

# Hospitalizations for Poisoning by Prescription Opioids, Sedatives, and Tranquilizers

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**Background:** Unintentional poisoning deaths have been increasing dramatically over the past decade, and the majority of this increase has resulted from overdoses of specific prescription drugs. Despite this trend, there are limited existing data examining hospitalizations for poisonings, both unintentional and intentional, associated with prescription drugs. A better understanding of these hospitalizations may help identify high-risk populations in need of intervention to prevent subsequent mortality.

**Purpose:** This article aims to describe the incidence and characteristics of hospitalizations resulting from poisoning by prescription opioids, sedatives, and tranquilizers in the U.S. from 1999 to 2006 and make comparisons to hospitalizations for all other poisonings during this time period.

**Methods:** Hospitalizations for poisonings were selected from the Nationwide Inpatient Sample (NIS), a stratified, representative sample of approximately 8 million hospitalizations each year, according to the principal discharge diagnosis. Intentionality of the poisoning was determined by external cause of injury codes. SAS callable SUDAAN software was used to calculate weighted estimates of poisoning hospitalizations by type and intentionality. Demographic and clinical characteristics of poisoning cohorts were compared. Data were analyzed in 2009.

**Results:** From 1999 to 2006, U.S. hospitalizations for poisoning by prescription opioids, sedatives, and tranquilizers increased a total of 65%. This increase was double the increase observed in hospitalizations for poisoning by other drugs and substances. The largest increase in the number of hospitalized cases over the 7-year period was seen for poisonings by benzodiazepines, whereas the largest percentage increase was observed for methadone (400%). In comparison to patients hospitalized for poisoning from other substances, those hospitalized for prescription opioids, sedatives, and tranquilizers were more likely to be women, aged >34 years, and to present to a rural or urban nonteaching hospital.

**Conclusions:** Prescription opioids, sedatives, and tranquilizers are an increasing cause of hospitalization. The hospital admission provides an opportunity to better understand the contextual factors contributing to these cases, which may aid in the development of targeted prevention strategies.

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## Introduction

Unintentional poisoning is now the second-leading cause of unintentional injury death in the U.S.<sup>1</sup> Among people aged 35–54 years, unintentional poisoning surpassed motor-vehicle crashes as the leading cause of unintentional injury death in 2005. Although several high-profile cases involving Hollywood celebrities have brought the problem to recent public attention, the rates of unintentional poisoning deaths have been increasing for more than 15 years.<sup>2</sup> From 1999 to 2004, unintentional drug poisoning deaths increased by 68%,<sup>3</sup> and the majority of this increase has been attributed to deaths associated with pre-

scription opioid analgesics.<sup>4</sup> In addition to opioids, other controlled substances including those classified as sedatives or tranquilizers (e.g., diazepam, alprazolam, phenobarbital) have been found to contribute to the recent rise in unintentional overdose fatalities.<sup>5</sup>

In the 1990s, several initiatives<sup>6–9</sup> were undertaken to increase awareness of the problem of inadequately treated pain. Since this time, data collected by the Drug Enforcement Agency<sup>10</sup> have shown substantial increases in the total quantity of opioids prescribed in the U.S. Along with the increase in legitimate use of opioids, the use of these drugs for recreational purposes has also increased. In 2007, the nonmedical use of prescription drugs ranked second to only marijuana as the most prevalent category of drug abuse (excluding alcohol), and was the category with the largest number of new initiates.<sup>11</sup> From 2004 to 2006, emergency department visits associated with prescription drugs increased by 44%, whereas there was no corresponding increase in emergency department visits associated with illegal drugs.<sup>12</sup>

Despite these recent trends, there are limited data examining hospitalizations for unintentional poisonings and the associated characteristics of these patients. Although emergency department data can demonstrate the prevalence and trends among nonfatal cases, these data provide little specific information on the most serious cases requiring hospitalization. To our knowledge, no previous report has de-

scribed the incidence and characteristics of hospitalizations for unintentional poisonings associated with prescription opioids, sedatives, and tranquilizers. In addition, few studies have examined the relative contribution of these prescription drugs to intentional overdoses. Hospitalization data may improve understanding of the epidemiology of this problem and may also help delineate a high-risk population in need of specific interventions.

