



# The Opioid Crisis: a Comprehensive Overview

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Published online: 23 February 2018

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## Abstract

**Purpose of Review** The opioid crisis most likely is the most profound public health crisis our nation has faced. In 2015 alone, 52,000 people died of drug overdoses, with over 30,000 of those people dying from opioid drugs. A recent community forum led by the Cleveland Clinic contrasted this yearly death rate with the loss of 58,000 American lives in 4 years of the Vietnam War. The present review describes the origins of this opioid epidemic and provides context for our present circumstances.

**Recent Findings** Alarmingly, the overwhelming majority of opioid abusers begin their addiction with prescription medications, primarily for chronic pain. Chronic postoperative pain, which occurs in 10–50% of surgical patients, is a major concern in many types of surgery. Nationwide, the medical community has made it a priority to ensure that postsurgical analgesia is sufficient to control pain without increasing non-medically appropriate opioid use.

**Summary** The opioid epidemic remains a significant pressing issue and will not resolve easily. Numerous factors, including the inappropriate prescription of opioids, lack of understanding of the potential adverse effects of long-term therapy, opioid misuse, abuse, and dependence, have contributed to the current crisis.

**Keywords** Opioids · Overdose deaths · Pain · Health policy

## Introduction

The opioid crisis in the USA has been worsening at an alarming rate and has grown into a major concern in the realm of health policy, health care guidelines, and management. Between 1999 and 2014, the reported drug overdose deaths increased by almost 3-fold [1•]. In 2014, of the 47,055 reported drug overdose deaths in the USA, 60.9% were opioid-

related [2]. The following year, nationwide drug overdose deaths were reported at 52,404, of which 63.1% were opioid-related [1•]. In an attempt to develop methods to manage and prevent the opioid crisis, the Centers for Disease Control and Prevention (CDC) [1•] investigated the overall drug overdose deaths over a 5-year span from 2010 to 2015, as well as the opioid-related overdose death rates from 2014 to 2015 by subgroups including semisynthetic/natural opioids, heroin, methadone, and synthetic opioids other than methadone. The CDC found that although progress has been made in the prevention of methadone deaths (rate decline of 9.1%), the rates of other opioid-related deaths, especially non-methadone synthetic opioids and heroin, increased significantly across the country. The rates of methadone-related deaths have been declining since 2008 as a result of efforts to decrease utilization of methadone for pain, including limits on high-dose formulations, Food and Drug Administration warnings, and clinical guidelines [3]. The increase in the death rates of non-methadone-related deaths is likely attributed mostly by the illegally manufactured fentanyl [4, 5]. Thus, the CDC has called for the pressing need of a collaborative, multifaceted law enforcement and public health approach.

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This article is part of the Topical Collection on *Other Pain*

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## The Progression of the Epidemic

An important point of consideration is to appreciate what has fueled the opioid epidemic and how it has developed into such a widespread crisis. Historically, in the nineteenth century, there was no form of regulation of cocaine and opioids in the USA. These drugs were prescribed and marketed as for the treatment of a myriad of conditions ranging from diarrhea to toothaches [6]. It was not until the Harrison Narcotics Tax Act was passed in 1914 that the manufacturing, distributing, and importing of cocaine and opium started to become regulated [6]. Further, since addiction at this time was not recognized as a disease, physicians who provided prescription maintenance stock of these drugs to addicted patients were by law incarcerated or lost their licenses [7]. Illegalization of addiction, in part, eventually led to inadequate treatment of pain states.

Weiner et al. [8] have identified three driving forces that have contributed to the evolution of opioid use: treatment of pain as a human right; pharmaceutical companies; and the response to the undertreatment of pain. The first driving force is the existing moral duty for physicians to relieve suffering and to manage pain. The paper cites the Declaration of Montreal, which asserts that the access to pain treatment is a fundamental human right [9].

The second driving force identified is the heavy influence of the pharmaceutical industry on the prescription of opioids. Pharma has started to assertively market the utilization of opioids for non-cancer pain [10, 11], and the sales of opioids have skyrocketed accordingly. For instance, Purdue Pharma, the manufacturer of Oxycontin, expended \$200 million promoting the drug in 2001, which resulted in an increase in the prescription of Oxycontin by almost 10-fold to nearly 6.2 million annual prescriptions the following year [12]. Purdue Pharma aggressively mobilized marketing techniques in the form of organizing 20,000 pain “education” programs and 40 all-expenses-paid conferences for 5000 health care providers. Free-starter coupons and branded promotional products for patients were offered, and the company targeted physicians who prescribe large amounts of opioids with sales representatives who were incentivized by a bonus system. Furthermore, Purdue Pharma also distorted the risk of addiction associated with Oxycontin in its supplies to physicians and patients. Ultimately, the executives and manufacturer were fined \$634 million on the grounds of misbranding [12]. Furthermore, distribution of morphine milligram equivalents per person increased from 96 to 700 between the years of 1997 to 2007, an upsurge of greater than 600% [13]. In 2013, a drug study based on workers’ compensation prescription drugs found that narcotics make up 25% of all paid prescription costs and that 45% of the narcotic costs were for drugs containing oxycodone HCl [14]. In 2011, Oxycontin made up 25.5% of all prescribed narcotics and ranked no. 1 in the top 20 drug list

