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Trends in opioid exposures among young children reported to United States poison centers from 2016 to 2023

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ABSTRACT

Introduction: The objective of this study was to update and expand on previous studies of opioid exposures among young children reported to America's Poison Centers, and to describe how fentanyl and medications for opioid use disorder have contributed.

Methods: This retrospective study investigated 34,632 reports of single-substance opioid exposure from 2016 to 2023 involving pediatric patients aged one month to six years old. Descriptive statistics, tests for data normality, and significance testing were performed where applicable.

Results: Of 34,632 reported exposures, 96.7% were unintentional. The median age of exposure was 2.0 years (IQR 1.33-3.0 years). Reported exposures decreased by 57.5% over the study period ($r=-0.96$; $P<0.001$). However, there was a 300% absolute increase in deaths and major effects ($r=0.96$; $P<0.001$). Exposures resulting in minor, no effect, not followed, or unable to follow decreased 66.2% ($r=-0.99$; $P<0.001$). Buprenorphine was most frequently involved, comprising 23.4% of reported exposures. Buprenorphine (OR 1.93; $P<0.001$) and methadone (OR 14.98; $P<0.001$) were associated with an increased risk of severe effects when compared to other prescription drugs (OR: 1). There was an absolute increase of 512% over time in reports of heroin, fentanyl, synthetic non-pharmaceutical opioids ($r=0.92$; $P<0.001$), which were also associated with severe effects (OR 20.1; $P<0.001$).

Discussion: Pediatric opioid exposures have previously been reported to be relatively stable. It is likely the 57.5% reduction is exaggerated due to underreporting from health care providers. However, decreases in exposures are presumed to be balanced throughout the dataset and, therefore, without differential impact on other points of analysis. Our study highlights the continued need for enhanced poisoning prevention strategies.

Conclusions: The relative severity of poisonings reported to poison centers worsened over the study period. The opioids implicated have shifted away from hydrocodone, oxycodone, and tramadol, and towards fentanyl and buprenorphine.

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Buprenorphine; drug endangerment; fentanyl; harm reduction; poison prevention

Introduction

Prescription opioids have led to serious consequences in the United States (US). The number of national overdose deaths with any opioid as the underlying cause has surged nearly 4-fold, escalating from 21,089 in 2010 to 80,411 in 2021 [1]. This alarming spike in fatalities can largely be attributed to the clandestine production and distribution of illicitly manufactured fentanyl, which was first reported by the US Drug Enforcement Agency in late 2013 [2,3]. Moreover, the infiltration of illicit synthetic opioids and other pharmacologically potent substances into the drug market has been accompanied by an increase in the circulation of counterfeit prescription drugs since 2017 [4-6]. Unfortunately, the surge in opioid-related morbidity and mortality is mirrored in the pediatric population, including in young children.

When considering the 0-18 age cohort, it has been reported that children under five years old account for 60% of pediatric opioid exposures [7,8]. Underlying these younger

pediatric exposures are cases which are predominantly "unintentional", and therefore, largely preventable [9,10]. Other recent studies examining fatal poisonings reported to the US Centers for Disease Control and Prevention [11,12], and the National Fatality Review-Case Reporting System [13], have uncovered opioids as the predominant substances contributing to pediatric poisoning deaths.

The purpose of this study is to evaluate the trends in reported exposures to central opioid receptor agonists among young children from 2016 to 2023 and evaluate risk factors for poisoning severity in the instance of primarily unintentional opioid exposures.

Methods

Data sources and study design

This Institutional Review Board-exempt retrospective study investigates the year-to-year trends in opioid exposures from

2016 to 2023 reported by 55 US poison centers to the National Poison Data System® (NPDS). The NPDS is a data warehouse owned and operated by America's Poison Centers™ [14]. Poison centers all use a standardized America's Poison Centers case form and definitions to record patient information, interventions, clinical effects, and medical outcomes [15].

Case selection criteria

We included children aged one month to six years old with exposure to a single opioid as specified by an America's Poison Centers generic code. Patients under one month were excluded from neonatal opioid withdrawal syndrome cases [16]. The dataset included those up to the age of 12, and we removed individuals over six years (7–12 years) ($n=5,704$) and those with only a designated age range of 6–12 ($n=14$). Next, we removed polysubstance exposures ($n=6,053$) and those with the outcome “unrelated effect” ($n=407$), “confirmed non-exposure” ($n=863$), and “death-indirect report” ($n=16$). Product codes were not analyzed as they were not provided in entirety.

Variables

America's Poison Centers generic codes analyzed are included in numerical form in [Supplementary Appendix I](#). Exposures with age entered only as ≤ 5 years ($n=50$) were included in all analyses but removed from the calculation of mean and standard deviation of ages implicated in exposures. Ages provided in months were translated to a year value (i.e., 1-month/12-months = 0.083 years). Distribution of gender (variable defined by America's Poison Centers field) was also investigated.

Reason for exposure, exposure site, and caller site are selected by specialists in poison information at the time of the first call pertaining to the exposure as specified by the NPDS Annual Report [15]. Potential poison exposures are followed by specialists in poison information until the known effects and outcome can be documented with reasonable

certainty. The known medical outcomes included in our analysis were “no effect”, “minor effect” (minimal symptoms with rapid resolution), “moderate effect” (symptoms are more pronounced or prolonged), “major effect” (symptoms were life-threatening or resulted in residual disability), and “death” (patient died as result of the poisoning). Unknown medical outcomes included “judged as nontoxic exposure”, “minimal clinical effects possible”, and “unable to follow, potentially toxic exposure”. We defined a composite outcome of “severe effect” to include exposure outcomes which resulted in death or major effect. More detailed information can be found in the NPDS Annual Report [15].

