Prevalence and Characteristics of Pediatric Opioid Exposures and Poisonings in the United States

Anisha M. Patel, PhD, MS, BPharm[1,*], David C. Wheeler, PhD, MPH, MS, MA, BA[2], S. Rutherfoord Rose, PharmD, FAACT, BS Pharm, BA[2], Pramit A. Nadpara, PhD, MS, BPharm[2], Amy L. Pakyz, PhD, MS, PharmD, BS Pharm, BS[2], and Norman V. Carroll, PhD, MS, BS Pharm[2]

Objective To examine the prevalence and characteristics of pediatric opioid exposures and poisonings in the US.

Study design This was a retrospective, cross-sectional analysis using the National Poison Data System from January 1, 2010 to December 31, 2014. Records of children aged <18 years with exposure to opioid-containing medications were identified. Standardized prevalence rates were calculated, and the annual trend was examined. Pediatric opioid exposures were characterized descriptively, and logistic regression was performed to estimate the association between various clinical and sociodemographic characteristics and exposures with serious (ie, moderate, major, or death) outcomes. The association of pediatric opioid exposures and area-level socioeconomic status factors at 5-digit ZIP code level was examined descriptively.

Results The prevalence of opioid exposures was 22.6 per 100 000 children and was particularly high among ≤5-year-olds. Prevalence declined from 25.5 to 20 per 100 000 children from 2010 to 2014. There were 83 418 pediatric opioid exposures over the 5-year period and nearly one-half resulted in poisoning. Over 60% of exposures were among children ≤5 years of age, 73.4% were unintentional, and over 90% occurred at home. One in every 2 pediatric opioid exposures was evaluated in a healthcare facility. Annually 4912 children aged ≤5 years were treated in the emergency department or admitted for care. Older age, nonaccidental intent, and single-substance opioid, especially buprenorphine and methadone, were associated with serious outcomes ($P < .05$). Positive correlations were observed for area-level socioeconomic status factors including proportion of adults and pediatric opioid exposures.

Conclusions Pediatric opioid exposures and poisonings decreased from 2010 to 2014 but morbidity remains high. The epidemiology of opioid exposures differed considerably by age. *(J Pediatr 2019;206:148-55).*

Previous studies have examined opioid overdoses and poisonings in adults but opioid exposures and poisonings in children, particularly in young children, are not well described. An increase in adults' opioid use is found to be significantly associated with an increase in opioid exposures among children.[1,2] The number of opioid analgesic prescriptions per 100 persons rose by 35% in the last decade, nearly at a rate of 1 prescription per person per year, with an increase that was more apparent for stronger opioids.[3,4] In 2012 alone, nearly 5 million people aged 12 years or older were nonmedical users of prescription opioid analgesics.[5] This wide accessibility of opioid analgesics and parallel surge in their nonmedical use has resulted in an increased number of opioid overdoses and poisonings among children.[6]

Poison centers receive over 500 000 calls annually for drug ingestions among young children, and opioid analgesics are reported to be the most common substance involved.[7] In fact, drug poisonings send 1 of every 150 two-year olds to the emergency department (ED).[8] The number of ED visits because of opioid analgesic ingestions increased by 101% among children aged ≤5 years from 2001 to 2008.[9] The annual incidence of pediatric hospitalizations for opioid poisonings rose by 165% from 1997 to 2012,[10] and the number of hospitalizations for opioid poisonings requiring pediatric critical care almost doubled between 2004 and 2015.[11] Opioid analgesics are also commonly involved in exposures and poisonings among teenagers.[7] Adolescent opioid exposures reported to Indiana poison center almost doubled, and resulting medical complications more than doubled following the release of new pain management standards in early 2000s.[12]

AAPCC	American Association of Poison Control Centers
APAP	Acetaminophen
ED	Emergency department
HCF	Healthcare facility
NPDS	National Poison Data System
NSAID	Anti-inflammatory drug
SES	Socioeconomic status

From the [1]Genentech, Inc, South San Francisco, CA; and [2]Virginia Commonwealth University, Richmond, VA

*This author was a graduate student at Virginia Commonwealth University at the time this research was done.

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Over 10 000 opioid exposures were recorded for teenagers in the Researched Abuse, Diversion, and Addiction-Related Surveillance system from 2007 to 2009.[13]

Of the studies that have examined pediatric opioid exposures and poisonings, a few studies focused on single-ingredient opioids[1,14] or single ingestions alone.[9] Other research included only specific opioid agents.[2,15,16] or limited the analyses to opioid exposures that resulted in a healthcare facility (HCF) use.[10,11,17] The objectives of the current study were to examine the prevalence and characteristics of opioid exposures and poisonings in children and to analyze factors associated with serious opioid exposures. Further, we examined pediatric opioid exposures in children at 5-digit ZIP code level and studied the association with area-level socioeconomic status (SES) factors. Our research is comprehensive (ie, opioid exposures were not limited to specific agents or single substances or ingestions) and included exposures that may have not resulted in HCF visit but were still recorded by the poison center; additionally, we inspected area-level SES factors.

Methods

This was a retrospective, cross-sectional study using the American Association of Poison Control Centers' (AAPCC) National Poison Data System (NPDS), from January 1, 2010 through December 31, 2014. The NPDS is a poisoning surveillance database that logs information from poison centers nationally. Poison centers receive about 6000 exposure calls daily from the public or healthcare providers. These calls are managed by trained specialists and exposure-related information is captured in standard data collection fields in near real-time. Poison centers attempt to follow-up on cases postexposure. A case is closed when all related follow-up has been completed.[7]

Sample Selection

Closed records of ≥1 opioid containing product exposure involving children under 18 years of age were extracted. Cases that were confirmed as nonexposures during follow-up were excluded. The resulting cohort was used as the final sample for examining prevalence and characteristics of opioid exposures (N = 83 418). From this, further exclusions were made for subsequent analyses as follows. A flowchart of sample selection is shown in **Figure 1** (available at www.jpeds.com). First, records involving >1 product exposure were excluded from serious outcome analysis (n = 64 045) to eliminate confounding in the association between exposure severity and various characteristics because of involvement of additional products. Second, records where exposure and caller site were not one's residence were excluded from area-level analysis (n = 43 701), in an attempt to restrict exposures to those that occurred in one's own area. The ZIP code provided in the NPDS represents caller's site, this ZIP code was used as a proxy for the ZIP code of exposure site as long as, reported caller and exposure site were one's own residence.

Variables

For this study, opioids were defined as any opioid-containing medications and were identified using generic codes maintained by the AAPCC. This included single-ingredient opioids (or "single-opioids") such as oxycodone, buprenorphine, hydrocodone, and others, and combination-opioids containing acetaminophen (APAP), acetylsalicylic acid, and anti-inflammatory drugs (NSAIDs), gastrointestinal agents, and cough and cold products. Exposure comprised any suspected opioid exposure, and poisoning was operationalized as any opioid exposure with a related clinical symptom or medical effect.[7] Exposures were categorized as single product (single-opioid or combination-opioid) or multiple product exposures (at least one product was an opioid).

