

Conceptualization of the Epidemiology of Opioid Use in the United States

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Abstract

The United States is in the midst of an opioid epidemic, necessitating a shift in the conceptualization of the harm caused by opioids. Harm may be caused through exposure, misuse, addiction, and overdose. This article proposes the use of a pyramid diagram in which the volume of individuals in a category decreases as movement progresses up the pyramid, with most individuals in the exposure category and the least in overdoses. The article reviews definitions for each category. Further, the article summarizes current volume for each category. As volume changes, it is important for stakeholders to be aware of the different databases and the sources used to create them.

Keywords: Opioid; Epidemic; Overdose; Misuse; Epidemiology

The United States is currently experiencing an opioid epidemic. The etiology of this tragedy is complex and multifactorial. Causal factors include an increased emphasis on treating pain, aggressive marketing that opioid use in treatment of pain is not harmful, lack of oversight, and a high level of national growth in consumption and demand.¹ The first decade of the 21st century was characterized by a significant increase in the availability, use, and abuse of prescription opioids.¹ As medical use became more prevalent, so did nonmedical use, contributing to adverse outcomes.¹

Prescription opioid sales quadrupled between 1999 and 2010.² Hydrocodone with acetaminophen was the number one prescribed medication in the United States from 2006 through 2011.³ With increased prescribing, there has been a massive increase in the rate of

overdose deaths. The age-adjusted rate of drug overdose deaths in 2015 (16.3 per 100,000) was more than 2.5 times the rate in 1999 (6.1 per 100,000).⁴ There has also been a change in the types of drugs found in overdose deaths. In 2010, 29% of drug overdose deaths were due to natural and semisynthetic opioids and 12% were from methadone.⁴ In 2015, natural and semisynthetic opioids accounted for 24% and methadone just 6%.⁴ This shift was largely due to the rise of heroin usage which was involved in 8% of deaths in 2010 and increased to 18% in 2015.⁴ Among heroin users today, 75% were introduced to opioids through prescription drugs compared to the 1960s when 80% of heroin users started with heroin as their first opioid drug of abuse.⁵ As access to prescription opioids becomes more tightly regulated and restricted, many prescription opioid users are turning to heroin as their drug of choice.⁶ This is even more exaggerated in US Veterans, with 27.3% that had no previous history of illicit opioid use initiated heroin within 10 years of new-onset non-medical prescription opioid use.⁷

Opioid addiction (formally known as Opioid Use Disorder) is a gradual process characterized by a progressive loss of control. This rate of progression differs among individuals, but the steps taken are common. For example, it has been shown that heroin users follow a drug use trajectory that begins with opioid analgesic initiation followed by a switch to a higher dose or single-entity pill. The next step is characterized by sniffing as a primary route of administration culminating in physical opioid dependence. Finally, heroin usage is initiated.⁸

The purpose of this article is to introduce a conceptualization of opioid use and subsequent harm utilizing a pyramid diagram (Figure 1). Representing the base of the pyramid is opioid exposure. This includes anyone who has ever used any sort of opioid. Above exposure is opioid misuse which includes those who have used an opioid without a prescription or outside of its intended purpose. The next level is opioid use disorder, representing those individuals that fulfill the criteria for a long standing maladaptive pattern of use. At the top of the pyramid is unintentional overdose. It is believed that opioid users gradually progress up this pyramid, and users at higher levels are at an increased risk for adverse outcomes of opioid use. By utilizing this concept, stakeholders will be able to understand the characteristics of each step and fight the epidemic in strategic pieces.

Exposure

Opioid exposure is at the bottom of the pyramid and includes the highest number of individuals. Anyone who has ever been prescribed any type of opioid falls into this category. In 2017, 56,778,428 people in the United States had at least one prescription filled for an opioid, accounting for 17.4% of the national population.⁹ 191,146,822 opioid prescriptions were dispensed, averaging 3.4 prescriptions per person prescribed opioids.⁹ The average days of supply per prescription was 18.3, the average Morphine Milligram Equivalent (MME) per capita was 511.1, the average MME per prescription was 873.4, and the average daily MME per prescription was 45.3.⁹ In 2015, an estimated 91.8 million or 37.8% of US adults aged 18 and older had used a prescription opioid in the past year.¹⁰

