Trends in opioid prescriptions among children and adolescents in the United States: a nationally representative study from 1996 to 2012

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Introduction

Prescription opioid misuse and its related health consequences is a major public health concern among children and adolescents in the USA and exert an enormous economic burden on society [1; 2]. Opioids are the most commonly abused drugs and constitute the fastest growing drug problem among adolescents in the USA [14]. Recently, 8.7% of 12th graders reported opioid misuse in the past year[8]. From 1999 to 2008 the number of accidental poisonings involving opioids more than quadrupled [19]. Among children, opioids are the most frequent cause of serious injury or death resulting from unintentional drug poisoning [3]. In 2008, the annual rate of unintentional deaths related to opioids was 0.1 per 100,000 for children 0–14 years of age and 3.7 per 100,000 for adolescents 15–18 years of age[30].

Understanding the epidemiology of opioid prescribing patterns is critical to identifying the scope of the problem to begin to address opioid misuse and poisonings. The increased rate of opioid prescriptions to adults is strongly associated with increased rates of opioid misuse and overdose due to larger amounts of available opioids [18; 31]. Furthermore, increased rates of adult opioid prescriptions have also been associated with increased rates of opioid poisoning and overdose among children and adolescents who have access to these substances at home [3]. Data on opioid prescriptions to children and adolescents are lacking and the few studies on the epidemiology of prescription opioids in pediatrics are equivocal. Fortuna et al. demonstrated that rates of opioid prescriptions to adolescents presenting to

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ambulatory offices and emergency departments increased from 1994 to 2007[5]. Similarly, Richardson et al. found increased rates of opioid prescriptions to adolescents with non-cancer pain from 2001 to 2005 in the USA [22]. In contrast to these studies Kaiser et al. found that rates of opioid prescriptions did not increase among children and adolescents presenting to emergency departments in the USA between 2001 and 2010[9]. However, these studies did not provide critically important information on opioid prescriptions among family members to allow for understanding the context of opioid availability in the home to children and adolescents in the USA.

Our objective was to examine patterns of opioid prescriptions among children and adolescents 0– 17 years of age in the USA between 1996 and 2012, using a set of nationally representative large databases, the Medical Expenditure Panel Surveys. Our primary aim was to estimate the effect of time as well as of sociodemographic and clinical characteristics on opioid prescriptions to children and adolescents. Based on previous reports, our primary hypothesis was that prescription opioid use among children and adolescents would increase over time. Because family members are an important source of prescription opioids that are misused by children and adolescents, our secondary aim was to estimate rates of opioid prescriptions to family members of children and adolescents. Based on previous publications reporting increased rates of opioids to adults, we hypothesized that rates of opioid prescription to family members of children and adolescents would also increase over time.

Methods

Data source

In this cross sectional analysis we used data from the Medical Expenditure Panel Surveys (MEPS) for years 1996 through 2012 which include all years currently available for analysis. MEPS are a nationally representative set of surveys conducted annually by two United States governmental agencies: the National Center for Health Statistics and the Agency for Healthcare Research and Quality. The primary goal of MEPS is to provide comprehensive estimates of health care use among the civilian, non-institutionalized population in the United States. Individuals included in MEPS are sourced from the previous year's National Health Interview Survey. Americans are sampled at the household level, allowing for analyses at both the individual level, as well as the family level. MEPS also samples households' health care providers (doctors, pharmacies, hospitals, etc.) and health insurance companies. MEPS participants are followed with five in-person interviews (rounds) over the course of two years during which comprehensive sociodemographic data are collected and all medical encounters are documented (including medications prescribed). In-person interviews are supplemented by record abstractions from medical providers, hospitals, pharmacies, and health insurance agencies to provider further information on health care utilization. A comprehensive description of MEPS is available online at http://meps.ahrq.gov/mepsweb/. MEPS has previously been used to estimate trends in opioid prescriptions to adults in the United States [23].

Study Design

This study was deemed exempt from review by the Institutional Review Board at Seattle Children's Hospital. We abstracted the following information from MEPS for years 1996 through 2012: 1) demographics, 2) type of opioid prescribed, 3) number of opioid prescriptions per participant, 4) whether a family member received an opioid prescription, and 5) medical diagnoses associated with opioid prescriptions. Data were not available to report on quantity and duration of opioid use among participants. We obtained U.S. population estimates for children and adults for years 1996 through 2012 from the U.S. Census Bureau[27].