The objective of this study was to describe hospitalizations for poisonings in the U.S. from 1999 to 2006 with specific focus on poisonings from prescription opioids, sedatives, and tranquilizers. For the current study, the focus was on these classes of drugs because of their well-documented contribution to the increasing number of poisoning fatalities. Both intentional and unintentional drug poisonings were examined, and hospitalizations for prescription opioids, sedatives, and tranquilizers were compared with hospitalizations for all other poisonings to determine similarities and differences within selected demographic and clinical variables.

## Methods

### Design

Data were obtained from the Nationwide Inpatient Sample (NIS), a data set from the Agency for Healthcare Research and Quality's Healthcare Cost and Utilization Project (HCUP), for the 7-year

**Table 1.** National estimates of U.S. poisoning hospitalizations by substances and intent, 1999–2006<sup>a</sup>

	1999	2000	2001
<b>Prescription opioids, sedatives, and tranquilizers</b>	43,210 (41,763, 44,691)	48,310 (46,739, 49,914)	54,332 (52,786, 55,906)
	24.9 (24.0, 25.7)	26.5 (25.6, 27.3)	27.6 (26.8, 28.4)
Intentional	10,385 (9,849, 10,941)	11,054 (10,468, 11,662)	11,692 (11,047, 12,363)
	24.1 (22.8, 25.3)	22.9 (21.7, 24.1)	21.5 (20.3, 22.8)
Unintentional	24,342 (23,590, 25,087)	26,742 (25,913, 27,565)	29,619 (28,758, 30,474)
	56.3 (54.6, 58.1)	55.4 (53.6, 57.1)	54.5 (52.9, 56.1)
Unknown intent	8,483 (7,667, 9,363)	10,514 (9,614, 11,473)	13,022 (12,059, 14,037)
	19.6 (17.7, 21.7)	21.8 (19.9, 23.8)	24.0 (22.2, 25.8)
<b>Other drugs, medicinal, and biological substances</b>	130,670 (129,189, 132,117)	134,369 (132,764, 135,940)	142,440 (140,866, 143,986)
	75.2 (74.3, 76.0)	73.6 (72.7, 74.4)	72.4 (71.6, 73.2)
Intentional	37,479 (35,452, 39,575)	35,242 (33,332, 37,220)	35,938 (34,093, 37,848)
	28.7 (27.1, 30.3)	26.2 (24.8, 27.7)	25.2 (23.9, 26.6)
Unintentional	66,430 (64,015, 68,843)	68,292 (65,905, 70,677)	72,362 (69,863, 74,857)
	50.8 (49.0, 52.7)	50.8 (49.1, 52.6)	50.8 (49.1, 52.6)
Unknown intent	26,760 (24,255, 29,452)	30,835 (28,348, 33,470)	34,140 (31,384, 37,058)
	20.5 (18.6, 22.5)	23.0 (21.1, 24.9)	24.0 (22.0, 26.0)
<b>All other hospital admissions</b>	35,467,714	36,417,575	37,187,646

Note: Values are *n* (95% CI) and % total (95% CI).

<sup>a</sup>Hospitalization numbers and rates are weighted estimates.

period 1999–2006, and were analyzed in 2009. The NIS is the largest inpatient database in the U.S., and contains data for approximately 8 million hospitalizations each year. Because it contains a stratified sampling of U.S. community hospitals, NIS data can be weighted to produce national estimates. The sampling frame for the 2006 NIS contained 1045 hospitals in 38 states that represented approximately 90% of all hospital discharges in the U.S.<sup>13</sup> This sampling frame changes annually, depending on the number of states participating in HCUP, and weighting adjustments are made annually by HCUP staff to account for these changes.

Approximately 5% of the principal diagnoses in the NIS are for some type of injury, and approximately 86% of these injury diagnoses have an external cause of injury code.<sup>14</sup> These injury diagnoses include poisonings, and drug overdoses are included as a form of poisoning. Data from the NIS have been used to estimate hospitalizations for various injuries such as all-terrain-vehicle accidents<sup>15</sup> and firearm-related injuries.<sup>16</sup> The NIS Trends Supplemental files<sup>17</sup> were used to facilitate multiyear trend estimation and ensure that data elements were consistently defined across all data years. The West Virginia University IRB waived the requirement for review of this research because NIS data are deidentified.

