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Comorbidities and Risk of Admission following an Emergency Department Presentation for an Opioid Overdose, United States, 2014

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The Ohio State University

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Abstract

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Opioid overdoses place considerable burden on U.S. hospitals and emergency departments (ED). This study aimed to assess the demographic and clinical factors associated with admission following an ED presentation for an opioid overdose. Using data from the 2014 National Emergency Department Sample, a retrospective cohort study was conducted. ED visits were classified according to opioid type (non-heroin opioid or heroin). The main outcome measure was admission or other further care following the ED visit. The cohort contained 147,654 total visits for opioid overdoses. 81,631 (55%) presented due to non-heroin opioid overdoses and 66,023 (45%) presented due to heroin overdoses. Non-heroin opioid overdoses occurred more frequently among older populations, females, in the South, and among Medicare enrollees. Non-heroin opioid overdoses had a greater prevalence of comorbid conditions such as diabetes, hypertension, and chronic obstructive pulmonary disease (COPD). Among heroin overdose visits, 57% of patients also had a diagnosis of a substance-related disorder compared to 43% of non-heroin opioid overdose visits. Among non-heroin opioid overdose visits, 67% of patients had at least one mental health condition compared to 64% of heroin overdose visits. The risk of admission following a non-heroin opioid overdose, when controlling for age, sex, hospital region, and primary insurance payer, was 2.14 times the risk of admission following a heroin overdose (95% CI: 2.01, 2.28). When considering interaction with prevalent comorbidities, the risk of admission varied by condition. Allowing for interaction with substance-related disorders, the relative risk of admission was 2.59 (95%CI: 2.40, 2.80). Among overdoses with at least one mental health condition, the risk of admission was 1.92 greater among non-heroin opioid overdoses than heroin overdoses (95% CI: 1.92, 2.06). The study found that patients who presented at U.S. EDs with a non-heroin opioid overdose differed both demographically and clinically from heroin overdose patients and had a greater risk of admission following the ED visit.

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CHAPTER I: MANUSCRIPT

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A. Title, Authors, Abstract

Comorbidities and Risk of Admission Following an Emergency Department Presentation for an Opioid Overdose, United States, 2014

Meghan R. Shea, BS, Gery P. Guy Jr., PhD, MPH, Timothy L. Lash, DSc, MPH

Opioid overdoses place considerable burden on U.S. hospitals and emergency departments (ED). This study aimed to assess the demographic and clinical factors associated with admission following an ED presentation for an opioid overdose. Using data from the 2014 National Emergency Department Sample, a retrospective cohort study was conducted. ED visits were classified according to opioid type (non-heroin opioid or heroin). The main outcome measure was admission or other further care following the ED visit. The cohort contained 147,654 total visits for opioid overdoses. 81,631 (55%) presented due to non-heroin opioid overdoses and 66,023 (45%) presented due to heroin overdoses. Non-heroin opioid overdoses occurred more frequently among older populations, females, in the South, and among Medicare enrollees. Non-heroin opioid overdoses had a greater prevalence of comorbid conditions such as diabetes, hypertension, and chronic obstructive pulmonary disease (COPD). Among heroin overdose visits, 57% of patients also had a diagnosis of a substance-related disorder compared to 43% of non-heroin opioid overdose visits. Among non-heroin opioid overdose visits, 67% of patients had at least one mental health condition compared to 64% of heroin overdose visits. The risk of admission following a non-heroin opioid overdose, when controlling for age, sex, hospital

region, and primary insurance payer, was 2.14 times the risk of admission following a heroin overdose (95% CI: 2.01, 2.28). When considering interaction with prevalent comorbidities, the risk of admission varied by condition. Allowing for interaction with substance-related disorders, the relative risk of admission was 2.59 (95%CI: 2.40, 2.80). Among overdoses with at least one mental health condition, the risk of admission was 1.92 greater among non-heroin opioid overdoses than heroin overdoses (95% CI: 1.92, 2.06). The study found that patients who presented at U.S. EDs with a non-heroin opioid overdose differed both demographically and clinically from heroin overdose patients and had a greater risk of admission following the ED visit.

B. Introduction

Driven by a medical and pharmaceutical push to reduce the amount and degree of pain felt by patients, the number of prescriptions written in the United States for opioid pain relievers (OPRs), such as oxycodone and hydrocodone, has quadrupled over the past two decades (1). Before science was able to indicate their addictive potential, the use, and misuse, of OPRs became commonplace. Opioid overdoses are a serious, often fatal, unintended consequence of the pain management campaigns of the late 1990s. In 2014, over 47,000 Americans died from a drug overdose; of these deaths, approximately sixty percent were due to an opioid (2). Heroin use has also driven the opioid crisis and some OPR users transition to the drug (3). Overdose deaths from synthetic opioids such as fentanyl have also been on the rise, further exacerbating the crisis (4). As of 2015, over 2 million Americans had been diagnosed with a substance use disorder related to OPRs and around one-half million suffered from a heroin use disorder (2).

Opioid overdoses, both fatal and non-fatal, place considerable burden on the U.S. economy, healthcare system, and other societal institutions. The Centers for Disease Control and Prevention estimates the yearly cost of the opioid crisis to be at least $78 billion dollars (2). Every component of the U.S. healthcare system has been burdened by the increase in opioid overdoses; however, emergency medicine has been heavily impacted. Along with the frequency of fire department and/or emergency medical technician administration of overdose-reversal medications such as naloxone, presentation to emergency departments (EDs) for an opioid-related overdose provides an important measure of the national

morbidity of opioid intoxication (5, 6). Between 2004 and 2011, ED visits for opioid-related overdoses increased by over 180% (7). Moreover, inpatient hospitalizations for both prescription opioid and heroin overdoses have increased steadily from 2007 to 2014; these rates varied according to the urban/rural location of the patient, with higher rates of heroin hospitalizations among urban residents (8).

