The use of cough syrup in the management of acute cough in young children

Janssens Jules, KU Leuven

Verfaillie Pieter, KU Leuven

Promotor: Dr. Spitaels David

Co-promotor: Dr. Van den Bulck Steve

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Abstract (Nederlands)

Achtergrond: In een poging om acute hoest symptomen bij kinderen te verlichten, worden over the counter (OTC) hoestmedicijnen veelvuldig gebruikt. Ondanks talrijke studies die een gebrek aan doorslaggevend bewijs voor hun doeltreffendheid aantonen, worden vrij verkrijgbare hoestsiropen nog steeds vaak voorgeschreven door huisartsen. Dezelfde trend wordt waargenomen in het Belgische gezondheidszorgsysteem. Ouders zijn zich vaak niet bewust van het beperkte effect en mogelijke schadelijke gevolgen van hoestmedicatie.

Doel: Ons doel is om het gebruik van hoestmedicatie bij kinderen jonger dan 10 jaar met een acute hoest in de Belgische huisartspraktijk te verkennen. Daarnaast willen we inzicht verwerven in de motieven, verwachtingen en algemene kennis van ouders met betrekking tot het gebruik van vrij verkrijgbare hoestmedicatie. Gezien de beperkte effectiviteit van hoestsiropen, kan het nodig zijn om het bewustzijn in deze groepen te vergroten. Een beter inzicht in de denkpatronen van ouders kan de communicatie en patiëntenvoorlichting vergemakkelijken en verbeteren.

Methoden: Als eerste voerden we een retrospectieve audit uit in het EMD (CareConnect) van onze huidige praktijk. We includeerden alle relevante patiëntencontacten van kinderen jonger dan 10 jaar van wie het globaal medisch dossier (GMD) geregistreerd was in deze praktijk en die op raadpleging kwamen voor een acute hoest tijdens een vooraf bepaalde periode. Informatie zoals patiëntprofielen, gebruik van hoestmedicatie en diagnoses werden systematisch geëxtraheerd en later ingevoerd voor data-analyse. Ten tweede ondervroegen we ouders met kinderen jonger dan 10 jaar over hun gebruik, ervaring en kennis van hoestmedicatie. We stelden een online Qualtrics-enquête op die toegankelijk was voor ouders door een unieke QR-code te scannen. De gegevens werden verzameld en later ingevoerd voor data-analyses.

Resultaten: Voor de audit werden in totaal 302 geregistreerde patiëntencontacten beoordeeld, waarvan er 105 voldeden aan de vooraf gedefinieerde inclusiecriteria. Er was een gelijke verdeling van geslacht. De gemiddelde leeftijd van de kinderen was 3,4 jaar. Hoesten was acuut (<21 dagen) in 93,8% van de gevallen, met een gemiddelde duur van 6,4 dagen voordat de huisarts werd geconsulteerd. Het gebruik van vrij verkrijgbare medicatie voor zelfmedicatie werd gedocumenteerd bij 50 patiënten, waarvan 8 uit eigen initiatief een siroop begonnen te gebruiken. In 26,0% van de patiëntencontacten schreef de huisarts hoestsiroop voor. Indien hoestsiroop werd voorgeschreven was dit een antihistaminica (53,7%) of een mucolytica (42,3%).

In totaal reageerden 110 ouders op de vragenlijst. De gemiddelde leeftijd van de kinderen was 5,3 jaar. 83,5% van de respondenten gaf aan ooit hoestsiroop aan hun kinderen te hebben gegeven. De meerderheid van de ouders, ofwel 51,1%, diende de siroop op eigen initiatief toe, gevolgd door ouders die handelden op advies van de huisarts (21,4%) en de apotheker (16,6%). 67% van de ouders was tevreden over de doeltreffendheid van de hoestsiroop, terwijl 28,5% niet volledig tevreden was over de snelheid van werking. 75% van de ouders uitte geen bezorgdheid over bijwerkingen en er werden geen bijwerkingen gerapporteerd. 64,3% van de ouders is van plan in de toekomst opnieuw hoestsiroop te gebruiken, terwijl 21,4% onbeslist bleef.

Conclusie: Onze studie benadrukt het veelvuldige gebruik van hoestsiroop voor acute hoest bij kinderen, vaak zonder medisch advies. Hoewel het bewijs voor de werkzaamheid onvoldoende blijkt, zijn ouders over het algemeen tevreden over deze geneesmiddelen. Het gebruik van hoestsiropen lijkt overmatig aanwezig te zijn en hoewel bijwerkingen zeldzaam zijn, is er een gebrek

aan bewustzijn met betrekking tot het veiligheidsprofiel van deze medicijnen. Er is behoefte aan sensibilisatie binnen deze populatie. Door ouders voor te lichten over het natuurlijke verloop van bovenste luchtweginfecties, het beperkte bewijs en de veiligheidszorgen in verband met hoestsiroop, kan onnodige toediening van medicatie, ongewenste bijwerkingen en onnodige kosten in de toekomst voorkomen worden.

Abstract

Background: Over the counter (OTC) cough medicines are widely used in an attempt to relieve acute cough symptoms in children. Despite numerous studies indicating a lack of conclusive evidence for their efficacy, OTC cough medications are still often prescribed by primary care physicians. The same trend is observed in the Belgian health care system. Parents are often unaware of the limited effects and potential harms of cough medicines.

Objective: Our objective is to explore the usage of cough medicine in children under 10 years old with an acute cough in the Belgian primary practice. Additionally, we want to gain insight into parents' motives, expectations and overall knowledge regarding the use of OTC cough medicine. Considering the limited effect of cough syrups, it may be necessary to raise awareness in these groups. Getting a better understanding of parents' thinking patterns may facilitate and improve communication and patient education.

Methods: Firstly, we performed a retrospective audit in our Electronic health record CareConnect. We included all relevant patient encounters of children under 10 years old with a global medical record registered in the practice, who were consulted for an acute cough between a predetermined period of time. Information such as patients' profiles, use of cough medicine and diagnoses were systematically extracted and later entered for data analyses.
Secondly, we questioned parents with children under 10 years old about their usage, experience and knowledge of cough medicine. We created an online Qualtrics survey accessible for parents by scanning a unique QR code. Data were collected and later entered for data analyses.

Results: For the audit a total of 302 registered patient encounters were reviewed, 105 of which met the predefined inclusion criteria. There was an equal distribution of sex. The mean age of children was 3.4 years. Of all durations reported in the patients' files, coughing was acute (<21 days) in 93.8% of cases, with a mean duration of 6.4 days before consulting the GP. The use of OTC medication for self-medication was documented in 50 patients, of whom 8 initiated a syrup on their own accord. In 26,0% of cases, the physician prescribed cough syrup. Of these prescriptions, antihistamines were prescribed in 53.7% of cases, while mucolytics were prescribed in 42.3% of cases.
In total 110 parents responded to the questionnaire. The mean age of children was 5.3 years old.
83.5% of respondents reported giving cough syrup to their children at some point in the past. The majority of parents or 51.1% administered the syrup at their own initiative, followed by parents who acted on the advice of the general practitioner (21.4%) and the pharmacist 14 (16.6%). 67% of parents were satisfied with the overall effectiveness of the cough syrup whereas 28.5% were not fully pleased with the onset of time. 75% of parents expressed no concerns about adverse events and none such events were reported. 64.3% of parents intend to use a cough syrup again in the future while 21.4% stayed indecisive.

Conclusion: Our study underscores the widespread use of cough syrup for acute cough in children in the Belgian practice, often without medical guidance. Although evidence supporting the efficacy remains insufficient, parents generally express satisfaction with the use of these medications. The use of OTC cough medicines seems to be overly apparent and while adverse events are rare, a lack of awareness regarding the safety profile of these medications is present. There's a need for sensibilization within this population. By educating parents about the natural course of upper

respiratory tract infections, the limited evidence and safety concerns associated with cough syrup, unnecessary medication administration, unwanted side effects and unneeded costs can be avoided in the future.

Introduction

Acute cough is the leading cause worldwide for seeking primary medical care for both adults and children(1). By definition, an acute cough has a duration of less than 3 or 4 weeks. In literature, this duration varies depending on which guideline is applied(2). Acute cough is primarily attributed to viral upper respiratory tract infections (URTI). In 2021, URTIs had an incidence rate of 76.98 per 100.000 patients across all age groups in the Belgian primary care according to data from the Intego database(3). Less frequently but still prevalent, acute cough results from lower respiratory tract infections(2,4). Symptoms arising from URTIs include coughing, nasal congestion, rhinorrhea, sore throat, general malaise, and/or low-grade fever. These symptoms typically exhibit a self-limited course, often lasting up to 10 days. In children under medical care, the median duration is 8 days, and approximately 90% of cases resolve within 23 days. Notably, acute bronchitis in children tends to have a longer resolution period, with a median duration of 12 days (5,6).
Coughing is a complex physiological reaction of the body that acts as a protection mechanism to clear excess mucus or aspirated foreign material. It is a mere symptom rather than an independent condition, necessitating a primarily symptomatic approach to management(1,7).

