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PATIENT, HOSPITAL AND STATE-LEVEL POLICY CHARACTERISTICS ASSOCIATED WITH PREVALENCE OF TREATING OPIOID USE DISORDER IN UNITED STATES EMERGENCY DEPARTMENTS

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PATIENT, HOSPITAL AND STATE-LEVEL POLICY CHARACTERISTICS
ASSOCIATED WITH PREVALENCE OF TREATING OPIOID USE
DISORDER IN UNITED STATES EMERGENCY DEPARTMENTS

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2020

DEDICATION

To

Rafiu Olalekan Yusuf & Ramat Adunni Yusuf;

Zenab Yusuf;

Raadiyah, Aamanee, Reedah & Rahma Yusuf.

PATIENT, HOSPITAL AND STATE-LEVEL POLICY CHARACTERISTICS
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DISORDER IN UNITED STATES EMERGENCY DEPARTMENTS

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for the Degree of

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SCHOOL OF PUBLIC HEALTH

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PREFACE

My inspiration for completing this degree program stemmed from my life long desire for learning and self-improvement. My motivation for pursuing this research was from my professional experiences interacting with patients as a physician. I was personally motivated to complete this work because I believe strongly that it will contribute significantly to knowledge and practice in the fields of clinical medicine, public health, and health informatics while having far reaching policy implications on how individuals, populations, and the public in general receive health and healthcare services.

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DISORDER IN UNITED STATES EMERGENCY DEPARTMENTS

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The opioid crisis in the United States was declared a public health emergency due to escalating and untoward human, financial, and systemic consequences and effects on the nation. Opioid use disorder (OUD) comprising opioid abuse and dependence is devastating because of its associated chronic relapsing nature, overutilization of healthcare services, rising morbidity and mortality rates, and high cost of care. Efforts to address this have not made significant positive impacts. It is thus imperative to reassess the influence of factors associated with OUD.

This study answered the question, what patient-, hospital-, and state-level policy factors were associated with prevalence of diagnosing and treating OUD in U.S. emergency departments (ED), since the ED which were usually first point-of-contact with the healthcare system by patients with OUD witnessed significantly increased visits related to nonmedical use of opioids.

A retrospective secondary data analysis of the cross-sectional Nationwide Emergency Department Sample of patients 12 years and older from January 1 to December 31, 2016;

ASAM state reports; SAMHSA Office of Policy, Planning and Innovation State Medicaid coverage reports; and KFF report on opioid epidemic was performed. Outcome variable was prevalence of diagnosing and treating OUD in the ED. Primary predictor variable was OUD condition, and covariates included, patient characteristics – primary payer, annual median income, patient location, and ED event; hospital characteristics – control/ownership, region, and designation; and state-level policy characteristics – medication-assisted treatment (MAT) policy, MAT medication coverage, Medicaid expansion, and Medicaid section 1115 behavioral health waiver statuses. Descriptive statistics was reported for all variables. Pearson's chi-squared was test used to determine statistically significant differences between opioid abuse and opioid dependence diagnosis. Hierarchical linear regression model (HLM) was used to estimate association between outcome and predictor variables.

In total, 32,680,232 ED visits in 953 hospitals across 35 states and District of Columbia which when generalized to the entire United States amounted to 144,842,742 visits to the ED in 4,639 hospitals across the 50 states including the District of Columbia were analyzed. The total number of opioid-related incidents to the ED was 1,623,490. The overall prevalence of any opioid-related incident was 1.12% while overall prevalence of diagnosis and treatment of uncomplicated OUD in U.S. ED was 0.5%. Significant regional disparities existed in state-level opioid policies, prevalence of uncomplicated OUD and other characteristics influencing treatment of OUD in U.S. ED. Opioid dependence patients (55.6%) were preponderantly of upper-lower income class, micropolitan residents, covered by Medicare; admitted to same hospital they presented, attended to largely in privately-owned not-for-profit ED, in micropolitan areas, and in Southern and Western U.S. Opioid

abuse patients (44.4%) were predominantly of lower-lower income status, metropolitan dwellers, Medicaid covered; presented commonly to privately-owned not-for-profit ED, in metropolitan locations, and in Northeastern and Midwestern U.S. Combined, patient and hospital-level policy characteristics accounted for 25.4% ($R^2=0.254$, Adj. $R^2=0.254$, $F(3,734618)=31937.906$, $p<0.0001$) of variance in prevalence of treating OUD in ED. Patient characteristics only accounted for 15.6% ($R^2=0.156$, Adj. $R^2=0.156$, $F(5,734621)=27245.686$, $p<0.0001$) and hospital characteristics only for 9.7% (R^2 change=0.097, $F(3,734618)=31937.906$, $p<0.0001$) of the variance. Proportion of variance accounted for by each predictor variable was, control/ownership of hospital (9.67%), patient location (6.35%), annual median income (1.44%), hospital designation (1.21%), OUD diagnosis (0.20%), primary payer (0.04%), region of hospital (0.02%), and ED event (0.008%).

Patient and hospital level characteristics significantly influenced prevalence of treating OUD in U.S. ED. Hospital-level characteristics contributed more than patient-level characteristics. A socioecological approach, which ensures an integrated and holistic method, is required to understand factors influencing OUD with the view to developing innovative policies and programs that can positively and significantly address the opioid crisis.

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BACKGROUND

Introduction

This dissertation will determine the prevalence of emergency care of opioid use disorder in the United States population 12 years and older with a view to guiding drug policy and program implementation.

The devastating effects of opioids in developed and developing nations is no longer news. What may be news is the context in which the problem is framed which invariably affects perceptions of the scope of the problem and how it is addressed subsequently. The President of the United States, under federal law declared the opioid crisis in America as a national public health emergency on October 26, 2017 (The White House, 2017).

Current research on opioids focuses on prescribing and dispensing practices (Jayawardhana et al, 2018; Cochran et al, 2017; Dowell et al, 2016); treatment of specific conditions such as chronic pain, back disorders, arthritis, inflammatory bowel disease (Hayes et al, 2018; Cohen-Mekelburg et al, 2018); prevention of opioid overdoses (Peglow et al, 2018; Huhn et al, 2018; McGinty et al, 2018; Lynch et al, 2017); treatment of substance use disorders especially opioid overdoses (Zhu et al, 2018; Vipler et al, 2018; Garland et al, 2018; Brinkley-Rubinstein et al, 2018; Borodovsky et al, 2018; Heslin et al, 2017; Mosher et al, 2017); adherence/non-adherence to treatment (Lo-Ciganic et al, 2018); prevalence of specific conditions (e.g. obesity, HIV, mental health disorders) among opioid use disorder (OUD) populations (Hu et al, 2018; Shrestha et al, 2018; Cochran et al, 2017); substance use disorders including opioids (Serdarevic et al, 2018; Hawk et al, 2018); cost of providing treatment (Chang et al, 2018; Burgos et al, 2018; Xie et al, 2014; Chandwani et al, 2013); and molecular and pharmacogenetic

basis of treating substance use disorders including OUD (Fang et al, 2018; Schroeder et al, 2018, Crist et al, 2018; Laudénbach et al, 2018).

Furthermore, recent opioid research has focused on community-based populations (Serdarevic et al, 2018; Cochran et al, 2017), specific populations such as children and adolescents 12-17 years old (Borodovsky et al, 2018; Levy et al., 2016; Wu et al., 2016; Hadland et al., 2016; Xie et al, 2014; Muhuri et al., 2013, SAMHSA, 2013a), women (Hayes et al, 2018; Serdarevic et al, 2018), pregnant women (Jayawardhana et al, 2018; Peglow et al, 2018), incarcerated individuals (Brinkley-Rubinstein et al, 2018), individuals enrolled in clinical trials (Hu et al, 2018); and privately insured individuals (Sun et al, 2017).

The sites of these studies have been mainly inpatient-based (Zhu et al, 2018; Peglow et al, 2018; Cohen-Mekelburg et al, 2018; Heslin et al, 2017; Mosher et al, 2017; Gaither et al, 2016), a combination of inpatient-based and emergency department visits (Peterson et al, 2018; Tedesco et al, 2017; Wu et al., 2016) or ambulatory clinics only (Peglow et al, 2018; Wu et al., 2016). Few have focused on patients with OUD visiting the emergency department only (Hawk et al, 2018; Wu et al., 2016; Xie et al, 2014; Chandwani et al, 2013).

This research fills an important gap in providing current estimates of the prevalence of diagnosing and treating OUD in emergency departments (ED) in the United States. The implications of this research include guiding policymaking, resource allocation, program planning and implementation regarding management of OUD in the ED (Burgos et al, 2018; Friedmann et al, 2017; Molfenter et al, 2017; Ford et al, 2017).

Why study disease prevalence?

Estimating burden of disease specifically prevalence may potentially influence health policy development and implementation regionally and globally (Degenhardt et al, 2014a).

How does prevalence estimations influence policy?

Prevalence of disease influence policy by driving change and leading to meaningful differences in health outcomes (Aldrich et al, 2015).

Literature Review

In this review of the literature, the timeline of the opioid crisis in the United States is highlighted, opioid crisis as a public health emergency is discussed, the opioid crisis is evaluated using the quadruple aim framework and the significance of opioid use disorder is emphasized.

Advocacy for better treatment of pain in the United States started in 1991 (Tsang et al., 2008). This resulted in introduction of opioid analgesics (pain relievers) to manage both acute and chronic pain. Opioids are a class of drugs consisting of Schedule II analgesics such as codeine, oxycodone, hydrocodone, morphine, and legally prescribed fentanyl; and the Schedule I drug – heroin – considered illicit. The achievement of pain relieving effects of opioids are through stimulation of neurotransmitter production in the central nervous system and gastrointestinal tract (National Institute on Drug Abuse, 2015). When taken as prescribed by healthcare providers and over a short period, opioid analgesics are essentially safe. However, because of the added euphoric effects, opioids may not be taken as prescribed, taken in quantities larger than prescribed or taken without being prescribed (National Institute on Drug Abuse, 2015). Notwithstanding legally prescribed or illicitly obtained, opioids readily result in abuse leading to opioid use disorder (OUD) such as dependency and addiction. Consequences of iatrogenic or recreational long-term use of opioids include physical and/or psychological dependence, overdose, and death (National Institute on Drug Abuse, 2015). Specifically, problematic uses of opioids are categorized and defined as (1) Misuse – “opioid use contrary to the directed or prescribed pattern of use, regardless of the presence or absence of harm or

adverse effects”. (2) Abuse – “intentional use of the opioid for a nonmedical purpose, such as euphoria or altering one’s state of consciousness”. (3) Addiction – “pattern of continued use with experience of, or demonstrated potential for, harm” which may include inability to control use of the drug, habitual drug use, constant drug use in the face of harm, and insatiable craving (Naliboff et al., 2011; Smith et al., 2013; Butler, 2013; Sullivan, 2013; Vowles et al., 2015). There is controversy over using the term “addiction” or “dependence” (O’Brien et al., 2006; Regier et al, 2013). However, in the American Psychiatric Association Diagnostic and Statistical Manual of Mental Disorders, fifth Edition (DSM-5) Classification, “dependence” is the preferred term. According to the DSM-5 classification, the two disorders, opioid abuse and opioid dependence, have now been combined into a single term – Opioid Use Disorder (Hartney & Gans, 2008; Regier et al, 2013).

An unintended consequence of the advocacy efforts and subsequent escalation in pain treatment of the early 1990s was an increase over four times of prescription opioid induced overdose mortality between 1999 and 2018 (Seth et al., 2018). A proportion of opioid users began their dependence on the drug following legal prescription of opioids by healthcare providers (Schoenfeld et al, 2017). Furthermore, attributed to use of prescription opioids was the initiation of drug abuse in 80% of heroin users (Muhuri et al., 2013). Over 116 million individuals are living with chronic pain in the United States (Seth et al., 2018). Concerning chronic pain treatment, between 21% and 29% percent of individuals on prescription opioids ultimately misuse their medication with 8% to 12% becoming addicted (Vowles et al., 2015). Consequently, the United States is currently experiencing a significant opioid misuse crisis (Trasolini et al, 2018).

Opioid Crisis in America

Timeline of opioid analgesic use and opioid crisis

Pre 1800 to 1800 – Prior to 1800, clinicians viewed pain as part of human existence and experience. It was considered a result of aging (Meldrum, 2003a). As such, not regulating use of cocaine and opioids in this era resulted in pervasive marketing and prescription for various illnesses from toothache to diarrhea (Clarke et al, 2016).

1801 to 1979 – During the 19th century, opioids were used as standard treatment for acute and recurrent pain. In 1804, Friedrich Wilhelm Sertürner produced morphine from crude opium (Schmitz, 1985). By the 1820s, Germany had commenced industrial production of morphine followed a decade later by the United States. In 1855, Alexander Wood invented the technique of using a hypodermic syringe and fine bore needle to deliver morphine subcutaneously to pain sites. The convenience of this mode of ensuring pain relieve may have heralded overuse of morphine for analgesia (Howard-Jones, 1947). Furthermore, non-regulation and easily available over the counter formulations of opium and alcohol-based preparations as pills, liquids and powders made self-medication convenient. This trend continued into the 1870s during which physicians started observing the “repeated indulgence inducing bodily and mental prostration and mental perversion” associated with “the morphine habit” or “narcomania” of using morphine (Kerr, 1894). Germany’s Bayer Company started marketing diacetylated morphine pills for treatment of cough under the trade name of “Heroin” in 1898. This diacetylated morphine introduced as less habit-forming was an alternative to morphine. However, by 1910, diacetylated morphine pills were being crushed into powder and inhaled for concentrated high by the young working-class in the United States. The rising trend of morphine (heroin) addiction due to legal and illicit use resulted in overwhelming support of the Harrison Narcotic Control Act of 1914.

A consequence of this Act was “opiophobia”, where both physicians and patients avoided prescribing and using opioid analgesics respectively. (Meldrum, 2003a; Meldrum, 2003b; Jones et al., 2018). Thus, by the 1920s, patients with unexplained pain were categorized as deluded, malingers or abusers looking for a “heroin fix” while into the 1950s, patients with cancer were encouraged to self-wean off opioids (Schiffman, 1956). Opiophobia continued into the second half of the twentieth century (Meldrum, 2003a; Jones et al., 2018). Therefore, under-treatment of pain, another consequence, led to advocacy to bring awareness to this issue especially following a 1973 *Annals of Internal Medicine* publication by Richard Marks and Edward Sachar (Marks & Sachar, 1973).

1980 to 1989 – Generally, in the 1980s, several physicians were fearful of prescribing opioids in spite of an extensively cited article suggesting opioid-induced addiction was rare with opioids taken for short-term pain (Porter & Jick, 1980). Specifically, John Morgan in 1985 in the United States and Michael Zenz and Anne Willweber-Strumpf in 1992 in Europe stressed the issue of less reliance on opioid analgesics and resultant under-treatment of pain. This was due to physicians’ conflict arising from their desire to relieve adequately the pain of patients and their fear of inducing addiction in these patients (Morgan, 1985; Zenz & Willweber-Strumpf, 1993). In spite of education, clinical guidelines, and advocacy to change the perceptions, attitudes, and beliefs of physicians towards prescribing opioids for pain management, practice had not change (National Institutes of Health, 1986; American Pain Society, 1987, WHO, 1986, 1996; Carr & Jacox, 1997). Thus, due to the attendant problem of underassessment and under-treatment of pain, opinion leaders and experts in the field called for improved assessment, robust and more vigorous treatment methods to address the problem of inadequate pain management including the use of opioids (Max, 1990, Baker, 2017).

1990 to 1999 – Following the work of Morgan and Zenz and Willweber-Strumpf, the clear call for a change in the strategy for assessment and management of pain intensified in the 1990s. The American Pain Society through its then president, Dr. Mitchell Max was at the forefront of these efforts. He wrote an editorial in *Annals of Internal Medicine* criticizing the lack of improvement in assessment and treatment of pain over the preceding two decades (Max, 1990). In addition, education, advocacy, and clinical guidelines in the prior decade from Ubaker.S. Agency for Health Care Policy and Research, American Pain Society, and World Health Organization had not worked (National Institutes of Health, 1986; American Pain Society, 1987, WHO, 1986, 1996; Carr & Jacox, 1997). Reasons proffered for this failure included patients not informing their healthcare providers about their pain, nurses' inability to adjust pain medication doses, and physicians' reluctance to prescribe opioids. In taking a new approach to pain management, Dr. Max stressed then conventional wisdom that “therapeutic use of opiate analgesics rarely results in addiction”. He thus recommended (1) making pain “visible”. (2) Giving practitioners “bedside” tools for change to guide physicians and nurses to initiate and modify analgesic treatments. (3) Assuring patients a place in the “communications loop”. (4) Increasing clinician accountability by developing “quality assurance guidelines”, improving care systems, and assessing patient satisfaction. (5) Facilitating innovation and exchange of ideas. (6) Working with narcotics control authorities to encourage therapeutic opiate use. Consequently, in response to greater awareness of pain levels of patients and more therapeutic use of opioids, and prior to acknowledgement of the opioid crisis, healthcare providers were motivated to treat pain generously with opioid analgesics (Max, 1990; Baker, 2017). The resultant effect was pressure to prescribe opioid analgesics every time pain was reported (Trasolini et al, 2018). As such, pain was promoted as the “fifth vital sign” and an “enemy that

needed to be eradicated” (Baker, 2017). For instance, in 1999, California’s legislature voted for an act necessitating that facilities record pain levels together with routine vital sign measurements (Escutia, 1999).

In 1995, the Food and Drug Administration approved OxyContin® (Oxycodone) for treatment of pain. Misleadingly and aggressively marketed as a non-addicting opioid analgesic, OxyContin quickly developed into a widely prescribed pain reliever. Consequently, there was a 153% rise in opioid analgesics prescribing between 1990 and 1999 from 76 to 116 million prescriptions respectively (Baker, 2017). In many ways, the discovery that OxyContin® was an opioid with a high risk for addiction and dependence may have driven the second wave of the opioid crisis (Van Zee, 2009).

2000 to 2009 – The Joint Commission in collaboration with the University of Wisconsin-Madison School of Medicine and experts nationwide started to develop its first pain standards in 1997 and completed it in 2000. The Joint Commission initiative followed the advocacy by American Pain Society for novel quality assurance standards for acute and cancer pain, and as a result of the overall paucity of knowledge regarding pain management, and misunderstandings concerning tolerance and addiction to drugs (American Pain Society, 1987; Institute of Medicine, 1987; Campbell, 1995). Part of the requirements of the Joint Commission’s standards was that all healthcare organizations were to assess systematically and quantitatively every patient for pain (Morone & Weiner, 2013; Barker, 2017). Furthermore, the United States Congress declared a “Decade on Pain Control and Research,” from 2001 to 2011. Following this, there was increase in opioid analgesics prescribing. Equally, due to public health research efforts, there were increasing reports of misuse, addiction, and deaths due to opioid-related overdoses (Interagency

Pain Research Coordinating Committee, 2015). All these coincided with when OxyContin® had become a leading drug of abuse in the United States in 2004 (Van Zee, 2009).

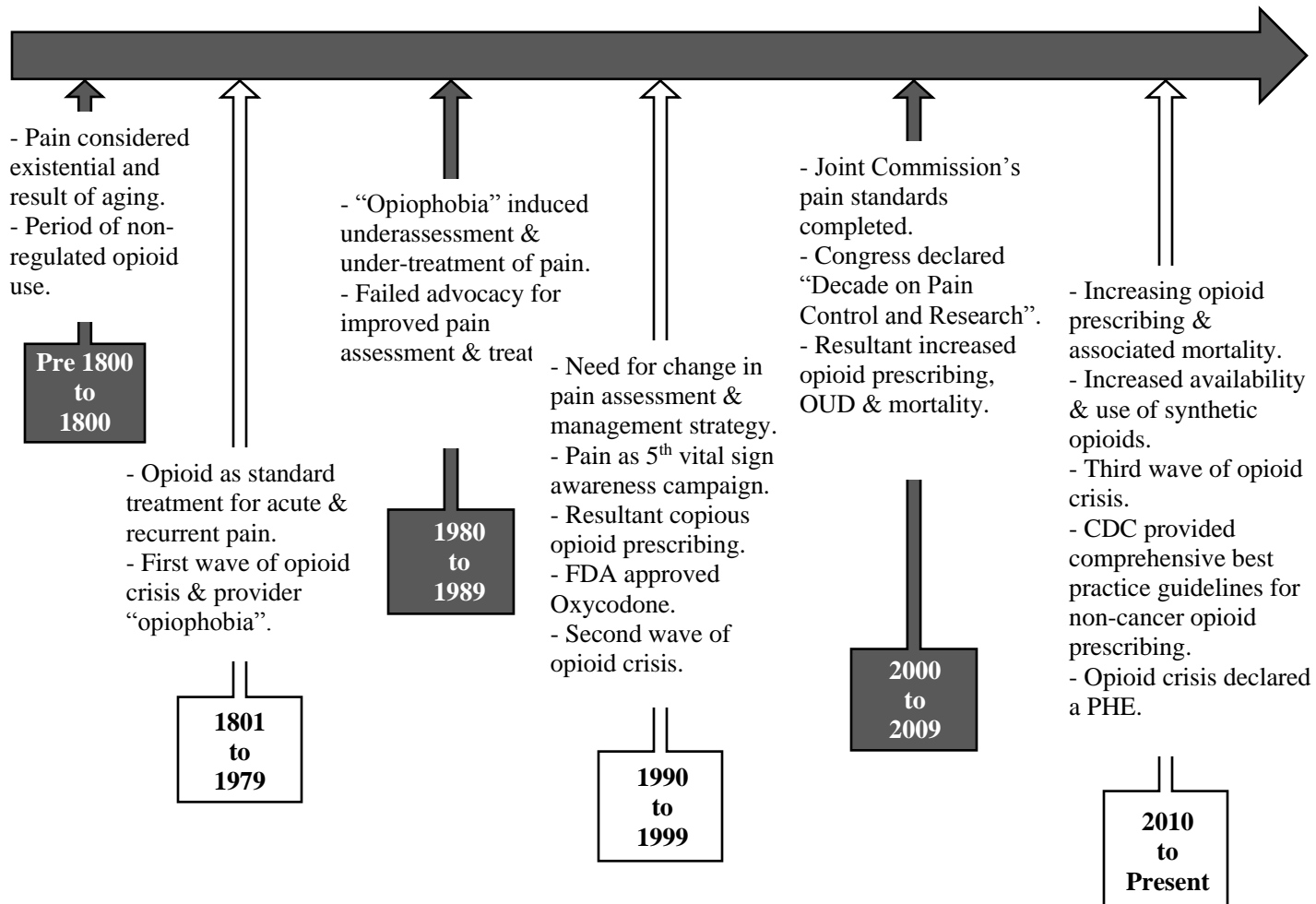
2010 to present – In 2011, the prescription of opioid analgesics had risen to 219 million prescriptions – a 288% and 189% rise from 1990 and 1999 levels respectively. It was 255 million prescriptions in 2012 (335%, 219%, and 116% rise from 1990, 1999, and 2011 levels respectively) (Baker, 2017; Centers for Disease Control and Prevention, 2018b). By 2015, over 33,000 Americans had died from opioid overdose due to prescription opioids, heroin, and illegally manufactured synthetic opioid – Fentanyl (Centers for Disease Control and Prevention/National Center for Health Statistics, 2018). Reported in 2015 in the United States were approximately 2 million cases of substance use disorders associated with prescription opioids and 591,000 cases of heroin use disorder not mutually exclusive from the former (Center for Behavioral Health Statistics and Quality, 2016).

The third wave of the opioid crisis ushered in in 2013 was due to synthetic opioids such as fentanyl. By 2016, mortality related to illegally manufactured fentanyl and not diverted medical fentanyl and associated drugs was over 20,000. Illegally manufactured fentanyl was being used to adulterate or as a replacement for other drugs of abuse (Ciccarone, 2017; Dismukes, 2018; Liu et al., 2018).

In 2016, Centers for Disease Control and Prevention (CDC) provided comprehensive guidelines for best practices regarding prescribing opioids for non-cancer related chronic pain, in an effort to curb risks associated with prescribing opioid analgesics and to maximize available benefits accruable from different pain treatment alternatives (Dowell et al., 2016). Some of these recommendations include using non-opioid treatment regimens as the first line of approach to treating non-cancer related chronic pain; and using opioid analgesics only following cautious

pain control assessment and constant evaluations for their continued indication (Dowell et al., 2016). Figure 1 shows a timeline summary of opioid analgesic use and opioid crisis in America.

Figure 1. Timeline of Opioid Analgesic Use and Opioid Crisis



Opioid Crisis as a Public Health Emergency

The opioid crisis in the United State was declared a public health emergency (PHE) on October 26, 2017 by Eric D. Hargan, then Acting Secretary of Health and Human Services (Hargan, 2017; Health and Human Services, 2017). This declaration made at the behest of the President and following necessary consultation with public health officials was extended through April 24, 2018 (Health and Human Services, 2017; Haffajee et al., 2018). The declaration of the

opioid crisis in America as a public health emergency was necessary due to the escalating and untoward consequences and impacts of the crisis on the nation (Haffajee et al., 2014). Prior to the declaration, over 190 deaths per day in the United States were due to drug overdoses. Of these, over 130 deaths per day were the result of opioid overdoses (Centers for Disease Control and Prevention/National Center for Health Statistics, 2018). In addition, between 1999 and 2017, there was a 256% increase in age-adjusted rate of drug overdose mortality from 6.1 to 21.7 per 100,000 (Hedegaard et al., 2018). Furthermore, in fiscal year 2017 ending September 30, approximately \$900 million had been invested on training, education, treatment and recovery, and other support services for opioid-related conditions by the United States' Department of Health and Human Services (Health and Human Services, 2017). As such, declaring the crisis a public health emergency (PHE) was intended to, allow the federal government take legitimate actions devoid of legislative bureaucracy to address the opioid crisis, permit use of new funds or repurposing of existing funds to deal with the crisis, expedite *ad hoc* subject-matter expert appointments to proffer solutions, ensure collaboration with agencies such as the Drug Enforcement Agency to increase telemedicine access for opioid dependence treatment for specific patients requiring such services, and to ensure that HIV/AIDS programs have flexibilities that included managing associated opioid-related conditions (Haffajee et al., 2014; Health and Human Services, 2017).

Opioid Crisis in context of the Quadruple Aim

The Quadruple Aim is a modification to and expansion of the Triple Aim Framework of healthcare improvement by inclusion of a fourth dimension – Improving provider experience of care. The justification for including this fourth dimension is based on the argument that attaining a truly effective health system performing at optimal levels requires a satisfied, motivated, and

engaged healthcare workforce devoid of burnout (Bodenheimer & Sinsky, 2014; Sikka et al., 2015; West, 2016). Triple Aim on the other hand, is a framework describing an approach to enhancing performance of health systems. The Triple Aim framework posits that improving performance of health systems through new systems designs must consider three interdependent dimensions (Triple Aim): 1) Improving care experience of patients; 2) Improving population health; and 3) Reducing per capita healthcare cost. The Institute for Healthcare Improvement (IHI) developed the Triple Aim framework (Institute of Healthcare Improvement, n.d; Berwick et al., 2008).

Opioid crisis and individual experience of care

An approach to evaluating the opioid crisis is to view it at the individual level as a person-specific problem, which influences individual experience of care. Prolonged use and/or use at higher doses of prescription opioids potentially increases risk of opioid use disorder, overdose, and death. Some of the individual patient-level person-specific factors shown to drive the opioid crisis include: previous history of substance abuse and mental health status (Ives et al. 2006; Sullivan et al. 2010; Fischer et al. 2012); economic circumstances of individuals including employment and income (Case and Deaton, 2015; 2017). Over 30% of individuals in the United States suffer from acute or chronic pain (Johannes et al., 2010; Simon, 2012). The high prevalence of chronic pain coupled with its frequently debilitating effects underscores the reason for opioid analgesics being the most frequently prescribed category of medications in the United States (Centers for Disease Control and Prevention, 2012). Given the rising rates of patients progressing from use of opioid analgesics for treatment of pain to misuse and subsequent dependence, advocates are calling for more controlled prescribing of opioids. However, the

opioid crisis is a multi-faceted problem of which curbing prescribing rates is just one part (Patient Engagement HIT, 2018).

Concerning chronic pain, prevalence is increasing in United States adults. Studies have estimated that the prevalence of chronic pain in U.S adults ranges between 11% and 40% (National Institute of Health, 2016). In 2012, 11.2% of adults in U.S experienced chronic pain (Nahin, 2015) which increased to 20.4% in 2016 (Dahlhamer et al., 2016). Living with chronic pain can rapidly develop into problems of quality of life. Since the pain affects the experience of patients during daily activities, it can limit their participation in daily routines including school, work, and social activities. However, long-term treatment with opioids predisposes these patients to a higher risk misuse, dependence and progression to heroin addiction (Volkow et al., 2016).

