

# Trends of Outpatient Prescription Drug Utilization in US Children, 2002–2010

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## KEY WORDS

ADHD, antibiotic use, children, drug market, drug safety, frequency, pediatric, trends, utilization

## ABBREVIATIONS

ADHD—attention-deficit/hyperactivity disorder

CI—confidence interval

FDA—US Food and Drug Administration

OTC—over-the-counter

PPI—proton pump inhibitor

VONA—IMS Vector One: National

WLSLR—weighted least squares linear regression

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**WHAT'S KNOWN ON THIS SUBJECT:** A wide variety of prescription drugs are prescribed to US children. Although one of the steps in assessing the risk/benefit of therapies in the pediatric population is to understand how they are used, pediatric drug utilization is not well characterized.



**WHAT THIS STUDY ADDS:** By using large prescription databases, this study examines the frequency and patterns of national outpatient drug utilization (acute and chronic medications) in US infants, children, and adolescents for 2002 through 2010.

## abstract

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**OBJECTIVE:** To describe trends in outpatient prescription drug utilization in US children and the changes in major areas of pediatric therapeutic use for the years 2002 through 2010.

**METHODS:** Large prescription databases (the IMS Vector One: National and Total Patient Tracker) were used to examine national drug utilization patterns for the US pediatric population (ages 0–17 years) from 2002 through 2010.

**RESULTS:** In 2010, a total of 263.6 million prescriptions were dispensed to the US pediatric population, 7% lower than in 2002, while prescriptions dispensed to the adult population increased 22% during the same time. Analysis of pediatric drug utilization trends for the top 12 therapeutic areas in 2010 compared with 2002 showed decreases in systemic antibiotics (–14%), allergies (–61%), pain (–14%), depression (–5%), and cough/cold without expectorant (–42%) prescriptions, whereas asthma (14%), attention-deficit/hyperactivity disorder (46%), and contraceptive (93%) prescriptions increased. In 2010, amoxicillin was the most frequently dispensed prescription in infants (aged 0–23 months) and children (aged 2–11 years). Methylphenidate was the top prescription dispensed to adolescents (aged 12–17 years). Off-label use was identified, particularly for lansoprazole; ~358 000 prescriptions were dispensed in 2010 for infants <1 year old.

**CONCLUSIONS:** Changes in the patterns of pediatric drug utilization were observed from 2002 to 2010. Changes include a decrease in antibiotic use and an increase in attention-deficit/hyperactivity disorder medication use during the examined time. This article provides an overview of pediatric outpatient drug utilization, which could set the stage for further in-depth analyses. *Pediatrics* 2012;130:23–31

For decades, clinicians have prescribed therapies to children, relying on data from adult clinical studies because data from appropriate pediatric safety or efficacy studies were lacking.<sup>1–3</sup> The application of adult data to children is often complicated by different expressions of adverse effects and varying pharmacokinetic and pharmacodynamic profiles, even within the pediatric population (neonates versus adolescents). One study found that children were prescribed at least 1 “off-label” prescription in 62% of office visits during the years 2001 through 2004.<sup>4</sup> Until recently, conducting drug development studies in children has not been of great interest for industry. Efforts in the form of legislation, the pediatric exclusivity component of the Food and Drug Modernization Act of 1997, the Best Pharmaceuticals for Children Act of 2002, the Pediatric Research Equity Act of 2003, and the Food and Drug Administration Amendments Act, either provided incentives for or required pediatric studies in drug development.<sup>5–8</sup> Since 1997, legislation has resulted in ~400 products studied in children and >150 products with pediatric-focused postmarketing safety reviews.<sup>9,10</sup> Although the impact of these studies on clinical practice has yet to be formally analyzed, this article seeks to provide, as an initial effort, an overview of pediatric outpatient drug utilization.