In children, a cough can significantly impact the quality of life, which may cause distress or anxiety for the parents as it interferes with daily activities and often disrupts both the parents' and child's sleep(8). Consequently, both over the counter (OTC) and prescription cough medicines are widely used as an attempt to reduce coughing. In the Belgian healthcare system, a distinction is made between OTC medicines and prescription drugs (e.g., codeine and antihistamines). In the literature both OTC and prescription drugs are frequently combined and referred to as just OTC medications. Therefore, in this article, we also adopt this convention.

Many parents administer these OTC cough syrups to their children before seeking medical care and even general practitioners (GP) will often recommend cough medicines as a first line treatment. There is a significant variation among countries in the availability and guidelines for the use of these preparations(9).

Cough medicines used for symptomatic relief in children are typically classified based on their mechanism of action. Below, the working mechanism is briefly explained per group, each with a selection of frequently used substances as exemplified for each group:
(Note that this is not an extensive list of all available products.)

1. <u>Antitussives</u>
   Antitussives function by inhibiting the cough reflex through either a central or peripheral mechanism, or a combination of both. Opioid derivatives work by depressing the cough reflex in the central nervous system. Peripheral antitussive agents function by attenuating the reactivity of one or more vagal sensory receptors responsible for inducing cough reflex (10).
   Examples:
   - opioids: codeine, dihydrocodeine, ethylmorphine, pholcodine
   - non-opioids: dextromethorphan, noscapine, levodropropizine

2. Mucolytics

   These medications act on the mucus itself, disrupting the structure of the mucus molecules. This results in the liquefaction of thick and sticky mucus, making it more fluid (11).

   Examples:

   - cysteine derivatives: acetylcysteine, carbocisteine, erdosteine

3. Expectorants

   Expectorants work by increasing the volume and reducing the viscosity of mucus. By stimulating the production of more fluid mucus, it facilitates a smoother process for the body to expel mucus from the airways via the mechanism of coughing (11).

   Examples:

   - guaifenesin
   - erdosteine

4. Antihistamines

   Antihistamine H1-receptor agonists act by reducing histamine release, thereby reducing local congestion and secretion production (6).

   Examples:

   - diphenhydramine
   - hydroxyzine
   - chlorpheniramine
   - terfenadine
   - (des)loratadine
   - clemastine
   - (levo)cetirizine

5. Antihistamine-decongestant combinations

   Drugs that combine antihistamine H1-receptor antagonists and alpha adrenoceptor agonists. Decongestants function by inducing vasoconstriction in mucosal blood vessels, consequently alleviating congestion (12).

   Examples:

   - pseudoephedrine + antihistamine
   - phenylephrine + antihistamine

6. Other

   Examples:

   - plant based cough syrups

Despite the frequency of URTIs and coughing in children, there is limited evidence to support the use of cough medicine.
A 2014 Cochrane review by Smith SM et al. failed to show a superior effect of antitussives or antihistamines (whether used in monotherapy or combined with decongestants) in children with acute cough compared to placebo (9). It is noteworthy that this systematic review did not include any studies that tested expectorants in children.
An argument can be made that mucolytics are the only cough syrup that has been proven effective in children. Smith SM et al included a study that favored active treatment with letosteine in comparison to placebo from day 4 until day 10 (P value < 0.01) (13). Another cochrane review of 6 low to moderate quality studies involving 497 participants, suggests actual but limited efficacy of acetylcysteine (e.g. reduction in cough severity at day 7) in children older than 2 years (14). However, the authors of both Cochrane reviews stated that these results have to be interpreted with caution because of the limited number of participants included in these studies whose methodological quality is questionable.
Herbal cough medicines have also shown a lack of efficacy as reflected in a recent systematic review for ivy leaf (15).
Apart from the limited efficacy, various adverse events related to the use of cough medicines have been described. The occurrence of adverse effects associated with these medicines is low though, with a rate of 1 case per 1.75 million units of cough medicines sold (1 case per 0.23 million units sold for liquid product types)(16). However, it is likely that this is an underestimation because many drug related side effects remain unreported due to either a lack of recognition or reluctance to engage in the reporting process(17).
A diverse array of adverse effects has been reported, ranging from mild to very severe. The most frequent side effects include tachycardia, ataxia, somnolence, agitation, mydriasis and hallucinations. Concerns are mainly raised when used in young children (under the age of 4) and when more than one cough medicine is administered at the same time(18). Adverse events occur mostly due to medication errors, including accidental overdose, and even lethal cases were described where cough medicine overdose was the underlying cause of death (16,19,20).

Insufficiently defined guidelines regarding dosing and treatment duration, a proliferation of available pharmaceuticals, the presence of diverse active ingredients in products, and the involvement of multiple caregivers in administering medication to children are identified as factors contributing to an increased risk of inappropriate prescription, unintentional overdosing, and adverse events (21). Professional caregivers do play an essential role in this matter.

Despite the lack of evidence and safety concerns, OTC cough medicines are still commonly used in the Belgian primary practice. Even after a statement from the Belgian federal agency for Medicines and Health Products (FAGG) discouraging the use of products such as mucolytics/expectorants and antitussives in children under the age of 6 years old (22).

In our experience, most parents seem to be unaware of the limited effects and potential harms of cough medicines.

Our first objective is to gain insight into the usage and prescription behavior of cough medicine for children with acute cough in the Belgian primary practice (By audit in Electronic Health Record). The secondary objective is to learn more about the parents' motives, expectations, and overall knowledge regarding the use of OTC cough medicine for their children (By questionnaires).

By doing this we hope to obtain a better understanding of the use of cough medicine in young children by their parents and in the Belgian primary practice. Given the insufficiently proven effect of cough medicines, sensitization in these groups may be necessary. This could potentially avoid (over) usage due to misinformation, unprecedented side effects, hospitalization and unnecessary costs in the future.

To our knowledge questionnaires have not previously been used to determine the parents' motivations regarding cough syrups for children.

Methods

Audit in Electronic health record

We conducted a retrospective practice audit in the Electronic health record (EHR) software CareConnect (23), to search for all relevant patient files and contacts. The exact search string is listed in the appendix A. The general practitioner's office where we performed the audit was "Huisartsenpraktijk Medi-Vorst" in Laakdal, Belgium, a group practice comprising 5 individual physicians.

The inclusion criteria were as followed:

[1] Children younger than 10 years old (born after 31-12-2011).
[2] The patient's global medical record is registered in Medi-Vorst practice.
[3] The diagnosis in EHR was coughing or a condition that included coughing as a symptom.
[4] The patient was seen with acute cough between 01/10/2021 - 31/12/2021.

Exclusion criteria:

[1] The presence of a chronic cough (>3 weeks) whether or not as part of an underlying condition
[2] Patients using medication other than cough syrup in an attempt to treat the acute cough.
[3] Absence of the child at the consultation.

All patient files obtained by this audit search were screened by PV and JJ, if a patient had multiple contacts concerning an acute cough between the inclusion period, all contacts were screened for exclusion criteria. When patients consulted more than once for the same cough episode, this was considered as one event.

Data from all relevant files that remained were systematically extracted.

All extracted data from the patient's file, as shown in Table 1, was listed in a Microsoft Excel file. For confidentiality reasons patients were given a unique number. The names and the allocated number were kept in a secure file that is only accessible by the researchers if necessary.

Table 1: Extracted data from patient files.

- Date of presentation - Date of birth - Sex (male/female) - Duration of symptoms (days) - Self-medication started by parents (yes/no) - Type of self-medication (Antitussives/mucolytics/antihistamines/other) - Cough syrup prescribed or recommended by physician (yes/no) - Type of cough syrup prescribed or recommended by physician (Antitussives/mucolytics/antihistamines/other) - Date of prescription by physician - Physician's diagnosis

After extraction, the results were analyzed by DS using SPSS (IBM SPSS Statistics for Windows, Version 28. Armonk, NY: IBM Corp.)(24)

Our main objectives for this audit were: [1] percentage of children seen for acute cough that were treated with a cough medicine, self-medicated or prescribed by physician, [2] type of cough medicine most commonly used and [3] differences in age groups.

Other topics of interest were the ICE (Ideas-concerns-expectations) of the parents.