Adequately treating both acute (such as post-surgical pain) and chronic pain (such as non-cancer related chronic pain) is critical to a positive individual patient experience of care – including quality of care and satisfaction with care. Healthcare providers however find themselves put in a position of conflict between satisfactorily relieving patients' pain, improving their experience of care, quality of life, and preventing misuse of and dependence on opioid analgesics. Thus, reconciliation between the current opioid crisis, treatment of pain, and ensuring patient satisfaction with care received puts healthcare providers in a difficult position (Morgan, 1985; Zenz & Willweber-Strumpf, 1993; Patient Engagement HIT, 2018). Furthermore, efforts at addressing the opioid crisis by limiting supply may be depriving patients who rightfully need opioids from receiving life-sustaining treatment and for those on long-term treatment with opioids from legitimately filling their prescriptions (Nicholson, 2018; Schultz, 2018). This may ultimately result in lack of improved experience of care.

As such, a vital point to addressing the opioid crisis requires understanding the role of opioids in care of patients with pain. Treatment for pain in some patients may require opioid analgesics leading to improved satisfaction with care while others may benefit from alternative pain management options. On the other hand, patients need to understand how to use opioid analgesics responsibly while appreciating the risks associated with taking these medications. Therefore, patient and provider education is important in efforts to address the opioid crisis (Patient Engagement HIT, 2018).

Opioid crisis and population health

Another approach of framing the opioid crisis is as a population health problem. This potentially broadens the scope of the problem beyond the individual. This population health approach involves confronting root causes, trans-sectoral collaborations, eradicating inequalities in access to treatment, and tackling and decreasing racial biases and stigma (Gourevitch, 2018) compared to focusing more on individual experience of care or lack thereof. This approach ensures multi-pronged efforts to reversing the trend on the crisis and subsequently improving the health of populations. This in other words would require a systems approach to the opioid crisis ((Martin et al., 2016); Martin & Laderman, 2016).

There are demographic, socioeconomic, and healthcare-related characteristics associated with the opioid crisis. Demographic characteristic includes: (i) Race – predominantly Caucasian and/or African American. Socioeconomic characteristics include: (i) Poverty. (ii) Unemployment. (iii) Low educational attainment. Healthcare-related characteristics include: (i) Uninsured. (ii) High healthcare services utilization such as those suffering with chronic pain. (Ghertner & Groves, 2018; Karamouzian & Kerr, 2018; Keyes et al., 2014; Muhuri et al., 2013; Cicero et al., 2014; Vowles et al., 2015; Carlson et al., 2016; National Institute on Drug Abuse,

2018c; Guy et al., 2017; Webster et al., 2009; McDonald et al., 2012; Wennberg, 2011; McDonald & Carlson, 2014). There are however, four different types of patient sub-populations associated with the opioid crisis. These distinct but interdependent sub-populations include the: (1) naïve patient; (2) high-dose chronic use patient; (3) opioid-dependent, seeking within healthcare patient; and (4) opioid-dependent, seeking outside of healthcare patient (Martin et al., 2016). Based on the risk factors above, approximately 21% to 29% of patients with chronic pain prescribed opioid eventually misuse the prescribed opioids. Eight percent to 12% ultimately develop opioid use disorder while about 4% to 6% of those misusing the prescribed opioids switch to using heroin (Muhuri et al., 2013; Cicero et al., 2014; Vowles et al., 2015; Carlson et al., 2016; National Institute on Drug Abuse, 2018c).

To adequately address the opioid crisis and subsequently improve the health of populations, policy makers and health systems should make decisions and allocate resources that specifically target these populations.

Opioid crisis and per capita cost of care

Per capita cost – Regarding the opioid crisis, per capita cost of care refers to the average cost of caring for opioid use disorder per person or average cost of healthcare for opioid use disorder per member of the population (Institute of Healthcare Improvement, n.d; Berwick et al., 2008). Total cost – The total cost of the opioid crisis to the United States is immense. This total cost includes: (1) tangible cost – such as healthcare, criminal justice, lost productivity cost; and (2) intangible cost – comprising cost to quality of life, emotional cost, and cost of pain/suffering endured (Brill & Ganz, 2018). In 2015, the total cost of the opioid crisis including mortality, healthcare, criminal justice and lost productivity costs to the United States economy was 2.8% of GDP and estimated to be \$504 billion. This total cost of the opioid crisis is a combination of; (1)

mortality cost – consisting of value of statistical lives lost due to opioid overdoses – of \$431.7 billion (85.7%) and (2) non-mortality cost – consisting of average cost of non-fatal consequences of opioid use disorder – of \$72.3 billion (14.3%) (Council of Economic Advisers, 2017). This total cost is over six to forty-eight times more than previously estimated cost of the crisis to the US economy (Birnbaum et al., 2006, Birnbaum et al., 2011, Florence et al., 2016). It is important to note that other prior estimated costs focused on estimating the cost of prescription opioids only. However, the current total cost of \$504 billion is six to forty-eight times higher because it includes the cost of both prescription and illicit opioids; fatalities due to opioid overdoses have increased significantly; and value of lives lost were fully accounted for in the \$504 billion estimate. In addition, there are geographical variations to the distribution of this cost that need to be accounted for at the federal, state and local levels when policies are being enacted to address the opioid crisis (Council of Economic Advisers, 2017; Brill & Ganz, 2018).

In 2015 dollars, while total healthcare expenditures per capita by state of residence in the United States revealed a national average of \$8,054.55, total health care expenditures per capita for states with the top five highest total per capita cost of the opioid crisis were all above the national average and within the top 20 highest health care expenditures per capita for that year. Specifically, West Virginia was 12th at 118% (\$9,473.23) of national average; Washington, D.C. 1st at 148% (\$11,958.18); New Hampshire 9th at 119% (\$9,600.38); Ohio 17th at 108% (\$8,722.34); and Maryland 19th at 106% (\$8,612.21). For states with the top five lowest total per capita cost of opioid crisis, Iowa, Montana, and Nebraska had total health care expenditures per capita by state of residence above the national average while those for Mississippi and Texas were below national average. Specifically, Iowa was 25th at 101% (\$8,209.73) of national

average; Mississippi 34th at 95% (\$7,655.08); Texas 45th at 86% (\$7,006.31); Montana 24th at 102% (\$8,230.76); and Nebraska 20th at 104% (\$8,421.98).

State-level total and non-mortality per capita cost of the opioid crisis are spatially distributed. In 2015, states with the top five highest total per capita cost of the opioid crisis included West Virginia – \$4,378; Washington, D.C. – \$3,657; New Hampshire – \$3,640; Ohio – \$3,385; and Maryland – \$3,337. These states mostly in the Appalachian region are all in the eastern United States except for Ohio, which is in the Midwest. States with the top five lowest total per capita cost included Iowa – \$705; Mississippi – \$703; Texas – \$653; Montana – \$596; and Nebraska – \$394. These states are in the Midwestern and southern United States. (Brill & Ganz, 2018). Similarly, states with the top five highest non-mortality per capita cost of the opioid crisis were Washington, D.C. – \$493; New Hampshire – \$360; Connecticut – \$358; Washington – \$331; and New York – \$320. These states are all in the eastern United States except for Washington, which is in the west. States with the top five lowest non-mortality per capita cost were Texas – \$144; Arkansas – \$143; Mississippi – \$138; Nebraska – \$126; and Iowa – \$118. These states are in the Midwestern and southern United States. (Brill & Ganz, 2018).

Regarding states with the top five highest and lowest non-mortality per capita cost of the opioid crisis, health care expenditure per capita by state of residence not already mentioned were Connecticut 6th at 122% (\$9,870.70) of national average, Washington 31st at 98% (\$7,922.39), New York 9th at 121% (\$9,789.61); and Arkansas 38th at 92% (\$7,416.39) respectively in 2015. It is important to note here that health care expenditure per capita (also known as health spending per capita) is “spending for all privately and publicly funded personal health care services and products (hospital care, physician services, nursing home care, prescription drugs, and so on) by state of residence (aggregate spending divided by population)”. Where included hospital costs

represent total net revenue comprised of gross charges less contractual adjustments, bad debts, and charity care. Excluded from this total health care expenditure per capita are insurance program administration, research, and construction-related costs (Kaiser Family Foundation, 2017b).

Also, of significance is the percentage of total health care expenditure per capita by state of residence that both the total and non-mortality per capita cost of the opioid crisis constitute respectively. Concerning states with the top five highest total per capita cost of the opioid crisis, West Virginia's opioid crisis comprises about 46%; Washington, D.C. 30%; New Hampshire 37%; Ohio 38%; and Maryland 38% of the total health care expenditure per capita by state of residence respectively. For states with the top five lowest total per capita cost of opioid crisis, Iowa's opioid crisis constitutes about 8%; Mississippi 9%; Texas 9%; Montana 7%; and Nebraska 4% of the total health care expenditure per capita by state of residence respectively.

In relation to states with the top five highest non-mortality per capita cost of the opioid crisis, Washington, D.C.'s opioid crisis consist of approximately 4%; New Hampshire 3%; Connecticut 3%; Washington 4%; and New York 3% of the total health care expenditure per capita by state of residence respectively. For states with the lowest non-mortality per capita cost of the opioid crisis, Texas was 2%; Arkansas 1%; Mississippi 1%; Nebraska 1%; and Iowa 1% of the total health care expenditure per capita by state of residence respectively. Table 1 shows the total health care expenditure per capita by state of residence, total per capita cost of the opioid crisis (as a percentage of the total health care expenditure per capita by state of residence), and non-mortality per capita cost of the opioid crisis (as a percentage of the total health care expenditure per capita by state of residence) of the top five states in the United States.

Table 1. Total Health Care Expenditure per Capita by State of Residence, Total per Capita Cost and Non-Mortality per Capita Cost of Opioid Crisis of Top Five States in United States.

Top Five States				
Total Health Care Expenditure per Capita by State (a)		Total per Capita Cost of Opioid Crisis (b)		Non-Mortality per Capita Cost of Opioid Crisis (c)
Value (\$)	State	% ([b/a]*100)	% ([c/a]*100)	State
11,958.18	Washington D.C.	30.58	4.12	Washington D.C.
9,600.38	New Hampshire	37.91	3.75	New Hampshire
9,473.23	West Virginia	46.21	3.78	Connecticut
8,722.34	Ohio	38.81	3.79	Washington
8,612.21	Maryland	38.75	3.72	New York

The spatial variations in the opioid crisis and per capita cost of care in the United States can be attributed to geography and socioeconomic factors (Keyes et al., 2014; Ghertner & Groves, 2018; Karamouzian & Kerr, 2018). (1) Rural-urban geographic divide – where as noted above, rural areas including most of the Appalachian region, parts of the West and the Midwest, and New England, are disproportionately more affected by the opioid crisis compared to more urban areas; (2) socioeconomic factors – specifically high unemployment and high poverty have been shown to be associated with the opioid crisis (Ghertner & Groves, 2018). However, there are exceptions to these observed association in which urban areas experience and some economically disadvantaged areas do not experience the opioid crisis (Ghertner & Groves, 2018). These geographic and socioeconomic factors attributable to the opioid crisis have resulted in varying; (1) Opioid prescribing and dispensing practices in the United States in which more opioids are prescribed and dispensed in the Appalachian region, Southern, and Western states of the United States (McDonald et al., 2012). (2) Internal migration patterns in which there is movement of people between and within states and counties in search of economic prosperity

and better healthcare services (Finkelstein et al., 2018). Furthermore, counties within states in the Appalachian region, Southern, and Western United States tend to have more opioids prescribed and dispensed. This is due to those counties having greater (i) resident population size (ii) white non-Hispanic or African American (iii) economically disadvantaged, uninsured (iv) urban classified dwelling population and (v) number of opioid prescribing providers (Wennberg, 2011; McDonald et al., 2012; McDonald & Carlson, 2014). In addition, other factors such as political affiliations, higher healthcare utilization, greater income disparities, and lower educational attainment predispose these counties to prescribing and dispensing more opioids (Webster et al., 2009; Goodwin et al., 2018; Guy et al., 2017).

Opioid crisis and provider experience of care

The quantity of opioid analgesics prescribed grew from 76 million prescriptions in 1990 to 116 million in 1999 to 255 million in 2012 and declined to 191 million in 2017 – the lowest in over 10 years (Baker, 2017, Centers for Disease Control and Prevention, 2018b). However, in spite of the overall rate of opioid analgesics prescribing rate in United States climaxing and leveling off from 2010 to 2012 and decreasing since 2012, the quantity of opioids in morphine milligram equivalents (MME) prescribed per person is still estimated at three times higher than it was in 1999 (Centers for Disease Control and Prevention, 2017). This may have contributed in part to the rising overall opioid-related deaths in the nation. Such that between 1999 and 2017, approximately 218,000 deaths were reported in United States due to overdoses connected to prescription opioids – a fivefold increase from 1999 to 2017 (WONDER, 2016). In addition, in 1999 and 2017, age-adjusted prescription opioid overdose mortality rates were 4,030 and 40,051 per 100,000 population respectively. This represents an estimated 10-fold increase in deaths due to prescription opioids between 1999 and 2017 (Kaiser Family Foundation, 2018). Furthermore,

in 2017, 46 deaths/day were attributed to prescription opioid overdoses accounting for over 35% of all deaths related to opioid overdoses in that year (Scholl et al., 2018; Centers for Disease Control and Prevention, 2018a).

Annual prescribing rates between 2006 and 2017 declined by over 19% with most of the decline occurring from 2012 to 2017. In addition, prescribing rates of high-dose opioids has been reducing since 2008 (Centers for Disease Control and Prevention, 2018a). All indicative of cautious prescribing practices on the part of healthcare providers. However, not all healthcare provider experiences of caring for individuals with opioid use disorder and opioid related drug overdoses during the opioid crisis can be explained by adherence to best prescribing practices only.

The experiences of healthcare providers caring for patients during the opioid crisis may be influenced by certain factors. These include: (1) General overutilization of healthcare services by individuals with substance use disorders (Walley et al., 2011; National Drug Intelligence Center, 2011; Neighbors et al., 2013). (2) Repeated presentations at emergency departments and readmissions to hospital of patients with opioid use disorder related conditions and opioid related drug overdoses (Walley et al., 2011; National Drug Intelligence Center, 2011; Neighbors et al., 2013). (3) Disproportionately high costs of healthcare incurred by patients with substance use disorders including opioids (Walley et al., 2011; National Drug Intelligence Center, 2011; Neighbors et al., 2013). (4) Underutilization or lack of use of substance use disorder-specific interventions during inpatient admissions and at discharge (Knudsen et al., 2011; Knudsen & Roman, 2012; Rosenthal et al., 2016; Donroe et al., 2016; McCarty et al., 2018).

Other plausible reasons related to the aforementioned include: (Ia) Associated regulations and other treatment policies of patients with opioid use disorder related conditions and opioid

related drug overdoses such as certification to dispense opioid drugs in the treatment of OUD (CFR Title 42: Part 8: Subparts A through C). (Ib) Policies influencing opioid prescribing practices (National Academies of Sciences, Engineering, and Medicine, 2017). (Ic) Additional provider requirement to report pain and OUD data (National Academies of Sciences, Engineering, and Medicine, 2017). (IIa) Healthcare provider biases such as fears related to deception and manipulation by patients with opioid use disorder when presenting with or reporting pain. (IIIa) Challenges associated to using agonist and antagonist medication such as, patients and families explicitly requesting nondrug treatment, persistently expecting abstinence as only appropriate outcome of treatment, resistance of healthcare staff to use of medications, and medication cost. (IIIb) Lack of providers capable of prescribing required medications on staff in many addiction treatment centers (Knudsen et al., 2011). (IV) Barriers related to routine usage of extended-release naltrexone such as, difficulty ordering and administering the medication, policies of health plans demanding prior authorization and review of utilization, requirements of first failing at use of other treatment options, need for patients being free of opioids the prior 7 to 10 days before injection, lack of care continuity by physicians, and cultures that are resistant use of medication (Alanis-Hirsch et al., 2016).

All of these factors may result in healthcare provider dissatisfaction and burnout, which adversely affects their experience of caring for patients with opioid use disorder related conditions, and opioid related drug overdoses. This may ultimately lead to poor patient experience of care including dissatisfaction and poor quality of care, poor population health outcomes, and increased per capita cost of care (Bodenheimer & Sinsky, 2014).

Why is Opioid Use Disorder (OUD) important?

Opioids – The estimated cost of the opioid crisis the United States between 2001 and 2017 exceeded \$1.0 trillion and is projected to rise to \$1.5 trillion by 2020 (Altarum, 2018). Evidence shows that prescription opioids, not heroin, are the first opioids frequently abused (Cicero et al, 2014). Approximately 67% of primary heroin users also use prescription opioids (Rosenblum et al, 2007). Use of heroin and heroin-related mortality in the United States have been on the rise since 2000 (Rudd et al, 2016).

Opioid Use Disorder (OUD) – OUD is a chronic relapsing condition involving frequent misuse of prescription opioids, diversion and use of opioids, or use of heroin acquired illegally. OUD is usually associated with considerably high rates of morbidity and mortality (Strain et al, 2015). Opioid use disorder, according to the DSM-V combines two disorders, namely; Opioid Dependence and Opioid Abuse. OUD encompasses use of a wide range of illegal and prescribed drugs of the opioid class (Hartney & Gans, 2018; Regier et al, 2013). Adverse events – such as overdosing, abuse, dependence, and death – from using prescription opioids in the United States have risen over the last 20 years (Chang et al, 2018). Opioid abusers have greater odds of visiting the emergency departments, physician outpatient clinics; longer inpatient stays compared to non-abusers of opioids (Meyer et al, 2014).

Identifying individuals with OUD particularly in the ED can be challenging. This is partly because there are no existing clinical guidelines for such tasks (Duber et al., 2018). Clinically, individuals with OUD may present to the ED with somatic symptoms and signs such as headaches and pain involving the joints, back, neck, chest or abdomen, elevated heart rate and blood pressure; and psychological symptoms like agitation, panic attacks, and restlessness (Braden et al., 2010; Kampman & Jarvis, 2015; Duber et al., 2018). Several different tools have been developed for identifying patients or individuals with OUD (Duber et al., 2018). The

similarities between these tools are that they accurately and reliably identify patients with OUD while being easy to administer and integrate into providers' existing workflows (Johnson et al., 2013; Duber et al., 2018).

Prevalence of opioid use disorder

Approximately 12 million individuals 12 years and older misused prescription opioids in the United States in 2016 (Reinhart et al, 2018). Over 130 people are estimated to die per day from opioid-related overdoses (Centers for Disease Control and Prevention/National Center for Health Statistics, 2018). According to the National Survey on Drug Use and Health, an estimated total of 7.7 million, 7.4 million, and 7.6 million people 12 years and older suffered from OUD in the 12 months preceding the survey in 2015, 2016, and 2017 respectively (SAMHSA – Center for Behavioral Health Statistics and Quality, 2017, 2018). In addition, results from the National Survey on Drug Use and Health revealed that in the 12 months prior to the survey, 2.1 million people 12 years and older were first time misusers of prescription opioids. (SAMHSA – Center for Behavioral Health Statistics and Quality, 2018). In 2015 or the most recent year, there was significant state-level variability in OUD diagnosed in healthcare settings; aggregated data revealed an estimated 10-fold difference in diagnosed OUD prevalence between South Dakota (least impacted state at 1.32 per 1,000) and Vermont (most impacted state at 12.56 per 1,000) (Davenport & Matthews, 2018).

Economic burden of opioid use disorder

Prescription abuse costs society \$55 billion each year, with \$20 billion in emergency department and inpatient care alone (Fuehrlein et al, 2017). Approximately 75% treatment costs for alcohol & other drug use disorder (DUD) including OUD is publicly funded alone (Mark et al, 2005). Treatment expenditure for substance use disorder including OUD in the United States

increased from \$9 billion in 1986 to \$21 billion in 2003 to \$24 billion in 2009 and \$31 billion in 2014 (Mark et al., 2007; SAMHSA, 2013b; SAMHSA, 2014). This amount is projected to increase to about \$42 billion in 2020 (SAMHSA, 2014).

Importance of opioid use disorder prevalence and cost in adolescents and young adults

Significant increases in opioid prescribing across all age groups have been observed in recent years with parents more likely to share opioids with their children and/or diversion of parents' opioid pain relievers by children thus predisposing to OUD (Binswanger & Glanz, 2015). The most commonly initiated drugs of abuse among children, adolescents, and young adults are opioids (SAMHSA, 2010). Adolescents (12-17 year old) and young adults (18-25 year old) presenting to primary care with OUD and overdoses has been on the rise in the last 15 years (Saloner et al., 2017). Misuse and abuse of prescription opioids in individuals 12-17 years old and 18-25 years old more than doubled between 1991 and 2012 (SAMHSA, 1993, 2013a). An estimated 5.4% of 12-17 year olds and 10% of 18-25 year olds reported nonmedical use of prescription opioids (Binswanger & Glanz, 2015). In addition, 16.1% of 12-17 year olds and 20.9% of 18-25 year olds were at-risk of initiation of heroin use in the past year following prior nonmedical opioid pain reliever use between 2002 and 2011 (Muhuri et al., 2013). The proportion of admissions into substance abuse treatment facilities due to opioid use in individuals 12 years and older increased from 18% in 2004 to 30% in 2014 (SAMHSA, 2014, 2017). There has been a six-fold increase of unintentional opioid poisonings in youth in the last 10 years (Binswanger & Glanz, 2015). In spite of expanded access to medications, on average only 11.1% of 13 to 17 year olds received Buprenorphine and Naltrexone for OUD between 2001 and 2014 (Hadland et al., 2017). Disparities based on age, gender, and race/ethnicity exist for OUD treatment among 13 to 25 year olds (Hadland et al., 2017; Feder et al., 2017). In

addition, other characteristics such as; census region, insurance status, annual income, patient location, hospital designation/location, treatment setting (e.g. ED, inpatient, and outpatient), and disposition have been shown to influence prevalence and cost of OUD treatment (Wu et al., 2016; Peterson et al., 2018; Hadland et al., 2017; Mosher et al., 2017; Gaither et al., 2016; Xie et al., 2014). Specifically, studies using the Nationwide Emergency Department Sample (NEDS) have used the following: (1) individual variables – age, gender, primary payer, annual median income, patient location; and (2) hospital variables – control/ownership, region, designation; and type of emergency department event (disposition) including treated & released, admitted to same hospital, transferred to another or died (Chandwani et al., 2013; Mejia et al., 2018; Upadhyay et al., 2018; Rivera et al., 2017; Singh et al., 2016; Wall et al., 2015; Wang et al., 2015). In 2013, only 0.4% of 15-17 year olds compared to 12.0% of 18 year olds and older with prescription OUD; and only 2.4% of 15-17 year olds compared to 26.3% of 18 year olds and older with heroin use disorder received medication-assisted treatment (MAT) (Feder et al., 2017).

Importance of emergency departments in opioid use disorder

Emergency departments (EDs) are engaged in managing the untoward consequences of inappropriately prescribed opioids (Xie et al, 2014; Duber et al., 2018; Salzman et al., 2020). About 305,900 ED visits were related to the nonmedical use of opioids in 2008, a 111% increase from the 144,600 ED visits in 2004 (Xie et al, 2014).

State-level opioid policies

State lawmakers in the United States are engaging different sectors such as health, criminal justice, human services, and so on to create innovative policies aimed addressing the current opioid crisis deemed as a public health emergency (U.S HHS, 2017). These efforts are going on in addition to ensuring appropriate and needed access to pain management. A minimum

of 33 states had enacted legislation related to opioid prescription limits as of October 1, 2018 (Blackman, 2017).

As of July 1 2017, in United States, 49 States, District of Columbia, and St. Louis County in Missouri have operational Prescription Drug Monitoring Programs (PDMPs) that have capacity to receive and distribute controlled substance prescription information to authorized users (National Alliance for Model State Drug Laws, 2017).

As of 2019, in United States, 49 States and the District of Columbia with exception of Wyoming have operational Opioid Treatment Programs (OTP) that provide medication-assisted treatment (MAT) – use of medications with counseling and behavioral therapies to provide holistic treatment – for individuals diagnosed with opioid use disorder (OUD) and to prevent opioid overdose (Kaiser Family Foundation, 2019; SAMHSA, 2015, 2019).

In spite of state-level opioid policies, there are still geographic variations to the opioid crisis. In addition to causes of the geographic variations in opioid crisis and per capita cost of care stated above, other factors may be responsible for observed state-level variations in opioid usage in United States. These include (Martin et al., 2016): (1) Availability of, access to, scope of regulation, and use of Prescription Drug Monitoring Programs (PDMPs). (2) Attitudes of the population regarding pain and opioid-containing substances. (3) Attitudes of law enforcement towards individuals using opioids and incarceration of such individuals. (4) Judicial enforcement using drug courts or mandating treatment versus imprisonment. (5) Addiction treatment availability and referrals to these facilities and other treatment resources. (6) Addiction treatment reimbursement. (7) Reimbursement of insurance for screening and analysis of risk. (8) Heroin and other illicitly produced synthetic opioids availability in the community. (9) Healthcare providers and patients education. (10) Oversight of patients taking and providers prescribing

controlled substances. (11) Community resources and involvement in response to opioid crisis.
(12) Probable effects of genetic variations or cultural influences on specific populations.

Therefore, to address convincingly the opioid crisis, an understanding of the specific features of the opioid crisis in individual states and geographic regions is necessary in addition to policies.

Policy/intervention evaluation

Effect of policies on prescribing practices – Following a uniform rise in overall national rate of opioid prescribing beginning in 2006, the total quantity of opioid prescriptions written and dispensed reached a climax in 2012 at approximately 255.2 million prescriptions equivalent to a prescribing rate of 81.3 prescriptions per 100 persons (Centers for Disease Control and Prevention, 2018b). Thereafter, from 2012 to 2017, overall national prescribing rates of opioids analgesics decreased. This decline in overall national opioid analgesic prescribing rate reached its ebb in 2017, the lowest in over 10 years for an estimated total of 191.2 million prescriptions equivalent to a prescribing rate per 100 persons of 58.7 prescriptions (Bao et al., 2016, 2018; Centers for Disease Control and Prevention, 2018b; Bohnert et al., 2018;). Policies related to use of state prescription drug monitoring programs (PDMPs) particularly comprehensive legislative mandates to use PDMPs and laws allowing healthcare providers who prescribe opioids to delegate use of PDMPs to their office staff have been more effective compared to laws compelling state participation in interstate sharing of PDMP data at reducing opioid prescribing rates (Bao et al., 2018).

In 2017, however, certain areas across the United States still witnessed very high opioid prescribing rates perhaps due in part to consistently higher quantity of opioids in morphine milligram equivalents (MME) prescribed per person, causes of geographic variations, and other

factors discussed earlier. For instance, some United States counties had prescribing rates per 100 persons that were seven times higher than the national average of 58.7. In addition, opioid analgesics prescriptions still being dispensed in 16% of counties in United States were enough for everyone in the nation to have one (Centers for Disease Control and Prevention, 2018b). Thus, it is reasonable to conclude that though policies limiting supply of prescription and other sources of legal opioids are necessary, they are not sufficient to address the opioid crisis.

Effect of policies on opioid overdoses – The prescribing rate of opioid analgesics had declined annually since 2012 reaching a 10-year low in 2017 (Centers for Disease Control and Prevention, 2018b). However, national and state-level opioid overdose deaths continued to rise within the same period from 2012 to 2017 (Kaiser Family Foundation, 2017a; National Institute on Drug Abuse, 2018a). Plausible reasons for this may be as discussed earlier, persistently higher MMEs of opioids still prescribed per person, clusters of counties around the country still prescribing opioids over five times that of the national average, and high dispensing rate of opioid analgesics by almost 20% of counties nationwide (Centers for Disease Control and Prevention, 2018b). In addition to over-prescription in some parts of the country, it is not possible to rule out diversion and misuse of prescription opioids. Furthermore, prescription opioids even when prescribing rates have declined are still precursors to addiction and transitioning to illegal opioids and a reason for rising opioid overdose mortalities (Compton & Wargo, 2018). The above reasons were supported in a systematic review by Fink and colleagues in 2018, which revealed that the impact of implementing PDMPs on opioid overdoses was equivocal because there were evidences that implementing PDMPs was associated with declining or rising nonfatal or fatal opioid overdoses (Fink et al, 2018).

Effect of policy on opioid use disorder – Medication-assisted treatment (MAT) is effective for treating opioid use disorder (OUD). Use of MAT leads to: (1) increased social functioning and retention in treatment program of affected individuals; (2) reduced, use of opioids, overdosing on opioids, criminal activities, risky behaviors promoting transmission of HIV and hepatitis C virus (HCV), morbidity and mortality (Mattick et al., 2009, 2014; Schwartz et al., 2013; SAMHSA, 2015; Connery, 2015; US HHS, 2016).

