



Research Paper

CAM treatments for cough and sore throat as part of an uncomplicated acute respiratory tract infection: a systematic review of prescription rates and a survey among European integrative medical practitioners

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ABSTRACT

Introduction: Most Complementary & Alternative Medicine (CAM) interventions have not been tested in clinical trials and systematic reviews (SRs). It is therefore important to collect knowledge from experienced practitioners to identify (lower level) evidence to support their use and to prioritize interventions for future research. This study aimed to document the CAM treatments for cough and sore throat as part of uncomplicated, acute respiratory tract infections (RTI), most frequently recommended by experienced integrative medical practitioners; and to assess whether these approaches have been tested in clinical trials and SRs.

Methods: Data on treatment approaches were collected by means of (1) a SR on prescription rates of CAM treatments for RTIs in CAM practice by searching Pubmed and CINAHL databases; and (2) a survey among integrative medical doctors and TCM practitioners in five European countries.

Results: The SR identified 336 articles. After screening five studies were included (Anthroposophic Medicine (AM): two and homeopathy (HOM): three). The survey resulted in 262 responses (including 99 AM and 95 HOM experts). Of 19 products that were described in both the SR and the survey, two (22%) AM (*Hustenelixier*, *Echinacea*) and three (30%) homeopathic products (*Belladonna*, *Hepar sulphuris*, *Mercurius solubilis*) had been studied in a clinical trial and one AM treatment (*Echinacea*) in a SR for this indication.

Conclusions: CAM treatments for RTI related cough and sore throat were identified (medicinal products, syrup, external applications, tea and acupuncture). These treatments have hardly been studied in clinical trials (26%) and SRs (5%) and require further evaluation.

1. Background

1.1. The AMR problem

Resistance to antibiotics is a complex and growing international public health problem with important consequences such as increased mortality and economic impact [1]. In most global, regional and national policies on antimicrobial resistance (AMR), six main strategies are used to achieve the goal of reducing the AMR problem: infection prevention and control of resistant bacteria, monitoring of both

infection prevention and control of resistant bacteria, research on antibiotic resistance and antibiotic use, appropriate use of antibiotics (e.g. not for viral infections), less antibiotic use (e.g. delayed prescription and alternatives), and development of new antibiotics [2]. In human medicine, Complementary & Alternative Medicine (CAM) treatment strategies, including CAM medicinal products and fever management strategies, are not included in these official AMR policies [3]. However, national guidelines for uncomplicated, acute respiratory tract infections (RTIs) in many EU countries demonstrate entry points for delayed prescription and options for CAM treatments as part of delayed

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prescription strategies [4].

1.2. The hypothetical value of CAM in bridging the gap between guidelines and practice

There is a gap between guidelines and current practice in Europe regarding the non-use of antibiotics for RTIs. The guidelines for treatment of uncomplicated, acute RTIs in five European countries (France, Germany, Switzerland, the Netherlands and the UK) demonstrate that antibiotics are only indicated in high risk groups and for complications. However, antibiotics are often prescribed for uncomplicated, acute RTIs, motivated in various ways by patients and health care professionals [5,6].

Primary care is of high relevance for AMR policies. For example, in the UK 74% of antibiotics for human use are prescribed in primary care, making it one of the most important contributors to the development of AMR [7]. Reducing the use of antibiotics in primary care and counteracting the development of AMR are pressing international priorities.

CAM competence can make a difference. There is a growing amount of evidence that GP surgeries employing doctors with additional qualification in Integrative Medicine (IM doctors) prescribe fewer antibiotics overall and for RTIs than conventional GP surgeries. This could be because IM doctors have additional treatments to offer for infections, and/or patients who do not want to use antibiotics visit these IM surgeries [3,8].

1.3. The need to collect and systematize expert knowledge of expert CAM professionals

There is a paradox as far as CAM is concerned. On the one hand many surveys and other studies demonstrate that many people would like to be treated with CAM [9–13]. Surveys conducted among patients in university hospitals show that more than 50% of patients at the departments of oncology, gastroenterology and even cardiology are requesting CAM treatment and wish to be better informed about it [14]. On the other hand, there is only limited funding for CAM treatment studies in many EU countries, unlike in the US and China which provide substantial budgets to study the efficacy of traditional medicine and herbals. In addition, other than in China, funding by EU industry is limited by the fact that several CAM medicinal products are generic and cannot be patented; thus, in the current EU policy, there are no large profits to be expected from investments in research as for many new biomedical drugs. There is a gap between the public need and the recognition by the politicians and universities. There is only scattered and isolated research activity in the medical faculties in European countries [3,15].

A European research strategy on deepening knowledge about the potential contribution of CAM should address the need to make use of the large amount of professional CAM expertise, data on CAM daily practices and/or patient experiences, because most CAM interventions have not yet been tested yet and very likely will not be tested in clinical trials in the foreseeable future, due to the described lack of sufficient financial resources and methodological issues [16].

