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National Trends in Hospitalizations for Opioid Poisonings Among Children and Adolescents, 1997 to 2012

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Abstract

IMPORTANCE—National data show a parallel relationship between recent trends in opioid prescribing practices and hospitalizations for opioid poisonings in adults. No similar estimates exist describing hospitalizations for opioid poisonings in children and adolescents.

OBJECTIVE—To describe the incidence and characteristics of hospitalizations attributed to opioid poisonings in children and adolescents.

DESIGN, SETTING, AND PARTICIPANTS—Retrospective analysis of serial cross-sectional data from a nationally representative sample of US pediatric hospital discharge records collected every 3 years from January 1, 1997, through December 31, 2012. The Kids' Inpatient Database was used to identify 13 052 discharge records for patients aged 1 to 19 years who were hospitalized for opioid poisonings. Data were analyzed within the collection time frame.

MAIN OUTCOMES AND MEASURES—Poisonings attributed to prescription opioids were identified by codes from the *International Classification of Diseases, Ninth Revision, Clinical Modification*. In adolescents aged 15 to 19 years, poisonings attributed to heroin were also

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identified. Census estimates were used to calculate incidence per 100 000 population. The Cochran-Armitage test for trend was used to assess for changes in incidence over time.

RESULTS—From 1997 to 2012, a total of 13 052 (95% CI, 12 500–13 604) hospitalizations for prescription opioid poisonings were identified. The annual incidence of hospitalizations for opioid poisonings per 100 000 children aged 1 to 19 years rose from 1.40 (95% CI, 1.24–1.56) to 3.71 (95% CI, 3.44–3.98), an increase of 165% (*P* for trend, <.001). Among children 1 to 4 years of age, the incidence increased from 0.86 (95% CI, 0.60–1.12) to 2.62 (95% CI, 2.17–3.08), an increase of 205% (*P* for trend, <.001). For adolescents aged 15 to 19 years, the incidence increased from 3.69 (95% CI, 3.20–4.17) to 10.17 (95% CI, 9.48–10.85), an increase of 176% (*P* for trend, <.001). In this age group, poisonings from heroin increased from 0.96 (95% CI, 0.75–1.18) to 2.51 (95% CI, 2.21–2.80), an increase of 161% (*P* for trend, <.001); poisonings involving methadone increased from 0.10 (95% CI, 0.03–0.16) to 1.05 (95% CI, 0.87–1.23), an increase of 950% (*P* for trend, <.001).

CONCLUSIONS AND RELEVANCE—During the course of 16 years, hospitalizations attributed to opioid poisonings rose nearly 2-fold in the pediatric population. Hospitalizations increased across all age groups, yet young children and older adolescents were most vulnerable to the risks of opioid exposure. Mitigating these risks will require comprehensive strategies that target opioid storage, packaging, and misuse.

Poisonings attributed to prescription drugs are now the leading cause of injury-related mortality in the United States[1,2]; this epidemic is driven by the increased use of opioid analgesics to treat chronic pain.[3–6] From 1999 to 2010, retail sales of prescription opioids quadrupled,[4] and during this time, deaths attributed to opioid overdose rose 4-fold in those 15 to 64 years of age and 6-fold in those 15 to 24 years of age.[7] In 2014 alone, opioids were blamed for 18 893 deaths in the United States.[8]

These mortality data, however, represent only a fraction of the serious adverse events attributed to prescription opioids.[5,9–16] The increased availability of these medications has resulted in an unprecedented rise in opioid addiction and nonfatal overdoses.[5] Emergency department (ED) visits for opioid-related indications have risen substantially in children and adults during the past 2 decades; ED visits for prescription opioid overdose, abuse, and misuse now rival those for illicit drugs, including heroin and cocaine.[17–21] Even in children younger than 6 years, opioids, followed closely by benzodiazepines, now account for most of the drug poisonings in this age group[18]; in nearly all these poisonings, the child was exposed to a prescription intended for an adult in the household.[22]

How many children and adolescents are hospitalized each year for opioid poisonings and how hospitalization rates have changed over time remain unknown. In young adults and those middle-aged and older, inpatient hospitalizations for opioid-related indications, such as for opioid dependence, abuse, and overdose, have increased 2- and 5-fold, respectively, in less than a decade.[23,24] We hypothesized that similar trends in opioid poisonings have occurred in children and adolescents.