Participants

The study population included all sampled participants in MEPS between 1996 and 2012. We performed subgroup analysis on 3 populations captured in MEPS: (1) children and adolescents 0–17 years of age, (2) adults 18 years and older, and (3) any family members of children and adolescents. MEPS characterizes a family as consisting of two or more persons living together in the same household who are related by blood, marriage, or adoption, as well as foster children. MEPS also defines unmarried persons living together who consider themselves a family, as a family. Relatives identified as usual residents of the household (even if not present at the time of the interview, such as college students living away from their parents' home during the school year), were considered as members of the family. In our subpopulation analysis the group containing family members is not mutually exclusive to either the child or adult groups. This means that individuals identified as family members could also be captured and surveyed as part of either the child or adult subgroups. Approximately 34,000 individuals (25,000 adults and 9,000 children and adolescents) were included in MEPS each year between 1996 and 2012 and our final sample included 548,401 participants of which 403,483 were adults and 144,918 were children and adolescents.

Identification and classification of prescription opioids

MEPS survey participants were asked about their prescription medications and then asked permission to collect further information about these medications from their pharmacies. Data collected from pharmacies included type of opioid prescribed. MEPS collected data on medications prescribed during outpatient visits (e.g. hospital outpatient visits, office-based visits, and dental office visits), however no information was collected on medications prescribed during hospital inpatient visits. We used Cerner's Multum Lexicon therapeutic drug class classification system to identify opioid prescriptions to MEPS participants. We defined opioid prescriptions as any prescription that fit the "narcotic analgesic" and "narcotic analgesic combination" classification according to the Multum Lexicon classification; the former definition includes all pure opioid agonists (e.g. oxycodone), while the latter includes all opioid combination drugs (e.g. oxycodone/acetaminophen combinations). Between 1996 and 2012 we identified 250 unique prescription types of opioid analgesics among children and adolescents, each containing varying aspects of manufacturer, formulation, and route of administration (e.g. oral, transdermal). We assigned these 250 unique opioid products to one of 6 opioid classes including both pure opioids and opioid combinations: (1) codeine and codeine combinations, (2) hydrocodone and

hydrocodone combinations (3) oxycodone and oxycodone combinations, (4) propoxyphene and propoxyphene combinations, (5) meperidine and meperidine combinations, (6) morphine and morphine combinations, (7) other opioids (incl. methadone, fentanyl, and opium products). Prescription opioid users were classified as those survey participants who received one or more prescription opioids in a given calendar year. We were also interested in estimating whether the number of individuals with multiple or long term opioid prescriptions had increased over time. However, MEPS does not reliably collect data on the quantity or duration of opioid use and therefore we classified individuals with increased opioid requirements as those who received 5 or more prescriptions in a single year. This classification is consistent with previous reports in Norway (children) [6] and the USA (adults)[23] that used the same definition to classify high opioid users as those receiving 5 or more opioid prescriptions per year.

Medical diagnoses

Participants reported on the medical conditions associated with each individual opioid prescription. Medical conditions provided by participants were recorded by interviewers as verbatim text, which were then recoded to fully specified International Statistical Classification of Diseases and Related Health Problems (ICD-9) codes, including medical condition, V-codes, and E-codes by professional coders. MEPS aggregated ICD-9 codes into clinically meaningful categories generated by Clinical Classification Code Software (CCC). This classification resulted in 263 mutually exclusive CCC categories. To ease interpretability, we further categorized these 263 CCC categories into 13 general categories which included: infections, hematologic/oncologic, neurologic and migraine, ear-nose-throat, cardiorespiratory, gastrointestinal, dental, urogenital, skin/dermatological, non-traumatic orthopedic, traumatic, procedures, and "other" conditions. Our classification was intended to simplify presentation of data in this report.