Specific clinical symptoms following an exposure were captured in the NPDS and recorded as "related" or "unrelated" to the exposure. The level of medical effect was separately assigned for each exposure by the poison center staff, depending on the specific symptoms exhibited. Information from both these standard data fields was combined and reclassified into medical outcome of an exposure as follows. None: Patient did not exhibit any symptoms, or was not followed but judged as nontoxic with no related clinical symptom; Minor outcome: Patient exhibited some minimally bothersome symptoms, or was not followed but minimal clinical effects were possible; Moderate outcome: Patient developed symptoms that were more pronounced, prolonged or systemic but were not life-threatening; Major outcome: Patient exhibited symptoms that were life-threatening or resulted in significant residual disability; Death: Patient died due to the exposure or its direct complication.

Medical outcome was assigned as unknown for exposures that poison center staff were "unable to follow but judged as potentially toxic." Outcomes were operationalized as serious, if the exposure resulted in moderate, major, or death outcome. Related clinical symptoms were categorized under system organ classes, based on Medical Dictionary for Regulatory Activities and the AAPCC symptoms classification.

NPDS provides other exposure related information including intent, chronicity, scenario leading to exposure and treatment. An intentional exposure included suspected suicide, or intentional abuse or misuse, and an unintentional exposure comprised general accidental exposure, therapeutic error, and unintentional misuse and other. Chronicity was operationalized as acute if any single or repeated exposure occurred for ≤8 hours. Scenarios were grouped as storage or access-related, therapeutic error, or others. Performed therapies included decontamination, therapeutic intervention, and naloxone. Data on HCF use and management site was combined to identify the level of healthcare utilization. Age was categorized into ≤5 (young children), 6-12 (middle-aged children), and 13-17 (teenagers) years, which is consistent with the child development literature.[18] Other variables included route of exposure, sex, exposure and caller site, and state. Operational definitions of study variables were reviewed by a clinical expert on the team.

For area-level analysis, the final sample from the NPDS was aggregated at 5-digit ZIP code level and merged with the ZIP code file obtained from the Environmental Systems Research Institute (ESRI) Updated Demographics data from Census 2010. Census data on total population of adults, minorities, and different racial and ethnic groups in an area were examined. Area-

level variables for median household income, average household size, and older adults' population (aged >65 years) in household were also included.

Statistical Analyses

Annual and 5-year prevalence rates were calculated for pediatric opioid exposures and poisonings. National- and state-level population estimates for children aged <18 years were obtained from the 2010 US Census. Annual prevalence estimates of opioid exposures were adjusted for the number of child exposure calls reported to the AAPCC in that respective year. Total and annual case fatality rates were also calculated. Age-specific and state-specific prevalence rates of opioid exposures were computed to account for population-level differences. A generalized linear mixed model with Poisson distribution and log-link function was used to examine the statistical significance of pediatric opioid exposure trend and inspect state-level differences. The exposure year was a fixed-effect variable and state was a random-effect variable in this model. The log of state's total child population for the respective year was used as an offset, which accounts for different state-level pediatric population sizes.

Descriptive statistics were calculated for sociodemographic and clinical characteristics of children with opioid exposures. Separate analyses were done by age group and intent, and by exposures involving one opioid and ≥1 product (at least 1 opioid). χ^2 tests and logistic regression were performed to estimate the association between serious opioid exposures and various characteristics. Spearman correlation tests were used to examine the correlation between the proportion of pediatric opioid exposures and the corresponding SES variables at ZIP code level. All statistical tests were performed with a 2-sided significance level of 0.05, and analyses were done in SAS v 9.4 (SAS Institute, Cary, North Carolina), Microsoft Excel 2013 (Microsoft Corporation, Redmond, Washington), and ArcGIS v 10.3.1 (ESRI, Redlands, California). The study was approved under exempt status by the local Institutional Review Board (#HM20004393).

Results

From 2010 to 2014, there were 83 418 pediatric opioid exposures with 52.2% that resulted in poisoning. Five-year prevalence rates of opioid exposures and opioid poisonings were 22.6 and 11.8 per 100 000 children, respectively. Prevalence rate of opioid exposures was higher in children ≤5 years of age, especially among toddlers 1-2 years of age (**Figure 2**, A). Total prevalence rates also varied by state with some clustering of highest rates in the western states (**Figure 3**). Case fatality rate was 0.1%, and was slightly higher among teenagers compared with younger children.

Trend analysis of pediatric opioid exposures showed that the annual prevalence decreased from 25.5 to 20 per 100 000 children from 2010 to 2014. This decline was greater among 1- to 2-year-olds compared with other age groups (**Figures 2**, B and C). Mean number of pediatric opioid exposures decreased from 28 to 22 per 100 000 children from 2010 to 2014, after adjusting for random effects of states ($P < .0001$). There was a significant amount of variability in the rate of pediatric opioid exposures across states (covariance parameter estimate = 0.077, $P < .0001$).

Sociodemographic and Clinical Characteristics

Of total exposures identified, 61.1% were among children aged ≤5 years and over 90% occurred at home, involved ingestion, and were acute in nature. Of exposures, 73.4% were unintentional, and nearly one-half were treated in an ED or admitted for care and experienced a medical outcome. Over three-fourths were single-product exposures, and these involved single-opioids particularly tramadol, oxycodone, and buprenorphine, or APAP combinations mainly with hydrocodone and oxycodone. Subsequent poisoning, naloxone treatment, medical admissions, and serious (ie, moderate-to-major) medical outcomes were more common among single-opioid exposures (**Table I**, **Table II** [available at www.jpeds.com]), and **Figure 4** (available at www.jpeds.com).

Characteristics of opioid exposures varied by age group and intent. Exposures in children ≤5 years of age were more common among boys, largely involving unintentional exposures to single-opioids. A total of 17 888 (35%) of children aged ≤5 years were treated in the ED and another 6672 (13.1%) were admitted for medical care with nearly 6.3% experiencing a serious medical outcome. On the contrary, exposures in teenagers had a higher involvement of combination opioids, were mostly intentional, and commonly occurred among female teenagers. Nearly one-half of these exposures involved co-ingestants of which roughly 13% involved another opioid product. A majority of teenage exposure cases had a related clinical symptom documented, especially neurologic symptoms. Almost 3 out of every 4 teenage exposures resulted in poisoning and were treated in the ED or admitted for care, with 24.2% experiencing serious outcomes (**Table III** and **Table IV**; available at www.jpeds.com).

Serious Outcomes

Of the total 64 045 cases with one opioid product exposure, from either a single-opioid or combination opioid, 7% had a serious outcome. All factors except sex were found to be statistically significant in bivariate analyses. Compared with the counterparts, serious exposures were more common among teenagers (37.9% vs 15.8%) and had a single-opioid (78.3% vs 46.7%), especially buprenorphine (21.7% vs 5.7%) or methadone (10.9% vs 1.8%) involved. One-third of serious exposures were intentional and 45.8% were treated with naloxone. A majority were treated in the ED or admitted for medical care (94.1%), especially for critical care (unadjusted analyses results not shown here).

