The Critical Care Crisis of Opioid Overdoses in the United States

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Abstract

Rationale: Opioid abuse is increasing, but its impact on critical care resources in the United States is unknown.

Objectives: We hypothesized that there would be a rising need for critical care among opioid-associated overdoses in the United States.

Methods: We analyzed all adult admissions, using a retrospective cohort study from 162 hospitals in 44 states, discharged between January 1, 2009, and September 31, 2015 to describe the incidence of intensive care unit (ICU) admissions for opioid overdose during this time. Admissions were identified using the Clinical Database/Resource Manager of Vizient, the successor to the University Health System Consortium.

Results: Our primary outcome was opioid-associated overdose admissions to the ICU. The outcome was defined on the basis of previously validated ICD-9 codes. Our secondary outcomes were in-hospital death and markers of ICU resources. The final cohort

included 22,783,628 admissions; 4,145,068 required ICU care. There were 52.4 ICU admissions for overdose per 10,000 ICU admissions over the entire study (95% confidence interval [CI], 51.8–53.0 per 10,000 ICU admissions). During this time period, opioid overdose admissions requiring intensive care increased 34%, from 44 per 10,000 (95% CI, 43–46 per 10,000) to 59 per 10,000 ICU admissions (95% CI, 57–61 per 10,000; $P < 0.0001$). The mortality rate of patients with ICU admissions with overdoses averaged 7% (95% CI, 7.0–7.6%) but increased to 10% in 2015 (95% CI, 8.8–10.8%).

Conclusions: The number of deaths of ICU patients with opioid overdoses increased substantially in the 7 years of our study, reflecting increases in both the incidence and mortality of this condition. Our findings raise the need for a national approach to developing safe strategies to care for patients with overdose in the ICU, to providing coordinated resources in the hospital for patients and families, and to helping survivors maintain sobriety on discharge.

Keywords: critical care; opioid overdoses; epidemiology

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Opioid use and subsequent opioid-related overdose deaths are rapidly rising in the United States, with a 200% increase in opioid-related overdose deaths since 2000 as documented by the Centers for Disease Control and Prevention (1). Multiple state governments have begun major policy efforts toward the prevention and treatment of opioid use disorder (2–4).

As increasing numbers of patients are admitted to hospitals with overdoses from opioids, including prescription opioids, synthetically derived opioids, and heroin, the critical care community will be required to care for the most complex admissions. Further, these admissions may also contribute to additional hospital and societal costs, as this population may necessitate increasing rates

of complex and expensive multiorgan support.

Consequently, understanding the use of intensive care services for patients with opioid overdose may serve as a bellwether of the severity of the opioid epidemic and allow hospitals to anticipate critical care needs for patients with opioid overdose. Little is known, however, about the fundamental epidemiology of opioid overdoses among

admissions to intensive care units. We therefore used a large, national database of hospital admissions to understand the epidemiology of opioid overdose admissions to intensive care units. We hypothesized that overdose admissions to ICUs have increased significantly over time, as have mortality and the use of critical care resources.

Methods

Study Population and Data Source

We studied acute care hospital inpatient admissions of patients 18 years or older in 162 hospitals in 44 states, who were discharged between January 1, 2009, and September 31, 2015. The data source was the Clinical Database/Resource Manager of Vizient (Irving, TX). Vizient is the largest member-owned health services company, and is the successor to the University Health System Consortium, which previously operated the Clinical Database/Resource Manager. Hospitals were included only if they had participated in the database for the entire study period.

Study Variables

Outcome. Our primary outcome of interest was the incidence of ICU admissions for opioid-related overdose per month per hospital. We defined admissions for overdoses as those with the discharge *International Classification of Diseases, 9th Revision* (ICD-9) code for any diagnosis or presence on admission of prescription drug overdose (965.00, 965.09, or E code E850.0, E850.2), methadone overdose (965.02), or heroin overdose (965.01 or E code E850.0) present on admission, as was previously used in the literature (5). We further validated the use of these codes within the Beth Israel Deaconess Medical Center (Boston, MA) and found that these functioned with a sensitivity of 100% and specificity of 100% among 100 patients, 50 randomly chosen patients with these ICD-9 codes and 50 patients without these ICD-9 codes. We identified ICU stay using Vizient's ICU Encounter definition, which applies each hospital's best information source for identifying ICU utilization.