Sociodemographic and health status variables

We abstracted child and adolescent characteristics including age (categories: 0–5, 6–11, 12–17 years), sex, race/ethnicity (white non-Hispanic, black non-Hispanic, Hispanic, other), insurance (private, public, uninsured), USA census region (Northeast, Midwest, South, West), and urbanization (living in a metropolitan statistical area vs living in a non-metropolitan statistical area). We also abstracted parent-reported child and adolescent physical health status (categorized as excellent, very good, good, fair, and poor) and parent-reported child mental health status (categorized as excellent, very good, good, fair, and poor).

Statistical analysis

All analyses were conducted with Stata version 12.1 (StataCorp, College Station, TX); α level was set at .05. We adjusted for the complex probability survey design of MEPS using sampling weights, stratification, and clustering to provide nationally representative estimates of the USA population. We calculated the prevalence rates of opioid prescriptions for each year, the number of opioid prescriptions given each year, the mean number of prescriptions per participant, as well as the number of children and adolescents receiving more than 5 prescriptions each year. We also determined which opioids children and adolescents received

and the primary diagnosis associated with opioid prescriptions across years. Finally, we performed multivariable logistic regression analysis to examine child and adolescent participant characteristics (age, sex, race/ethnicity, insurance status, region, urbanization, physical health, and mental health) associated with receipt of opioid prescription(s). In our logistic regression model, all years 1996–2012 were included for analysis as a continuous variable. Odds ratio for year presented in our tables represents the linear test of trend across 17 years (1996–2012).

Results

Sociodemographic and clinical characteristics

We included data on all 144,918 children and adolescents (average 9,057 each year) available in the 1996–2012 MEPS databases. Table 1 presents the characteristics of child and adolescent participants. On average MEPS surveyed 9,057 children and adolescents each year and after applying survey weights these 9,057 participants represented approximately 70 million children and adolescents annually in the USA, which are consistent with estimates of the child and adolescent population in the USA according to the US Census Bureau[27]. Consistent with findings from the US Census Bureau, there was a slight preponderance of males (51.2%) and most were white, non-Hispanic (59.2%)

Trends in opioid prescriptions: Children and adolescents

The total number of opioid prescriptions to children and adolescents 0–17 years of age for each year from 1996 to 2012 is presented in Figure 1. In 1996 the total number of opioid prescriptions to all children and adolescents in the USA was 2.2 million (95% CI, 1.76 – 2.63 million) and in 2012 this number had only slightly increased to 2.5 million prescriptions (95% CI, 1.91 – 3.08 million), a non-significant increase based on overlapping confidence intervals around point estimates. Therefore, while there were significant differences in year to year opioid prescriptions, the overall trend showed stability over time in prescriptions to children and adolescents. During this time the childhood population in the USA increased from 67.7 million to 69.9 million, a relative increase of 2.1%. As a percentage of all children in the USA, 2.68% (95% CI, 2.24–3.21) received an opioid prescription in 1996, while 2.91% (95% CI, 2.71–3.01) received an opioid prescription in 2012, also a non-significant difference. On average 2.86% of children and adolescents received an opioid prescription each year from 1996 to 2012 (Table 1).

In 1996 1.81 million children and adolescents received at least one opioid prescription (95% CI, 1.47–2.15 million), while in 2012 2.03 million children and adolescents received at least one opioid prescription (95% CI 1.55–2.52 million). Among those children and adolescents receiving opioid prescriptions, the mean number of prescriptions per user was 1.21 (95% CI, 1.12–1.30) in 1996 and 1.22 (95% CI, 1.10–1.36) in 2012. In 1996, among children and adolescents receiving at least one opioid prescription, none had received 5 or more opioid prescriptions; however in 2012 1.14% (95% CI, 0.35–3.62%) received 5 or more opioid prescriptions.

Predictors of opioid prescriptions

The results of the multivariable logistic regression analysis examining survey year, and child and adolescent participant characteristics associated with opioid prescriptions are presented in Table 1. Increasing survey year (1996 through 2012) was not associated with an increased likelihood of receiving an opioid prescription (odds ratio (OR) linear test of trend: 1.01; 95% CI, 0.99–1.02, p=0.34). Sociodemographic characteristics associated with higher rates of opioid prescriptions between 1996 and 2012 included older child age, being white non-Hispanic, having private or public insurance, and being from a region other than the Northeastern United States. Poorer parent-reported physical and mental health was also associated with a higher likelihood of prescription opioid use (Table 1).