1.4. The objectives of this study

This study therefore aims first to identify the CAM treatments most frequently recommended by integrative medical practitioners in five European countries for cough and sore throat as part of an uncomplicated, acute RTI by (1) analysing prescription rates of CAM treatments and by (2) collecting recommendations of integrative medical doctors and Traditional Chinese Medicine (TCM) practitioners with regard to the CAM treatment for these indications, in order to provide evidence from observational studies and professional opinion. Secondly, the study aims to explore the percentages of identified CAM treatments that have been tested in clinical trials and systematic

reviews for uncomplicated, acute RTIs.

2. Methods

2.1. Research questions

- 1 What are the CAM treatments used for cough and sore throat as part of uncomplicated, acute RTIs and are most frequently recommended according to:
 - the prescription rates of CAM treatment by integrative medical doctors? (see 2.3)
 - the expert knowledge of experienced integrative medical doctors and TCM practitioners? (see 2.4)
- 2 To what extent have recommended CAM treatments (for uncomplicated, acute RTIs) been studied in clinical trials and systematic reviews? (see 2.5)

2.2. Operationalization

The following definitions were used for:

- Most frequently recommended CAM treatments:
 - o Most frequently recommended CAM treatments by integrative medical practitioners (survey)
 - o Most frequently prescribed CAM treatment in CAM daily practices of doctors and therapists (SR)
- CAM:
 - o Anthroposophic medicine (AM)
 - o Ayurveda
 - o Homeopathy (HOM)
 - o Traditional Chinese Medicine (TCM)
 - o Western herbal medicine (phytotherapy)
- Cough:
 - o Dry cough as part of an uncomplicated, acute RTI
 - o Wet cough as part of an uncomplicated, acute RTI
- Sore throat:
 - o Sore throat with fever as part of an uncomplicated, acute RTI
 - o Sore throat without fever as part of an uncomplicated, acute RTI

2.3. Systematic review on prescription rates of CAM practices

2.3.1. Search strategy

A literature search was executed in two databases: PubMed and CINAHL. The search period was from 15 years before the search date until the search date (03-07-2019). Search terms were combinations of:

- CAM search terms: complementary, alternative, integrative, CAM, Ayurveda/ ayurvedic, anthroposophy/ anthroposophic, herbal, traditional Chinese medicine/ TCM, homeopathy/ homeopathic, and
- RTI search terms: respiratory tract infection, cough, sore throat.

Language restrictions: only publications in Dutch, English, German, French were included, because publications with other languages could not be read by the researchers involved in the screening and analyses processes (see 2.3.3 and 2.3.4).

2.3.2. Inclusion criteria

Studies were included that:

- monitored CAM practices in Europe, and
- included RTIs and/ or cough and/ or sore throat, and
- presented prescription rates of CAM treatments of RTIs

Studies were excluded that:

- monitored CAM practices outside Europe, or

- included cough and/ or sore throat but not as part of an uncomplicated, acute RTI, or
- did not present prescription rates of CAM treatments for RTIs

2.3.3. Data management and selection process

A single Endnote file of all references identified through the search process, was produced by EBe. Duplicates were removed from this file.

Two researchers (EBa, EBe) then independently subsequently screened the titles, abstracts and full texts of the searched studies, performed study selection, and recorded their decisions on a standardised eligibility form. Disagreements between the two reviewers were resolved via discussion or ultimately, by consulting a third reviewer.

2.3.4. Data collection process

Two researchers (EBa, EBe) read the full text of each included article and independently extracted the relevant data, using a standard and piloted extraction form. Any disagreement between the authors was resolved by discussion with a group of authors. When the reported data were insufficient or ambiguous, the corresponding authors were contacted to request for the additional information.

2.3.5. Data-analyses

Lists of 'best CAM treatments' for each indication were made, based on a ranking of number of times prescribed. For each indication, per CAM modality, CAM treatments were ranked from most prescribed to least prescribed. When there were two or more articles on prescription rates for the same CAM modality and the same indication, these CAM treatments were listed.

2.4. Survey

2.4.1. Population

A survey in four languages (Dutch, English, French and German) was conducted and disseminated among medical doctors practicing at least one of five CAM types (anthroposophic medicine (AM), Ayurveda, homeopathy, western herbal medicine (phytotherapy) and traditional Chinese medicine (TCM)) in five European countries (France, Germany, Switzerland, the Netherlands, UK) to collect and systematize their knowledge on CAM treatments for four indications. A purposive sample of integrative medical practitioners was approached through national CAM associations (members of EuroCAM) in each of the five countries to complete an online survey. Members of associations received from their own national CAM association an invitation per email that was written by the researchers. In the email a link to the online questionnaire in the right language was provided. Only CAM professionals that fulfilled the criteria of being an integrative medical practitioner with at least 5 years of experience in practice were able to complete the questionnaire. The researchers did not have access to or information on the total number of the target population per association, so therefore estimations of the population size of integrative medical practitioners were made (see 2.4.3). By completing the survey, practitioners had therefore provided their consent to participate.

2.4.2. Content of the survey

Integrative medical practitioners were invited in the survey to describe, according to their experience, their top 3 best CAM treatments for the following indications: (1) dry cough, (2) wet cough, (3) sore throat without fever, and (4) sore throat with fever, all as part of an uncomplicated, acute RTI.