The population seeking medical care for opioid overdoses tend to be affected by many other underlying health conditions. Several comorbid conditions, both chronic and acute, have been found to be associated with overdoses or to be common among populations that abuse opioids. These conditions include kidney failure, liver disease, hypertension, heart disease and circulatory disorders, respiratory disorders such as chronic obstructive pulmonary disease (COPD), cancer, diabetes, and neurological disorders (9-15). Additionally, opioid users have a high prevalence of chronic mental health conditions such as anxiety, depression and other mood disorders, alcohol-related disorders, and substance abuse disorders (9-16).

Given the economic and human costs associated with the opioid overdose crisis, preventing overdoses is of significant interest to policy makers, researchers, and public health practitioners. However, data on non-fatal opioid overdoses is not as readily available as data on fatal overdoses. Death certificates include information on primary and secondary causes of death, as well as the manner and mechanism of death, which allows for a somewhat robust understanding of opioid overdose mortality (3). While studies on opioid overdose morbidity have been conducted, most are among limited populations such as

Medicaid enrollees, Veterans Health Administration patients, health plan members, or residents of specific states (6, 9-11, 13-15). Nationally-representative studies on overdose morbidity have largely been descriptive in nature (12, 17-19).

To address these gaps in the current epidemiologic understanding of the opioid crisis, this study analyzed data from a large, nationally-representative, all-payer dataset. The study aimed to assess the demographic factors, such as urban/rural patient location and insurance coverage, that are associated with admission or other continued care following presentation to an ED for an opioid overdose. Specifically, we sought to add to the literature by examining whether comorbidities, such as mental health conditions, diabetes, or kidney disease, are associated with admission, as they may exacerbate the severity of an opioid overdose.

C. Methods

Data Source & Study Design

Data were obtained from the 2014 Nationwide Emergency Department Sample (NEDS), Healthcare Utilization Project (HCUP), Agency for Healthcare Research and Quality (AHRQ). NEDS is the country's largest sample of hospital-based emergency department (ED) visits, containing weighted data from over 140 million ED discharges annually, from 953 hospitals in 34 states and the District of Columbia (20). Utilizing a single-stage cluster design, the sample contains discharge-level data from approximately 20% of U.S. emergency departments (20).

This study used a cohort design to assess the factors associated with admission or other further medical care following presentation to a U.S. Emergency Department in 2014. ED visits for non-fatal opioid overdoses were classified as either non-heroin opioid or heroin related according to their diagnostic codes and external injury codes, as classified by the International Classification of Disease, Ninth Revision, Clinical Modification (ICD-9). Non-heroin opioid overdose discharges were identified as those with a primary diagnostic code of 965.00, 965.02, or 965.09, or an external injury code of E8501 or E8502. Heroin overdoses were identified as discharges with a primary diagnostic code of 965.01 or external injury code of E8500. Visits that had a diagnostic code indicating a non-heroin opioid overdose and an external injury code indicating a heroin overdose, or vice versa, were classified according to their primary diagnostic code. All descriptive analyses were performed in SAS 9.4.

Once the data were classified according to type of overdose, NEDS weights were applied to account for the sampling design and to obtain national estimates. Estimates of demographic characteristics of the two groups (age, sex, region, income, urban-rural classification, hospital type, primary payer, and total charge) were generated to assess the characteristics of those presenting to an ED for each type of opioid overdose and to compare these characteristics across the types of overdose.

Covariate Definitions

NEDS data contain the age of the patient at the time of presentation to an ED. Age was transformed into a categorical variable separating the population into the following groups: Under 18, 18 to 25, 26 to 30, 31 to 40, 41 to 64, and 65

years and older. Sex was defined in this study as it is contained in NEDS, male or female. NEDS uses the National Center for Health Statistics' (NCHS) urban-rural scheme to approximate the urban classification of the patient's zip code as provided in the discharge record. Discharges are classified into six levels from central large metropolitan to non-core (21). This study further collapsed the urban-rural classification into large metro, medium metro, small metro, micro, and non-core. The median income in the zip code of the patient presenting to the ED was used as a proxy for socioeconomic status. NEDS divides patient income levels into quartiles; the lowest income quartile is less than $40,000 and the highest income quartile is a median zip-code level income of more than $66,000.

Insurance status of the individual presenting to the ED is indicated through the primary payer variable, which NEDS defines as the expected primary payer for the services provided at the ED. Values for expected primary payer are Medicare, Medicaid, private insurance, self-pay, no charge, and other. Private insurance includes Blue Cross, all commercial carriers, and private Health Maintenance and Preferred Provider Organizations. Those discharges with a listed primary payer of "other" indicate visits that were expected to be paid by Worker's Compensation, Veteran Affairs, Title V, and other government programs (21). The total charge for all ED services was also included on the discharge record; the mean total charge was calculated for each group of overdose discharges.

The region of the hospital of each ED presentation was defined using the U.S. Census Bureau's regional designations: Northeast (CT, MA, ME, PA, NH, NJ, NY, RI, VT), Midwest (IA, IL, IN, KS, MI, MN, MO, NE, ND, OH, SD, WI),

South (AL, AR, DC, DE, FL, GA, KY, LA, MD, MS, NC, OK, SC, TN, TX, VA, WV), and West (AZ, AK, CA, CO, HI, ID, MT, NM, NV, OR, UT, WA, WY) (22). NEDS also contains data regarding the urban/rural designation and teaching status of the hospital where the patient presented to the ED.

For the purpose of this study, comorbidities were defined as concurrent diagnoses on an ED discharge record, as recorded in the NEDS data, which allows for a maximum 30 diagnoses per visit. The primary diagnosis, which determined inclusion into this study, is listed first in the discharge record. All subsequent diagnoses are listed as secondary diagnoses (21). A thorough review of the literature identified over thirty comorbidities that have been found to be prevalent among opioid and/or heroin users. These include: diabetes, hypertension, heart disease, COPD, HIV, hepatitis, cancer, renal failure, and kidney disease. Prevalent comorbid mental health diagnoses included mood disorders, anxiety, substance-abuse disorders, and alcohol-related disorders.