Therapies performed were only considered in analysis if coded as “recommended and performed” or “performed”. Level and location of care were determined by aggregating data from two fields: level of health care facility care and management site. Health care facility utilization was defined by exposures in which the patient was reported to have been admitted to a critical care unit, non-critical care unit, or psychiatric facility, or when the exposure was coded as treated/evaluated and released, or patient lost to follow-up/left against medical advice [15].

Exposures were categorized by the America's Poison Centers generic opioid code provided; combination medications were grouped by primary opioid type if applicable, and opioids involved in <400 exposures were grouped as “other prescriptions” as seen in [Supplementary Appendix II](#). A composite grouping of “medications for opioid use disorder” was created and comprised of buprenorphine and methadone exposures. Another composite grouping of “illicit opioids and fentanyl” was created and included exposures involving prescription fentanyl, illicitly manufactured fentanyl, heroin, and non-prescription synthetic opioids. While fentanyl exposures remain separated in [Supplementary Appendix 1](#) and [Table 1](#) by prescription versus non-prescription, both types were considered alongside illicit opioids due to their high-risk profile, lack of an illicitly manufactured fentanyl America's Poison Centers code before 30 October 2019 [17], and trends which make us suspect illicit fentanyl continued to be coded as prescription even after 2019.

Table 1. Change in exposure drug type 2016–2023.

Parent opioid name	2016	2023	Relative change	Absolute change	Pearson's correlation/ Spearman's rho	P-value
Prescription opioids	6,539	2,327	−16.3%	−64.4%	0.94	<0.001
Codeine alone or in combination	1,014	197	−54.3%	−80.6%	−0.97	<0.001
Hydrocodone alone or in combination	1,500	415	−35.0%	−72.3%	−0.97	<0.001
Oxycodone alone or in combination	1,309	510	−8.4%	−61.0%	−0.48	0.12
Other specific prescriptions (<400) ^a	224	44	−53.8%	−80.4%	−0.95	<0.001
Buprenorphine	996	724	70.9%	−27.3%	0.77	0.01
Methadone	195	98	18.2%	−49.7%	0.72	0.02
Morphine	202	68	−20.9%	−66.3%	−0.77	0.01
Tramadol	1,099	271	−42.0%	−75.3%	−0.97	<0.001
Illicit opioids and fentanyl	65	398	1,339.6%	512.3%	0.92	<0.001
Fentanyl (prescription)	46	144	636.0%	213.0%	0.95	<0.001
Diacetylmorphine (heroin)	19	23	184.6%	21.1%	0.76	0.02
Fentanyl (non-prescription) ^b	0	229	Not applicable ^d	Not applicable ^d	0.98	<0.001
Synthetic opioids, analogs and precursors (excluding pharmaceutical preparations) ^c	0	2	Not applicable ^d	Not applicable ^d	0.77	0.01
Other or unknown opioids	73	115	270.4%	57.5%	0.94	<0.001

^aIf a prescription drug had under 400 exposures, it was grouped into this category.

^bFentanyl (non-prescription) generic code activated 30 October 2019.

^cSynthetic opioids, analogs, and precursors generic code activated 24 October 2017.

^dStatistic unable to be calculated due to denominator of 0.

Statistical analysis

Descriptive statistics were used to describe data. We reported absolute change and relative rates of change. Relative change measures the change in the annual proportion of exposures over a period of time, whereas absolute measures the percentage difference in the number of exposures over time without accounting for the number of annual exposures. Sample calculations of absolute and relative change are included as a footnote in Table 2. To compute the mean rate of change, year-to-year absolute change was calculated, summed, and then divided by the total number of intervals between the years. This approach determined the average annual change in the variable of interest over the study period. Shapiro-Wilk's test was used to test data normality where applicable; linear change was not assumed. Pearson's correlation (r) or Spearman's rho (r_s) were used to test whether there was a trend, the strength of trends, and significance. Furthermore, multinomial logistic regression was used to determine significant predictors of medical outcomes (i.e., major effect, death, minor effect, and moderate effect). We adjusted for age and gender. Cox, Snell, and Nagelkerke methods were used to determine model fit. Predictor variables included in the model were: exposure site (health care facility, own residence, public

area, workplace or school, other), reason (adverse reaction, intentional, unintentional, other), and substance type (codeine alone or in combination with other drugs, other or unknown opioids alone or in combination, hydrocodone alone or in combination, oxycodone alone or in combination, other specific prescriptions, buprenorphine, non-pharmaceutical synthetic opioids, fentanyl, diacetylmorphine (heroin), methadone, morphine, and tramadol. Adjusted odds ratios (aORs), and P -values were reported for the results of the regression, as well as prior described analyses. All P -values were reported at the 0.05 significance level. Confidence intervals were reported at 95% (95% CI) for the regression analysis and included odds ratios. All error bars in the figures were reported using standard error.

Results

Characteristics of exposures

Over the study period, there were 34,632 reported opioid exposures, which met the study criteria. Reported exposures decreased at a mean rate of 11.4% per year (range -5.6 to -17.6%), with an absolute decrease of 57.5% from 2016 to 2023 ($r = -0.97$; $P < 0.001$). The median age of exposure was

Table 2. Change in pediatric opioid exposure severity.

