

Risks of Concurrent Use of OTC Medicines and Prescription Drugs in Children

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In this presentation I will discuss

- Pharmacoepidemiology of Prescription and OTC use in children
- Safety concerns in US over cough and cold medicines for young children as an example of risks of concurrent use of OTC medicines and prescription drugs (2007)
- Mechanisms leading to safety problems in concurrent use of OTC medicines and prescription drugs

Recent drug history in children visiting a pediatric emergency room and documentation in medical records

Elin Kimland · Ylva Böttiger · Synnöve Lindemalm

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Abstract

Aims We performed a systematic analysis of which drugs, prescribed, over the counter (OTC), and/or natural remedies, children had used prior to visiting a pediatric emergency room (ER), and to compare this information with the documentation of drug use in the medical records.

Methods A questionnaire study was performed at a pediatric ER in a Swedish university hospital during 3 weeks in April 2008. The questionnaire was validated through an interview with a subgroup of participants. Only drug use associated with the time of that hospital visit was requested. Information was compared with information in medical records related to the same visit.

Results Two hundred and seventy-four children aged 0–18 (median 2) years were enrolled, representing 28% of the total number of patients visiting the ER within the time frame. Forty% ($n=109$) of participants reported use of

and omega fatty acids, respectively. In the medical records, no more than 50% of the reported drug intake could be found, representing 74% of prescribed drugs but only 34% of OTC drugs and 27% of natural remedies.

Conclusions The majority of children had used drugs, both prescribed and OTC, before coming to the ER, but this drug intake, and especially that of nonprescribed drugs, was often not documented in the medical records.

Keywords Child · Emergency room · Drug use · OTC · Safety · Medical records · History · Natural remedies

Abbreviations

OTC over the counter
ER emergency room

Drugs documented from questionnaire and in the medical records (number and percentages compared with the questionnaire). One patient could have received drugs from more than one category

	All age groups* (n=274)		Infants (n=131)		Children (n=111)	
	Drugs	Patients	Drugs	Patients	Drugs	Patients
All drug use in questionnaires	460	227	195	131	214	111
- Prescribed	187	109	62	41	109	57
- OTC	249	172	127	89	94	66
- Natural remedies	22	17	6	5	11	7
All drug use in medical records	229 (50%)	125	85 (44%)	55	117 (55%)	52
- Prescribed	138 (74%)	76	49 (79%)	31	75 (69%)	36
- OTC	83 (34%)	52	34 (27%)	18	38 (40%)	26
- Natural remedies	6 (27%)	5	2 (33%)	2	3 (27%)	1

* Includes adolescents (n=29), data not shown separately for the age group

Kimland E, Böttiger Y, Lindemalm S. Recent drug history in children visiting a pediatric emergency room and documentation in medical records. Eur J Clin Pharmacol. 2011Oct.;67(10):1085–9.

The most commonly used prescribed drugs and OTC substances among participating children (n=274)

Prescribed drugs (n=182)		OTC drugs (n=254)	
Drug substances	n (%)	Drug substances	n (%)
Salbutamol	34 (19)	<i>Paracetamol</i>	135 (53)
Penicillin V, penicillins	22 (12)	Nasal decongestants	29 (11)
Budesonide	19 (10)	<i>Ibuprofen</i>	25 (10)
<i>Bromhexin/ephedrine</i>	13 (7.1)	AD-vitamin drops	13 (5.1)
<i>Unspecified cough syrup</i>	6 (3.3)	Nasal potassium chloride	8 (3.1)
Terbutaline	5 (2.7)	Multivitamins	7 (2.8)
<i>Paracetamol</i>	5 (2.7)	Oral rehydration solution	6 (2.4)
<i>Ibuprofen</i>	4 (2.2)	Dimethicone	4 (1.6)
<i>Clemastine</i>	4 (2.2)	<i>Cough syrup</i>	3 (1.2)
Betamethasone	3 (1.6)	<i>Loratadine</i>	23 (1.2)

Kimland E, Böttiger Y, Lindemalm S. Recent drug history in children visiting a pediatric emergency room and documentation in medical records. *Eur J Clin Pharmacol.* 2011Oct.;67(10):1085–9.

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ORIGINAL REPORT

The use of prescription medicines and self-medication among children—a population-based study in Finland[†]

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SUMMARY

Purpose The aim of this study was to investigate the prevalence and concomitant use of prescription medicines and self-medication, including over-the-counter (OTC) medicines, vitamins, and complementary and alternative medicines (CAMs) among Finnish children aged under 12 years.

Methods We carried out a nationwide postal survey of the use of medicines by a representative sample ($n = 6000$) of Finnish children aged under 12 years in spring 2007. A response rate of 67% ($n = 4032$) was achieved. The current use of prescription medicines and the use of OTC medicines, vitamins, and CAMs in the preceding 2 days were the main outcome measures.