Understanding pediatric drug utilization is an important component in the assessment of therapies used in the pediatric population. Drug utilization data can provide information on the frequency and patterns of use, grouped according to therapeutic areas and patient demographic characteristics. Areas of extensive off-label pediatric use can be identified, providing insight into where potential therapeutic needs exist for pediatric drug development and clinical safety and efficacy studies. Nationwide utilization data can be used to examine the impact of US Food and

Drug Administration (FDA) regulatory actions, help target risk management/mitigation messages, and inform decisions made in clinical practice.<sup>11</sup>

The Centers for Disease Control and Prevention annually publishes a summary of health statistics for US children with highlights on selected topics, including prescription drug use.<sup>12</sup> Although a few studies have also examined pediatric drug use, studies on national drug utilization are not widely available. In 1 study, data obtained from the Slone Survey were used to estimate medication use in patients aged <12 years.<sup>13</sup> This study provided a sampling of pediatric over-the-counter (OTC) and prescription drug use based on a random-digit-dial telephone survey. However, the Slone Survey relied on self-reported use, which may be subject to response bias or misclassification of medications. In another study, chronic medication use in patients aged 5 to 19 years was examined but was limited to the commercially insured population.<sup>14</sup> By using large prescription claims databases, our study seeks to examine national outpatient drug use (acute and chronic medications) in US patients aged 0 to 17 years, including cash, Medicaid, and commercially insured populations from 2002 through 2010. Due to the recent interest in proton pump inhibitors (PPIs) and medications used to treat attention-deficit/hyperactivity disorder (ADHD), our study also includes a focus on lansoprazole use and ADHD treatment.<sup>15–17</sup>

## METHODS

Dispensed prescription and patient utilization data were obtained from the IMS Vector One: National (VONA) and Total Patient Tracker, 2 large commercial prescription and patient databases of drugs dispensed from outpatient retail pharmacies. IMS contracts with retail pharmacies, software providers, and pharmacy claims aggregators to

obtain dispensed prescription data from two-thirds of the universe of roughly 59 000 retail pharmacies. IMS maintains a stable data feed through its multiyear contracts with its data suppliers. The data captured by IMS account for approximately one-half of all retail prescriptions dispensed in the United States. IMS projected these data to the national level by using a proprietary projection method incorporating geography, pay type, and class of trade (eg, retail, independent, mass merchandisers). All data were de-identified. An exemption for use of these data was granted by the FDA institutional review board chairperson under 45CFR46.101 (b)(4).

Utilization data were subdivided according to patient age: pediatric (0–17 years) and adult ( $\geq 18$  years). Further subdivisions were infants (0–23 months), children (2–11 years), and adolescents (12–17 years), age classifications similar to those in an FDA guidance regarding the pediatric population.<sup>18</sup> Neonatal patients aged 0 to 27 days could not be separately identified by using the databases available.

Drug products were examined in terms of therapeutic areas or drug markets and active ingredients or molecules, both predefined by IMS and mapped to each drug product in the database. IMS grouped drug products within a drug market on the basis of the drug product's first approved indication. For example, montelukast is included in the asthma market but not in the allergy market. However, products included in a therapeutic area may not necessarily have an approved pediatric indication. Drug products were also grouped into molecules, which refer to the active ingredient(s) in a drug product. For example, the drug product Augmentin includes 2 active ingredients mapped to the molecule “amoxicillin/clavulanate.” For this analysis, the term molecule included all

brands/generics and dosage forms of the active ingredient(s) dispensed in the outpatient setting. Data on OTC medications, herbals, and supplements, or in mail order prescriptions, were not included.

Weighted least squares linear regression (WLSLR) was used to assess the annual trend of the estimated prescriptions dispensed and the annual trend of the rate of prescriptions dispensed per million residents. Estimates of US residents were derived from US census data.<sup>19</sup> Unlike standard linear regression, WLSLR corrects the unequal variance in estimates by inversely weighting the estimates according to their precision. The 95% confidence intervals (CIs) for VONA's estimates of prescriptions dispensed, as well as the 95% CIs for the calculated rates, provided the measure of precision (specifically, variance) required for WLSLR. Annual trends were statistically significant if likelihood-ratio tests derived from the WLSLR models yielded *P* values <.05. WLSLR was conducted by using PROC MODEL in SAS version 9.2 (SAS Institute, Inc, Cary, NC). Sensitivity analyses assessed the presence of autoregressive correlation in the drug utilization trends.