In adjusted analysis, exposures involving children aged 6-12 years and 13-17 years were 1.72 (95% CI 1.02-2.91) and 2.34 (95% CI 1.57-3.48) times more likely to be serious compared with those in younger children. Exposures to single-opioids were 4.34 (95% CI 3.79-4.96) times more likely to be serious than exposures to combination opioids. Exposures to buprenorphine or methadone were 5.15 (95% CI 4.66-5.69) to 6.44 (95% CI 5.54-7.48) times more likely to be serious (**Table V**).

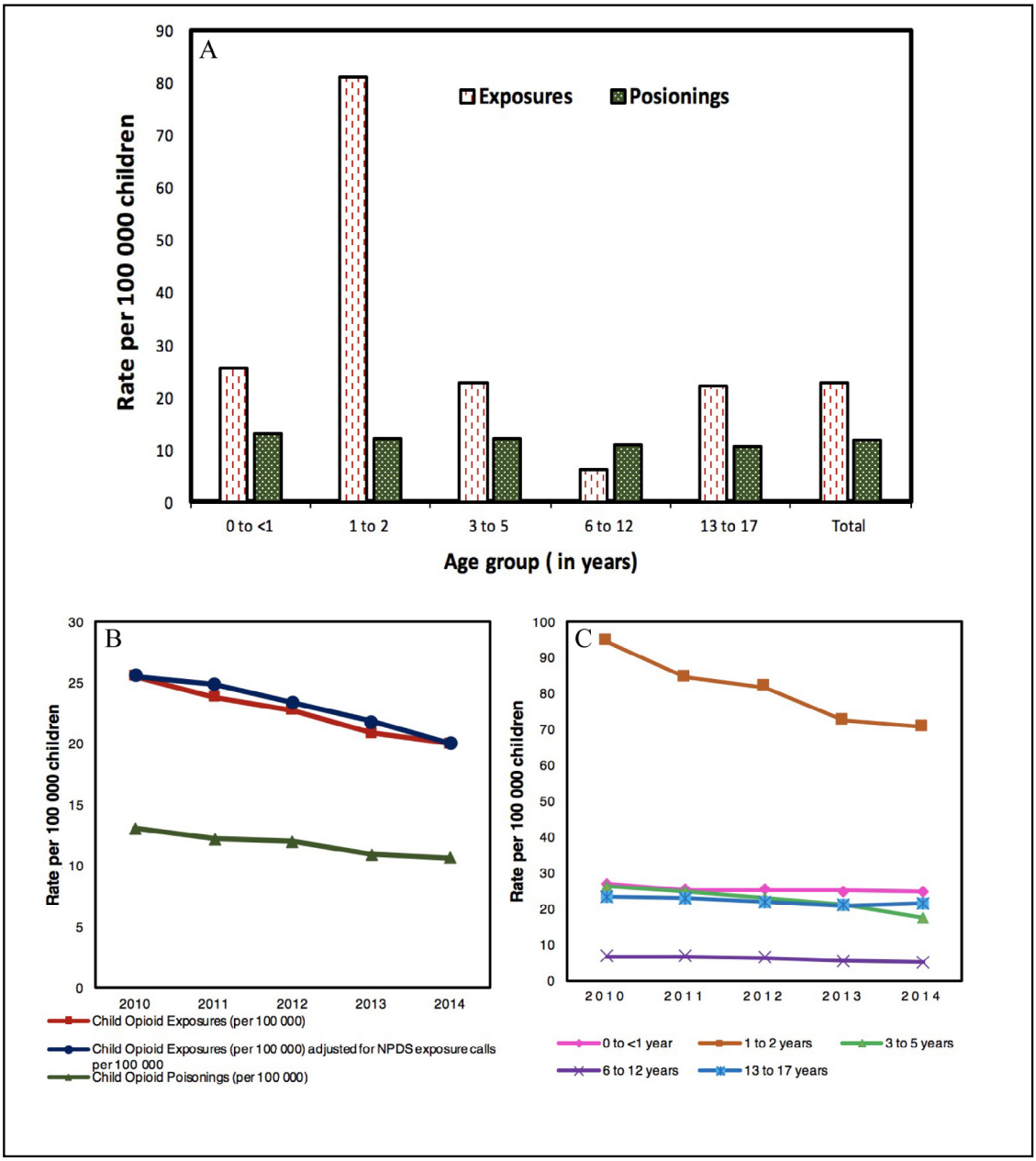

Figure 2. Prevalence rates of opioid exposures and poisonings among children aged <18 years, NPDS, 2010-2014 (legend enclosed in the figure). **A,** Total 5-year prevalence rates; **B,** Annual prevalence rates; **C,** Age-specific annual prevalence rates.

Area-Level SES Characteristics

SES characteristics of areas with pediatric opioid exposures were descriptively compared using ZIP code area-level averages obtained from US Census. A total of 12 809 areas had ≥1 pediatric opioid exposure. These areas had a slightly higher mean proportion of minorities, higher median household income and a lower proportion of non-Hispanic whites. Bivariate analyses showed statistically significant associations between SES characteristics and area-level proportion of pediatric opioid exposures. Positive correlations were observed for proportion of adults, male, non-Hispanic whites, and older adults in household (**Table VI**; available at www.jpeds.com).

Discussion

From 2010 through 2014, there were 16 684 pediatric opioid exposures per year and roughly one-half resulted in poisonings. By comparison, Allen et al reported 11 779 yearly prescription opioid exposures among children aged <20 years; however, these analyses did not include combination opioids.[14] The majority of exposures occurred in young children, particularly children 1-2 years of age, consistent with previous reports of drug exposures.[1,2,9,19,20] This has been attributed to a combination of childhood factors such as increased mobility

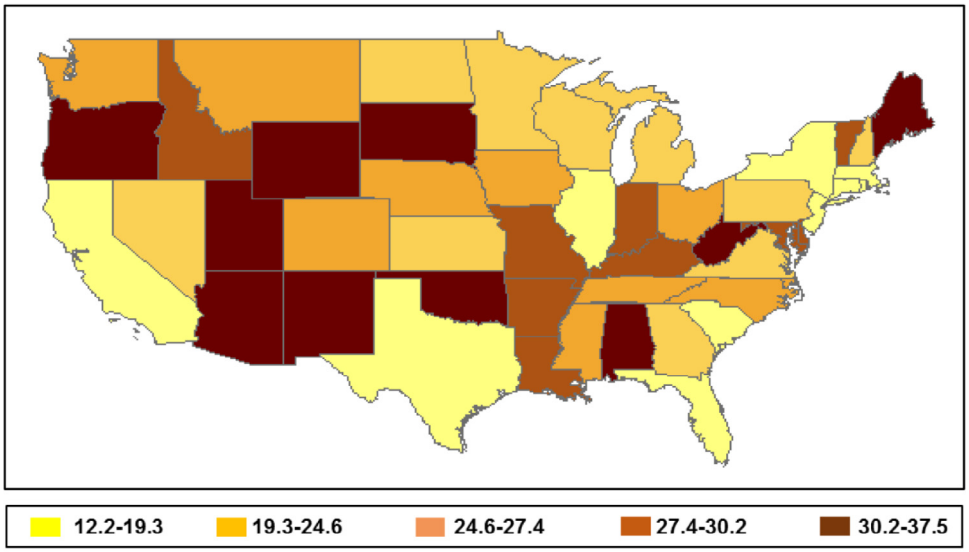

Figure 3. Prevalence rates of opioid exposures among children aged <18 years by state (per 100 000 children), NPDS 2010-2014 (legend enclosed in the figure).

