we could find no clinical evidence of effectiveness of the other ingredients. Honey is itself a complex and heterogeneous substance; DNA analysis has shown it contains plant material from multiple taxa.²⁷ The 'usual care' interventions were also highly varied and could have had different effects. Some studies used comparators that attempted to replicate the look and consistency of honey. If the effect of honey is mediated through forming a soothing mechanical barrier, then these comparators could have a similar effect to honey, biasing the results towards the null. On the other hand, studies that made less of an attempt to blind patients to their allocation risk biased reporting and patients taking honey outside of the trial context, with less predictable results. The low heterogeneity of our results, and our sensitivity analyses, are reassuring. Finally, we could not explore the effectiveness of different types or doses of honey due to lack of data.

Implications for clinicians and policy makers

Existing research shows that most usual care therapies produce no, or relatively small, improvements in URTI symptoms.^{28,29} Antibiotics, which are frequently prescribed despite guidance, are associated with significant adverse effects in children and adults.^{2,3,30} Given that a lack of alternative therapies⁶ and a desire to preserve the patient–doctor relationship⁵ are two key contributors to antibiotic over prescription by general practitioners, our finding that honey may be effective is important in the clinical context: honey is a reasonable alternative. Adverse effects were not observed in most patients given honey, and they were relatively mild, such as nausea. Honey is commercially consumed and is safe for use by the majority of the population, apart from allergic individuals and infants under 1 year of age.³¹ Data on the use of honey and other complementary and alternative medicines in the UK, and doctors' and patients' perceptions of these therapies, are limited.

However, the low cost and easy accessibility of honey would likely contribute to the acceptability of this treatment to patients, clinicians and policy makers. Because of the limitations to the evidence, particularly for adults, we would support large, high quality placebo controlled trials.

Conclusion

We found that honey likely improves URTI symptoms, with the strongest evidence in the context of cough frequency and cough severity. Moderate evidence supports its use in preference to usual care for other URTI symptoms, and most evidence comes from studies of children. Honey is a frequently used lay remedy that is well known to patients. It is also cheap, easy to access and has limited harms. When clinicians wish to prescribe for URTI, we would recommend honey as an alternative to antibiotics. Honey is more effective and less harmful than usual care alternatives and avoids causing harm through antimicrobial resistance.

Twitter Charlotte Albury @AlburyCharlotte

Acknowledgements The authors thank Filippo Bianchi, Kerstin Frei, Milad Sherafati and Marina Al Basri for translating, and Nia Roberts for training and reviewing the search strategy. The authors also thank Merlin Wilcox for sharing the search terms and Oliver Van Hecke for reviewing the search terms.

Funding No external funding was received for this work. HA: medical student, University of Oxford. CA: NIHR SPCR trainee. JL: NIHR SPCR Career Progression Fellow.

Competing interests JL is a hobby beekeeper.

Patient consent for publication Not required.

Provenance and peer review Not commissioned; externally peer reviewed.

Data availability statement We are unable to share primary data as these are published papers that we do not have permission to share. All references are provided, although subscriptions may be required for access.