Therefore, the purpose of this study was to examine trends in hospitalizations for opioid poisonings in children and adolescents (aged 1–19 years). Moreover, because of the

association between prescription opioid misuse and progression to heroin use,[3,25–28] we examined trends in heroin overdose among those 15 to 19 years of age. In this same age group, we also examined poisonings attributed to methadone, a prescription opioid used to treat illicit and prescription opioid addiction and severe intractable pain. Recent analyses[29] have shown that despite the low frequency with which methadone is prescribed, it is responsible for a disproportionate number of drug poisonings. Given that opioids are already among the most widely prescribed medications in the United States—available in millions of US households[6,30]—and that the US Food and Drug Administration Recently approved the use of oxycodone hydrochloride (OxyContin) for children meeting certain criteria,[31] a clearer understanding of pediatric opioid-related morbidity and mortality is needed.

Methods

Study Overview

From a national database of pediatric hospitalizations, we identified children and adolescents admitted to US hospitals for opioid poisonings in 1997, 2000, 2003, 2006, 2009, and 2012. We conducted a retrospective analysis of serial cross-sectional data abstracted from the Kids' Inpatient Database (KID).[32] The KID, created by the Agency for Healthcare Research and Quality aspart of the Healthcare Cost and Utilization Project, is the only US database to provide all-payer data on pediatric services and clinical outcomes for children admitted as inpatients, routinely or through the ED.[32,33] This study involved deidentified data and was determined to be exempt from approval and the need for informed consent by the Yale School of Medicine's institutional review board.

The KID has been released every 3 years since 1997 and is compiled from a random sample of pediatric discharge records collected from acute-care hospitals across the United States (the unit of observation is the inpatient record, regardless of the length of stay).[32] For the most recent year of data, 2012, approximately 3.2 million records were selected from 4179 hospitals across 44 states. For a given year, 10%of uncomplicated hospital births and 80% of other pediatric hospitalizations (ie, patients younger than 19 years in 1997 and younger than 20 years beginning in 2000) are then sampled from among these records. Each discharge record is then weighted to facilitate national estimates. Weighting is accomplished by stratifying hospitals according to the following 6 characteristics: number of beds, teaching status, ownership or control (eg, private), hospital type (eg, children's hospital), rural or urban location, and US region. For each year of the KID, the unweighted database contains information on approximately 2 to 3 million annual pediatric discharges. When weighted, the KID provides estimates on approximately 6 to 7 million discharges.

Identification of the Sample

We identified hospitalizations attributed to opioid poisonings using diagnostic codes from the *International Classification of Disease, Ninth Revision, Clinical Modification* (*ICD-9-CM*).[34] Admissions for prescription opioid poisonings were identified by the following *ICD-9-CM* poisoning codes: 965.00 (opium), 965.02 (methadone), and 965.09 (other opiates and narcotics). Among those 15 to 19 years of age, we also identified admissions for illicit opioid poisonings using the *ICD-9-CM* code 965.01 (heroin). We restricted the heroin and

methadone analyses to those 15 to 19 years of age because most of these poisonings occurred in this age group.

To further characterize poisonings, we used E codes for external causes of injury to establish intent. These codes includedE850.xtoE858.x(unintentional[ie, accidental]),E950.0 to E950.5 (intentional [ie, suicide or self-inflicted]), and E980.x (undetermined).

We restricted the sample to those 1 to 19 (inclusive) years of age. Infants were excluded to primarily capture those poisonings related to self-administration. To be consistent with the age categories used by the Centers for Disease Control and Prevention WISQARS (Web-based Injury Statistics Query and Reporting System) for reporting fatal and nonfatal injuries,[35] we grouped children into the following age categories: 1 to 4, 5 to 9, 10 to 14, and 15 to 19 years. The estimates for those aged 5 to 9 years (n = 135, unweighted), however, did not meet the criteria[36] for statistical reliability, and thus are not shown.

Statistical Analysis

Data were collected and analyzed from January 1, 1997, to December 31, 2012. Descriptive statistics were used to characterize the sample according to each year of the KID. Differences according to demographic and clinical characteristics were assessed with χ^2 tests for categorical variables and, as appropriate, 2-tailed *t* tests, analysis of variance, or Wilcoxon rank sum tests for continuous variables.