Type of opioid prescriptions

The most common opioids prescribed to children and adolescents between 1996 and 2012 were codeine, hydrocodone, and oxycodone (Figure 3). In 2012 codeine, hydrocodone, and oxycodone was prescribed to 39.9%, 42.1%, and 15.5% of children and adolescents respectively. Figure 4 lists the general diagnostic categories associated with opioid prescriptions in children and adolescents. In 2012, most opioid prescriptions were prescribed during medical provider visits for trauma (36.5%), followed by dental visits (15.7%), and visits related to procedures (13.2%) performed on children and adolescents. The disproportionate drop in opioids for procedures and increase in opioids for trauma in 2000 may have represented a sampling variance or coding error.

Trends in opioid prescriptions: Families and adults

In 1996 the total number of all opioid prescriptions to adults in the USA were 62.5 million prescriptions (95% CI, 54.8–70.2), however by 2012 this had increased to 141 million prescriptions (95% CI, 129–154), a relative increase of 125.6% (Figure 2). During this time, the adult population in the United States increased from 201 million to 243 million, a relative increase of 20.8%. We also found that opioid prescriptions to family members of children and adolescents in the USA increased from 19 million prescriptions (95% CI, 14.5–23.4) in 1996 to 29.6 million prescriptions (95% CI, 23.2–35.9) in 2012, a relative increase of 55.8%.

Discussion

Contrary to our primary hypothesis we found that trends in opioid prescriptions to children and adolescents in the United States remained stable between 1996 and 2012. This included both the annual number of child and adolescent opioid users and the average number of opioid prescriptions per child and adolescent between 1996 and 2012. However, an increase over time was found for rate of high opioid users (children and adolescents who received 5 or more opioid prescriptions) between 1996 and 2012. The most commonly prescribed opioids to children and adolescents in 2012 were codeine, hydrocodone, and oxycodone. Although children's opioid prescriptions were fairly stable over time, in stark contrast, opioid prescriptions to family members of children and adolescents, and to adults in general, significantly increased (more than doubled) between 1996 and 2012.

Prior studies of rates of opioid prescriptions to children and adolescents have been equivocal, likely due to differences in the settings of care (e.g., emergency department vs outpatient) and time periods chosen for evaluation. Using emergency department data from the National Hospital Ambulatory Medical Care Survey, two studies reported increased rates of opioid prescriptions to children[5; 16]. Similarly, Richardson et al. using data from a national commercially insured population and a state Medicaid plan also found increased rates of opioid prescriptions among children and adolescents in the USA [22]. Our data extends these previous findings by presenting opioid trends over a larger time frame, 1996–2012, in a nationally representative sample of civilian, noninstitutionalized children and adolescents across multiple outpatient care settings. To our knowledge, outside of the USA, there are limited data describing child and adolescent opioid prescriptions. A few studies conducted in Norway and Denmark provide some comparison data. National data from Norway indicated an increase in opioid prescriptions between 2004 and 2007, however overall rates were low with only 0.79% of Norwegian children receiving opioids in 2007[6], and very few children receiving 5 or more opioid prescriptions in any given year. Similarly, in Denmark, the proportion of children receiving opioid prescriptions increased between 2000 and 2014, with the largest surge among adolescents 15–19 years of age (increasing from 0.86% in 2000 to 1.1% in 2013)[21].

In contrast to the relative stability found in opioid prescriptions to children, our findings demonstrated significantly increased rates in opioid prescriptions to adults (including adult family members) in the USA between 1996 and 2012, that is consistent with previous publications [14; 19; 23]. Sites et al. also used MEPS databases and found significant increases in opioid prescriptions to adults in the USA between 2000 and 2010 [23]. Our methods differ slightly from Sites' in that we analyzed years 1996 through 2012, and used a different drug classification system to identify opioids. However, even with these slight methodological differences, both studies point to substantially greater opioid prescriptions among adults over time.