2.4.3. Sample size calculation

Based on an estimated population of a maximum of 1000 integrative medical professionals (GPs and pediatricians) per CAM modality in all five countries, a confidence level of 95% and a margin of error of 10%, a minimum of 88 respondents per CAM modality was required to get valid results.

2.4.4. Data-analysis: ranking of expert practices

Lists of 'best CAM treatments' for each indication were made based on a ranking of number of times mentioned by the respondents.

2.5. Analysis of the extent to which recommended CAM treatments are studied in clinical trials and systematic reviews

Per CAM modality, a list of 'best CAM treatments' (identified in both the survey and the SR) was made. Then, for each CAM treatment in PubMed a search was executed on the existence of a clinical trial on RTI treatment in the last 20 years. In addition for each CAM treatment it was checked whether or not the treatment was analyzed in a SR for this indication.

2.6. Ethical approval

Because this study included only a literature review and a survey among healthcare professionals, without patient involvement, ethical approval according to the Dutch law was not needed as is described at the website of the Centrale Commissie Mensgebonden Onderzoek (<https://www.ccmo.nl/onderzoekers/wet-en-regelgeving-voor-medisch-wetenschappelijk-onderzoek/uw-onderzoek-wmo-plichtig-of-niet>).

3. Results

3.1. Systematic review on prescription rates for uncomplicated, acute RTIs in CAM practices

3.1.1. Search results

The search resulted in 336 hits. From these, five studies matched the inclusion and exclusion criteria: two on AM and three on HOM (Fig. 1) (Table 1).

3.1.2. Anthroposophic medicine

Jeschke et al. [17] studied in a prospective, multicenter observational study prescribing patterns of AM in pediatric primary care (38 primary care physicians in Germany with a total of 57893 prescriptions for 18440 children under 12 years of age). *Hustnelixier* (cough elixir), *Nasenoel* (nose oil), and *Apis/Belladonna cum mercurio* were the most frequently prescribed anthroposophic remedies for acute upper respiratory tract infections (percentages not described) (See Table 8 for active ingredients of the anthroposophic medicinal products).

Hamre et al. [18] analyzed prescription data of 21 AM primary care practices in Europe (13) and the USA (8) in total; there were no separate analyses for Europe. The cohort comprised 715 consecutive outpatients aged > 1 month, treated for *acute otitis* and *respiratory infections*. The most frequently prescribed anthroposophic medicinal products were: *Plantago Bronchial Balm* (16.4%), *Erysidoron*® 1 Liquid (13.7%), *Cinnabar comp. Powder* (13.4%), *Pneumodoron*® 1 Liquid (9.8%), *Cinnabar/Pyrit Tablets* (9.7%), *Bolus Eucalypti comp. Powder* (8.3%), *Pine Reviving Bath Milk* (7.4%), *Berdonia Nose Spray* (7.0%), *Echinacea comp. Mouthspray* (6.9%), *Sticta Liquid* (6.7%), *Hepar Sulfuris Powder* (6.6%), *Chamomilla comp. suppository* (6.0%), *Aconitum comp. Eardrops* (5.9%), *Infludo*® Liquid (5.6%), *Levisticum Rh Liquid* (5.6%), *Kalium carbonicum Liquid* (4.8%), *Silicea (Quarz) 1% Eardrops* (4.8%), *Nose Balm for Children* (4.5%), and *Capsicum annuum Liquid* (4.5%).

A comparison of the two studies demonstrates that there is no overlap; none of the products are reported in both studies.

3.1.3. Homeopathy

Haidvogel et al. [19] conducted an international, multicenter, comparative non-randomized cohort study of the homeopathic treatment of acute respiratory and ear complaints of 857 patients. The most prescribed medicinal products for children were: *Belladonna* (13.3%), *Pulsatilla* (10.6%), *Hepar sulphuris* (6.6%), *Mercurius solubilis* (6.4%),

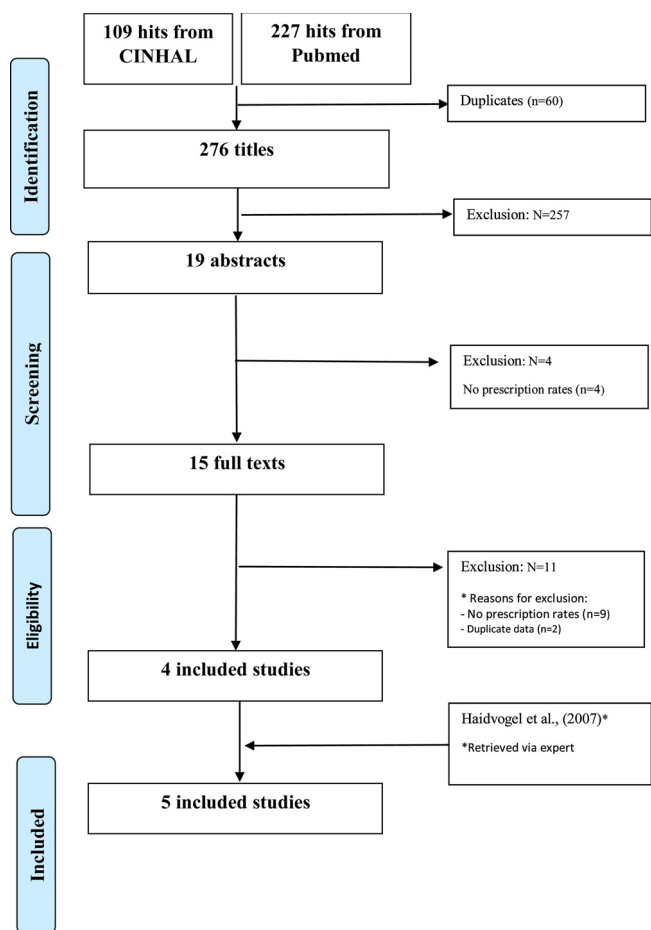


Fig. 1. Flow diagram.