Nationally representative estimates were calculated using methods that take into account the complex survey design of the KID. Specifically, we used weights, strata, and cluster variables provided by the Healthcare Cost and Utilization Project to produce weighted estimates and SEs, which were then used to establish 95% CIs.[37] Unless otherwise noted, all counts, proportions, and incidence rates are based on weighted estimates.

To calculate the annual incidence of hospitalizations, we divided the weighted number of hospitalizations for opioid poisonings for a given year by the intercensal number of children at risk in that year.[38] The Cochran-Armitage test for trend[39] was used to assess changes in incidence over time.

All analyses were performed using SAS software (version 9.3; SAS Institute Inc). We applied a 2-sided statistical significance level of .05 to all analyses.

Results

Demographic Characteristics

Among children and adolescents aged 1 to 19 years admitted to US hospitals every 3 years from 1997 through 2012, we identified a total of 13 052 (95% CI, 12 500–13 604) hospitalizations for prescription opioid poisonings. Demographic characteristics for each of the 6 assessment periods are shown in the Table. Those in the oldest group accounted for the largest proportion of poisonings, whereas those aged 5 to 9 years accounted for the smallest. In 1997, males accounted for 34.7% (95% CI, 31%−39%) of hospitalizations; by 2012, this proportion was 47.4% (95% CI, 45%−50%). Children were predominately white (73.5%;

95% CI, 72%−75%) and covered by private insurance (48.8%; 95% CI, 48%−50%); however, the proportion insured by Medicaid increased from 24.1% (95% CI, 20%−28%) in 1997 to 44.0% (95% CI, 42%−46%) in 2012 (*P* for trend, <.001). Across the 6 years of the KID, 176 children (1.3%; 95% CI, 1.1%−1.6%) died during hospitalization (in compliance with Healthcare Cost and Utilization Project privacy protections, we do not present these data stratified by year because of small cell frequencies).

Trends in Hospitalizations for Prescription Opioid Poisonings

From 1997 to 2012, the annual incidence of hospitalizations for opioid poisonings per 100 000 children rose from 1.40 (95% CI, 1.24–1.56) to 3.71 (95% CI, 3.44–3.98), an increase of 165% (*P* for trend, <.001). As shown in Figure 1 and eTable 1 in the Supplement, when examined by age category, the greatest change occurred among the group aged 1 to 4 years, among whom the incidence rose from 0.86 (95% CI, 0.60–1.12) in 1997 to 2.62 (95% CI, 2.17–3.08) in 2012, an increase of 205% (*P* for trend, <.001). For adolescents aged 15 to 19 years, the incidence rose from 3.69 (95% CI, 3.20–4.17) in 1997 to 10.17 (95% CI, 9.48–10.85) in 2012, an increase of 176% (*P* for trend, <.001).

When prescription opioid poisonings were examined by intent, among children younger than 10 years, 16 poisonings (0.92%; 95% CI, 0.37%−1.47%) were attributed to suicide or self-inflicted injury from 1997 to 2012. In children 10 to 14 years of age, the incidence of poisonings attributed to suicide or self-inflicted injury increased from 0.62 (95% CI, 0.44–0.79) in 1997 to 0.85 (95% CI, 0.68–1.02) in 2012, an increase of 37% (*P* for trend, <.001). The incidence of poisonings attributed to accidental intent increased from 0.17 (95% CI, −0.04 to 0.39) in 1997 to 0.31 (95% CI, 0.21 to 0.42) in 2012, an increase of 82% (*P* for trend, <.001).

These trends were more marked in adolescents 15 to 19 years of age. Poisonings attributed to suicide or self-inflicted injury increased by 140% (*P* for trend, <.001), whereas those attributed to accidental intent increased 303% (*P* for trend, <.001). Incidence rates, stratified by year, for this age group are shown in Figure 2 and eTable 2 in the Supplement.