ORCID iD

Hibatullah Abuelgasim <http://orcid.org/0000-0002-2498-090X>

References

- Goossens H, Ferech M, Vander Stichele R, *et al.* Outpatient antibiotic use in Europe and association with resistance: a cross-national database study. *Lancet* 2005;365:579–87.
- Kenealy T, Arroll B. Antibiotics for the common cold and acute purulent rhinitis. *Cochrane Database Syst Rev* 2013;6:CD000247.
- Arroll B. Common cold. *BMJ Clin Evid* 2011;2011:1510.
- Hersh AL, Jackson MA, Hicks LA, *et al.* Principles of judicious antibiotic prescribing for upper respiratory tract infections in pediatrics. *Pediatrics* 2013;132:1146–54.
- Kumar S, Little P, Britten N. Why do general practitioners prescribe antibiotics for sore throat? Grounded theory interview study. *BMJ* 2003;326:138.
- Bradley CP. Uncomfortable prescribing decisions: a critical incident study. *BMJ* 1992;304:294–6.
- Ventola CL. The antibiotic resistance crisis: Part 1: causes and threats. *Pharmacy & Therapeutics P T* 2015;40:277–83.
- The Review on Antimicrobial Resistance. Tackling drug-resistant infections globally: final report and recommendations [Internet], 2016. Available: https://amr-review.org/sites/default/files/160525_Final paper_with cover.pdf
- van Hecke O, Wang K, Lee JJ, *et al.* Implications of antibiotic resistance for patients' recovery from common infections in the community: a systematic review and meta-analysis. *Clin Infect Dis* 2017;65:371–82.
- Oduwole O, Meremikwu MM, Oyo-Ita A, *et al.* Honey for acute cough in children. *Cochrane Database Syst Rev* 2014:CD007094.
- Higgins JPT, Altman DG, Sterne JAC. Chapter 8: Assessing risk of bias in included studies. In: Higgins JPT, Green S, eds. *Cochrane Handbook for Systematic Reviews of Interventions Version 5.1.0 (updated March 2011) [Internet]*. The Cochrane Collaboration, 2011. www.handbook.cochrane.org
- The Cochrane Collaboration. *Review Manager (RevMan) [computer program]. Version 5.3*. Copenhagen Nord Cochrane Cent, 2014.
- Ahmadi M, Moosavi SM, Zakeri S. Comparison of the effect of honey and diphenhydramine on cough alleviation in 2–5-year-old children with viral upper respiratory tract infection. *J Gorgan Univ Med Sci* 2013;15:8–13.
- Ayazi P, Mahyar A, Yousef-Zanjani M, *et al.* Comparison of the effect of two kinds of Iranian honey and diphenhydramine on nocturnal cough and the sleep quality in coughing children and their parents. *PLoS One* 2017;12:e0170277.
- Raessi MA, Aslani J, Raessi N, *et al.* Honey plus coffee versus systemic steroid in the treatment of persistent post-infectious cough: a randomised controlled trial. *Prim Care Respir J* 2013;22:325–30.
- Shadkam MN, Mozaffari-Khosravi H, Mozayan MR. A comparison of the effect of honey, dextromethorphan, and diphenhydramine on nightly cough and sleep quality in children and their parents. *J Altern Complement Med* 2010;16:787–93.
- Waris A, Macharia M, Njeru EK, *et al.* Randomised double blind study to compare effectiveness of honey, salbutamol and placebo in treatment of cough in children with common cold. *East Afr Med J* 2014;91:50–6.
- Miceli Sopo S, Greco M, Monaco S, *et al.* Effect of multiple honey doses on non-specific acute cough in children. An open randomised study and literature review. *Allergol Immunopathol* 2015;43:449–55.
- Canciani M, Murgia V, Caimmi D, *et al.* Efficacy of Grintuss pediatric syrup in treating cough in children: a randomized, multicenter, double blind, placebo-controlled clinical trial. *Ital J Pediatr* 2014;40:56.
- Cohen HA, Rozen J, Kristal H, *et al.* Effect of honey on nocturnal cough and sleep quality: a double-blind, randomized, placebo-controlled study. *Pediatrics* 2012;130:465–71.
- Cohen HA, Hoshen M, Gur S, *et al.* Efficacy and tolerability of a polysaccharide-resin-honey based cough syrup as compared to carbocysteine syrup for children with colds: a randomized, single-blinded, multicenter study. *World J Pediatr* 2017;13:27–33.
- Gupta A, Gaikwad V, Kumar S, *et al.* Clinical validation of efficacy and safety of herbal cough formulation "Honitus syrup" for symptomatic relief of acute non-productive cough and throat irritation. *Ayu* 2016;37:206–14.
- Nanda M, Mittal S, Gupta V. Role of honey as adjuvant therapy in patients with sore throat. *Natl J Physiol Pharm Pharmacol* 2017;7:1–5.
- Paul IM, Beiler J, McMonagle A, *et al.* Effect of honey, dextromethorphan, and no treatment on nocturnal cough and sleep quality for coughing children and their parents. *Arch Pediatr Adolesc Med* 2007;161:1140–6.
- Pourahmad M, Sobhanian S. Effect of honey on the common cold. *Arch Med Res* 2009;40:224–5.
- Raessi M, Aslani J, Gharai H, *et al.* Honey with coffee: a new finding in the treatment of persistent postinfectious cough. *Iran J Otorhinolaryngol* 2011;23:1–8.
- Hawkins J, de Vere N, Griffith A, *et al.* Using DNA metabarcoding to identify the floral composition of honey: a new tool for investigating honey bee foraging preferences. *PLoS One* 2015;10:e0134735.
- Smith SM, Schroeder K, Fahey T. Over-The-Counter (OTC) medications for acute cough in children and adults in community settings. *Cochrane Database Syst Rev* 2014:CD001831.
- Smith SM, Henman M, Schroeder K, *et al.* Over-The-Counter cough medicines in children: neither safe or efficacious? *Br J Gen Pract* 2008;58:757–8.
- Kenealy T. Sore throat. *BMJ Clin Evid* 2011;2011:1509.
- Arnon SS, Midura TF, Damus K, *et al.* Honey and other environmental risk factors for infant botulism. *J Pediatr* 1979;94:331–6.
- Chung KF. Assessment and measurement of cough: The value of new tools. In: *Pulmonary pharmacology and therapeutics*. , 2002: 15, 267–72.