The increased opioid prescriptions to adults in the community are concerning because they put children and adolescents at higher risk for opioid misuse and poisoning due to a larger supply of available opioids. Studies at population and community levels report strong associations between increased opioid prescriptions and sales and increased rates of opioid misuse and overdose among adults [31; 19]. Furthermore increases in adult opioid prescriptions are associated with increases in pediatric opioid poisonings [3]. Opioid prescriptions to family members are also a common source of drugs for adolescent misuse [17; 14]. Future studies should further explore the association between opioid prescriptions to family members and rates of opioid misuse and poisonings among children and adolescents, and identify potential targets for prevention efforts (e.g., adults with chronic pain who have young children).

Health care providers must balance the need to adequately treat pain with opioids with the risk of potential diversion and misuse of these drugs. However despite health agencies advocating for improved pain control, increased opioid prescriptions to adults over the last 10 years have not been associated with improved physical and psychological health among users [24; 15; 23]. In fact, the present trend of increased opioid use by adults is a significant

public health concern contributing to an increase in opioid misuse, abuse, and overdose[14]. Furthermore, recent research suggests a mismatch between the amount of opioids prescribed versus the amount of opioids needed to treat children's acute pain, with children using less than 50% of prescribed opioids[29]. Such practices results in a large amount of unused opioid medications in the homes of children which may contribute to opioid misuse and unintentional poisonings. There is an urgent need among clinicians and policymakers to develop guidelines and recommendations for the appropriate use of opioids among children and adolescents. As such, the American College of Physicians recently recommended that physicians develop guidelines to limit the amounts of opioid prescribed[10]. To develop these guidelines, future studies should focus on the roles of providers and parents in the prescription of opioids to children, as well as gather data on how opioid prescriptions to adults in the community put children at risk for opioid misuse and unintentional poisoning. The U.S. Food and Drug Administration has published guidelines on how to dispose of unused opioid medications and it is important that the public be made aware of these[4].

Our study identified several predictors of opioid prescriptions among children and adolescents including age, ethnicity, health insurance, and region. Adolescents had a higher likelihood of receiving opioid prescriptions as compared to younger children which may be due to increased pain complaints among adolescents compared to children [12]. However it is also likely that providers feel more comfortable prescribing opioids to adolescents, which could mean that pain in children as compared to pain in adolescents, is undertreated. We found that opioids were more often prescribed to white, non-Hispanic children and adolescents and also those with health insurance, patterns that have previously been found in both pediatric and adult populations[20; 16]. Future research should monitor pain management practices among minorities and lower socioeconomic groups in order to improve quality and equity of healthcare [7]. Regional variances in opioid prescriptions demonstrated that children from Southern, Midwestern, and Western states had higher rates of opioid prescriptions as compared to children from Northeastern states, which is consistent with previous findings [5; 9]. Regional variance also exists in rates of opioid misuse and poisonings, with children in the Western and Southern states at higher risk for opioid misuse.

An unexpected finding from this study is the high rate of codeine prescriptions for children and adolescents. Due to variability in its metabolism, codeine can either lead to toxicity or inadequate pain relief in a large proportion of children and adolescents[11]. Consequently, in 2013 the U.S. Food and Drug Administration issued guidelines to limit codeine prescriptions to children[28]. Although codeine prescriptions declined over time, in 2012 codeine still made up nearly 40% of all opioid prescriptions to adolescents, consistent with recent data on codeine prescriptions to children in USA emergency departments [9]. Safer alternatives to codeine, including hydrocodone, are available to treat children's pain[26; 25]. There is an urgent need for future epidemiological studies aimed at identifying patient and provider characteristics associated with codeine prescriptions.

There are several limitations to our study. We were unable to estimate whether quantities of opioid prescription to participants increased over time. The primary reason for this was that data on opioid dose and duration is largely missing from MEPS. This is an important limitation, because increased quantities of opioids available to children and adolescents may

also result in increased rates of opioid misuse and abuse. MEPS relies in part on participant-reported information; our results would be affected by under- or over-reporting of opioid prescriptions. Participants only reported on how medications were prescribed and not on how they ultimately used them, therefore we were unable to assess whether opioid medications were used for medical indications or ultimately diverted for non medical use. We were also unable to assess opioid prescriptions to peers of children and adolescents, another important source of prescription opioid misuse. This study also has several strengths as compared to other epidemiological studies examining rates of opioid use among children and adolescents: (1) we included a very large nationally representative sample spanning 17 years, from 1996 to 2012 rendering multiple years of data available for analysis, and (2) we analyzed opioids obtained from a wide range of outpatient prescribers including hospital outpatient departments, other office based visits, dental offices, emergency departments, and other healthcare providers.

