Prescribing Patterns and Safety of *Mezclitas* for Respiratory Illnesses

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Objective: To evaluate the prescribing patterns of compound mixtures of cough and cold liquid medications, known as *mezclitas*, which are prescribed to patients with respiratory illnesses in Puerto Rico. Secondary objectives include assessing the potential safety of these mixtures and patients' perception of them.

Methods: Using a cross sectional study approach, a convenience sample was obtained from five pharmacies in Puerto Rico, from October 2008 to October 2009. Patients were asked to complete a 9-item questionnaire about demographic information, in addition to their *mezclita* prescription data.

Results: The mean age of patients was 43 years with a range of less than 12 months to 101 years. For children < four years of age, 71% were prescribed cough and cold medications. Sixty-four percent of the prescriptions were given to females. The most prevalent ingredient employed was guaifenesin, which appeared in about 77% of the *mezclitas*. 'Common cold' was the principal diagnosis for 62% of the prescriptions, of which 75% of these prescriptions contained a corticosteroid and 17% contained a beta2 agonist bronchodilator. The top medical prescribing specialty was general medicine (51%). Thirty-eight percent of hypertensive patients were prescribed a decongestant. The majority of diabetic patients (60%) were dispensed a corticosteroid. Most (74%) patients reported that they had a rapid and good response to their *mezclita*.

Conclusion: *Mezclitas* were most commonly prescribed for acute symptoms of upper respiratory illness by general physicians despite possible side effects. This study suggests that the prescription patterns of *mezclitas* do not always consider evidence-based medicine treatment guidelines. [*P R Health Sci J 2012;3:138-144*]

Key words: Mezclitas, Over-the-counter, Adverse drug reactions, Cough and cold medications, Food and Drug Administration, Treatment guidelines, Puerto Rico

Mezclitas are liquid mixtures of cough and cold medications combined with other prescription products including corticosteroids, bronchodilators, and narcotic antitussives. *Mezclitas* is the term in Spanish used by both health care professionals and patients when referring to these mixtures. These *mezclitas* are commonly prescribed by physicians in Puerto Rico to treat respiratory illnesses, including coughs related to the common cold, bronchitis and asthma. Anecdotal evidence seems to indicate that prescribing and utilizing *mezclitas* is a practice limited to the territory of Puerto Rico. In spite of their popular use, there is limited and conflicting evidence as to the safety and efficacy of this practice (1- 4). However, in the United States, the inappropriate use and the questionable efficacy and safety of cough and cold medications (CCM) has already been a major concern for authorities like the FDA and CDC, especially in children and the elderly (5-10). These authorities have raised significant concerns about CCM misuse, including serious cases of intoxication and adverse drug reactions (5, 9, 10). In spite of this, little is known regarding the effects of complex mixtures composed of over-the-counter CCM and other prescription products for respiratory illnesses.

This study moves beyond simple CCM misuse, to address *mezclitas*, which are complex mixtures that may have higher potential to cause adverse drug reactions (ADRs) and drug-drug interactions, especially in vulnerable populations such as children and the elderly.

So far, treatment guidelines for the management of cough associated with the common cold, bronchitis, asthma or cough-variant asthma, as defined by the American College of Chest Physicians (ACCP) and Global Initiative for Asthma (GINA),

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do not support the use of most of these drugs; especially in a compounded mezclita form for the symptomatic scenarios under which they are prescribed (11-14). The Food and Drug Administration (FDA) recognizes some cough and cold medicine combinations as safe and outlines warnings of potential side effects (5). An epidemiologic profile of the diagnosis and management of asthma in Puerto Rico has already reported a concern that health care professionals are not adhering to treatment guidelines (15).

Children constitute a special population in which there is limited evidence for the safety and efficacy of these products (6-8). In the United States (US), nearly 7,000 children ≤ 11 years old are treated in hospital emergency departments due to intoxication with cough and cold medications (9). In 2004 -2005, about 1,500 children < 2 years-old experienced adverse events, including death, related to CCM (10). The average adult over 65 years takes between six to nine medications concurrently, making the risk of polypharmacy and drug reactions a major concern (16, 17). ADRs are up to seven times more common in the elderly than young adults (16, 18). A potential harmful adverse event may occur when there is duplication of ingredients from prescribed medications and commercially available over-the-counter (OTC) preparations.