### Selecting Poisoning Hospitalizations

Hospitalizations for drug poisonings were selected from the NIS ICD-9-CM diagnosis codes.<sup>18</sup> Although the NIS provides up to 15 diagnoses per record, cases were selected based solely on the principal diagnosis field, in order to specify that it was the condition responsible for the admission of the patient to the hospital. Any

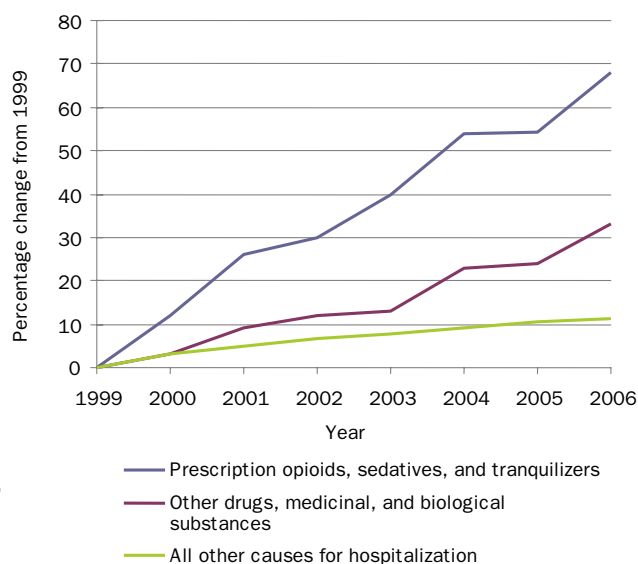
case having a principal ICD-9-CM code in the Poisonings by Drugs, Medicinal, and Biological Substances injury category (ICD-9-CM 960–979) was selected for inclusion in the study. The following codes within this injury category were defined as poisonings by prescription opioids, sedatives, and tranquilizers: 965.02 (methadone); 965.09 (other narcotics including codeine, meperidine, morphine); 965.5 (pyrazole derivatives); 965.8 (pentazocine); 967.0 (barbiturates); 969.4 (benzodiazepine-based tranquilizers); 969.5 (other tranquilizers including hydroxyzine, meprobamate); 967.8 (other sedatives and hypnotics); and 967.9 (unspecified sedatives and hypnotics). All other cases with a principal ICD-9-CM code within the 960–979 range, excluding the codes specified above, were defined as poisonings by other drugs, medicinal, and biological substances. Poisoning hospitalizations for substances such as heroin (965.01); cocaine (968.5 and 970.8); acetaminophen (965.4); and antidepressants (969.0) were all included in this other drug category.

### Determining Intentionality of the Poisoning

Intentionality of the poisoning was determined by examining the presence of Supplementary Classification of External Causes of Injury and Poisoning codes (E-codes).<sup>18</sup> The NIS provides up to four E-codes per record, and poisoning injuries were defined as intentional, unintentional, or undetermined based on the presence of the codes in any of the four E-code fields on each record. Poisonings were classified as unintentional if there was an E-code present in the E850–E858 range (accidental poisonings by drugs, medicinal substances, and biologicals) and intentional if there was an E-code present in the E950.0–E950.5 range (suicide and self-

**Table 1.** National estimates of U.S. poisoning hospitalizations by substances and intent, 1999–2006<sup>a</sup> (continued)