Results In total, 17% of children had used prescription medicines and 50% some self-medication. The corresponding figures for OTC medicines, vitamins, and CAMs use were 17, 37, and 11%, respectively. Drugs for obstructive airway diseases were the most common prescription medicines, whereas analgesics and antipyretics, including non-steroidal-anti-inflammatory-medicines (NSAID), were the most common OTC medicines reported. Vitamin D was the most common vitamin, while fish oils and fatty acids were the most common CAMs used. Ten percent of the children had used prescription medicines and self-medication concomitantly.

Conclusions Most of the children's medication consists of self-medication, and especially of vitamin use. However, also a considerable proportion had used prescription medicines, and a minority prescription medicines and self-medication concomitantly. In three of the cases, a combination of prescription and OTC medicine with a potential risk for interactions were found. Physicians should be aware of this wide use of self-medication when prescribing medicines. Copyright © 2010 John Wiley & Sons, Ltd.

KEY WORDS—child; drug utilization; population survey; self-medication; vitamin; complementary and alternative medicine

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The legal requirements and selling pathways of prescription medicines and self-medication in Finland

	Legal requirements	Retail outlet
Prescription medicine	Marketing authorisation by EMA ¹ /FIMEA ²	Community pharmacies, with a prescription
OTC-medicine	Marketing authorisation by EMA ¹ /FIMEA ²	Community pharmacies, without a prescription
Self-medication		
Traditional herbal medicinal product	Registration by EMA ¹ /FIMEA ²	Community pharmacies and some preparations also from grocery stores and health food shops
Homeopathic and anthroposophic product	Marketing authorisation or registration by EMA ¹ /FIMEA ²	
Food supplement	Reporting to the Finnish Food Safety Authority	Community pharmacies grocery stores and health food shops

¹ European Medicines Agency

² Finnish Medicines Agency

Ylinen S, Hämeen-Anttila K, Sepponen K, Lindblad ÅK, Ahonen R. The use of prescription medicines and self-medication among children--a population-based study in Finland. *Pharmacoepidemiol Drug Saf.* 2010Oct.;19(10):1000-

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The prevalence of the use of prescription medicines and self-medication, and furthermore of over-the-counter (OTC) medicines, vitamins, and complementary and alternative medicines (CAMs) among Finnish children aged under 12 years

	Total		0-2 years		3-6 years		7-11 years	
	%	n	%	n	%	n	%	n
Prescription medicine use	17	676/3 974	20	197	17	217	15	262
Self-medication use ¹	50	1 991/3 986	73	723	48	606	39	662
- OTC use	17	655/3 942	24	232	16	202	13	221
- Vitamin use	37	1459/3 986	62	612	34	439	24	408
- CAM use	11	452/3 958	12	121	10	124	12	207

¹ Use of OTC medicines, vitamins and CAMs

Concomitant use prevalence prescription medicines and self-medication 10%

Ylinen S, Hämeen-Anttila K, Sepponen K, Lindblad ÅK, Ahonen R. The use of prescription medicines and self-medication among children--a population-based study in Finland. *Pharmacoepidemiol Drug Saf.* 2010Oct.;19(10):1000-

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Six most commonly used prescription and OTC medicines among Finnish children aged under 12 years according to age

	Total		0-2 years		3-6 years		7-11 years	
	%	n	%	n	%	n	%	n
Prescription medicine								
Salbutamol	4	151	4	43	4	47	4	61
Flutikason	2	84	2	16	2	26	3	42
Naproxen	2	67	3	29	2	26	1	12
Ointment (base cream)	2	61	2	21	2	22	1	18
Amoxicillin	1	40	2	20	1	11	1	9
Cetirizin	1	40	1	5	1	9	2	26
OTC medicine								
Paracetamol	5	202	9	90	4	52	4	60
Dekspanthenol	2	87	4	39	2	30	1	18
Ibuprofen	2	59	0	2	1	7	3	50
Xylometatsolin	1	55	2	19	1	17	1	19
Topical Hydrocortison	1	51	2	21	2	20	1	10
Sodiumfluoride	1	53	1	14	2	27	1	12

Ylinen S, Hämeen-Anttila K, Sepponen K, Lindblad ÅK, Ahonen R. et. al Drug Saf. 2010Oct.;19(10):1000-8.

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Medication Use Among Children <12 Years of Age in the United States: Results From the Slone Survey



WHAT'S KNOWN ON THIS SUBJECT: A wide variety of medications, both OTC and prescription, are available to US children, and the safety of pediatric medications is an important public health issue. However, the precise prevalence of use of pediatric medications is not well understood.