The objectives of this study are to: 1) evaluate the prescribing patterns and utilization of *mezclitas*, including ingredient composition, distributed by age, gender, prescribing diagnosis, physician specialty, and patients' underlying medical condition(s); 2) assess the potential safety of these compound mixtures in patients with known chronic diseases; and 3) assess the patient's perception of the effectiveness of the *mezclitas*.

Methods

Utilizing a cross sectional study design, a convenience sample of prescriptions containing different combinations of ingredients such as corticosteroids, $beta_2$ agonists, xanthenes, and cough and cold medications, were obtained from five pharmacies in Puerto Rico. Three of the pharmacies were from the southern area (Ponce, Juana Diaz and Yauco), and two were from the northern side of the island (Carolina and Rio Piedras). Written permission from the pharmacy owners was obtained and the study received Institutional Review Board (IRB) approval from the Universidad Central del Caribe, University Hospital.

Included were all prescriptions for any of the different combinations of liquids (suspensions, syrups, elixirs, solutions, etc.) whose ingredients included corticosteroids, $beta_2$ agonists, xanthenes, antitussives, decongestants, expectorants, or antihistamines. Prescriptions for OTC drugs that contained a *mezclita* of the above categories were also included. Excluded from the study were all prescriptions for non-oral preparations, oral preparations prescribed for other illnesses and prescriptions for oral CCM to be dispensed separately. Minors, patients or care takers with impaired decisional capacity with no legal representative to consent to participate in the study were also excluded. Patients with prescriptions meeting the inclusion criteria were invited to participate in the study by trained pharmacy personnel and their informed consent was obtained.

Participants completed a validated 9-item questionnaire containing demographics, diagnosis, prescribing physician's specialty and the patient's perception of their *mezclita's* effectiveness. This questionnaire had been previously designed and revised by the authors (researchers, pharmacists, and a physician), verifying that the common subject with a "mezclita" prescription would understand what was being asked. The patient completed the survey while waiting for their prescription(s) in a waiting room or similar area. Trained pharmacy staff assisted subjects by answering any questions related to the survey.

In order to protect the patient's identity, a pharmacy code and a number were given to each questionnaire and to the patient's prescription. Information about the ingredients of the *mezclita* was obtained from copies of the original prescriptions, where the name and personal information of the participant were removed. Data were collected over one year (October 2008 - October 2009). Descriptive statistics were performed using the mean, standard deviation (SD), and median and range (maximum – minimum) for continuous variables. Categorical variables were described as frequencies and proportions. Relationships between the most common ingredients and age categories, sex and medical specialty were evaluated using the Chi-square test. STATA 11.2 software was utilized for the analysis (19). Any probability value < 0.05 was considered statistically significant.

Results

Epidemiologic profile

A total of 317 prescriptions were evaluated. Each of the 5 pharmacies contributed between 39 and 95 prescriptions. There were 66 different medication class combinations of ingredients that were compounded together. The most prevalent ingredient was guaifenesin which appeared in about 77% of the *mezclitas*. The most common combination (22%) contained an expectorant, non-narcotic antitussive, steroid, and decongestant. The other two most common combinations were an expectorant, non-narcotic antitussive, and steroid (13%) and an expectorant, non-narcotic antitussive, decongestant, beta-agonist, and steroid (5%).

The mean age was 43 years with an age range of less than 12 months of age to 101 years old. For children under age four, 71% were prescribed cough and cold medications. Sixty-four percent of the prescriptions were given to females.

Influenza or the common cold was the principal diagnosis for 62% of the prescriptions. Other common diagnoses included asthma (27%), bronchitis (16%), and sinusitis (13%). The top medical prescribing specialty was general medicine (52%), followed by pediatricians (17%), pneumologists (11%), and internists (10%) (Table 1). Table 2 shows the six most common ingredients overall; whereas Table 3 shows the top six ingredients across five age groups. There were no significant differences between the age groups in the percentages in which the top six ingredients were prescribed.

Combining the ingredients of dexamethasone and prednisolone shows that 75% of the prescriptions for patients with a diagnosis of influenza or the common cold contained a corticosteroid and 17% a $beta_2$ agonist bronchodilator. Among the most prescribed agents, there were no statistically significant differences between medical specialties (Table 3).