## RESULTS

Approximately 263 million prescriptions were dispensed to the pediatric population in 2010, 7% lower than the number of prescriptions dispensed in 2002. From 2002 to 2010, the number of pediatric prescriptions significantly decreased on average by 2.4 million prescriptions per year. In the adult population, 3.3 billion prescriptions were dispensed in 2010, 22% higher than the number dispensed in 2002 and significantly increasing on average by 86 million prescriptions per year (Table 1). When annual population size is taken into account, prescriptions dispensed to pediatric patients decreased by 43 900 prescriptions per million residents per year, a -9% change from 2002 to 2010, and adult prescriptions increased by 229 600 prescriptions per million residents per year, an 11% change (Fig 1).

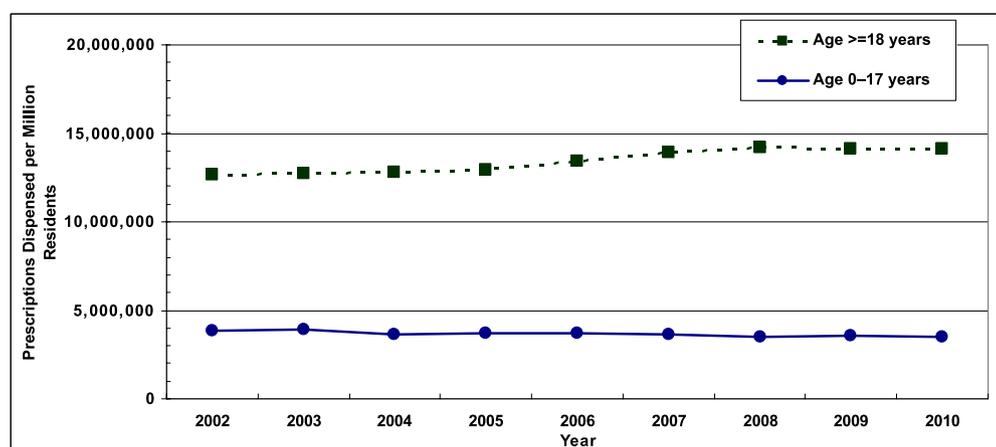
Of nearly 2200 molecules examined, 30 molecules were identified as having the highest number of unique pediatric patients who received prescriptions dispensed for the respective molecules from outpatient retail pharmacies in 2010 (Table 2). Each of these 30 molecules had >1 million unique pediatric patients who received a prescription for the respective molecule in 2010. For example, 18.3 million unique pediatric patients received  $\geq 1$  prescription for amoxicillin during 2010. However, for the majority of molecules available on the market, >1700 molecules each had <10 000 pediatric patients in 2010. Similar proportions of use were found in an analysis conducted for the total population, including adults, although the top drug molecules differed (data not shown).

Figures 2 and 3 show trends in pediatric drug utilization for the top 12

**TABLE 1** Total Number of Outpatient Retail Prescriptions Dispensed (in Millions) to the Pediatric and Adult Populations From US Retail Pharmacies, 2002 Through 2010

Prescription	2002	2003	2004	2005	2006	2007	2008	2009	2010
Total	3038.9	3084.0	3116.2	3193.0	3307.8	3456.9	3545.8	3566.7	3596.3
Pediatric (0 to <18 y)	283.3	286.7	266.8	272.3	273.3	272.2	262.2	266.6	263.6
Adult ( $\geq 18$ y)	2736.7	2779.4	2820.2	2892.0	3034.3	3184.6	3283.6	3299.5	3332.5

Source: VONA, 2002 through 2010; extracted March 2011.



**FIGURE 1**

Estimated number of outpatient prescriptions dispensed per million residents according to patient age (0-17 and  $\geq 18$  years) from US retail pharmacies, 2002 through 2010. \*Statistically significant linear trend at *P* value = .05. Estimates were derived from the following sources: US census projections and estimates and VONA. Years 2002 through 2010; extracted December 2011. CIs for estimates are suppressed because the relative SEs of the estimates are <1%.