WHAT THIS STUDY ADDS: Using data from the Slone Survey, this study defines the prevalence and patterns of use of the most commonly used OTC and prescription medications among US children <12 years of age.

abstract

OBJECTIVES: Using data from the Slone Survey, we sought to define the prevalence of over-the-counter and prescription medication use among US children <12 years of age and to determine the prevalence and patterns of use of the most commonly used medications.

METHODS: The Slone Survey was a random-digit-dial telephone survey of medication use in the previous 7 days for a representative sample of the US population. Between February 1998 and April 2007, we enrolled 2857 children 0 to 11 years of age from the 48 contiguous US states.

RESULTS: The survey response rate was 61%. Overall, 56% of children had used ≥ 1 medication product in the 7 days preceding the interview, with 15%, 7.1%, 3.1%, and 1.9% taking 2, 3, 4, and ≥ 5 medications, respectively, during that time period. Twenty percent of children took ≥ 1 prescription-only medications, but <6% used ≥ 2 prescription-

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KEY WORDS: drug utilization, over-the-counter drugs

ABBREVIATION

OTC—over-the-counter

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TABLE 2 Weighted Prevalence of Use of Most Commonly Used Medication Products, According to Age

0–23 mo (N = 478)		2–5 y (N = 1000)		6–11 y (N = 1379)	
Product	Prevalence, %	Product	Prevalence, %	Product	Prevalence, %
Acetaminophen	23	Multivitamin	24	Multivitamin	19
Multivitamin	7.4	Acetaminophen	7.7	Acetaminophen	8.6
Ibuprofen	7.2	Ibuprofen	7.2	Ibuprofen	7.3
Amoxicillin ^a	5.1	Albuterol ^a	3.4	Albuterol ^a	3.2
Albuterol ^a	4.3	Amoxicillin ^a	2.9	Loratadine	2.8
Multivitamin-fluoride ^a	2.3	Cetirizine ^a	2.8	Methylphenidate ^a	2.0
Benzocaine	3.8	Multivitamin-fluoride ^a	2.7	Diphenhydramine (oral)	1.9
Acetaminophen-pseudoephedrine	2.4	Montelukast ^a	2.5	Vitamin C	1.9
Simethicone	2.1	Diphenhydramine (oral)	1.6	Montelukast ^a	1.8
Iron	1.7	Cough medication NOS	1.6	Multivitamin-fluoride ^a	1.8
Diphenhydramine (oral)	1.6	Vitamin C	1.5	Amoxicillin ^a	1.5
Ranitidine ^a	1.4	Triple-antibiotic ointment ^b	1.5	Cetirizine ^a	1.5
Pseudoephedrine	1.4	Hydrocortisone ^b	1.5	Triple-antibiotic ointment ^b	1.3
Hydrocortisone ^b	1.3	Fluticasone ^a	1.3	Fluticasone ^a	1.3
Cold/fever medication NOS	1.3	Fluoride ^a	1.3	Mixed amphetamine salts ^a	1.1
Dextromethorphan-pseudoephedrine	1.0	Dextromethorphan	1.1	Hydrocortisone ^b	0.9
Pimecrolimus ^{a,b}	1.0	Chlorpheniramine-phenylpropanolamine	1.0	Pseudoephedrine	0.8
Cream/ointment NOS ^b	1.0	Brompheniramine-pseudoephedrine	0.9	Guaifenesin	0.8
Cetirizine ^a	0.9	Loratadine	0.8	Fluticasone-salmeterol ^a	0.8
Cough medication NOS	0.9	Bismuth subsalicylate	0.8	Fluoride	0.8
Dextromethorphan	0.8	Iron	0.8	Bismuth subsalicylate	0.7
Amoxicillin-clavulanate ^a	0.7	Acetaminophen-chlorpheniramine-dextromethorphan-pseudoephedrine	0.8	Azithromycin ^a	0.6
Triple-antibiotic ointment ^b	0.6	Azithromycin ^a	0.6	Fexofenadine ^a	0.6
Brompheniramine-pseudoephedrine	0.6	Budesonide ^a	0.5	Mometasone ^a	0.6
Fluoride ^a	0.5	Amoxicillin-clavulanate ^a	0.5	Amoxicillin-clavulanate ^a	0.5
Chlorpheniramine-phenylpropanolamine	0.5			Atomoxetine ^a	0.5

The table includes all products with a prevalence of use of $\geq 0.5\%$. NOS indicates not otherwise specified. Multivitamin refers to a product containing ≥ 2 vitamins without fluoride.

^a Products available only by prescription during the study period.

^b Dermal products.

Vernacchio L, Kelly JP, Kaufman DW, Mitchell AA. Medication use among children. PEDIATRICS. 2009Aug.;124(2):446–54.