Table 1. Demographic characteristics

	Freq.[1] (n=317)	%
Gender		
Male	113	35.6
Female	204	64.4
Age		
< 18	71	22.4
18 – 35	38	12.0
36 – 50	61	19.2
51 – 64	67	21.1
> 65	80	25.2
Medical condition		
Diabetes	60	18.9
Hypertension	116	36.6
Asthma	96	30.3
Osteoporosis	20	6.3
CHF	20	6.3
Diagnosis		
Asthma	85	26.8
Influenza / cold	196	61.8
Bronchitis	51	16.1
Sinusitis	40	12.6
Medical specialty		
General medicine	162	51.1
Pediatrics	53	16.7
Internal medicine	33	10.4
Pneumology	34	10.7
Effectiveness perception (n=173)		
Good	153	88.4
Regular	16	9.3
No improvement	3	1.7
Symptoms worsened	1	0.6
Days before improvement (n=165)		
< 5 days (rapid)	122	73.9
> 5 days (slow)	43	26.1

[1]Sample size (n) = 317 except where noted otherwise. The n values below 317 are due to subjects not completing some questions in questionnaire.

Table 2. Top six most common ingredients

Ingredient (n=317 prescriptions)	Freq.	%*
Guaifenesin	244	76.9
Dextromethorphan	230	72.8
Dexamethasone	129	40.8
Phenylephrine	117	37.0
Prednisolone	115	36.4
Albuterol	55	17.4

*Percentage represents the ingredient's presence in the total prescriptions (n=317). More than one ingredient could exist in the same prescription.

Safety

The top five comorbidities affecting individuals prescribed a *mezclita* were hypertension (37%), asthma (30%), diabetes (19%), osteoporosis (6%), and congestive heart failure (6%). Thirty eight percent of hypertensive patients were prescribed a decongestant. For diabetic patients, 60% were dispensed a corticosteroid and 30% and 40% of patients with congestive heart failure were given a decongestant and a $beta_2$ agonist, respectively. Of the patients with a diagnosis of asthma, 74% were prescribed guaifenesin. About 18% of patients with sinusitis were given a $beta_2$ agonist bronchodilator (Table 3).

The mean day's supply of a *mezclita* was 8 days with prescriptions having a day's supply ranging from 2 to 180 days. One infant was prescribed betamethasone for 45 days for the treatment of asthma.

There were a total of 29 prescriptions that contained duplication of therapy. Seventeen of the duplications combined more than two antitussives. Six combined up to three antihistamines, while three prescriptions combined two bronchodilators, two combined two corticosteroids, and one prescription had a duplication of decongestants.

Patient perception

Subjects were asked about the effectiveness of their prescribed *mezclita*. The vast majority (88%) reported a good response to their prescription, with 74% saying that the response was rapid (less than 5 days).

The missing data derived from the questionnaire (as reflected by some n values in tables) is due to some subjects not answering every question primarily because they unrecalled or were unsure of information asked.

Discussion

In our study, the two largest age groups for *mezclita* prescriptions were comprised of patients less than 18 years of age or older than 65 years old. This raises the concern that the two most vulnerable age groups for adverse drug reactions are the primary consumers of *mezclitas*. A systematic review by Smith et al., involving 51 clinical trials from 1950 to 1991, revealed that there was a lack of high quality clinical trials on

the effects of cough and cold medications in children. Studies reviewed yielded conflicting results, indicating no clear benefit of giving CCM to this population (3). The doses approved by the FDA for children were extrapolated from adults, due to the limited or non-existent data available (20, 21). The duration of therapy for the cough and cold medications reviewed varied from as little as a single dose treatment to "as long as necessary" (3). The trials included in the systematic reviews were fixed manufacturer prepared combinations, not compounded *mezclitas*. For children under age four, 71% were prescribed cough and cold medications in combination with corticosteroids or/and bronchodilators for upper respiratory infections (URI). Medical guidelines currently discourage the use of cough and cold medications in children younger than 4 years of age (6-8). No statistically significant differences were seen between age groups and the top ingredients prescribed, suggesting that there is little consideration of age by prescribers, despite the fact that age is an important issue for ADRs and FDA regulations.

Outcomes from our study are similar to the findings from a nationwide retrospective study by Korelitz et al (22). In that study, 4,259,103 children in the US, from birth to age 17, were enrolled over a two year period (2004-05), for which 398,880 children without an asthma diagnosis were dispensed asthma-related medications. A large number of children in the United States were dispensed asthma medications for acute pharyngitis, acute bronchitis and bronchiolitis (22). In our study, over 90% of patients < 18 years old with a diagnosis of a common cold or bronchitis received asthma medications like oral albuterol and/or corticosteroids. All patients with sinusitis where given this same class of treatment.