Outcome characteristics	2016	2023	Relative change ^a	Absolute change ^b	Pearson's correlation/ Spearman's rho	P -value
Total exposures among young children ^c	1,044,484	868,856	Not applicable	-16.8%	-0.98	<0.001
Total opioid exposures among young children ^d	6,677	2,840	Not applicable	-57.5%		
Outcome						
Severe effect ^e	78	312	840.4%	300.0%	0.96	<0.001
Moderate effect	401	430	152.1%	7.2%	0.98	<0.001
Minor effect, no effect, not followed and unable to follow ^f	6,198	2,098	-20.4%	-66.2%	-0.99	<0.001
Effects						
Acidosis	11	80	1,609.9%	627.3%	0.99	0.01
Asystole	2	10	1,075.5%	400.0%	0.85	0.004
Bradycardia	20	36	323.2%	80.0%	0.94	<0.001
Coma or major central nervous system depression	37	225	1,329.7%	508.1%	0.96	<0.001
Cyanosis	18	57	644.5%	216.7%	0.92	<0.001
Respiratory arrest	18	57	644.5%	216.7%	0.93	<0.001
Respiratory depression	242	374	263.3%	54.5%	0.94	<0.001
Therapies						
Cardiopulmonary resuscitation	25	38	257.4%	52.0%	0.91	<0.001
Endotracheal intubation	24	39	282.0%	62.5%	0.94	<0.001
Naloxone	464	670	239.5%	44.4%	0.90	0.001
Mechanical ventilation	24	44	331.0%	83.3%	0.97	<0.001
Level of care						
Health care facility utilization ^g	4,026	2,038	19.0%	-49.4%	0.98	<0.001
Managed on site (non-health care facility)	2,340	667	-33.0%	-71.5%	-0.97	<0.001
Other	28	7	-41.2%	-75.0%	-0.33	0.21
Patient refused referral/did not arrive at health care facility	230	109	11.4%	-52.6%	0.35	0.20
Unknown	53	19	-15.7%	-64.2%	-0.5	0.10

^aRelative change example of severe effect: $\frac{\left(\frac{312}{2840}\right) - \left(\frac{78}{6677}\right)}{\left(\frac{78}{6677}\right)} \times 100\% = 840.40\%$.

^bAbsolute change example of severe effect: $\left(\frac{312 - 78}{78}\right) \times 100\% = 300.0\%$.

^cControl for pediatric exposures.

^dAges 1 month to 6-years old.

^eIncludes: major effect, death.

^fIncludes: not followed, judged as nontoxic exposure (clinical effects not expected), not followed, minimal clinical effects possible (no more than minor effect possible), unable to follow, judged as a potentially toxic exposure.

^gIncludes: admitted to critical care unit, admitted to noncritical care unit, admitted to psychiatric facility, patient lost to follow-up/left AMA, treated/evaluated and released.

2.0 years (IQR 1.33–3.0 years). Incidents involving children aged one month to two years old constituted 74.1% of exposures. Gender distribution was relatively balanced, with 52.4% of incidents involving boys, 47.1% involving girls, and 0.5% involving a child of unknown gender.

The reason for exposure was predominantly unintentional, accounting for 96.7% of exposures. A minority of incidents were attributed to adverse reactions, intentional, malicious, other, and unknown causes. Site of exposure was 92.3% at the child's own residence, 4.9% of exposures at an "other residence", and 2.9% occurred at other and unknown sites. Over half (54.8%) of the calls originated from the home, 34.6% originated from a health care facility, 8.7% from other or unknown sites, and 1.9% from other residences.

Overall trends in severity

Outcomes, specific effects, and therapies performed revealed significant relative and absolute changes, as reflected in Table 1. Exposure outcomes with severe effects increased from 1.2 to 11.0% of annual exposures ($r=0.96$; $P<0.001$) and are summarized year by year in Figure 1. Similarly, reports of moderate effect outcomes increased from 6.0% in 2016 to 15.2% in 2023 ($r=0.98$; $P<0.001$). Conversely, reports of minor effect, no effect, not followed-judged as nontoxic exposure, not followed-minimal clinical effects possible, decreased from 92.8 to 73.9% of annual exposures over the study period ($r=-0.99$; $P<0.001$). Naloxone administration increased from 6.9 to 23.6% of exposures over the study period ($r=0.90$; $P=0.001$). Table 1 summarizes other changes in related clinical effects and performed therapies.

Severe effects were most strongly associated with illicit opioids and fentanyl (OR 20.1; 95% CI: 17.6–23.0; $P<0.001$) and other or unknown opioid exposures (OR 15.8; 95% CI: 13.4–17.5; $P<0.0001$), compared to prescription opioid

exposures (OR 1). Within the prescription opioids, severe effects were most associated with methadone exposures (OR 15.0; 95% CI: 11.1–15.7; $P<0.001$) and buprenorphine exposures (OR 1.9; 95% CI: 1.5–2.1; $P<0.001$), when compared with other types of prescription opioids.