and dexterity around the age of 12 months, imitating adult drug-taking behavior, or attraction to "candy-like" appearance of the pills.[20-22]

There was an overall decline in the prevalence of pediatric opioid exposures and poisonings between 2010 and 2014 as seen in another recent study.[14] This decrease was largely among toddlers 1-2 years of age. This may be attributed to various interventions such as Centers for Disease Control and Prevention's Preventing Overdoses and Treatment Errors in Children Taskforce collaborative initiative in 2008,[23,24] poison prevention outreach efforts of poison centers,[25] advances in the use of child-resistant packaging such as unit-dose packaging,[15,20] or the release of abuse-deterrent opioid formulations.[26] However, the decline in poisonings was smaller indicating that more opioid exposures among children are resulting in poisonings, which is consistent with recent studies that examined opioid-poisoning related pediatric hospitalizations.[10,11] This may be attributed to the corresponding rise in the use of stronger opioids among adults.[4] State-level variations were observed in prevalence rates of pediatric opioid exposures. Prior research has indicated that these states with higher prevalence also had a corresponding higher number of opioid prescriptions per 100 persons in 2012.[6]

Roughly one-half of total opioid exposures in children were from single-ingredient opioids, and about one-fourth involved multiple products. The morbidity following such opioid exposures and poisonings is high. Over one-half of single-ingredient opioid exposures and 75% of multiple product exposures resulted in an HCF admission. Buprenorphine and methadone were significantly associated with negative medical outcomes in children following an exposure. Buprenorphine exposures in young children have been associated with medically significant effects such as respiratory or central nervous system depression.[15] Intentional exposures to methadone have been associated with major medical complications and deaths among teenagers.[13] Buprenorphine and methadone are used for the treatment of opioid dependence and addiction, but there is increasing evidence of misuse and abuse of these agents.[27,28] It is important to educate adults, including those undergoing treatment for opioid dependence or addiction, of the dangers of pediatric opioid exposures. In addition, a majority of pediatric opioid exposures occurred at home irrespective of the child's age. Thus, it is imperative to increase awareness and provide instructions on safe storage and disposal practices, especially when adults commonly report storing leftover opioid medications at home for future use.[29]

The epidemiology of opioid exposures varied by age, congruent with the findings of recent investigations.[14,17] Exposures in children ≤5 years of age were mainly unintentional with higher involvement of single-ingredient opioids. Young children are generally not the intended recipients of these drugs, hence, they are accidentally exposing themselves to adults' opioids. Intentional opioid exposures with multiple products or APAP opioid combinations were common among teenagers. Nearly one-fourth of opioid exposures in teens were serious and about 41% were admitted for care, which is higher than previous reports, but our study was not limited to single-ingredient or single-product exposures.[14] Adolescent nonmedical users frequently use opioids in conjunction with alcohol or other drugs.[30] One out of every 12 high-schoolers reported a previous nonmedical use of APAP-hydrocodone combination, making it one of the top abused drugs among adolescents.[31,32] This may suggest higher accessibility of such opioids among teenagers.

Pediatric opioid exposures in general were associated with considerable morbidity. One in every 2 opioid exposures in children was presented to an HCF. Among children aged ≤5 years, 4912 (48%) opioid exposures resulted in ED or hospital

Table I. Sociodemographic and clinical characteristics of pediatric opioid exposures, NPDS 2010-2014

Characteristics, n (%)	Total opioid exposures (n = 83 418)	Single product exposures* (n = 64 045)		Multiple products exposures§ (n = 19 373)
		Single-opioid† (n = 31 775)	Combination-opioid‡ (n = 32 270)	
Age group (y)				
0 < 1	5042 (6.04)	2388 (7.52)	2163 (6.7)	491 (2.53)
1-2	32 204 (38.61)	14 771 (46.49)	12 987 (40.24)	4446 (22.95)
3-5	13 744 (16.48)	5994 (18.86)	6052 (18.75)	1698 (8.76)
6-12	8819 (10.57)	3463 (10.9)	4031 (12.49)	1325 (6.84)
13-17	23 245 (27.87)	4982 (15.68)	6912 (21.42)	11 351 (58.59)
Sex				
Male	41 081 (49.25)	16 505 (51.94)	16 183 (50.15)	8393 (43.32)
Female	42 022 (50.38)	15 117 (47.58)	15 973 (49.5)	10 932 (56.43)
Opioid involved				
Single substance	40 651 (48.73)	31 775 (100)	n/a	8876 (45.82)
APAP combinations	37 472 (44.92)	n/a	26 657 (82.61)	10 815 (55.83)
Cough and cold product combinations	5406 (6.48)	n/a	4825 (14.95)	581 (3)
Other combinations¶	1028 (1.23)	n/a	788 (2.44)	240 (1.24)
Reason				
Unintentional	61 206 (73.37)	26 925 (84.74)	26 137 (80.99)	8144 (42.04)
Intentional	20 064 (24.05)	4143 (13.04)	5361 (16.61)	10 560 (54.51)
Adverse reaction	1088 (1.30)	223 (0.70)	495 (1.53)	370 (1.91)
Other**	227 (0.27)	132 (0.42)	36 (0.11)	59 (0.30)
HCF use				
None	30 093 (36.07)	10 830 (34.08)	16 114 (49.93)	3149 (16.25)
T/E and R	25 983 (31.15)	10 089 (31.75)	9316 (28.87)	6578 (33.95)
Critical care	7097 (8.51)	3012 (9.48)	662 (2.05)	3423 (17.67)
Noncritical care	6122 (7.34)	2869 (9.03)	895 (2.77)	2358 (12.17)
Psychiatric care	3658 (4.39)	459 (1.44)	975 (3.02)	2224 (11.48)
Other††	9836 (11.79)	4259 (13.40)	4021 (12.46)	1556 (8.03)
Medical outcome				
None	32 944 (39.49)	12 478 (39.27)	14 599 (45.24)	5867 (30.28)
Minor	32 443 (38.89)	11 820 (37.2)	13 120 (40.66)	7503 (38.73)
Moderate	7709 (9.24)	2900 (9.13)	888 (2.75)	3921 (20.24)
Major	1368 (1.64)	581 (1.83)	81 (0.25)	706 (3.64)
Death	111 (0.13)	46 (0.14)	7 (0.02)	58 (0.3)
Poisoning	43 503 (52.15)	16 180 (50.92)	14 714 (45.60)	12 609 (65.09)

n/a, not applicable; *T/E and R*, treated/evaluated and released.
The subcategories do not add up to 100% because of a small proportion of missing data.
Additional results are shown in **Table II**.
Analyses were limited to cases with: *One product (opioid) exposures.
†One product (single-substance opioid) exposures.
‡One product (combination opioid) exposures.
§Multiple products exposures of which at least one of the products was an opioid.
¶Other opioid combinations include combinations with acetylsalicylic acid, nonsteroidal anti-inflammatory drugs, and gastrointestinal agents.
**Other reasons include tampering, malicious, or withdrawal attempts.
††Other HCF include cases wherein the patient refused referral or left against medical advice but were documented to be either in or en route to a HCF.

admissions annually. Naloxone was commonly used for the treatment of opioid exposures with serious outcomes.