Conclusions

In summary, in a large, nationally representative database, we found that the overall trend in opioid prescriptions to children 0–17 years of age remained stable between 1996 and 2012. However, consistent with previous findings in adults, rates of opioid prescriptions to family members of children and adolescents rose substantially between 1996 and 2012, placing children at greater exposure to opioids in their homes and communities.

Acknowledgments

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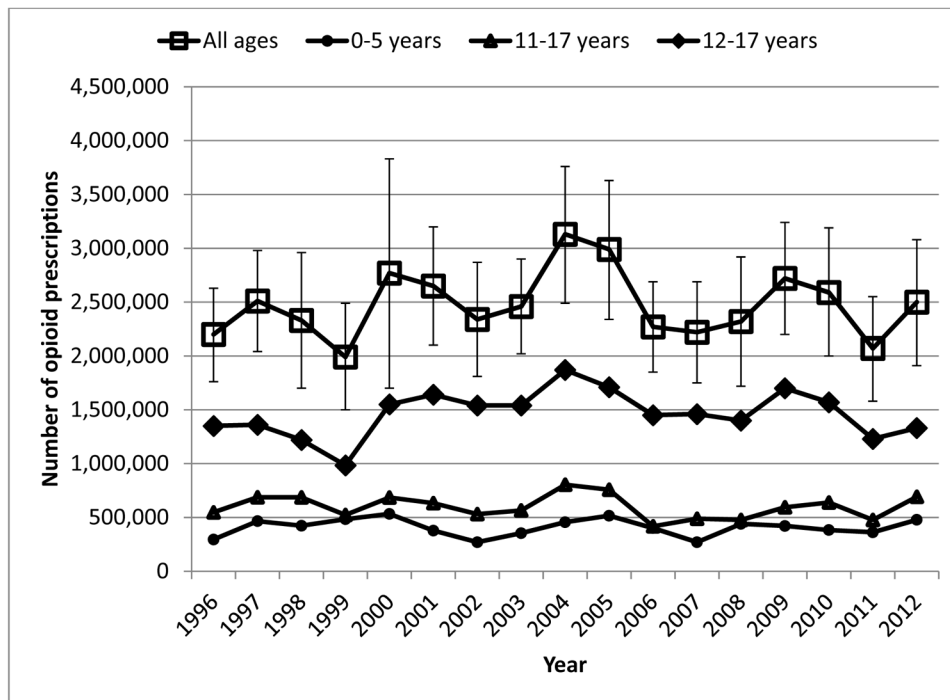
Figure 1.
Estimated total number of opioid prescriptions per year for all children and adolescents in the USA and grouped by ages: 0–5 years of age, 6–11 years of age, and 12–17 years of age (point estimates and confidence intervals). Data source: Medical Expenditure Panel Surveys 1996–2012.