Secondary outcomes. Our secondary outcomes of interest included incidence of in-hospital death after ICU admission for overdose, and markers of ICU resources

including use of mechanical ventilation, noninvasive ventilation, vasopressor use, and use of renal replacement therapy, average length of stay per hospital per month, and average cost of admission per hospital per month. Mechanical ventilation (ICD-9 96.72), noninvasive ventilation (93.90), vasopressor use (00.17), and renal replacement therapy (39.95) were all ascertained with ICD-9 codes, acknowledging that these estimates likely underestimated the rate of resource use (6). We report costs based on Vizient cost estimation which normalize hospital data, using cost-to-charge ratios from each member's Medicare Cost Report, as well as area wage indices, to facilitate comparison across regions with diverse labor markets.

Patient demographics and comorbidities. Demographic information, including age (divided into 18–19, 20–29, 30–39, 40–49, 50–59, 60–69, and 70+ yr), race (white or nonwhite), insurance provider (divided into Medicaid, uninsured, commercial payer, and other), and sex, was obtained per hospital. To characterize other complications of opioid overdose, we extracted rates of aspiration pneumonia (ICD-9 507.0), septic shock (ICD-9 785.52), rhabdomyolysis (ICD-9 728.88), and anoxic brain injury (ICD-9 348.1 and 437.9), per hospital.

Hospital characteristics. The number of acute care beds (<150 beds, between 150 and 250 beds, and >250 beds), the number of hospitalizations with an ICU stay per month, as well as the state and region (South, West, Northeast, and Midwest) were included. Hospitals were characterized as being in a rural area, a large rural city, or an urban area (defined using the Rural Health Research Center definitions for identifying rural status based on ZIP codes) (7). State-level data are presented only when five or more hospitals in the state participated in the data set for the entire study period, so as to ensure confidentiality in presented data.

Statistical Analysis

All statistical tests were formed with SAS (v. 9.4; Cary, NC). We first classified hospitals into quartiles by critical care overdose density, which we defined as the mean ICU admissions for opioid-related overdose per 10,000 ICU admissions. We then compared patient, hospital, and geographic characteristics of hospitals by quartile, using χ^2 tests for categorical variables, and by

Kruskal–Wallis test for continuous variables. We examined the effects of time, hospital, and geographic characteristics using a generalized estimating equations approach for multivariable negative binomial regression models that accounted for clustering by hospital, with the hospital discharge as the unit of analysis. We used the number of discharges from ICU associated with overdose as an offset variable, when an overdose-related mortality rate was modeled. We accounted for seasonality of discharges by adjusting to an indicator variable of summer. The point estimates of an association between the independent factors and an outcome were expressed as relative risks (RRs) and described along with their 95% confidence intervals (CIs). The RRs presented showed a multiplicative change in the outcome variable, following 10-unit change in the independent factors.

As part of a sensitivity analysis, the models were repeated using a generalized estimating equations approach with a Poisson-distributed outcome, where estimates were scaled by Pearson to correct for overdispersion. Data points are presented graphically, using a locally weighted scatterplot smoothing technique, in the figures in the online supplement.

Our study was approved by the institutional review boards at the University of Chicago Medical School and the Beth Israel Deaconess Medical Center with a waiver of informed consent.

Results

We studied a total of 22,783,628 hospital admissions and 4,145,068 ICU admissions between January 1, 2009, and September 31, 2015 from 162 hospitals. These admissions were 55% female, 35% nonwhite, with 32% with commercial insurance, 4% uninsured, and 18% with Medicaid. Twenty-five percent of patients were 70 years or older. Among ICU patients, the population was 44% female, 33% nonwhite, with 29% of the population 70 years or older.