2002	2003	2004	2005	2006
56,488 (54,913, 58,090)	60,308 (58,554, 62,092)	65,885 (64,010, 67,792)	65,956 (63,815, 68,139)	71,355 (69,179, 73,571)
28.0 (27.2, 28.8)	29.1 (28.3, 30.0)	29.1 (28.2, 29.9)	28.9 (27.9, 29.8)	29.1 (28.2, 30.0)
14,593 (13,928, 15,279)	17,180 (16,432, 17,949)	18,658 (17,886, 19,451)	19,926 (19,106, 20,766)	23,844 (22,762, 24,952)
25.8 (24.7, 27.1)	28.5 (27.3, 29.8)	28.3 (27.2, 29.5)	30.2 (29.0, 31.5)	33.4 (31.9, 35.0)
29,304 (28,385, 30,222)	30,705 (29,753, 31,655)	34,089 (33,123, 35,052)	32,595 (31,624, 33,567)	33,402 (32,298, 34,511)
51.9 (50.3, 53.5)	50.9 (49.3, 52.5)	51.7 (50.3, 53.2)	49.4 (48.0, 50.9)	46.8 (45.3, 48.4)
12,590 (11,573, 13,671)	12,423 (11,322, 13,601)	13,138 (12,053, 14,294)	13,435 (12,351, 14,588)	14,109 (12,861, 15,446)
22.3 (20.5, 24.2)	20.6 (18.8, 22.6)	19.9 (18.3, 21.7)	20.4 (18.7, 22.1)	19.8 (18.0, 21.7)
145,151 (143,549, 146,727)	146,739 (144,955, 148,492)	160,741 (158,835, 162,616)	162,591 (160,409, 164,732)	174,135 (171,919, 176,311)
72.0 (71.2, 72.8)	70.9 (70.0, 71.7)	70.9 (70.1, 71.8)	71.1 (70.2, 72.1)	70.9 (70.0, 71.8)
39,616 (37,770, 41,518)	42,821 (40,566, 45,148)	47,287 (45,111, 49,523)	49,978 (47,408, 52,623)	57,314 (54,495, 60,205)
27.3 (26.0, 28.6)	29.2 (27.7, 30.8)	29.4 (28.1, 30.8)	30.7 (29.2, 32.4)	32.9 (31.3, 34.6)
72,298 (69,976, 74,621)	74,237 (71,628, 76,844)	81,709 (79,119, 84,297)	79,748 (76,969, 82,531)	80,503 (77,418, 83,605)
49.8 (48.2, 51.4)	50.6 (48.8, 52.4)	50.8 (49.2, 52.4)	49.1 (47.3, 50.8)	46.2 (44.5, 48.0)
33,237 (30,639, 35,986)	29,680 (27,125, 32,411)	31,745 (29,026, 34,652)	32,865 (29,732, 36,238)	36,318 (32,999, 39,876)
22.9 (21.1, 24.8)	20.2 (18.5, 22.1)	19.8 (18.1, 21.6)	20.2 (18.3, 22.3)	20.9 (19.0, 22.9)
37,804,054	38,220,591	38,661,786	39,163,834	39,450,216



**Figure 1.** Increasing hospitalizations in the U.S. by selected causes, 1999–2006

inflicted poisoning) or E962.0 (assault by poisoning). The cause of the poisoning was considered to be undetermined if there was an E-code in the E980 range present (poisoning by solid or liquid substances, undetermined whether accidentally or purposely inflicted); if there were E-codes unrelated to poisonings; or if no E-code was present.

## Analyses

Data were analyzed using SAS-callable SUDAAN 10.0 to produce unbiased SEs that account for the multistage sampling design of the NIS. Weighted national estimates of poisoning hospitalizations were calculated for each data year to observe trends. A 95% CI was constructed around each estimate. The following demographic and clinical characteristics of prescription opioids, sedatives, and tranquilizers and other poisonings were compared: age, race, gender,

geographic residence, hospital location/teaching status, payer type, total hospital charges, and hospital length of stay. Differences were considered significant if the 95% CIs did not overlap. In situations where the interval overlap was slight, pairwise contrasts were constructed to determine the presence of a significant difference. An alpha of .05 was set a priori as the threshold for significance. All analyses were performed in 2009.

## Results

### Incidence of Poisoning Hospitalizations

From 1999 to 2006, estimated hospitalizations in the U.S. for poisoning by prescription opioids, sedatives, and tranquilizers increased by a total of 65%. In comparison, during this same period, hospitalizations for poisoning by other drugs, medicinal, and biological substances increased by 33%, whereas all other hospitalizations increased by little more than 11% (Table 1 and Figure 1). Unintentional poisonings involving prescription opioids, sedatives, and tranquilizers increased by 37% during the 7 years examined, whereas unintentional poisonings by other substances increased by 21%. Intentional poisonings from prescription opioids, sedatives, and tranquilizers rose by a total of 130% compared to a 53% increase in intentional poisonings from other substances over the 7-year period (Table 1).

For specific types of drugs, the largest increase in the number of estimated hospitalizations was observed for poisonings by benzodiazepines (10,379 more hospitalizations in 2006 vs 1999, an increase of 39%). The largest percentage increase in poisoning hospitalizations over the 7-year period among specific drugs was observed for methadone (400%). Hospitalizations for poisoning by barbiturates actually decreased 41%, as did hospitaliza-