The same methods were used to compare opioids to health care facility utilization, and similar trends were observed. Health care facility utilization increased from 60.3 to 71.8% over the study period ($r=0.98$; $P<0.001$). Health care facility utilization was most strongly associated with illicit opioids and fentanyl (OR 2.6; 95% CI: 2.3–3.0; $P<0.001$) and other or unknown opioids (OR 2.3; 95% CI: 2.0–2.9; $P<0.001$) than with a prescription opioid. Regarding known prescription opioid exposures, health care facility utilization was most correlated to methadone exposure (OR 3.8; 95% CI: 3.2–4.4; $P<0.0001$) and buprenorphine exposure (OR 5.6; 95% CI: 5.1–5.9; $P<0.0001$), when compared to other types of prescription opioids.

Type of opioid

Pharmaceutical preparations were implicated in most exposures (93.9%) yet declined over the study period from 97.9 to 81.9% of annual exposures ($r=-0.94$; $P<0.001$). Relative and absolute changes are described in detail by opioid agent in Table 2. Buprenorphine was unique as it was the only known prescription opioid to increase in its proportion of annual exposures, from 14.9% in 2016 to 25.5% in 2023 ($r=0.77$; $P=0.01$). All other prescriptions revealed decreases or statistically insignificant changes. Illicit opioids and fentanyl exposures increased from 1.0 to 14.0% ($r=0.92$; $P<0.001$), and other or unknown opioid exposures increased from 1.1 to 4.1% ($r=0.94$; $P<0.001$) of annual exposures. Relative annual reports of prescription, illicit opioids and fentanyl, medications for opioid use disorder (buprenorphine and methadone), and other or unknown opioids are shown in Figure 2.

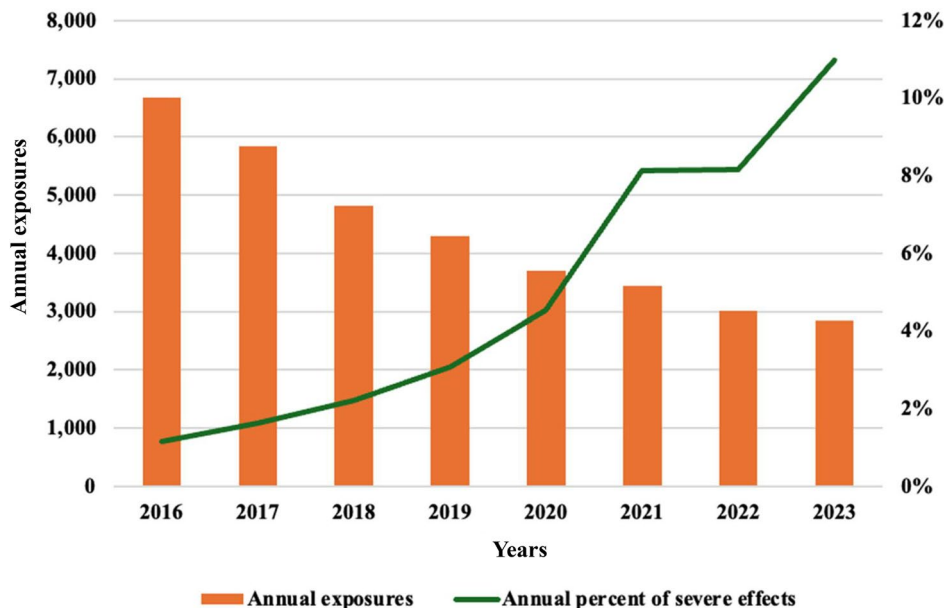


Figure 1. Number of exposures per year and percentage of severe effects or death (2016–2023).

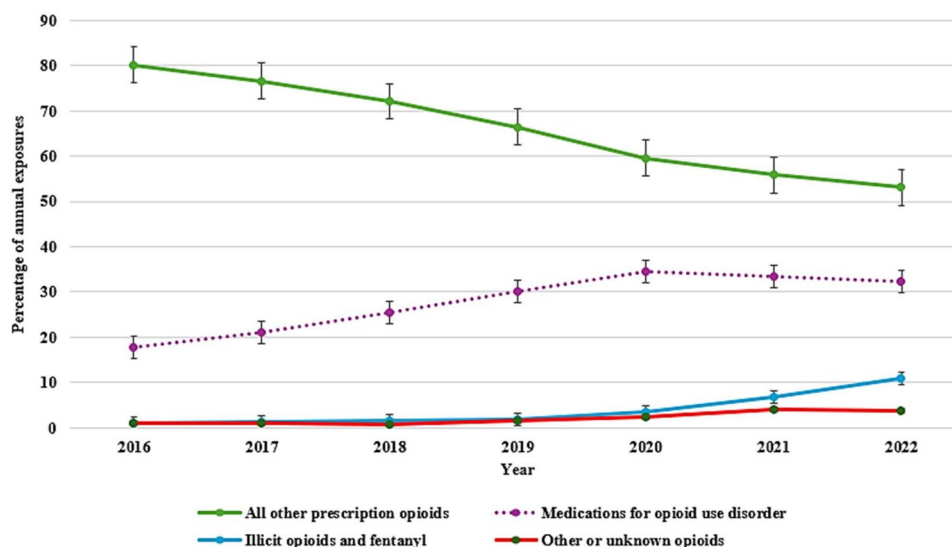


Figure 2. Opioids implicated in exposures (2016–2023).