A total of 21,705 overdose admissions required ICU care during this period, an average of 52.4 admissions for overdose per 10,000 ICU admissions. The distribution of patient demographics and hospital characteristics by quartile of critical care overdose density is presented in Table 1, and the annual incidence of

Table 1. Distribution of patient demographics and hospital characteristics by quartile of critical care overdose density

Hospital Characteristic	Below 25th Percentile (0–30.7 per 10,000) (n = 40)	25–50th Percentile (30.7–47.7 per 10,000) (n = 41)	50–75th Percentile (47.7–83.5 per 10,000) (n = 40)	Above 75th Percentile (83.5 and above per 10,000) (n = 41)	P Value
Female, %	54%, 52–60%	56%, 52–59%	55%, 53–60%	56%, 54–58%	0.970
White, %	58%, 50–70%	63%, 48–79%	77%, 58–89%	75%, 63–87%	0.001
Percentage of patients at the age of					
18–19 yr	2%, 1–2%	2%, 1–2%	2%, 1–2%	2%, 1–2%	0.868
20–29 yr	12%, 9–15%	13%, 10–16%	12%, 8–14%	12%, 8–15%	0.648
30–39 yr	12%, 10–15%	14%, 12–16%	12%, 9–14%	12%, 8–15%	0.035
40–49 yr	13%, 11–14%	13%, 10–15%	13%, 10–14%	13%, 10–16%	0.793
50–59 yr	19%, 16–21%	18%, 15–20%	17%, 15–20%	17%, 14–20%	0.565
60–69 yr	19%, 16–21%	17%, 16–19%	18%, 16–19%	16%, 15–18%	0.002
70+ yr	22%, 18–28%	24%, 16–30%	28%, 17–38%	29%, 18–38%	0.061
Number of overdose patients with mechanical ventilation/ 10,000 ICU patients*	1.91, 1.15–3.18†	3.48, 1.70–5.95	5.60, 2.84–7.29	10.63, 7.10–14.55	<0.001
Number of overdose patients with renal replacement therapy/10,000 ICU patients*	1.00, 0.64–1.86†	1.91, 1.05–2.69	2.36, 0.62–3.36	4.86, 1.89–6.38	<0.001
Percentage of patients without insurance	3%, 1–5%	3%, 1–8%	4%, 1–7%	4%, 2–7%	0.449
Percentage of patients with commercial insurance	37%, 29–40%	32%, 27–41%	27%, 19–34%	24%, 21–31%	<0.001
Percentage of patients with Medicaid	16%, 10–22%	14%, 9–25%	14%, 11–21%	19%, 14–26%	0.139
Number of acute care beds					
<150	7.5%	2.4%	15.0%	12.2%	0.087‡
150–250	2.5%	17.1%	17.5%	19.5%	
>250	90.0%	80.5%	67.5%	68.3%	0.001
Number of patients hospitalized per month*	2,087.88, 1,394.8–2,714.7	1,809.32, 1,147.2–2,558.6	1,491.44, 772.5–2,153.7	1,262.11, 737.0–1,594.3	
Average length of stay in hospital, d*	10.73, 9.42–12.00†	10.20, 8.54–11.39	9.25, 7.38–10.21	7.43, 6.54–9.53	<0.001
Percentage of ICU patients out of all hospitalized patients	20%, 13–25%	16%, 12–20%	17%, 13–23%	15%, 11–21%	0.250
Urban hospitals	95.0%	100.0%	92.5%	100.0%	0.129‡
Region					
Northeast	17.5%	22.0%	32.5%	41.5%	0.119‡
Midwest	30.0%	22.0%	35.0%	34.1%	
South	35.0%	36.6%	22.5%	12.2%	
West	17.5%	19.5%	10.0%	12.2%	

Definition of abbreviations: ICU = intensive care unit; IQR = interquartile range.

*Median, IQR.

†Entries calculated with 3 missing hospitals from the total denominator for a total of 38 hospitals. All other cells have complete data.

‡Tests of difference performed by χ^2 test; all remaining tests of difference performed by Kruskal-Wallis test.

Figure 1. Changes in monthly overdose-related intensive care unit (ICU) admissions, mortality rates, and overall number of ICU deaths from overdose. Shown is the change in monthly incidence of ICU admission for (A) overdose and (B) mortality rates, as compared with the overall ICU population. (C) Data demonstrate that the number of opioid overdoses is rising at an even faster rate. Plots represent the unadjusted data and a LOESS function with 95% confidence intervals. LOESS = locally weighted scatterplot smoothing technique.

overdose-related ICU admissions is presented in Figure 1.

Patients with Opioid Overdose Requiring ICU Admission

The incidence of opioid overdoses admitted to the ICU increased significantly per month per year. On average, there was an increase of 0.6% per month (RR, 1.006; 95% CI, 1.005–1.007; $P < 0.0001$).