Trends in Hospitalizations for Heroin and Methadone Poisonings Among 15- to 19-Year-Olds

As shown in Figure 3 and eTable 2 in the Supplement, prescription opioids accounted for most opioid poisonings across all time points. However, poisonings involving heroin increased from 0.96 (95% CI, 0.75–1.18) in 1997 to 2.51 (95% CI, 2.21–2.80) in 2012, an increase of 161% (*P* for trend, <.001). Poisonings involving methadone increased from 0.10 (95% CI, 0.03–0.16) in 1997 to 1.05 (95% CI, 0.87–1.23) in 2012, an increase of 950% (*P* for trend, <.001).

Discussion

Using a nationally representative sample of pediatric hospital discharge records, we found that the incidence of hospitalizations for prescription opioid poisonings among children and adolescents 1 to 19 years of age increased nearly 2-fold from 1997 to 2012. Although rates increased across all age groups, the largest percentage increase occurred among the youngest

children aged 1 to 4 years. The second largest increase occurred among adolescents 15 to 19 years of age, among whom hospitalizations for prescription opioid and heroin poisoning increased. Adolescents in this age group had the highest incidence overall for each of the 6 years examined.

In contrast to poisoning intent in younger children, poisonings in those older than 10 years were primarily attributed to suicide or self-inflicted injury. During the 16-year period, poisonings attributed to suicide or self-inflicted injury among those aged 15 to 19 years increased by 140%. These data underscore the dangers associated with the widespread availability of prescription opioids, particularly for adolescents at risk for depression (many adolescents are also thought to self-medicate with prescription opioids).[16,40]

Although poisonings attributed to suicide or self-inflicted injury among those aged 15 to 19 years exceeded those attributed to accidental poisonings across all time points, accidental poisonings increased at a more rapid rate, 3-fold from 1997 to 2012. Increasing rates of prescription opioid misuse and abuse, rather than therapeutic errors or adverse effects among adolescents prescribed opioids for pain management, are likely driving these trends in accidental poisonings.[19]

Mirroring demographic trends seen in adults,[23,24] we found that approximately three-quarters of hospitalizations occurred in white individuals. Similarly, private insurers were found to be the largest payer. However, the percentage of hospitalizations covered by private payers decreased over time, whereas the percentage paid by Medicaid increased. In 2012, Medicaid covered 44.0% of hospitalizations for pediatric opioid poisonings, up from 24.1% in 1997. This change may reflect trends in Medicaid payments for all hospitalizations; from 1997 to 2011, the percentage of hospitalizations where Medicaid was the primary payer increased by 34%.[41] This increase, however, has largely been attributed to a rise in hospitalizations for a small number of conditions. Thus, the shift over time in payers for opioid hospitalizations may instead be indicative of the widening effect of opioid use across sociodemographic groups.

This study—to our knowledge, the first to extensively examine pediatric hospitalizations due to opioid poisonings— contributes to a broader understanding of the public health crisis caused by the now widespread availability of prescription opioids in the United States. Our findings are consistent with previous research demonstrating that as physicians have increasingly relied on prescription opioids to treat chronic pain during the past 2 decades, rates for opioid poisonings have risen in tandem.[1–4,9] For young children, calls to poisoning control centers for opioid ingestion have increased markedly in recent years,[19,20,22] as have ED visits across all age groups.[17–21] In addition, a number of studies have examined trends in ED visits and subsequent hospitalizations for pharmaceutical poisonings and found that prescription opioids were among the most commonly implicated medications and that these poisonings frequently resulted in hospital admission.[17,19,20]

Emerging data suggest that in recent years physicians have been prescribing opioids less frequently. From 2011 to 2013, the number of opioid prescriptions dispensed in the United States slightly decreased.[25,42] Our data show a similar marginal decrease in the overall

incidence of hospitalizations for prescription opioid poisonings from 2009 to 2012. This change, however, was driven entirely by a slight (7%) but statistically significant decrease in hospitalizations among those aged 15 to 19 years. In contrast, in this age group, hospitalizations involving heroin overdose continued to rise. This finding is consistent with research suggesting that prescription opioid abuse may be a precursor to initiation of heroin use,[3,25–28] which can be explained in part by the low cost of heroin compared with opioid analgesics such as oxycodone.[26–28]