**TABLE 2** Top Drug Molecules According to Number of Unique Pediatric Patients (Ages 0–17 Years) Who Received Prescriptions Dispensed From US Retail Pharmacies in 2010

Drug Molecule	Pediatric Patients ( <i>N</i> )
Amoxicillin	18 292 768
Azithromycin	10 171 046
Albuterol	7 343 063
Amoxicillin/clavulanate	4 454 926
Cefdinir	4 308 857
Cephalexin	4 009 275
Fluticasone	3 144 844
Prednisolone sodium phosphate	2 932 124
Ibuprofen	2 887 667
Montelukast	2 629 494
Sulfamethoxazole/trimethoprim	2 568 202
Codeine phosphate/acetaminophen	1 993 396
Hydrocodone bitartrate/ acetaminophen	1 967 638
Mupirocin	1 927 453
Nystatin	1 892 573
Methylphenidate	1 879 178
Dextromethorphan/phenylephrine/ chlorpheniramine	1 859 851
Mometasone	1 859 475
Triamcinolone	1 516 887
Prednisone	1 466 328
Sodium fluoride	1 393 819
Multivitamins with fluoride	1 340 073
Amphetamine/dextroamphetamine	1 237 154
Hydrocortisone	1 179 002
Budesonide	1 174 880
Ciprofloxacin/dexamethasone	1 134 611
Promethazine	1 107 342
Prednisolone	1 106 900
Antipyrine/benzocaine	1 027 768
Lisdexamfetamine	1 022 442

Source: IMS Total Patient Tracker, year 2010; extracted April 2011.

therapeutic areas or drug markets from 2002 through 2010. Systemic antibiotics were the most frequently dispensed, accounting for 24% to 27% of all pediatric prescriptions between 2002 and 2010. Five drug markets had a statistically significant decreasing trend in prescriptions dispensed to pediatric patients. The allergies (–61%), cough/cold without expectorant (–42%), depression (–5%), pain (–14%), and systemic antibiotics (–14%) markets decreased in prescriptions dispensed for 2010 compared with 2002. The allergies market had the largest decreasing trend (–2.2 million prescriptions/year) and the largest decrease (–61%) in prescriptions

dispensed for 2010 compared with 2002. Only the acne market had no statistically significant trend in prescriptions, although its prescriptions dispensed in 2010 was 13% lower than in 2002. When accounting for the annual pediatric population size, the rate of prescriptions dispensed per million US residents aged 0 to 17 years decreased in a statistically significant trend for the acne market but did not significantly change for the asthma market, which had a statistically significant trend when not accounting for population size. Statistical significance did not change for all other drug markets after accounting for the pediatric population size per year.

Six drug markets had a statistically significant increasing trend in prescriptions dispensed to pediatric patients. The ADHD (46%), asthma (14%), corticosteroids dermal (10%), corticosteroids oral (22%), contraceptive (93%), and seizure disorder (10%) markets increased in prescriptions dispensed for 2010 compared with 2002. The ADHD market had the largest increasing trend (0.8 million prescriptions/year), followed by the contraceptive market (0.5 million prescriptions/year). The contraceptive market had the largest increase in prescriptions dispensed in 2010 compared with 2002 (93% in prescriptions dispensed and 88% in prescriptions dispensed per million US female residents aged 0–17 years). However, compared with the other categories, the contraceptive market also had the lowest number of prescriptions dispensed in 2002.

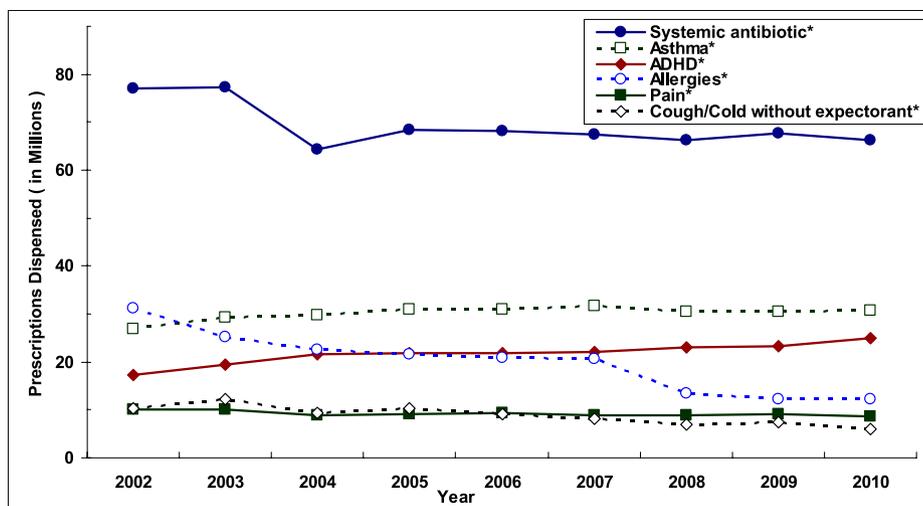
Table 3 shows the top molecules by the number of prescriptions dispensed for patients aged 0 to 23 months, 2 to 11 years, and 12 to 17 years in 2010. Among infants (0–23 months), antibiotics, asthma, and gastrointestinal medications were among the most frequently dispensed prescriptions. PPI use in children was a topic of interest at the