These comorbidity group diagnostic variables were defined using HCUP's Clinical Classifications Software (CCS). CCS streamlines ICD-9 codes into groups of codes that indicate one diagnosis (23). For example, there are 14 ICD-9 codes that correspond to an HIV infection; CCS groups these codes and assigns a CCS value of 5 if the diagnosis was one of 14 respective ICD-9 codes. Using the CCS for all secondary diagnoses, indicator variables were created to denote if any of a record's subsequent diagnoses indicated a CCS value for any of the comorbidities of interest for this study. This coding allowed for estimation of the overall prevalence of a particular secondary diagnosis. The NEDS CCS scheme does not

differentiate between types of hepatitis; thus, any diagnosis for hepatitis A, B, and C are grouped together in this study.

Descriptive Analysis and Modeling

In order to account for NEDS study design, logistic regression was conducted in SAS-callable SUDAAN® 11.0.1. Risk ratios and 95% confidence intervals were generated to estimate the risk of admission or further treatment among non-heroin opioid and heroin overdose ED visits. The outcome (disposition from the ED) was collapsed into a binary variable based on if the patient received further care if they were admitted as an inpatient to the same hospital as the ED visit, transferred to a skilled nursing facility, intermediate care facility, or short-term hospital, or referred to home health care. The remaining dispositions, including routine treatment and release or release against medical advice were classified as not receiving further medical care.

Individuals who died in the ED were excluded from the study, as this study aimed to assess non-fatal overdoses (0.1% of non-heroin opioid overdoses and 0.3% of heroin overdoses died in the ED). Individuals who died in transport to the ED are not accounted for in NEDS data, thus they were also excluded from this study. Additionally, visits for which the patient's disposition from the ED was missing were excluded from the study (0.2% of non-heroin opioid overdoses and 0.6% of heroin overdoses). This resulted in a study population of 81,341 non-heroin opioid overdoses and 65,457 heroin overdoses. See Figure 1 for a visualization of the determination of the study population.

An initial logistic regression model was run to generate the unadjusted risk of admission among non-heroin opioid overdoses compared to that of heroin

overdoses. A subsequent model adjusted for meaningful confounders (age, gender, region, and primary payer). Additional models were run that adjusted for the aforementioned confounders while allowing for interaction with specific comorbidities (any mental health condition, anxiety disorders, mood disorders, substance-related disorders, alcohol-related disorders, cancer, thyroid conditions, diabetes, hypertension, heart diseases, COPD, respiratory failure, liver disease, acute renal failure, and chronic kidney disease). Risk ratios were also generated within strata of specific comorbidities.

D. Results

In 2014, there were 147,631 ED visits for opioid overdoses. 81,631 (55%) were due to non-heroin opioids and 66,023 (45%) were due to heroin overdoses. Table 1 provides a summary of the demographic characteristics of those presenting to a U.S. ED for an opioid overdose, separated by opioid type: non-heroin opioids and heroin. Individuals presenting with a non-heroin opioid overdose were older than those presenting with a heroin overdose. For example, 30% of heroin overdoses were among individuals aged 18 to 25 years, compared to 11% of non-heroin opioid overdoses. Additionally, 16% of non-heroin opioid overdoses were among those age 65 years and older, compared to 1.0% of heroin overdoses. Non-heroin opioid overdoses were approximately equal across sex, with 53% of overdoses occurring among females. In contrast, 70% of heroin overdose presentations were male.

Differences in opioid overdoses were also noted across regions of the country. The most common U.S. region for non-heroin opioid overdose was the

South (39%), followed by the Midwest (22%), the West, (22%), and the Northeast (17%). In contrast, the most common region for heroin overdoses was the Northeast (37%), followed by the Midwest (30%), the South (23%), and the West (9.9%). Figure 2 contains the regional distribution of opioid overdoses. Figure 4 is a reference map of the U.S. Census Bureau that identifies which states correspond to the designated regions.

Both populations tended to be low income; 33% percent of non- heroin opioid overdoses and 29% of heroin overdoses resided in zip codes with a median income less than $39,000. Most opioid overdoses, heroin or non-heroin, presented to metropolitan, non-teaching hospitals (54% of non-heroin opioid overdoses and 64% of heroin overdoses).

Considerable differences were found in the primary payer among heroin and non-heroin opioid overdose patients. For example, 35% of non-heroin opioid overdose discharges listed Medicare as the primary payer, compared to 6.8% of heroin overdose discharges. In contrast, 28% of non-heroin opioid overdoses listed Medicaid as the primary payer, compared to 41% of heroin overdoses.

Differences were also noted in the outcome of interest: disposition from the ED. Among non-heroin opioid overdoses, 39% left the ED under routine protocol (treat and release), compared to 72% of heroin overdoses. Moreover, 51% of non-heroin opioid discharges were admitted to the same hospital where they presented to the ED, compared to 18% of heroin overdose discharges. 6.6% of heroin overdose discharges left the ED against medical advice, compared to 2.5% of non-heroin opioid discharges.

Table 2 contains the prevalence of each comorbidity, or secondary diagnosis, stratified by the type of overdose. Non-heroin opioid overdoses had a higher prevalence of comorbidities**.** The most prevalent comorbidity among both non-heroin opioid and heroin overdoses was substance-related disorder, which was a concurrent diagnosis among 43% of non-heroin opioid overdoses and 57% of heroin overdoses. However, this diagnosis may not be best defined as a comorbidity, but as a concurrent presenting condition. Except for substance-abuse disorder, each comorbidity had a higher percent prevalence among non-heroin opioid overdoses than among heroin overdoses.