**Table 2.** U.S. poisoning hospitalizations (*n* [95% CI]), by selected substances, 1999–2006<sup>a</sup>

	1999	2000	2001
<b>Prescription opioids, sedatives, and tranquilizers</b>	43,210 (41,763, 44,691)	48,310 (46,739, 49,914)	54,332 (52,786, 55,906)
Methadone	1,073 (887, 1,297)	1,459 (1,242, 1,715)	1,644 (1,437, 1,880)
Other narcotics	7,742 (7,306, 8,203)	9,274 (8,763, 9,813)	11,480 (10,921, 12,066)
Barbiturates	2,953 (2,682, 3,251)	2,718 (2,473, 2,986)	2,605 (2,360, 2,875)
Benzodiazepines	26,321 (25,143, 27,543)	28,507 (27,298, 29,760)	31,410 (30,225, 32,633)
Other sedatives and hypnotics	2,936 (2,677, 3,219)	3,865 (3,575, 4,179)	4,438 (4,109, 4,792)
Unspecified sedatives and hypnotics	1,123 (971, 1,299)	1,350 (1,188, 1,533)	1,488 (1,308, 1,693)
<b>Other drugs, medicinal, and biological substances</b>	130,670 (129,189, 132,117)	134,369 (132,764, 135,940)	142,440 (140,866, 143,986)
Heroin	3,971 (3,468, 4,546)	4,467 (3,846, 5,186)	3,806 (3,300, 4,387)
Aromatic analgesics (includes acetaminophen)	20,189 (19,398, 21,008)	21,566 (20,650, 22,518)	22,714 (21,808, 23,652)
Antidepressants	23,286 (22,304, 24,305)	22,911 (21,949, 23,909)	23,813 (23,105, 24,636)

<sup>a</sup>Hospitalization numbers and rates are weighted estimates.

tions for poisoning by antidepressants (a decrease of 13%;  
T2 Table 2).

### Characteristics of Hospitalizations for Prescription Opioids, Sedatives, and Tranquilizers

Patients hospitalized for poisoning by prescription opioids, sedatives, and tranquilizers were predominately women, aged 35–54 years, and residents of large or small urban areas. The most common type of insurance among this cohort was private coverage (31%) followed by Medicare (27%) and Medicaid (21%). Hospitalizations lasted about 3 days on average, and transfers to other facilities occurred in almost one third of the patients.

### Prescription Opioids, Sedatives, and Tranquilizers Versus Other Drug Poisonings

In comparison to patients hospitalized for other drug poisonings, those hospitalized for poisoning by prescription opioids, sedatives, and tranquilizers were more likely to be women, aged >34 years, have Medicare as the primary payer, and to present to a rural or urban non-teaching hospital. These patients were also less likely to live in a large urban area, and were significantly more likely to be transferred to another facility or to a home health agency compared to those hospitalized for other drug poisonings. No differences were observed in hospital length of stay or in the proportion of patients dying in the hospital.

There were significant differences in the intentionality of poisoning hospitalizations by gender, with men more likely to be hospitalized with unintentional poisoning and women more likely to be hospitalized with intentional poisonings. These findings were consistent for

those poisoned by prescription opioids, sedatives, and tranquilizers, and for all other poisonings as well. Within gender categories, there were not significant differences in the intentionality of the poisoning according to the type of drug or substance used (Table 3). Those aged  $\geq 55$  years were more likely to be classified as intentional, whereas those aged between 18 and 54 years were more likely to be coded as unintentional poisoning (Table 3). There were no significant changes in the demographic and hospital characteristics of poisoning hospitalizations over the 7-year period examined.

### Discussion

These data provide the first comprehensive examination of nationwide hospitalizations associated with prescription opioids, sedatives, and tranquilizers. Between 1999 and 2006, hospitalizations in the U.S. for these increased by 65%, almost twice as much as the increase observed in hospitalizations for poisonings by all other drugs and medicinal substances. This overall trend parallels recent reports examining fatality trends in the U.S.<sup>3,19</sup> In addition, these data reveal an increasing involvement of prescription opioids, sedatives, and tranquilizers in hospitalizations for both unintentional and intentional poisonings. Few prior studies have examined the contribution of prescription opioids, sedatives, and tranquilizers to intentional overdoses.<sup>20</sup> Hospitalizations most frequently involved middle-aged women residing in urban settings and the majority of cases were unintentional, although intent in a large number of cases was undetermined.