Phosphorus (4.9%), Bryonia alba (3.7%), Calcarea carbonica (3.7%), Lycopodium clavatum (3.7%), Sulphur (3.7%) and Phytolacca decandra (3.4%); and for adults: Hepar sulphuris (9.7%), Belladonna (8.3%), Bryonia alba (7.2%), Lycopodium clavatum (7.2%), Kalium bichromicum (5.8%), Mercurius solubilis (4.9%), Allium cepa (4.5%), Phosphorus (3.4%), Causticum (3.1%) and Gelsemium sempervirens (2.7%).

Salatino and Gray [20] studied with a survey in seven countries the management of pediatric tonsillopharyngitis, with a focus on natural remedies. 138 pediatricians, general practitioners and ear-nose-throat (ENT) specialists in 7 countries responded. SilAto-5-90 (Tonsilotren®, containing: Atropinum sulfuricum D5, Hepar Sulfuris D3, Kalium bichromicum D4, Silicea D2, Mercurius bijodatus D8) was the most frequently prescribed (38%), followed by Mercurius solubilis (6%), AcoBry-6-78 (Influcid®, containing: Aconitum D3, Gelsemium D3, Phosphorus D5, Bryonia D2, Ipecacuanha D3, Eupatorium perfoliatum D1) (6%), Belladonna (5%) and CalSuli-4-02 (Immunokind®, containing: Calcium carbonicum Hahnemanni D6, Calcium fluoratum D6, Calcium phosphoricum D6, Sulfur jodatum D12) (4%).

Vincent et al. [21] studied in a prospective observational study the treatment of influenza-like illnesses by homeopathic GPs in France. The 124 homeopathic GPs prescribed most often: Belladonna (33.8%), Eupatorium (30.5%), Gelsemium (22.5%), Oscilloccinum (21.9%), Bryonia (21.2%), Influenzinum (15.2%) and L52 (a mixture of several homeopathic dilutions of ILI medications) (12.6%).

A comparison of the three studies demonstrates that Belladonna and Bryonia were reported in all three studies, and that Hepar Sulfuris, Mercurius solubilis, Phosphorus, Calcium carbonicum, Sulphur, Kalium bichromicum and Gelsemium are reported in two studies.

Table 1 Study characteristics.

	CAM type	Design	Population	Indication
Jeschke et al. [17]	AM	Prospective, multicenter observational study (38 German primary care physicians)	18440 children under 12 years of age	Acute upper respiratory tract infections
Hamre et al. [18]	AM	Cohort study (21 AM primary care practices in Europe and the USA)	715 outpatients aged > 1 month	Acute otitis and respiratory infections
Haidvogel et al. [19]	HOM	International, multicenter, comparative non-randomized cohort study (57 primary care practices in Austria (8), Germany (8), the Netherlands (7), Russia (6), Spain (6), Ukraine (4), United Kingdom (10) and the USA (8))	857 patients presenting themselves with at least one chief complaint: acute (≤ 7 days) runny nose, sore throat, ear pain, sinus pain or cough	Acute respiratory and ear complaints
Salatino and Gray [20]	HOM	Survey (138 pediatricians, general practitioners (GPs) and ear-nose-throat specialists in 7 countries (Bulgaria, Spain, Israel, Italy, Portugal, Romania and Serbia))	138 pediatric patients with tonsillopharyngitis	Pediatric tonsillopharyngitis
Vincent et al. [21]	HOM	Prospective observational study (124 French homeopathic GPs)	151 patients with influenza-like illnesses	Influenza-like illnesses

AM = Anthroposophic Medicine.
HOM = Homeopathy.

Table 2
Response rates per CAM type and per language (country).

	German speaking countries (Germany & Switzerland)	French (France)	Dutch (The Netherlands)	English (UK)	Total
Anthroposophic medicine	88	0	8	3	99
Ayurveda	3	0	2	3	8
Homeopathy	45	3	39	8	95
Traditional Chinese medicine	10	0	8	7	25
Phytotherapy	23	1	4	7	35
Total	169	4	61	28	262

3.2. Survey

3.2.1. Response of the survey

With 262 respondents in total, the highest and sufficient responses (≥ 88 respondents per CAM modality) were for AM ($n = 99$) and homeopathy ($n = 95$) (Table 2).

Low and insufficient responses were in France and UK and for Ayurveda, TCM and phytotherapy.