Due to the large number of people in the exposure category, the likelihood of people elevating into the misuse, opioid use disorder, and overdose categories is increased. Studies have shown¹¹ that 5.0% of previously opioid naïve patients initially prescribed opioids progress to long-term opioid use, and the risk of progression increases with a higher number of fills and increased morphine milligram equivalent in the initiation month, as well as use of long-acting opioids. Another study found that those with an initial exposure of at least one day of opioid therapy had a 6.0% risk of still being on opioids one year later, but that risk increases to 13.5% when the initial exposure is at least eight days and 29.9% when the initial exposure is at least 31 days.¹² In a study where the participants were heroin or nonmedical prescription opioid users, 59% were initially exposed to opioids through a legitimate prescription by a medical provider. Of note, 29% reported that their initial exposure came from an emergency department.¹³ In a cohort study of 1.14 million hospital admissions, 51% of adult nonsurgical admissions to US hospitals were given opioids and 0.6% of this group developed severe opioid-related adverse events during their admission. Of those exposed, more than half were still receiving opioids on the day of discharge. The opioid prescribing rates by hospital ranged from 5% to 72%, and hospitals with higher opioid prescribing rates had a higher rate of severe opioid-related adverse events.¹⁴

Despite the high levels of opioid use in the United States, there is a general downward trend in opioid prescriptions. The number of opioids prescribed annually peaked in 2010 then decreased each year. This decline is thought to be due to increased awareness among physicians and patients of the high level of risk of opioids. Despite these reductions, the amount of annually prescribed opioids is currently approximately three times as high as it was in 1999.¹⁵ From 2006 to 2017, the high dose (daily dosage of ≥ 90 MME) opioid prescriptions dispensed per 100 persons annually decreased from 11.5 to 5.0.⁹ This is indicative of increased recognition of the particular danger of high dose opioids. Opioid use is not equal across the United States. Average per capita opioid prescriptions in the top prescribing counties are approximately six times higher than in the lowest prescribing counties. County factors associated with higher prescribing counties include a larger percentage of non-Hispanic whites, a higher prevalence of diabetes and arthritis, areas with a population between 10,000 and 50,000, and higher unemployment and Medicaid enrollment.¹⁵

There are several tools providers can use to monitor the prevalence of opioid exposure. CMS Opioid Prescribing provides more transparency on opioids prescribed through Medicare and Medicaid. It allows visualization of the number and percentage of opioid prescriptions among Medicare and Medicaid patients based on state and county statistics.¹⁶ The DEA's Automation of Reports and Consolidated Orders System (ARCOS) is a comprehensive drug reporting system used to track the distribution of controlled substances. Manufacturers and distributors are obligated to report transaction of controlled substances, and cumulative and quarterly sales are available for viewing based on state and zip codes.¹⁷ To enable providers to learn about individual patient's prescriptions of controlled substances, prescription drug monitoring programs (PDMPs) utilize statewide electronic databases that collect prescribing and dispensing data submitted by pharmacies and dispensing practitioners. Practitioners can obtain PDMP reports on patients under their care to determine if they may be misusing controlled substances.¹⁸

Misuse

Those in the exposed category of the pyramid are at risk to elevate into the misuse category. The term misuse can be defined as use in a manner other than indicated or prescribed. This category also includes those who abuse opioids which had previously been defined as unlawful use or when use is detrimental to the user or others.¹³ The misuse category is fairly extensive and ranges from anyone who has taken an opioid without a prescription on a single occasion to someone who is on the cusp of diagnosis with opioid use disorder. Such variation necessitates the need for a standard definition. The risk to the next elevation in the pyramid likely varies based on the extent of misuse. The misuse category includes those who have misused opioids but does not include those who qualify for Opioid Use Disorder which is the next elevation in the pyramid.

In 2015, 11.5 million people in the United States aged 18 or older misused opioids, accounting for 4.7% of that population.¹⁰ The 2015 National Survey on Drug Use and Health (NSDUH) had respondents who were told that misuse is considered use without a prescription of one's own, use in greater amounts, more often, or longer than told to take a drug, or use in any other way not directed by a doctor; 66.3% of misusers reported that their primary motivation for misuse was to relieve physical pain. Among adults who misuse opioids, 59.9% use opioids without a prescription, and 40.8% obtained prescription opioids for free from friends or relatives for their most recent episode of misuse.¹⁰ The high percentage of misusers who used opioids without a prescription is likely because any use of opioids without a prescription would cause them to surpass the exposure category and would automatically place them in the misuse category.