Notably, we found that the incidence of hospitalizations for methadone poisonings increased 950% among 15-to19-year-olds from 1997 to 2012. Methadone is among the most misused of prescription drugs and is commonly diverted for illicit (nonmedical) purposes, such as getting high or to enhance the effects of alcohol or other drugs.[3] Our data suggest that the incidence of poisonings attributed to methadone misuse may be slowing. From 2009 to 2012, hospitalization rates for methadone misuse decreased slightly among those aged 15 to 19 years. These findings are consistent with recent data showing that rates for prescription opioid abuse, misuse, and diversion for nonmedical use have plateaued or decreased in the general adult population.[43] Declining rates for abuse and diversion have also been seen among those aged 12 to 17 years.[44]

Nonmedical use of prescription opioids, nevertheless, remains a substantial problem, particularly for adolescents. In 1 study,[44,45] nearly 10% of high school seniors reported using opioids nonmedically. Although most acquired these medications from family and friends, the source for nearly 40% of students was their own prior prescription.[46] This information is in keeping with findings that adolescents are frequently prescribed opioids for common injury- and non–injury-related indications.[46] A recent study of ambulatory care visits in the United States, for example, reports that from 2005 to 2007, opioids were prescribed at 22% of visits among adolescents presenting with back pain.[47] A separate study of commercial medical and pharmacy claims data from 2007 to 2008 found that nearly 50% of patients aged 13 to 17 years presenting with first-time complaints of headache received an opioid prescription during the 2-year follow-up, and nearly one-third received 3 or more prescriptions.[31] Of note, the US Food and Drug Administration recently extended the off-label use of oxycodone for children as young as 11 years with certain types of intractable pain—namely cancer pain.[48] Despite these trends, however, the new national opioid prescribing guidelines[49] by the Centers for Disease Control and Prevention fail to include recommendations for patients younger than 18 years.[50]

Limitations

This study has at least 4 limitations. The major limitation is that the national estimates are based on *ICD-9-CM* codes, which are subject to miscoding and errors of omission. Although limited data are available regarding the accuracy of opioid poisoning codes, validation studies involving other common pediatric medications (eg, acetaminophen) support the use of *ICD-9-CM* codes for identifying poisonings in children.[51] Second, we were unable to provide a full clinical picture or psychosocial profile (eg, the circumstances that led to the poisoning) of the children admitted for opioid poisonings or to validate the poisoning codes with toxicologic results. Similarly, we were not able to distinguish between opioids

prescribed for chronic pain and those, such as buprenorphine hydrochloride and methadone, prescribed for opioid dependence (ie, methadone maintenance treatment). Third, each record within the KID represents a hospitalization; thus, children admitted within a given year for 1 or more repeated opioid poisonings would be counted multiple times. We believe, however, that this limitation is minor because such instances are likely rare. Finally, similar to other recent studies[17,19,20] examining trends in opioid poisonings in the young, we lacked the data to determine whether the trends we report continued beyond 2012.

Conclusions

The current public health crisis caused by prescription opioids is a systemic issue that affects individuals across the age spectrum. To date, numerous initiatives at the local, state, and federal levels have been implemented to combat prescription opioid poisonings and overdose; most of these efforts, however, have focused on modifying physician prescribing practices for those treating adults with chronic pain.[52] The full effect of these initiatives remains to be seen, but recent data indicate that the United States is making progress in gaining control of the epidemic caused by opioid analgesics.[3]

Our research, however, suggests that poisonings by prescription and illicit opioids are likely to remain a persistent and growing problem in the young unless greater attention is directed toward the pediatric community, who make up nearly one-quarter of the US population. A combination of public health interventions (eg, parental education), policy initiatives, and consumer-product regulations is needed to reduce pediatric exposure to opioids.[50,52] In addition, further resources should be directed toward addressing opioid misuse and abuse during adolescence. Of particular importance are prevention programs that address the overlap in opioid misuse and depression among adolescents.[16] Finally, for clinicians who treat acute and chronic pain in children, national clinical practice guidelines for opioid prescribing that include pediatric-specific recommendations are urgently needed.[50]

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Key Points

Question

How has the prescription opioid epidemic affected pediatric hospitalization rates in the United States?

Findings

This retrospective analysis of 13 052 national hospital discharge records found that pediatric hospitalizations for opioid poisonings increased nearly 2-fold from 1997 to 2012. Hospitalization rates were highest in older adolescents, but the largest percentage increase in hospitalizations over time occurred among the youngest children (toddlers and preschoolers).