June 2010 Pediatric Advisory Committee.<sup>17</sup> Because of the recent interest in pediatric PPI use, lansoprazole use in the off-label population of patients aged <1 year was also examined. Approximately 70% (358 000 prescriptions out of 515 000 prescriptions) of outpatient lansoprazole prescriptions dispensed to infants were to patients aged <1 year. In children (2–11 years), antibiotics and asthma products along with ADHD products ranked among the top drugs used. In adolescent patients (12–17 years), contraceptives and pain medications, along with antibiotics, asthma, and ADHD products, were among the most frequently dispensed prescriptions in 2010.

Our analyses of utilization trends by therapeutic areas show an increase in the use of ADHD products from 2002 through 2010. Due to the increase in use and interest in this topic, trends in ADHD product usage were also examined (Fig 4). Methylphenidate remained the most frequently dispensed ADHD product during the examined time and had no significant change between 2002 and 2010. Amphetamine/dextroamphetamine was the second most frequently dispensed molecule, although prescriptions dispensed for amphetamine/dextroamphetamine were 15% lower in 2010 than in 2002. Prescriptions dispensed for dextroamphetamine also decreased (–69%) between these years. On the other hand, dispensed prescriptions for dexmethylphenidate, lisdexamfetamine, and guanfacine increased after 2004. The number of atomoxetine prescriptions dispensed to pediatric patients had a large uptake between 2002 and 2004 but significantly decreased from 2004 to 2010 at a rate of 376 800 prescriptions per year.

## DISCUSSION

By using prescription claims databases, this article provides an overview of outpatient prescription use in the US

**FIGURE 2**

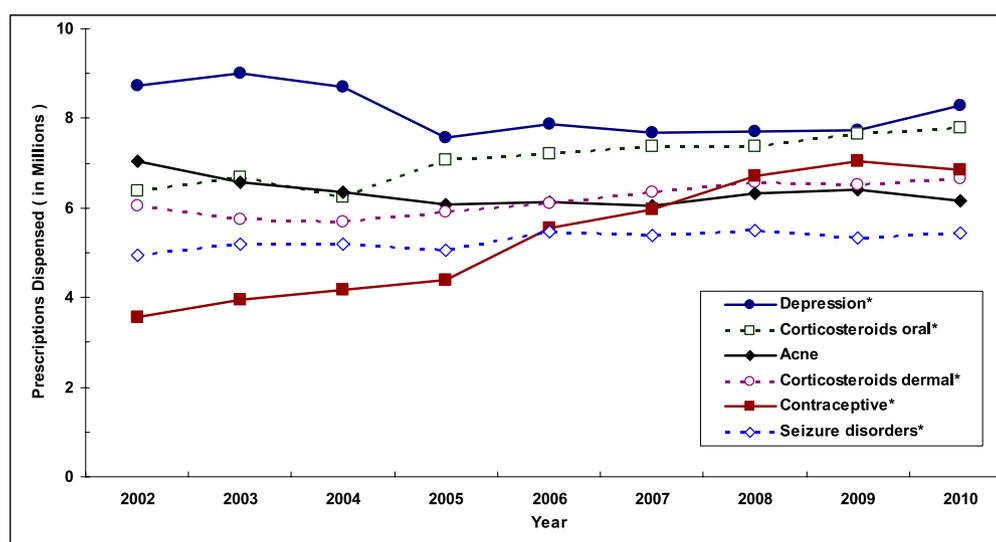
Top 1 through 6 drug markets according to the total estimated number of outpatient prescriptions dispensed to the US pediatric population (ages 0–17 years) from US retail pharmacies, 2002 through 2010. \*Statistically significant linear trend at  $P$  value = .05. Estimates were derived from the following source: VONA. Years 2002 through 2010; extracted December 2011. CIs for estimates are suppressed because the relative SEs of the estimates are <1%.