Previous studies show lack of efficacy for oral corticosteroids in the pediatric population for the treatment of acute virus-induced wheezing and acute bronchiolitis (23-26). Overall, there are limited data for the use of corticosteroids for the treatment of upper respiratory illness (URI) and corticosteroids do not have an FDA indication for URI (27). In our study, corticosteroids were prescribed to 75% of the patients with a diagnosis of URI. Many of our study's elderly population were prescribed *mezclitas* containing systemic corticosteroids and bronchodilators for presumed diagnoses of URI or sinusitis. Current treatment guidelines for these diagnoses also do not recommend use of such therapy, (11, 28, 29) causing an unnecessary exposure to both potential drug side effects and drug-drug interactions. In general, the elderly are large consumers of multiple prescriptions and OTC medications (including CCM) due to their overall higher prevalence of comorbidities (30). CCM are particularly

Table 3. Most common ingredients by gender, age, medical condition, diagnosis and medical specialty

(Total n = 317)	Guaifenesin		Dextromethorphan		Dexamethasone		Phenylephrine		Prednisolone		Albuterol	
	Freq.	%	Freq.	%	Freq.	%	Freq.	%	Freq.	%	Freq.	%
Gender												
Male	87	35.7	88	38.3	47	36.4	34	29.1	33	28.7	26	47.3
Female	157	64.3	142	61.7	82	63.6	83	70.9	82	71.3	29	52.7
	p = 0.005		p < 0.001		p = 0.003		p < 0.001		p < 0.001		p = 0.689	
Age												
< 18	49	69.01	52	73.24	34	47.89	30	42.25	25	35.21	7	9.86
18 – 35	28	73.68	30	78.95	13	34.21	12	31.58	15	39.47	9	23.68
36 – 50	47	77.05	48	78.69	26	42.62	20	32.79	26	42.62	12	19.67
51 – 64	58	86.57	48	71.64	26	38.81	30	44.78	26	38.81	13	19.40
> 65	62	77.50	52	65.00	30	37.50	25	31.25	23	28.75	14	17.50
	p= 0.180		p = 0.371		p = 0.607		p = 0.324		p = 0.491		p = 0.371	
Medical conditions												
Diabetes	49	81.67	38	63.33	20	33.33	19	31.67	16	26.67	15	25.00
Hypertension	98	84.48	81	69.83	43	37.07	44	37.93	33	28.45	22	18.97
Asthma	71	73.96	64	66.67	40	41.67	30	31.25	33	34.38	21	21.88
Osteoporosis	14	70.00	8	40.00	10	50.00	4	20.00	7	35.00	1	5.00
CHF	15	75.00	11	55.00	6	30.00	6	30.00	5	25.00	8	40.00
Diagnosis												
Asthma	64	75.29	56	65.88	32	37.65	29	34.12	34	40.00	16	18.82
Influenza / cold	155	79.08	145	73.98	79	40.31	77	39.29	68	34.69	34	17.35
Bronchitis	39	76.47	38	74.51	21	41.18	19	37.25	19	37.25	10	19.61
Sinusitis	30	75.00	31	77.50	11	27.50	16	40.00	14	35.00	7	17.50
Medical specialty												
General medicine	130	80.24	120	74.07	73	45.06	55	33.95	54	33.33	34	20.99
Pediatrics	36	67.92	37	69.81	28	52.83	23	43.40	17	32.08	4	7.55
Internal medicine	29	87.87	25	75.76	9	27.27	14	42.42	13	39.39	7	21.21
Pneumology	23	67.65	22	64.71	8	23.53	11	32.35	15	44.12	3	8.82
	p = 0.063		p = 0.655		p = 0.012		p = 0.507		p = 0.590		p = 0.061	

used and misused by the elderly (31). This again represents a higher risk for potential ADRs when combining some *mezclitas* with common cold medications that are commonly self-prescribed (32-35).