Meaning

Reducing pediatric opioid exposure and misuse will require a combination of public health interventions, policy initiatives, and consumer-product regulations.

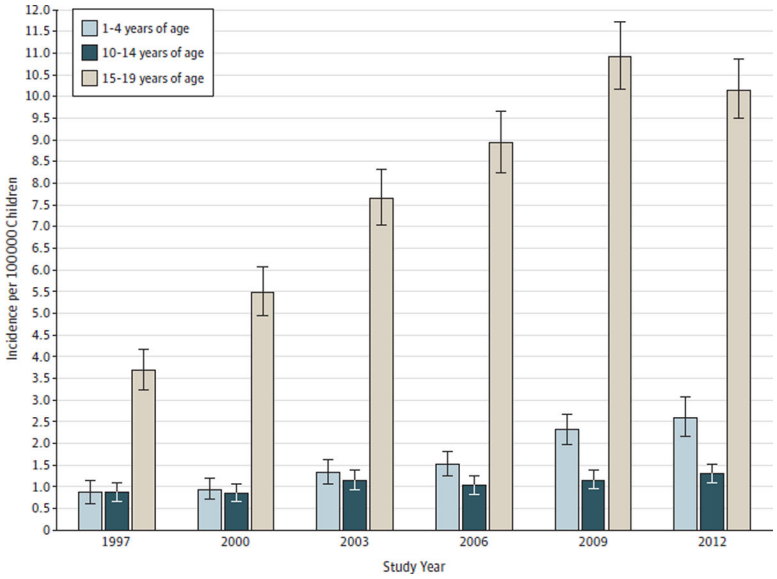

Figure 1. Weighted National Estimates of Temporal Trends in Hospitalizations for Prescription Opioid Poisonings Stratified by Age Category

Error bars indicate 95% CI (*P* for trend, <.001 for all ages). Estimates for 5- to 9-year-olds do not meet the criteria for statistical reliability and thus are not shown.

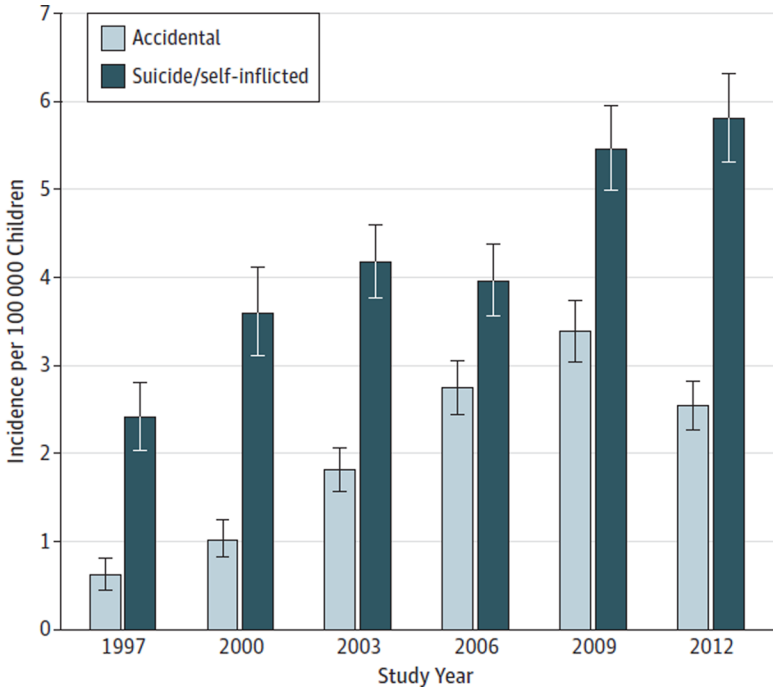

Figure 2. Weighted National Estimates of Temporal Trends in Prescription Opioid Poisonings by Intent in the Group Aged 15 to 19 Years

Error bars indicate 95% CI (*P* for trend, <.001 for poisonings attributed to accidental and suicidal intent).