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The NEW ENGLAND JOURNAL of MEDICINE

N Engl J Med. 2007 Dec.6;357(23):2321–4.

Perspective
DECEMBER 6, 2007

Over the Counter but No Longer under the Radar —
Pediatric Cough and Cold Medications

Joshua M. Sharfstein, M.D., Marisa North, B.A., and Janet R. Serwint, M.D.

In recent weeks, over-the-counter cough and cold medications for children have received unprecedented attention from regulators, physicians, the media, and parents. This scrutiny represents a

long-overdue reassessment of products that were purchased by 39% of U.S. households during the past

community, however, concern over the effectiveness and safety of such drugs has been growing for more

medications does not support the efficacy of such products in the pediatric age group.¹

Meanwhile, poison-control centers have reported more than 750,000 calls of concern related to cough and cold products since January 2000.² A recent report from the Centers for Disease Con-

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Why the attention?

- Poison-control centers had reported more than 750,000 calls of concern related to cough and cold products since January 2000
- A recent report from the CDC identified more than 1 500 emergency room visits in 2004 and 2005 for children under 2 years of age who had been given cough or cold products
- A review by the FDA identified 123 deaths related to the use of such products in children under six during the past several decades

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Background

- Over-the-counter cough and cold medications were purchased by 39% of U.S. households during the past 3 years
- Consumers purchase about 95 million packages of such medication for use in children each year
- There is no standard for describing these products; two products marketed similarly may have different types of ingredients

Sharfstein JM, North M, Serwint JR. Over the counter but no longer under the radar--pediatric cough and cold medications. N Engl J Med. 2007Dec.6;357(23):2321-4.

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Cough and cold preparations had remained on then market although:

- Since 1985, all six randomized, placebo-controlled studies of the use of cough and cold preparations in children under 12 years of age have not shown any meaningful differences between the active drugs and placebo
- In 1997, the American Academy of Pediatrics noted in a policy statement on cough medications that "indications for their use in children have not been established."
- In 2006, the American College of Chest Physicians found that "literature regarding over-the-counter cough medications does not support the efficacy of such products in the pediatric age group."

Sharfstein JM, North M, Serwint JR. Over the counter but no longer under the radar--pediatric cough and cold medications. N Engl J Med. 2007Dec.6;357(23):2321-4.

Sharfstein JM, North M, Serwint JR. Over the counter but no longer under the radar--pediatric cough and cold medications. N Engl J Med. 2007Dec.6;357(23):2321-4.

Ingredients and Marketing of Some of the Available Pediatric Cough and Cold Products.*		
Ingredients	Brand Name	Marketed Use
Antihistamine	Pediacare	Nighttime cough
	Triaminic	Cough and runny nose
Antitussive	Robitussin	Long-acting cough
Decongestant	Dimetapp	Decongestant
Antihistamine and antitussive	Robitussin	Long-acting cough and cold
	Tylenol Plus	Cough and runny nose
Antihistamine and decongestant	Dimetapp	Cold and allergy
	Pediacare	Nighttime multisymptom cold
	Triaminic	Nighttime cough and cold
Antitussive and decongestant	Dimetapp	Decongestant plus cough
	Pediacare	Multisymptom cold
	Triaminic	Daytime cough and cold
Decongestant and expectorant	Dimetapp	Cold and chest congestion
	Triaminic	Chest and nasal congestion
Antihistamine, antitussive, and decongestant	Dimetapp	Cold and chest congestion
	Tylenol Plus	Flu
	Tylenol Plus	Multisymptom cold
Antitussive, decongestant, and expectorant	Robitussin	Cough and cold

* The antihistamines include brompheniramine, chlorpheniramine, and diphenhydramine; the antitussive is dextromethorphan, the decongestant is phenylephrine, and the expectorant is guaifensin. All formulas of Tylenol Plus also contain acetaminophen.

Examples of common ingredients in cough and cold medications on US market in 2007 by class of medication

Class	Examples
Antihistamine (first generation)	Acrivastine, bromipheniramine, cabinoxamine, chlorpheniramine, cyproheptadine, diphenhydramine, doxylamine, triprolidine
Antipyretic and analgesic	Acetaminophen (paracetamol), ibuprofen
Cough suppressant (antitussive)	Benzonate, codeine, dextromethorphan, hydrocodone
Expectorant	Guaifenesin
Nasal decongestant	Ephedrine, phenylephrine, phenylpropanoamine, pseudoephedrine

Centers for Disease Control and Prevention CDC. Infant deaths associated with cough and cold medications--two states, 2005. MMWR Morb Mortal Wkly Rep. 2007Jan.12;56(1):1-4.