Results of regression analysis

The only predictor of a severe outcome was substance type, particularly illicit opioids and fentanyl (aOR 2.7; 95% CI: 2.3–3.2) or methadone (aOR 1.4; 95% CI: 1.1–1.9). Substance type also emerged as the only significant predictor of a moderate effect, particularly methadone (aOR 3.8; 95% CI: 3.1–4.2). Exposure site and reason were not significant predictors of either severe or moderate effects.

Discussion

The objective of this study was to update and expand on previous reports of opioid exposures among young children reported to US poison centers. To our knowledge, there has not been a similar detailed study examining both fatal and non-fatal outcomes of pediatric opioid exposures and poisonings using NPDS data post-2015 [7]. By that time, it was already well known that increased prescribing and general availability of drugs was directly associated with rising pediatric poisonings, particularly among children 0–5 years old [18], and the US Centers for Disease Control and Prevention implemented the Prevention of Overdoses and Treatment Errors initiative to reduce these exposures [19]. Unfortunately, the infiltration of fentanyl into the illicit drug market has counteracted these efforts and increased pediatric opioid-related deaths [20]. We hypothesized the implications of such concomitant substances in the illicit drug market would reveal worsening fatal and non-fatal trends regardless of a potential decrease in exposures. We also sought to better understand the changing trends among reported prescription opioid exposures.

Our study found that opioid exposures among young children reported to poison centers decreased by 57.5% from 2016 to 2023. This contradicts previous studies which concluded pediatric opioid exposures may be stable [21]

but similarly reflects recent reports of declines in prescription opioid poisoning per 10,000 prescriptions [22]. When compared to the decline in all pediatric poison exposures reported to poison control centers over the study period (–16.8%), we realize it is likely this decrease is exaggerated due to underreporting from health care providers who have become increasingly comfortable treating opioid exposure. Still, decreases in exposures are presumed to be balanced throughout the dataset and, therefore, without differential impact on other points of analysis. Our study showed an increase in reports of illicit opioid and fentanyl exposure from 65 in 2016 (0.97%) to 398 in 2023 (14.0%). It is these illicit opioids, fentanyl, buprenorphine, methadone, and other or unknown opioids which underlie 83.5% of reported exposures with severe effects and are largely responsible for the 300.0% absolute increase in severe effects reported over the study period. Given that opioids have long been the most common substance to contribute to poisoning-related deaths among children [13,23], our study highlights the continued need for enhanced poisoning prevention strategies aimed at parents and other childcare providers, physicians, and pharmaceutical companies [24,25].

While opioid prescribing has decreased overall, prescription opioids still comprise most pediatric opioid exposures, and efforts to promote knowledgeable prescribing practices may make an additional impact. All patients being prescribed opioids, regardless of their age or familial status, should be educated on safe pharmaceutical storage, given that 4.9% of exposures occurred in another residence; this includes education on the safe disposal of unused medications, as a recent study revealed 78% of individuals retained their unused opioid prescriptions [26]. The conversation can be extended to include the proper disposal of partially used drugs and proper storage of drugs and paraphernalia, and it remains relevant to illicit opioids as well. In addition, prescribing naloxone along with all opioid prescriptions,

including medications for opioid use disorder, and its safe use in children should be discussed and become common practice as it may reduce the risk of opioid-related emergency room visits [27,28].

Despite pediatricians historically writing only 0.2% of total opioid prescriptions [29], their educational role remains important. Pediatricians should similarly emphasize the importance of proper drug and paraphernalia storage and disposal to parents and caregivers. This is paramount, given that the lack of proper drug storage is frequently reported [30], and poisonings involving children ≤ 5 years tend to be the unintentional result of exploratory behavior [31]. These discussions can begin as early as prenatal visits and include the topic of potential substance use in the household. Emphasizing the risks posed by individuals beyond the parents can also remind parents of other sources of legitimate risk while also encouraging productive discussions about substance abuse and its consequences. Pediatricians may also consider framing a naloxone prescription as an item that should be in every household.

Further exploring the instance of exposure to medications for opioid use disorder, it is important to note that although buprenorphine revealed an absolute decrease of 23.3%, it was the only prescription with a statistically significant relative increase. This epidemiologic shift was expected, given national efforts to increase prescribing to curb worsening overdose rates [1,32]; such efforts have included lessened prescribing restrictions and increased Medicaid coverage for these drugs [33,34]. While opioid-based medications for opioid use disorder are specifically effective at decreasing withdrawal [35], limiting feelings of euphoria [36], and decreasing overdose mortality among adults [37], they do pose unique dangers to children. Partial agonist effect from buprenorphine exhibits a respiratory depression ceiling effect in adults [38,39]. However, this may not be present in children who may instead experience a delayed onset and long-lasting symptoms [40,41]. For this reason, clinicians should counsel on these facts, and possibly, newer extended-release injections of buprenorphine formulations should take precedence as a treatment for patients with opioid use disorder given the reduced risk for diversion, misuse, and unintentional pediatric poisonings while remaining covered by most insurance and Medicaid [42].

Lastly, pharmaceutical companies may be able to reduce unintentional exposures more through improved formulation and packaging safeguards. Opioid compound formulations, especially sublingual, should be made to taste and look less appealing to children. Packaging warnings, such as “One Pill Can Kill” for opioids can serve as safe-storage reminders. More importantly, unintentional pediatric buprenorphine exposures were reported to have greatly decreased with the manufacturer’s transition to unit dose packaging [43]; moving towards unit dose packaging for all opioid prescriptions may decrease pediatric access as it has for buprenorphine. In the instance of illicit opioid exposure, unit dose packaging may also make it easier to identify counterfeit pills and subsequently reduce severe poisonings due to drugs produced in clandestine laboratories [44].