based on total claims paid. Other substances that also ranked as a top 20 agent included Percocet at no. 20, oxycodone-HCl at no. 15, oxycodone HCL-acetaminophen at no. 13, and hydrocodone-acetaminophen at no. 5 [6].

The third driving force was identified as the recent trend in the more aggressive management of pain secondary to the observed undertreatment of pain, designated “oligoanalgesia.” As a consequence of findings of significant discrepancies in pain treatment in ethnic and racial minorities [15–17] and age [18], the American Pain Society pronounced “pain as the fifth vital sign” and promoted the assessment of pain at each clinical assessment [19], further advocating the widespread use of opioids. In 2000, the Joint Commission accepted pain as the fifth vital sign as a standard [20]. Gradually, the indication for opioid use expanded from that of cancer and palliative care to patients with non-cancer pain, and opioids became synonymous with pain management. This was the beginning of the opioid crisis which has seen a quadrupling of prescriptions and associated overdose deaths that now affects the entire nation.

Another significant contributor to the current drug epidemic is recent postoperative pain management practices. Related to their potency, opioids have been a main drug in the acute postoperative pain management setting. Typically lengthy and high dose prescriptions were routinely provided to patients, even though acute pain typically lasts less than a week. Over a period of weeks to months, suppression of endogenous opioid production results in dependents on these opioid medications and addiction.

Nationwide, the medical community has made it a priority to ensure that postsurgical analgesia is sufficient to control pain. As an example, orthopedic and other extremity trauma is extremely common with reconstruction and rehabilitation from these injuries being both prolonged and painful. Despite the opportunity to provide multimodal strategies such as ultrasound guided local anesthetic nerve blocks and catheters to help manage postsurgery-related acute pain, it is more likely that the patient will only receive a large dose of opioid medication from his orthopedic surgeon. Alarmingly, the majority of opioid abusers begin their addiction with prescription medications, and as a result, many states have created limits in dosing interval and quantity for acute pain management.

In fact, opioids are commonly continued under the context of management of postoperative pain and often only stopped with obvious adverse life-threatening side effects being identified or when there is hampering of the recovery process and negative affect to the patient.

In order to improve the treatment options of postoperative pain management, alternate routes and drugs have been identified, including the development of adjunctive medications such as gabapentinoid agents to reduce the need for high doses of pain medicine postoperatively. This has resulted in decreasing amounts of opioids and consequent reduced side effects,

resulting in lower analgesic dosages with shorter durations of dosing and a lower likelihood of contribution to long-term opioid dependence. The recent reforms in many states that have limited the number of opioid prescriptions in both quantity and in days post surgery in the setting of acute pain management are excellent practical strategies in combating certain aspects of our opioid epidemic at present.

Education of prescribers has been discussed at many national and state-led meetings as something that should be on a regular basis and mandatory. It should be noted that the two most common opioid prescriber groups in the USA are family practice and internal medicine physicians.

The increase in options for postsurgical pain management ironically has contributed to the mismanagement of opioids by unwittingly exposing patients to opioid formulations at more potent dosages, and in greater quantities. Clarke et al. [6] propose that because prescriptions of these newer formulations were prescribed under the inaccurate assumption that opioids administered for patients with acute pain are associated with minimal risk for misuse, abuse, or addiction, patients were often discharged from the surgical center or hospital without adequate education regarding risks. In fact, two thirds of patients who are abusing opioids are taking medication that was not prescribed to them, but are the unused pills of another patient's prescription [6]. Rodgers et al. [21] found that 245/250 patients who underwent upper extremity surgery were prescribed postsurgical opioids for pain management. Patients were typically prescribed 30 tablets, although patients took an average of 10 pills and reported a surplus of 19 pills, with a total of 4639 excess tablets in the study. This creates a large pool of opioids that can potentially be used by the patient later or by someone it was not prescribed for [22•].