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Existence of these cold and cough preparations on the market explained partly by their regulatory history

- This class of drugs was first marketed well before 1972, the year that the FDA began a comprehensive review of hundreds of OTC cough and cold preparations
- In 1976 FDA advisory panel endorsed the use of some OTC ingredients for cough or cold symptoms in adults but, in the face of "negligible or nonexistent" data on pediatric use, recommended against their marketing for children under two
- For older children, it endorsed the extrapolation of doses from those recommended for adults, using a crude formula: half the adult dose for children 6-11 years of age and a quarter of the adult dose for children 2-5 years.

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Adverse effects of OTC Cough and Cold medicines

Class	Potentially serious adverse effects
Sympathomimetics (ephedrine, pseudoephedrine, phenylpropanolamine)	(CNS) stimulation: extreme agitation, restlessness, insomnia, psychosis, and seizures, hypertension, and tachycardia, bradycardia, Dysrhythmias, myocardial infarction, stroke, and cerebral hemorrhage,
Antihistamines (chlorpheniramine, brom-pheniramine)	Anticholinergic symptoms and CNS depression, tachycardia, blurred vision, agitation, hyperactivity, toxic psychoses, and seizures may be evident. Cardiac dysrhythmias including torsades de pointes
Antitussives (codein, dextromethorphan)	Lethargy, stupor, hyperexcitability, ataxia, abnormal limb movements, and coma

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Serious adverse effects of Cough and Cold medicines have been associated with

- Accidental overdose
- In children given standard doses
 - Inadvertent misuse
 - Drug–drug or drug–host interactions

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Accidental overdose

- Paediatric OTC liquid medications contained highly variable and inconsistent dosing directions and measuring devices
- Child is given two products (OTC + OTC) with same/similar active ingredient for different indications

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ORIGINAL CONTRIBUTION

Evaluation of Consistency in Dosing Directions and Measuring Devices for Pediatric Nonprescription Liquid Medications

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Ruth M. Parker, MD

IN NOVEMBER 2009, THE US FOOD and Drug Administration (FDA) released new voluntary guidelines to industry groups responsible for manufacturing, marketing, or distributing over-the-counter (OTC) liquid medications, particularly those intended for use by children.¹ These guidelines were developed in response to numerous reports of unintentional overdoses that were attributed, in part, to products with inconsistent or confusing labels and measuring devices.² At roughly the same time the FDA guidance was released, the Consumer Health Products Association (CHPA), a group representing manufacturers of OTC medications, issued a similar set of voluntary guidelines for its members.²

The FDA recommendations include the following provisions: (1) il l d d d h ld

Context In response to reports of unintentional drug overdoses among children given over-the-counter (OTC) liquid medications, in November 2009 the US Food and Drug Administration (FDA) released new voluntary industry guidelines that recommend greater consistency and clarity in OTC medication dosing directions and their accompanying measuring devices.

Objective To determine the prevalence of inconsistent dosing directions and measuring devices among popular pediatric OTC medications at the time the FDA's guidance was released.

Design and Setting Descriptive study of 200 top-selling pediatric oral liquid OTC medications during the 52 weeks ending October 30, 2009. Sample represents 99% of the US market of analgesic, cough/cold, allergy, and gastrointestinal OTC oral liquid products with dosing information for children younger than 12 years.

Main Outcome Measures Inclusion of measuring device, within-product inconsistency between dosing directions on the bottle's label and dose markings on enclosed measuring device, across-product use of nonstandard units and abbreviations, and presence of abbreviation definitions.

Results Measuring devices were packaged with 148 of 200 products (74.0%). Within this subset of 148 products, inconsistencies between the medication's dosing directions and markings on the device were found in 146 cases (98.6%). These included missing markings (n=36, 24.3%) and superfluous markings (n=120, 81.1%). Across all products, 11 (5.5%) used atypical units of measurement (eg, drams, cc) for doses listed. Milliliter, teaspoon, and tablespoon units were used for doses in 143 (71.5%), 155 (77.5%), and 37 (18.5%) products, respectively. A nonstandard abbreviation for milliliter (not mL) was used by 97 products. Of the products that included an abbreviation, 163 did not define at least 1 abbreviation.

Conclusion At the time the FDA released its new guidance, top-selling pediatric OTC liquid medications contained highly variable and inconsistent dosing directions and measuring devices.

JAMA. 2010;304(23):2595-2602

www.jama.com

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Yin HS, Wolf MS, Dreyer BP, Sanders LM, Parker RM. Evaluation of consistency in dosing directions and measuring devices for pediatric nonprescription liquid medications. JAMA. 2010Dec.15;304(23):2595-602.