After adjustment for other variables influencing the increase in critical care needs

for patients with opioid overdose, the rise per month persisted with an increase at a level of 0.5% per month (RR, 1.005; 95% CI, 1.003–1.006; $P < 0.0001$). The other variables that had a statistically significant effect on the increase in critical care admissions for opioid overdose are presented in Table 2. Admission during the summer and the overall increase in ICU admissions also significantly influenced the prevalence of opioid overdose-related admissions from the ICU.

Patients admitted to the ICU with overdose had several comorbidities associated with their hospitalization. Among all adult patients with overdoses admitted to an ICU, 25% experienced aspiration pneumonia, 6% had septic shock, 15% had rhabdomyolysis, and 8% experienced anoxic brain injury.

Mortality

Deaths among patients admitted to the ICU with opioid overdose also increased

Table 2. Hospital and environmental characteristics associated with admissions to intensive care unit for opioid overdose, based on multivariable model

Variable	RR	95% CI	P Value
Increase per month, after January 2009	1.005	1.003–1.006	
ICU volume (number of admissions of nonoverdose patients per month)	1.002	1.001–1.002	<0.001
Proportion of patients with Medicaid in the hospital, in quartiles	1.397	1.258–1.551	<0.001
Proportion of white patients in the hospital, in quartiles	1.257	1.141–1.386	<0.001
Urban versus rural location of hospital	3.817	1.184–12.304	0.025
Summer admission	1.089	1.053–1.125	<0.001

Definition of abbreviations: CI = confidence interval; ICU = intensive care unit; RR = relative risk.

significantly. The mortality rate in ICU patients with overdose on average was 7.3% but increased to 9.81% by 2015. The monthly mortality of patients admitted to the ICU with overdose increased at a rate of 0.5% per month (RR, 1.005; 95% CI, 1.002–1.007; $P < 0.0001$) (Figure 1C); this U-shaped graph has an inflection point in April 2012. After

adjustment for other significant hospital and patient characteristics, the mortality from overdose in the ICU remained significant at 0.4% per month (RR, 1.004; 95% CI, 1.001–1.006; $P = 0.003$).

In the multivariable model, the number of all hospitalizations with heroin overdose each month was associated with an increase

in the monthly mortality among ICU patients with opioid-related overdoses (RR, 1.247; 95% CI, 1.137–1.368; $P < 0.001$) (Figure 2). The number of patients admitted with overdose from prescription drugs, however, was not significantly associated with ICU mortality from overdose (RR, 1.031; 95% CI, 0.992–1.071; $P = 0.125$) (Figure 2). ICU admission with overdose during the summer months was associated with lower mortality (RR, 0.871; 95% CI, 0.782–0.970; $P = 0.012$). The full model is presented in Table E1 in the online supplement.

Critical Care Resources and Cost

The average cost per ICU overdose admission increased from \$58,517 in 2009 to \$92,408 in 2015, in 2015 dollars, an increase of 58% ($P < 0.0001$). On average, approximately 10% of ICU patients with overdose required mechanical ventilation, and this did not change appreciably over time. Seven percent of this population required noninvasive ventilation, and 4%

Figure 2. Change in overdose-related mortality among intensive care unit (ICU) admissions for opioid overdose as compared with monthly prevalence of heroin, prescription drugs, and methadone admissions per month. Shown is the change in incidence of heroin, prescription drugs, and methadone hospital admissions normalized to January 2009 on the primary y-axis. The secondary y-axis illustrates the opioid overdose-related mortality in the ICU, also normalized to January 2009. In each case, the unadjusted rate is described using a LOESS function. LOESS = locally weighted scatterplot smoothing technique.

Figure 3. Opioid overdose critical care density per state heatmap, as defined as intensive care unit (ICU) admissions for opioid overdose per 10,000 ICU admissions. (A) The change in number of ICU admissions for opioid overdose per year among states with five or more hospitals participating in the study continuously between January 2009 and September 2015. (B) Normalization of the rate of change to 2009. All results are presented as unadjusted rates. In each panel, the darker the color, the greater the value.

required vasopressors. Critically ill patients with overdose required renal replacement therapy 37% more often in 2015 than in 2009 (of ICU admissions for overdose, 4.5% in 2009 to 6.1% in 2015; $P = 0.007$).