Common comorbidities among patients presenting with a non-heroin opioid overdose included: diabetes (17%), hypertension (33%), heart diseases (19%), COPD (13%), respiratory failure/arrest (19%), acute renal failure (14%), anxiety disorders (19%), mood disorders (34%), and alcohol-related disorders (12%). This is in contrast to the prevalence among heroin overdoses: diabetes (4.8%), hypertension (7.8%), heart diseases (4.9%), COPD (2.1%), respiratory failure (9.0%), acute renal failure (4.6%), anxiety disorders (7.6%), mood disorders (13%), and alcohol-related disorders (11%). Percent prevalence of each comorbidity can be seen in Figure 4.

Among non-heroin opioid overdoses, 6.3% had a concurrent cancer diagnosis, compared to 0.7% of heroin overdoses. Less than 1% of non-heroin opioid (0.9%) and heroin overdoses (0.7%) had a concurrent HIV infection. The prevalence of hepatitis was similar across overdose groups as hepatitis was a listed diagnosis in 5.4% of non-heroin opioid and 5.5% of heroin overdoses.

The unadjusted risk of admission among non-heroin opioid overdoses was 2.84 times the risk of admission among heroin-opioid overdoses (95% CI: 2.63, 3.05). When adjusting for important confounders (age, sex, hospital region, and primary payer), the relative risk of admission for non-heroin opioid overdoses was 2.14 (95% CI: 2.01, 2.28).

The risk of admission varied when accounting for interaction with specific comorbid conditions. When accounting for interaction between opioid type and prevalence of at least one mental health condition, the risk of admission among non-heroin opioid overdoses was 2.37 times that of heroin overdoses (95%CI: 2.19, 2.56). The risk of admission, when allowing for interaction with mood disorders, was 1.94 times greater among non-heroin opioid overdoses than among heroin overdoses (95% CI: 1.82, 2.07). When accounting for interaction between opioid type and substance abuse disorder, the risk of admission among non-heroin opioid overdoses was 2.59 times that of heroin overdoses (95%CI: 2.40, 2.80.). The risk of admission, when allowing for interaction with hypertension, was 2.05 times greater among non-heroin opioid overdoses than among heroin overdoses (95% CI: 1.92, 2.18). Table 3 contains risk ratios that allowed for interaction with a specific comorbidity.

The relative risk of admission among non-heroin opioid overdoses compared to heroin opioid overdoses differed across strata of comorbidity prevalence. Among visits with no concurrent mental health diagnoses, the risk of admission was 3.47 times greater among non-heroin opioid overdoses (95% CI: 2.89, 4.17). In contrast, among visits with at least one concurrent mental health diagnosis, the risk of admission was 1.92 times greater among non-heroin opioid

overdoses (95% CI: 1.78, 2.06). For each comorbidity, the risk ratio of admission was greater among the visits that did not have a concurrent diagnosis than among the visits that did have a concurrent diagnosis. Table 4 contains the risk ratios stratified according to the prevalence of the comorbidities of interest in this study.

E. Discussion

Principal Findings

Consistent with the literature, this study found that non-heroin opioid overdoses were more likely to result in a hospital admission or other further medical care, compared to heroin overdoses that presented to an emergency department in the United States in 2014. Additionally, considerable demographic differences among patients presenting with non-heroin opioid overdoses and heroin overdoses were observed. Notable differences included age, gender, region, and insurance status, with non-heroin opioid overdoses occurring more frequently among older populations, females, in the south, and among Medicare enrollees. Most notably, this study revealed considerable differences in the prevalence of comorbidities, or secondary diagnoses, according to the type of overdose. However, this finding may be related to the age difference between the two groups; those who presented an ED for a non-heroin opioid overdose were considerably older than those who presented for a heroin overdose.

Strengths and weaknesses

There are several strengths of this study including the use of NEDS data, a large, nationally-representative, multi-payer data set. This dataset allowed for a

very large sample size of over 140 million ED visits; 147,654 of which had a primary diagnosis of an opioid overdose. Both inclusion into the study and comorbidity diagnoses were determined using ICD-9 codes, which are uniformly used throughout U.S. hospitals and emergency departments. This allows for easy replication of the study in the future, while providing a strong standard of measurement for both exposure and interaction variables. Additionally, a thorough review of the current literature was conducted before the study to ensure that all relevant comorbidities were considered in the analyses.

However, there are several weaknesses of the study that must be considered. First, use of the NEDS data does not allow for a clear prior definition of chronic conditions, which raises concerns regarding misclassification of interaction variables. Comorbidities were defined using concurrent diagnoses from the ED discharge data. This is not likely to be a complete list of every comorbid health condition of each patient from each discharge. Moreover, these data did not indicate whether the individual had the condition before presenting to the ED, or if it was diagnosed upon presentation. Thus, patients could have received their first diagnosis of a condition such as substance abuse disorder during their ED visit. It is possible that the risk of admission would depend on the time of diagnosis with a particular comorbidity, but these data cannot account for this.

Another concern is repeat patients; in this study, the population is all opioid overdose ED discharges, not individuals who overdosed in 2014. It is likely that there were individuals who overdosed and presented to an ED multiple times during 2014 and were counted more than once in this study. This could have

contributed to the high prevalence of certain comorbid conditions. These data provide no mechanism for identifying these patients through this study.

This study adds to the current literature by evaluating the risk of admission among a nationally-representative sample of ED visits. Most studies of opioid overdose morbidity have focused on trends in visits as well as descriptive epidemiology (12, 17-19). For instance, Guy et al. (2018) observed higher rates of admission following non-heroin opioid overdoses compared to heroin overdoses, but potential mechanisms for the finding were not explored (18). This study sought to evaluate the relationship between opioid type and further medical care after an ED visit for an overdose, while allowing for the assessment of interaction by several key comorbidities such as mental health disorders, hypertension, diabetes, and renal diseases. However, other studies, while descriptive in nature, have analyzed several years of ED data, allowing for trend analyses of ED visits. This study only includes visits from the year 2014. Further research should asses the risk of admission across several years of data in order to better understand the interaction between opioid type and comorbid conditions.