pediatric population. Prescription claims data can provide insight into postmarketing “real-world” use of drugs. These data can be used for research without perceived harm to children because of the de-identified nature of the data. Prescription claims data include information from a variety of geographic regions and socioeconomic subpopulations, such as cash payors, those with private insurance, and those

covered under state insurance programs (eg, Medicaid), guaranteeing representativeness across much of the US population. The data can also be used to help identify off-label use in pediatrics, highlighting areas for further research. The pediatric studies resulting from the legislative initiatives mentioned here found that in nearly 20% of cases in which a product was used off-label in children, the product was found not to be effective

at the dose used when finally studied in children.<sup>20</sup> Additional information showed that children often manifest a new, more frequent, or severe form of adverse events described in adults.<sup>21</sup>

However, drug utilization data obtained through large health care databases are not without limitations. Data are available only up to the point of dispensing and do not track whether the patient actually used the medication.<sup>22</sup>

**FIGURE 3**

Top 7 through 12 drug markets according to the total estimated number of outpatient prescriptions dispensed to the US pediatric population (ages 0–17 years) from US retail pharmacies, 2002 through 2010. \*Statistically significant linear trend at  $P$  value = .05. Estimates were derived from the following source: VONA. Years 2002 through 2010; extracted December 2011. CIs for estimates are suppressed because the relative SEs of the estimates are <1%.

**TABLE 3** Top Drug Molecules Dispensed to the Pediatric Population From US Retail Pharmacies According to Patient Age in 2010

0–23 Months (N = 31.6 million prescriptions)		2–11 Years (N = 134.2 million prescriptions)		12–17 Years (N = 96.6 million prescriptions)	
Drug Molecule	Share, %	Drug Molecule	Share, %	Drug Molecule	Share, %
Amoxicillin	17.3	Amoxicillin	11.3	Methylphenidate	4.5
Azithromycin	6.1	Azithromycin	5.8	Albuterol	3.7
Nystatin	5.9	Albuterol	5.6	Azithromycin	3.5
Albuterol	5.8	Montelukast	4.5	Amoxicillin	3.5
Cefdinir	4.9	Methylphenidate	3.9	Amphetamine/dextroamphetamine	3.1
Prednisolone	4.2	Fluticasone	2.9	Montelukast	2.2
Amoxicillin/clavulanate	3.4	Prednisolone	2.7	Norgestimate-ethinyl estradiol	2.2
Dextromethorphan/phenylephrine/ chlorpheniramine	2.4	Cefdinir	2.6	Lisdexamfetamine	2.2
Ranitidine	2.2	Cephalexin	2.3	Fluticasone	1.9
Hydrocortisone	2.0	Amoxicillin/clavulanate	2.2	Hydrocodone bitartrate/apap	1.9
Ibuprofen	1.8	Amphetamine/dextroamphetamine	2.0	Ibuprofen	1.7
Multivitamins with fluoride	1.7	Multivitamins with fluoride	1.7	Amoxicillin/clavulanate	1.5
Budesonide	1.6	Lisdexamfetamine	1.6	Sulfamethoxazole/trimethoprim	1.5
Lansoprazole <sup>a</sup>	1.6	Sodium fluoride	1.5	Doxycycline hyclate	1.5
Cephalexin	1.5	Ibuprofen	1.4	Cephalexin	1.5
Mupirocin	1.4	Mometasone	1.4	Sertraline	1.4
Sulfamethoxazole/trimethoprim	1.3	Dexamethylphenidate	1.4	Fluoxetine	1.4
Polymyxin b sulfate/tmp	1.0	Sulfamethoxazole/trimethoprim	1.2	Minocycline	1.1
Triamcinolone	1.0	Clonidine	1.1	Prednisone	1.1
Montelukast	0.9	Budesonide	1.1	Clindamycin phosphate/benzoyl peroxide	1.1
All others	32.0	All others	41.8	All others	57.5