A recent study examining hospitalizations due to opioid poisonings in Denmark found that hospitalizations

**Table 2.** U.S. poisoning hospitalizations (*n* [95% CI]), by selected substances, 1999–2006<sup>a</sup> (continued)

2002	2003	2004	2005	2006
56,488 (54,913, 58,090)	60,308 (58,554, 62,092)	65,885 (64,010, 67,792)	65,956 (63,815, 68,139)	71,355 (69,179, 73,571)
2,548 (2,264, 2,868)	3,244 (2,911, 3,615)	4,195 (3,794, 4,637)	4,549 (4,160, 4,973)	5,362 (4,898, 5,869)
12,946 (12,347, 13,573)	14,351 (13,623, 15,115)	15,766 (15,039, 16,524)	15,847 (15,048, 16,685)	17,545 (16,712, 18,415)
2,303 (2,093, 2,534)	2,202 (1,997, 2,428)	1,973 (1,783, 2,182)	1,846 (1,653, 2,060)	1,749 (1,556, 1,965)
31,567 (30,349, 32,825)	32,531 (31,332, 33,768)	35,264 (33,958, 36,611)	34,801 (33,375, 36,275)	36,700 (35,301, 38,145)
4,627 (4,305, 4,973)	5,166 (4,821, 5,535)	5,666 (5,305, 6,050)	6,033 (5,643, 6,448)	6,713 (6,296, 7,158)
1,412 (1,240, 1,609)	1,743 (1,545, 1,967)	1,813 (1,609, 2,044)	1,983 (1,761, 2,233)	2,421 (2,181, 2,686)
145,151 (143,549, 146,727)	146,739 (144,955, 148,492)	160,741 (158,835, 162,616)	162,591 (16,049, 164,732)	174,135 (171,919, 176,311)
4,572 (4,017, 5,201)	4,146 (3,661, 4,692)	3,961 (3,512, 4,466)	3,693 (3,140, 4,342)	4,858 (4,159, 5,671)
22,810 (21,981, 23,667)	22,427 (21,604, 23,277)	25,395 (22,601, 24,428)	26,192 (25,152, 27,270)	27,930 (26,812, 29,088)
23,229 (22,315, 24,175)	22,011 (21,162, 22,890)	23,499 (22,601, 24,428)	20,919 (20,129, 21,738)	20,348 (19,478, 21,253)

**Table 3.** Poisoning hospitalizations (% [95% CI]) by intentionality and demographic characteristics, 2006

	Prescription opioids, sedatives, and tranquilizers			Other drugs, medicinal, and biological substances		
	Intentional	Unintentional	Undetermined	Intentional	Unintentional	Undetermined
<b>Gender</b>						
Male	31.4 (29.8, 33.0)	50.0 (48.4, 51.7)	18.6 (16.9, 20.5)	28.8 (27.5, 30.1)	52.9 (51.2, 54.5)	18.4 (16.6, 20.3)
Female	36.4 (34.5, 38.4)	42.2 (40.3, 44.0)	21.5 (19.5, 23.6)	37.7 (35.5, 39.8)	38.6 (36.7, 40.6)	23.8 (21.6, 26.1)
<b>Age (years)</b>						
≤18	44.2 (38.9, 49.7)	37.4 (32.7, 42.7)	18.4 (13.4, 24.6)	34.6 (31.5, 37.9)	50.1 (46.8, 53.4)	15.3 (11.8, 19.5)
18–34	23.6 (21.7, 25.6)	55.9 (53.6, 58.1)	19.8 (17.9, 21.8)	21.8 (20.4, 23.2)	58.8 (57.0, 60.7)	19.4 (17.6, 21.4)
35–54	28.7 (27.1, 30.3)	51.6 (49.7, 53.4)	19.8 (17.9, 21.8)	30.8 (28.6, 33.2)	46.0 (43.5, 48.4)	23.2 (21.0, 25.6)
≥55	50.7 (48.4, 52.9)	30.1 (28.4, 32.0)	19.2 (17.2, 21.4)	57.0 (54.7, 59.2)	21.1 (19.8, 22.5)	21.9 (19.9, 24.1)

for poisonings by strong analgesics increased from 0.6 per 100,000 person-years in 1998 to 2.1 per 100,000 person-years in 2004, and methadone poisoning hospitalizations increased from 0.1 per 100,000 person-years in 1998 to 1.1 per 100,000 person-years in 2004.<sup>21</sup> The current results indicate a similar trend in the U.S. The 400% increase in methadone poisoning hospitalizations over the study period may be related to the substantial increase in the overall retail sales of this drug from 1997 to 2006. During this time period, retail sales of methadone increased 1177%.<sup>22</sup> The large increase in hospitalizations reported here from benzodiazepine poisoning (>10,000 more hospitalizations in 2006 compared to 1999) also mirrors the trend of increasing emergency department visits associated with benzodiazepines. More specifically, between 1995 and 2005, the number of emergency department visits involving benzodiazepine abuse reported to the DAWN network increased 141% (from 71,609 to 172,388).<sup>22</sup> Because most prescription drug injury reports have focused on opioids, it is possible that poisonings from benzodiazepines have been somewhat overlooked.