Medications used in MAT include, buprenorphine (Suboxone[®], Subutex[®]), methadone, and extended release naltrexone (Vivitrol[®]), with buprenorphine and methadone considered essential medicines (WHO, 2004; National Institute on Drug Abuse, 2018a, 2016). However, these medications are not extensively used and where they are used; access to the medications is a major issue (Jones et al., 2018). The nationwide percentage of admissions for opioid treatment with treatment plans including receipt of medications such as MAT decreased from 35.2% in 2002 to 27.6% in 2013 before increasing to 36.9% in 2015 then decreasing again to 33.5% in 2016. This trend was occurring while total opioid admissions increased between 2002 and 2016. (SAMHSA, 2014, 2017, 2018). This fluctuating trend may have been due to initially insufficient treatment capacity (responsible for the 2002-2013 decline) (Jones et al, 2015; Jones et al., 2018) which progressively improved and/or availability of multiple treatment options in U.S. States (responsible for the 2013-2015 rise and 2015-2016 decline) (Jones et al., 2018).

Overall, the impact of MAT on OUD has been equivocal (Kampman & Jarvis, 2015; Potter et al., 2015; Weiss et al., 2015). Medication assisted treatment (MAT) has proven effectiveness in treating OUD following initiation of MAT in an estimated 50% of patients with prescription OUD at 18 months (Potter et al., 2015) and 61% of patients with prescription OUD at 42 months (Weiss et al., 2015). Conversely, it has proven to be ineffective in approximately

50% and 39% of patients with prescription OUD at 18 and 42 months follow-up post-initiation of MAT respectively (Potter et al., 2015; Weiss et al., 2015).

Selected state-level comparison of the opioid crisis

The states of Texas, New York, and Kentucky are selected to highlight the variation in statistics of the opioid crisis in the United States.

Texas – Is located in southern United States. Specifically, in the West South Central division where the overall burden of the opioid epidemic is light. There are very few available facilities located in Texas, which, provide some but not all three forms of MAT. The state of Texas has not expanded Medicaid (SAMHSA, 2017; National Institute on Drug Abuse, 2018b; Jones et al., 2018).

New York – Is located in the northeast United States. Specifically, in the Middle Atlantic division where the overall burden of the opioid epidemic is relatively heavy. There are many facilities located in New York providing all three forms of MAT. These facilities are clustered together. The state of New York has expanded Medicaid (SAMHSA, 2017; National Institute on Drug Abuse, 2018b; Jones et al., 2018).

Kentucky – Is located in the southern United State. Specifically, in the East South Central division where the overall burden of the opioid epidemic is heavy. There are very few available facilities located in Kentucky, which provide some but not all three forms of MAT. The state of Kentucky has expanded Medicaid. (SAMHSA, 2017; National Institute on Drug Abuse, 2018b; Jones et al., 2018).

In 2016, Texas had an opioid-related overdose death rate of 4.9 deaths per 100,000 persons. However, the number of heroin and synthetic opioids death rates has steadily increased since 2010. New York State had an opioid-related overdose death rate of 15.1 deaths per 100,000

persons in the same year. The heroin-related and synthetic opioids deaths were over two times and ten times more since 2012. Similarly, in Kentucky with an opioid-related overdose death rate of 23.6 deaths per 100,000 persons, the heroin-related deaths more than doubled and synthetic opioids deaths were over six times more since 2012.

A comparative analysis of the opioid crisis by the numbers between Texas, New York, and Kentucky is shown below.

Table 2. Comparative Analysis of Opioid Crisis between the States of Texas, New York, and Kentucky

Characteristics	States			National Average
	Texas	New York	Kentucky	
Opioid pain reliever prescriptions (opioid prescriptions per 100 persons) (2016)	57.6	42.7	97.2	70.6
Total number of prescriptions (millions) (2016)	15.44	9.53	4.18	214.88
Opioid related overdose deaths (2016)	1,375	1,641	989	42,000
Opioid related overdose death rates (deaths per 100,000 persons) (2016)	4.9	15.1	23.6	13.3
Total per capita cost of opioid crisis (\$ per resident) (2015)	653	1,850	2,412	---
Non-mortality per capita cost of opioid crisis (\$ per resident) (2015)	144	320	205	---
Total healthcare expenditure per capita by state of residence (\$) (2015)	7,006.31	9,789.61	8,013.50	8,054.55

Sources: (Kaiser Family Foundation, 2017b; National Institute on Drug Abuse, 2018b; Centers for Disease Control and Prevention, 2018b).

Public Health Significance

The opioid crisis in America appears to be worsening. State-level policies legitimizing interventions such as use of Prescription Drug Monitoring Programs (PDMPs) that have capacity to receive and distribute controlled substance prescription information and Opioid Treatment Programs (OTP) that provide medication-assisted treatment (MAT) for opioid use disorder (OUD) and to prevent opioid overdose have made modest impacts on prescribing practices, opioid overdoses, and opioid use disorder. These interventions though promising have challenges, which need to be adequately addressed if they are to make significant positive impacts on the opioid crisis.

This research will provide most current prevalence of diagnosing and treating OUD in 12-18 year olds and those over 18 with OUD based on their ED disposition. In addition, this research will use a robust sample of nationally representative data including those 12 years of age and older. Furthermore, it will provide accurate estimates to guide policy and program implementation regarding management of opioid use disorder in the emergency department.

Specific Aims

The specific aims of this research are:

Aim 1:

To systematically identify, appraise, and collect state-by-state level data on status of medication-assisted treatment (MAT) policies, MAT medication coverage status for OUD treatment, Medicaid expansion status, and Medicaid section 1115 behavioral health waiver status for OUD treatment in all 50 states and the District of Columbia captured in the literature.

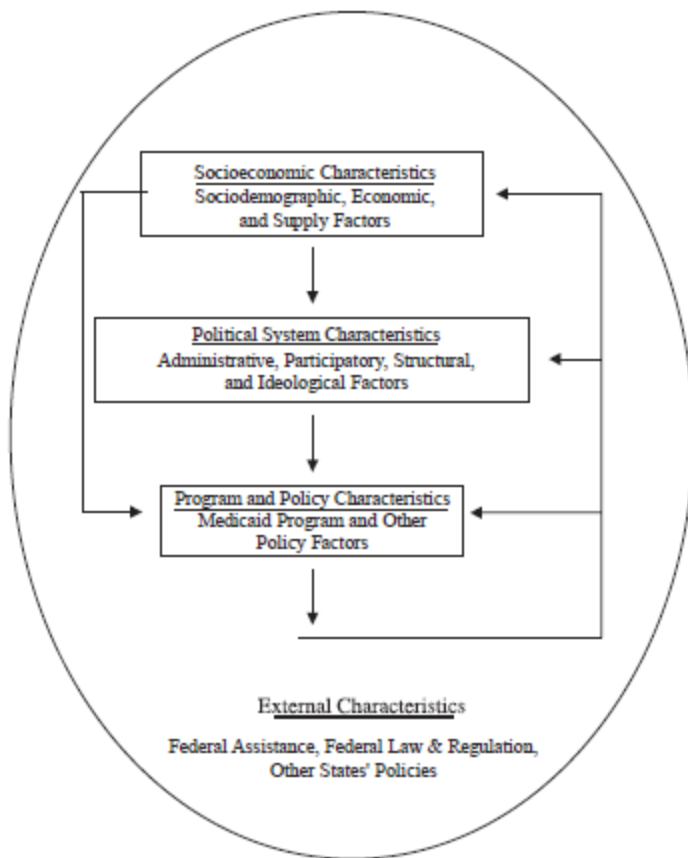
Aim 2:

To examine individual characteristics (Primary payer, Annual median income, Patient location, and Type of emergency department event), hospital characteristics (Control/Ownership, Region, and Designation), and state-level policy characteristics (MAT policy status, MAT medication coverage status for treating OUD, Medicaid expansion status, and Medicaid section 1115 behavioral health waiver status for OUD treatment) associated with prevalence of emergency department diagnosis and treatment of any opioid use disorder (OUD) in U.S. population 12 years and older from January 2016 to December 2016 captured in the Nationwide Emergency Department Sample (NEDS) database.

Conceptual Research Model

Research Models Referenced in the Literature

General Model of State Policy Adoption (Miller, 2005) – The general model of state policy adoption posits that the determinants of adoption of policy arise from both a state's external and internal environment. External factors include policy adoptions by other states and federal assistance, law and regulation. Internal factors comprise the economic and political circumstances of a particular state in addition to baseline program and policy characteristics. Socioeconomic factors directly influence Medicaid program and other policy attributes; and indirectly influence Medicaid program and other policy attributes by first influencing political system development, which, in turn, produces policy outputs that feedback into the socioeconomic and/or political environment.



Source: <https://www.sciencedirect.com/science/article/pii/S0277953605002376>

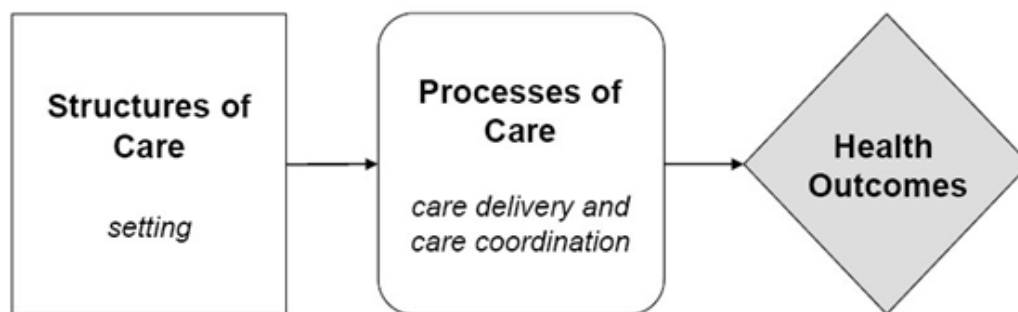
Structure, Process and Outcomes Framework by Avedis Donabedian – Avedis

Donabedian described a widely adopted and adapted framework for assessing, investigating, and understanding quality of care using the structure, process and outcomes constructs (Donabedian, 1966; Donabedian, 2005).

Donabedian's reasoning was that the definition of outcomes and types of measures selected for measurement of outcomes were both imperative for understanding quality in health care. In addition, in his landmark article Donabedian described the significant role process-related factors played in understanding and evaluating quality. He noted that rooted in the processes of care are values, standards and normative judgments that drive performance of patient care activities to improve patient health. Furthermore, Donabedian also highlighted the

important influence of structure of care or physical and organizational context such as personnel, equipment, facilities, financial and operational processes and so on that support healthcare on quality (Donabedian, 1966; McDonald et al., 2007).

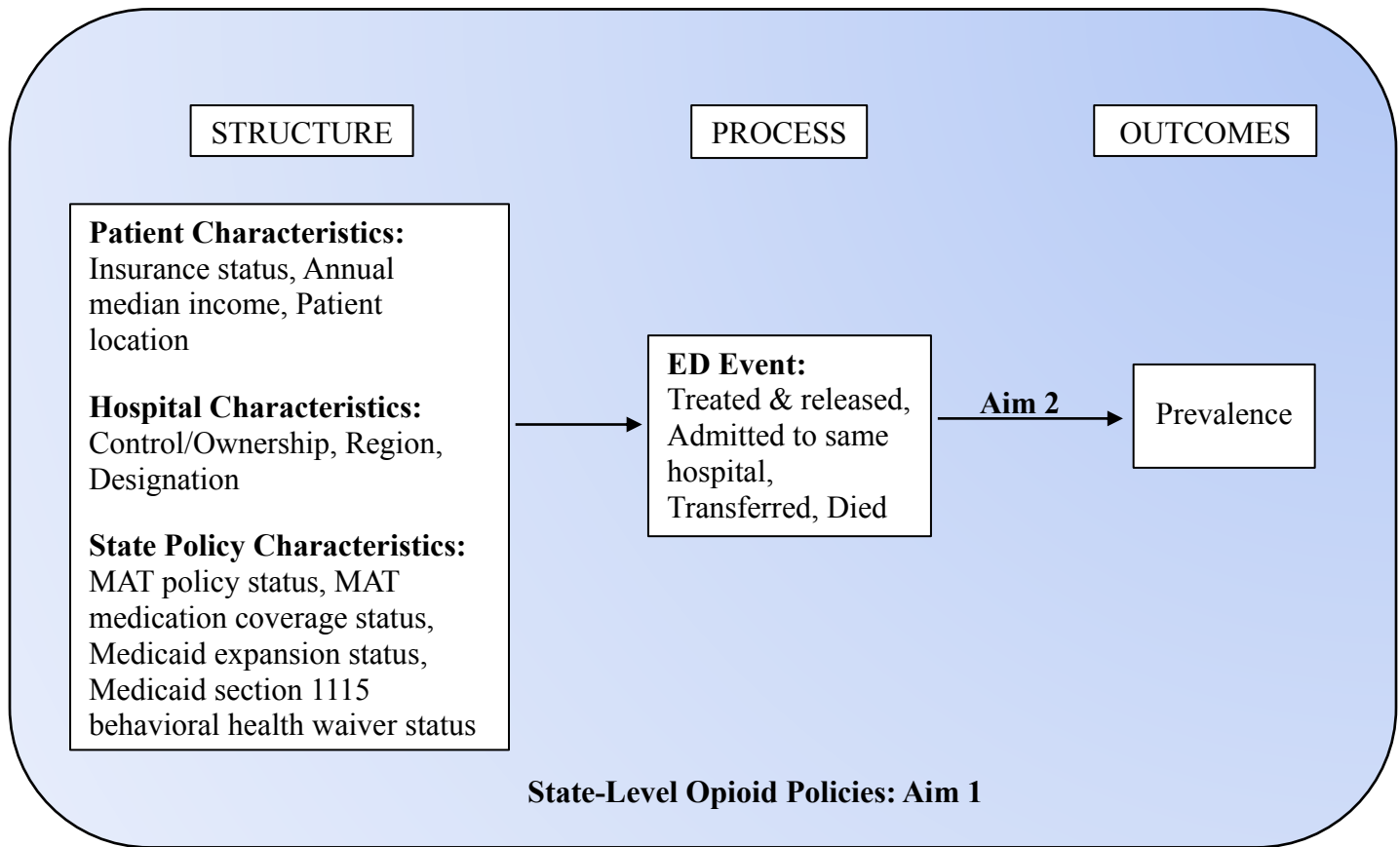
Donabedian's structure-process-outcomes framework is flexible and allows for different interpretations and applications in different circumstances (Donabedian, 1966; Donabedian, 2005).



Source: <https://www.ncbi.nlm.nih.gov/books/NBK44008/figure/A25995/?report=objectonly>

Research Model

The model for this study combined Donabedian's structure-process-outcomes framework and the General Model of State Policy Adoption. In this study, Donabedian's framework was embedded within the General Model of State Policy Adoption. The relationships between both models and the study aims are depicted thus:



METHODS

Study Design

This research involved a retrospective secondary data analysis of the Nationwide Emergency Department Sample (NEDS) from January 1, 2016 to December 31, 2016.

Data Sources

Nationwide Emergency Department Sample (NEDS) – The NEDS is the largest all-payer emergency department (ED) database in the United States, yielding national estimates of hospital-based ED visits. NEDS was developed for the Healthcare Cost and Utilization Project (HCUP) and is maintained by the Agency for Healthcare Research and Quality (AHRQ). NEDS produces regional and national estimates about hospital-owned emergency department (ED) visits across the United States. The NEDS describes ED visits, regardless of whether they result in admission. Information includes geographic characteristics, hospital characteristics, patient characteristics, and the nature of visits (e.g., common diagnoses for ED visits). The NEDS was constructed using the Healthcare Cost and Utilization Project (HCUP) State Emergency Department Databases (SEDD) and the State Inpatient Databases (SID). HCUP data inform decision-making at the national, state, and community levels. The SEDD capture discharge information on ED visits that do not result in an admission (i.e., treat-and-release visits, transfers to another hospital, and deaths). The SID contain information on patients initially seen in the ED and then admitted to the same hospital.

The 2016 NEDS includes a full calendar year of data with diagnosis and procedure codes reported using the International Classification of Diseases, Tenth Revision, Clinical Modification/Procedure Coding System ICD-10-CM/PCS).

American Society of Addiction Medicine (ASAM) state reports (American Society of Addiction Medicine et al., 2013); Substance Abuse and Mental Health Services Administration (SAMHSA) Office of Policy, Planning and Innovation State Medicaid coverage reports (Substance Abuse and Mental Health Services Administration et al., 2014, 2018); and Kaiser Family Foundation (KFF) report on the opioid epidemic (Kaiser Family Foundation, 2018b, 2019a, 2019b) – for nationwide state level medication-assisted treatment (MAT) policy, MAT medication coverage status, Medicaid expansion status, and Medicaid section 1115 behavioral health waiver status data. These data provided the state-by-state summary of medication-assisted treatment (MAT) policy status, Medicaid coverage status of the MAT medications for treating OUD, Medicaid expansion status, and Medicaid section 1115 behavioral health waiver status used in this study.

Study Population

Target Universe

Emergency departments (ED) in community, nonrehabilitation U.S. hospital-owned ED that reported total ED visits in the American Hospital Association (AHA) Annual Survey Database. Equivalent to 144,842,742 ED events in 2016.

Exclusion criterion – non-rural hospitals that reported less than ten ED visits in a year.

Sampling Frame

Hospital-owned ED in the 35 States and the District of Columbia that provided information on ED visits that result and do not result in admission. The sampling frame of the NEDS was limited to a subset of the universe: hospital-owned ED in the States and District of Columbia for which Healthcare Cost and Utilization Project (HCUP) ED data (SID and SEDD) were available. The list of hospital-owned ED in the sampling frame consisted of all AHA

community, nonrehabilitation hospitals that reported total ED visits in each of the sampling frame States and District of Columbia that could be matched to the ED data provided to HCUP. If an ED in the AHA survey could not be matched to the ED data provided by the HCUP data source, it was eliminated from the sampling frame (but not from the target universe). The HCUP hospitals were required to be represented in the AHA data and have no more than 90 percent of their ED visits resulting in admission. Equivalent to 113,306,272 ED events in 2016.

Exclusion criterion – HCUP hospitals that were not represented in the AHA data and had more than 90 percent of their ED visits resulting in admission.

Sample Size Calculation and/or Study Power

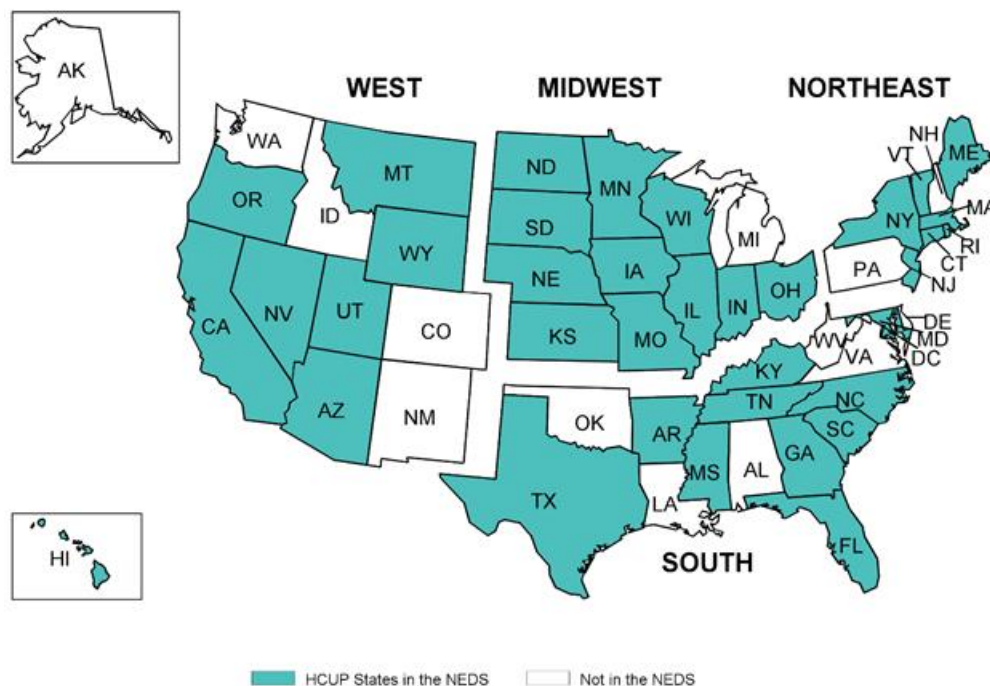
Sample size

The 2016 NEDS is a 20% stratified probability sample of target universe drawn from the sampling frame based on five hospital-based stratification variables including, United States Census region, trauma center designation, urban-rural hospital location, ownership, and teaching status. It therefore represented the diversity of hospitals across the United States. A sample size of 20 percent was based on previous experience with similar research databases. A larger sample would be cumbersome for data users, given that a 20 percent sample contains about 30 million records. A 20 percent sample also enables the user to split the NEDS into two 10 percent subsamples for estimation and validation of models. Therefore, the 2016 NEDS contained 32,680,232 ED visits in 953 hospitals across 35 states and the District of Columbia. Post-stratification discharge weights defined by the Healthcare Cost and Utilization Project (HCUP) were used to calculate national estimates. The use of these weights enabled each HCUP database discharge entry to be adjusted to estimate values from specific portions of the overall United States population. The number of ED visits weighted for national estimates was 144,842,742. In

2016, the national rate of opioid-related ED visits per 100,000 population was 243.5 with a range of 223 to 268.

The HCUP states in the 2016 NEDS included; Arizona, Arkansas, California, Connecticut, District of Columbia, Florida, Georgia, Hawaii, Illinois, Indiana, Iowa, Kansas, Kentucky, Maine, Maryland, Massachusetts, Minnesota, Mississippi, Missouri, Montana, Nebraska, Nevada, New Jersey, New York, North Carolina, North Dakota, Ohio, Oregon, Rhode Island, South Carolina, South Dakota, Tennessee, Utah, Vermont, Wisconsin, and Wyoming.

Figure of HCUP States and the District of Columbia included in the 2016 NEDS.



Source: https://www.hcup-us.ahrq.gov/db/nation/neds/NEDS_Introduction_2016.jsp#ta1

Note: The above graphic outlines states in the NEDS by Region. In the Western region, AZ, CA, HI, MT, NV, OR, UT, WY were in the HCUP NEDS. The following states were not in the NEDS in this region - AK, CO, ID, NM, WA. In the Midwestern region, IA, IN, IL, KS, MN, MO, ND, NE, OH, SD, WI were in the HCUP NEDS. The following state was not in the NEDS

in this region - MI. In the Northeastern region, CT, MA, ME, NJ, NY, RI, VT were in the HCUP NEDS. The following states were not in the NEDS in this region - NH, PA. In the Southern region, AR, DC, FL, GA, KY, MD, MS, NC, SC, TN, TX were in the HCUP NEDS. The following states were not in the NEDS in this region - AL, DE, LA, OK, VA, WV.

Cases of opioid use disorder (OUD) were identified using International Classification of Disease, Tenth Revision, Clinical Modification (ICD-10-CM) codes. These cases were assessed for characteristics associated with prevalence including, (1) Patient (Primary payer, Annual median income, Patient location, and Type of emergency department event – treated & released, admitted to same hospital, transferred to another or died). (2) Hospital (Control/Ownership, Region, and Designation).

The American Psychiatric Association Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5) Classification recommended ICD-10-CM codes for opioid use disorder (OUD) beginning October 1, 2017 are F11.1* for opioid abuse and F11.2* for opioid dependence. The code for uncomplicated opioid abuse is F11.10, which is applicable to mild OUD. The code for uncomplicated opioid dependence is F11.20 which is applicable to moderate and severe OUD (ICD-10-CM Diagnosis Code, 2018; American Psychiatric Association, 2013).

Study Power

For the systematic review, following good research practice, a convenience sample size of the 35 states and the District of Columbia which contributed to the 2016 NEDS database was used in this study.

For the secondary analysis of the 2016 NEDS cross-sectional dataset of this study, the minimal required sample size was calculated based on a power of 80% and a significance level (α) of 0.05.

To calculate the sample size required for this survey study, the follow were needed (Abramson, 2008; Selwyn, 2011):

“p” – A reasonably close estimate of estimate of the actual prevalence – if in doubt, 50% was used; this maximized the sample size and, hence, erred on the safe side.

“d” – The maximum acceptable difference between the estimated prevalence (based on the sample) and the actual prevalence; this “acceptable margin of error” was half the confidence interval.

“t” – The required confidence interval – usually 95%

Also, the size of the population; its effect on the calculated sample size – the Finite Population Correction (f.p.c) was small, unless the population was very small.

Initial sample size (n) calculation;

Using the formula, $n = (t^2pq)/d^2$

Where n=sample size; t=Z of 95% confidence=1.96; p=prevalence estimate=50%;

q=1-p=50%; d=absolute error or sampling error=10%.

$$n = (1.962*0.5*0.5)/0.12 = 96.04 = 97$$

Sample size calculation corrected for Finite Population Correction (f.p.c);

Based on good sampling practice, sample was $\geq 10\%$ of the sample size of 32,680,232 ED visits. In this research, 2016 NEDS was 20% of probability sample of target universe drawn from the sampling frame.

Using the sample size of emergency departments (ED) in community, nonrehabilitation U.S. hospital-owned EDs that reported total ED visits in the American Hospital Association (AHA) Annual Survey Database, $N = 32,680,232$

Initial sample size, $n = 97$

Thus, sampling fraction = $n/N = 97/144,842,742 = 6.7 \times 10^{-7} \times 100\% = 6.7 \times 10^{-5}\%$

Therefore, since the sampling fraction was very low, the f.p.c was close to unity and the correction had a negligible influence and was omitted (Armitage et al., 2002).

Sample size calculation corrected for nonresponse (NR);

Based on good sampling practice, an NR of 10% was expected.

Therefore, the new sample size, $n_1 = n/(1-NR) = 97/(1-0.1) = 107.8 = 108$.

Based on a sample size of 108, calculated power using STATA version 15.0 = 55%. But based on good sampling practice, a power of at least 80% was expected which amounted to a calculated sample size of 194. However, 2016 NEDS sample size was 32,680,232 which provided adequate size to detect any significant difference.

Data Collection and Management

Discharge-level administrative NEDS data was collected based on efforts of hospitals in participating states that maintain statewide data systems. Unweighted ED visit data were collected on actual visits, then weighted proportionately to total number of ED visits in the country based on the sampling strategy. The NEDS is a stratified single-stage cluster sample of state-level ED data reported to healthcare cost and utilization project (HCUP).

All emergency department (ED) discharge-level data totaling 32,680,232 ED visits in 953 hospitals across 35 states and the District of Columbia contributing to and collected in the 2016 NEDS were used in this study. This dataset provided the largest repository of individual level discharge data from all ED visits nationwide capable of providing patient and hospital characteristics associated with prevalence of diagnosing and treating OUD in U.S. Emergency Departments.

Data security and confidentiality – Data in the 2016 NEDS database were recoded to ensure ease of analysis. Missing data were excluded from the final dataset for analysis.

Data location and management – Final dataset for analysis was password protected and study materials secured in a locked cabinet.

Quality Control

The following quality control procedures were used to assess data quality and perform basic editing for the NEDS:

Quality control editing procedures – Data editing was performed using the following explicit rules. (a) Made the data usable without extensive further editing. (b) Confirmed that data values were valid, internally consistent, and consistent with established norms, when feasible. (c) Used some edit procedures to set questionable and inconsistent values to inconsistent (.C or negative 6-filled). Used other edit procedures only to tabulate edit failures. Used the latter to evaluate whether systematic problems exist. (d) Never "fix" or imputed data. Set invalid or inconsistent values to special missing values. This preserved the analyst's ability to investigate data anomalies. (e) Some data elements were coded more reliably because they related to reimbursement. For example, diagnoses, procedures, age, sex, and discharge disposition were part of the algorithm to assign Diagnosis Related Group (DRG) on an inpatient record. (f) Tabulated instances of edit failures and used these to assess data quality for each data source.

Quality review procedure – An independent contractor reviewed the following statistics for the 2016 NEDS. (a) Means, number of missing and non-missing values, minimum, and maximum for all numeric data elements. (b) Mean, median, and extreme values for continuous variables such as length of stay and charges. (c) Frequency distributions for all categorical and

some continuous data elements. (d) Cross frequencies for closely related data elements (e.g., point of origin compared to admission type).