Limitations

Limitations exist within our methodologies and are also inherent to the voluntary nature of reporting, which comprise NPDS datasets. Exposures involving multiple substances ($n=6,053$) were excluded from our analysis to avoid confounding variables but may have contained pertinent findings. The validity of the included dataset is assumed even though quantity, dosage, and formulation of a drug involved in an exposure is often unavailable, and confirmatory testing of drug exposure is rarely done. This highlights how the selection of a specific prescription drug can be misleading because it may be an assumption and/or “prescription drugs” purchased on the street may be counterfeit and contain other potent pharmacologically active components [4].

A past study reported that NPDS only captured 1 in 61 deaths when compared to US death certificates and National Vital Statistics Systems [45]. In addition, NPDS data on the number of exposures, therapies provided, and effects experienced are reported to be underestimated when compared to details of hospital chart data [46]. Conversely, there may be over-admission for some types of opioid exposures due to presumed-risk bias (i.e., the potential for delayed onset of long-lasting symptoms without respiratory depression ceiling from buprenorphine), which would mean these drugs have overestimated risk in relation to health care facility use. The type and level of health care facility use were not dissected, as past studies have shown the level of pediatric care is not necessarily indicative of risk [47]. Regarding our analysis of therapies, there were counts of “recommended, not known if performed” within the provided dataset, which were excluded from our statistics. We also did not count “unknown if related” in our analysis with regard to specific clinical effects. These may have amounted to preformed therapies and related effects missing in our counts. Data included for 2023 is also considered provisional before the database is locked in 2024. This means some data involving exposure severity from 2023 may have changed after our analysis was completed.

Conclusion

This study demonstrates an increase in the severity of opioid exposures among young children despite a decrease in the reported number of exposures to poison centers. A significant proportion of severe effects were attributed to illicit opioids, fentanyl, buprenorphine, methadone, and other or unknown opioids. Further advocacy and prevention efforts are needed to reverse these trends.

Acknowledgements

America’s Poison Centers maintains the National Poison Data System (NPDS), which houses de-identified case records of self-reported information collected from callers during exposure management and poison information calls managed by the country’s poison centers. The NPDS data do not reflect the entire universe of exposures to a particular substance as additional exposures may go unreported to poison centers; accordingly, NPDS data should not be construed to represent the

complete incidence of US exposures to any substance(s). Exposures do not necessarily represent a poisoning or overdose and America's Poison Centers is not able to completely verify the accuracy of every report. Findings based on NPDS data do not necessarily reflect the opinions of America's Poison Centers.

Author contributions

Perry Rosen and Christine Ramdin: data curation; formal analysis; investigation; methodology; project administration; writing—original draft; writing—review and editing. James Leonard: data curation; methodology; supervision; writing—review and editing. Bruce Ruck: investigation; methodology; resources; supervision. Lewis Nelson: conceptualization; methodology; supervision; writing—review and editing. Diane Calello: conceptualization; methodology; project administration; supervision; writing—review and editing. All authors approved the final manuscript as submitted and agreed to be accountable for all aspects of the work.

Disclosure statement

No potential conflict of interest was reported by the authors.

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Data availability statement

This study utilized data from the National Poison Data System, which is a proprietary database owned by the America's Poison Centers. Data requests should be directed to America's Poison Centers.