Questionnaire

Starting January 2023, we systematically handed out information letters to parents that did meet the inclusion criteria listed below.

Inclusion criteria:

- Parents of children <10 years old regardless of parent's age, gender, race, nationality or social status.

The reason for the parents' doctor's visit was not taken into account nor did the children have to be present. The information letters were only handed out in the practice where the researchers were employed at that time.

These letters invited the parents to participate in a questionnaire by scanning a QR code with their smartphone (Appendix B). Scanning the QR-codes with a smartphone or tablet led parents to an anonymous Qualtrics questionnaire. (25) (Appendix C). Except for the informed consent, there was no obligation to answer as parents could easily skip any question and proceed to the next one. Data was stored in Qualtrics and later extracted and entered for data analysis in SPSS.

Our main objectives were to learn more about parents' motives, expectations, and overall knowledge regarding the use of OTC cough medicine for their children.

Data analysis with SPSS:
Counts with percentages were used to calculate the number of children that were prescribed a cough syrup. Descriptive statistics of person data (age, gender) showing number, mean, standard deviations and skewness.

This Master's thesis (MP023299) was approved by the Research Ethics Committee UZ/KU Leuven.

Results

Audit

Together, JJ and PV manually screened a total of 302 registered patient encounters pertaining 265 patients in the period between November 12, 2022 and January 8, 2023. Among these 302 contacts, 105 were deemed eligible based on our predefined inclusion criteria, necessitating the exclusion of 197 contacts.
The main reason for exclusion stemmed from instances in which patient encounters occurred either preceding or following the temporal bounds of October 1, 2021, through December 31, 2021.
This accounted for 196 exclusions, 1 exclusion resulted from a registration error where no data was recorded for a patient encounter.

Sex

There is an equal gender distribution with 48.6% of the 105 contacts belonging to male patients and 51.4% to female patients.
If we focus on the distribution based on the number of patients, thus after removing multiple contacts attributed to one patient, we still see an equal distribution with 50.5% of the patients being male and 49.5% being female.

Age

The age of children varied between 0-9 years at the moment of presentation with a mean age of 3,55 years (+/- 2,61 SD). There was missing data regarding the date of birth for one patient encounter due to a registration error. Distribution of ages is shown in graphic 1.

Graphic 1: Distribution of age at moment of consultation

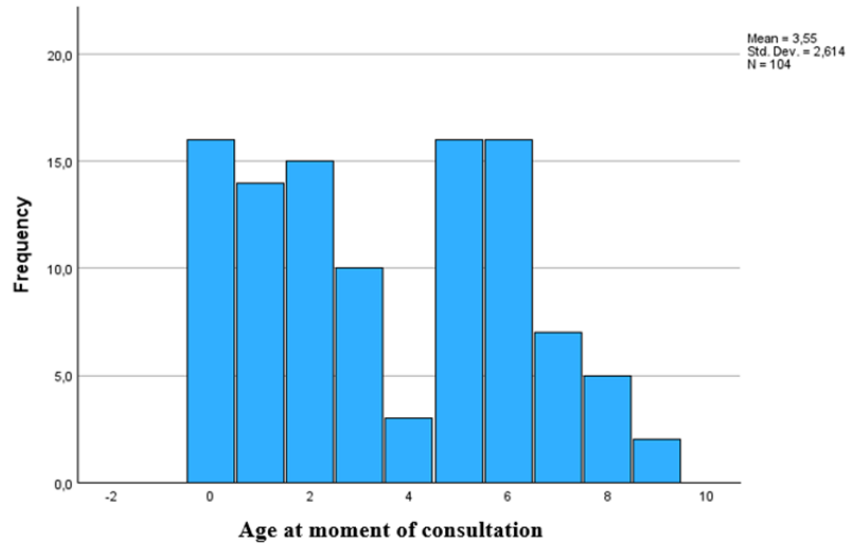


Table 2: Age at time of registration

	Age	Frequency	Percent	Valid Percent	Cumulative Percent
Valid	0	16	15,2	15,4	15,4
	1	14	13,3	13,5	28,8
	2	15	14,3	14,4	43,3
	3	10	9,5	9,6	52,9
	4	3	2,9	2,9	55,8
	5	16	15,2	15,4	71,2
	6	16	15,2	15,4	86,5
	7	7	6,7	6,7	93,3
	8	5	4,8	4,8	98,1
	9	2	1,9	1,9	100,0
	Total	104	99,0	100,0	
Missing	System	1	1,0		
Total		105	100,0		

Duration of symptoms

In 40 cases (38.1%) the care provider did not specifically register the duration of symptoms. When we divided the 65 patient encounters where the duration of symptoms was reported into acute cough (<21 days) and chronic coughing (>21days), coughing was considered acute in 93.8% of the cases with a mean duration of 6.36 days (+- 0,902 SD).

Table 3: Duration of symptoms

		Frequency	Percent	Valid Percent
Valid	acute	61	58,1	93,8
	chronic	4	3,8	6,2
	Total	65	61,9	100,0
Missing	unknown	40	38,1	
Total		105	100,0	

Use of OTC Auto-medication

The general practitioner registered the use of OTC auto-medication in the EHR program for 50 patients (47.6%). Among them, 8 patients reported using medication on their own initiative (7.6%). This means that no data on the use of cough syrups was recorded for 55 out of 105 patient encounters (52.4%).

Table 4: Cough syrup as auto-medication

		Frequency	Percent	Valid Percent
Valid	Yes	8	7,6	16,0
	No	42	40,0	84,0
	Total	50	47,6	100,0
Missing	2	54	51,4	
	unknown	1	1,0	

	Frequency	Percent	Valid Percent
Total	55	52,4	
Total	105	100,0	

For our data extraction we divided cough syrups used as auto-medication into 5 categories.

1. antitussives
2. mucolytics
3. antihistamines
4. other
5. unknown (the patient mentioned using auto-medication but the specific type was not documented by the caregiver.)

In only 4 out of the 8 cases where parents initiated self-medication, the type medicine was documented by the caregiver. Antihistamines were reported in 2 cases and in 2 cases the type of auto-medication was categorized as "other" medication. The type in the 4 remaining cases was unknown.

Cough syrup prescribed by physicians

Cough syrup prescribed by a physician was reported in 26 cases (26.0%). The two syrups prescribed were antihistamines (15 cases, 57.7%) and mucolytics (11 cases, 42.3%). There was no reported data of a physician prescribing any other type of cough syrup than antihistamines or mucolytics. Of these 26 cases regarding 26 individual patients, 14 (53.8%) were under the age of 4 years, whereas 12 (46.2%) children were above the age of 4 years old.

Table 5: Age cohorts, cough syrup prescribed by GP

			Cough syrup prescribed by GP		
			Yes	No	Total
Age cohorts	Age < 4y	Count	14	37	51
		% within Age cohort	27,5	72,5	100,0
		% within total cough syrup prescribed	53,8	50,0	51,0
		% of Total	14,0	37,0	51,0

	Age between 4-10y	Count	12	37	49
		% within Age cohort	24,5	75,5	100,0
		% within total cough syrup prescribed	46,2	50,0	49,0
		% of Total	12,0	37,0	49,0
Total		Count	26	74	100

Physicians diagnosis

A diagnosis was made by the physician for 98 out of the 105 contacts. The diagnoses and their distribution are presented in Table 6.

Table 6: Physicians diagnosis

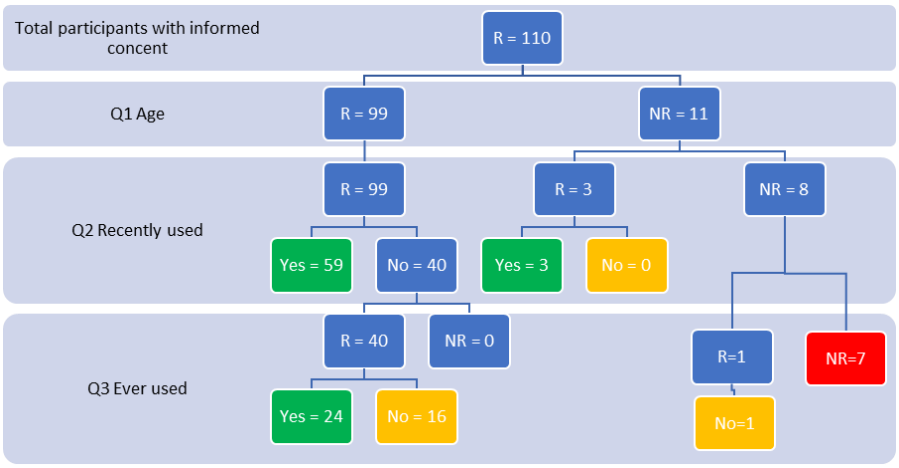
		Frequency	Percent	Valid Percent
Valid	LRTI	13	12,4	13,3
	OMA	10	9,5	10,2
	viral URTI	35	33,3	35,7
	covid	17	16,2	17,3
	bacterial URTI	6	5,7	6,1
	acute cough	15	14,3	15,3
	chronic cough	2	1,9	2,0
	Total	98	93,3	100,0
Missing	99	6	5,7	
	System	1	1,0	
	Total	7	6,7	

Total	105	100,0	

LRTI: lower respiratory tract infection; OMA: otitis media acuta; URTI: upper respiratory tract infection

Questionnaire

A total of 110 individuals replied to the questionnaire. All participants provided their informed consent before partaking in the survey. Number of responses throughout the first three questions (Appendix B) are displaced in flowchart.