Automated quality review control procedures – Each discharge record was subjected to the following procedures. (a) To assess validity of values – For numeric data: Verifying numeric data as numeric. Checking the range against legal values documented by the data source. Checking the range against standard norms (e.g., length of stay is a non-negative value; age in years is between 0 and 124, the maximum allowed by the DRG grouper). Checking the values against the maximum allowed for the data element (e.g., birth weight less than 20 pounds). For character data: Verifying against norms, when feasible (e.g., diagnosis codes and procedure codes). (b) To assess internal consistency – Comparing values of related data elements (e.g., a procedure of *hysterectomy* should appear with a sex of *female*; admission date should occur *before* discharge date). If an inconsistency involved a critical data element (such as discharge date and admission date), as much information as reasonable was retained. For example, If discharge date fell before admission date, discharge date was retained and admission date and length of stay set to inconsistent (.C or negative 6-filled). If discharge date was invalid (e.g., February 30), discharge quarter and discharge year were retained. (c) To assess consistency with established norms – Comparing values to an established norm (e.g., maternal diagnoses should occur with an age between 10 and 55 years).

Measures

Individual patient encounters resulting in a diagnosis of any opioid-related incidents including the diagnosis of OUD were identified in NEDS using ICD-10-CM diagnostic codes. According to the DSM-5 classification of the American Psychiatric Association, beginning October 1, 2017, ICD-10-CM codes for OUD are F11.1* for opioid abuse and F11.2* for opioid

dependence (WHO, 1992, 1993). This study used F11.10, the code for uncomplicated opioid abuse which was applicable to mild OUD and F11.20, the code for uncomplicated opioid dependence which was applicable to moderate and severe OUD (ICD-10-CM Diagnosis Code, 2018; American Psychiatric Association, 2013). A composite variable “OUD_Condition” based on whether the individual patient encounter resulted in a diagnosis and treatment of OUD, specifically uncomplicated opioid abuse or uncomplicated opioid dependence was created. Depending on the presence of opioid abuse or opioid dependence, “OUD_Condition was then recoded as ‘0’ – Uncomplicated opioid abuse; and ‘1’ – Uncomplicated opioid dependence. These cases of OUD were assessed for factors associated with prevalence (patient demographic – Primary payer, Annual median income, Patient location, and Type of emergency department event – treated & released, admitted to same hospital, transferred to another or died; hospital – Control/Ownership, Region, and Designation; and state-level policy – MAT policy status, MAT medication coverage status, Medicaid expansion status, and Medicaid section 1115 behavioral health waiver status).

The cohort of cases in this study were patients 12 years and older. Children from 12 years were included in this study because there has been significant increases in opioid prescribing across all age groups observed in recent years (Binswanger & Glanz, 2015). In addition, opioids have become the most commonly initiated drugs of abuse among youth. There has been a six-fold increase of unintentional opioid poisonings in youth in the last 10 years. Furthermore, 5.4% of 12-17 year olds and 10% of 18-25 year olds reported nonmedical use of prescription opioids in 2012 (Binswanger & Glanz, 2015). Therefore, treatment plans that are effective, practical, and scalable are needed for the young population with OUD (Borodovsky et al, 2018).

Variables

Outcome variables: The outcome variables for this study included: (i) State-level opioid policy – which was defined as the type of state-by-state opioid policy in existence. Specifically, state-level opioid policy were characterized by, (a) MAT policy status – presence or not of state-level MAT policy. (b) MAT medication coverage status – coverage of all three MAT medications used for OUD treatment (comprehensive coverage) or coverage of two or less of MAT medication used for OUD treatment (non-comprehensive coverage) (Grogan et al, 2016; Blanchard et al, 2018). (c) Medicaid expansion status – number of states that have adopted and not adopted Medicaid expansion. (d) Medicaid section 1115 behavioral health waiver status – number of states that have approved and not approved for behavioral health exclusion waivers for OUD treatment. (ii) Prevalence – which was defined as the proportion of cases of opioid use disorder (OUD) diagnosed and treated in the Emergency Department (ED) within a 12-month period from January 2016 to December 2016.

Predictor variables: The predictor variables in this study were grouped into two categories. (1) Primary predictor variable – (i) Opioid use disorder (OUD) condition – which was defined as the presence of a diagnosis of uncomplicated opioid abuse and uncomplicated opioid dependence during an individual patient encounter at the ED within a 12-month period from January 2016 to December 2016. (2) Covariates – (i) Patient characteristics – primary payer, annual median income, patient location and ED event. (ii) Hospital characteristics – control/ownership, region, and designation. (iii) State-level policy characteristics – MAT policy status, MAT medication coverage status, Medicaid expansion status, and Medicaid section 1115 behavioral health waiver status.

Measurement Matrix

Outcome Variables

Variable category	Variable	Definition	Source	Related Aim	Type
State-Level Opioid Policy	Opioid Policy	Characteristics of state-level opioid policy (including: MAT policy status – not present=0, present=1; MAT medication status – non-comprehensive=0, comprehensive=1; Medicaid expansion status – not adopted=0, adopted=1, and Medicaid section 1115 behavioral health waiver status – not approved=0, approved=1)	American Society of Addiction Medicine (ASAM) State Report, Substance Abuse and Mental Health Services Administration (SAMHSA), and Kaiser Family Foundation (KFF) Report	Aim 1	Systematic review of state-by-state opioid policies
Prevalence	Prevalence	The proportion of cases of opioid use disorder (OUD) diagnosed and treated for in the Emergency Department (ED) within a 12-month period from January 2016 to December 2016	Nationwide Emergency Department Sample (NEDS)	Aim 2	Continuous
Predictor variables					
Variable category	Variable	Definition	Source	Related Aim	Type
Primary					
OUD Diagnosis	OUD_Condition	Presence of a diagnosis of opioid abuse or dependence during an individual patient encounter at the ED within a 12-month period from January 2016 to December 2016. (including, 0= diagnosed opioid abuse , 1= diagnosed opioid dependence)	Composite derived from Nationwide Emergency Department Sample (NEDS)	Aim 2	Categorical (Binary)
Covariates					

Patient Characteristics	Primary payer	Expected primary payer of ED services (including, 1=Medicare, 2=Medicaid, 3=Private including HMO, 4=Self-pay, 5=No charge, 6=Other)	NEDS	Aim 2	Categorical (Nominal)
	Annual Median Income	National quartile of median household income estimated using patient's residential zip code (include, 1=\$1-\$42,999, 2=\$43,000-\$53,999, 3=\$54,000-\$70,999, and 4=≥\$71,000)	NEDS	Aim 2	Categorical (Ordinal)
	Patient location	Urban-rural designation of patient's county of residence (include, 1=large central metropolitan, 2=large fringe metropolitan, 3=medium metropolitan, and 4=small metropolitan, 5=micropolitan, 6=not metropolitan or micropolitan)	NEDS	Aim 2	Categorical (Nominal)
	ED Event	Type of patient ED event (include, 1=treated & released, 2=admitted to same hospital, 3=transferred to another hospital, 9=died)	NEDS	Aim 2	Categorical (Nominal)
Hospital Characteristics	Control/Ownership	Ownership status of ED/hospital (include, 0=all, 1=public[government, non-Federal, 2=voluntary[private, not-for-profit], 3=proprietary[private, investor-owned/for-profit], 4=private[private voluntary/proprietary])	Nationwide Emergency Department Sample (NEDS)	Aim 2	Categorical (Nominal)
	Region	Region of the U.S. hospital is located (include, 1=Northeast,	NEDS	Aim 2	Categorical (Nominal)

State-Policy Characteristics		2=Midwest, 3=South, and 4=West)			
	Designation	Hospital urban-rural designation (include, 1=large metropolitan area, 2=small metropolitan area, 3=Micropolitan area, and 4=Non-urban residual)	NEDS	Aim 2	Categorical (Nominal)
	MAT Policy Status	Presence or absence of MAT policy. (including, 0=Not present, 1=Present)	ASAM State Report, SAMHSA, and KFF Report	Aims 1& 2	Categorical (Binary)
	MAT Medication Coverage Status	Presence or absence of MAT medication coverage status. (including, 0= non- comprehensive coverage, 1=has comprehensive coverage)	ASAM State Report, SAMHSA, and KFF Report	Aims 1& 2	Categorical (Binary)
	Medicaid Expansion Status	Adoption or not Medicaid expansion. (including, 0= not adopted, 1=Adopted)	KFF Report	Aims 1& 2	Categorical (Binary)
	Medicaid Section 1115 Behavioral Health Waiver Status	Section 1115 behavioral health waiver status. (including, 0=not approved, 1=Approved)	KFF Report	Aims 1& 2	Categorical (Binary)

Data Analysis

Overview

The final dataset for analysis was organized, recoded and analyzed manually by research staff.

Descriptive statistics including frequency and proportions were used to analyze the final data collected. In addition to hierarchical linear regression model (HLM) was used to analyze the final data collected.

Data analysis was performed using Statistical Package for Social Sciences (SPSS) version 25.0 developed by IBM Corporation.

Secondary analyses

Aim 1: To systematically identify, appraise, and collect state-by-state level data on status of medication-assisted treatment (MAT) policies, MAT medication coverage status for OUD treatment, Medicaid expansion status, and Medicaid section 1115 behavioral health waiver status for OUD treatment in all 50 states and the District of Columbia captured in the literature.

Methods – Review of the identified data sources – American Society of Addiction Medicine (ASAM) state reports; Substance Abuse and Mental Health Services Administration (SAMHSA) Office of Policy, Planning and Innovation State Medicaid coverage reports; and Kaiser Family Foundation reports on the opioid epidemic was performed to identify, appraise and collect relevant data on nationwide state-level opioid policy status, MAT medication coverage status for treating OUD, Medicaid expansion status, and Medicaid section 1115 behavioral health waiver status for OUD treatment. While, the aim of the review which was to identify, appraise, and collect state-level opioid policies in all 50 states and the District of Columbia in the United States captured in the literature was accomplished, only policies specifically within the 35 states of the US and the District of Columbia contribution to the 2016 NEDS were used in the analysis. These included; Arizona, Arkansas, California, Connecticut, District of Columbia, Florida, Georgia, Hawaii, Iowa, Illinois, Indiana, Kansas, Kentucky, Maine, Maryland, Massachusetts, Minnesota, Missouri, Mississippi, Montana, North Carolina,

North Dakota, Nebraska, New Jersey, Nevada, New York, Ohio, Oregon, Rhode Island, South Carolina, South Dakota, Tennessee, Utah, Vermont, Wisconsin, and Wyoming. The University of Texas Health Science Center at Houston Committee for the Protection of Human Subjects – also known as Institutional Review Board (IRB) – approval was not required for this process as no human subjects were needed.

Results – Findings from each of the 50 States opioid policy evaluated for specific criteria including MAT policy status, MAT medication coverage status for treating OUD, Medicaid expansion status and Medicaid section 1115 behavioral health waiver status was presented Table 2 shown below.

Aim 2: To examine individual or patient characteristics (Primary payer, Annual median income, Patient location and Type of emergency department event), hospital characteristics (Control/Ownership, Region, and Designation), and state-level policy characteristics (Opioid policy status, MAT medication coverage status for treating OUD, Medicaid expansion status, and Medicaid section 1115 behavioral health waiver status for OUD treatment) associated with prevalence of emergency department diagnosis and treatment of any opioid use disorder (OUD) in U.S. population 12 years and older from January 2016 to December 2016 captured in the Nationwide Emergency Department Sample (NEDS) database.

Method – Data preparation: Core dataset – For this study, this dataset was also known as the patient-level dataset. Only the variables of interest were retained in the core (patient-level) dataset. These included, “DX_OUD” – the ICD-10-CM Diagnosis for OUD; “PAY1” – the primary expected payer (uniform), “ZIPINC_QRTL” – the median household income national quartile for patient zip code, “PL_NCHS” – the patient location: NCHS urban-rural code, and “EDEVENT” – the type of ED event. A new variable “nDX_OUD” was created to represent the

string to numeric recode of OUD diagnosis variable “DX_OUD”. Using ICD-10-CM codes, the diagnoses of any opioid-related incident in the ED were identified from the patient-level dataset. The identification of occurrence of any opioid-related was classified using ICD-10-CM codes into: (1) opioid abuse, (2) adverse effects of opioids, (3) opioid dependence and unspecified use, and (4) opioid poisoning. This approach of using ICD codes to categorize any opioid-related incident has been documented and used in previous studies (More & Barrett, 2017; Vivolo-Kantor et al., 2018; Litaker et al., 2019; Geller et al., 2019; Salzman et al., 2020). Subsequently, the ICD-10-CM Diagnosis for uncomplicated opioid abuse was recoded as “0” and the ICD-10-CM Diagnosis for uncomplicated opioid dependence was recoded as “1”.

Hospital dataset – only the variables of interest were retained in the hospital dataset. These included, “HOSP_CONTROL” – the control/ownership of hospital, “HOSP_REGION” – the region of hospital, “HOSP_URCAT4” – the hospital urban-rural designation, and “TOTAL_EDVisits” – the total number of ED visits from this hospital in the NEDS. A new variable “PREV_RXOUD_ED” was derived to represent the prevalence of diagnosing and treating OUD in ED at the hospital level. To determine the prevalence of diagnosing and treating OUD in the ED at the hospital level, it was assumed that: (1) patients were diagnosed and treated for OUD at least during one ED visit; (2) the total ED visits – “TOTAL_EDVisits” – for each hospital represented the total number of times each patient was treated at least once for OUD. Therefore, the prevalence of diagnosing and treating OUD in the ED at the hospital level (“PREV_RXOUD_ED”) was calculated by dividing each TOTAL_EDVisits per hospital by the total number of ED visits for all hospitals for the duration of the study under consideration, which was 32,680,232 emergency department (ED) visits. In other words, $PREV_RXOUD_ED = TOTAL_EDVisits \text{ per hospital} / \text{Sum of } TOTAL_EDVisits$ (Woltman et al., 2012).

“HOSP_ED” – the HCUP ED hospital identifier and “DISCWT” – the weight to ED visits in AHA universe for each of the cases in the core and hospital datasets were also retained.

The hospital dataset was then merged with the core (patient-level) dataset in a one-to-many merger using HOSP_ED, the unique identifier common to both the core (patient-level) and hospital datasets.

State-level policy dataset – the state-level policy dataset was created by abstracting the required data from the identified sources. Four variables were identified and categorized as “MAT_POL” – representing the MAT policy status which was coded as “0” when not present and “1” when present, “MAT_COV” – representing MAT medication coverage status which was coded as “0” for “No” when not comprehensive and as “1” for “Yes” when comprehensive, “MED_EXP” – representing Medicaid expansion status which was coded as “0” for “No” when not adopted and “1” for “Yes” when adopted, and “MED_1115” – representing Medicaid section 1115 behavioral health waiver status which was coded as “0” for “No” when not approved and “Yes” when approved.

As part of the data preparation requirements for the statistical analysis, the patient-, and hospital-level datasets were merged into a single dataset file and the cases in the final dataset file sorted in ascending order – that is, from lowest to highest value – using HOSP_ED, the unique identifier common to all individual data files.

Pearson’s chi-squared test was used following cross-tabulation of “nDX_OUD” by the patient and hospital characteristics to determine if the differences between the diagnosis of opioid abuse and opioid dependence were statistically significant. Pearson’s chi-squared test was also used after cross-tabulation of “HOSP_REGION” by the patient and hospital characteristics to determine if the differences between the regions were statistically significant.

Statistical analysis – Hierarchical linear models (HLM) (Huta, 2014; Anderson, 2012; Woltman et al., 2012; Aiken, et al., 2018) were used to estimate the association between the outcome variable (prevalence) and predictor variables (patient demographic –primary payer, annual median income, patient location and type of emergency department event – treated & released, admitted to same hospital, transferred to another or died; and hospital – control/ownership, region, and designation). HLM was used as the inferential statistical analysis method of choice for this study because: (1) there were two levels of units in the dataset for this study, i) patients – were level 1 units because of multiple individual per hospital, and ii) hospitals – were level 2 units because there were multiple hospitals per state in the dataset. As such, the final dataset used for analysis in this study consisted of 2-level hierarchies. (2) The unweighted sample sizes of the levels in the hierarchy differed from patient-level (174,061) to hospital-level (953). (3) There were missing values at the patient-level, the lowest level of the hierarchy, which HLM can handle. (4) There were no missing data at the hospital-level of the hierarchy thus HLM was more suitable as there was no need for imputing missing data at this levels before performing HLM regression. (5) The cases or records at the patient-level were indistinguishable [HLM can be utilized when cases are distinguishable or not] (Huta, 2014; Anderson, 2012; Woltman et al., 2012).

Tests of Normality – The outcome variable, PREV_RXOUD_ED, was tested to determine if it was normally distributed (See Appendix A - Tests of Normality Results). It was not normally distributed. Therefore, PREV_RXOUD_ED was log transformed to “PREV_RXOUD_ED_Log” and re-tested for the normality assumption (See Appendix A - Tests of Normality Results). It was relatively more normally distributed. Additionally, the tests of HLM assumptions using PREV_RXOUD_ED and PREV_RXOUD_ED_Log revealed more violations of these

assumptions with PREV_RXOUD_ED than PREV_RXOUD_ED_Log (See Appendix C - HLM Regression and Test of Assumptions Results). Thus, it was determined to proceed with the HLM regression analysis using the transformed outcome variable, PREV_RXOUD_ED_Log.

Furthermore, the relationship between outcome variable, PREV_RXOUD_ED_Log and all the predictor variables was assessed for linearity and was found to be linear.

Missing Data – Little’s Missing Completely at Random (MCAR) Test was performed on the transformed outcome and predictor variables in the dataset to determine the proportion of missing data for each variable and how to handle the missing data (See Appendix B - MVA) (Little & Schenker, 1995). There were no missing data in the transformed outcome variable – Prevalence (“PREV_RXOUD_ED_Log”). The predictor variables were all categorical as such; expectation maximization (EM) statistics were not computed. Only patient-level variables – specifically PAY1, ZIPINC_QRTL, PL_NCHS – had missing data to the proportions of 0.1%, 3.1%, and 1.7% respectively (See Appendix B - MVA). Given the large sample size of this study, the missing data were not replaced (Allison, 2001; Dong & Peng, 2013).

Test of HLM Assumptions – HLM assumptions were tested for the purposes of this study and no major violations of these assumptions were found (See Appendix C). Specifically, error or residual structure and predictor variables assumptions were tested. For this study, error structure assumptions tested for included ensuring that: patient-level (Level 1) residuals were independent and normally distributed; hospital-level (Level-2) random effects were independent, multivariate and normally distributed; and inter level residuals were independent. Predictor variables assumptions tested for in this study included ensuring that: no multicollinearity exist between predictor variables and residuals at all levels – that is, patient-level (Level 1) predictor variables were independent of patient-level residuals and hospital-level (Level-2) predictor variables were

independent of hospital-level residuals respectively and the predictor variables at the patient-, and hospital-levels were independent of the random effects at the other levels (Huta, 2014; Anderson, 2012; Woltman et al., 2012). The statistical analyses for this study was conducted using IBM SPSS Statistics version 25. All tests of hypotheses were two-tailed with a type-1 error rate set at 5%.

Human Subjects, Animal Subjects, or Safety Considerations

This study used data from the 2016 Nationwide Emergency Department Sample (NEDS). The 2016 NEDS is publicly available data developed for the Healthcare Cost and Utilization Project (HCUP). The HCUP was developed through a Federal-State-Industry partnership sponsored by the Agency for Healthcare Research and Quality. HCUP data inform decision making at the national, state, and community levels. There was no need for submission of a public use file data agreement form to access the dataset. The dataset does not contain personal identifiers that can be linked back to individual level emergency department visits. The proposal for this study was reviewed by the University of Texas Health Science Center, School of Public Health Office of Research. The status of this study was determined by the University of Texas Health Science Center at Houston Committee for the Protection of Human Subjects to be exempt. The researcher of this study completed human subject ethics training through the Collaborative Institutional Training Initiative prior to the commencement of the project.

RESULTS

A total of 32,680,232 ED visits to 953 hospitals across 35 states and the District of Columbia which when generalized to the entire United States in 2016 amounted to 144,842,742 visits to the ED in 4,639 hospitals across the 50 states including the District of Columbia were analyzed in this study. Of these weighted ED visits, 1,623,490 visits were due to opioid-related incidents.

Descriptive Statistics

The overall prevalence of any opioid-related incident in a U.S. ED observed in the 2016 NEDS was 1.12%. Figure 1 reveals the proportions of the broad categories of opioid-related incidents that were diagnosed and treated for across the ED in the United States in 2016. Almost half of these opioid-related incidents were the results of opioid dependence (47.21%). Over 1 in 5 (21.92%) of the incidents were due to opioid abuse. Opioid poisoning constituted just less than 20% while just over 10% of the incidents were because of adverse effects of opioids (Figure 1).

Figure 1. Proportions of the Categories of Any Opioid-Related Incident in U.S. Emergency Departments

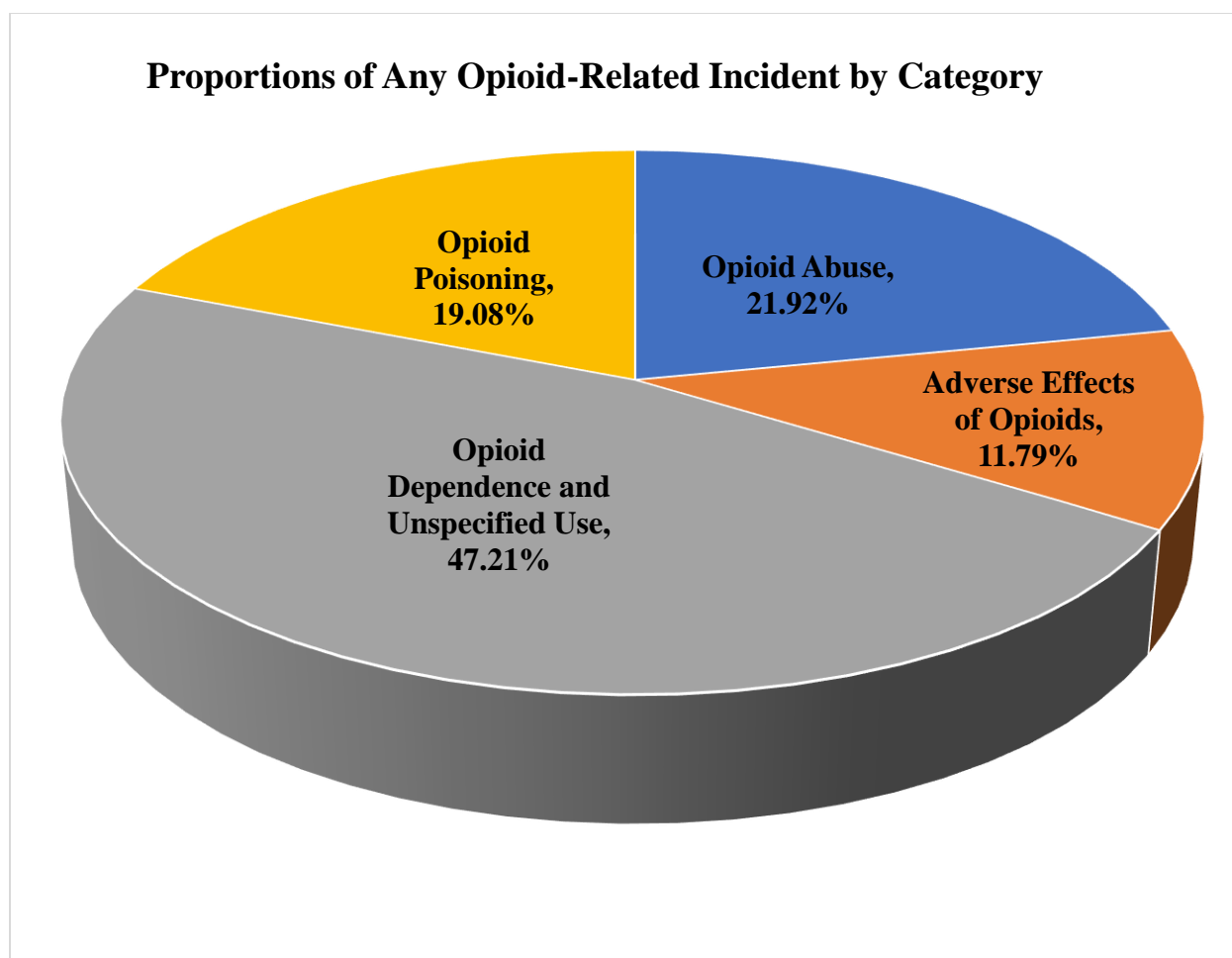


Table 1 details the categories, ICD-10-CM codes, descriptions, frequencies, and proportions of all opioid-related incidents observed in 2016. There were 132 ICD-10-CM diagnosis codes identified for any opioid-related incident; 119 (90.15%) of these were observed in the 2016 NEDS (Table 1). There were preponderant opioid-related incidents diagnosed and treated in the U.S. ED in 2016. These included: uncomplicated opioid dependence (26.01%); uncomplicated opioid abuse (20.80%). Opioid dependence with withdrawal (11.35%); initial encounter with accidental poisoning by heroin (8.37%); initial encounter with adverse effect of other opioids (6.67%); unspecified, uncomplicated opioid use (5.52%). Initial encounter with adverse effect of unspecified narcotics (3.54%); initial encounter with accidental poisoning by other opioids (3.35%). Initial encounter with accidental poisoning by unspecified narcotics

(2.43%); opioid dependence in remission (1.77%); initial encounter with intentional self-harm through poisoning by other opioids (1.09%); and initial encounter with adverse effect of synthetic narcotics (1.00%) (Table 1) (Figure 2).

Table 1. Categories, Descriptions, Frequencies, and Proportions of Any Opioid-Related Incident Observed in 2016.