Table 2. Level of Industry Adherence in Study Sample With FDA Recommendations¹

Area of Concern	Relevant Product Sample	Rate Among Surveyed Products		a,b
		No./Total No. ^a	% (95% CI)	
No standardized measuring device	All	52/200	26.0 (20.1-32.7)	1.0
Within-product inconsistency between directions and measuring device ^c	Measuring device included	146/148	98.6 (95.2-99.8)	1.0
Inconsistent doses listed or marked	Measuring device included	122/148	82.4 (75.3-88.2)	1.0
Missing necessary markings on device	Measuring device included	39/148	26.3 (17.7-35.1)	1.0
Superfluous markings on device	Measuring device included	123/148	83.1 (73.8-87.9)	1.0
Inconsistent text used for unit of measurement ^d	MilliL, teaspoon, or tablespoon expression on both label and device	121/136	89.0 (82.5-93.7)	1.0
Inconsistent text for milliL	MilliL on both label and device	40/78	51.3 (39.7-62.8)	0.97
Inconsistent text for teaspoon	Teaspoon on both label and device	9/1105	0.8 (0.4-1.5)	1.0
Inconsistent text for tablespoon	Tablespoon on both label and device	6/7	85.7 (42.1-99.8)	1.0
Across-product variability ^e	All	172/200	86.0 (80.4-90.3)	1.0
Atypical units of measurement (other than milliL, teaspoon, or tablespoon) ^f	All	11/200	5.5 (2.8-9.6)	1.0
Nonstandard ^g abbreviations for unit of measurement	Abbreviation used for milliL, teaspoon, or tablespoon	120/165	72.7 (65.3-79.4)	0.99
Any nonstandard abbreviation for milliL (not mL) ^h	Abbreviation used for milliL	97/143	67.8 (59.4-75.4)	0.97
Any nonstandard abbreviation for teaspoon (not tsp) ⁱ	Abbreviation used for teaspoon	69/110	62.7 (53.0-71.8)	1.0
Abbreviation used for tablespoon other than most common (not TBS) ^j	Abbreviation used for tablespoon	7/22	31.8 (13.0-54.9)	1.0
Missing ≥1 definitions of abbreviations for unit of measurement (eg, tsp = teaspoon)	≥1 Abbreviations used ^k	163/165	98.8 (95.7-99.9)	1.0
≥1 Definitions present for abbreviation for unit of measurement	≥1 Abbreviations used ^l	152/165	92.1 (86.9-95.7)	0.96
Unclear use of numeric text (decimal/fraction)	Decimal dose <1 or fraction used	76/147	51.7 (43.3-60.0)	1.0
No use of leading zeros before decimal for dose <1	Decimal dose <1 used	5/40	12.5 (4.2-26.8)	1.0
Use of large font size for numerals in fractions (eg, 1/2 instead of 1⁄2)	Fraction used	7/110	6.4 (3.4-10.4)	1.0
Lack of consumer guidance on appropriate use ^m	Measuring device included	149/148	100.0 (97.5-100.0)	
No strategy to ensure measuring device used only with its product	Measuring device included	9/1148	0.8 (0.3-1.8)	0.91
No statement that only enclosed device be used with its product	Measuring device included	32/148	21.6 (15.3-29.0)	0.91
No mechanism securing measuring device to product	Measuring device included	143/148	96.6 (92.3-98.9)	1.0
No warning about use of appropriate delivery device when physician-recommended doses do not match a dose amount marked on enclosed device	Measuring device included	149/148	100 (97.6-100.0)	

Abbreviations: CI, confidence interval; FDA, Food and Drug Administration.
^aNo. represents the number of products that do not adhere to the FDA recommendation; Total No. represents the total number of products relevant to the area of concern.
^bDegree of inter-rater agreement for each outcome of interest determined by calculation of the κ statistic; product packaging was independently assessed by 2 investigators. No κ was calculated when No./Total No. = 1; however, there was 100% agreement between investigators in these instances.
^cAny inconsistency between directions and measuring device with respect to dose listed or marked, or text used for unit of measurement.
^dFor milliL, teaspoon, and tablespoon units of measurement, inconsistency was defined as different terms of the abbreviation used in the labeled dosing directions compared with that used on the measuring device, as well as when milliL was used in one location and an abbreviation used in the other location.
^eAcross-product variability including use of atypical units of measurement, use of nonstandard abbreviations for unit of measurement, absence of 1 or more definitions of abbreviations for unit of measurement, or unclear use of numeric text.
^fUnits of measurement considered atypical, including drams, cc, fluid ounces.
^gAmong products using a milliL abbreviation, use of mL, ml, or M; rather than the standard term, mL.
^hAmong products using a teaspoon abbreviation, use of tsp or TSP rather than the standard term, tsp.
ⁱAmong products using a tablespoon abbreviation, use of Tbsp, tbs, or TBS instead of TBSP (most commonly used abbreviation).
^jMilliL, teaspoon, or tablespoon abbreviations.
^kEither no strategy to ensure measuring device used only with the product with which it was included, or no warning about use of appropriate delivery device when physician-recommended doses do not match a dose amount marked on the enclosed device.