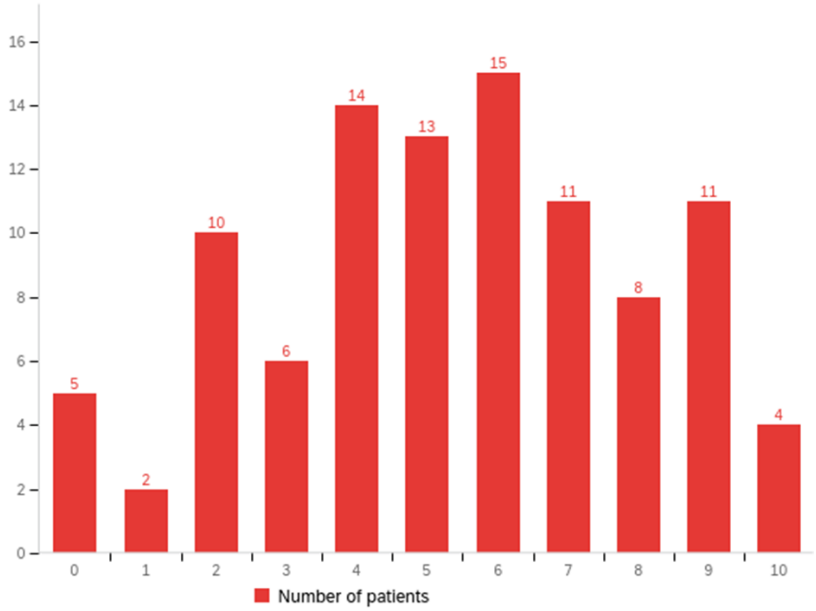
Flowchart 1: responses on first 3 questions. Q=question); R= responders; NR= non responders green: produced to Q4; yellow: responders who did not proceed to Q4; red: non responders after informed consent

A total of 86 parents continued to question 4. Out of these, 83 respondents answered all the following questions, while one did not respond to any of them. Additionally, one parent only answered on the fifth question and one did answer every question except question eight.

Age

Ninety-nine people responded to this question (flowchart 1). The mean age of the parents' children was 5.36 years (+-2.6 SD). Of these 99 children, 23 or 23.2% were under the age of 4 years.

Age distribution



Use of cough syrup

102 respondents answered the question if they had used cough medicine the last time their child had an acute cough. Among them, 62 individuals or 60.8% answered positively.

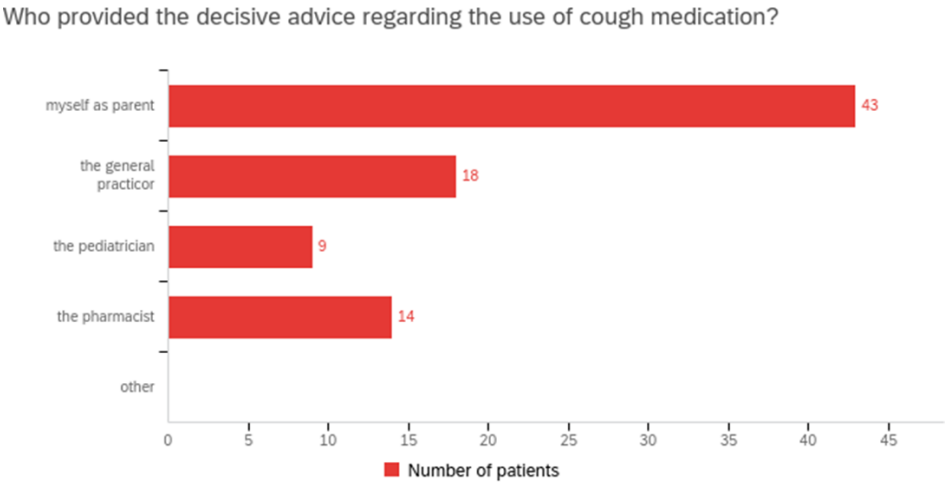
41 respondents, who either answered negatively or did not respond to the previous question, were asked if they had ever used cough medicine for their children in the past. Out of these 41, 24 respondents (58.4%), answered positively.

Overall, 86 out of the 103 or 83.5% of the total respondents, reported having used cough syrup for their children at some point in the past.

Of these 86, 14 or 16.2% of children were under the age of 4.43 Among them, eight received a cough syrup the most recent episode of acute cough and the other 6 also did somewhere in the past.

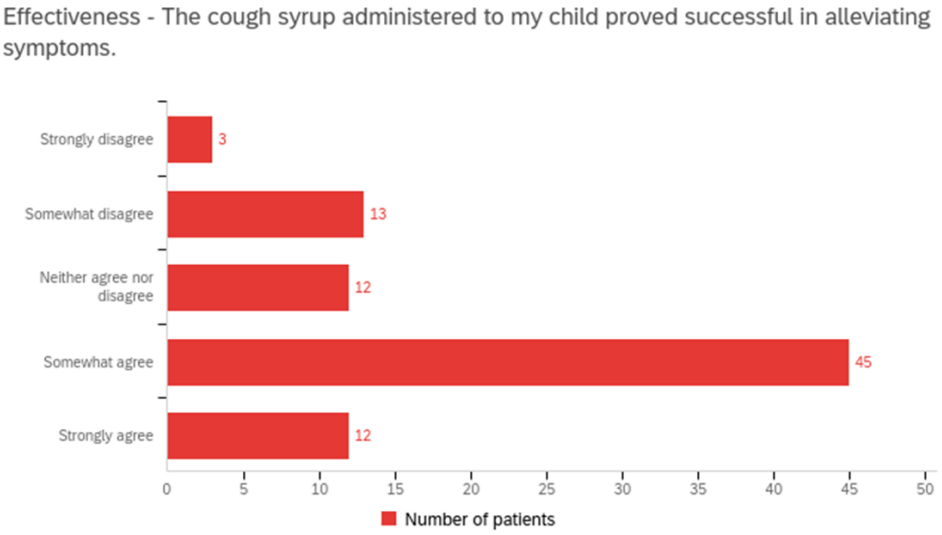
Advice on use of cough syrup

84 out of 86 participants responded to the question regarding who gave the decisive advice for the use of cough medication. The distribution of responses is summarized in the table below. The majority of children (43 in total or 51.1%) received cough medicine at the initiative of the parents themselves. Following this, advice from a general practitioner or pharmacist accounted for 18 (21.4%) and 14 (16.6%) individuals respectively. Pediatricians recommended the use of cough medication the least with a reported incidence of 10.7%. None of the parents reported receiving advice from any other source than the previously stated four options.



Self-reported effectivity

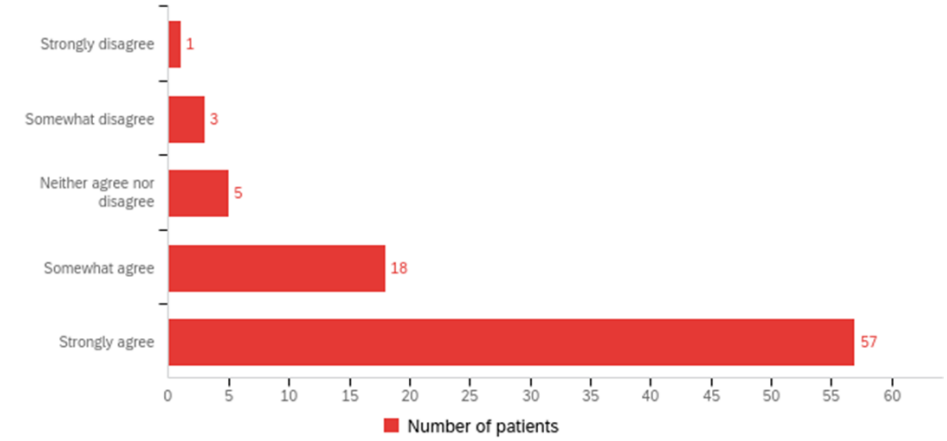
The question regarding parents' thoughts on the effectiveness of cough syrup was answered by 85 people. Among these participants, 57 (67%) either somewhat agreed or strongly agreed (52.9% and 14.1% respectively) with the statement that the cough medicine helped to reduce the cough symptoms for their children. Conversely, 16 parents (15.3% and 3.5% respectively) indicated partial or strong disagreement. An additional 14.1% did neither agree nor disagree.