## Populations Impacted

The breadth of patients who have become addicted to opioids following the opioid epidemic has expanded across numerous demographics and socioeconomic populations [23]. In the 1960s, greater than 80% of the patients enrolling in opioid abuse treatment programs were males living in urban, inner-city regions who abused heroin [24]. Contrastingly, in 2010, the majority of patients who were enrolling in these programs were middle-class women from rural or less urban regions, of which 90% were Caucasian [24]. Currently, the USA makes up less than 5% of the world's population all the while making up more than 80% of the world's consumption of opioid pain analgesics [25].

Among those affected by this opioid epidemic include the veteran population in the USA. A study conducted on patients of the Veterans Health Administration from 2001 to 2009 demonstrated a comparable increase in levels of opioid overdoses between the general population and the population of

the health system [26]. Furthermore, veterans from Afghanistan and Iraq suffering from mental health disorders, particularly posttraumatic stress disorder, have been associated with a greater risk of being prescribed opioids, high-risk opioid use, and adverse clinical outcomes [27].

Children who participate competitively in sports are also a group that is at especially high risk of opioid misuse. Adolescents contending for sports scholarships regularly suffer from injuries that necessitate surgeries and physical rehabilitation. Opioids are often given prophylactically to facilitate rapid return to sports practice [6]. A longitudinal study by Veliz et al. [28] found that compared to adolescents who were not involved in sports, adolescents involved in organized sports were two times more likely to be prescribed an opioid, at greater risk for medical misuse of an opioid with the intention of getting high by 4-fold, and at greater risk for medical misuse of an opioid by 10-fold. In this regard, in a recent FDA Advisory Board meeting in 2016 that focused on pain in children under the age 18, it was referenced that approximately 85% of adolescents obtained opioids from unknowing family members who have not secured their own prescribed medications.

The rise in prescription opioid abuse has also contributed to the increase in the use and overdose in heroin [29]. Since 2010, the rate of reported heroin use and heroin-related overdose deaths has increased by more than 3-fold, partially due to the increase in the affordability and availability of heroin [2].

## The Cost and Effect of Long-Term Opioid Use

Part of the opioid crisis can be attributed to the poor management with which oncologists, primary care physicians, dentists, surgeons, and emergency room physicians direct opioid therapy in regards to continuing prescriptions in opioid-dependent patients, and starting opioid therapy in patients who are opioid-naïve.

Despite the acute analgesic efficacy in taking opioids, numerous harmful effects have been associated with its administration. These effects are mostly dose-dependent and are well documented in the literature. The unfavorable effects include addiction, abuse, overdose, hyperalgesia, cardiovascular events, hormonal changes, fracture, potential for propagation of infection and cancer progression through suppression of natural killer cells, incidence of pneumonia, and death [30•]. Higher doses of opioids are associated with a greater incidence of ileus postoperatively. Administering opioids to patients with ileus is associated with increased costs, prolonged hospital stays, and greater readmissions [31]. Opioid-associated adverse events have significantly impacted health care costs. One retrospective analysis of 320,000 surgeries found that 12.2% of patients with opioid-related adverse drug events had prolonged hospital stays (7.6 vs.

4.2 days) and greater costs (\$22,000 vs. \$17,000) relative to patients without opioid-related adverse drug events [32]. Another retrospective study found that patients with reported opioid-related adverse drug events had 36% increased risk 30-day readmission, 55% prolonged hospitalization, increased risk of inpatient mortality by 3.4-fold, and 47% increased cost of care compared to patients who did not report opioid-related adverse drug events [33].

Furthermore, the efficacy of long-term opioid use is not well studied in non-cancer pain. In most chronic pain conditions, there is limited to no clear evidence that opioids are significantly effective. Despite this lack in evidence, many health providers continue to prescribe opioids. Krashin et al. [34] discuss the potential factors that pressure health providers to continue this practice. They propose that as a result of the increasing number of clinics and physicians who refuse to prescribe opioids for non-cancer pain, the burden on other providers to prescribe those who seek pain relief has increased. To complicate these matters, many patients on chronic opioids are “inherited” patients who were initially prescribed opioids by providers who have since either left the practice or retired. Krashin et al. [34] also point out that the majority of providers were once largely unaware of the addictive properties of opioids, and the potential harm in continuing chronic opioid therapy. Studies have shown that patients on opioid therapy that is continued for 90 days or more are more likely to stay on chronic opioid therapy for years [35]. Clinics and providers have been shut down by authorities for inappropriate prescribing of opioids, leaving hundreds to thousands of patients on chronic opioid therapy without someone to prescribe them opioids [34].