Opioid-Related Incident Category	ICD-10-CM Code	Description	Frequency (N=1,623,490)	Proportion (%)
Opioid Abuse (n=13)	F1110	Opioid abuse, uncomplicated	337,639	20.80
	F11120	Opioid abuse with intoxication, uncomplicated	2,062	0.13
	F11121	Opioid abuse with intoxication delirium	1,023	0.06
	F11122	Opioid abuse with intoxication with perceptual disturbance	130	0.01
	F11129	Opioid abuse with intoxication, unspecified	8,614	0.53
	F1114	Opioid abuse with opioid-induced mood disorder	1,813	0.11
	F11150	Opioid abuse with opioid-induced psychotic disorder with delusions	130	0.01
	F11151	Opioid abuse with opioid-induced psychotic disorder with hallucinations	242	0.01
	F11159	Opioid abuse with opioid-induced psychotic disorder, unspecified	483	0.03
	F11181	Opioid abuse with opioid-induced sexual dysfunction	0	0.00
	F11182	Opioid abuse with opioid-induced sleep disorder	57	0.00
	F11188	Opioid abuse with other opioid-induced disorder	2,270	0.14
	F1119	Opioid abuse with unspecified opioid-induced disorder	1,447	0.09
Adverse Effects of Opioids (n=18)	T400X5A	Adverse effect of opium, initial encounter	3,282	0.20
	T400X5D	Adverse effect of opium, subsequent encounter	20	0.00
	T400X5S	Adverse effect of opium, sequela	18	0.00
	T402X5A	Adverse effect of other opioids, initial encounter	108,298	6.67
	T402X5D	Adverse effect of other opioids, subsequent encounter	325	0.02
	T402X5S	Adverse effect of other opioids, sequela	229	0.01
	T403X5A	Adverse effect of methadone, initial encounter	2,923	0.18
	T403X5D	Adverse effect of methadone, subsequent encounter	10	0.00
	T403X5S	Adverse effect of methadone, sequela	32	0.00
	T404X5A	Adverse effect of synthetic narcotics, initial encounter	16,243	1.00
	T404X5D	Adverse effect of synthetic narcotic, subsequent encounter	39	0.00
	T404X5S	Adverse effect of synthetic narcotic, sequela	43	0.00
	T40605A	Adverse effect of unspecified narcotics, initial encounter	57,489	3.54
	T40605D	Adverse effect of unspecified narcotics, subsequent encounter	86	0.01
	T40605S	Adverse effect of unspecified narcotics, sequela	107	0.01
	T40695A	Adverse effect of other narcotics initial encounter	2,215	0.14
	T40695D	Adverse effect of other narcotics, subsequent encounter	14	0.00
	T40695S	Adverse effect of other narcotics, sequela	0	0.00
Opioid Dependence and Unspecified Use (n=29)	F1120	Opioid dependence, uncomplicated	422,249	26.01
	F1121	Opioid dependence, in remission	28,727	1.77
	F11220	Opioid dependence with intoxication, uncomplicated	1,214	0.07
	F11221	Opioid dependence with intoxication delirium	1,005	0.06
	F11222	Opioid dependence with intoxication with perceptual disturbance	171	0.01
	F11229	Opioid dependence with intoxication, unspecified	3,183	0.20
	F1123	Opioid dependence with withdrawal	184,301	11.35
	F1124	Opioid dependence with opioid-induced mood disorder	5,100	0.31

Opioid Poisoning (n=72)	F11250	Opioid dependence with opioid-induced psychotic disorder with delusions	124	0.01
	F11251	Opioid dependence with opioid-induced psychotic disorder with hallucinations	331	0.02
	F11259	Opioid dependence with opioid-induced psychotic disorder, unspecified	506	0.03
	F11281	Opioid dependence with opioid-induced sexual dysfunction	0	0.00
	F11282	Opioid dependence with opioid-induced sleep disorder	197	0.01
	F11288	Opioid dependence with other opioid-induced disorder	2,706	0.17
	F1129	Opioid dependence with unspecified opioid-induced disorder	14,253	0.88
	F1190	Opioid use, unspecified, uncomplicated	89,635	5.52
	F11920	Opioid use, unspecified, with intoxication, uncomplicated	291	0.02
	F11921	Opioid use, unspecified, with intoxication delirium	1,465	0.09
	F11922	Opioid use, unspecified, with intoxication with perceptual disturbance	42	0.00
	F11929	Opioid use, unspecified, with intoxication, unspecified	908	0.06
	F1193	Opioid use, unspecified with withdrawal	4,037	0.25
	F1194	Opioid use, unspecified with opioid-induced mood disorder	1,197	0.07
	F11950	Opioid use, unspecified with opioid-induced psychotic disorder with delusions	45	0.00
	F11951	Opioid use, unspecified with opioid-induced psychotic disorder with hallucinations	234	0.01
	F11959	Opioid use, unspecified with opioid-induced psychotic disorder, unspecified	364	0.02
	F11981	Opioid use, unspecified with opioid-induced sexual dysfunction	0	0.00
	F11982	Opioid use, unspecified with opioid-induced sleep disorder	126	0.01
	F11988	Opioid use, unspecified with other opioid-induced disorder	704	0.04
	F1199	Opioid use, unspecified with unspecified opioid-induced disorder	3,374	0.21
	T400X1A	Poisoning by opium, accidental (unintentional), initial encounter	2,143	0.13
	T400X1D	Poisoning by opium, accidental (unintentional), subsequent encounter	5	0.00
	T400X1S	Poisoning by opium, accidental (unintentional), sequela	0	0.00
	T400X2A	Poisoning by opium, intentional self-harm, initial encounter	252	0.02
	T400X3A	Poisoning by opium, assault, initial encounter	6	0.00
	T400X4A	Poisoning by opium, undetermined, initial encounter	274	0.02
	T400X4D	Poisoning by opium, undetermined, subsequent encounter	0	0.00
	T400X4S	Poisoning by opium, undetermined, sequela	0	0.00
	T400X6A	Underdosing of opium, initial encounter	174	0.01
	T401X1A	Poisoning by heroin, accidental (unintentional), initial encounter	135,963	8.37
	T401X1D	Poisoning by heroin, accidental (unintentional), subsequent encounter	194	0.01
	T401X1S	Poisoning by heroin, accidental (unintentional), sequela	137	0.01
	T401X2A	Poisoning by heroin, intentional self-harm, initial encounter	6,939	0.43
	T401X2D	Poisoning by heroin, intentional self-harm, subsequent encounter	20	0.00
	T401X2S	Poisoning by heroin, intentional self-harm, sequela	17	0.00
	T401X3A	Poisoning by heroin, assault, initial encounter	125	0.01
	T401X3S	Poisoning by heroin, assault, sequela	4	0.00
	T401X4A	Poisoning by heroin, undetermined, initial encounter	8,877	0.55

T401X4D	Poisoning by heroin, undetermined, subsequent encounter	54	0.00
T401X4S	Poisoning by heroin, undetermined, sequela	19	0.00
T402X1A	Poisoning by other opioids, accidental (unintentional), initial encounter	54,432	3.35
T402X1D	Poisoning by other opioids, accidental (unintentional), subsequent encounter	61	0.00
T402X1S	Poisoning by other opioids, accidental (unintentional), sequela	36	0.00
T402X2A	Poisoning by other opioids, intentional self-harm, initial encounter	17,689	1.09
T402X2D	Poisoning by other opioids, intentional self-harm, subsequent encounter	38	0.00
T402X2S	Poisoning by other opioids, intentional self-harm	9	0.00
T402X3A	Poisoning by other opioids, assault, initial encounter	96	0.01
T402X4A	Poisoning by other opioids, undetermined, initial encounter	4,588	0.28
T402X4D	Poisoning by other opioids, undetermined, subsequent encounter	17	0.00
T402X4S	Poisoning by other opioids, undetermined, sequela	0	0.00
T402X6A	Underdosing of other opioids, initial encounter	1,757	0.11
T402X6D	Underdosing of other opioids, subsequent encounter	9	0.00
T403X1A	Poisoning by methadone, accidental (unintentional), initial encounter	7,013	0.43
T403X1D	Poisoning by methadone, accidental (unintentional), subsequent encounter	15	0.00
T403X1S	Poisoning by methadone, accidental (unintentional), sequela	13	0.00
T403X2A	Poisoning by methadone, intentional self-harm, initial encounter	1,398	0.09
T403X2D	Poisoning by methadone, intentional self-harm, subsequent encounter	8	0.00
T403X3A	Poisoning by methadone, assault, initial encounter	10	0.00
T403X4A	Poisoning by methadone, undetermined, initial encounter	805	0.05
T403X4D	Poisoning by methadone, undetermined, subsequent encounter	5	0.00
T403X4S	Poisoning by methadone, undetermined, sequela	4	0.00
T403X6A	Underdosing of methadone, initial encounter	274	0.02
T404X1A	Poisoning by synthetic narcotics, accidental (unintentional), initial encounter	11,322	0.70
T404X1D	Poisoning by synthetic narcotics, accidental (unintentional), subsequent encounter	15	0.00
T404X1S	Poisoning by synthetic narcotics, accidental (unintentional), sequela	27	0.00
T404X2A	Poisoning by other synthetic narcotics, intentional self-harm, initial encounter	5,859	0.36
T404X2D	Poisoning by other synthetic narcotics, intentional self-harm, subsequent encounter	27	0.00
T404X3A	Poisoning by other synthetic narcotics, assault, initial encounter	54	0.00
T404X4A	Poisoning by synthetic narcotics, undetermined, initial encounter	791	0.05
T404X4D	Poisoning by synthetic narcotics, undetermined, subsequent encounter	0	0.00
T404X4S	Poisoning by synthetic narcotics, undetermined, sequela	4	0.00
T404X6A	Underdosing of other synthetic narcotics, initial encounter	211	0.01
T40601A	Poisoning by unspecified narcotics, accidental (unintentional), initial encounter	39,448	2.43
T40601D	Poisoning by unspecified narcotics, accidental (unintentional), subsequent encounter	29	0.00

T40601S	Poisoning by unspecified narcotics, accidental (unintentional), sequela	40	0.00
T40602A	Poisoning by unspecified narcotics, intentional self-harm, initial encounter	3,677	0.23
T40602D	Poisoning by unspecified narcotics, intentional self-harm, subsequent encounter	7	0.00
T40603A	Poisoning by unspecified narcotics, assault, initial encounter	82	0.01
T40604A	Poisoning by unspecified narcotics, undetermined, initial encounter	3,185	0.20
T40604D	Poisoning by unspecified narcotics, undetermined, subsequent encounter	8	0.00
T40604S	Poisoning by unspecified narcotics, undetermined, sequela	5	0.00
T40606A	Underdosing of unspecified narcotics, initial encounter	85	0.01
T40691A	Poisoning by other narcotics, accidental (unintentional), initial encounter	1,105	0.07
T40691D	Poisoning by other narcotics, accidental (unintentional), subsequent encounter	0	0.00
T40691S	Poisoning by other narcotics, accidental (unintentional), sequela	0	0.00
T40692A	Poisoning by other narcotics, intentional self-harm, initial encounter	151	0.01
T40693A	Poisoning by other narcotics, assault, initial encounter	4	0.00
T40694A	Poisoning by other narcotics, undetermined, initial encounter	74	0.00
T40694D	Poisoning by other narcotics, undetermined, subsequent encounter	0	0.00
T40694S	Poisoning by other narcotics, undetermined, sequela	0	0.00
T40696A	Underdosing of other narcotics, initial encounter	23	0.00
T40696S	Underdosing of other narcotics, sequela	5	0.00

Note: Total proportions do not add up to 100% because compared to the absolute values; these relative values were rounded up.

Figure 2. Most Preponderant Opioid-Related Incidents in U.S. Emergency Departments

2016 Most Preponderant Opioid-Related Incidents in U.S. EDs

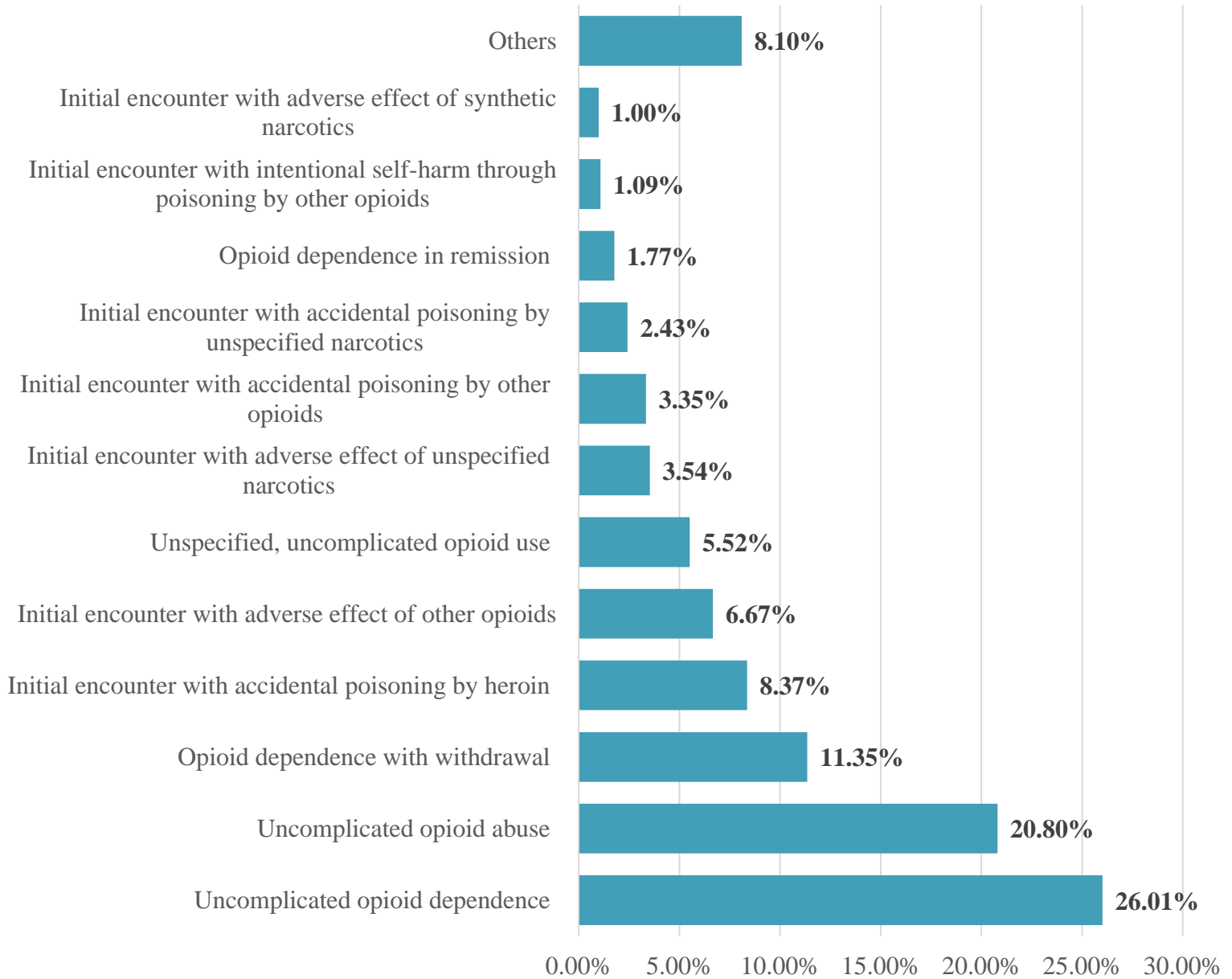


Table 2 summarizes state-level opioid policies of all the 50 states of the United States and the District of Columbia. Forty-nine states including the District of Columbia (98.0%) had medication-assisted treatment policies in place for treating opioid use disorder (OUD). Wyoming (2.0%) was the only state that did not have a medication-assisted treatment policy. Forty states and the District of Columbia (80.4%) provided comprehensive medication-assisted treatment

coverage. Ten states (19.6%) comprising Arkansas, Idaho, Kansas, Kentucky, Louisiana, Nebraska, North Dakota, South Carolina, Tennessee and Wyoming did not provide comprehensive medication-assisted treatment coverage. Of the 50 states and the District of Columbia, thirty-seven (72.6%) had expanded Medicaid. The 14 states (27.4%) that had not expanded Medicaid included Alabama, Florida, Georgia, Kansas, Mississippi, Missouri, North Carolina, Oklahoma, South Carolina, South Dakota, Tennessee, Texas, Wisconsin, and Wyoming. In addition, while 31 states (60.8%) had approved Medicaid section 1115 behavioral health waiver status, twenty (39.2%) consisting of Alabama, Arkansas, Colorado, Connecticut, District of Columbia, Georgia, Idaho, Iowa, Maine, Mississippi, Missouri, Nevada, North Dakota, Oklahoma, Oregon, South Carolina, South Dakota, Tennessee, Texas, and Wyoming had not approved Medicaid section 1115 behavioral health waiver status (Table 2).

Table 2. Characteristics of State-Level Opioid Policies for all 50 States and District of Columbia

State	Criteria			
	MAT Policy status	MAT medication coverage status	Medicaid expansion status	Medicaid section 1115 behavioral health waiver status
Alabama*	Yes	Yes	No	No
Alaska*	Yes	Yes	Yes	Yes
Arizona	Yes	Yes	Yes	Yes
Arkansas	Yes	No	Yes	No
California	Yes	Yes	Yes	Yes
Colorado*	Yes	Yes	Yes	No
Connecticut	Yes	Yes	Yes	No
Delaware*	Yes	Yes	Yes	Yes
District of Columbia	Yes	Yes	Yes	No
Florida	Yes	Yes	No	Yes
Georgia	Yes	Yes	No	No
Hawaii	Yes	Yes	Yes	Yes

State	Criteria			
	MAT Policy status	MAT medication coverage status	Medicaid expansion status	Medicaid section 1115 behavioral health waiver status
Idaho*	Yes	No	Yes	No
Illinois	Yes	Yes	Yes	Yes
Indiana	Yes	Yes	Yes	Yes
Iowa	Yes	Yes	Yes	No
Kansas	Yes	No	No	Yes
Kentucky	Yes	No	Yes	Yes
Louisiana*	Yes	No	Yes	Yes
Maine	Yes	Yes	Yes	No
Maryland	Yes	Yes	Yes	Yes
Massachusetts	Yes	Yes	Yes	Yes
Michigan*	Yes	Yes	Yes	Yes
Minnesota	Yes	Yes	Yes	Yes
Mississippi	Yes	Yes	No	No
Missouri	Yes	Yes	No	No
Montana	Yes	Yes	Yes	Yes
Nebraska	Yes	No	Yes	Yes
Nevada	Yes	Yes	Yes	No
New Hampshire*	Yes	Yes	Yes	Yes
New Jersey	Yes	Yes	Yes	Yes
New Mexico*	Yes	Yes	Yes	Yes
New York	Yes	Yes	Yes	Yes
North Carolina	Yes	Yes	No	Yes
North Dakota	Yes	No	Yes	No
Ohio	Yes	Yes	Yes	Yes
Oklahoma*	Yes	Yes	No	No
Oregon	Yes	Yes	Yes	No
Pennsylvania*	Yes	Yes	Yes	Yes
Rhode Island	Yes	Yes	Yes	Yes
South Carolina	Yes	No	No	No

State	Criteria			
	MAT Policy status	MAT medication coverage status	Medicaid expansion status	Medicaid section 1115 behavioral health waiver status
South Dakota	Yes	Yes	No	No
Tennessee	Yes	No	No	No
Texas*	Yes	Yes	No	No
Utah	Yes	Yes	Yes	Yes
Vermont	Yes	Yes	Yes	Yes
Virginia*	Yes	Yes	Yes	Yes
Washington*	Yes	Yes	Yes	Yes
West Virginia*	Yes	Yes	Yes	Yes
Wisconsin	Yes	Yes	No	Yes
Wyoming	No	No	No	No

Note: * = States not participating in 2016 NEDS; MAT policy status as of September 9, 2019 (present [Yes]/not present [No]); MAT medication coverage status as of July 1, 2018 (comprehensive [Yes]/non-comprehensive [No]); Medicaid expansion status as of October 9, 2019 (adopted [Yes]/not adopted [No]); Medicaid section 1115 behavioral health waiver status as of October 9, 2019 (approved [Yes], not approved [No]).

Table 3 shows the weighted summary statistics of uncomplicated OUD, patient, hospital, and state-level opioid policy characteristics of the 35 states and the District of Columbia that contributed to the data analyzed for this study. An estimated 0.5% (759,888/144,842,742) of the entire patients who visited the ED in the United States in 2016 were diagnosed with and treated for uncomplicated OUD. Of this less than one per cent, more than half of these patients (55.6%) were diagnosed with and treated for uncomplicated opioid dependence. The remaining 44.4% were diagnosed with and treated for uncomplicated opioid abuse (Table 3).

The indicators of financial security for the entire patients diagnosed with and treated for uncomplicated OUD were largely low with over a third (43.9%) having their treatment paid for by Medicaid and slightly less than 1 in 4 (24.8%) were covered by Medicare. Only about 12% of the patients paid out-of-pocket. In addition, more than half of these patients earned an annual

median income less than \$54,000 – just over 1 in 3 (33.8%) earned between \$1 and \$42,999; and less than a quarter earned between \$43,000 and \$53,999. However, over three-quarters (86.6%) of them resided in metropolitan areas (33.3% in large central metropolitan, 23.9% in large fringe metropolitan, 21.6% in medium metropolitan, and 7.8% in small metropolitan locations respectively).

Upon visiting the ED, slightly over half (50.8%) of these patients were treated and released; 47.4% were admitted to the same hospital for further management, and 1.4% were transferred to another hospital. Less than one per cent (0.1%) of patients with OUD died in the ED.

Less than 1 in 5 of the hospital-owned emergency departments visited by the patients diagnosed with and treated for OUD were owned by, government (16.6%), private voluntary entities (16.3%), private not-for-profit organizations (13.3%), and private for-profit establishments (10.0%) respectively. Over two-thirds of these hospital-owned emergency departments were located in the southern (35.9%) and midwestern (34.3%) United States respectively. Over 50% of these hospital-owned emergency departments were located in metropolitan areas. Specifically, 27.5% each in large and small metropolitan areas respectively (Table 3).

Of the 35 states and the District of Columbia analyzed for this study, over three-quarters (77.8%) provided comprehensive MAT medication coverage. More than 2 in 3 (69.4%) of the states had adopted Medicaid expansion and over half (58.3%) had approved Medicaid section 1115 waiver (Table 3).

Table 3. Summary Statistics of OUD, Patient, Hospital, and State-Level Opioid Policy Characteristics

Variable Category/Variables	Frequency (N=144,842,742)	Proportion
	(n=759,888)	(%)
OUD Diagnosis		
Opioid abuse	337,639	44.4
Opioid dependence	422,249	55.6
Patient Characteristics		

Primary Payer:		
Medicare	187,853	24.8
Medicaid	333,228	43.9
Private including HMO	118,521	15.6
Self-pay	91,999	12.1
No charge	4,455	0.6
Other	21,993	2.9
Annual Median Income (\$):		
1-42,999	256,209	33.8
43,000-53,999	186,780	24.6
54,000-70,999	160,080	21.1
≥71,000	132,315	17.4
Patient Location:		
Large central metropolitan	252,420	33.3
Large fringe metropolitan	181,384	23.9
Medium metropolitan	163,816	21.6
Small metropolitan	59,483	7.8
Micropolitan	59,506	7.8
Not metropolitan or micropolitan	29,327	3.9
Type of Emergency Department Event:		
Treated & released	385,157	50.8
Admitted to same hospital	359,988	47.4
Transferred to another hospital	10,244	1.4
Died	897	0.1
Other (Not admitted in same hospital & discharged alive)	2,549	0.3
Hospital Characteristics	(n=4,639)	(%)
Control/Ownership:		
All [government or private]	2,033	43.8
Public [government, non-Federal]	770	16.6
Voluntary [private, not-for-profit]	617	13.3
Proprietary [private, investor-owned/for-profit]	462	10.0
Private [private voluntary/proprietary]	758	16.3
Region:		
Northeast	535	11.5
Midwest	1,590	34.3
South	1,665	35.9
West	849	18.3
Designation:		
Large metropolitan area	1,274	27.5
Small metropolitan area	1,274	27.5
Micropolitan area	679	14.6
Non-urban residual	1,255	27.1
Other (Metropolitan [1/2] & Non metropolitan [3/4])	157	3.4
State-level Opioid Policy Characteristics	(n=36)	(%)
MAT medication coverage status:		

Non-comprehensive	8	22.2
Comprehensive	28	77.8
Medicaid expansion status:		
Not adopted	11	30.6
Adopted	25	69.4
Medicaid section 1115 waiver status:		
Not approved	15	41.7
Approved	21	58.3

Note: For OUD Diagnosis, Patient Characteristics, and Type of Emergency Department Event, weighted n = 759,888. For Hospital Characteristics, weighted n = 4,639. For State-level Opioid Policy Characteristics, weighted n = 36 (35 States & D.C.). Overall N=144,842,742. Sum of some variable percentages did not attain 100% because missing values were not included.

Table 4 and Figure 3 display the associated state-level opioid policies by hospital region of the 35 states and the District of Columbia that contributed to the 2016 NEDS dataset analyzed in this study. In the northeast region, there were seven states. All of these States in the northeastern region had MAT policies in place and 100% provided comprehensive MAT medication coverage. All (100%) of these states had adopted Medicaid expansion while 71.4% with the exception of Connecticut and Maine had approved the Medicaid section 1115 behavioral health waiver. The Midwest region had 11 states, all of which had existing MAT policies. However, of these midwestern states, 72.7% excluding Kansas, Nebraska, and North Dakota, provided comprehensive MAT medication coverage; 63.6% apart from Kansas, Missouri, South Dakota, and Wisconsin had adopted Medicaid expansion; while 63.6% not including Iowa, Missouri, North Dakota, and South Dakota had approved the Medicaid section 1115 behavioral health waiver. The south region comprised 10 states. Of these southern states, all (100%) had MAT policies in place, 60% without Arkansas, Kentucky, South Carolina, and Tennessee, provided comprehensive MAT medication coverage. While only 40% exclusive of Florida, Georgia, Mississippi, North Carolina, South Carolina, and Tennessee had expanded Medicaid; and 40% except for Arkansas, Georgia, Mississippi, South Carolina, Tennessee, and District of Colombia approved the Medicaid section 1115 behavioral health waiver. Finally, the

west region consisted of eight states. In these states, 87.5% with the exception of Wyoming had existing MAT policies, provided comprehensive MAT coverage, and had expanded Medicaid respectively. The Medicaid section 1115 behavioral health waiver had been approved in 62.5% of these western regional states apart from Nevada, Oregon, and Wyoming (Table 4) (Figure 3).

Table 4. Descriptive Statistics of the 35 State-Level and District of Columbia Opioid Policies by Hospital Region

Hospital Region	States	MAT Policy status	MAT medication coverage status	Medicaid expansion status	Medicaid section 1115 behavioral health waiver status
Northeast (n=7)	Connecticut	Yes	Yes	Yes	No
	Maine	Yes	Yes	Yes	No
	Massachusetts	Yes	Yes	Yes	Yes
	New Jersey	Yes	Yes	Yes	Yes
	New York	Yes	Yes	Yes	Yes
	Rhode Island	Yes	Yes	Yes	Yes
	Vermont	Yes	Yes	Yes	Yes
Midwest (n=11)	Illinois	Yes	Yes	Yes	Yes
	Indiana	Yes	Yes	Yes	Yes
	Iowa	Yes	Yes	Yes	No
	Kansas	Yes	No	No	Yes
	Minnesota	Yes	Yes	Yes	Yes
	Missouri	Yes	Yes	No	No
	Nebraska	Yes	No	Yes	Yes
	North Dakota	Yes	No	Yes	No
	Ohio	Yes	Yes	Yes	Yes
	South Dakota	Yes	Yes	No	No
	Wisconsin	Yes	Yes	No	Yes
South (n=10)	Arkansas	Yes	No	Yes	No
	District of Columbia	Yes	Yes	Yes	No
	Florida	Yes	Yes	No	Yes
	Georgia	Yes	Yes	No	No
	Kentucky	Yes	No	Yes	Yes
	Maryland	Yes	Yes	Yes	Yes
	Mississippi	Yes	Yes	No	No
	North Carolina	Yes	Yes	No	Yes
	South Carolina	Yes	No	No	No
	Tennessee	Yes	No	No	No
West (n=8)	Arizona	Yes	Yes	Yes	Yes
	California	Yes	Yes	Yes	Yes
	Hawaii	Yes	Yes	Yes	Yes

Montana	Yes	Yes	Yes	Yes
Nevada	Yes	Yes	Yes	No
Oregon	Yes	Yes	Yes	No
Utah	Yes	Yes	Yes	Yes
Wyoming	No	No	No	No

Note: MAT policy status as of September 9, 2019 (present [Yes]/not present [No]); MAT medication coverage status as of July 1, 2018 (comprehensive [Yes]/non-comprehensive [No]); Medicaid expansion status as of October 9, 2019 (adopted [Yes]/not adopted [No]); Medicaid section 1115 behavioral health waiver status as of October 9, 2019 (approved [Yes], not approved [No]).