Received information before usage.

In total 84 people responded to the question about properly being informed regarding the use of a cough syrup. Of these 84, 57 or 67.8% strongly agreed that they were properly informed. Only 4 people were not satisfied as they somewhat or strongly disagreed, 1.1% and 3.6% respectively. Additionally, 5% of respondents remained neutral as they neither disagreed nor agreed.

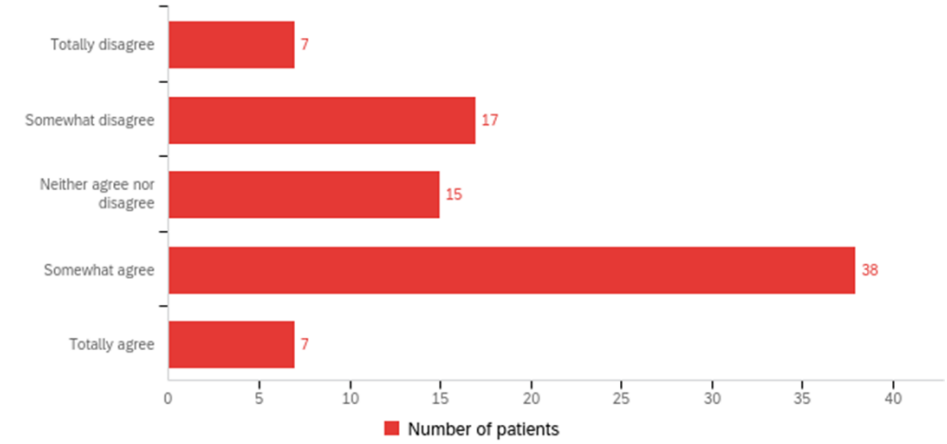
I received proper guidance from my doctor/pharmacist regarding the usage of the cough medicine.



Onset of time

The question of whether the expectations regarding speed of action were met was answered by 84 parents. Among them, 45 parents or 53,6% indicated that they were satisfied with the onset of time, 7 of them even strongly agreed. For 24 parents (28.5%) expectations were not fulfilled as 17 somewhat disagreed and 7 strongly disagreed, constituting 20.2% and 8.3% respectively.

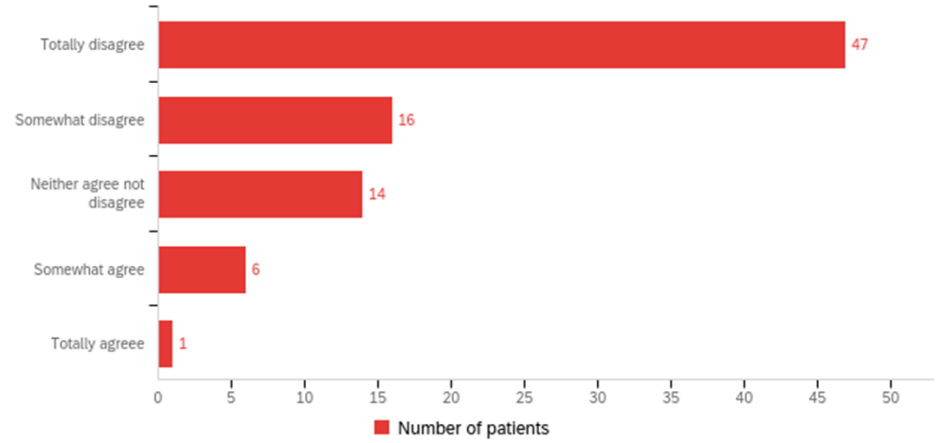
Onset time - My expectations regarding the speed of action were met



Adverse events

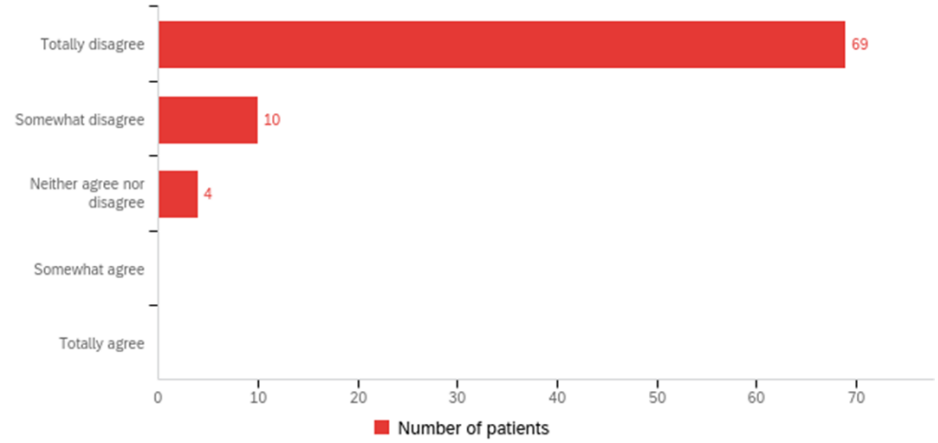
Out of 84 parents who replied, the majority of parents expressed no concern about adverse events. In total 63 parents indicated that they were not worried. In fact, 47 parents strongly affirmed not being worried. Only one parent was strongly concerned about adverse events. Additionally, 6 parents (7.1%) expressed some level of concern and 14 parents responded neutral.

Adverse Events - I was concerned about adverse events occurring in my children during the use of cough medicine.



The vast majority of parents did not experience any side effects in their children when cough medicine was administered, as 79 out of 83 respondents disagreed or strongly disagreed with the statement. The remaining 4 parents neither agreed nor disagreed. No parents stated that they totally agree on the question whether their child did experience any side effects during the use of cough syrups.

During the use of cough medicine, my child experienced side effects.



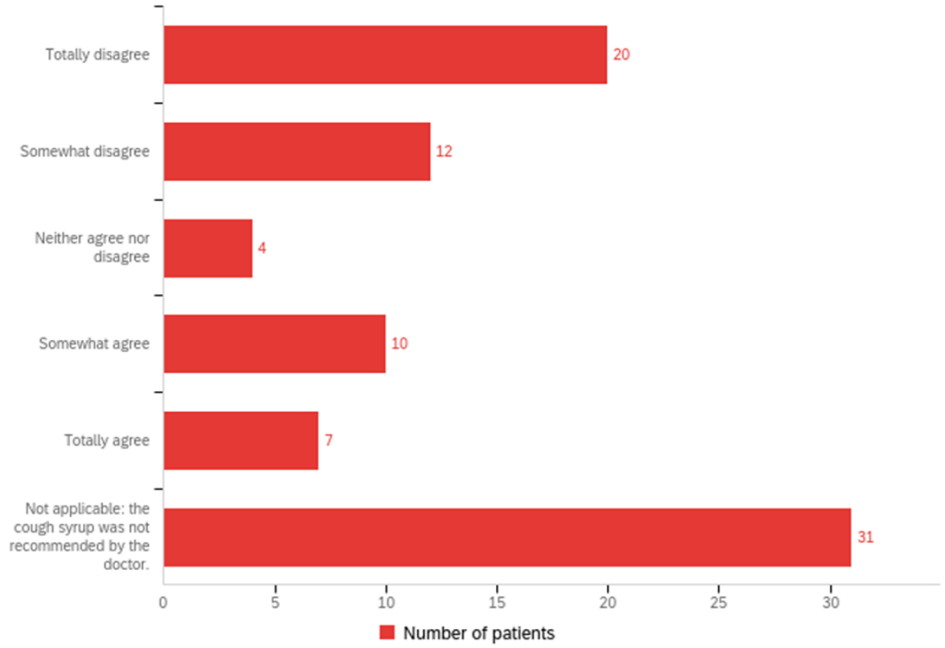
Evidence of cough syrup

In total 84 parents answered the question whether they were informed by the general practitioner about the limited evidence regarding the effectiveness of cough syrups.

Among them, 32 parents (38%) responded that they were not informed by their GP, with 20 individuals stating that they strongly disagree with the statement and 12 parents somewhat disagreeing. Out of the 84 participants, 17 individuals (20%) felt they were informed about the lack of evidence with 7 participants strongly agreeing.