Implications for Public Health Practice

This study provides important insights into the differences, both demographic and clinical, between the populations who present to an ED for an overdose on non-heroin opioids and those who overdose on heroin. Much of the media surrounding the opioid epidemic concerns its effects on rural populations throughout the U.S. However, this study found that urban areas also have a high morbidity of ED overdoses. Public health practitioners and law-makers should consider place, especially region and urban/rural location, when developing

programs and policies to prevent and mitigate overdoses. Additionally, given the differences in the populations according to opioid type, those who use non-heroin opioids and those who use heroin should not always receive the same interventions.

This study, consistent with the literature, found that non- heroin opioid users were approximately two times more likely to be admitted after an ED visit; this pattern is potentially due to the high prevalence of comorbidities among this population. As clinicians treat overdose patients and work to reduce future ED visits and hospitalizations, they should consider the impact of comorbidities on the overall severity of an overdose.

Recent literature has focused on using EDs as a point of intervention in order to transition overdose patients directly into treatment (24, 25). The results of this study allow for a more complete understanding of the clinical and demographic characteristics of these patients, which is essential for linking this population to treatment for opioid misuse outside of an ED. Given the high prevalence of comorbidities among this population, treatment programs should include care management for chronic diseases such as heart disease and diabetes as well as medication-assisted treatment for opioid use disorder.

Given the high prevalence of mental health conditions among this population, it is of utmost importance that public health practitioners continue work to increase access to mental health services and counseling among opioid users. Integrating coordinated care into opioid treatment programs has the potential to reduce costs and prevent future overdoses.

Considerations for Further Research

This study posed several unanswered questions that are necessary for researchers and public health practitioners to further investigate in order to better understand the opioid overdose epidemic. Specifically, this study found that those who presented to an ED for a heroin overdose on heroin were more likely to leave an ED against medical advice than those who presented for a non-heroin opioid overdose. However, further research is necessary to understand the mechanisms that led to this finding. It would be advantageous to see if this difference is also found in more recent years or among populations from different data sources such as Medicaid data repositories or managed care claims databases. Additionally, this study was a point-in-time analysis that considered the risk of admission in 2014. Since 2014, the number of opioid overdoses, both fatal and non-fatal have increased and the use of synthetic and semi-synthetic opioids such as fentanyl has risen (24). Thus, it is necessary to evaluate the risk of admission during subsequent years and determine if similar patterns persist.

Conclusion

As our knowledge of the opioid overdose crisis in the United States continues to grow, it is imperative that we invest time, effort, and funding into understanding the factors associated with both opioid overdose mortality and morbidity. This study sought to add to the understanding of opioid morbidity in the United States by assessing the demographic and clinical differences among heroin and non-heroin opioid overdoses. It is clear that comorbidities contribute heavily to opioid overdose morbidity and they should be considered in future clinical, policy, and research decision-making regarding the opioid crisis.

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G. Tables

Table 1. Characteristics of Emergency Department Discharges for Opioid Overdose, United States, 2014, N= 147,654				
	Non-Heroin Opioid Discharges n= 81,631		Heroin Discharges n=66,023	
	Frequency	%	Frequency	%
Patient Age				
Under 18	4,382	5.4%	418	0.6%
18 to 25	8,921	11%	19,793	30%
26 to 30	6,394	7.8%	14,656	22%
31 to 40	11,699	14%	15,966	24%
41 to 50	13,439	16%	8,117	12%
51 to 64	23,629	29%	6,425	9.7%
65 and older	13,167	16%	648	1.0%
Gender				
Male	38,683	47%	46,428	70%
Female	42,934	53%	19,595	30%
Missing	14	0.0%	0	0.0%
Hospital Region				
Northeast	14,029	17%	24,491	37%
Midwest	17,942	22%	19,855	30%
South	32,104	39%	15,123	23%
West	17,556	22%	6,554	9.9%
Median Income of Patient's Zip Code				
Less than $39,000	26,813	33%	18,929	29%
$40,000 - $50,999	23,342	29%	15,705	24%
$51,000 - $65,999	16,736	21%	15,423	23%
Greater than $66,000	12,512	15%	13,920	21%
Missing	2,228	2.7%	2,046	3.1%
Patient Location According to NCHS Urban Rural Code				
Large Metropolitan Area	37,099	45%	39,439	60%
Medium Metro Area	22,037	27%	16,230	25%
Small Metro Area	8,373	10%	4,143	6.3%
Micropolitan county	8,084	9.9%	3,773	5.7%
Non-core	5,298	6.5%	1,244	1.9%
Missing	740	0.9%	1,194	1.8%
Hospital Type				
Metropolitan teaching	26,260	32%	19,528	30%
Metropolitan non-teaching	44,114	54%	42,483	64%
Non-metropolitan hospital	11,257	14%	4,012	6.1%
Primary Payer				
Medicare	28,167	35%	4,505	6.8%
Medicaid	22,937	28%	26,817	41%
Private	16,402	20%	12,316	19%
Self-Pay	10,409	13%	17,621	27%
No charge	453	0.6%	847	1.3%
Other	3,142	3.8%	3,748	5.7%
Missing	121	0.1%	169	0.3%
Total Charge, mean (SD)				
	$3,670	$108	$2,672	$113
Discharge Status				
Routine (Treat and Release)	31,652	39%	47,562	72%
Admitted	41,368	51%	11,581	18%
Transferred facilities	6,026	7.4%	1,914	2.9%
Home Health Care	252	0.3%	25	0.0%
Against Medical Advice	2,043	2.5%	4,375	6.6%
Died in ED	87	0.1%	198	0.3%
Unknown	203	0.2%	368	0.6%

Table 2. Comorbidities/Concurrent Diagnoses of Emergency Department Discharges for Opioid Overdose, United States, 2014, N= 147,654