Regional Variation in Overdoses Requiring ICU Care

Eight states included more than five hospitals with data during the entire study period and were included in state-level

subgroup analyses of changes in ICU overdose admissions over time. Massachusetts and Indiana were both substantially higher than the other states included in the analysis (Figures 3A and 3B), with the average opioid-related overdose critical care density twice that of other states. Whereas some states appear to have declining prevalence of ICU admissions for opioid overdoses, others have risen sharply since 2009. In Pennsylvania, in particular, the rates of

critical care admissions for overdose have nearly doubled.

Discussion

We found that the United States experienced a marked increase in critically ill patients with overdoses from opioids between 2009 and 2015. Not only did the number of patients with opioid-related overdose requiring ICU care increase above and beyond the increasing supply of critical care admissions, the mortality among this population increased as well, leading us to estimate that there was a near doubling of ICU deaths from opioid overdoses in September 2015 compared with January 2009. These patients also required more intense care, as reflected by the use of more renal replacement therapy at significantly higher costs. Further, our findings identify two states with substantial critical care use by patients with opioid overdoses.

Our results provide the first description of the impact of the current opioid addiction crisis on the critical care community. We would propose that any admission to the ICU for opioid overdose is a preventable admission. We have presented only one aspect of how health care systems interact with these patients, but critical care represents the most technologically advanced part of our care. Our findings are agnostic as to whether local community emergency response teams are doing better at rescuing people with overdoses (leading to more ICU admissions due to higher numbers of patients surviving) or whether this represents an opportunity for improvement (if more immediate care had been available, patients may have required lower levels of care rather than the ICU). Prior research found that prevention strategies such as nasal naloxone distribution for bystanders change overall mortality from opioid overdose, but do not change acute care hospital utilization (8–10). However, our findings do describe a growing demand for critical care support for this population, particularly in some regions of the country where the critical care need for patients with overdoses is already high. Further, if each of these admissions is preventable and, by extension, the growing number of deaths from overdoses are also preventable, we would suggest that these findings represent a growing and urgent call for additional

critical care resources and expanded primary prevention strategies.

Although our data are not definitive, they suggest that overdoses from heroin, rather than prescription opioids, appear to be a major contributor to the rise in critical care mortality for this population. Beginning in April 2012, the severity of illness of these overdoses, as reflected in the sudden rise in mortality, increased. Okie described a growing epidemic in 2010 from accidental deaths from unintentional drug overdoses, with increasing concern by clinicians, health departments, and the Food and Drug Administration (11). This was associated with areas with high rates of prescriptions for opioid pain killers. Unick and colleagues identified that hospitals with increases in prescription overdose admissions increased their likelihood of subsequent increases in heroin overdose admissions the following year by a factor of 1.26 (5). In the interim, the economy and patterns of drug abuse have changed (12, 13). Our results describe the increasing association of heroin with the most severe

opioid overdoses, those that necessitate critical care support.

Our study does have several notable limitations. First, we examined only the population participating in Vizient's Clinical Database/Resource Manager, which have historically been academic centers of care and the hospitals in this study are almost universally in urban centers. This raises concerns about whether our estimates of prevalence can be generalized to community settings where critical care resources may be less available. Second, we used administrative data, which lack the clinical nuance of a manual record review. We would hypothesize that use of administrative data may underestimate the critical care demands of opioid-related admissions, such as the frequency of mechanical ventilation and use of vasopressors (6). Third, we identified overdoses only through billing, which likely misses many admissions for opioid-related complications. Fourth, we used hospital rather than patient-level data. Data through the Clinical Database/Resource Manager

are available at a hospital level rather than patient level, which prevents patient-level risk adjustment or further investigations into patterns of care. Fifth, we did not provide population-level controls for critical care use for opioid overdoses given that hospitals in this study were likely representative of more urban and academic centers. However, we did attempt to control for the contribution of increasingly available critical care beds by adjusting for overall increases in critical care admissions.

In conclusion, there is substantial demand for critical care resources secondary to the opioid overdose epidemic in the United States. Early recognition for states with rising crises—such as Pennsylvania—may allow for early action in these areas to both prepare critical care units for the needs of this population and to better equip front-line providers to prevent these critical care admissions from occurring. ■

Author disclosures are available with the text of this article at www.atsjournals.org.

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