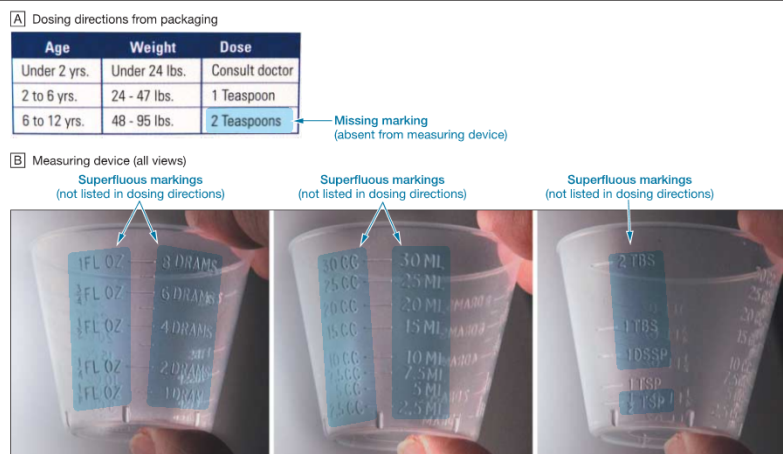
2598 JAMA, December 15, 2010—Vol 304, No. 23 (Reprinted)

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Figure 3. Use of Atypical Unit Markings on Measuring Device and Inconsistency With Listed Doses



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Yin HS, Wolf MS, Dreyer BP, Sanders LM, Parker RM. Evaluation of consistency in dosing directions and measuring devices for pediatric nonprescription liquid medications. JAMA. 2010Dec.15;304(23):2595-602.

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Sharfstein JM, North M, Servint JR. Over the counter but no longer under the radar--pediatric cough and cold medications. N Engl J Med. 2007;Dec 6;357(23):2321-4.

Ingredients and Marketing of Some of the Available Pediatric Cough and Cold Products.*		
Ingredients	Brand Name	Marketed Use
Antihistamine	Pediacare	Nighttime cough
	Triaminic	Cough and runny nose
Antitussive	Robitussin	Long-acting cough
Decongestant	Dimetapp	Decongestant
Antihistamine and antitussive	Robitussin	Long-acting cough and cold
	Tylenol Plus	Cough and runny nose
Antihistamine and decongestant	Dimetapp	Cold and allergy
	Pediacare	Nighttime multisymptom cold
	Triaminic	Nighttime cough and cold
Antitussive and decongestant	Dimetapp	Decongestant plus cough
	Pediacare	Multisymptom cold
	Triaminic	Daytime cough and cold
Decongestant and expectorant	Dimetapp	Cold and chest congestion
	Triaminic	Chest and nasal congestion
Antihistamine, antitussive, and decongestant	Dimetapp	Cold and chest congestion
	Tylenol Plus	Flu
	Tylenol Plus	Multisymptom cold
Antitussive, decongestant, and expectorant	Robitussin	Cough and cold

* The antihistamines include brompheniramine, chlorpheniramine, and diphenhydramine; the antitussive is dextromethorphan; the decongestant is phenylephrine; and the expectorant is guaifensin. All formulas of Tylenol Plus also contain acetaminophen.

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Inadvertent misuse

- Use of OTC cough and cold medicine in children < 2 yrs. because parents misinterpret the information on the package
- Child is given two products (OTC+ Prescription) with same/similar active ingredient for different indications because the prescriber has not been told about OTC use, or not told correctly

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ARTICLE

Parental Misinterpretations of Over-the-Counter Pediatric Cough and Cold Medication Labels

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What's Known on This Subject
The misuse or overuse of OTC cold and cough medications has been implicated in many adverse events and the deaths of >100 infants. Caregivers may have difficulties understanding OTC label directions, but this has not been well studied.

What This Study Adds
OTC labels can be misleading and difficult for many caregivers to understand. Label graphics and items can lead to misinterpretation and understanding of the age indication of products. Poorer understanding may be more common among caregivers with lower numeracy skills.

ABSTRACT

OBJECTIVE Concerns about the safety and efficacy of over-the-counter cold medications have led to a recent US Food and Drug Administration public health advisory against their use in children <2 years of age. Our goal was to examine caregiver understanding of the age indication of over-the-counter cold medication labels and identify factors, associated with caregiver understanding.