	Non-Heroin Opioid Discharges n= 81,631		Heroin Discharges n=66,023	
	Frequency	%	Frequency	%
Number of Additional Diagnoses				
Zero	5,038	6.2%	8,565	13%
One to Four	25,016	31%	40,278	61%
Five to Nine	19,928	24%	11,029	17%
Ten to Fourteen	15,899	19%	3,938	6.0%
Fifeen to Nineteen	9,186	11%	1,463	2.2%
Twenty or more	6,565	8.0%	749	1.1%
Concurrent Diagnoses[1]				
HIV Infection	747	0.9%	438	0.7%
Hepatitis	4,391	5.4%	3,635	5.5%
Cancer	5,175	6.3%	437	0.7%
Thyroid disorders	6,211	7.6%	593	0.9%
Diabetes	13,969	17%	3,199	4.8%
Hypertension	26,573	33%	5,160	7.8%
Heart diseases and conditions	15,812	19%	3,256	4.9%
Pneumonia (except that caused by TB or STD)	3,668	4.5%	1,050	1.6%
Chronic obstructive pulmonary disease	10,724	13%	1,366	2.1%
Asthma	5,375	6.6%	2,580	3.9%
Respiratory failure; insufficiency; arrest	15,242	19%	5,913	9.0%
Liver disease (alcohol-related or other)	5,068	6.2%	1,694	2.6%
Nephritis, nephrosis, renal sclerosis	333	0.4%	59	0.1%
Acute and unspecified renal failure	11,716	14%	3,054	4.6%
Chronic Kidney Disease	5,025	6.2%	432	0.7%
Arthritis	4,728	5.8%	294	0.4%
Concurrent Mental Health Diagnoses[1]				
At least one mental health condition	54,310	67%	42,448	64%
Anxiety disorders	15,172	19%	5,037	7.6%
Mood disorders	27,513	34%	8,456	13%
Alcohol-related disorders	10,071	12%	7,077	11%
Substance-related disorders	34,767	43%	37,656	57%
Suicide and intentional self inflicted injury	2,582	3.2%	898	1.4%
Miscelleanuous mental health	4,213	5.2%	1,774	2.7%

Notes:

[1]ICD-9 codes for concurrent diagnoses were grouped using the Clinical Classifications Software (CCS) of the Health Care Utilization Project (HCUP).

Table 3. Risk of Admission/Further Care Among Opioid Overdose ED Visits by Comorbidity/Concurrent Diagnosis[1], United States, 2014, N=

	Risk Ratio, (95% CI)	SE
Unadjusted Model		
Risk of admission among non-heroin opioid compared to heroin overdoses	2.84, (2.63, 3.05)	0.11
Adjusted Model		
Adjusts for age, sex, hospital region, and expected primary payer	2.14, (2.01, 2.28)	0.07
Interaction with Mental Health Conditions		
Any mental health condition	2.37, (2.19, 2.56)	0.09
Anxiety disorders	2.04, (1.92, 2.17)	0.06
Mood disorders	1.94, (1.82, 2.07)	0.06
Substance abuse disorders	2.59, (2.40, 2.80)	0.10
Alcohol-related disorders	2.17, (2.03, 2.32)	0.07
Interaction with Other Comorbid Conditions		
Cancer	2.10, (1.98, 2.24)	0.07
Thyroid Conditions	2.09, (1.96, 2.23)	0.07
Diabetes	2.09, (1.96, 2.22)	0.07
Hypertension	2.05, (1.92, 2.18)	0.07
COPD	2.10, (1.97, 2.24)	0.07
Respiratory failure; arrest	2.17, (2.04, 2.32)	0.07
Liver disease	2.10, (1.97, 2.24)	0.07
Acute renal failure	2.00, (1.88, 2.14)	0.07
Chronic kidney disease	2.07, (1.94, 2.21)	0.07

Notes:

[1]ICD-9 Codes for concurrent diagnoses were grouped using the Clinical Classifications Software (CCS) of the Health Care Utilization Project (HCUP)

Table 4. Risk of Admission Among Non-Heroin Opioid Overdoses, Stratified by Comorbidity/Concurrent Diagnosis Prevalence[1], United States, 2014, N= 146,798

	Discharges without a subsequent diagnosis for listed comorbidity			Discharges with a subsequent diagnosis for listed comorbidity		
	Risk Ratio	95% CI	SE	Risk Ratio	95% CI	SE
Mental Health Conditions						
Any mental health condition	3.47,	(2.89, 4.17)	0.32	1.92,	(1.78, 2.06)	0.07
Anxiety disorders	2.24,	(2.10, 2.40)	0.08	1.28,	(1.19, 1.37)	0.05
Mood disorders	2.26,	(2.10, 2.43)	0.08	1.30,	(1.22, 1.38)	0.04
Substance abuse disorders	3.80,	(3.30, 4.37)	0.27	1.83,	(1.69, 1.97)	0.07
Alcohol-related disorders	2.28,	(2.12, 2.44)	0.08	1.54,	(1.42, 1.67)	0.06
Other Comorbid Conditions						
Cancer	2.15,	(2.01, 2.29)	0.07	1.37,	(1.08- 1.73)	0.16
Thyroid conditions	2.16,	(2.03, 2.30)	0.07	1.25,	(1.06, 1.48)	0.11
Diabetes	2.22,	(2.08, 2.37)	0.07	1.41,	(1.27, 1.55)	0.07
Hypertension	2.24,	(2.09, 2.39)	0.08	1.52,	(1.37, 1.69)	0.08
COPD	2.18,	(2.05, 2.33)	0.07	1.42,	(1.25, 1.61)	0.09
Respiratory failure; arrest	2.51,	(2.33, 2.69)	0.09	1.13,	(1.09, 1.16)	0.02
Liver disease	2.23,	(2.09, 2.38)	0.08	1.04,	(0.97, 1.11)	0.03
Acute renal failure	2.32,	(2.18, 2.48)	0.08	1.03,	(1.00, 1.05)	0.01
Chronic kidney disease	2.16,	(2.03, 2.30)	0.07	1.05,	(0.97, 1.21)	0.07

Notes:

[1]ICD-9 Codes for concurrent diagnoses were grouped using the Clinical Classifications Software (CCS) of the Health Care Utilization Project (HCUP).