3.2.2. Results for the indications cough and sore throat

The ranked lists of most often mentioned treatments for AM, homeopathy, TCM and phytotherapy for the indications dry cough, wet cough, sore throat and sore throat and fever are presented in Tables 3–6 (if applicable, treatments for children and adults are separately listed). In addition to medicinal products, mentioned in all four CAM types, AM uses external applications and tea, phytotherapy uses inhalations, and TCM uses acupuncture/ acupressure, cupping and massage. Comparing the four CAM types demonstrates that there is some overlap in substances of medicinal products between AM and homeopathy (for dry cough: *Bryonia* and *Spongia*; for sore throat and fever: *Belladonna* and *Mercurius*) and for AM and phytotherapy (for wet cough: thyme; for sore throat: *Echinacea* and *Salvia*).

3.2.3. Other results

Many (especially homeopathic) respondents answered that more information than provided in the survey questions was necessary to be able to make an individualized treatment. Acupuncture was mentioned often in the TCM group, but this may be (also) have been due to the fact that members of the acupuncture association were among these respondents.

Table 3
CAM treatments for dry cough, most frequently recommended by integrative medical practitioners.

Anthroposophic medicine (n = 99)	Homeopathy (n = 95)	Phytotherapy (n = 35)	Traditional Chinese medicine (n = 25)
Medicinal products: <ul style="list-style-type: none"> ● <i>Bronchi plantago</i> (15%) ● <i>Cuprum aceticum comp.</i> (Pertudoron 2) (13%) ● <i>Tartarus stibiatus</i> (13%) ● <i>Bryonia Spongia</i> (7%) 	Medicinal products: <ul style="list-style-type: none"> ● <i>Spongia</i> (27%) ● <i>Bryonia</i> (21%) ● <i>Drosera</i> (24%) ● <i>Aconitum</i> (11%) ● <i>Phosphorus</i> (9%) ● <i>Coccus cacti</i> (6%) 	Medicinal products: <p>Children</p> <ul style="list-style-type: none"> ● Thyme (34%) ● Marshmallow (31%) ● Ivy (26%) ● Inhalation with hot damp (20%) <p>Adults</p> <ul style="list-style-type: none"> ● Thyme (29%) ● Inhalation ● with hot damp (26%) 	Medicinal products: <ul style="list-style-type: none"> ● <i>Mai Men Dong</i> (<i>Tuber Ophiopogonis Japonici</i>) (14%) <p>Other treatments</p> <ul style="list-style-type: none"> ● Acupuncture (36%)
External applications on the chest: <ul style="list-style-type: none"> ● <i>Plantago bronchial balsam</i> (18%) ● Lavender (11%) 			
Cough syrup: <ul style="list-style-type: none"> ● <i>Flechtenhonig/ Plantago cough</i> (10%) ● <i>Weleda cough juice or syrup</i> (6%) 			

3.3. A comparison of the results of the survey and the SR on prescription rates in CAM daily practices for anthroposophic medicine and homeopathy

3.3.1. Anthroposophic medicine

Nine AM medicinal products (respectively 33% and 41% of the products described in the survey and the SR) were mentioned both in the survey and the SR: *Hustenelixier*, *Apis/Belladonna cum mercurio*, *Plantago Bronchial Balm*, *Erysidoron 1*, *Pneumodoron 1*, *Bolus Eucalypti comp.*, *Echinacea*, *Hepar Sulfuris* and *Infludo*® (Table 7).

3.3.2. Homeopathy

Ten homeopathic products (respectively 56% and 56% of the products described in the survey and the SR) were described both in the survey and the SR: *Aconitum*, *Belladonna*, *Bryonia alba*, *Gelsemium*, *Hepar sulphuris*, *Ipecacuanha*, *Mercurius solubilis*, *Phosphorus*, *Phytolacca* and *Pulsatilla* (Table 7). Both Tonsilotren and Influcid, combinations of single remedies, were studied in a clinical trial.

3.4. Identified CAM treatments studied in clinical trials and systematic reviews

Of the AM treatments, nine of all 42 (21%), and two of the nine (22%) AM treatments described both in the survey and the SR, had been studied in a clinical trial and one (11%) in a systematic review of clinical trials for the indication acute RTI (Table 7).

Of the HOM treatments, eight of all 20 (40%), and three of the ten (30%) homeopathic products described both in the survey and the SR, had been studied as a single product in a clinical trial and zero (0%) in a systematic review for the indication acute RTI (Table 7).

4. Discussion

Most CAM interventions are not, and very likely will not be, tested in clinical trials and included in systematic reviews in the foreseeable future, due to a lack of sufficient financial resources, a lack of scientific

Table 4
CAM treatments for wet cough, most frequently recommended by integrative medical practitioners.