This study also examined the association of area-level factors with pediatric opioid exposures. We found that area-level factors such as proportion of adults, Non-Hispanic whites, and older adults in household were associated with higher pediatric exposure rates. This may be related to the higher opioid use in these populations.[4,33] These findings may provide a good starting point for further investigating predisposing factors and planning interventions at the community level.

These findings are limited by the biases inherent in a retrospective study design. NPDS data is voluntarily reported and may be subject to self-reporting bias such as lower reporting of intentional exposures among adolescents. These data do not capture every occurrence of exposure, hence, the identified number of exposures is likely an underestimate. Prevalence rates were calculated assuming that each exposure case was unique. It is possible that a child may have had repeated opioid exposures during the study period, which may have led to some double-counting in our analyses. Opioid exposures recorded in the NPDS can only be considered suspected because of lack of confirmatory clinical data, and it cannot be determined if the exposure was to a prescribed or an illicitly obtained opioid. Lastly, age was unknown for 0.4% of exposure cases in the study. These records were included in prevalence analysis; however, some of these records could involve children aged 18-19 years as the AAPCC considers exposures in <20 year-olds as pediatric cases.[7] Despite these limitations, the NPDS has been validated as an effective pharmaceutical poisoning surveillance system and the data have been shown to correlate well with hospital poisoning data.[34,35] Census data used are estimates based on the 2010 base year and are likely to be reported with margins of errors. However, it is standard practice to use these data because margins of errors are expected to be small.[36] Lastly,

Table V. Adjusted analysis of characteristics associated with serious pediatric opioid exposures, NPDS 2010-2014

Characteristics (n = 64 045)*,†	Estimate, β (SE)	aOR (95% CI)	*P* value
Intercept‡	−4.21 (0.16)	n/a	<.0001
Age group (y)‡			
≤ 5		Reference	
6-12	0.54 (0.27)	1.72 (1.02-2.91)	.0413
13-17	0.85 (0.20)	2.34 (1.57-3.48)	<.0001
Sex‡			
Female		Reference	
Male	0.14 (0.03)	1.15 (1.08-1.23)	<.0001
Chronicity			
Non-acute		Reference	
Acute§	-0.08 (0.15)	0.92 (0.69-1.24)	.5833
Reason‡			
Unintentional		Reference	
Intentional	0.98 (0.37)	2.66 (1.29-5.47)	.0081
ADR	1.45 (0.24)	4.25 (2.63-6.86)	<.0001
Other¶	1.35 (0.28)	3.85 (2.23-6.66)	<.0001
Opioid involved‡			
Combination opioid		Reference	
Single	1.47 (0.07)	4.34 (3.79-4.96)	<.0001
Buprenorphine‡			
No		Reference	
Yes	1.64 (0.05)	5.15 (4.66-5.69)	<.0001
Methadone‡			
No		Reference	
Yes	1.86 (0.08)	6.44 (5.54-7.48)	<.0001

ADR, adverse drug reaction; *n/a*, not applicable.
The characteristics in the model were chosen based on practical significance and past research. Goodness-of-fit tests showed that the model fits the data well ($P = .8248$). AIC = 24965.93 and -2 Log L = 24915.93. Interaction terms of age were included in the final model (results not shown here).
*Represents single product exposures including single-ingredient opioids and combination opioids.
†Of these, 8382 observations were not included in the analysis because of missing values for the response or explanatory variables. About 12% cases (n = 7525) had no data on medical outcomes (ie, unknown if serious/nonserious). These cases were excluded in the initial logistic model. Sensitivity analysis was performed to avoid biases because of missing data. Medical outcome was re-coded by reclassifying exposures with unknown outcome that were unable to be followed, but judged as potentially toxic exposure by the poison center, as serious outcome (these cases were grouped as unknown and excluded in the initial model). Similar results were found in sensitivity analysis except that older age was no longer significantly associated, while acute exposures were significantly associated with higher odds of a serious outcome.
‡$P < .05$.
§An exposure was categorized as acute if any single, repeated, or continuous exposure occurred over ≤8 hours.
¶Other reasons include tampering, malicious, or withdrawal attempts.

area-level analysis did not include poison center calls that originated from a hospital. To evaluate the effect of this on our results, we compared the total sample of exposures to those with exposure and caller site as own residence. The latter group, which was the sample used in our area-level analysis, had a lower proportion of teenagers (14% vs 28%) and more unintentional exposures (89% vs 73%), and a smaller proportion of exposures resulted in moderate-to-major outcomes (2% vs 11%). This indicates that more serious cases were not captured in area-level analysis.

Development of public educational efforts and targeted prevention strategies particularly those that are age- and agent-specific is warranted. ■