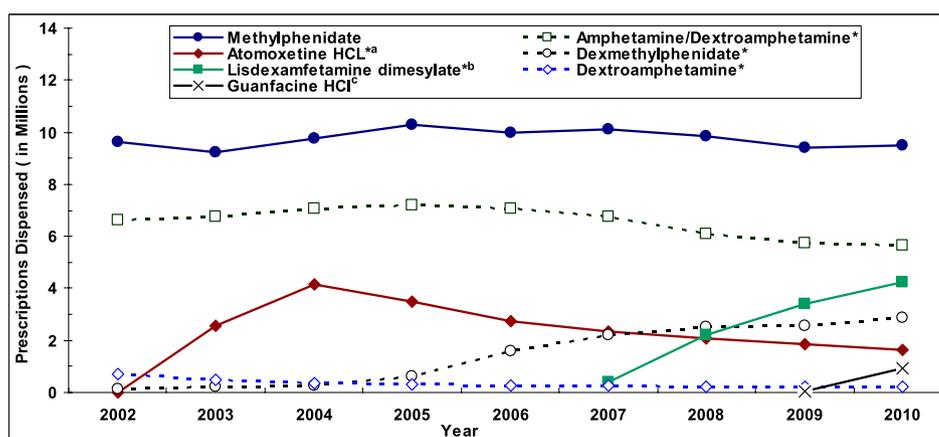
Data include all formulations (eg, oral tablet, oral syrups, topical cream). Source: VONA, 2002 through 2010; extracted March 2011.

<sup>a</sup> A total of 515 000 lansoprazole prescriptions (358 000 prescriptions in patients aged 0 to <1 year and 157 000 prescriptions in patients aged 1 to <2 years).

Utilization data in the neonatal population are difficult to obtain because many databases are unable to provide data for patient age down to days or months; children aged <1 year are generally grouped, as in our analysis.

Although drug utilization information may be used as a surrogate in assessing the impact that regulatory actions and clinical study results have on use, further analyses are needed to establish direct causal relationships.<sup>23</sup>

Our data do not reflect pediatric utilization in settings other than outpatient, such as inpatient or clinic settings, where seriously ill children are often treated. Data on OTC medications, herbals, and supplements, or on mail order



**FIGURE 4**

Total estimated number of outpatient prescriptions for ADHD drug market drug products dispensed to the US pediatric population (ages 0–17 years) from US retail pharmacies, 2002 through 2010. \*Statistically significant linear trend at  $P$  value = .05. <sup>a</sup> Atomoxetine HCl's analysis of trend starts from 2004 because atomoxetine HCl (Strattera) had an increasing trend from 2002 through 2004 but a decreasing trend from 2004 to 2010. <sup>b</sup> Lisdexamfetamine dimesylate's analysis of trend starts from 2007 because lisdexamfetamine dimesylate (Vyvanse) was approved on February 23, 2007. <sup>c</sup> Guanfacine HCl's estimates were not trended because guanfacine HCl (Intuniv) was approved on September 23, 2009. Estimates were derived from the following source: VONA. Years 2002 through 2010; extracted December 2011. CIs for estimates are suppressed because the relative SEs of the estimates are <1%, except for atomoxetine HCl's estimate for 2002.

prescriptions, were not included in this analysis.

Statistical analyses were performed to assess annual trends. Although assuming that the estimates are independent from 1 year to the next is reasonable, sensitivity analyses were conducted to assess the robustness of the annual trends if correlations between estimates were present. However, the sensitivity analyses did not show significant changes in the estimated trends if autoregressive correlation among estimates was truly present. From 2002 through 2010, there was a statistically significant decreasing trend in prescriptions dispensed to the pediatric population. However, this decrease was small compared with the increase in prescriptions dispensed to the adult population, even after accounting for population growth. Our analyses found that only 1% of outpatient drugs (30 molecules) had >1 million pediatric patients who received prescriptions for each respective molecule in 2010. In contrast, >1700 molecules were each used by <10 000 pediatric outpatients. Identification of these 30 molecules can help focus research efforts on the drugs used by the greatest number of pediatric patients.<sup>24</sup> However, low outpatient utilization of the majority of products underscores the difficulty in obtaining adequate sample sizes to conduct clinical studies in the pediatric population. Our analyses show that the systemic antibiotics market decreased from 2002 through 2010. Systemic antibiotics accounted for approximately one-fourth of all the prescriptions dispensed to the pediatric population, contributing to the overall decrease seen in total pediatric drug utilization. Over the last decade, the American Academy of Pediatrics and others have made an enormous effort to decrease antibiotic use in the pediatric population by educating parents about the futility of treating viral infections with antibiotics and about

concerns of antibiotic resistance.<sup>25–27</sup> Some articles cite that 40% to 50% of antibiotic use is inappropriate.<sup>28,29</sup> A variety of initiatives have been launched in the past decade promoting the judicious use of antibiotics, particularly for acute respiratory tract infections and acute otitis media.<sup>30–33</sup> Our analyses suggest such efforts may be working.