Anthroposophic medicine (n = 99)	Homeopathy (n = 95)	Phytotherapy (n = 35)	Traditional Chinese medicine (n = 25)
Children <i>Medicinal products:</i> <ul style="list-style-type: none"> ● Bronchi/ Plantago comp. (25%) ● Petasites comp. (16%) ● Plantago Hustensaft (8%) ● Pneumodoron 2 (8%) ● Hustenelixier (7%) ● Pneumodoron 1 (6%) <i>External applications:</i> <ul style="list-style-type: none"> ● Plantago bronchial balsam (32%) Adults <i>Medicinal products:</i> <ul style="list-style-type: none"> ● Pneumodoron 2 (16%) ● Bronchi/Plantago comp. (14%) ● Petasites comp. (10%) ● Thyme (9%) ● Pneumodoron 1 (8%) <i>External applications:</i> <ul style="list-style-type: none"> ● Plantago bronchial balsam (29%) 	Children <i>Medicinal products:</i> <ul style="list-style-type: none"> ● Pulsatilla (34%) ● Antimonium Tartaricum (16%) ● Ipecacuana (11%) Adults <i>Medicinal products:</i> <ul style="list-style-type: none"> ● Pulsatilla (24%) ● Antimonium Tartaricum (16%) ● Ipecacuana (9%) 	Children <i>Medicinal products:</i> <ul style="list-style-type: none"> ● Thyme (46%) ● Inhalation (20%) ● Efeu (14%) ● Liquorice Syrup (11%) ● Marrubium vulgare (11%) ● Salbei (9%) ● Inula eleT&CMpane (9%) Adults <i>Medicinal products:</i> <ul style="list-style-type: none"> ● Thyme (40%) ● Inhalation (14%) ● Salbei (11%) ● Efeu (11%) 	<i>Other treatments:</i> <ul style="list-style-type: none"> ● Acupuncture (72%)

interest and methodological issues. It is therefore important to collect and systematise knowledge of CAM practitioners in order to provide evidence of effectiveness of CAM treatments at the levels of evidence III and IV (observational study) and V (expert opinion) [22]. The first aim of this study was therefore to collect the knowledge of doctors practicing CAM / integrative medicine and practitioners of TCM with regard to the treatment of (wet or dry) cough and sore throat (with or without fever) as part of an uncomplicated, acute RTI. A SR on prescription rates of CAM treatments for these indications, and a survey on expert knowledge of CAM doctors and CAM therapists (TCM) in five European countries on CAM treatments of RTIs, cough and/ or sore throat was therefore carried out. Secondly, the study aimed at analyzing the percentages of identified CAM treatments that have been tested in clinical trials and systematic reviews.

A SR on prescription rates of CAM treatments for uncomplicated, acute RTIs resulted in five included studies: two on AM and three on HOM. The overall response of the survey among CAM doctors (AM, Ayurveda, HOM, phytotherapy, TCM) and CAM therapists (TCM) in five European countries (France, Germany, Switzerland, The Netherlands, UK) was low (n = 262), with highest and sufficient response on AM (n = 99) and homeopathy (n = 95). The most frequently recommended treatments are reported. A comparison of results of the survey and the review demonstrated that nine AM (respectively 33% and 41% of the products described in the survey and the monitoring studies) and ten

homeopathic medicinal products (respectively 56% and 56% of the products described in the survey and the monitoring study) were described both in the survey and the monitoring studies of prescription rates. CAM treatments for uncomplicated, acute RTIs, described both in the survey and the SR, are hardly studied in clinical trials (26%) or in systematic reviews (5%).

The importance of this study is that it contributes to Evidence-Based Practice (EBP) by addressing all three EBP pillars: clinical expertise, patient values and preferences, and research [23]. Practicing true EBP requires clinicians to understand the interplay of these three factors, and to make judicious clinical decisions regarding the care of an individual patient based upon this knowledge. As described, several studies demonstrate that a large group of patients wants to be treated with natural medicines (= second EBP pillar: patient values and preferences) [10]. The other two EBP pillars are addressed by the study of CAM clinical expertise. This type of research is very important to acquire at least some evidence of effectiveness of CAM treatments, because, as previously described, most CAM interventions have not been tested. The value of this type of evidence is larger when the collected expertise in surveys is combined with a literature review on prescription rates, and subsequent triangulation of knowledge sources [24]. These results can be of interest for the relevant stakeholders (doctors, patients, pharmacists), in order to choose as part of a shared decision-making process or in self-management for an expertise-based best CAM

Table 5
CAM treatments for sore throat, most frequently recommended by integrative medical practitioners.

Anthroposophic medicine (n = 99)	Homeopathy (n = 95)	Phytotherapy (n = 35)	Traditional Chinese medicine (n = 25)
<i>Medicinal products:</i> <ul style="list-style-type: none"> ● Apis Belladonna (28%) ● Bolus/Eukalyptus comp. (28%) ● Pyrit /Zinnober (17%) ● Apis Belladonna cum Mercurio (14%) ● Echinacea Rachenspray (14%) ● Zinnober comp. (10%) <i>External applications on the neck:</i> <ul style="list-style-type: none"> ● Citrus (18%) <i>Tea:</i> <ul style="list-style-type: none"> ● Salvia/ salbei tea (16%) 	<i>Medicinal products:</i> Children <ul style="list-style-type: none"> ● Lachesis (12%) ● Bryonia (11%) ● Aconitum (9%) ● Belladonna (8%) ● Spongia (7%) ● Phosphorus (7%) ● Pulsatilla (7%) ● Drosera (6%) ● Phytolacca (6%) Adults <ul style="list-style-type: none"> ● Spongia (17%) ● Lachesis (12%) ● Bryonia (11%) ● Aconitum (11%) ● Drosera (8%) ● Phytolacca (7%) 	<i>Medicinal products:</i> <ul style="list-style-type: none"> ● Echinacea (13%) ● Salbei (13%) ● Zinc lozenges (6%) 	<i>Other treatments:</i> <ul style="list-style-type: none"> ● Acupuncture (32%)

Table 6
CAM treatments for sore throat and fever, most frequently recommended by integrative medical practitioners.