Prescription opioid misuse has been shown to be a key feature of trajectory into heroin use.¹⁹ Those who transition from prescription opioid to heroin abuse typically escalate by sniffing prescription opioids, then injecting prescription opioids, and finally injecting heroin. One of the key reasons for trajectory into heroin use is that heroin can be purchased cheaper than prescription opioids.¹⁹ The dwindling supply of opioids relative to 2010 levels has increased the demand for heroin. To meet this increased demand, dealers have increased the supply of cheap, accessible heroin. From 2010 to 2016 in the US, the price per pure gram of heroin decreased from \$1,090 to \$750 and the total pure metric tons consumed increased from 27 in 2010 to 47 in 2016.²⁰ The number of chronic heroin users also increased from an estimated 1.6 million in 2006 to 2.3 million in 2016.²⁰ In 2005, 8.7% of new regular opioid users started with heroin.²¹ This dramatically changed in the next decade, and in 2015, 33.3% of new regular opioid users began with heroin.^{21,22}

It is important for providers to be aware of patients' risk of opioid misuse and further progression up the pyramid. Several screening assessments are available to providers to determine a patient's risk for opioid misuse, including the Pain Catastrophizing Scale (PCS) and the Screener and Opioid Assessment for Patients with Pain-Revised (SOAPP-

R). It has also been demonstrated that a single item from the Coping Strategies Questionnaire (CSQ) has a fair discrimination in determining patients at risk for opioid misuse.²³ The item states, “When I feel pain... It is terrible and I feel it is never going to get better,” and the responses range from 0 (“never”) to 6 (“always”).²³ It is suggested that primary care physicians cover this question during their conversations with patients in instances where time constraints prohibit a more extensive assessment.²³ Additional information regarding a state population’s health problems and opioid misuse can be found through the state’s Behavioral Risk Factor Surveillance System (BRFSS), a telephone survey asking about health-related risk behaviors.²⁴ The survey questions regarding opioid misuse vary by state, and prevalence of risk factors can be localized to state, city, and county levels.²⁴

The misuse of opioids can have far-reaching consequences. It is estimated that the total economic burden of prescription opioid overdose, abuse, and dependence is \$78.5 billion. These costs include healthcare, criminal justice, and lost productivity. Approximately one quarter of the costs is through the public sector.²⁵ This demonstrates that opioids not only negatively impact users and those around them but society as a whole.

Opioid Use Disorder

The next elevation in the pyramid from misuse is Opioid Use Disorder (OUD). The criteria for OUD is outlined in the Diagnostic and Statistical Manual, 5th Edition (DSM 5).²⁶ The diagnosis requires having two out of 11 of the following conditions: hazardous use, social/interpersonal problems related to use, neglected major roles to use, withdrawal, tolerance, used larger amounts or for longer than intended, repeated attempts to quit/control use, great deal of time spend using, physical/psychological problems related to use, activities given up to use, and cravings.²⁶ However, the DSM 5 states that tolerance and withdrawal (known as physical dependence) are omitted from the criteria if the user is taking the opioids as prescribed and under the supervision of a physician.²⁷ It is important to note that OUD includes use of medical opioids (e.g. hydrocodone), illicit opioids (e.g. heroin), or both.

In 2016, it was estimated that 2.1 million Americans, or 0.8% of the population, aged 12 and older met the criteria for OUD.⁹ Among those with OUD, 81.93% had prescription OUD only, 9.75% had heroin use disorder only, and 8.32% had both prescription and heroin use disorder.²⁸

Medication Assisted Treatment (MAT) is an effective treatment option for OUD. However, widespread use has not yet been achieved.²⁹ For example, despite buprenorphine being an effective treatment for OUD, only 2.2% of US physicians had obtained waivers for using this treatment protocol as of 2012. 90.4% of these physicians practiced in urban counties, and 53.4% of total counties, most of them rural, did not have a physician authorized to prescribe buprenorphine.³⁰ This is especially relevant since rural communities are particularly affected by the opioid epidemic.¹⁵

Use of opioids for pain does not prohibit the development of OUD, thus physicians must be cautious when prescribing opioids for chronic pain. One study demonstrated that of

non-cancer patients on chronic opioid therapy, 23.9% met the criteria for OUD.³¹ It is estimated that 25.3 million, or 11.2%, of US adults suffer from chronic pain³², demonstrating that there is a probability that 6 million individuals could develop OUD if treated with opioids. According to the CDC guidelines, primary care physicians should consider the following when initiating opioids for chronic pain: opioids are not first-line therapy, establish goals for pain and function with the patient, and discuss risks and benefits.³³ If opioid therapy is initiated, physicians should begin with immediate-release, low dosage opioids, prescribe short durations for acute pain, and evaluate benefits and harm frequently. When assessing risk and addressing harms, physicians should adopt strategies to mitigate risk, review prescription drug monitoring program (PDMP) data, use urine drug testing, avoid concurrent opioid and benzodiazepine prescribing, and offer treatment for OUD.³³ It is essential to minimize the population with OUD given that these individuals are have a high risk to elevate to the last and most dangerous category in the pyramid: overdose.