As stated above, Smith et al. concluded that it is difficult to say if cough and cold medications are safe and effective due to the conflicting scientific evidence (36). Many of these CCM are fixed combinations in which there is no indication that the ingredients are more effective together than individually. Overall, it is not recommended for physicians to resort to them (37). Two non-US articles included in the Smith et al. review evaluated the combination of dextromethorphan and albuterol in children (Finland, ~4yo) and adults (Scandinavia, ~38yo) for URI. For the children's trial, there was no statistical difference between the product and placebo. However, the study had a very small sample size and limited statistical power. For the adult trial, the combination of dextromethorphan and albuterol, compared to plain dextromethorphan, was statistically superior for suppressing cough at night on day 3 of taking the medication ($p<0.01$). However, an increase in side effects was seen including tremors ($p< 0.05$) (36). Though tremors can be a tolerable side effect of albuterol, there are cases where a patient's stable chronic condition, like heart failure or cardiac arrhythmias, can be exacerbated due to an indiscrete use of this type of medication (38). In our study, systemic corticosteroids, decongestants (sympathomimetics), and $beta_2$ agonist bronchodilators were routinely prescribed to patients with co-morbid conditions including diabetes, cardiovascular disease, and osteoporosis. Thirty-eight percent of hypertensive patients were prescribed a decongestant. For diabetic patients, 60% were dispensed a corticosteroid and patients with congestive heart failure were given a decongestant (30%) and a $beta_2$ agonist (40%).

The FDA continues to report and issue warnings about the potential adverse reactions caused by cough and cold medications, especially in children and in patients with underlying conditions (20, 21). While scenarios exist where a therapy's benefit outweighs its potential for causing adverse reactions, our study reveals a large number of cases where the prescribing of some of *mezclitas* ingredients was not justified based on the presumed primary diagnosis. This potentially leads to an unnecessary exposure of the patients to side effects. The World Health Organization (WHO) indicates that most combinations of cough and cold medications are not logical (39). Often they are in a combination of ineffective ingredients with subtherapeutic doses, with additive therapeutic effects, or with opposite effects (e.g., dextromethorphan with guaifenesin). The WHO recommends avoiding these products, especially in combinations, including combinations containing bronchodilators (39). Evidence-based practice guidelines issued by both the ACCP and GINA do not recommend compounded liquid cough and cold medications in combination with systemic corticosteroids and bronchodilators for the treatment of asthma, bronchitis or the common cold cough (11-14). In our study, *mezclitas* were often prescribed for these conditions. The FDA regards expectorants use in patients with asthma as controversial because there is little evidence in the clinical literature to support their use in this condition (40). This modality is inconsistent and is not recommended by current asthma management guidelines (5, 13, 14). In our study, 74% of patients with a diagnosis of asthma received guaifenesin.

For chronic cough due to acute bronchitis, $beta_2$ agonist bronchodilators should not be routinely used to alleviate cough; however, it may be used in some adults with wheezing and cough. Non-narcotic antitussives are sometimes useful for short term alleviation of coughing and the mucokinetics (expectorant, mucolytic) are not recommended (41). In our study, patients with bronchitis were mostly prescribed a combination containing guaifenesin (77%), dextromethorphan (75%), corticosteroid (78%), and phenylephrine (37%) and some of them had a prescription which combined a $beta_2$ agonist bronchodilator.

ACCP and GINA guidelines recommend giving oral corticosteroids as a last option, reserving this treatment for severe and or refractory cough due to asthma. This recommendation is for a short course (1 to 2 weeks) of systemic (oral) followed by inhaled corticosteroids (13, 14). In our study, systemic corticosteroids were prescribed in 78% of the cases of asthma-induced cough or bronchial asthma exacerbations. It is suspected that most of these cases had no prior trial of being refractory to first line therapy.

The majority of patients perceived that they had a rapid response to their prescribed *mezclitas* since their symptoms improved in less than 5 days. However, the symptoms of the common cold or influenza may last about a week and the patient's symptoms may have improved regardless of the medication (42-44). Patients may be misinformed about the symptoms, duration, and recovery processes associated with the common cold and/or influenza.

Another important finding of our study is the problem of duplication of therapy and hence greater risk for drug side effects or intoxication. Many *mezclitas* prescribed contained duplication of therapy or contained up to three ingredients of the same medication class.

There were 17 *mezclitas* with duplicity of antitussive therapy by mixing narcotic and non-narcotic antitussives, whereas 6 *mezclitas* contained double antihistamine therapy. In addition to duplication within the prescriptions, there is the possibility that some patients might have mixed these *mezclitas* with OTCs medications already found in the home, leading to higher toxicity potential, especially in children and elderly populations.