Figure 3. Overall and Regional Prevalence of State-Level Opioid Policies of the 35 States and District of Columbia

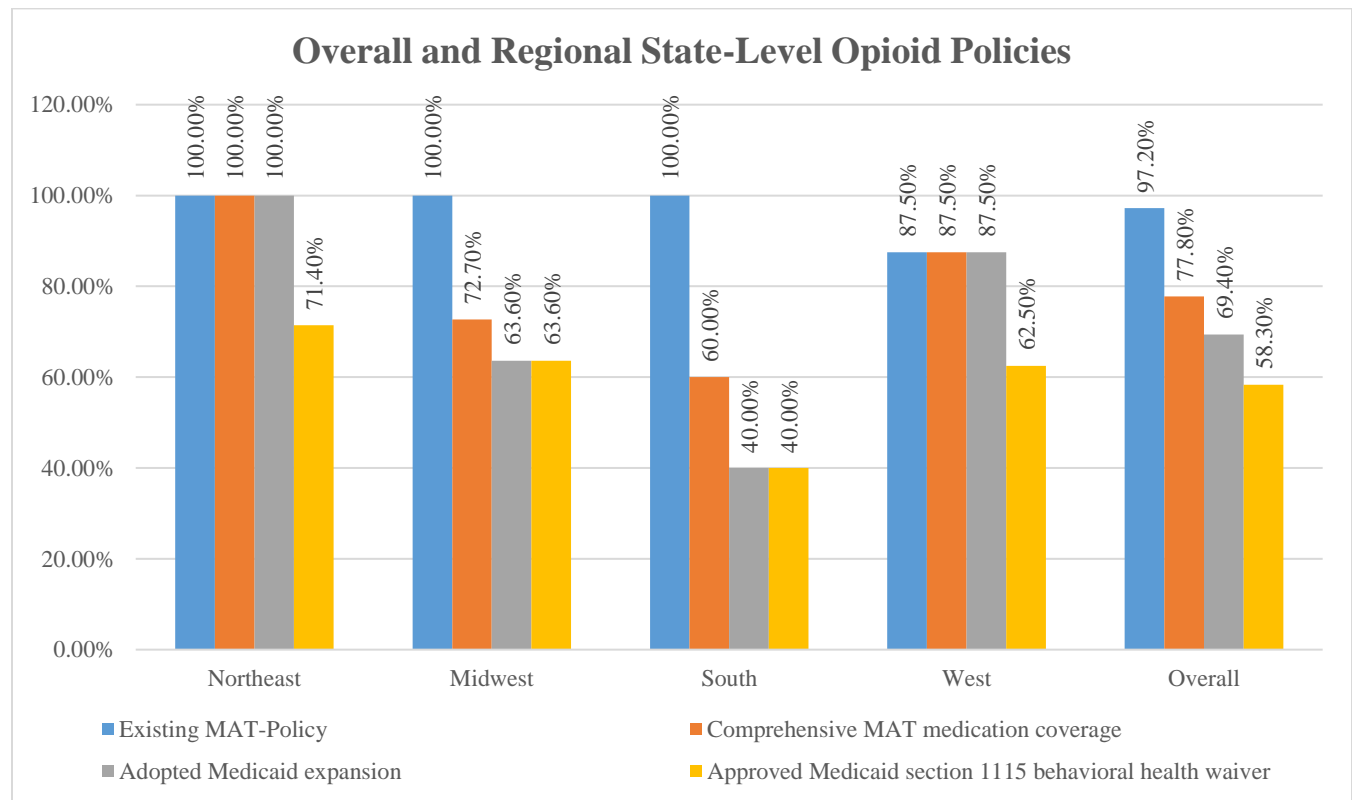
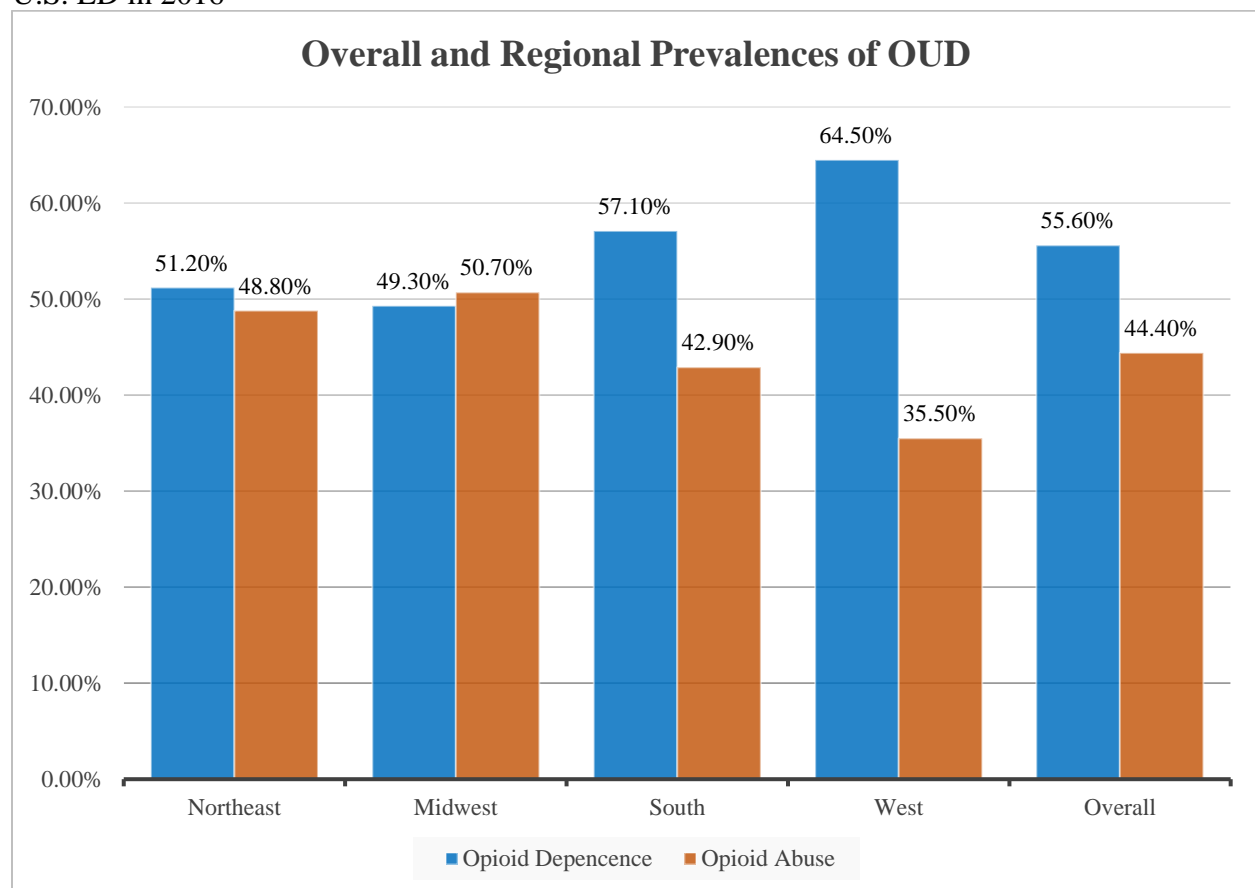


Figure 4 represents the overall and regional prevalence of uncomplicated OUD – comprised of opioid dependence and opioid abuse – diagnosed and treated in U.S. ED in 2016. Overall, over 5 of every 10 patients who presented at a U.S. ED had uncomplicated opioid dependence while just over 4 of every 10 patients had uncomplicated opioid abuse. The figure however showed noteworthy regional differences. The western region of the U.S. revealed that over 6 of every 10 patients seen in the ED in that region was diagnosed and treated for

uncomplicated opioid dependence and just over 3 in 10 of the patients had uncomplicated opioid abuse. On the other hand, similar to the national average, over 5 of every 10 patients had uncomplicated opioid dependence and just over 4 of every 10 patients had uncomplicated opioid abuse in southern U.S. However, in northeastern region of the U.S., approximately 5 of every 10 patients who presented at the ED had uncomplicated opioid dependence or uncomplicated opioid abuse. Similarly, in midwestern U.S., about 5 of every 10 patients had either uncomplicated opioid dependence or uncomplicated opioid abuse (Figure 4).

Figure 4. Overall and Regional Prevalence of Uncomplicated OUD Diagnosed and Treated in U.S. ED in 2016



In Table 5, overall patient and hospital characteristics between all patients diagnosed with and treated for opioid abuse and opioid dependence in the U.S. ED were compared. There were significant differences between patients who were diagnosed with and treated for opioid abuse

and opioid dependence in the ED in all forms of patient and hospital characteristics ($p < 0.0001$).

The following patient characteristics depicted these distinct differences more: among patients diagnosed with and treated for OUD in the ED, Medicaid paid more for opioid abuse (49.2% vs. 39.8%) while Medicare paid more for opioid dependence (34.6% vs. 12.4%). In addition, the proportion of self-paying (out-of-pocket payment) patients were higher in those diagnosed with and treated for opioid abuse (18.2% vs. 7.3%). More patients in the \$1-\$42,999 annual median income bracket were diagnosed with and treated for opioid abuse (36.6% vs. 33.5%).

Conversely, more patients in the \$43,000-\$53,999 annual median income bracket were diagnosed with and treated for opioid dependence (26.1% vs. 24.6%). There were more patients diagnosed with and treated for opioid abuse located in metropolitan areas (89.1% vs. 87.3%). In contrast, more patients diagnosed with and treated for opioid dependence were located in micropolitan areas (8.5% vs. 7.3%). Concerning the type of ED event that occurred to patients when they visited the ED, more patients with opioid abuse were treated and released (64.7% vs. 39.6%). On the other hand, the proportion of patients diagnosed with and treated for opioid dependence who were admitted to the same hospital was more (59.1% vs. 32.8%).

There was a higher proportion of patients with opioid dependence diagnosed with and treated in hospital-owned ED controlled by private not-for-profit entities (10.3% vs. 8.8%) and private voluntary organizations (5.0% vs. 3.2%). More patients diagnosed with and treated for opioid abuse were seen northeastern (30.7% vs. 25.7%) and midwestern (21.5% vs. 16.7%) United States. On the contrary, more of the patient seen in the southern (31.5% vs. 29.8%) and western (26.1% vs. 18.0%) regions of the country were diagnosed with and treated for opioid dependence. Similarly, the proportion of patients diagnosed with and treated for opioid abuse

seen in hospital-owned ED designation as been located in metropolitan areas was more (88.8% vs. 87.4%) (Table 5).

Table 5. Weighted Descriptive Statistics of Patient and Hospital Characteristics Comparing Opioid Abuse and Opioid Dependence

Variable Category/Variables	Opioid Abuse (n=337,639)		Opioid Dependence (n=422,249)		p value
	Frequency	Proportion (%)	Frequency	Proportion (%)	
Patient Characteristics					
Primary Payer:					<0.0001
Medicare	41,777	12.4	146,076	34.6	
Medicaid	165,389	49.2	167,839	39.8	
Private including HMO	53,828	16.0	64,693	15.3	
Self-pay	61,086	18.2	30,913	7.3	
No charge	2,712	0.8	1,743	0.4	
Other	11,367	3.4	10,627	2.5	
Annual Median Income (\$):					<0.0001
1-42,999	118,746	36.6	137,463	33.5	
43,000-53,999	79,774	24.6	107,006	26.1	
54,000-70,999	70,251	21.6	89,828	21.9	
≥71,000	55,972	17.2	76,342	18.6	
Patient Location:					<0.0001
Large central metropolitan	109,662	33.3	142,759	34.3	
Large fringe metropolitan	84,805	25.7	96,579	23.2	
Medium metropolitan	73,892	22.4	89,924	21.6	
Small metropolitan	25,465	7.7	34,018	8.2	
Micropolitan	24,032	7.3	35,474	8.5	
Not metropolitan or micropolitan	11,778	3.6	17,550	4.2	
Type of Emergency Department Event:					<0.0001
Treated & released	217,928	64.7	167,229	39.6	
Admitted to same hospital	110,378	32.8	249,610	59.1	
Transferred to another hospital	6,123	1.8	4,121	1.0	
Died	676	0.2	221	0.1	
Other	1,479	0.4	1,069	0.3	
Hospital Characteristics					
Control/Ownership:					<0.0001
All [government or private]	272,668	81.0	325,728	77.1	
Public [government, non-Federal]	8,784	2.6	12,114	2.9	
Voluntary [private, not-for-profit]	29,656	8.8	43,561	10.3	
Proprietary [private, investor-owned/for-profit]	14,873	4.4	19,685	4.7	
Private [private voluntary/proprietary]	10,604	3.2	21,161	5.0	<0.0001
Region:					
Northeast	103,397	30.7	108,457	25.7	

Midwest	72,449	21.5	70,449	16.7	<0.0001
South	100,152	29.8	133,196	31.5	
West	60,588	18.0	110,147	26.1	
Designation:					
Large metropolitan area	193,179	57.4	237,509	56.2	
Small metropolitan area	105,635	31.4	131,767	31.2	
Micropolitan area	18,553	5.5	28,057	6.6	
Non-urban residual	5,800	1.7	8,387	2.0	
Other (Metropolitan [1/2] & Non metropolitan [3/4])	13,449	4.0	16,531	3.9	

Note: For Patient Characteristics, Type of Emergency Department Event and Hospital Characteristics, weighted n = 759,888. Overall N=144,842,742. Sum of some variable percentages did not attain 100% because missing values were not included.

Table 6 presents the weighted summary statistics of uncomplicated OUD diagnosis, patient and hospital characteristics by hospital region. In all the four hospital regions, there were significant differences in patient and hospital characteristics ($p < 0.0001$). Specifically, the diagnoses of uncomplicated opioid dependence were more preponderant in the western (64.5%), southern (57.1%), and northeastern (52.2%) regions. Uncomplicated opioid abuse was the predominant diagnosis in the midwestern region at 50.7%. Patient characteristics that exhibited these unique regional differences included: primary payers of diagnosing and treating OUD in the ED – where in spite of Medicaid being the predominant payer across all the regions, an additional more than 1 in 5 patients were self- (or out-of-pocket) paying in the southern region compared to the less than 1 in 10 self-paying patients in the other regions. Annual median income revealed that patients in the \$1-\$53,999 income bracket were mainly in the southern (72%), midwestern (57%), and western (54%) regions. The northeastern region comprised patients mostly in the \$54,000 and higher income bracket (52.5%). Patient location showed that over 1 in 10 patients resided in micropolitan areas in the midwestern region compared to other regions in addition to the fact that most patients across all regions were overwhelmingly metropolitan area dwellers. Over half of the patients presenting to ED in the northeastern and midwestern regions respectively were treated and released while about 1 in 2 of the patients seen

in ED in the southern and western regions were admitted to the same hospital of the ED to which they presented. Regional differences were more pronounced in the following hospital characteristics: hospitals' urban-rural designation revealed that just over 10% of hospitals with ED were designated as micropolitan in the midwestern region compared to other regions. This is in addition to the overwhelming metropolitan designation of all hospitals across all the regions (Table 6).

Table 6. Weighted Summary Statistics of Opioid Use Disorder Diagnosis, Patient and Hospital Characteristics by Hospital Region

Variable Category/ Variables	Northeast Region (n=211,854)		Midwest Region (n=142,898)		South Region (n=233,348)		West Region (n=170,735)		p value
	Frequency	(%)	Frequency	(%)	Frequency	(%)	Frequency	(%)	
OUD Diagnosis									<0.0001
Opioid abuse	103,397	48.8	72,449	50.7	100,152	42.9	60,588	35.5	
Opioid dependence	108,457	51.2	70,449	49.3	133,196	57.1	110,147	64.5	
Patient Characteristics									
Primary Payer:									<0.0001
Medicare	39,275	18.5	33,597	23.6	62,178	26.7	52,803	31.0	
Medicaid	117,281	55.4	66,811	46.8	73,498	31.5	75,638	44.4	
Private including HMO	33,451	15.8	22,568	15.8	35,168	15.1	27,333	16.0	
Self-pay	15,895	7.5	14,007	9.8	52,247	22.4	9,849	5.8	
No charge	1,140	0.5	714	0.5	2,490	1.1	111	0.1	
Other	4,704	2.2	4,956	3.5	7,639	3.3	4,695	2.8	
Annual Median Income (\$):									
1-42,999	59,219	28.8	53,589	38.0	100,793	44.4	42,608	26.3	
43,000-53,999	38,442	18.7	40,908	29.0	62,582	27.6	44,849	27.7	
54,000-70,999	51,150	24.9	28,742	20.4	42,668	18.8	37,520	23.2	
≥71,000	56,601	27.6	17,877	12.7	20,989	9.2	36,848	22.8	
Patient Location:									<0.0001
Large central metropolitan	56,585	27.3	49,281	34.6	65,989	28.6	80,564	48.6	
Large fringe metropolitan	80,168	38.7	28,183	19.8	58,503	25.4	14,530	8.8	
Medium metropolitan	45,017	21.7	24,076	16.9	53,234	23.1	41,489	25.0	
Small metropolitan	11,529	5.6	15,819	11.1	19,072	8.3	13,063	7.9	
Micropolitan	9,409	4.5	17,954	12.6	19,111	8.3	13,033	7.9	
Not metropolitan/micropolitan	4,334	2.1	7,133	5.0	14,813	6.4	3,047	1.8	
Type of ED Event:									<0.0001
Treated & released	117,465	55.4	74,526	52.2	109,366	46.9	83,800	49.1	
Admitted to same hospital	89,405	42.2	64,813	45.4	120,707	51.7	85,064	49.8	
Transferred to another hospital	3,334	1.6	2,276	1.6	2,920	1.3	1,714	1.0	
Died	405	0.2	191	0.1	214	0.1	87	0.1	
Other	1,245	0.6	1,093	0.8	140	0.1	71	0.0	
Hospital Characteristics									
Control/Ownership:									<0.0001
All [government or private]	211,854	100.0	124,075	86.8	153,118	65.6	109,349	64.0	

Public [government, non-Federal]	0	0.0	4,194	2.9	11,845	5.1	4,859	2.8	
Voluntary [private, not-for-profit]	0	0.0	0	0.0	49,122	21.1	24,096	14.1	
Proprietary [private, investor-owned/for-profit]	0	0.0	0	0.0	19,262	8.3	15,296	9.0	
Private [private voluntary/proprietary]	0	0.0	14,629	10.2	0	0.0	17,136	10.0	
Designation:									<0.0001
Large metropolitan area	137,704	65.0	79,320	55.5	131,908	56.5	81,756	47.9	
Small metropolitan area	58,872	27.8	44,003	30.8	78,568	33.7	55,959	32.8	
Micropolitan area	8,412	4.0	15,599	10.9	13,693	5.9	8,905	5.2	
Non-urban residual	3,155	1.5	3,224	2.3	6,166	2.6	1,642	1.0	
Other (Metropolitan [1/2] & Nonmetropolitan [3/4])	3,711	1.8	752	0.5	3,014	1.3	22,472	13.2	

Note: For Patient Characteristics and Hospital Characteristics, weighted n = 759,888. Sum of some variable percentages did not attain 100% because missing values were not included.

Tests of HLM Assumptions Results

The collinearity statistics revealed no multicollinearity between the predictor variables. This is confirmed by the tolerance for each of the predictor variable in models 1 to 2 shown to be greater than $1-R^2$ (i.e. >0.746); and the variance inflation factor (VIF) for each of the predictor variable in models 1 to 2 was less than 10 (See Appendix C - Coefficients). In addition, the points on the normal probability-probability plot are close to and follow the line (multivariate normality); the scatter plot showed relatively scattered dots which were mostly between -3 and +3 on both axes indicating that the errors of the data in this study were normally distributed and the variance of the residuals were constant (homoscedasticity) (See Appendix C – Normal P-P Plot and Scatterplot). Furthermore, the maximum value of the Cook's Distance – a measure of influential outliers within the predictor variables – was 0.001 (normal <1) which indicated that there was no influential value within the predictor variables that could have negatively affected models 1 to 2 of the HLM. The minimum and maximum values of the standard residuals were expected to be between -3 to +3. In this study, the minimum was -7.446 which was far from -3, however, the maximum value was not too far from +3 at +3.900 (See Appendix C – Residual Statistics).

HLM Regression Results

In the model 1 of the HLM regression, patient-level characteristics comprising OUD diagnosis, primary payer, annual median income, patient location, and type of ED event accounted for a significant 15.6% of the variance in prevalence of patients diagnosed with and treated for OUD in the ED ($R^2=0.156$, Adjusted $R^2=0.156$, $F(5,734621)=27245.686$, $p<0.0001$). When the hospital-level characteristics consisting of control/ownership of hospital, region of hospital, and hospital urban-rural designation were entered in model 2, they accounted for an additional and significant 9.7% of the variance in prevalence of patients diagnosed with and treated for OUD in the ED (R^2 change=0.097, $F(3,734618)=31937.906$, $p<0.0001$). Combined, all 8 predictor variables – OUD diagnosis, primary payer, annual median income, patient location, type of ED event, control/ownership of hospital, region of hospital, and hospital urban-rural designation – accounted for a significant 25.4% of the variance in prevalence of patients diagnosed with and treated for OUD in the ED ($R^2=0.254$, Adjusted $R^2=0.254$, F change (3,734618)=31937.906, $p<0.0001$). Overall, the patient- and hospital-level predictor variables all accounted for a significant proportion of unique variance in the final regression model (Appendix C – Model Summary).

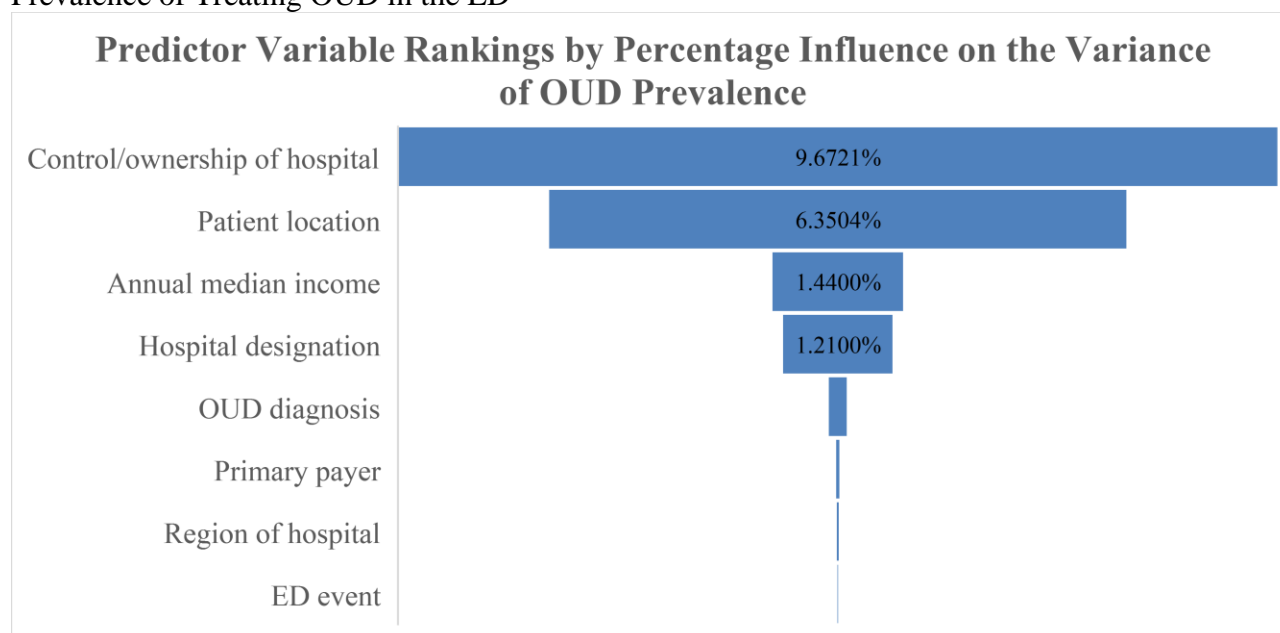
In model 2, the final HLM regression, the ranking of each of the 8 predictor variables based on the proportion of the variance accounted for in the prevalence of patients diagnosed with and treated for OUD in the ED was reported. These include, control/ownership of hospital (9.672%), patient location (6.350%), annual median income (1.440%), hospital designation (1.210%), OUD diagnosis (0.202%), primary payer (0.040%), region of hospital (0.025%), ED event (0.008%) (Table 7) (Figure 5).

Table 7. Unstandardized Coefficients, Standardized Coefficients, and Proportion of Variance Accounted for by each Predictor Variable in the Hierarchical Linear Models

Regression Models/ Predictor Variables	B (95%CI)	Std. Error B	β	p value	sr²
Model 1					
OUD diagnosis	0.017(0.016,0.019)	0.001	0.026	<0.0001	0.001
Primary payer	0.006(0.005,0.007)	0.000	-0.021	<0.0001	0.000
Annual median income	-0.028(-0.028,-0.027)	0.000	-0.094	<0.0001	0.010
Patient location	-0.092(-0.093,-0.092)	0.000	-0.399	<0.0001	0.155
ED event	0.000(0.000,0.000)	0.000	-0.006	<0.0001	0.000
Model 2					
OUD diagnosis	0.027(0.026, 0.028)	0.001	0.040	<0.0001	0.002
Primary payer	0.005(0.004,0.006)	0.000	0.018	<0.0001	0.000
Annual median income	-0.031(-0.032,-0.031)	0.000	-0.106	<0.0001	0.014
Patient location	-0.060(-0.061,-0.060)	0.000	-0.259	<0.0001	0.063
ED event	0.000(-0.001,0.000)	0.000	-0.008	0.251	0.000
Control/ownership of hospital	-0.096(-0.096,-0.095)	0.000	-0.320	<0.0001	0.096
Region of hospital	0.005(0.004,0.005)	0.000	0.016	<0.0001	0.000
Hospital designation	-0.023(-0.024,-0.023)	0.000	-0.105	<0.0001	0.012

Note: B=unstandardized coefficient, CI=confidence interval, β =standardized coefficient (indicates the contribution of each predictor variable to the prevalence of treating OUD in the ED); sr²=squared semi-partial correlation (indicates proportion of unique variance in prevalence of treating OUD in the ED accounted for by each predictor variable).

Figure 5. Ranking of Predictor Variables by their Percentage Influence on Variance of the Prevalence of Treating OUD in the ED



DISCUSSION

The overall prevalence of any opioid-related incident diagnosed and treated the U.S. ED was 1.12%. This represents a greater than 900% increase in similar visits since 1999 (Salzman et al., 2020) and an increase of over 1,000% since 2004 (Xie et al, 2014). Over two-thirds of the patients who presented at U.S. ED in 2016 with any opioid-related incident were diagnosed and treated for OUD. Specifically, uncomplicated OUD accounted for almost half of these cases. It is important however to note that these numbers may have been overestimated since there may have been multiple visits to the ED and multiple diagnosis for any given patient. Nevertheless, uncomplicated OUD – comprising uncomplicated opioid dependence and uncomplicated opioid abuse – was the most prevalent opioid-related incident in 2016 compared to accidental opioid poisoning, adverse effect of opioids or intentional opioid poisoning. The implications of this finding is that interventions targeted at adequately addressing OUD may potentially reduce the burden of the opioid crisis by more than 50%.

The overall prevalence in this study of ED visits in the entire United States resulting in the diagnosis and treatment of uncomplicated OUD was 0.5%. Of these, an estimated fifty-six per cent or more than 1 in 2 of the patients who visited the ED had uncomplicated opioid dependence. This is in spite of 98% of States in the U.S having functional opioid treatment centers, 80.4% of which deliver comprehensive medication-assisted treatment (MAT) with this MAT administered in 72.6% of States that have expanded Medicaid and 60.8% that have approved Medicaid section 1115 behavioral health waiver (Kaiser Family Foundation, 2019; SAMHSA, 2015, 2019).

Generally, the patients with uncomplicated OUD who visited the hospital-owned ED were mostly of low-income status, metropolitan areas residents, covered by Medicaid, and

treated and released from the ED. These hospital-owned ED were majorly, controlled by the government and privately-owned voluntary organizations, in metropolitan areas, and in the Southern and Midwestern United States. Notwithstanding the general characterization of the patients with uncomplicated OUD and the hospitals that they presented, there were significant patient-, hospital-, and state-policy level differences between uncomplicated opioid dependence and uncomplicated opioid abuse. Additionally, significant regional differences were noted for all uncomplicated OUD diagnosis and across all categories of patient-, hospital-, and state-level policy characteristics.

From a diagnosis perspective, the patients with uncomplicated opioid dependence were preponderantly upper-lower income class, micropolitan residents, covered by Medicare, admitted to the same hospital as ED to which they presented; and attended to largely in hospital-owned ED that were privately-owned not-for-profit entities, in micropolitan areas, and in the Southern and Western U.S. On the other hand, patients with uncomplicated opioid abuse were predominantly of lower-lower income status, metropolitan dwellers, Medicaid covered; and presented commonly to privately-owned not-for-profit organizations (though less in proportion than opioid dependence case), in metropolitan locations, and in the Northeastern and Midwestern United States.

Regionally, however, the relationship between patient-, hospital-, and state-level policy characteristics have not been studied in great detail prior to this study. In the northeastern U.S. where all the states in this study had MAT policies, comprehensive MAT medication coverage, adopted Medicaid expansion, and more than two-thirds approved Medicaid section 1115 behavioral health waiver, uncomplicated opioid dependence was the main diagnosis. However, it was surprising that more of the patients who were in the higher income bracket, still had

Medicaid as their predominant insurer and were mostly treated and released from the ED after their uncomplicated OUD diagnosis. In the midwestern region, however, with all states in this study having existing MAT policies but with less than three-quarters providing comprehensive MAT medication coverage and less than two-thirds haven adopted Medicaid expansion and Medicaid section 1115 behavioral health waiver respectively, uncomplicated opioid abuse was the predominant diagnosis. It was not surprising that the patients who were mostly low income and had Medicaid as their primary payer were typically treated and released post-uncomplicated OUD diagnosis in the ED. In contrast, states in the southern region of this study, all of which have MAT policies in place but with less than two-thirds providing comprehensive MAT medication coverage and just over one-third haven expanded Medicaid and approved the Medicaid section 1115 behavioral health waiver respectively, a diagnosis of uncomplicated opioid dependence was more preponderant. It was thus not surprising that the patients diagnosed and treated for OUD in this region though in the lower income bracket, had the highest proportion of self-paying patients and lowest proportion of Medicaid paying patients of all the regions. In addition, they were mostly admitted to the same hospital as the ED they were seen. Lastly, within the western U.S. in this study, where more than four-fifths had MAT policies, comprehensive MAT medication coverage, adopted Medicaid expansion respectively, and just less than two-thirds approved Medicaid section 1115 behavioral health waiver, uncomplicated opioid dependence was the highest diagnosis of all the regions. It was interesting that the proportion of patients in both the lower and higher income brackets was almost evenly split. Similarly in this western region of the U.S., about the same number of those patients that were treated/released were admitted following the diagnosis of OUD.