Anthroposophic medicine (n = 99)	Homeopathy (n = 95)	Phytotherapy (n = 35)	Traditional Chinese medicine (n = 25)
Medicinal products: Children <ul style="list-style-type: none"> ● Apis belladonna cum mercurio (31%) ● Apis belladonna (27%) ● Zinnober comp (12%) ● Infludoron (12%) ● Erysidoron 1 (11%) ● Pyriet zinnober (6%) ● Echinacea Mund und Rachenspray (6%) ● Chamomilla (4%) Adults <p><i>Medicinal products:</i></p> <ul style="list-style-type: none"> ● Apis belladonna cum mercurio (23%) ● Erysidoron 1 (21%) ● Bolus Eucalypti comp. (20%) ● Apis belladonna (17%) ● Infludoron (11%) ● Pyriet zinnober (12%) ● Infludo (11%) ● Echinacea Mund und Rachenspray (10%) ● Zinnober comp. (8%) ● Bio salie keelspray (4%) <p><i>External applications:</i></p> Children <ul style="list-style-type: none"> ● Citrus neck wrap (17%) Adults <ul style="list-style-type: none"> ● Citrus neck wrap (16%) 	Medicinal products: Children <ul style="list-style-type: none"> ● Belladonna (42%) ● Aconitum (22%) ● Mercurius (15%) ● Pulsatilla (11%) ● Lachesis (9%) ● Ferrum Phosphoricum (7%) ● Hepar sulphuris (6%) ● Gelsemium (5%) Adults <ul style="list-style-type: none"> ● Belladonna (31%) ● Aconitum (19%) ● Mercurius (15%) ● Lachesis (13%) ● Hepar sulphuris (11%) ● Pulsatilla (7%) ● Ferrum phosphoricum (7%) 	Medicinal products: Children <ul style="list-style-type: none"> ● Salvia (20%) ● Acupuncture (14%) ● Echinacea (14%) ● Linden blossom (11%) ● Thyme (11%) Adults <p><i>Medicinal products:</i></p> <ul style="list-style-type: none"> ● Salvia (34%) ● Echinacea (14%) ● Achillea (11%) <p><i>External applications:</i></p> Children <ul style="list-style-type: none"> ● Wadenwickel (23%) Adults <ul style="list-style-type: none"> ● Wadenwickel (20%) 	<p><i>Other treatments</i></p> <ul style="list-style-type: none"> ● Acupuncture (24%)

Table 7

Anthroposophic medicinal products and homeopathic products described both in the survey and the systematic review studied in clinical trials and systematic reviews.

Anthroposophic medicinal products	Homeopathic products
Hustenelixier ^a	Aconitum
Apis/Belladonna cum mercurio	Belladonna ^a
Plantago Bronchial Balm	Bryonia alba
Erysidoron 1	Gelsemium
Pneumodoron 1	Hepar sulphuris ^a
Bolus Eucalypti comp.	Ipecacuanha
Echinacea ^b	Mercurius solubilis ^a
Hepar Sulfuris	Phosphorus
Infludo ^a	Phytolacca
	Pulsatilla

^a Studied in one or more clinical trials.

^b Studied in one or more clinical trials and one or more SRs.

treatment for these indications, as an alternative for antibiotics. A second strength of this study is that it provides guidance in which CAM treatment strategies should be prioritized (Table 7) for further testing of safety and (cost)effectiveness/ efficacy in controlled clinical studies, based on prescription rates of integrative medical practitioners.

Limitations of the study are, firstly the limited number of databases and languages used in the search strategy. Due to for example excluding Chinese language studies, prescription rates studies performed by Chinese scientists in Europe are expected to be missed. Secondly, the survey results are limited by a low response, specifically for France and the UK and for Ayurveda, TCM and phytotherapy. Therefore, the results are representative for AM and homeopathy only and are tentative for the other CAM modalities. Thirdly, because only experts were included that are licensed and educated in both conventional and complementary medicine, and that are registered as members of one of the national complementary medicine associations, many TCM expert therapists without a license in conventional medicine were not included and therefore unable to respond to the survey. Fourthly, no exact response rates by CAM type and by country could be calculated. Fifthly, there is insufficient information regarding several identified CAM

treatments (e.g. which species of Echinacea is referred to by the professional; what are optimal doses of treatments?) for direct use in clinical practice. Finally, patient experiences and sales figures of CAM OTC products have not been included.