Limitations

The small sample size of our study may limit the extrapolation of results to the general population. There was a potential for

response bias since the information gathered from the surveys were based on patients' truthful answers. Another limitation is that frequently the diagnosis given on the prescription was not very specific. We were unable to identify or differentiate chronic versus acute bronchitis or acute asthma from refractory cough asthma. We did not verify that active ingredients were given at effective doses in the *mezclitas*. However, to our knowledge, this study is the first evaluation of prescribing patterns of *mezclitas* or cough and cold medication compounding mixtures practice in Puerto Rico. These data may increase the awareness of the prescribing pattern of *mezclitas* in different age groups.

Conclusion

Mezclitas were mostly prescribed for symptoms of upper respiratory illness by general physicians to children and the elderly. Though the majority of patients perceived a positive effect of their *mezclita*, the potential safety and efficacy for many of these *mezclitas* remains controversial (9, 10, 20, 45, 46). This study suggests that the prescribing patterns of *mezclitas* do not always consider evidence-based medicine treatment guidelines, including patient's age and underlying comorbidities. It may be important to develop and implement new policies about this practice in Puerto Rico to change the prescribing patterns of physicians for these medications. This may also aid in ensuring better adherence to evidence-based treatment guidelines with more effective and safe treatments delivered for these respiratory conditions.

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Resumen

Objetivo: Evaluar los patrones de prescripción de mezclas, llamadas *mezclitas*, compuestas de medicamentos líquidos para tos y resfriado, las cuales son recetadas en Puerto Rico para enfermedades respiratorias. Objetivos secundarios incluye evaluar la seguridad de estas mezclas y la percepción de ellas por los pacientes. Métodos: Utilizando un diseño de estudio transversal, se obtuvo una muestra de estudio de cinco farmacias en Puerto Rico de Octubre 2008 a Octubre 2009. Se les pidió a los pacientes completar un cuestionario de 9 elementos de información demográfica, en adición a los datos de la receta de la *mezclita*. Resultados: La edad promedio de los pacientes fue de 43 años, con un rango de menos de 12 meses a 101 años. En niños de cuatro años o menos, a un 71 % se les recetó medicamentos para tos y resfriado. Sesenta y cuatro por ciento de las recetas fueron dadas a mujeres. Guaifenesina fue el ingrediente más comúnmente empleado, presente en aproximadamente un 77% de las *mezclitas*. El 'resfriado común' fue el diagnóstico principal para 62% de las recetas, de las cuales 75% contenían un corticoesteroide y 17% un broncodilatador $beta_2$ agonista. Medicina general (51%) fue la especialidad médica que más las recetó. A 38% de los pacientes hipertensos se les recetó un descongestionante. La mayoría de los pacientes diabéticos (60%) se les dio un corticoesteroide. La mayoría (74%) de los pacientes reportaron una mejoría rápida gracias a su *mezclita*. Conclusión: Las *mezclitas* fueron más comúnmente recetadas por médicos generalistas para tratar síntomas agudos de enfermedades del tracto respiratorio alto. Este estudio sugiere que los patrones de prescripción de *mezclitas* no siempre consideran guías de tratamiento de medicina basada en evidencia.

References

1. The Proprietory Association of Great Britain. Annual Review and Report. PAGB London: 2000.
2. Schroeder K; Fahey T. Over-the-counter medications for acute cough in children and adults in ambulatory settings. Cochrane Database Syst Rev. 2004;4:CD001831.
3. Smith MB, Feldman W. Over-the-counter cold medications. A critical review of clinical trials between 1950 and 1991. JAMA 1993;269:2258-63.
4. Gunn VL, Taha SH, Liebelt EL, Serwint JR. Toxicity of over-the-counter cough and cold medications Pediatrics 2001;108:E52.
5. Food and Drug Administration 21 CFR Part 341[Docket No. 76N–052G] Cold, Cough, Allergy, Bronchodilator, and Antiasthmatic Drug Products for Over-The-Counter Human Use; Final Monograph for Combination Drug Products. Available from: Url: http://edocket.access.gpo.gov/2002/pdf/02-32158.pdf Cited: February 2, 2010.
6. Health Canada [website]. Health Canada's decision on cough and cold medicines. Ottawa, ON: Health Canada; 2008. Available from: Url: www.hc-sc.gc.ca/ahc-asc/media/advisoriesavis/_2008/2008_184info1-eng.php. Cited: January 31, 2010.
7. Food and Drug Administration. Using over-the counter cough and cold products in children. Silver Spring, M D: Food and Drug Administration; 2008. Available from: http://www.fda.gov/ForConsumers/ConsumerUpdates/ucm048515.htm Cited: February 2, 2010.