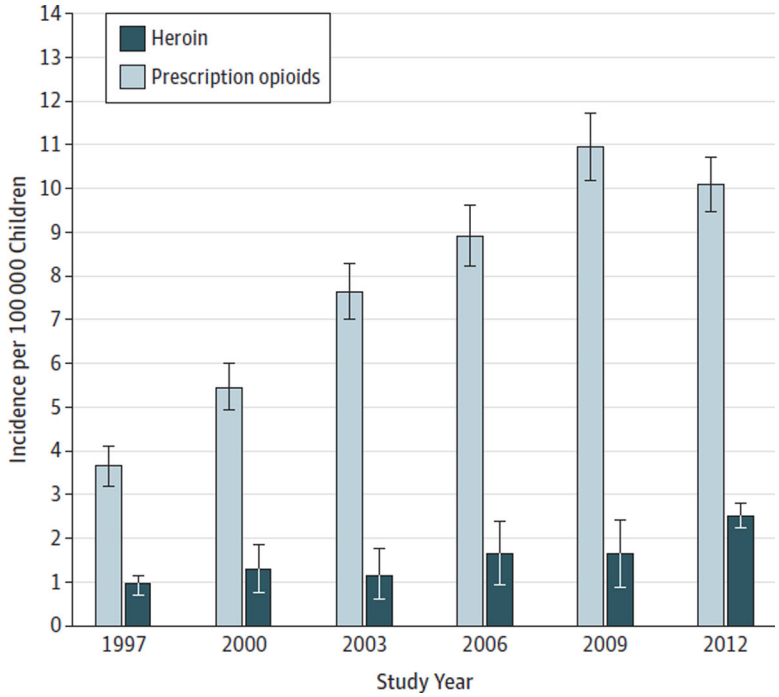

Figure 3. Weighted National Estimates of Temporal Trends in Hospitalizations for Illicit vs Prescription Opioid Poisonings in the Group Aged 15 to 19 Years

Error bars indicate 95% CI (*P* for trend, <.001 for poisonings attributed to heroin and prescription opioid drug use).

Table.

Weighted National Estimates of Demographic and Clinical Characteristics According to Year of Hospitalization for Prescription Opioid Poisoning

	Study Year, No. (%) of Patients						
Characteristic	**1997**	**2000**	**2003**	**2006**	**2009**	**2012**	***P* Value[a]**
Weighted No. of hospitalizations (95% Cl)	1049 (931–1167)	1474 (1333–1615)	2090 (1941–2238)	2436 (2267–2605)	3084 (2884–3283)	2918 (2706–3130)	NA
Age group, y							
1–4	133 (12.7)	146 (9.9)	210 (10.0)	244 (10.0)	377 (12.2)	421 (14.4)	<.001
5–9[b]	NA	NA	NA	NA	NA	NA	
10–14	171(16.3)	176(11.9)	247 (11.8)	216(8.9)	240 (7.8)	271 (9.3)	
15–19	715 (68.2)	1116(75.7)	1595 (76.3)	1950 (80.0)	2427 (78.7)	2171 (74.4)	
Male sex	364 (34.7)	661 (44.8)	976 (46.7)	1305 (53.5)	1636 (53.0)	1382 (47.4)	<.001
Race or ethnicity							
White	550(72.0)	938 (76.5)	1056 (72.3)	1270(75.2)	1907 (75.0)	1886 (70.6)	<.001
Black	118(15.4)	117 (9.5)	184(12.6)	152 (9.0)	251 (9.9)	315(11.8)	
Hispanic	64 (8.4)	118(9.6)	141 (9.7)	156(9.2)	210 (8.3)	271 (10.1)	
Other	33 (4.3)	54 (4.4)	80 (5.5)	111(6.6)	173 (6.8)	198 (7.4)	
Insurance							
Medicaid	253 (24.1)	392 (26.6)	651 (31.1)	816(33.5)	1164(38.0)	1280 (44.0)	<.001
Private	643 (61.4)	824 (56.4)	1107 (53.0)	1163 (47.9)	1362 (44.4)	1249 (43.0)	
Self-pay	103 (9.8)	190(13.0)	224(10.7)	312 (12.8)	356(11.6)	243 (8.4)	
Other	49 (4.7)	56 (3.8)	107(5.1)	140 (5.8)	184 (6.0)	133 (4.6)	

Abbreviation: NA, not applicable.

[a]Calculated using the χ^2 test.

[b]Estimates that do not meet the criteria for statistical reliability are not shown.