The allergies market had the largest decreasing trend in prescriptions dispensed to the pediatric population. However, the conversion of several non-sedating antihistamines from prescription to OTC (eg, Claritin [loratadine] products in 2002 and Zyrtec [cetirizine] products in 2007) may have contributed to the decrease in the number of prescriptions dispensed but not necessarily in the pediatric utilization of these medications.

Cough/cold without expectorant prescriptions also decreased significantly during the examined time. In 2004, a meta-analysis published in the Cochrane Review found that insufficient data and variable study quality complicated efforts to clarify the efficacy of cough/cold preparations in both children and adults.<sup>34</sup> An FDA Public Health Advisory, published in January 2008 discussing the safety and effectiveness of cough/cold products in children, recommended that OTC cough/cold products not be used in infants aged <2 years. Our data show a decrease in cough/cold without expectorant prescriptions in the pediatric population for 2008 through 2010.

In general, utilization data can be used to identify areas of interest for research in the pediatric population. In 2010, a total of 358 000 lansoprazole outpatient prescriptions were dispensed to infants aged <1 year. Prevacid (lansoprazole) labeling states that it is not effective in patients with symptomatic gastroesophageal reflux disease in ages 1 month to <1 year.<sup>35</sup> A number of studies conducted in adults

show that long-term PPI use might be a risk factor in the development of certain adverse events (eg, bone fractures).<sup>36</sup> Although these studies were primarily in adults, the safety of pediatric PPI use, especially off-label use, is of interest. Lansoprazole use in patients in whom the drug has been labeled as not effective is of interest as the safety of pediatric PPI use continues to be explored.<sup>37</sup> Dispensed prescriptions for the ADHD market also significantly increased from 2002 through 2010. The Centers for Disease Control and Prevention estimated the number of US children aged 3 to 17 years reported to have ADHD increased from 4.4 million in 2002 to 5 million children in year 2010.<sup>12,38</sup> Further analyses of the top ADHD medications found that although methylphenidate and amphetamine/dextroamphetamine prescriptions accounted for the largest proportions of use, these prescriptions remained steady or decreased while use of newer ADHD drugs (eg, lisdexamfetamine, dexamethylphenidate, guanfacine) increased. However, use of atomoxetine (approved in November 2002) has declined since 2005. Atomoxetine labeling changes and regulatory actions since December 2004 include a boxed warning and medication guide regarding the risk of suicidal ideation in children and adolescents. Our analyses did not include the use of other nonstimulant medications used on- or off-label for the treatment of ADHD, such as atypical antipsychotic or antidepressant agents.<sup>39,40</sup>

The number of contraceptive prescriptions dispensed to the pediatric population was 93% higher in 2010 than in 2002. Prescriptions for norgestimate–ethinyl estradiol ranked among the top 10 prescriptions dispensed to adolescent patients in 2010. However, household surveys conducted by the Centers for Disease Control and Prevention over the last 20 years have not found much of an increase in the percentage of young women taking birth control pills.<sup>41,42</sup>

Thus, the results presented in this article could reflect an increase in the duration of use (not measured here) and/or perhaps reflect use of contraceptive pills for secondary indications, such as acne.

## CONCLUSIONS

This article provides an overview of the frequency and trends of outpatient

prescription drug utilization in US pediatric patients over nearly a decade. Prescriptions dispensed to the pediatric population decreased whereas prescriptions dispensed to the adult population increased during the examined time. Identification of drugs with the highest numbers of patients exposed can help focus research efforts

on those drugs that could have a large impact on the pediatric population. Drug utilization data suggesting off-label use of products in children highlight areas for further research. It is important to continue to monitor patterns of drug utilization in the pediatric population as part of the risk/benefit evaluation of therapies for children.

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