F. Figures/Figure Legends

Figure 1. Flow Chart of Study Population

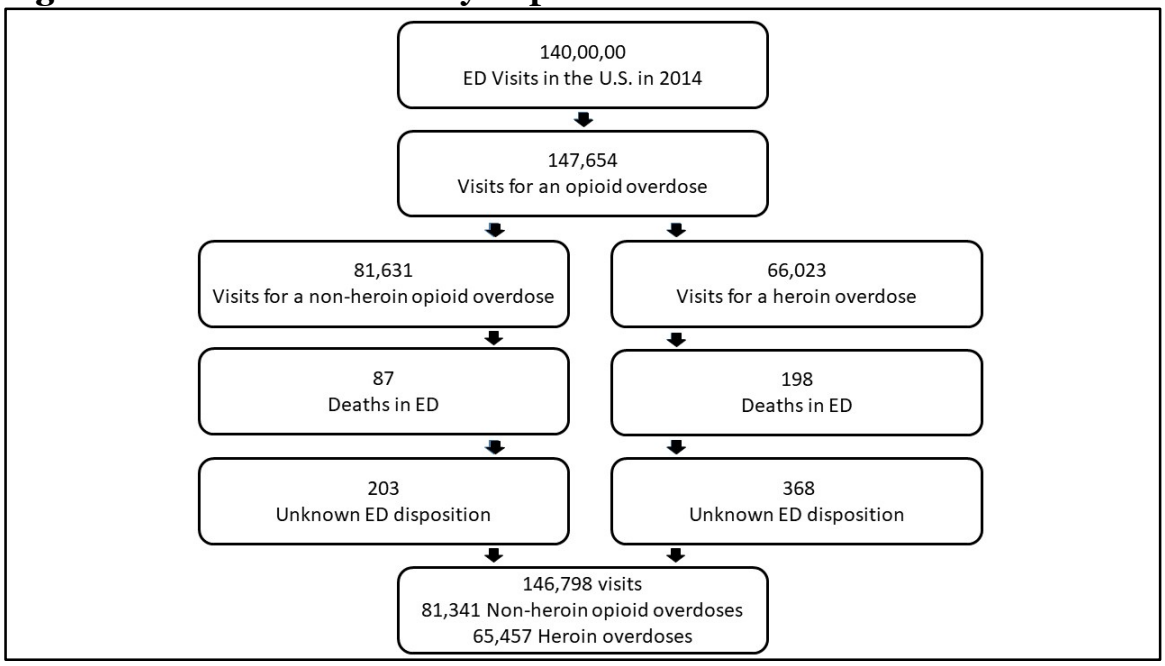

Figure 1 depicts how the final study population was determined. The 2014 National Emergency Department Sample contained 137,807,901 unique emergency department (ED) discharges, 147,654 of which had an opioid overdose listed as the primary diagnosis. After removing deaths in the ED and unknown dispositions, the final study population contained 136,697 visits- 81,341 for a non-heroin opioid overdose and 65,457 for a heroin overdose.

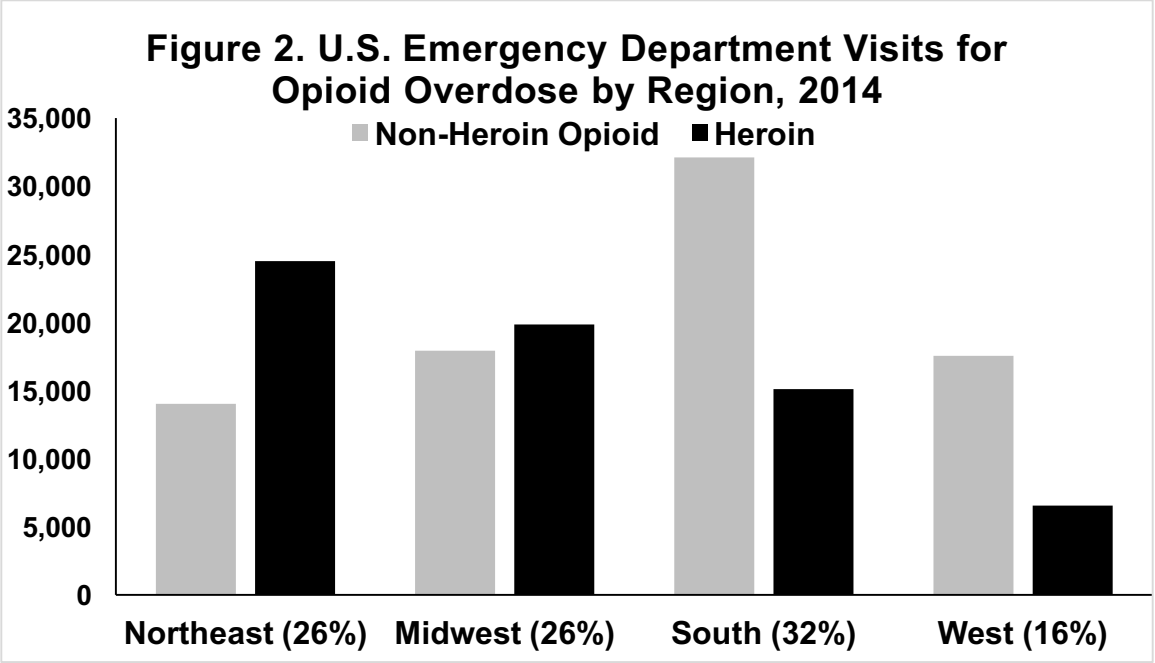

Figure 2 contains the counts of non-heroin opioid overdose and heroin overdose emergency department(ED) visits in 2014 per region, as designated by the United States Census Bureau. Percentages adjacent to the region indicate the percentage of the total U.S. opioid overdose ED visits in each region. Data were obtained from the National Emergency Department Sample, Healthcare Cost and Utilization Project, Agency for Healthcare Research and Quality.