For 31 participants this question was not applicable as the GP didn't recommend any cough syrup.

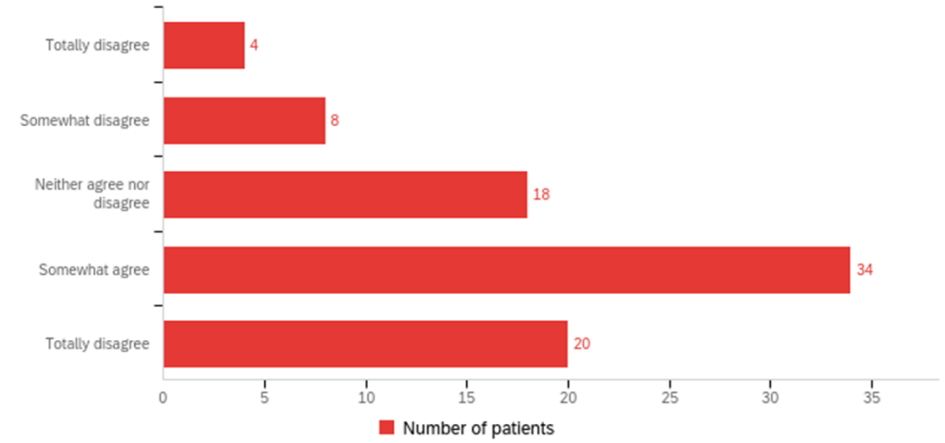
My general practitioner informed me about the limited evidence regarding the effectiveness of cough syrups.



Future intend

Again, 84 people replied to the question if they would ever use cough syrup again for their children in the future. 54 would use them again and 12 parents stated they do not intend to use them again. 18 parents or 21.4% seems to be indecisive.

In the future intend to use cough syrup again when my child coughs.



Discussion

Cough syrups are widely used in an attempt to symptomatically treat acute cough in children under ten years of age. A wide array of products is available, with a significant variability in their mechanisms of action. However, literature reflects a consensus regarding the lack of evidence concerning their efficacy. This is supported by various studies, including a 2014 Cochrane review by Smith SM et al.

In this study, we aimed to investigate the usage of cough medicine in the Belgian primary practice and the overall knowledge of parents about these medications.

In our experience, cough medicines still have a prominent place in the Belgian practice. This is confirmed by our findings from the questionnaire and to a lesser extent by the retrospective audit performed in the electronic health record at our own practice.

The audit revealed that in over one-fourth (26%) of patient contacts, a cough syrup was prescribed by a physician. The types of cough syrups prescribed were predominantly antihistamines and mucolytics. Additionally, a significant portion of parents reported using cough syrup for their children, often without medical advice. Our questionnaire showed that 83.5% of parents used cough syrup for their children at some point in the past, and 60.8% reported having used cough syrup for their child during the most recent episode of acute cough.

Surprisingly, 67.8% of children who received cough syrup did so without guidance from a medical professional, suggesting a common practice of self-medication among parents.

During patient file research, it was challenging to ascertain data regarding self-medication for a significant portion of the patients. This is because the usage of cough syrup as self-medication was poorly registered within the participating practices as it was only mentioned in 50 patient files (47.6%). Also determining the timeframe for initiating self-medication was challenging, as it was recorded for only 25 patients.

It's noteworthy that despite the majority of parents initiating cough syrup use on their own, many expressed satisfaction with the guidance received from healthcare professionals. This indicates that when medical advice is sought, parents generally feel well-informed about cough syrup usage. However, it's essential to recognize potential overestimation of understanding among parents who self-medicate their children.

Our questionnaire highlighted a discrepancy between parents' perception of cough syrup effectiveness and the lack of evidence supporting its efficacy. The majority of the parents seemed satisfied with the effectiveness of the cough syrup used. Indicating that the medicine helped alleviate symptoms in their child. This also accounts for the parents' expectations regarding the onset of action of cough syrups, albeit to a lesser extent. This is remarkable since studies have consistently shown limited evidence for their effectiveness, with most trials failing to demonstrate superiority over placebo. This discrepancy between perceived effectiveness and scientific evidence highlights the need for improved patient education and communication regarding the appropriate use of cough medicines.

It is important to recognize that expectations of parents regarding the onset of action is a rather subjective matter and parents' expectations can vary widely. Some parents may expect a rapid onset of action within minutes while others are satisfied if the symptoms diminish within a few days,

which can also be expected even without any medication. We intentionally did not ask about specific time intervals, as this seems a difficult question. We kept questions short and simple to avoid drop-out.

Parents did not mention any side effects associated with the cough syrups they gave to their children. As the prevalence of adverse effects associated with these medicines is rather low, we expected the probability of reported side effects to be low. It can be expected that with an increasing response rate, reports of adverse events will likely emerge.
Concerns about adverse events were minimal among respondents. This raises the question if there is a lack of awareness by parents regarding the safety profile of these medications. Therefore, healthcare providers should address these concerns and provide evidence-based guidance to ensure informed decision-making by parents.

A substantial number of parents seem to be unaware about the lack of evidence regarding the efficacy of cough syrups as well as possible side effects. This is evident in our questionnaire findings, which show high levels of satisfaction with self-reported effectiveness and minimal concern regarding adverse effects. Moreover, the majority of parents reported that they are likely to use cough syrup again in the future. This raises questions about the adequacy of education provided by physicians. Unfortunately, 38% of parents reported that they were insufficiently informed by their caregiver about the lack of evidence regarding cough syrup effectiveness. A possible explanation is that physicians themselves are unaware of this issue. Another plausible reason is the lack of effective alternatives for cough medicine, coupled with the desire to preserve a positive patient-doctor relationship, potentially leading to over-prescription of cough medicine.

The use of cough medicine is more discouraged in younger kids, especially those under the age of 4 years old. The findings of our audit were rather unsettling, as it revealed that in over half of the patient encounters where cough syrup was prescribed, children were younger than 4 years old at that time (53.8%). Our questionnaire showed that 27 out of 84 children were given a cough syrup based upon the recommendation of a physician (GP or pediatrician). Of these children, 6 were under the age of 4 years old. This indicates that among all patients prescribed cough syrup by a physician, 22.2% were under the age of 4 years.

When examining the prescription behavior of general practitioners regarding cough syrup, we observe similar results in both the conducted audit and the questionnaire we administered. The audit revealed that cough syrup was prescribed in 26% of the patient encounters. The questionnaire showed that 21.4% of parents indicated that the general practitioner provided decisive advice regarding the use of cough syrup.

<u>Clarification of the obtained results with the search command as shown in appendix A</u>
Our search string provided all contacts of children aged <10 years who had any contact during the period 01/10/2021 - 31/12/2021 and for whom a diagnosis of coughing or other respiratory related conditions (see appendix A) was ever established. Due to software limitations in CareConnect (23) it is not feasible to encode this in a manner that the search command explicitly

shows the contacts of children aged <10 years who were specifically assigned the diagnosis of coughing or other respiratory conditions within the aforementioned period.

Limitations of this study

The sample size of the audit was rather small. This is because we only examined a short period of time (3 months) in which children with acute cough presented themselves at our practice. Only 302 patient encounters resulted from this. Additionally, the practice where the research took place was small-scale. If this research were conducted in larger group practices or over a longer period of time, the number of patient encounters would be higher. Furthermore, manually screening these patient contacts is very intensive as each one must be reviewed individually. To conduct this study within a reasonable timeframe, a time window of only 3 months was applied.

For our questionnaire, we initially aimed to obtain a sample comprising 200 individuals. With margin of error set at 5% and a confidence interval of 95%, this necessitated the acquisition of 132 respondents. Unfortunately, we only achieved a total of 110 responses. Since our achieved number of responses was slightly lower than our target, the actual margin of error is 6.28%. Although the reliability of this study is slightly lower than initially targeted, the data still provides valuable insights into the motivation, reasons, and knowledge of parents regarding the use of cough syrup.
As expected, we encountered some dropouts. 6.3% of respondents did not pursue the questionnaire at all. Throughout the rest of the questionnaire dropout was low. Of all parents proceeding where kids ever used a cough syrup, 96.5% answered all questions without skipping a single one.

As both our retrospective audit and questionnaire were performed using only the patient population from the practices we were employed at that time, these results must be interpreted with some caution. It's important to note that there is a risk of selection bias, as patient populations as well as doctor's prescription habits can vary significantly upon different practices and regions.

During the patient file research (audit), there were instances of missing data for certain outcomes of interest. This occurred because the physician either failed to inquire about or neglected to document this information in the Electronic Health Record (EHR) at that time. As this is a retrospective audit, no standardized format for questioning or documenting was applied.
The duration of symptoms was not documented for 40 out of the 105 patient encounters (38.1%). Self-medication data was missing in 55 cases (52.4%). In 7 instances (6.7%), the physician did not register a diagnosis.