References

- [1] Abuse NID. Drug overdose death rates; 2023 [updated 2023 Jun 30; cited 2023 Nov 30]. Available from: <https://nida.nih.gov/research-topics/trends-statistics/overdose-death-rates>
- [2] Administration DE. National Heroin Threat Assessment summary; 2015. p. 12.
- [3] Administration USDoJDE. National Drug Threat Assessment; 2018 [cited 2023 Nov 30]. Available from: <https://www.dea.gov/sites/default/files/2018-11/DIR-032-18%202018%20NDTA%20final%20low%20resolution.pdf>
- [4] Nguyen L, Evans A, Frank G, et al. Genuine and counterfeit prescription pill surveillance in Washington, D.C. *Forensic Sci Int*. 2022;339:111414. doi: 10.1016/j.forsciint.2022.111414.
- [5] Singh VM, Browne T, Montgomery J. The emerging role of toxic adulterants in street drugs in the US illicit opioid crisis. *Public Health Rep*. 2020;135(1):6–10. doi: 10.1177/0033354919887741.
- [6] Cole C, Jones L, McVeigh J, et al. Adulterants in illicit drugs: a review of empirical evidence. *Drug Test Anal*. 2011;3(2):89–96. doi: 10.1002/dta.220.
- [7] Allen JD, Casavant MJ, Spiller HA, et al. Prescription opioid exposures among children and adolescents in the United States: 2000–2015. *Pediatrics*. 2017;139(4):e20163382. doi: 10.1542/peds.2016-3382.
- [8] Patel AM, Wheeler DC, Rose SR, et al. Prevalence and characteristics of pediatric opioid exposures and poisonings in the United States. *J Pediatr*. 2019;206:148–155.e4. doi: 10.1016/j.jpeds.2018.10.047.
- [9] Lee VR, Connolly M, Calello DP. Pediatric poisoning by ingestion: developmental overview and synopsis of national trends. *Pediatr Ann*. 2017;46(12):e443–e448. doi: 10.3928/19382359-20171121-01.
- [10] Tadros A, Layman SM, Davis SM, et al. Emergency department visits by pediatric patients for poisoning by prescription opioids. *Am J Drug Alcohol Abuse*. 2016;42(5):550–555. doi: 10.1080/00952990.2016.1194851.
- [11] Gaither JR, Shabanova V, Leventhal JM. US national trends in pediatric deaths from prescription and illicit opioids, 1999–2016. *JAMA Netw Open*. 2018;1(8):e186558. doi: 10.1001/jamanetworkopen.2018.6558.
- [12] Kelly BC, Vuolo M, Frizzell LC. Pediatric drug overdose mortality: contextual and policy effects for children under 12 years. *Pediatr Res*. 2021;90(6):1258–1265. doi: 10.1038/s41390-021-01567-7.
- [13] Gaw CE, Curry AE, Osterhoudt KC, et al. Characteristics of fatal poisonings among infants and young children in the United States. *Pediatrics*. 2023;151(4):e2022059016. doi: 10.1542/peds.2022-059016.
- [14] Centers AsP. NPDS interactive dashboard; 2022 [cited 2023 Nov 30]. Available from: <https://www.aapcc.org/national-poison-data-system>
- [15] Gummin DD, Mowry JB, Beuhler MC, et al. 2022 Annual report of the National Poison Data System (NPDS) from America's Poison Centers: 40th annual report. *Clin Toxicol*. 2023;61:717–939. doi: 10.1080/15563650.2023.2268981.
- [16] Weller AE, Crist RC, Reiner BC, et al. Neonatal Opioid Withdrawal Syndrome (NOWS): a transgenerational echo of the opioid crisis. *Cold Spring Harb Perspect Med*. 2021;11(3):a039669. doi: 10.1101/cshperspect.a039669.
- [17] Gummin DD, Mowry JB, Beuhler MC, et al. 2019 Annual report of the American Association of Poison Control Centers' National Poison Data System (NPDS): 37th annual report. *Clin Toxicol*. 2020;58(12):1360–1541. doi: 10.1080/15563650.2020.1834219.
- [18] Burghardt LC, Ayers JW, Brownstein JS, et al. Adult prescription drug use and pediatric medication exposures and poisonings. *Pediatrics*. 2013;132(1):18–27. doi: 10.1542/peds.2012-2978.
- [19] Promotion OoDPaH. PROTECT Initiative: using a healthy people 2030 objective to advance children's medication safety; 2023 [cited 2023 Nov 30]. Available from: <https://health.gov/news/202308/protect-initiative-using-healthy-people-2030-objective-advance-childrens-medication-safety#:~:text=Recent%20NEISS%20CADES%20data%20show,the%20Healthy%20People%202030%20target>
- [20] Gaither JR. National trends in pediatric deaths from fentanyl, 1999–2021. *JAMA Pediatr*. 2023;177(7):733–735. doi: 10.1001/jamapediatrics.2023.0793.
- [21] Roehler DR, Olsen EO, Mustaquim D, et al. Suspected non-fatal drug-related overdoses among youth in the US: 2016–2019. *Pediatrics*. 2021;147(1):e2020003491. doi: 10.1542/peds.2020-003491.
- [22] Wang GS, Olsen H, Severtson G, et al. The impact of the prescription opioid epidemic on young children: trends and mortality. *Drug Alcohol Depend*. 2020;211:107924. doi: 10.1016/j.drugalcdep.2020.107924.
- [23] Control CfD. Injuries among children and teens; 2021 [cited 2023 Nov 30]. Available from: <https://www.cdc.gov/injury/features/child-injury/index.html>
- [24] Administration HHRs. Prevention tips; 2024 [cited 2024 Jan 2]. Available from: <https://poisonhelp.hrsa.gov/what-you-can-do/prevention-tips>
- [25] <https://www.aap.org/en/news-room/news-releases/health-safety-tips/american-academy-of-pediatrics-offers-tip-s-on-poison-prevention-in-your-home> [Internet]; 2023 [cited 2023 Mar 14]. Available from: <https://www.aap.org/en/news-room/news-releases/health-safety-tips/american-academy-of-pediatric-s-offers-tips-on-poison-prevention-in-your-home>
- [26] Yeung C, Novak CB, Antflekk D, et al. Opioid medication disposal among patients following hand surgery. *Hand*. 2023;18(4):701–707. doi: 10.1177/15589447211063585.
- [27] Lebin JA, Chen BC, Valento MJ. Reversal of pediatric opioid toxicity with take-home naloxone: a case report. *J Med Toxicol*. 2019;15(2):134–135. doi: 10.1007/s13181-018-0695-z.
- [28] NIDA. Naloxone DrugFacts. National Institute on Drug Abuse; 2022 [updated 2022 Jan 11; cited 2024 Jan 2]. Available from: <https://nida.nih.gov/publications/drugfacts/naloxone#:~:text=Research%20indicates%20that%20clinicians%20prescribing>