Future studies regarding CAM treatments of uncomplicated, acute RTIs should at first focus on collecting data on expert knowledge of CAM doctors in surveys with larger responses (especially for Ayurveda, phytotherapy and TCM), in more countries (especially in France and the UK) and more languages (e.g. Italian), and on patient experiences and sales figures of CAM OTC products. Analyses of prescription rates of CAM treatments for uncomplicated, acute RTIs in CAM practices in EU countries could provide additional information on Integrative medical practitioner practice. The results on AM and HOM may form the basis to develop expertise-based CAM recommendations or guidelines for uncomplicated, acute RTIs and for designing and executing case reporting and more controlled clinical studies on the (cost)effectiveness of AM and HOM remedies. For the latter, the list of nine AM and ten homeopathic treatments described both in the survey and the SR (Table 7) can be used as a prioritized list for clinical studies. The clinical trials that have been executed should be assessed on methodological quality and results regarding effectiveness and safety. Finally, given the urgent need to reduce inappropriate antibiotic use, CAM treatments for uncomplicated, acute RTIs with sufficient evidence on safety and with some evidence of effectiveness, may already be suggested by doctors and patients, for example as part of a delayed prescription strategy for uncomplicated, acute RTIs. If so, the level of evidence on safety and uncertainty of effectiveness must be transparently communicated during physician-patient consultation or in a written adequately accessible format.

5. Conclusions

- 1 Most frequently recommended CAM treatments for cough and sore throat as part of uncomplicated, acute RTIs were identified, providing (1) input on non-antibiotic alternatives for the treatment of uncomplicated, acute RTIs from other knowledge sources than clinical trials and SRs of clinical trials, and (2) a prioritized list of CAM treatment for further testing in clinical trials.

Table 8
Active ingredients of AM treatments.

AM treatment	Ingredients
Apis belladonna	Apis mellifica, Atropa belladonna
Apis Belladonna cum Mercurio	Apis mellifica, Atropa belladonna, Mercurius solubilis
Bio salie keelspray	Salvia officinalis, Matricaria chamomilla L.
Bolus Eucalypti comp.	Apis mellifica, Atropa belladonna, Eucalyptus globulus
Bronchi/ Plantago comp.	Plantago lanceolata, Eupatorium cannabinum, Bryonia cretica, Pyrit
Chamomilla	Matricaria chamomilla L.
Citrus	Citrus limon
Echinacea Mund und Rachenspray	Echinacea pallida, Salvia officinalis, Calendula officinalis, Argentum nitricum
Erysidoron 1	Apis mellifica, Atropa belladonna
Flechtenhonig	Cetraria islandica, Cladonia rangiferina, Usnea barbata, Mel, Pimpinella anisum, Lobaria pulmonaria
Hustnelixier	Althaea officinalis, Solanum dulcamara, Stipites, Marrubium vulgare, Pimpinella anisi, Serpylli, Thymi vulgaris, Drosera, Cephaelis ipecacuanha, Pulsatilla vulgaris
Infludo	Aconitum napellus, Bryonia cretica, Eucalyptus globulus, Eupatorium perfoliatum, Phosphorus, Sabadilla
Infludoron	Aconitum napellus, Bryonia cretica, Eucalyptus globulus, Eupatorium perfoliatum, Sabadilla, Ferrum phosphoricum
Petasites comp.	Petasites, Plantago lanceolata
Plantago bronchial balsam	Plantago lanceolata, Terebinthina larinica, Campher, Cera flava, Thymi aetheroleum, Eucalypti aetheroleum, Drosera rotundifolia/ anglica, Petasites hybridus
Plantago cough/ Plantago Hustensaft	Petasites
Pneumodoron 1	Aconitum napellus, Bryonia
Pneumodoron 2	Phosphorus, Tartarus stibiatus
Pyrit zinnober	Pyrit, Cinnabarit
Salvia/ salbei tea	Salvia officinalis
Thyme	Thymus vulgaris L.
Weleda cough juice or syrup	Drosera rotundifolia, Althaea officinalis, Inula helenium, Marrubium vulgare, Pimpinella anisum, Plantago lanceolate, Thymus vulgaris, Citrus limon, Ipecacuanha, Pulsatilla vulgaris
Zinnober comp.	Apisinum, Atropa belladonna, Zinnober

2 Few identified CAM treatments for uncomplicated, acute RTIs have been studied in clinical trials and in SRs of clinical trials.

Authors Contribution

All authors have made substantial contributions to all of the following: (1) the conception and design of the study, or acquisition of data, or analysis and interpretation of data, (2) drafting the article or revising it critically for important intellectual content, (3) final approval of the version to be submitted.

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Erik W. Baars: Conceptualization, Data curation, Formal analysis, Investigation, Methodology, Project administration, Supervision, Writing - original draft, Writing - review & editing. **Eefje Belt-Van Zoen:** Conceptualization, Data curation, Formal analysis, Investigation, Methodology, Project administration, Writing - review & editing. **Merlin Willcox:** Conceptualization, Data curation, Investigation, Methodology, Writing - review & editing. **Roman Huber:** Conceptualization, Writing - review & editing. **Xiao-Yang Hu:** Conceptualization, Data curation, Investigation, Methodology, Writing - review & editing. **Esther T. van der Werf:** Conceptualization, Data curation, Investigation, Methodology, Writing - review & editing.

Declaration of Competing Interest

The authors report no declarations of interest.

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Appendix A. Supplementary data

Supplementary material related to this article can be found, in the online version, at doi:<https://doi.org/10.1016/j.eujim.2020.101194>.

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