Figure 3. U.S. Regions as designated by the U.S. Census Bureau

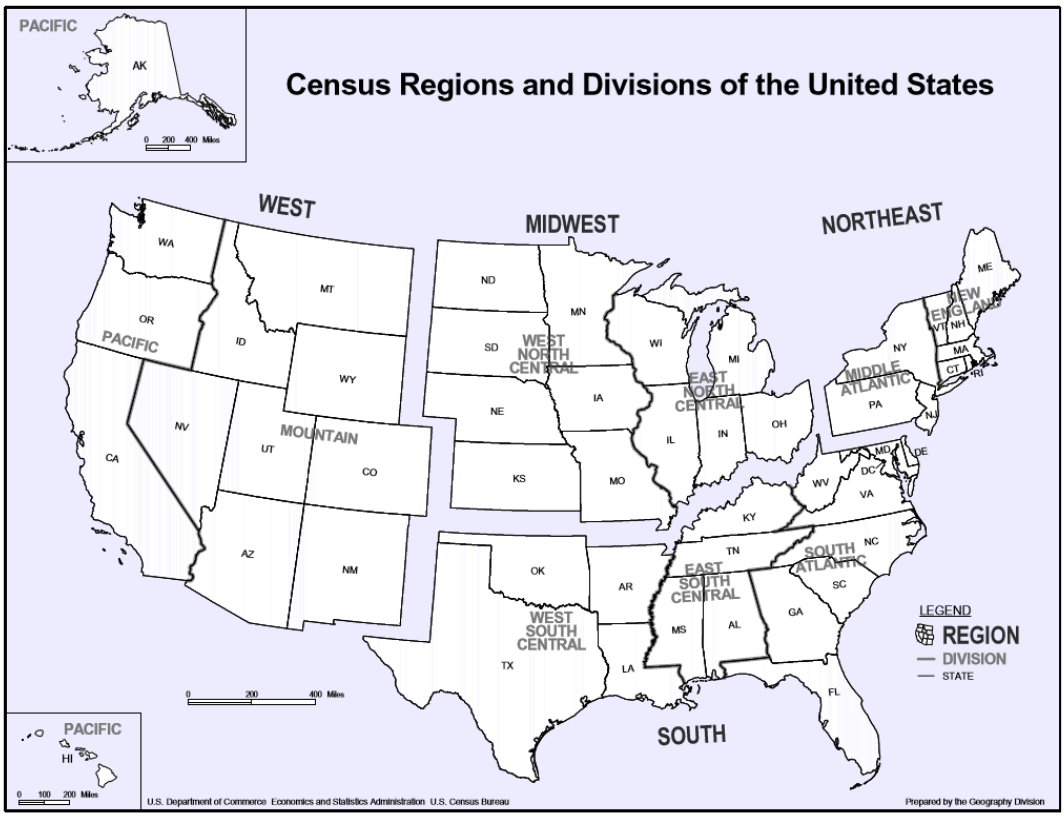

Figure 3, obtained from the U.S. Census Bureau, is a map of the United States according to the bureau's designated regions and divisions.

Figure 4. Percent Prevalence of Comorbidities/Concurrent Diagnoses, U.S. Emergency Department Visits for Opioid Overdose, 2014

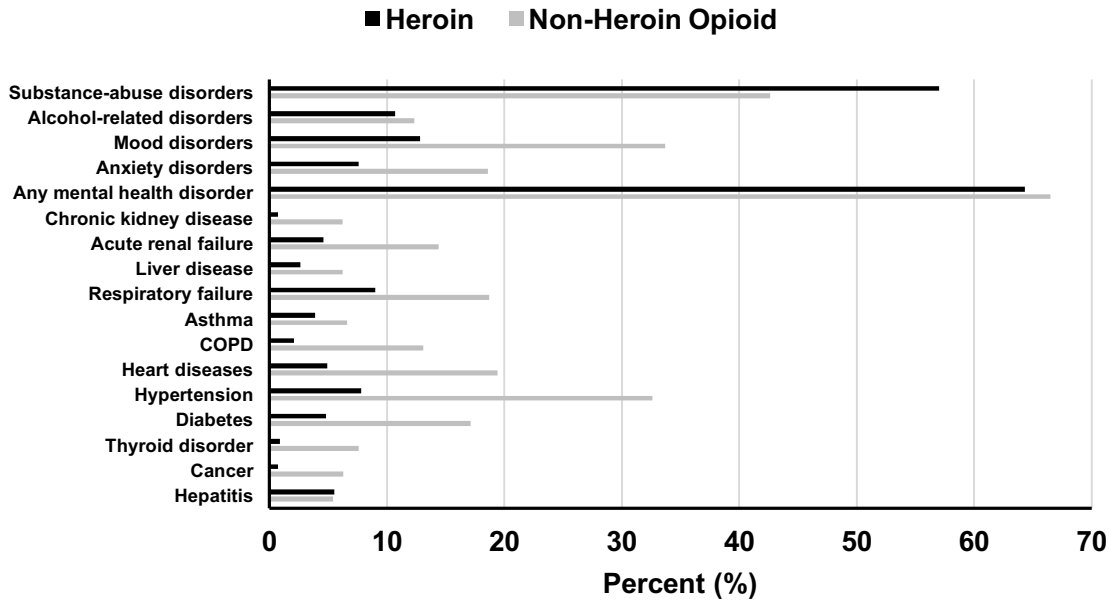

Figure 4 contains the percentage of non-heroin opioid overdose and heroin overdose presentations to a U.S. emergency department(ED) that had a subsequent diagnosis for the listed comorbid conditions. Data were obtained from the 2014 National Emergency Department Sample, Healthcare Cost and Utilization Project, Agency for Healthcare Research and Quality. Abbreviations: COPD, chronic obstructive pulmonary disease