8. Vernacchio L, Kelly JP, Kaufman DW, Allen AS, Mitchell. Cough and Cold Medication Use by US Children, 1999-2006: Results From the Slone Survey. Pediatrics 2008;122:e323-e329.
9. Centers for Disease Control and Prevention. Press Release. CDC Study Estimates 7,000 Pediatric Emergency Departments Visits Linked to Cough and Cold Medication. Available from: Url: http://www.cdc.gov/media/pressrel/2008/r080128.htm?s_cid=mediarel_r080128. Cited: March 3, 2010.
10. Centers for Disease Control and Prevention. Infant Deaths Associated with Cough and Cold Medication. 2007;56;1-4. Available from: Url: http://www.cdc.gov/mmwr/preview/mmwrhtml/mm5601a1.htm. Cited: February 26, 2010.
11. Pratter MR. Cough and the Common Cold: ACCP Evidence-Based Clinical Practice Guidelines. Chest 2006;129:72S-74S.
12. Braman SS. Chronic Cough Due to Acute Bronchitis: ACCP Evidence-Based Clinical Practice Guidelines. Chest 2006;129:95S-103S.
13. Dicpinigaitis PV. Chronic Cough Due to Asthma: ACCP Evidence-Based Clinical Practice Guidelines. Chest 2006;129:75S-79S.
14. Global strategy for asthma management and prevention. Global Initiative for Asthma (GINA); 2006. Available from: Url: http://www.ginasthma.org. Cited: January 28, 2010.
15. Bartolomei-Diaz J. Epidemiological profile of Asthma in Puerto Rico. San Juan, PR: Puerto Rico Department of Health, 2008.
16. Rolita L, Freedman M. Over-the-Counter Medication Use in Older Adults. J Gerontol Nurs 2008;34:p8-17.
17. Torrible SJ & Hogan DB. Medication use and rural seniors. Who really knows what they are taking? Can Fam Physician 1997;43:893-8.
18. Kongkaew C, Noyce PR, and Ashcroft DM. Hospital Admissions Associated with Adverse Drug Reactions: A Systematic Review of Prospective Observational Studies. Ann Pharmacother 2008;42:1017-1025.
19. STATA Data analysis and Statistical software. Available from: Url: http://stata.com/. Cited: December 15, 2011.
20. Food and Drug Administration, HHS. Nonprescription Drug Advisory Committee Meeting Cold, Cough, Allergy, Bronchodilator, Antiasthmatic Drug Products for Over-the-Counter Human Use. October 18 and 19, 2007. Available from: Url: http://www.fda.gov/ohrms/dockets/ac/07/briefing/2007-4323b1-02-FDA.pdf. Cited: March 4, 2010.
21. Dolansky G, Rieder M. What is the evidence for the safety and efficacy of over-the-counter cough and cold preparations for children younger than six years of age? Paediatr Child Health 2008;13:125-27.
22. Korelitz JJ, Zito JM, Gavin NI, Masters MN, McNally D, Irwin DE, Kelleher K, Bether J, Xu Y, Rubin J, Mattison DR. Asthma-related medication use among children in the United States. Ann Allergy Asthma Immunol 2008;100:222-229.
23. Panickar J, Lakhanpaul M, Lambert PC, Kenia P, Stephenson T, Smyth A and Grigg J. Oral Prednisolone for Preschool Children with Acute Virus-Induced Wheezing. N Engl J Med 2009;360:329-38.
24. Fernandes RM, Bialy LM, Vandermeer B, Tjosvold L, Plint AC, Patel H, Johnson DW, Klassen TP, Hartling L. Glucocorticoids for acute viral bronchiolitis in infants and young children. Cochrane Database Syst Rev 2010;10:CD004878.
25. Berger, Argaman,Schwartz SB, Segal, RN, Kiderman A, Branski D, Kerem E, Efficacy of corticosteroids in acute bronchiolitis: short-term and long-term follow-up. Pediatr Pulmonol 1998;26:162-6.
26. Oommen, A, Lambert, PC, Grigg, J Efficacy of a short course of parent-initiated oral prednisolone for viral wheeze in children aged 1–5 years: randomised controlled trial. Lancet 2003;362:1433-1438.
27. Prednisolone. In: DRUGDEX® System [Internet database]. Greenwood Village, Colo: Thomson Reuters (Healthcare) Inc. Updated November 20, 2009.