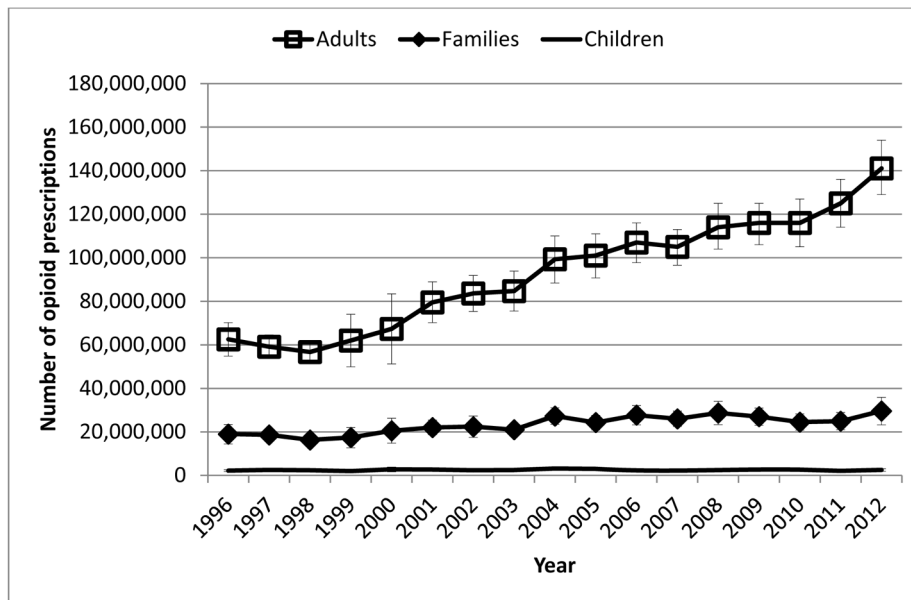
Figure 2.
Estimated total number of opioid prescriptions per year for children 0–17 years of age, family members of children, and adults 18 years and older in the United States (point estimated with 95 % confidence intervals). Data source: Medical Expenditure Panel.
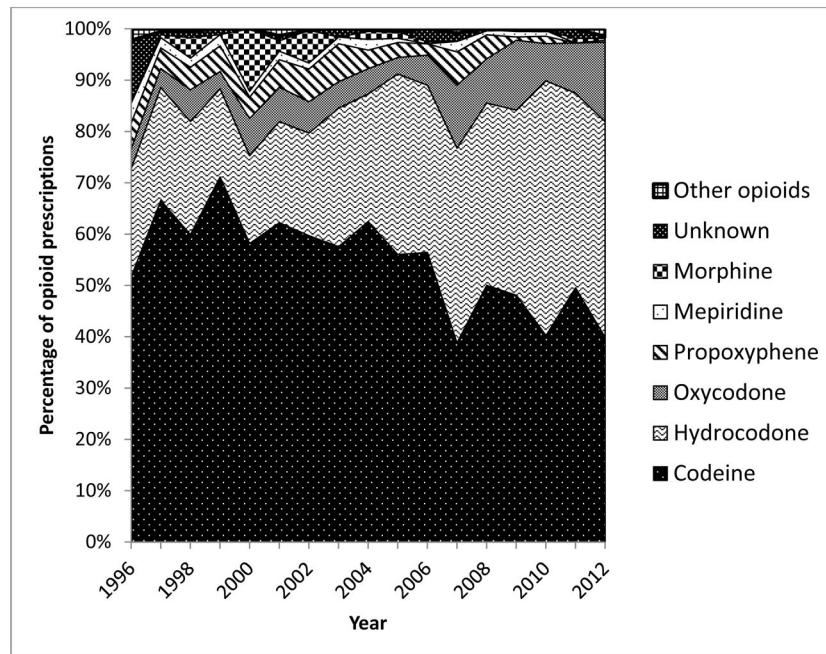
Figure 3.
Percentage of opioid prescriptions by opioid category in children 0–17 years of age in the United States (point estimates) between 1996 and 2012. Data source: Medical Expenditure Panel Survey 1996–2012
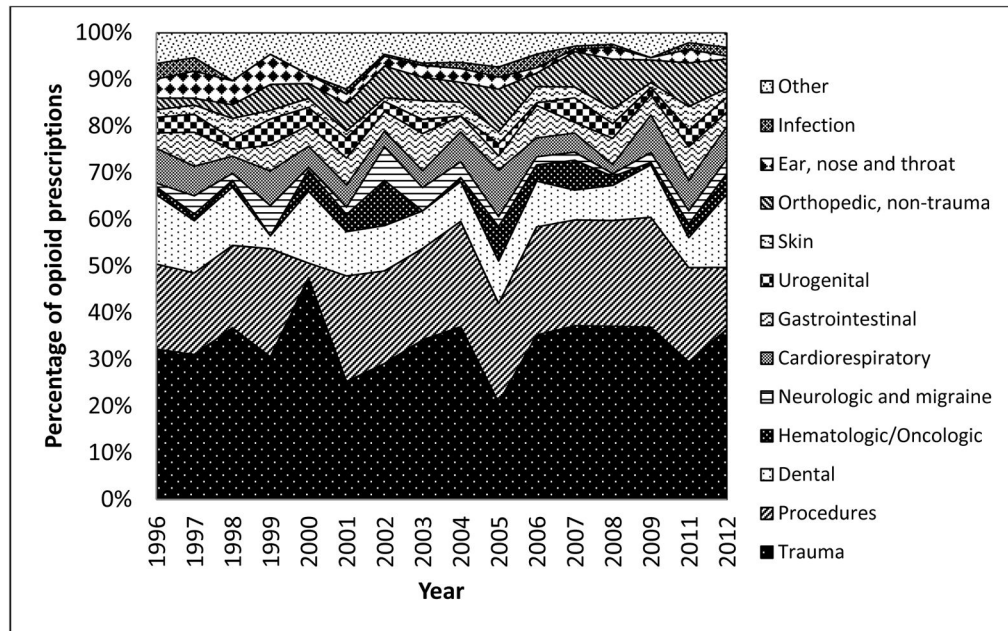
Figure 4.
General diagnostic categories associated with opioid prescriptions to children in the USA, 1996–2012. Data source: Medical Expenditure Panel Surveys 1996–2012