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References

1. Burghardt LC, Ayers JW, Brownstein JS, Bronstein AC, Ewald MB, Bourgeois FT. Adult prescription drug use and pediatric medication exposures and poisonings. Pediatrics 2013;132:18-27.
2. Bailey JE, Campagna E, Dart RC. The underrecognized toll of prescription opioid abuse on young children. Ann Emerg Med 2009;53:419-24.
3. Kenan K, Mack K, Paulozzi L. Trends in prescriptions for oxycodone and other commonly used opioids in the United States, 2000-2010. Open Med 2012;6:41-7.
4. Frenk SM, Porter KS, Paulozzi LJ. Prescription opioid analgesic use among adults: United States, 1999-2012. NCHS Data Brief 2015;1-8.
5. Substance Abuse and Mental Health Services Administration. Results from the 2012 National Survey on Drug Use and Health: summary of national findings. NSDUH Ser H-46, HHS. 2013.
6. Centers for Disease Control and Prevention (CDC). Morbidity and mortality vital signs: overdoses of prescription opioid pain relievers—United States, 1999-2008. MMWR Morb Mortal Wkly Rep 2011;60:1487-92.
7. Mowry JB, Spyker DA, Brooks DE, McMillan N, Schauben JL. 2014 annual report of the American association of poison control centers National Poison Data System (NPDS): 32nd Annual Report. Clin Toxicol 2015;53:962-1146.
8. Budnitz DS, Salis S. Preventing medication overdoses in young children: an opportunity for harm elimination. Pediatrics 2011;127:e1597-9.
9. Bond GR, Woodward RW, Ho M. The growing impact of pediatric pharmaceutical poisoning. J Pediatr 2012;160:265-70.
10. Gaither JR, Leventhal JM, Ryan SA, Camenga DR. National trends in hospitalizations for opioid poisonings among children and adolescents, 1997 to 2012. JAMA Pediatr 2016;170:1195.
11. Kane JM, Colvin JD, Bartlett AH, Hall M. Opioid-related critical care resource use in US children's hospitals. Pediatrics 2018;141:e20173335.
12. Tormoehlen LM, Mowry JB, Bodle JD, Rusyniak DE. Increased adolescent opioid use and complications reported to a poison control center following the 2000 JCAHO pain initiative. Clin Toxicol 2011;49:492-8.
13. Zosel A, Bartelson BB, Bailey E, Lowenstein S, Dart R. Characterization of adolescent prescription drug abuse and misuse using the researched abuse diversion and addiction-related surveillance (RADARS) system. J Am Acad Child Adolesc Psychiatry 2013;52:196.e2-204.e2.
14. Allen JD, Casavant MJ, Spiller HA, Chounthirath T, Hodges NL, Smith GA. Prescription opioid exposures among children and adolescents in the United States: 2000-2015. Pediatrics 2017;139:e20163382.
15. Lavonas EJ, Banner W, Bradt P, Bucher-Bartelson B, Brown KR, Rajan P, et al. Root causes, clinical effects, and outcomes of unintentional exposures to buprenorphine by young children. J Pediatr 2013;163:1377.e3-1383.e3.
16. Hayes BD, Klein-Schwartz W, Doyon S. Toxicity of buprenorphine overdoses in children. Pediatrics 2008;121:e782-6.
17. Tadros A, Layman SM, Davis SM, Bozeman R, Davidov DM. Emergency department visits by pediatric patients for poisoning by prescription opioids. Am J Drug Alcohol Abuse 2016;42:550-5.
18. Barton BK, Schwebel DC. A contextual perspective on the etiology of children's unintentional injuries. Health Psychol Rev 2007;1:173-85.
19. Lovegrove MC, Mathew J, Hampp C, Governale L, Wysowski DK, Budnitz DS. Emergency hospitalizations for unsupervised prescription medication ingestions by young children. Pediatrics 2014;134:e1009-16.
20. Schillie SF, Shehab N, Thomas KE, Budnitz DS. Medication overdoses leading to emergency department visits among children. Am J Prev Med 2009;37:181-7.
21. McFee RB, Caraccio TR. "Hang Up Your Pocketbook"—an easy intervention for the granny syndrome: grandparents as a risk factor in unintentional pediatric exposures to pharmaceuticals. J Am Osteopath Assoc 2006;106:405-11.
22. Rodgers GB, Franklin RL, Midgett JD. Unintentional paediatric ingestion poisonings and the role of imitative behaviour. Inj Prev 2012;18:103-8.

23. Centers for Disease Control and Prevention (CDC). The PROTECT initiative: advancing children's medication safety. http://www.cdc.gov/medicationsafety/protect/protect_initiative.html. Accessed August 27, 2016.
24. Food and Drug Administration (FDA). Timeline of selected FDA activities and significant events addressing opioid misuse and abuse. http://www.fda.gov/Drugs/DrugSafety/InformationbyDrugClass/ucm338566.htm. Accessed August 27, 2016.
25. American Association of Poison Control Centers (AAPCC). Prevention and education. https://aapcc.org/Prevention. Accessed October 30, 2017.
26. Coplan P, Kale H, Sandstom L, Chilcoat H. Effects of reformulated OxyContin® on opioid abuse in the National Poison Data System. J Pain 2012;13:S83.
27. Centers for Disease Control and Prevention (CDC). Prescription painkiller overdoses—use and abuse of methadone as a painkiller. https://www.cdc.gov/vitalsigns/methadoneoverdoses/index.html. Accessed September 2, 2018.
28. Centers for Disease Control and Prevention (CDC). Buprenorphine prescribing practices and exposures reported to a poison center—Utah, 2002-2011. MMWR Morb Mortal Wkly Rep 2012;61:997-1001.
29. Kennedy-Hendricks A, Andrea G, McDonald E, McGinty EE, Shields W, Barry CL. Medication sharing, storage, and disposal practices for opioid medications among US adults. JAMA Intern Med 2016;176:1027-8.
30. McCabe SE, West BT, Teter CJ, Cranford JA, Ross-Durow PL, Boyd CJ. Adolescent nonmedical users of prescription opioids: brief screening and substance use disorders. Addict Behav 2012;37:651-6.
31. Johnston LD, O'Malley PM, Miech RA, Bachman JG, Schulenberg JE. Monitoring the Future national survey results on drug use: 1975-2014: Overview, key findings on adolescent drug use. Ann Arbor, MI: Institute for Social Research, The University of Michigan; 2015.
32. Drug Enforcement Administration (DEA). How teens abuse medicine. https://www.dea.gov/pr/multimedia-library/publications/prescription_for_disaster_english.pdf. Accessed August 27, 2016. Published 2012.
33. Kuo YF, Raji MA, Chen NW, Hasan H, Goodwin JS. Trends in opioid prescriptions among part D medicare recipients from 2007 to 2012. Am J Med 2015;129:221.e21-30.
34. Naun CA, Olsen CS, Dean JM, Olson LM, Cook LJ, Keenan HT. Can poison control data be used for pharmaceutical poisoning surveillance? J Am Med Inform Assoc 2011;18:225-31.
35. Shah K, Barker KA. Out-of-hospital medication errors: a 6-year analysis of the national poison data system. Pharmacoepidemiol Drug Saf 2009;18:1080-5.
36. Berkley J. Using American community survey estimates and margins of error. U.S. Census Bureau. https://www.census.gov/content/dam/Census/programs-surveys/acs/guidance/training-presentations/20170419_MOE.pdf. Accessed September 29, 2017. Published 2017.

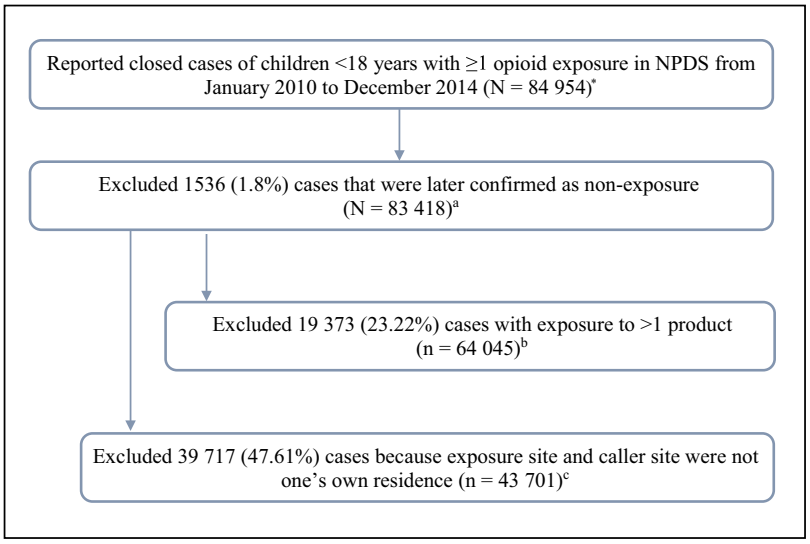

Figure 1. Study sample flow chart (legend below).
[a]Indicates the final sample used for pediatric opioid exposure prevalence and characteristics analysis.
[b]Indicates the final sample used for analyses of serious pediatric opioid exposures.
[c]Indicates the final sample used for area-level analyses of pediatric opioid exposures.
*Cases represent unique exposures and not unique patients.