In conclusion, our study underscores the widespread use of cough syrup for acute cough in children, often without medical guidance. While parents generally perceive cough syrup as effective, evidence supporting its efficacy remains insufficient. Additionally, a lack of awareness regarding the safety profile of these medications is present. Therefore, sensibilization in this population is needed. Efforts should be made to educate parents about the limited utility of cough syrups as well as the natural course of upper respiratory tract infections. By highlighting the often self-limiting nature of URTIs and pointing out alarm symptoms in case an infection escalates, they are better informed about the natural progression. A combined education of parents regarding the limited efficacy of cough syrups and the natural course of URTIs could contribute to a reduction in cough

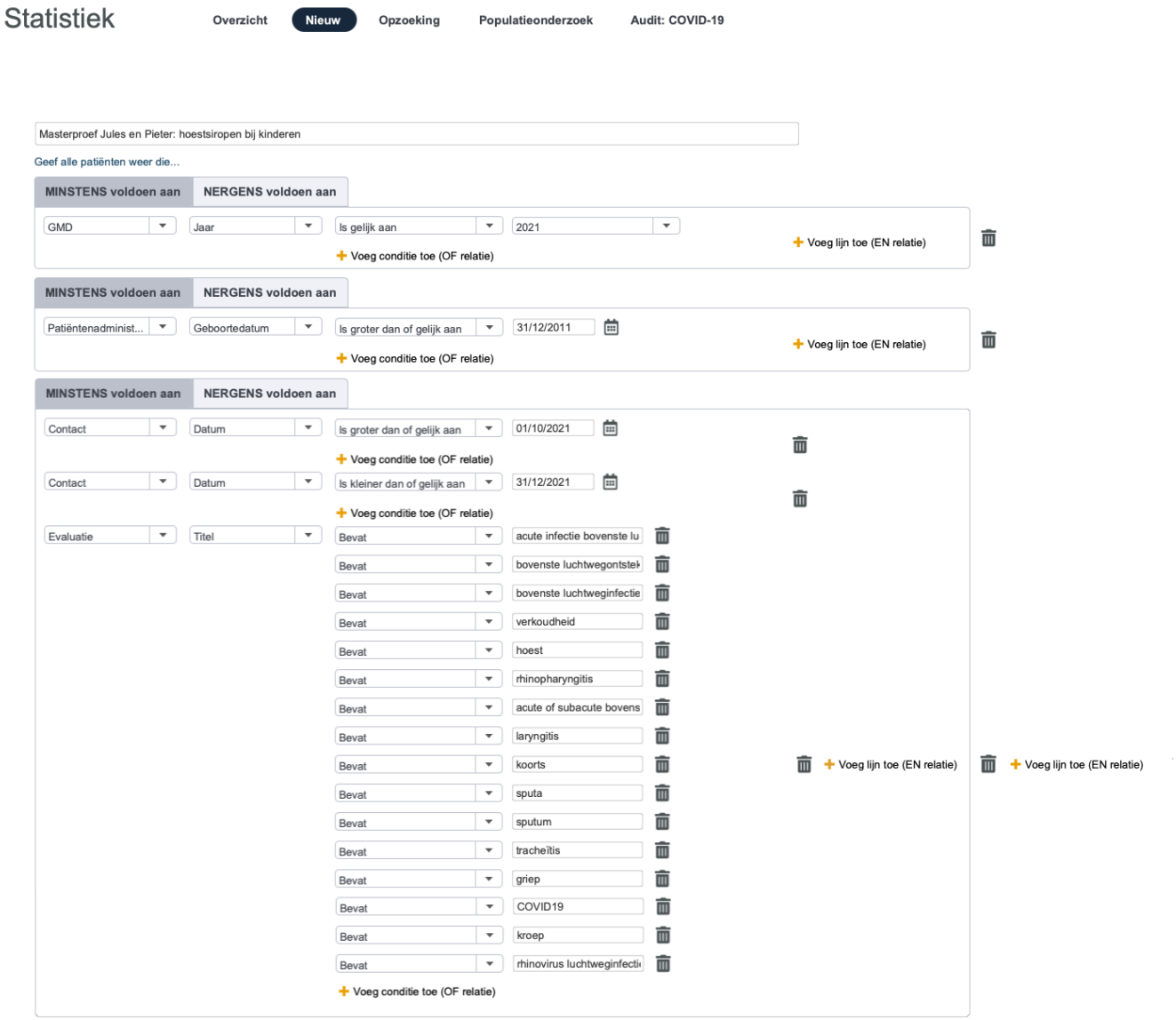
syrup usage. In the future, an intervention study incorporating this combined education could be compared with a control group to assess its effectiveness. For now we will utilize our results to inform the general practice where we conducted our research.

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Appendix A: search string used in EHR program, care connect



Appendix B: Questionnaire information letters (English translation of Dutch version)

Dear,

As part of our General Practice (GP) training, we're conducting research on the efficacy of cough syrups in young children, and we're interested in your opinion.

If you're a parent of a child **aged 10 or younger**, we invite you to participate in our anonymous questionnaire. It will only take about 5 minutes of your time.
You can join by scanning the QR code provided below using your smartphone or tablet (feel free to take a QR code home), or via on the survey link. Further instructions will be provided after scanning the QR code.

Thank you in advance for your participation!
Warm regards

General practitioner in training: Jules Janssens en Pieter Verfaillie
Promotors: Dr. David Spitaels en Dr. Steve Van den Bulck

https://kuleuven.eu.qualtrics.com/jfe/form/SV_eIZn17R0udPCL2u

Appendix C: Questionnaire (English translation of Dutch version)

Use of cough syrup in management of acute cough in children.

Informed consent

- ○ Yes
- ○ No

If Yes → proceed survey
If No → stop survey

Question 1

Age: What was the age of your child (10 years or younger) at the moment the last coughing symptoms (lasting less than 3 weeks) were present?

Indicate age on slider bar

0 1 2 3 4 5 6 7 8 9 10



Question 2

Administered recently - The last time your child had a cough for a period of less than 3 weeks, did you administer a cough syrup?

- ○ Yes
- ○ No

If Yes → forward to question 4
If No → question 3

Question 3:

Ever administered – Have you ever administered a cough syrup to your child ?

- ○ Yes
- ○ No

If Yes → question 4
If No → end of survey

Question 4a:

On whose advice - If you administered a cough syrup, who was decisive in this advice?

- ○ Myself as parent
- ○ The general practitioner (GP)
- ○ The pediatrician
- ○ The pharmacist
- ○ Other

If “Other” → question 4b

Question 4b:

Other advice - Who gave you the advice?

_____

Question 5:

Effectiveness - The cough syrup I used on my child helped reduce cough symptoms.

- ○ Strongly disagree
- ○ Somewhat disagree
- ○ Neither agree nor disagree
- ○ Somewhat agree
- ○ Strongly agree

Question 6:

Informed - I was properly informed by the doctor/pharmacist regarding the dosage, frequency and method of administration of the cough syrup
.

- ○ Strongly disagree
- ○ Somewhat disagree
- ○ Neither agree nor disagree
- ○ Somewhat agree
- ○ Strongly agree

Question 7:

Onset of action - My expectations regarding the onset of action of the cough syrup were met.

- ○ Strongly disagree
- ○ Somewhat disagree
- ○ Neither agree nor disagree
- ○ Somewhat agree
- ○ Strongly agree

Question 8:

Side effects 1 – During the use of the cough syrup, I was worried about side effects.

- ○ Strongly disagree
- ○ Somewhat disagree
- ○ Neither agree nor disagree
- ○ Somewhat agree
- ○ Strongly agree

Question 9:

Side effects 2 – During the using of a cough syrup, my child experienced side effects.

- ○ Strongly disagree
- ○ Somewhat disagree
- ○ Neither agree nor disagree
- ○ Somewhat agree
- ○ Strongly agree

Question 10:

Informed - I was informed by the GP about the limited evidence of effectiveness of cough syrups.

- ○ Strongly disagree
- ○ Somewhat disagree
- ○ Neither agree nor disagree
- ○ Somewhat agree
- ○ Strongly agree
- ○ Not applicable : the cough syrup was not on advice of the GP.

Question 11:

Future – I intent to use cough syrup again in te future when my child has a cough.

- ○ Strongly disagree
- ○ Somewhat disagree
- ○ Neither agree nor disagree
- ○ Somewhat agree
- ○ Strongly agree

END

Appendix D: Approval letter Research Ethics Committee UZ/KU Leuven

GROEP BIOMEDISCHE WETENSCHAPPEN
HERESTRAAT 49, O&N II – BUS 700
BE-3000 LEUVEN

English version below.