Most of the numbers involving the total population or percent of the US population in this category come from the National Survey on Drug Use and Health (NSDUH).³⁴ This is an annual survey of the US population conducted in all 50 states and the District of Columbia. The data is collected through face-to-face interviews of residents who are US civilians, older than 12 years old, and not institutionalized. It does not include people who are homeless or do not use shelters, military personnel on active duty, or residents of jails and hospitals. The survey provides a \$30 incentive for respondents.³⁴

Individuals seeking treatment is another valuable source of data. Substance treatment information is available through the Treatment Episode Data Set (TEDS).²⁹ This consists of client-level data for substance abuse treatment admissions from State Agency data systems. Records are collected from patients who are ages 12 and older and includes demographic information such as age, sex, race/ethnicity, and employment status and substance abuse characteristics such as substances used, age at first use, route of use, frequency of use, and number of previous admissions. Because each record represents an admission or discharge and not an individual person, individuals who are admitted more than once in a year are counted multiple times. Also, the degree of reporting varies by state. States are legally required to report publicly funded admissions. Some states only collect publicly funded admissions, while other states also collect privately funded admissions from facilities that receive public funding.²⁹

Overdose

The final category in the opioid pyramid is overdose. Overdose is defined as an event in which the documenting physician determined that a patient was unresponsive or not breathing adequately due to opioids.³⁵ The overdose category includes both fatal and nonfatal events and can be caused by both medical and illegal opioids. Because most of the research looks at opioid overdoses by year, it is possible for an individual to be counted multiple times in the overdose category, if that person survived an opioid overdose then subsequently overdosed again. It is difficult to calculate an exact number of opioid overdoses because they are either reported as emergency department (ED) visits or deaths. There are likely many more nonfatal opioid overdoses that were unreported or treated with

naloxone, an opioid antagonist commonly used to treat opioid overdoses, outside of a medical setting. Among patients presenting to the ED for an opioid overdose, 70% have a history of opioid overdose and 31% have access to a naloxone kit.³⁶ This seems to suggest that when those in the OUD category elevate to the overdose category and survive, they are more inclined to experience another overdose.

There were an estimated 140,077 ED visits for an opioid overdose in 2015, and 81,326 were due to heroin.⁹ These numbers were extracted from the Healthcare Cost and Utilization Project's (HCUP) National Inpatient Sample (NIS) and Nationwide Emergency Department Sample (NEDS). The percentage of visits resulting in death ranges from 2.2% if the overdose is due to multiples opioids to 1.1% if the overdose is due to prescription opioids.³⁷ This high survival rate indicates that most opioid overdose deaths occur outside of a medical setting. Among non-cancer patients on chronic opioid therapy, the annual risk for an overdose ranged from 0.2% to 1.8% depending on the average daily dose.³⁸ An increased annual risk of overdose is associated with a higher average daily dose.³⁸

In 2017, drug overdoses resulted in 70,237 deaths in the US, and 67.8% involved an opioid.³⁹ From 1999-2017, drug overdoses have resulted in 702,568 deaths, and 56.8% involved an opioid,³⁹ according to data from the National Vital Statistics System (NVSS), an important data set for monitoring the epidemic. The number of annual drug overdose deaths more than tripled since 1999, mostly due to the opioid epidemic.⁴⁰ Although opioid prescribing peaked around 2010⁹, opioid overdose deaths have continued to increase. The drug overdose death rate increased 23% from 2010 to 2014. This is largely due to the rapid rise in heroin and fentanyl deaths.⁴¹ In 2010, prescription opioids made up the largest share of opioid overdose deaths, but it is now ranked 3rd behind fentanyl and heroin.⁴² Fentanyl and fentanyl analogs now make up the largest share and have increased from a rate of 1.0 overdose deaths per 100,000 in 2013 to 9.0 in 2017.⁴² Heroin has increased at a rate from 1.0 deaths per 100,000 in 2008 to 4.9 in 2017.⁴² The continuing increase in opioid overdose deaths and shift in contributing opioids demonstrate the changing face of the opioid epidemic.

In conclusion, the opioid epidemic has evolved since its creation in the late twentieth century. The evolution requires constant vigilance of stakeholders, but also shifting strategies. By identifying prevention plans for each block of the pyramid of harm, measurements can be more precise and prevention plans can be better developed. Ultimately, such strategies will result in decreased morbidity and mortality.

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