One study evaluated the risk of injury in a Veterans population stemming from concomitant use of benzodiazepines with other drugs, and found a twofold increase in the odds of injury stemming from the use of a benzodiazepine with another drug versus a benzodiazepine alone (2.31, 95% CI=2.20, 2.41).<sup>23</sup> Benzodiazepines were also the most frequent concomitant drug detected (45% of all cases) in fatal opioid-related deaths in the United Kingdom, and were detected in 64% of the fatalities primarily attributable to methadone.<sup>24</sup> Interestingly, the blood concentration levels in these cases were within therapeutic ranges. These findings are similar to results based on data from New York City in which the presence of a benzodiazepine concomitant with methadone increased the odds of accidental death by 1.66 (95% CI=1.12, 2.45).<sup>25</sup>

Other studies have also noted the presence of benzodiazepines in methadone-related deaths in 18% to 60% of cases.<sup>25,26</sup> It is important to note that the current study examined only the primary pharmacologic agent responsible for hospitalization as assigned by coders. The presence of other drugs in these hospitalizations was not examined and toxicology results are not available within the NIS data. However, the current observed increases in benzodiazepine and methadone poisonings, coupled with these other reports, suggests the need for specific interventions targeting these substances.

Hospitalization for poisoning by prescription opioids, sedatives, and tranquilizers is a potentially serious and noteworthy event. With an average length of stay of 3 days, there exists a window of opportunity to both learn more about this escalating phenomenon and to implement preventive interventions. From a research perspective, there exists a paucity of information on the contextual factors leading to these types of poisonings. Interviews with survivors could provide important additional details regarding the pathways to abuse of these drugs, the methods used to obtain the medications, the sequencing and combination of drugs that result in overdose, and the immediate precursors to these serious events. The association between hospitalization for prescription opioids, sedatives, and tranquilizers and subsequent morbidity and mortality is another area in need of further research.

## Limitations

The primary limitation of this study is the retrospective design, which could negatively affect the internal validity of the study, because data were not originally collected for the purposes used in this study. Also, only the principal discharge diagnosis was used to classify cases. Therefore, it is entirely possible that the current hospitalization estimates are underestimates given that some drug poisonings may have been indicated in a secondary diagnosis

field. A further cause of underestimation may be that the case definition included only those who were considered acutely “poisoned” by these substances, and cases hospitalized for chronic use or dependence were not included. As previously noted, toxicology results are not included in these data. Also, E-codes were used to determine the intentionality of the overdose, and the accuracy of E-codes for these specific purposes has not been determined.

Further, although NIS data provide estimates of the total number of hospitalizations, it is possible that a single patient accounted for more than one hospitalization. Finally, there is a lack of predetermined standard definitions for use when describing poisonings associated with prescription drugs. For drugs, both prescribed and non-prescribed, the term *overdose* is more commonly used in clinical settings to denote an adverse consequence resulting from exposure to an excessive, large amount, and/or unusually potent amount of the drug. Also, there are varying definitions of the terms *illegal*, *illicit*, *recreational*, *abuse*, and *misuse* of prescription drugs across differing disciplines. The current analyses were confined to the information included in hospital discharge data and the lexicon used in discharge abstracts to classify these diagnoses.

## Conclusion

Hospitalizations for poisonings from prescription opioids, sedatives, and tranquilizers increased 65% from 1999 to 2006 in the U.S. This increase mirrors the trend observed in mortality from prescription drug overdose during this time period, and may point to an opportunity to intervene to prevent subsequent mortality. Although the majority of these hospitalized poisonings are classified as unintentional, substantial increases were also demonstrated for intentional overdoses associated with these drugs, likely reflecting their widespread availability in community settings. Future research should examine the contextual factors associated with these cases and the association between hospitalization for prescription drug poisoning and subsequent fatal overdoses. Enhanced surveillance activities and interventional trials are warranted.

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