To our knowledge, this is the first study to show the significant cumulative and individual effects of patient-level and hospital-level characteristics on the prevalence of diagnosing and treating OUD in the ED in the United States. Specifically, no previous work has attempted to highlight the relationship between state-level policy and patient/hospital-level characteristics regarding diagnosing and treating OUD in the ED. Prior research, even those that used datasets similar to this study, focused on patient-level only, hospital-level only or a combination of patient- and hospital-level factors only (Wu et al., 2016; Peterson et al., 2018; Hadland et al., 2017; Mosher et al., 2017; Gaither et al., 2016; Xie et al., 2014; Chandwani et al., 2013; Mejia et al., 2018; Upadhyay et al., 2018; Rivera et al., 2017; Singh et al., 2016; Wall et al., 2015; Wang et al., 2015). Additionally, findings from this study revealed over 1,000% increase in the total number of ED visits associated with nonmedical use of opioids in the United States between a 12-year period from 2004 to 2016 (Xie et al., 2014). Also, this study supports the findings of prior studies that showed that in spite of enacted state-level policies to address the opioid crisis (Blackman, 2017; National Alliance for Model State Drug Laws, 2017; Kaiser Family Foundation, 2019; SAMHSA, 2015, 2019), geographic, regional, and other factors still account for the rising numbers of patients with OUD visiting the ED (Martin et al., 2016). In addition, this study revealed that state-level policies such as the decision by a state to adopt Medicaid expansion, hospital-level factor such as the control and ownership of the hospital and its ED, and patient-level factor such as where patients are located play more significant roles in determining the prevalence of diagnosing and treating OUD in the United States than patient-level characteristics like the specific OUD diagnosis or primary payer of the OUD treatment. This may be due to issues related to access to and cost of caring for patients with OUD because those who really need the care cannot access or pay for it. Furthermore, to avoid the ecological fallacy of

using group-level (in this study, hospital-level) findings to make individual-level (in this study, patient-level) inferences or its opposite of using individual-level results to inform group-level decision making – the atomistic fallacy, a multi-faceted approach needs to be adopted in addressing the current opioid crisis. This is demonstrated in this study wherein factors at different levels were assessed for their individual influences on the prevalence of diagnosing and treating OUD in the ED.

Unlike prior studies (Chandwani et al., 2013; Mejia et al., 2018; Upadhyay et al., 2018; Rivera et al., 2017; Singh et al., 2016; Wall et al., 2015; Wang et al., 2015) however, that considered age, gender, and race/ethnicity as contributing factors to the treatment of their conditions of interest in the ED, this study did not want to duplicate such works. Thus, only patient-level variables – such as primary payer, annual median income, and patient location – that could be aggregated to higher levels such as the hospital-level were utilized. This approach of aggregating data for use at different levels has been used in previous research (Aiken, et al., 2018; Wright, et al., 2014; McHugh & Stimpfel, 2012; Claxton, et al., 2015; AHRQ, 2017). Similar to previous literature, this study’s findings revealed that total admissions for treatment of OUD increased in 2016 (SAMHSA, 2014, 2017, 2018). In addition, however, our study was able to provide previously unavailable information about the type of OUD majorly responsible for this increase. Our findings indicated that opioid dependence (59.1%) was more significantly responsible than opioid abuse (32.8%) for this increase in total admissions for OUD treatment. We were also able to show that significantly more patients with opioid abuse (64.7%) than with opioid dependence (39.6%) were treated and released from the ED.

The very low prevalence of diagnosing and treating uncomplicated OUD in the ED in the U.S. revealed in this study may be due to patient-related factors – such as fear of stigmatization

and reprisals by healthcare workers thus patients with OUD do not present in the ED (Martin et al., 2016); provider-related factors – consisting of lack of adequate knowledge, skills, and training necessary to treat OUD in the ED (Rubin, 2019; Yang, et al., 2018; Ho & Argáez, 2018; Knudsen et al., 2011); system-related factors – including lack of sufficient ED with capabilities and resources to treat OUD (Martin et al., 2016), negative attitude and perception of law enforcement and the judiciary about patients with OUD leading to incarceration rather than assistance; and policy-related factors – comprising dearth of policies for mandating education and training for providers to treat OUD, poor reimbursement policies for screening, risk assessment, and treatment of OUD particularly in the ED (Martin et al., 2016). The findings in this study that public insurance through Medicare and Medicaid were predominantly responsible for paying for OUD treatment followed by private insurance entities then self-paying patient aligns with the findings in previous research (Mark et al, 2005; SAMHSA, 2013c). This trend is projected to continue in the future with Medicaid playing an increasingly significant role as the primary payer for OUD treatment due to continuous expansion and enrollment in Medicaid (SAMHSA, 2014a).

In addition, this study revealed that patients with OUD irrespective of whether the specific diagnosis was opioid dependence or opioid abuse presented more at hospital-owned ED that were privately owned not-for-profit organizations. Perhaps, these voluntarily controlled private ED provide better access to and quality of care including shorter wait times brought about by better funding compared to publicly or government-controlled ED thus the attraction for patients with OUD. Regarding paying for OUD treatment, it is plausible that Medicaid was the major primary payer for patients with opioid abuse because these patients were usually younger than 65 years old (SAMHSA, 2010). However, for those patients less than 65 years who

did not initiate and/or complete treatment early and aged older than 65 years, Medicare then took over paying the cost of their care by which time they may have become opioid dependent.

Generally, the geographical variations and low markers of financial stability associated with patients having OUD highlighted in previous studies (Keyes et al., 2014; Ghertner & Groves, 2018; Karamouzian & Kerr, 2018; Davenport & Matthews, 2018) have persisted in this study findings. However, concerning the relationships between state-level policy, hospital regional and socioeconomic characteristics, this study was able to provide new and more detailed information described above.

Strengths and Limitations

In addition to the conceptualization- and finding-specific strengths highlighted above, there are methodological strengths to this study. First, this study utilizes a nationally representative dataset – the Nationwide Emergency Department Sample (NEDS) including children and adults. Second, this study provides most current estimates. Third, due to the size of the dataset, it provides accurate estimates to guide policy and decision-making. Fourth, use of hospital-based population allows for focus on specific population of interest and targeting of potential interventions (Setia, 2016). Fifth, there is reduction of type I error with the use of HLM because HLM bases the sample size it uses for its inferential statistical analysis on the group numbers and not the total number of cases. Finally, using HLM allows for separation of within group from between-group effects.

Limitations – NEDS only collected data from noninstitutionalized civilian US population. As such, non-civilian and institutionalized population are not included. Therefore, generalizability of the findings in this study is limited to noninstitutionalized civilian U.S. population only. Second, not all 50 states contributed to the 2016 NEDS, thus only policies

specifically within the 35 states of the U.S. and the District of Columbia contributing to the 2016 NEDS were used in the analysis for this study. Third, the dataset has limited patient variables thus restricting the robustness of the analysis. Fourth, generally, HLM is conservative when testing level 1 (in this study, patient-level) relationships thus has less power than using the generalized linear regression. However, the large sample size in this study addressed this limitation.

Policy Implications

All stakeholders particularly policy makers at the state-level need to continuously evaluate state-level policies and their impact on prevalence of diagnosing and treating OUD in the ED. In addition, there is need for continuous monitoring and evaluation of opioid treatment programs (OTP) in order to determine their usability and usefulness. Furthermore, there should be more funding of hospital-owned ED treatment of OUD (Carney, 2019; Miller, 2019). More importantly there is the need for State lawmakers to expedite current multi-sectoral efforts at developing novel policies to remedy the crisis (Petruzzelli, 2019). Innovative policies to consider include: encouraging alternative approaches such as the emerging non-medication or complementary modalities of pain management for patients simultaneously receiving OUD treatment (White, 2018; Barry, et al., 2012), expanding ED-based MAT programs (Carney, 2019; Miller, 2019), and developing creative reimbursement contracts with stand-alone Urgent/Emergency Care Centers to treat OUD. These have become necessary because it is possible that more patients with OUD visit other establishments other than the ED to receive treatment.

Health Information Technology Management Practice Implications

Regarding health information technology management, there are opportunities for creating policies on interoperability and best practices for information sharing (Center for Connected Health Policy, 2018). In addition, there are opportunities for using novel approaches such as telehealth for caring for patients with OUD since use of telemedicine has been piloted and shown to be promising (Rubin, 2019; Yang, et al., 2018; Ho & Argáez, 2018). These are imperative because the diagnosis and treatment prevalence of OUD in the ED maybe the result of hospitals and their ED still operating in individual silos, not communicating, being inaccessible due to their locations or lacking trained healthcare workers capable of prescribing for and treating OUD (Rubin, 2019; Yang, et al., 2018; Ho & Argáez, 2018; Knudsen et al., 2011). Finally, policies related to using these emerging types of care delivery modalities and reimbursement for OUD treatment are required (Centers for Medicare and Medicaid Services, 2019; Savage, 2019).

Future Research Directions

In the future, this OUD research will be expanded by creating dose-response models to capture incremental effects of varied OUD severity on prevalence of OUD diagnosed and treated in the ED. Additionally, the prevalence of OUD among the current study population will be quantified to determine potentially preventable cases of OUD by using targeted interventions to effectively address the opioid crisis. Furthermore, I will like to examine the association between patient, hospital, and state-level policy factors and actual cost (not charges) of caring for individuals with OUD in the ED. In addition, I will also want to evaluate through comparative analysis whether using MAT to provide treatment for individuals diagnosed with OUD is still cost effective and if not, what other approaches may be more cost effective.

Key Messages

- There was more than 1,000% increase in opioid-related incident visits from 144, 600 to 1,623,490 visits to the emergency departments (ED) in the United States (U.S.) between 2004 and 2016.
- There was a 32% increase in ICD-10-CM Diagnostic Codes for opioid-related incidents identified in the 2016 NEDS.
- Uncomplicated opioid use disorder (OUD) – comprising uncomplicated opioid dependence and uncomplicated opioid abuse constituted approximately 69% of any opioid-related incident ED visit in 2016.
- Uncomplicated opioid dependence was the more prevalent reason patients with any opioid-related incident visited the ED in 2016.
- More than 1 in 4 patients with uncomplicated opioid dependence were treated in U.S. ED in 2016 compared to about 1 in 5 patients with uncomplicated opioid abuse.
- Targeted interventions at addressing uncomplicated OUD may have potentially reduced the opioid crisis by about 50% in 2016.
- Significant regional disparities still exist between patient-, hospital-, and state-policy level characteristics influencing diagnosis and treatment of OUD in U.S. ED. This is in spite of existing efforts aimed at addressing the opioid crisis.
- Socioecological rather than discriminatory and punitive approaches may be required to understanding and addressing the opioid crisis.
- Comprehensive data collected, aggregated, and analyzed at the individual (patient)-level and group (interpersonal, organizational, community/environmental, and societal/policy)-level can potentially improve understanding of factors influencing the current opioid crisis.

- Continuous quality monitoring, evaluation, and improvement of existing opioid crisis-related policies are necessary but not sufficient to contain the current opioid crisis, which is constantly evolving.
- High quality data-driven innovative policy creation, decision-making, and resource allocation are critical to effectively addressing the current opioid crisis.

CONCLUSIONS

The prevalence of diagnosing and treating opioid use disorder in the emergency departments in the United States is very low. This is in spite of the significant rise in the total number of ED visits attributable to nonmedical use of opioids in the United States. Overall, a combination of patient-level, hospital-level, and state-level policy characteristics can potentially significantly influence the prevalence of diagnosing and treating opioid use disorder in the emergency departments. However, studied individually, hospital-level characteristics more than patient-level characteristics contributed significantly to explaining the variance in the low prevalence of caring for opioid use disorder in the emergency departments.

As such, in addressing the current opioid crisis, a socioecological approach may be required such that all levels contributing to this crisis are purposefully and simultaneously targeted discretely and in combination. Specifically, individual and group-level factors such as interpersonal, organizational, community/environmental and societal characteristics should be considered. This ought to be performed with the view to developing innovative policies and programs that can positively and significantly address this present opioid crisis. All of these efforts should be occurring while existing policies and programs are continuously monitored and evaluated for clinical efficiency, cost-effectiveness, quality, and public health impact.

Approaching the opioid crisis in this manner while not guaranteeing more effective decision-making, judicious allocation of scarce resources, and elimination of waste, will almost certainly ensure an integrated and holistic method to addressing the crisis.

APPENDICES

APPENDIX A: Tests of Normality Results

For PREV_RXOUD_ED:

Case Processing Summary

	Valid		Missing		Total	
	N	Percent	N	Percent	N	Percent
Prevalence of treating OUD in ED at hospital level	758835	100.0%	0	0.0%	758835	100.0%

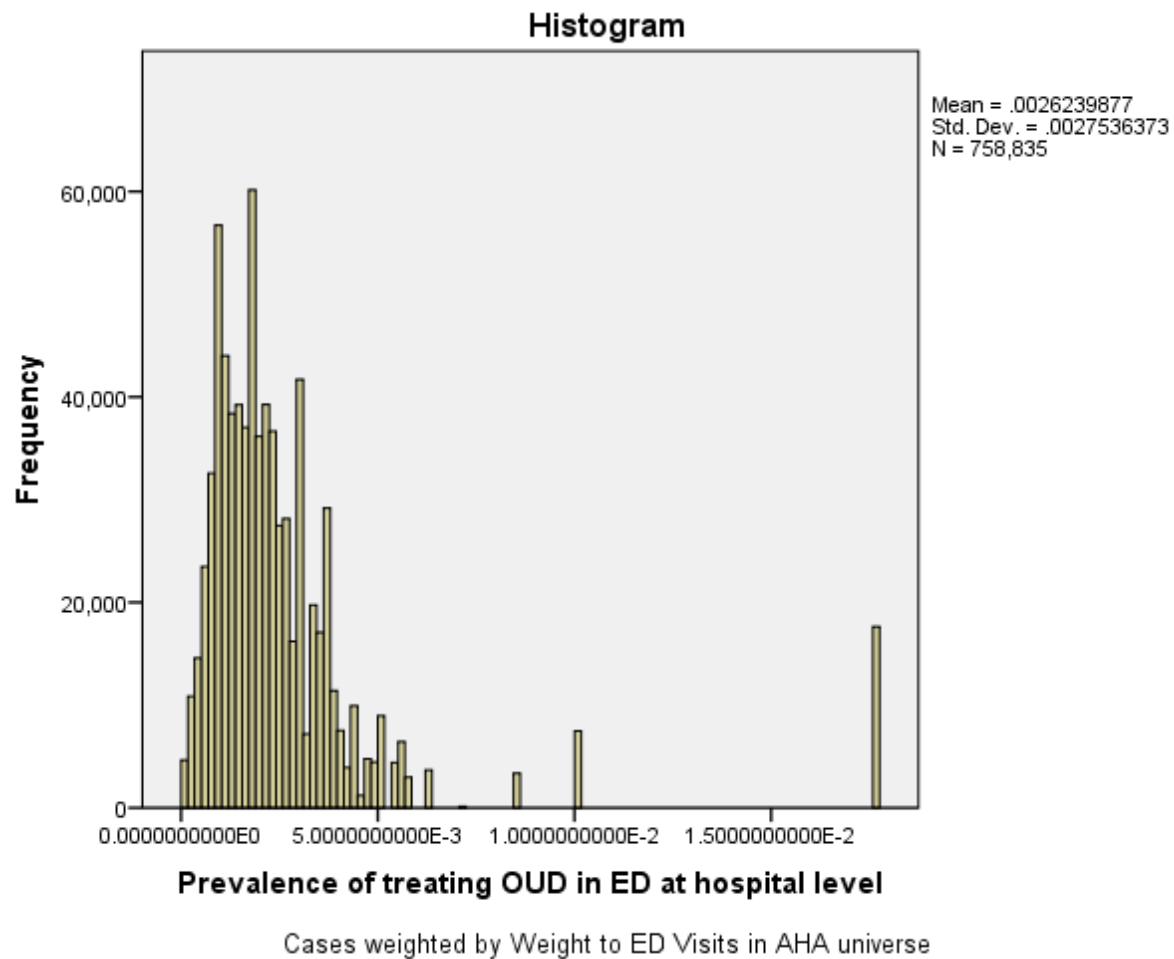
Descriptives

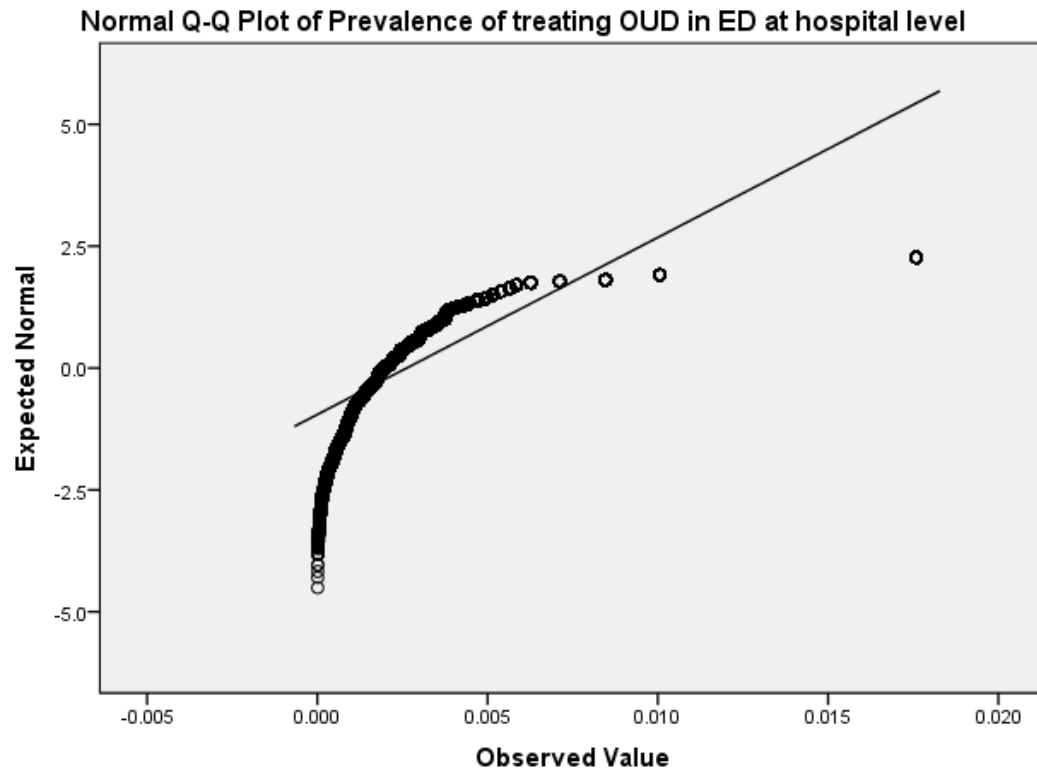
		Statistic	Std. Error
Prevalence of treating OUD in ED at hospital level	Mean	.002623987740	.0000031610619
	95% Confidence Interval for Mean	Lower Bound	.002617792160
		Upper Bound	.002630183310
	5% Trimmed Mean	.002205758840	
	Median	.001958003240	
	Variance	.000	
	Std. Deviation	.0027536373300	
	Minimum	.0000106180	
	Maximum	.0175897160	
	Range	.0175790980	
	Interquartile Range	.0017821477	
	Skewness	3.941	.003
	Kurtosis	18.011	.006

Tests of Normality

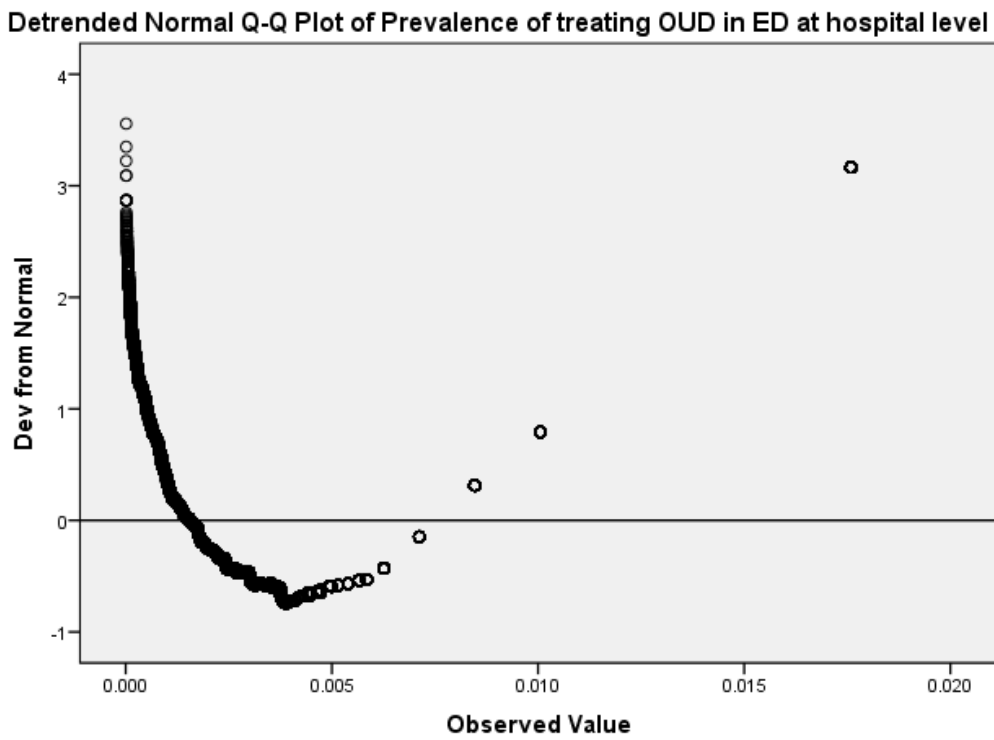
	Statistic	Kolmogorov-Smirnov ^a	
		df	Sig.
Prevalence of treating OUD in ED at hospital level	.212	758835	.000

a. Lilliefors Significance Correction

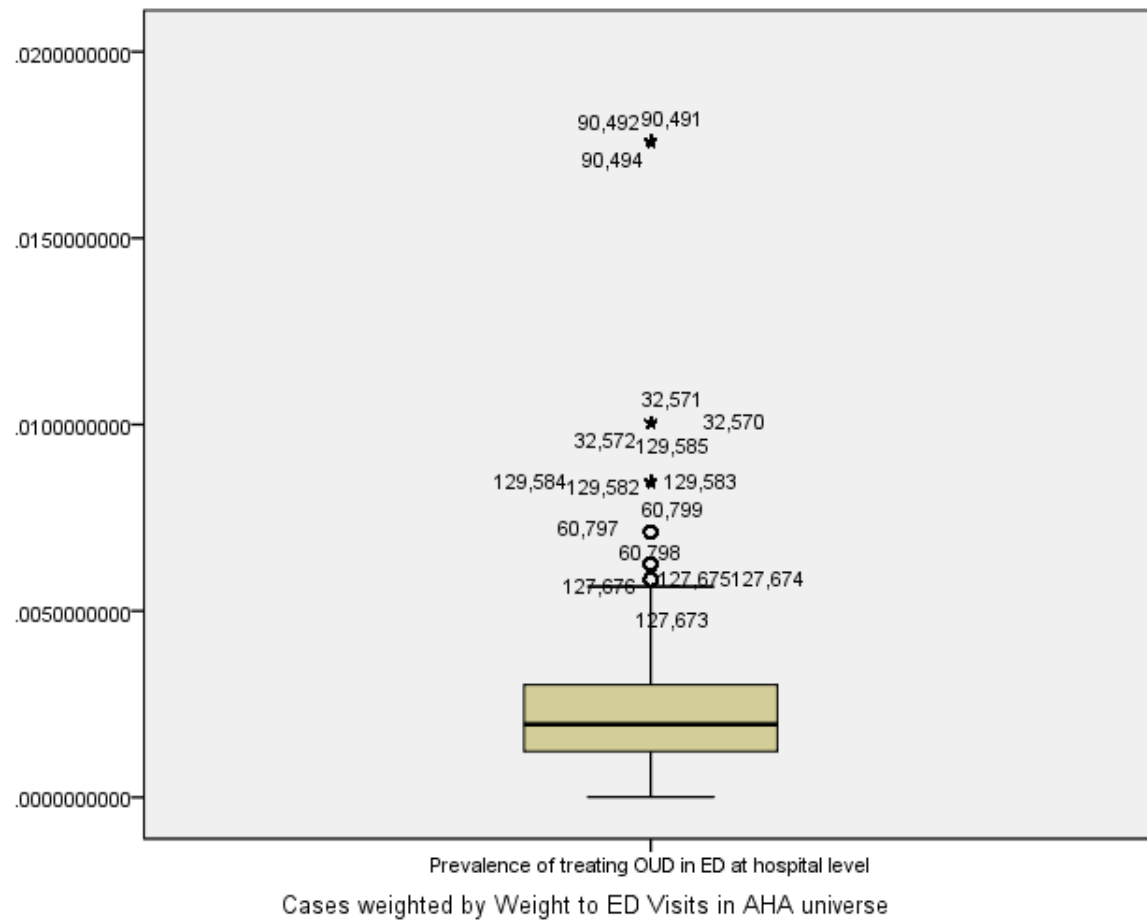




Cases weighted by Weight to ED Visits in AHA universe



Cases weighted by Weight to ED Visits in AHA universe



For PREV_RXOUD_Log:

Case Processing Summary

	Valid		Cases Missing		Total	
	N	Percent	N	Percent	N	Percent
PREV_RXOUD_ED_Log	758835	100.0%	0	0.0%	758835	100.0%

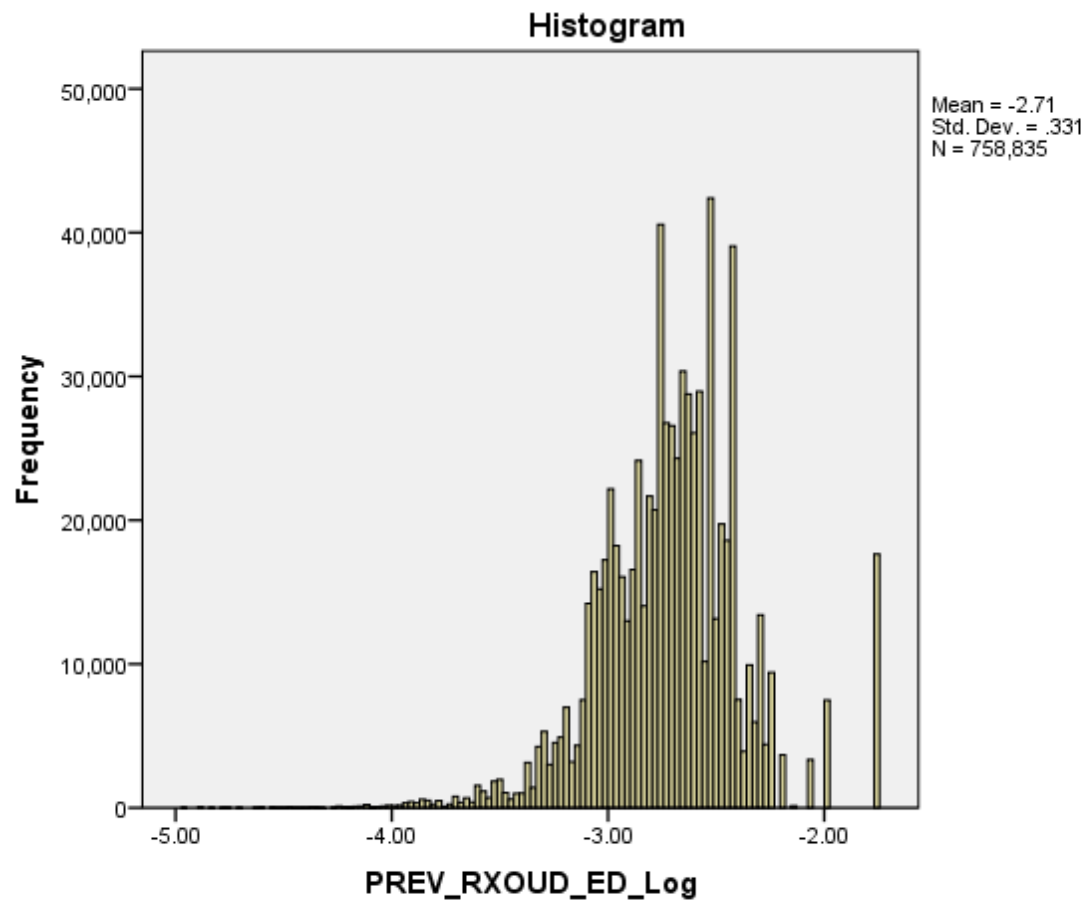
Descriptives

			Statistic	Std. Error
PREV_RXOUD_ED_Log	Mean		-2.7133	.00038
	95% Confidence Interval for Mean	Lower Bound	-2.7141	
		Upper Bound	-2.7126	
	5% Trimmed Mean		-2.7137	
	Median		-2.7082	
	Variance		.110	
	Std. Deviation		.33099	
	Minimum		-4.97	
	Maximum		-1.75	
	Range		3.22	
	Interquartile Range		.39	
	Skewness		-.125	.003
	Kurtosis		2.041	.006