28. American Academy of Pediatrics. Subcommittee on Management of Sinusitis and Committee on Quality Improvement. Clinical practice guideline: management of sinusitis. Pediatrics 2001;108:798-808. Erratum in: Pediatrics 2001;108:A24. Pediatrics 2002;109:40.
29. Hwang PH, et al. Acute sinusitis and rhinosinusitis in adults. Available from: Url: http://www.uptodate.com/home/index.html. Cited: May 15, 2011.
30. Crentsil V, Ricks M, Xue Qian-Li, Fried LP. A pharmacoepidemiologic study of community-dwelling, disabled older women: Factors associated with medication use. Am J Geriatr Pharmacother 2010;8;215-224.
31. Fillenbaum GG, Hanlon JT, Corder E, Ziqubu-Page T, Wall WE, Brock D. Prescription and Nonprescription Drug Use among Black and White Community-Residing Elderly. Am J Public Health 1993;83:1577-82. Available from: Url: http://ajph.aphapublications.org.ezp-prod1.hul.harvard.edu/cgi/reprint/83/11/1577. Cited: June 22, 2011.
32. Conn VS. Self-management of over-the-counter medications by older adults. Public Health Nurs 1992;9:29-36.
33. Simoni-Wastila L, Stuart BC, Shaffer T. Over-the-counter drug use by medicare beneficiaries in nursing homes: implications for practice and policy. J Am Geriatr Soc 2006;54:1543-9.
34. Baum C, Kennedy DL, Forbes MB, Jones JK. Drug use in the United States in 1981. JAMA 1984;251:1293-1297.
35. Sansgiry S.S, Nadkarni A, Doan T. Misuse of over-the-counter medications among community-dwelling older adults and associated adverse drug events. J Pharmaceut Health Serv Res 2010;1:175-179.
36. Smith SM, Schroeder K, Fahey T. Over-the-counter medications for acute cough in children and adults in ambulatory settings. Cochrane Database Syst Rev 2008;23:CD001831.
37. Stickler GB, Smith TF, Broughton DD. The Common Cold. Eur J Pediatr 1985;144:4-8.
38. Maak CA, Tabas JA, McClintock DE. Should Acute Treatment with Inhaled Beta Agonists be Withheld From Patients with Dyspnea Who May Have Heart Failure? J Emerg Med 2011;40:135-145.
39. World Health Organization. Cough and Cold Remedies for the treatment of Acute Respiratory Infections in young children. Child and adolescent health and development 2001; Available from: Url: http://www.who.int/child_adolescent_health/documents/fch_cah_01_02/en/ Cited: September 14, 2010.
40. Food and Drug Administration. Cough, Allergy, Bronchodilator, and Antiasthmatic Drug Products for Over-The-Counter Human Use; Proposed Amendment of the Tentative Final Monograph for Combination Drug Products. Available from: Url: http://www.federalregister.gov/articles/2005/07/13/05-13708/cold-cough-allergy-bronchodilator-and-antiasthmatic-drug-products-for-overthecounter-human-use#p-22. Cited: September 17, 2010.
41. Braman SS. Chronic cough due to acute bronchitis: ACCP evidence-based clinical practice guidelines. Chest 2006;129:95S-103S.
42. Information from Your Family Doctor. The Common Cold: What You Should Know. Am Fam Physician 2007;75:522.
43. Information from Your Family Doctor. Flu and Colds. Am Fam Physician 2004;69:383-384.
44. Centers for Disease Control and Prevention. Common Cold and Runny Nose. Overview of Common Cold. Available from: Url: http://www.cdc.gov/getsmart/antibiotic-use/URI/colds.html. Cited: June 22, 2011.
45. Cantu C, Arauz A, Murillo-Bonilla LM, López M, Barinagarrementeria F. Stroke associated with sympathomimetics contained in over-the-counter cough and cold drugs. Stroke 2003;34:1667-72. Epub 2003 Jun 5.
46. Braman SS, Hanania NA. Asthma in older adults. Clin Chest Med 2007;28:685-702.