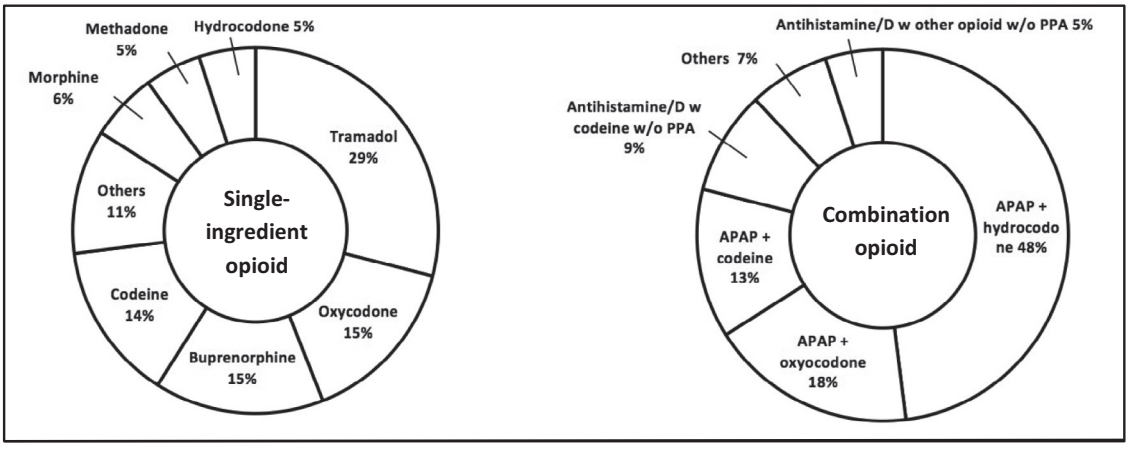

Figure 4. Opioid medications commonly involved in exposures among children, NPDS 2010-2014. *APAP*, acetaminophen; *D*, Decongestant; *PPA*, phenylpropanolamine; *w*, with; *w/o*, without.

Table II. Sociodemographic and clinical characteristics of pediatric opioid medication exposures, NPDS 2010-2014 (additional results from Table I)

Characteristics n (%)	Total opioid exposures (n = 83 418)	Single product exposures* (n = 64 045)		Multiple products exposures§ (n = 19 373)
		Single-substance opioid† (n = 31 775)	Combination opioid‡ (n = 32 270)	
Exposure site				
Own residence	76 577 (91.80)	29 057 (91.45)	30 110 (93.31)	17 410 (89.87)
Other residence	3518 (4.22)	1467 (4.62)	1236 (3.83)	815 (4.21)
School	949 (1.14)	325 (1.02)	319 (0.99)	305 (1.57)
Other¶	1131 (1.36)	477 (1.50)	329 (1.02)	325 (1.68)
Caller site				
Own residence	45 693 (54.78)	18 327 (57.68)	21 791 (67.53)	5575 (28.78)
HCF	29 749 (35.66)	10 148 (31.94)	7415 (22.98)	12 186 (62.9)
Other**	7699 (9.23)	3170 (9.98)	2961 (9.18)	1568 (8.09)
Route				
Ingestion	82 322 (98.69)	31 151 (98.04)	32 089 (99.44)	19 082 (98.5)
Other††	1602 (1.92)	541 (1.70)	189 (0.59)	872 (4.50)
Chronicity				
Acute‡‡	77 602 (93.03)	30,389 (95.64)	30 255 (93.76)	16 958 (87.53)
Non-acute	4609 (5.53)	1049 (3.30)	1770 (5.48)	1790 (9.24)

The subcategories do not add up to 100% because of a small proportion of missing data. Note that there can be >1 route recorded.
Exposure scenario, related clinical effect, and therapy performed following an exposure were missing for 60%-70% of cases, hence, these data are not shown here.
Analyses were limited to cases with: *One product (opioid) exposures.
†One product (single-substance opioid) exposures.
‡One product (combination opioid) exposures.
§Multiple products exposures of which at least one of the products was an opioid.
¶Other exposure site includes public area, restaurant, workplace, or others.
**Other caller site includes other residence, school, public area, restaurant, workplace, or others.
††Other route includes inhalation, ocular, otic, parenteral, rectal, or any other routes.
‡‡An exposure was categorized as acute if any single, repeated or continuous exposure occurred over a period of ≤8 hours.

Table III. Sociodemographic and clinical characteristics of pediatric opioid medication exposures by age, NPDS 2010-2014

Characteristics, n (%)	Age group* ≤5 y (n = 51 072)	6-12 y (n = 8819)	13-17 y (n = 23 245)
Sex†			
Male	26 935 (52.74)	4866 (55.18)	9159 (39.40)
Female	23 919 (46.83)	3933 (44.60)	14 056 (60.47)
Exposure site†			
Own residence	47 578 (93.16)	8253 (93.58)	20 510 (88.23)
Other residence	2660 (5.21)	290 (3.29)	552 (2.37)
School	50 (0.10)	89 (1.01)	805 (3.46)
Other‡	543 (1.06)	130 (1.47)	452 (1.94)
Opioid involved†			
Single-substance	26 752 (52.38)	3970 (45.02)	9765 (42.01)
APAP combinations	20 544 (40.23)	3564 (40.41)	13 249 (57.00)
Cough and cold product combinations	3442 (6.74)	1235 (14.00)	724 (3.11)
Other combinations§	695 (1.36)	99 (1.12)	230 (0.99)
No. of products†			
1	44 431 (87.00)	7494 (84.98)	11 894 (51.17)
≥2	6641 (13.00)	1325 (15.02)	11 351 (48.83)
No. of opioid products†			
1	50 322 (98.53)	8708 (98.74)	21 796 (93.77)
≥2	750 (1.47)	111 (1.26)	1449 (6.23)
Route†			
Ingestion	50 599 (99.07)	8708 (98.74)	22 742 (97.84)
Other¶	447 (0.88)	126 (1.43)	1017 (4.38)
Chronicity†			
Acute**	49 646 (97.21)	8018 (90.92)	19 702 (84.76)
Non-acute	1285 (2.52)	738 (8.37)	2561 (11.02)
Reason†			
Unintentional	50 390 (98.66)	7283 (82.58)	3361 (14.46)
Intentional	118 (0.23)	1035 (11.74)	18 829 (81.00)
Adverse reaction	253 (0.50)	258 (2.93)	560 (2.41)
Other††	127 (0.25)	23 (0.26)	74 (0.32)
HCF use†			
None	20 541 (40.22)	5595 (63.44)	3871 (16.65)
T/E and R	17 888 (35.03)	1539 (17.45)	6538 (28.13)
Critical care	3257 (6.38)	283 (3.21)	3551 (15.28)
Noncritical care	3415 (6.69)	315 (3.57)	2392 (10.29)
Psychiatric care	0 (0)	105 (1.19)	3550 (15.27)
Other‡‡	5635 (11.03)	899 (10.19)	3154 (13.57)
Medical outcome†			
None	25 441 (49.81)	2926 (33.18)	4532 (19.50)
Minor	17 188 (33.65)	4651 (52.74)	10 536 (45.33)
Moderate	2727 (5.34)	376 (4.26)	4601 (19.79)
Major	499 (0.98)	63 (0.71)	805 (3.46)
Death	40 (0.08)	8 (0.09)	63 (0.27)
Poisoning†	21 037 (41.19)	5237 (59.38)	17 128 (73.68)