## Pregnancy and Opioid Use Disorder

The prevalence of opioid-using women of reproductive age has climbed drastically high in the USA. From 2008 and 2012, a mean of 27.7% privately insured and 39.4% of Medicaid-insured women of childbearing age (between 15 and 44) filled an outpatient opioid prescription annually, with greater numbers reported among non-Hispanic white women and in the South [36]. Furthermore, in an assessment of over one million patients receiving Medicaid, one in five (21.6%) pregnant patients filled an opioid prescription, and 2.5% were prescribed an opioid prescription for more than 30 days [37]. This surge in the prescription of opioids to pregnant patients has caused a significant increase in the number of women that require treatment for opioid abuse. Between 1992 and 2012, the number of pregnant patients admitted to facilities for substance abuse treatment that reported a history of prescription opioid abuse increased from 2 to 28% [38].

Alongside the increasing rates of opioid use in pregnancy, there has been a rise in adverse neonatal outcomes including

neonatal abstinence syndrome. Relative to opioid-naïve neonates, those with neonatal abstinence syndrome are more likely to be white and have feeding difficulty, lower birth weights, respiratory complications, and seizures [39]. Between 2000 and 2012, the prevalence of neonates diagnosed with neonatal abstinence syndrome increased by almost 5-fold [39, 40]. States with the greatest rates of opioid prescriptions have the greatest rates of neonatal abstinence syndrome [40]. By 2012, on average, for every 30 min, there was one neonate born having drug withdrawal in the USA, which is responsible for an approximated health care cost of \$1.5 billion [40].

In efforts to combat the adverse effects that the opioid epidemic has caused on pregnant women and neonates, there has been a need to improve the accessibility and availability to medication-assisted treatment for pregnant women. Although the judicial and state legislative focuses on criminalizing pregnant women with opioid use disorder, there has been little to expand the programs available for treatment [29]. Substance abuse treatment programs specifically catered towards treating women during pregnancy are only available in 19 states, and only 12 states provide pregnant women priority access to state-sponsored programs [29]. These barriers to treatment accessibility further worsen the health care issue.

In February 2015, the “Prenatal Drug Use and Newborn Health” report was released by the Government Accountability Office, which pointed out the deficiency of federal programs and research allocated to neonates with neonatal abstinence syndrome and pregnant women struggling with opioid use disorder [29]. In response to the report, *The Protecting Our Infants Act of 2015* was signed by President Obama in November 2015, which guides the Department of Health and Human Services to manage a review of programs that organize services for neonates with neonatal abstinence syndrome and pregnant women with opioid use disorder, devise plans to decrease the research gap, offer technical aid to states collecting data, and develop prevention guidelines [29].

## Policy Changes and Trends

The former Surgeon General, Dr. Vivek Murthy, wrote a perspective letter titled “Ending the Opioid Epidemic—A Call to Action” [41•] detailing the steps that have been taken to combat the opioid crisis. The Department of Health and Human Services has invested millions of dollars to fund treatment programs and prescription-drug monitoring programs, increase naloxone accessibility, and develop guidelines for opioid prescribers to optimize care. However, Murthy also stresses the need to continue supporting measures to combat the opioid epidemic. He implores physicians to utilize prescription-drug monitoring programs and hone their prescription practices in order to decrease the risk of opioid abuse and the rate of overdoses. Additionally, he encourages



clinicians to consider alternatives such as non-opioid pain management wherever possible. Accessibility to affordable alternatives remains a challenge, and Murthy emphasizes that this initiative will require the cooperation of numerous organizations, including academia, the pharmaceutical industry, government, and payers. Murthy also points out that although the Mental Health Parity and Addiction Equity Act of 2008 was a major accomplishment in providing equal treatment by insurance plans of substance use disorders and other medical conditions, there is still a need to focus on the mental health of patients with these conditions [41•].

In addition to devising health policy initiatives, there is a need to develop curricula, enrich the education community, and develop guidelines so that health care providers can optimize the delivery and practice of opioid pain management.

## Conclusion

The opioid epidemic is one that remains a pressing issue that will not resolve easily. Numerous factors, including the inappropriate prescription of opioids, lack of understanding of the potential adverse effects of long-term therapy, opioid misuse, abuse, and dependence, have contributed to the current crisis. Targeting this issue will require collaborative efforts from numerous organizations, from health care providers, legislators, physicians, educators, pharmaceutical companies, and the public.

## Compliance with Ethical Standards

**Conflict of Interest** Nalini Vadivelu, Alice M. Kai, Vijay Kodumudi, and Julie Sramcik declare no conflict of interest. Dr. Kaye is a speaker for Depomed, Inc., and Merck, Inc.

**Human and Animal Rights and Informed Consent** This article does not contain any studies with human or animal subjects performed by any of the authors.

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