Table 1

Multivariate logistic regression testing survey year and participant characteristics associated with receiving prescription opioids among children 0–17 years of age in the United States, 1996–2012. Data source: Medical Expenditure Panel Surveys 1996–2012.

	Weighted percentage(SE)	% Receiving prescription opioids	OR	95 % CI	P
Year (1996 to 2012)		2.86	1.01	0.99–1.02	0.34
Age (year)					
0–5	29.1 (0.2)	1.72	(ref)		
6–11	35.2 (0.2)	2.02	1.19	1.06–1.34	0.004
12–17	35.7(0.3)	4.61	2.79	2.49–3.11	<.001
Sex					
Male	51.2 (0.2)	2.94	(ref)		
Female	48.8 (0.2)	2.77	0.93	0.86–1.02	0.11
Race/Ethnicity					
White	59.2 (0.8)	3.47	(ref)		
Black	14.9 (0.5)	2.13	0.56	0.49–0.63	<.001
Hispanic	19.4 (0.7)	1.81	0.50	0.43–0.57	<.001
Other	6.2 (0.1)	1.92	0.54	0.43–0.68	<.001
Insurance					
Any private	64.8 (0.6)	3.06	(ref)		
Public only	27.9 (0.5)	2.76	1.08	0.97–1.19	0.16
Uninsured	7.3 (0.2)	1.44	0.45	0.36–0.56	<.001
Region					
Northeast	17.3 (0.7)	2.06	(ref)		
Midwest	22.3 (0.8)	3.06	1.44	1.22–1.71	<.001
South	36.1 (1.0)	3.11	1.65	1.42–1.93	<.001
West	24.2 (1.0)	2.86	1.62	1.35–1.95	<.001
MSA					
Non-MSA	16.9 (0.7)	3.57	(ref)		
MSA	83.1 (0.7)	2.71	0.89	0.79–1.01	0.07
Physical Health					
Excellent	50.1 (0.4)	2.35	(ref)		

	Weighted percentage(SE)	% Receiving prescription opioids	OR	95 % CI	P
Very Good	30.6 (0.3)	2.96	1.44	1.27–1.64	<.001
Good	16.7 (0.3)	3.66	1.81	1.56–2.09	<.001
Fair	2.1 (0.1)	6.19	3.13	2.47–3.98	<.001
Poor	0.3 (0.0)	7.94	4.18	2.67–6.55	<.001
Mental Health					
Excellent	53.9 (0.4)	2.52	(ref)		
Very Good	28.1 (0.3)	2.88	0.85	0.75–0.97	0.01
Good	15.5 (0.3)	3.65	0.89	0.76–1.05	0.18
Fair	2.0 (0.1)	5.14	0.94	0.73–1.20	0.61
Poor	0.4 (0.0)	4.5	0.65	0.42–1.00	0.05

SE: standard error.

All years (1996–2012) included for analysis; odds ratio for year represents linear test for trend across 16 years