T/E and R, treated/evaluated and released.
The subcategories do not add up to 100% because of small proportion of missing data. Note that there can be more than 1 route and opioid involved recorded.
Exposure scenario, related clinical effect, and therapy performed following an exposure were missing for 60%-70% of cases hence these data are not shown here.
*Unknown age group not shown, however, exposures recorded as unknown age but documented to be ≤5 years were included in the ≤5 years subgroup here.
†χ^2, $P < .05$.
‡Other exposure site includes public area, restaurant, workplace, or others.
§Other opioid combinations include combinations with acetylsalicylic acid, nonsteroidal anti-inflammatory drugs, and gastrointestinal products.
¶Other route includes inhalation, ocular, otic, parenteral, rectal, or any other routes.
**An exposure was categorized as acute if any single, repeated or continuous exposure occurred over a period of ≤8 hours.
††Other reasons include tampering, malicious, or withdrawal attempts. Children ≤5 years of age can be coded as intentional if someone intentionally gave the child a wrong drug or dose.
‡‡Other HCF include cases wherein the patient refused referral or left against medical advice but were documented to be either in or en route to a HCF.

Table IV. Sociodemographic and clinical characteristics of pediatric opioid medication exposures by intent, NPDS 2010-2014

Characteristics, n (%)	Intent of exposure Unintentional (n = 61 206)	Intentional (n = 20 064)
Sex*		
Male	32 296 (52.77)	7745 (38.60)
Female	28 653 (46.81)	12 290 (61.25)
Age group (y)*,†		
≤5	50 312 (82.20)	117 (0.58)
6-12	7283 (11.90)	1035 (5.16)
13-17	3361 (5.49)	18 829 (93.84)
Exposure site*		
Own residence	57 285 (93.59)	17 546 (87.45)
Other residence	2910 (4.75)	540 (2.69)
School	138 (0.23)	768 (3.83)
Other‡	641 (1.05)	356 (1.77)
Opioid involved*		
Single-substance	30 936 (50.54)	8635 (43.04)
APAP combinations	25 003 (40.85)	11 493 (57.28)
Cough and cold product combinations	4866 (7.95)	441 (2.20)
Other combinations§	812 (1.33)	194 (0.97)
No. of products*		
1	53 062 (86.69)	9504 (47.37)
≥2	8144 (13.31)	10 560 (52.63)
No. of opioid products*	60 334 (98.58)	18 699 (93.20)
1		
≥2	872 (1.42)	1365 (6.80)
Route*		
Ingestion	60 746 (99.25)	19 636 (97.87)
Other¶	486 (0.79)	939 (4.68)
Chronicity*		
Acute**	58 817 (96.10)	17 203 (85.74)
Non-acute	2274 (3.72)	1954 (9.74)
HCF use*		
None	27 802 (45.42)	1529 (7.62)
T/E and R	19 473 (31.82)	6116 (30.48)
Critical care	3315 (5.42)	3537 (17.63)
Noncritical care	3564 (5.82)	2329 (11.61)
Psychiatric care	83 (0.14)	3543 (17.66)
Other††	6539 (10.68)	2880 (14.35)
Medical outcome*		
None	28 819 (47.09)	3813 (19.00)
Minor	22 945 (37.49)	8485 (42.29)
Moderate	2 960 (4.84)	4409 (21.97)
Major	485 (0.79)	786 (3.92)
Death	22 (0.04)	61 (0.30)
Poisoning*	27 137 (44.34)	14 749 (73.51)

T/E and R, treated/evaluated and released.
The subcategories do not add up to 100% because of a small proportion of missing data. Note that there can be more than one route and opioid involved recorded.
Exposure scenario, related clinical effect, and therapy performed following an exposure were missing for 60%-70% of cases, hence, these data are not shown here.
Exposures due to adverse reaction, others reasons including tampering, malicious or withdrawal attempts, or unknown are not shown here. Children ≤5 years can be coded as intentional if someone intentionally gave the child a wrong drug or dose.
*χ^2, $P < .05$.
†Unknown age group not shown, however, exposures recorded as unknown age but documented to be ≤5 years were included in the ≤5 years subgroup here.
‡Other exposure site includes public area, restaurant, workplace, or others.
§Other opioid combinations include combinations with acetylsalicylic acid, nonsteroidal anti-inflammatory drugs, and gastrointestinal products.
¶Other route includes inhalation, ocular, otic, parenteral, rectal, or any other routes.
**An exposure was categorized as acute if any single, repeated, or continuous exposure occurred over a period of ≤8 hours.
††Other HCF include cases wherein the patient refused referral or left against medical advice but were documented to be either in or en route to a HCF.

Table VI. Pediatric opioid medication exposures and area-level SES characteristics

Characteristics	Total ZIP code areas, mean (SD) (n = 32 086)†	ZIP code areas with ≥1 opioid exposure, mean (SD) (n = 12 809)‡,§	Spearman correlation (r)§
Pediatric opioid exposures			n/a
Number	n/a	3.07 (3.46)	
%		0.29 (2.47)	
% Adults	76.97 (5.04)	76.24 (4.85)	0.217*
% Minority	21.28 (23.87)	28.06 (24.92)	–0.392*
Sex			
% Male	50.18 (3.50)	49.48 (2.72)	0.270*
Race and ethnicity			
% Non-Hispanic whites	78.77 (23.90)	71.95 (24.93)	0.393*
% Hispanic whites	4.56 (9.11)	6.25 (10.32)	–0.367*
% Blacks	7.62 (15.39)	10.41 (16.78)	–0.323
% Other races¶	6.91 (11.73)	8.85 (11.33)	–0.380*
Median household income (in $000s)**	46.65 (19.75)	50.33 (20.60)	–0.267*
Average household size	2.56 (3.14)	2.58 (0.98)	–0.273*
% Population >65 y in households	15.30 (5.47)	13.79 (5.03)	0.312*

n/a, not applicable.
*$P < .0001$.
†Represents all 5-digit ZIP code areas from the US Census 2010 file (total).
‡Represents all 5-digit ZIP code areas with ≥1 pediatric opioid exposure (Sample).
§Spearman correlations computed for 5-digit ZIP code areas with ≥1 pediatric opioid exposures.
¶Other races = American Indians, Pacific Islanders, Asians, and others.
**Median household income was imputed using the corresponding per capita income to the extent possible.