Ons kenmerk: MP023299
Uw kenmerk: Masterproef studie: Het gebruik van hoestsiroop in de aanpak van acute hoest bij jonge kinderen **Leuven,** 23-01-2023

GEEN BEZWAAR BRIEF

Geachte Professor MD David Spitaels
Geachte Pieter Verfaillie, Jules Janssens
De Ethische Commissie Onderzoek UZ/KU Leuven bevestigt hierbij dat er geen bezwaren zijn tegen het uitvoeren van de voorgestelde studie, zoals ze werd beschreven in het protocol. De Commissie is van oordeel dat er vanuit ethisch standpunt geen bezwaren zijn bij de voorgestelde studie. De studie werd goedgekeurd op 23-01-2023
De Onderwijs-Begeleidings-Commissie voor Medische Ethiek (OBC) heeft in delegatie van het EC Onderzoek UZ/KU Leuven het vermeld protocol onderzocht en besproken op haar vergadering.
Deze studie richt zich op het gebruik van hoestsiroop in geval van acute hoest bij jonge kinderen. Het eerste deel van het onderzoek is bedoeld om zicht te krijgen op het gebruik en voorschrijfgedrag van hoestsiropen in de medische praktijk. Betreft een retrospectieve studie (medisch dossiersysteem van eigen praktijk) gebruikmaken van data tussen 01-10-2021 en 31-12-2021. Het tweede deel van het onderzoek is prospectief, om inzicht te krijgen in de toepasbaarheid van de richtlijnen in de praktijk. Het bestaat uit een vragenlijst voor ouders met kinderen < 10 jaar. Vragenlijst wordt via Qualtrics aangeboden, duurt 5 minuten. Rekrutering vindt plaats via de huisarts. Geen persoonlijke data, vragenlijst is OK. Data handling is goed, informatiebrief is in orde. Het protocol is voldoende uitgewerkt, er zijn geen bezwaren tegen de studie.
EC Onderzoek heeft geen bezwaar tegen het project mits vertrouwelijke behandeling van de gegevens en naleving van de Belgische wetgeving omtrent privacy. EC wenst de hoofdonderzoeker/promotor van de studie te wijzen op zijn/haar verantwoordelijkheid betreft de privacy van de persoons-/patiëntgegevens bij contact met levende personen, patiënten en/of inzage in het elektronisch medisch dossier, inclusief de correcte implementatie hiervan door medewerkers en studenten.
Deze geen bezwaar brief betreft de indiening van 23-01-2023 en wordt gegeven voor de duur van de Masterproef van de betrokken student(en). Elke wijziging aan het protocol doet dit advies vervallen. U dient in dat geval tijdig een amendement voor advies voor te leggen aan de OnderwijsBegeleidings-Commissie (OBC) die de initiële studie heeft geëvalueerd.
EC bevestigt dat ze werkt in overeenstemming met de ICH-GCP principes (International Conference on Harmonization Guidelines on Good Clinical Practice), met de meest recente

versie van de Verklaring van Helsinki en met de van toepassing zijnde wetten en regelgeving.
EC bevestigt dat in geval van belangenconflict, de betrokken leden niet deelnemen aan de besluitvorming omtrent de studie.
Met vriendelijke groet,
Prof. dr. Minne Casteels
Voorzitter
Ethische Commissie Onderzoek UZ/KU Leuven
Prof. dr. Pascal Borry
Voorzitter
Onderwijs-BegeleidingsCommissie voor Medische Ethiek KU Leuvenv

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Aandachtspunten (indien van toepassing)

EC benadrukt dat een GCP-opleiding van elke hoofdonderzoeker verwacht wordt. EC benadrukt tevens dat de hoofdonderzoeker/promotor verantwoordelijk is voor de uitvoering van het projectvoorstel in overeenstemming met de van toepassing zijnde wetten en voorschriften, waaronder, maar niet beperkt tot, de EU-verordening 2016/679 (Algemene Verordening Gegevensbescherming), de Belgische wet betreffende de rechten van patiënten van 22/8/2002, en het beleid van de instelling waar het onderzoek zal worden uitgevoerd.

Bij gebruik van elektronisch medische gegevens is een formeel akkoord van de dienstraad vereist. De opdrachtgever is verantwoordelijk voor de conformiteit van de anderstalige documenten met de Nederlandstalige documenten.

Dit advies van EC houdt niet in dat zij de verantwoordelijkheid voor de geplande studie op zich neemt. U blijft hiervoor zelf verantwoordelijk.

Bovendien dient u als hoofdonderzoeker erover te waken dat de resultaten van dit onderzoek, correct worden weergegeven in publicaties, rapporten voor de overheid enz.

U wordt eraan herinnerd dat bij klinische studies iedere door u waargenomen ernstige verwikkeling onmiddellijk zaan EC moet worden gemeld, ook al is het oorzakelijke verband met de studie onduidelijk.

Our reference: MP023299
Your reference: Master's thesis study: Het gebruik van hoestsiroop in de aanpak van acute hoest bij jonge kinderen
Leuven, 23-01-2023

DEFINITIVE FAVOURABLE ADVICE

Dear Professor MD David Spitaels
Dear Pieter Verfaillie, Jules Janssens
The Research Ethics Committee UZ/KU Leuven hereby confirms that there are no objections to conducting the proposed study, as it was described in the protocol. After a thorough ethical review, the Commission found no concerns regarding the study. The study was approved on 23-01-2023
De Onderwijs-Begeleidings-Commissie voor Medische Ethiek (OBC) heeft in delegatie van het EC Onderzoek UZ/KU Leuven het vermeld protocol onderzocht en besproken op haar vergadering.
Deze studie richt zich op het gebruik van hoestsiroop in geval van acute hoest bij jonge kinderen. Het eerste deel van het onderzoek is bedoeld om zicht te krijgen op het gebruik en voorschrijfgedrag van hoestsiropen in de medische praktijk. Betreft een retrospectieve studie (medisch dossiersysteem van eigen praktijk) gebruikmaken van data tussen 01-10-2021 en 31-12-2021. Het tweede deel van het onderzoek is prospectief, om inzicht te krijgen in de toepasbaarheid van de richtlijnen in de praktijk. Het bestaat uit een vragenlijst voor ouders met kinderen < 10 jaar. Vragenlijst wordt via Qualtrics aangeboden, duurt 5 minuten. Rekrutering vindt plaats via de huisarts. Geen persoonlijke data, vragenlijst is OK. Data handling is goed, informatiebrief is in orde. Het protocol is voldoende uitgewerkt, er zijn geen bezwaren tegen de studie.
The Committee has no objection to the project provided that the data are handled confidentially and there is compliance with the Belgian legislation concerning privacy. The Research Ethics Committee UZ/KU Leuven reminds the principal investigator/promotor of the study of their responsibilities with regard to the privacy of personal / patient details, when in contact with living persons, patients, and / or contained within electronic medical records, including the correct implementation by employees and students.
This letter of no objection concerns the submission of 23-01-2023v and is given for the duration of the Master's thesis of the student(s) concerned. Any amendment to the protocol will invalidate this advice. In that case, you must submit an amendment for advice to the committee that previously approved your file must be submitted.
The Committee confirms that they work in accordance with the ICH-GCP principles (International Conference on Harmonisation Guidelines on Good Clinical Practice), with the most recent version of the Helsinki Declaration, and with applicable laws and regulations.
The Committee confirms that in case of a conflict of interest, the members concerned have not participated in decision regarding the study.
Yours sincerely,
Prof. dr. Minne Casteels
President / Chairperson
Research Ethics Committee UZ/KU Leuven
Prof. dr. Pascal Borry
President / Chairperson
Education-Support Committee for Medical Ethics KU Leuven

Points of Interests (if applicable)

EC Research emphasizes that GCP-training is expected from every principal investigator. EC Research refers also to the Belgian legislation (Law from 8/12/1992 for the protection of personal privacy and Law from 22/8/2002 regarding the rights of the patient), and the General Data Protection Regulation (which comes into effect on May 25th 2018).

For use of electronic medical data, a formal agreement from the clinical departmental board is required. The study promotor is responsible for the conformity of foreign language documents with the Dutch language version.

This opinion from EC Research does not imply that it takes responsibility for the planned study. You remain responsible for this yourself. In addition, as the principal investigator, you must ensure that the results of this research are correctly displayed in publications, reports for the government, etc.

You are reminded that any serious complication you observe must be reported immediately to the Ethics Committee, even if the causal link with the study is unclear.