METHODS Caregivers of infant children (≤1 year old) were recruited from clinics at 3 institutions. Questions were administered regarding the use of 4 previously common "infant" over-the-counter cold and cough medicines labeled to consult a physician if used in children <2 years of age. Literacy and numeracy skills were assessed with validated instruments.

RESULTS A total of 182 caregivers were recruited; 87% were the infants' mothers. Mean education level was 12.5 years, and 99% had adequate literacy skills, but only 17% had >9th-grade numeracy skills. When examining the front of the product label, 86% of the time parents thought these products were appropriate for use in children <2 years of age. More than 50% of the time, parents stated they would give these over-the-counter products to a 13-month-old child with cold symptoms. Common factors that influenced parental decisions included label saying "infant," graphics (eg, infants, teddy bears, droppers), and dosing directions. Caregivers were influenced by the dosing directions only 47% of the time. Caregivers with lower numeracy skills were more likely to provide inappropriate reasons for giving an over-the-counter medication.

CONCLUSIONS Misunderstanding of over-the-counter cold products is common and could result in harm if medications are given inappropriately. Label language and graphics seem to influence inappropriate interpretation of over-the-counter product age indications. Poorer parental numeracy skills may increase the misinterpretation of these products. Opportunities exist for the Food and Drug Administration and manufacturers to revise existing labels to improve parental comprehension and enhance child safety. *Pediatrics* 2009;123:1464-1471

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Key Words
misinterpretation, drugs, literacy, safety
Abbreviations
OTC—over-the-counter
CDC—Centers for Disease Control and Prevention
FDA—Food and Drug Administration
OTCPL—Over-the-Counter Product Labeling
Health Literacy in Adults
WRMC—Wide Range Achievement Test 5
CEE—generalized estimating equations
OR—adjusted odds ratio
CI—confidence interval
Q—questionnaire
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TABLE 3 OTC-Label Survey Results

Product	Has Used Product Before, %	Thinks Product Is Appropriate for Children <24 Mo of Age, % ^a	Age Range Influenced by These Main Factors, % ^a	Would Give Product to 13-mo-Old With Cold ^b	Inappropriate Response ^b	Answer Influenced by These Main Factors, %
(A) decongestant nose drops	19	89	Says "infant": 9 Other language: 33 Graphics: 52 Experience: 12	52	58	Directions: 47 Other language: 24 Graphics: 6 Experience: 9
(B) infant drops, long-acting cough	14	80	Says "infant": 55 Other language: 13 Graphics: 27 Experience: 9	43	57	Directions: 48 Other language: 27 Graphics: 2 Experience: 9
(C) infant cough medicine	15	91	Says "infant": 72 Other language: 9 Graphics: 18 Experience: 10	50	57	Directions: 48 Other language: 27 Graphics: 2 Experience: 8
(D) infant drops for fever plus cold symptoms	33	86	Says "infant": 55 Other language: 14 Graphics: 29 Experience: 14	58	60	Directions: 43 Other language: 28 Graphics: 4 Experience: 12

^a Response based on examining the front of the package only.

^b Examined the entire package. Column is counted as inappropriate if the caregiver said he or she would give the product to a 13-month-old or that he or she would not give the product but did not have an appropriate explanation for why not.

Lokker N, Sanders L, Perrin EM, Kumar D, Finkle J, Franco V, et al. Parental misinterpretations of over-the-counter pediatric cough and cold medication labels. *PEDIATRICS*. 2009 Jun;123(6):1464-71.

Drug–drug interactions

- In children given standard doses
- Pharmacodynamic interaction (additive) of e.g. 2 sedating antihistamines in 2 different products
- Pharmacokinetic interactions may be less common but possible
 - Medicines with strong interaction potential usually not available OTC
 - Interactions leading to reduced effect possible (interaction with absorption)

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Drug-drug interactions in Concurrent Use of OTC and Prescription Drugs in Children

- In Finnish study (Ylinen et al. 2010) prevalence of concomitant use of prescription medicines and self-medication was 10%
- The prevalence of concomitant use of prescription medicines and OTC medicines was 4% (149/3892)
- Three of these cases (2%; 3/149) had a combination with potential risk for interaction (two NSAID or paracetamol containing products)

Ylinen S, Hämeen-Anttila K, Sepponen K, Lindblad ÅK, Ahonen R. The use of prescription medicines and self-medication among children—a population-based study in Finland. *Pharmacoepidemiol Drug Saf.* 2010Oct.;19(10):1000–8.

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Conclusions

- Data on concurrent use of OTC medicines and prescription drugs scarce
- Prevalence may vary between populations
- The prescriber often does not have a full picture of OTC use by the patient
- The patient does not know taking 2 products with same/similar active substance
- Risks are related to inadvertent overdosing (additive effect) or drug-drug interactions