- [29] Guy GPJr., Zhang K. Opioid prescribing by specialty and volume in the U.S. *Am J Prev Med.* 2018;55(5):e153–e155. doi: [10.1016/j.amepre.2018.06.008](https://doi.org/10.1016/j.amepre.2018.06.008).
- [30] Madden K, Reddy AS, De La Cruz MJ, et al. Patterns of storage, use, and disposal of prescription opioids by parents of children with cancer. *J Pain Symptom Manage.* 2020;59(2):320–326. doi: [10.1016/j.jpainsymman.2019.09.018](https://doi.org/10.1016/j.jpainsymman.2019.09.018).
- [31] Gummin DD, Mowry JB, Beuhler MC, et al. 2022 Annual report of the National Poison Data System((R)) (NPDS) from America's Poison Centers((R)): 40th annual report. *Clin Toxicol.* 2023;61(10):717–939. doi: [10.1080/15563650.2023.2268981](https://doi.org/10.1080/15563650.2023.2268981).
- [32] Krawczyk N, Rivera BD, Jent V, et al. Has the treatment gap for opioid use disorder narrowed in the U.S.: A yearly assessment from 2010 to 2019. *Int J Drug Policy.* 2022;110:103786. doi: [10.1016/j.drugpo.2022.103786](https://doi.org/10.1016/j.drugpo.2022.103786).
- [33] Taylor EA, Cantor JH, Bradford AC, et al. Trends in methadone dispensing for opioid use disorder after Medicare payment policy changes. *JAMA Netw Open.* 2023;6(5):e2314328. doi: [10.1001/jamanetworkopen.2023.14328](https://doi.org/10.1001/jamanetworkopen.2023.14328).
- [34] Ghanem N, Dromgoole D, Hussein A, et al. Review of medication-assisted treatment for opioid use disorder. *J Osteopath Med.* 2022;122(7):367–374. doi: [10.1515/jom-2021-0163](https://doi.org/10.1515/jom-2021-0163).
- [35] NIDA. How do medications to treat opioid addiction work? National Institute on Drug Abuse; 2021 [updated 2021 Apr 13]. Available from: <https://www.nida.nih.gov/publications/research-reports/medications-to-treat-opioid-addiction/how-do-medications-to-treat-opioid-addiction-work>
- [36] Mattick RP, Breen C, Kimber J, et al. Methadone maintenance therapy versus no opioid replacement therapy for opioid dependence. *Cochrane Database Syst Rev.* 2009;2009(3):CD002209. doi: [10.1002/14651858.CD002209.pub2](https://doi.org/10.1002/14651858.CD002209.pub2).
- [37] Wakeman SE, Larochelle MR, Ameli O, et al. Comparative effectiveness of different treatment pathways for opioid use disorder. *JAMA Netw Open.* 2020;3(2):e1920622. doi: [10.1001/jamanetworkopen.2019.20622](https://doi.org/10.1001/jamanetworkopen.2019.20622).
- [38] Kumar R, Viswanath O, Saadabadi A, et al. Buprenorphine. Treasure Island (FL): StatPearls; 2024.
- [39] Whelan PJ, Remski K. Buprenorphine vs methadone treatment: a review of evidence in both developed and developing worlds. *J Neurosci Rural Pract.* 2012;3(1):45–50. doi: [10.4103/0976-3147.91934](https://doi.org/10.4103/0976-3147.91934).
- [40] Kim HK, Smiddy M, Hoffman RS, et al. Buprenorphine may not be as safe as you think: a pediatric fatality from unintentional exposure. *Pediatrics.* 2012;130(6):e1700–e1703. doi: [10.1542/peds.2012-1342](https://doi.org/10.1542/peds.2012-1342).
- [41] Lo Re M, Chaplin M, Aronow B, et al. Buprenorphine overdose in young children: an underappreciated risk. *Clin Pediatr.* 2019;58(6):613–617. doi: [10.1177/0009922819829038](https://doi.org/10.1177/0009922819829038).
- [42] Institute U. Medicaid prescriptions for extended-release medications to treat opioid use disorder; 2021 [cited 2023 Nov 30].
- [43] Wang GS, Severtson SG, Bau GE, et al. Unit-dose packaging and unintentional buprenorphine-naloxone exposures. *Pediatrics.* 2018;141(6):e20174232. doi: [10.1542/peds.2017-4232](https://doi.org/10.1542/peds.2017-4232).
- [44] So T, Wertheimer A. Unit-of-Use Versus Traditional Bulk Packaging. *Innovations in Pharmacy* [Internet]. 2012 Jan 1 [cited 2024 Apr 1];3(1):3. Available from: <https://pubs.lib.umn.edu/index.php/innovations/article/view/251>
- [45] Mallama CA, Trinidad JP, Swain RS, et al. A comparison of opioid-involved fatalities captured in the National Poison Data System to data derived from US death certificate literal text. *Pharmacoepidemiol Drug Saf.* 2019;28(10):1377–1385. doi: [10.1002/pds.4869](https://doi.org/10.1002/pds.4869).
- [46] Hoyt BT, Rasmussen R, Giffin S, et al. Poison center data accuracy: a comparison of rural hospital chart data with the TESS database. *Toxic Exposure Surveillance System. Acad Emerg Med.* 1999;6(8):851–855. doi: [10.1111/j.1553-2712.1999.tb01220.x](https://doi.org/10.1111/j.1553-2712.1999.tb01220.x).
- [47] Patel MM, Travers CD, Stockwell JA, et al. Reducing Childhood Admissions to the PICU for Poisoning (ReCAP2) by predicting unnecessary PICU admissions after acute intoxication. *Pediatr Crit Care Med.* 2018;19(2):e120–e129. doi: [10.1097/PCC.0000000000001410](https://doi.org/10.1097/PCC.0000000000001410).