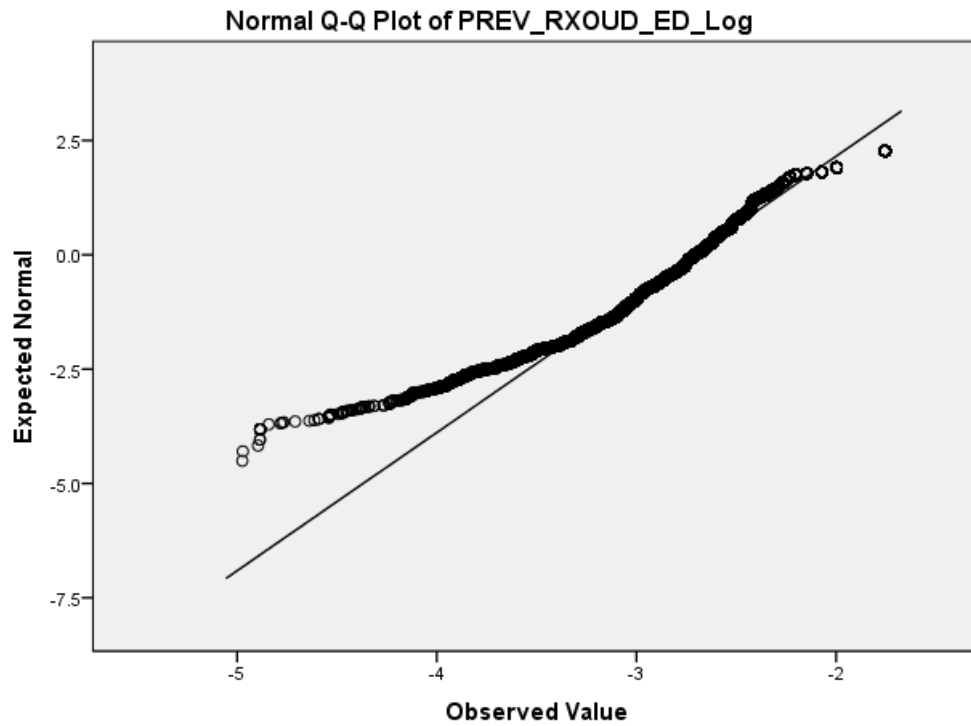
Tests of Normality

	Kolmogorov-Smirnov ^a		
	Statistic	df	Sig.
PREV_RXOUD_ED_Log	.067	758835	.000

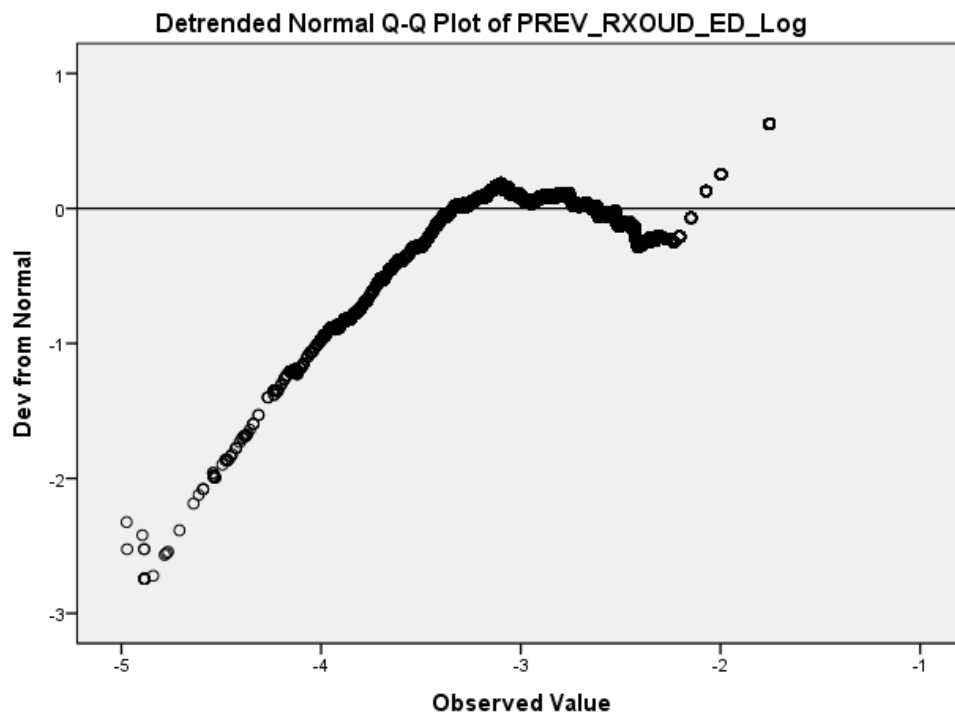
a. Lilliefors Significance Correction



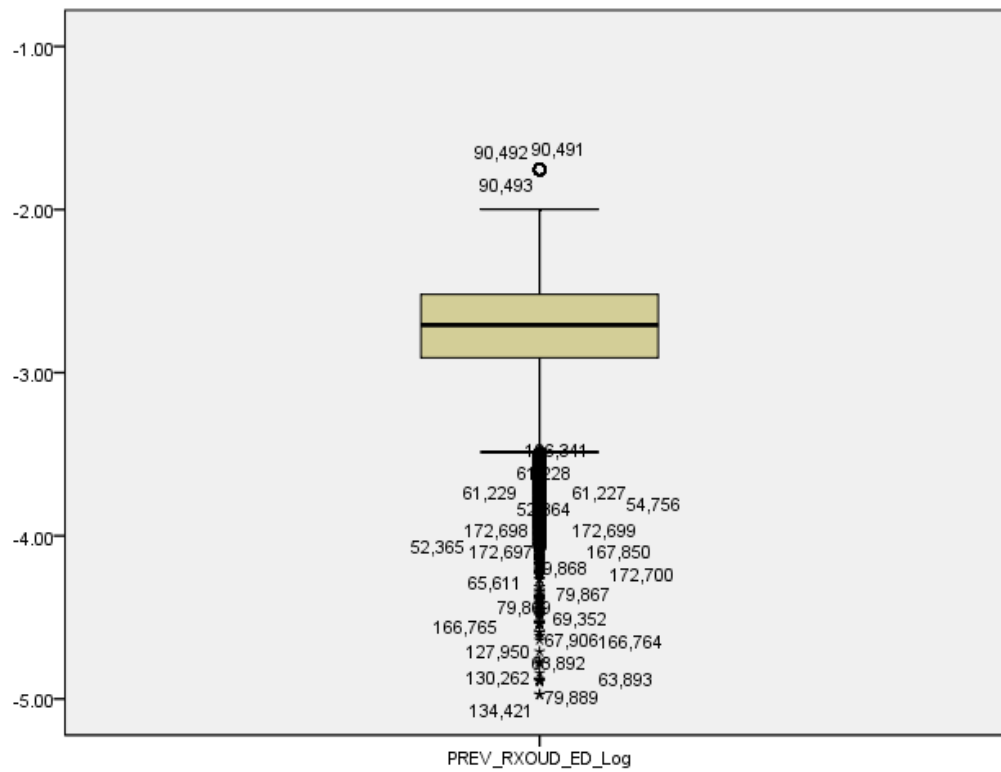
Cases weighted by Weight to ED Visits in AHA universe



Cases weighted by Weight to ED Visits in AHA universe



Cases weighted by Weight to ED Visits in AHA universe



Cases weighted by Weight to ED Visits in AHA universe

APPENDIX B: Little's Missing Completely at Random (MCAR) Test Results

MVA

Univariate Statistics							
	N	Mean	Std. Deviation	Missing		No. of Extremes ^a	
				Count	Percent	Low	High
PREV_RXOUD_ED_Log	663906	-2.7173	.32974	0	.0	3767	6406
nDX_OUD	663906			0	.0		
PAY1	663230			676	.1		
ZIPINC_QRTL	643396			20510	3.1		
PL_NCHS	652536			11370	1.7		
EDEVENT	663906			0	.0		
HOSP_CONTROL	663906			0	.0		
HOSP_REGION	663906			0	.0		
HOSP_URCAT4	663906			0	.0		

a. Number of cases outside the range (Mean - 2*SD, Mean + 2*SD).

EM Estimated Statistics

EM Means ^a	
PREV_RXOUD_ED_Log	
	-2.7180

a. Little's MCAR test: Chi-Square = 5.434, DF = 1, Sig. = .020

APPENDIX C: Hierarchical Linear Model (HLM) Regression and Test of Assumptions Results

The Hierarchical Linear Model (HLM) regression and test of assumptions results are shown below.

Descriptive Statistics

	Mean	Std. Deviation	N
Log Transformation of outcome variable PREV_RXOUD_ED	-2.7140	.33005	734627
String to numeric recode of OUD	.56	.497	734627
Primary expected payer (uniform)	2.28	1.148	734627
Median household income national quartile for patient ZIP Code	2.23	1.111	734627
Patient Location: NCHS Urban-Rural Code	2.43	1.423	734627
Type of ED Event	1.84	5.611	734627
Control/ownership of hospital	.52	1.103	734627
Region of hospital	2.47	1.117	734627
Hospital urban-rural designation	1.78	1.478	734627

Correlations

		Log Transformation of outcome variable PREV_RXOUD_ED	String to numeric recode of OUD	Primary expected payer (uniform)	Median household income national quartile for patient ZIP Code	Patient Location: NCHS Urban- Rural Code	Type of ED Event	Control/ownership of hospital	Region of hospital	Hospital urban-rural designation
Pearson Correlation	Log Transformation of outcome variable PREV_RXOUD_ED	1.000	.012	.008	-.032	-.384	-.005	-.402	-.100	-.219
	String to numeric recode of OUD	.012	1.000	-.211	.027	.018	.005	.056	.112	.010
	Primary expected payer (uniform)	.008	-.211	1.000	.018	.014	-.018	-.010	-.015	-.016
	Median household income national quartile for patient ZIP Code	-.032	.027	.018	1.000	-.152	.002	-.071	-.070	-.109
	Patient Location: NCHS Urban-Rural Code	-.384	.018	.014	-.152	1.000	-.004	.325	.005	.355
	Type of ED Event	-.005	.005	-.018	.002	-.004	1.000	-.009	-.039	-.002
	Control/ownership of hospital	-.402	.056	-.010	-.071	.325	-.009	1.000	.333	.116
	Region of hospital	-.100	.112	-.015	-.070	.005	-.039	.333	1.000	.185
	Hospital urban-rural designation	-.219	.010	-.016	-.109	.355	-.002	.116	.185	1.000

Sig. (1-tailed)	Log Transformation of outcome variable PREV_RXOUD_ED	.	.000	.000	.000	.000	.000	.000	.000	.000
	String to numeric recode of OUD	.000	.	.000	.000	.000	.000	.000	.000	.000
	Primary expected payer (uniform)	.000	.000	.	.000	.000	.000	.000	.000	.000
	Median household income national quartile for patient ZIP Code	.000	.000	.000	.	.000	.058	.000	.000	.000
	Patient Location: NCHS Urban-Rural Code	.000	.000	.000	.000	.	.000	.000	.000	.000
	Type of ED Event	.000	.000	.000	.058	.000	.	.000	.000	.090
	Control/ownership of hospital	.000	.000	.000	.000	.000	.000	.	.000	.000
	Region of hospital	.000	.000	.000	.000	.000	.000	.000	.	.000
	Hospital urban-rural designation	.000	.000	.000	.000	.000	.090	.000	.000	.
N	Log Transformation of outcome variable PREV_RXOUD_ED	734627	734627	734627	734627	734627	734627	734627	734627	734627
	String to numeric recode of OUD	734627	734627	734627	734627	734627	734627	734627	734627	734627
	Primary expected payer (uniform)	734627	734627	734627	734627	734627	734627	734627	734627	734627
	Median household income national quartile for patient ZIP Code	734627	734627	734627	734627	734627	734627	734627	734627	734627

Patient Location: NCHS Urban-Rural Code	734627	734627	734627	734627	734627	734627	734627	734627	734627	734627
Type of ED Event	734627	734627	734627	734627	734627	734627	734627	734627	734627	734627
Control/ownership of hospital	734627	734627	734627	734627	734627	734627	734627	734627	734627	734627
Region of hospital	734627	734627	734627	734627	734627	734627	734627	734627	734627	734627
Hospital urban-rural designation	734627	734627	734627	734627	734627	734627	734627	734627	734627	734627

Variables Entered/Removed^a

Model	Variables Entered	Variables Removed	Method
1	Type of ED Event, Median household income national quartile for patient ZIP Code, Primary expected payer (uniform), Patient Location: NCHS Urban-Rural Code, String to numeric recode of OUD ^b	.	Enter
2	Region of hospital, Hospital urban-rural designation, Control/ownership of hospital ^b	.	Enter

a. Dependent Variable: Log Transformation of outcome variable PREV_RXOUD_ED

b. All requested variables entered.

Model Summary^c

Model	R	R Square	Adjusted R Square	Std. Error of the Estimate	Change Statistics				
					R Square Change	F Change	df1	df2	Sig. F Change
1	.396 ^a	.156	.156	.30314	.156	27245.686	5	734621	.000
2	.504 ^b	.254	.254	.28512	.097	31937.906	3	734618	.000

a. Predictors: (Constant), Type of ED Event, Median household income national quartile for patient ZIP Code, Primary expected payer (uniform), Patient Location: NCHS Urban-Rural Code, String to numeric recode of OUD

b. Predictors: (Constant), Type of ED Event, Median household income national quartile for patient ZIP Code, Primary expected payer (uniform), Patient Location: NCHS Urban-Rural Code, String to numeric recode of OUD, Region of hospital, Hospital urban-rural designation, Control/ownership of hospital

c. Dependent Variable: Log Transformation of outcome variable PREV_RXOUD_ED

ANOVA ^a						
Model		Sum of Squares	df	Mean Square	F	Sig.
1	Regression	12518.475	5	2503.695	27245.686	.000 ^b
	Residual	67506.731	734621	.092		
	Total	80025.206	734626			
2	Regression	20307.279	8	2538.410	31226.166	.000 ^c
	Residual	59717.927	734618	.081		
	Total	80025.206	734626			

a. Dependent Variable: Log Transformation of outcome variable PREV_RXOUD_ED

b. Predictors: (Constant), Type of ED Event, Median household income national quartile for patient ZIP Code, Primary expected payer (uniform), Patient Location: NCHS Urban-Rural Code, String to numeric recode of OUD

c. Predictors: (Constant), Type of ED Event, Median household income national quartile for patient ZIP Code, Primary expected payer (uniform), Patient Location: NCHS Urban-Rural Code, String to numeric recode of OUD, Region of hospital, Hospital urban-rural designation, Control/ownership of hospital

Coefficients ^a													
Model		Unstandardized Coefficients		Standardized Coefficients	t	Sig.	95.0% Confidence Interval for B		Correlations			Collinearity Statistics	
		B	Std. Error	Beta			Lower Bound	Upper Bound	Zero-order	Partial	Part	Tolerance	VIF
1	(Constant)	-2.450	.001		-1781.271	.000	-2.453	-2.447					
	String to numeric recode of OUD	.017	.001	.026	23.976	.000	.016	.019	.012	.028	.026	.954	1.048
	Primary expected payer (uniform)	.006	.000	.021	19.217	.000	.005	.007	.008	.022	.021	.954	1.048
	Median household income national quartile for patient ZIP Code	-.028	.000	-.094	-86.365	.000	-.028	-.027	-.032	-.100	-.093	.975	1.025
	Patient Location: NCHS Urban-Rural Code	-.092	.000	-.399	-367.481	.000	-.093	-.092	-.384	-.394	-.394	.976	1.025
	Type of ED Event	.000	.000	-.006	-5.431	.000	.000	.000	-.005	-.006	-.006	1.000	1.000
2	(Constant)	-2.443	.002		-1596.472	.000	-2.446	-2.440					
	String to numeric recode of OUD	.027	.001	.040	38.940	.000	.026	.028	.012	.045	.039	.941	1.063
	Primary expected payer (uniform)	.005	.000	.018	17.052	.000	.004	.006	.008	.020	.017	.953	1.049
	Median household income national quartile for patient ZIP Code	-.031	.000	-.106	-103.329	.000	-.032	-.031	-.032	-.120	-.104	.968	1.033
	Patient Location: NCHS Urban-Rural Code	-.060	.000	-.259	-223.479	.000	-.061	-.060	-.384	-.252	-.225	.754	1.326
	Type of ED Event	.000	.000	-.008	-7.588	.000	-.001	.000	-.005	-.009	-.008	.998	1.002

Control/ownership of hospital	-.096	.000	-.320	-280.735	.000	-.096	-.095	-.402	-.311	-.283	.780	1.282
Region of hospital	.005	.000	.016	14.066	.000	.004	.005	-.100	.016	.014	.826	1.211
Hospital urban-rural designation	-.023	.000	-.105	-94.775	.000	-.024	-.023	-.219	-.110	-.096	.833	1.201

a. Dependent Variable: Log Transformation of outcome variable PREV_RXOUD_ED

Excluded Variables ^a							
Model		Beta In	t	Sig.	Partial Correlation	Collinearity Statistics	
						Tolerance	Minimum Tolerance
1	Control/ownership of hospital	-.315 ^b	-292.825	.000	-.323	.891	1.122
	Region of hospital	-.109 ^b	-101.718	.000	-.118	.981	1.020
	Hospital urban-rural designation	-.101 ^b	-88.292	.000	-.102	.870	1.149

a. Dependent Variable: Log Transformation of outcome variable PREV_RXOUD_ED

b. Predictors in the Model: (Constant), Type of ED Event, Median household income national quartile for patient ZIP Code, Primary expected payer (uniform), Patient Location: NCHS Urban-Rural Code, String to numeric recode of OUD

Collinearity Diagnostics^a

			Variance Proportions									
			Condition		String to numeric recode of	Primary expected payer	Median household income national quartile for patient ZIP	Patient Location: NCHS Urban-Rural	Type of ED	Control/ownership	Region of	Hospital
Model	Dimension	Eigenvalue	Index	(Constant)	OUD	(uniform)	Code	Code	Event	of hospital	hospital	urban-rural designation
1	1	4.190	1.000	.00	.02	.01	.01	.01	.01			
	2	.883	2.178	.00	.00	.00	.00	.00	.99			
	3	.433	3.111	.00	.76	.08	.01	.02	.00			
	4	.266	3.968	.00	.00	.02	.24	.60	.00			
	5	.178	4.852	.00	.10	.56	.39	.12	.00			
	6	.050	9.131	.99	.12	.34	.35	.25	.01			
2	1	5.924	1.000	.00	.01	.00	.00	.00	.00	.01	.00	.01
	2	.909	2.552	.00	.00	.00	.00	.00	.88	.07	.00	.00
	3	.769	2.775	.00	.01	.01	.01	.00	.11	.64	.00	.00
	4	.454	3.614	.00	.63	.02	.00	.02	.00	.01	.00	.15
	5	.380	3.948	.00	.13	.09	.08	.02	.00	.04	.00	.42
	6	.205	5.370	.00	.03	.05	.07	.51	.00	.02	.13	.20
	7	.184	5.676	.00	.03	.29	.53	.07	.00	.01	.10	.00
	8	.138	6.549	.01	.12	.34	.03	.17	.00	.15	.44	.23
	9	.037	12.632	.99	.05	.20	.27	.21	.01	.06	.32	.00

a. Dependent Variable: Log Transformation of outcome variable PREV_RXOUD_ED

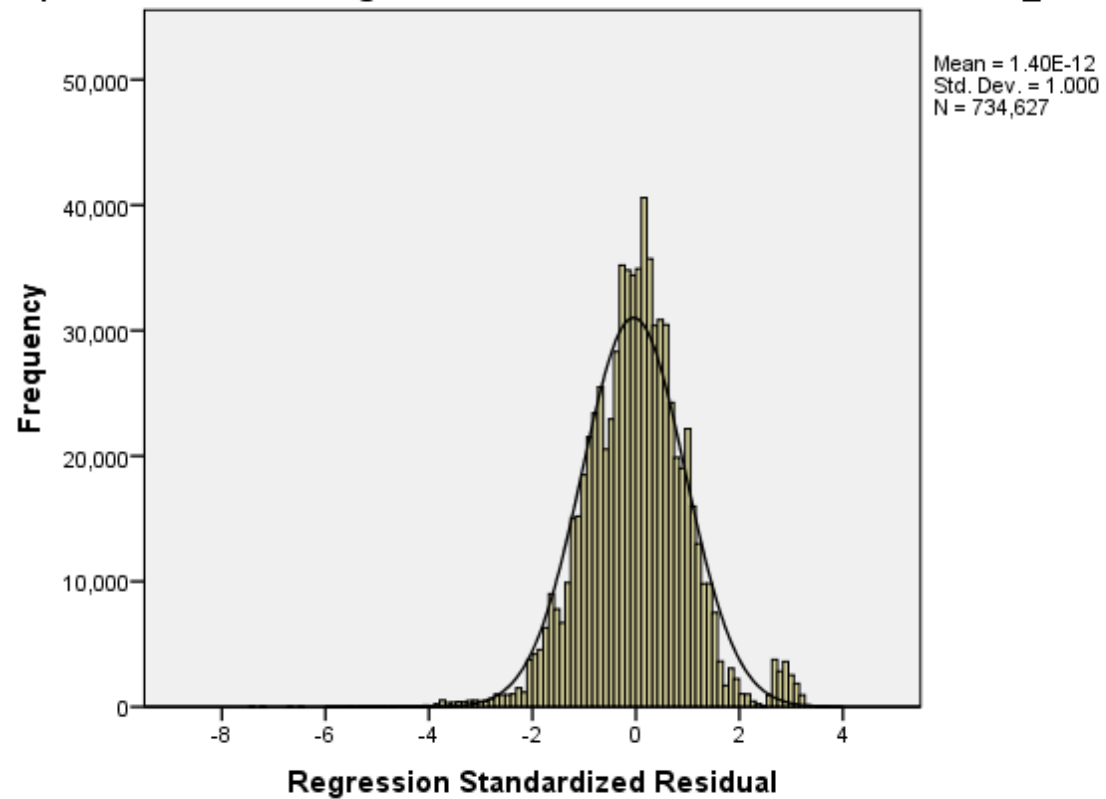
Residuals Statistics^a

	Minimum	Maximum	Mean	Std. Deviation	N
Predicted Value	-3.4049	-2.4827	-2.7140	.16626	734627
Std. Predicted Value	-4.156	1.391	.000	1.000	734627
Standard Error of Predicted Value	.000	.006	.001	.000	734627
Adjusted Predicted Value	-3.4048	-2.4827	-2.7140	.16626	734627
Residual	-2.12295	1.11190	.00000	.28511	734627
Std. Residual	-7.446	3.900	.000	1.000	734627
Stud. Residual	-7.446	3.900	.000	1.000	734627
Deleted Residual	-2.12298	1.11193	.00000	.28512	734627
Stud. Deleted Residual	-7.446	3.900	.000	1.000	734627
Mahal. Distance	1.135	332.138	8.000	17.795	734627
Cook's Distance	.000	.001	.000	.000	734627
Centered Leverage Value	.000	.000	.000	.000	734627

a. Dependent Variable: Log Transformation of outcome variable PREV_RXOUD_ED

Histogram

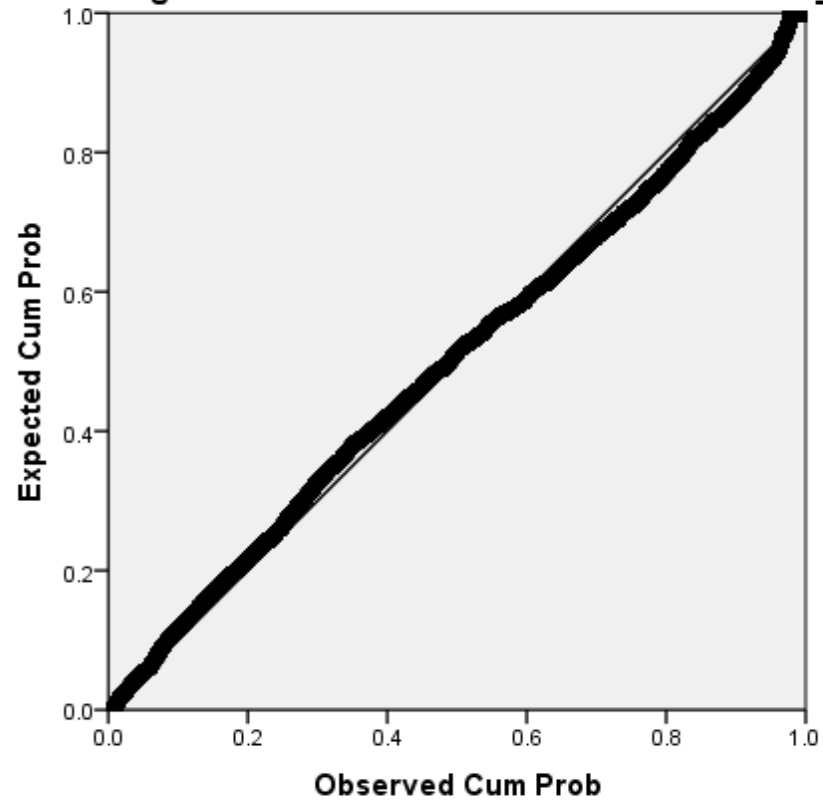
Dependent Variable: Log Transformation of outcome variable PREV_RXOUD_ED



Cases weighted by Weight to ED Visits in AHA universe

Normal P-P Plot of Regression Standardized Residual

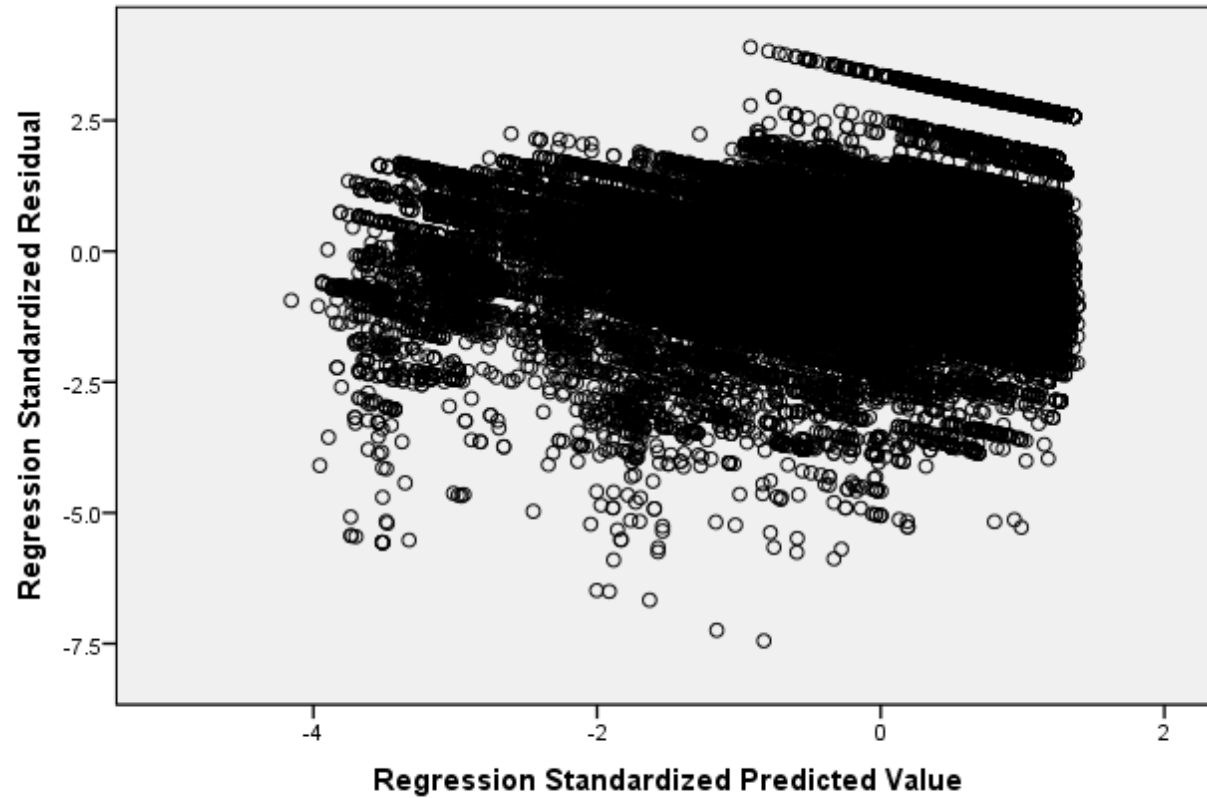
Dependent Variable: Log Transformation of outcome variable PREV_RXOUD_ED



Cases weighted by Weight to ED Visits in AHA universe

Scatterplot

Dependent Variable: Log Transformation of outcome variable PREV_RXOUD_ED



Cases weighted by Weight to ED Visits in AHA universe

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