The Opioid Epidemic: National Trends in Opioid-Related Overdose Deaths from 2000 to 2016

INTRODUCTION

For nearly two decades, the United States has experienced a growing crisis of drug abuse and addiction that is illustrated most starkly by deaths from drug overdose. Since 2000, the number of drug overdose deaths has more than tripled from 17,500 to 63,500 in 2016.\(^1\)\(^2\) Most of these deaths involved opioids, including heroin and prescription painkillers.\(^3\) In the years since the U.S. Centers for Disease Control and Prevention (CDC) declared overdoses from prescription painkillers an “epidemic” in 2011, the opioid overdose crisis has evolved rapidly from a problem tied mostly to prescription opioid painkillers to becoming increasingly driven by illicitly trafficked heroin and synthetic opioids.

This brief provides high-level information about opioids and opioid addiction, presents the historical context for the epidemic of opioid-related addiction and mortality in the United States, and examines trends in opioid-related mortality across the country and among population subgroups.

Background

Addictive properties of opioids

To better understand the development of the opioid crisis, it is important to recognize the addictive properties of opioids and the relationship between different opioid types. Generally, there are three kinds of opioids: 1) natural opiates, like morphine, which are made from the opium poppy plant; 2) semi-synthetic opioids, like hydrocodone and oxycodone, which are chemically derived from natural opiates; and 3) fully synthetic opioids, like fentanyl, which are chemically created to mimic natural opiates but are typically much more potent. In addition, opioids can be segmented into illicit opioids, such as heroin, and legal opioids, such as painkillers including oxycodone and hydrocodone.\(^4\) Illicit and legal opioids are chemically similar and stimulate the same opioid receptors in the reward centers in the brain, creating similar feelings of euphoria.\(^5\) Repeated use of opioids can affect the chemistry and wiring of the brain, causing addiction that prompts people to crave and use opioids habitually, and can cause symptoms of withdrawal if people stop using opioids.\(^6\)

Because all opioids act similarly in the same parts of the brain, someone who is chemically dependent on a prescription opioid painkiller and unable to obtain it may switch to an illicit opioid, such as a heroin, to relieve their cravings or withdrawal symptoms. In fact, studies have shown that many people who use heroin or misuse prescription opioids began with “legitimate” prescriptions for their own pain treatment or obtained these painkillers from friends or family members with prescriptions.\(^7\)\(^8\)\(^9\) For example, a national study found that 80 percent of people who reported using heroin also reported earlier misuse of prescription opioids.\(^5\) Research also shows that people often advance from misuse of prescription opioids to heroin because heroin provides stronger effects and is often less expensive than prescription opioids.\(^10\)
Rise of the epidemic
The rise of the opioid crisis is commonly attributed to an increase in the prescribing of opioid painkillers, which was driven by a confluence of several factors:

First, in the 1980s some peer-reviewed journals published letters and articles suggesting that opioids were an effective way to treat pain with little risk of addiction. Specifically, a commonly cited 1980 letter published in the *New England Journal of Medicine* and another commonly cited research article published in the journal *Pain* in 1986 are believed to have contributed to a belief that opioids did not pose a high risk for addiction.\(^{11,12,13,14}\)

Second, in the 1990s and 2000s, there was an increased emphasis among health care professionals on the importance of recognizing and treating pain. In 1996, the president of the American Pain Society raised the idea of “pain as a vital sign,” stating that “quality care means that pain is measured and treated”—a concept that was adopted by many health professionals and throughout many health care organizations.\(^{15}\) As examples, the Veterans Health Administration undertook efforts beginning in 1999 to regularly measure and record patients’ self-reported pain on a scale of 0 to 10, and the health care accreditation organization The Joint Commission introduced pain-management standards that encouraged the assessment and treatment of pain.\(^{16,17}\)

In 1995, around the same time that health professionals were focusing on under-treatment of pain, the Food and Drug Administration (FDA) approved the opioid painkiller OxyContin, which has become among the most commonly dispensed controlled substances in the U.S., and which the FDA has since described as “a focal point of opioid abuse issues.”\(^{18}\) In 2007, the maker of OxyContin, Purdue Pharma, settled criminal and civil claims by the U.S. Department of Justice that the company knowingly made false marketing claims that OxyContin was less addictive than other medications.\(^{19,20}\) Despite its renown, the case of OxyContin is not unique; use of other opioid painkillers also has increased substantially, and other pharmaceutical companies have settled charges of misrepresenting the abuse-resistance and addictive properties of their medications.\(^{21,22}\)

U.S. Opioid Deaths
Over more than a decade, the U.S. has experienced statistically significant increases in overdose deaths related to opioids; these increases have occurred throughout the country, with nearly every state having experienced increases in opioid-related deaths since 2000.\(^{23}\) However, data on overdose deaths show a nuanced story, with related but distinct trends in mortality from different types of opioids. Additionally, while opioid death rates have increased for most groups across age, sex, race/ethnicity, and metropolitan/non-metropolitan communities, not all groups have been affected equally.

The following section uses vital statistics data from the CDC to examine national increases in overdose deaths from heroin and other opioids since 2000, as well as differences across groups by age, sex, race/ethnicity, and metro/non-metro communities (state-level analysis can be found in the companion brief: *The Opioid Epidemic: State Trends in Opioid-Related Overdose Deaths from 2000 to 2016*). The analysis below focuses on the opioids that account for the bulk of opioid overdose deaths and are grouped according to how opioid overdose data are collected:

**Natural and semi-synthetic opioids:** Natural and semi-synthetic opioids include most prescription opioid painkiller pills, such as oxycodone and hydrocodone. Although these may be taken legitimately with a prescription, they are also sometimes used illicitly. For example, a person with a prescription may give them away or sell them, or a health care provider may improperly prescribe them (e.g., “pill mills”). Additionally, drug cartels manufacture and traffic counterfeit “prescription” opioid pills, which are sometimes mixed with other drugs.

**Synthetic opioids (except methadone):** Some synthetic opioids, such as fentanyl, also are used legitimately as a medication. However, because they are commonly much more potent than natural and semi-synthetic opioids, synthetic opioids are typically administered in more-controlled settings, such as in a hospital. Recently, drug cartels have begun manufacturing and trafficking synthetic opioids, which are sometimes mixed with other drugs such as counterfeit painkillers and heroin as a way to cheaply increase their potency.

Methadone is one of three medications approved by the FDA for treatment of opioid use disorders and also is used sometimes as a prescription pain reliever medication. Although methadone is a synthetic opioid, our analysis has excluded methadone deaths from the category of deaths from synthetic opioids, mainly because it has not followed the same trend of increasing overdose deaths, and methadone deaths have remained at a relatively low rate compared to other opioids described in this brief.
**Heroin:** Heroin is a form of opioid that is derived from opium poppies and trafficked by international drug cartels. Most heroin sold in the U.S. comes from Latin America, with a smaller amount coming from Afghanistan and Southeast Asia. Heroin is illegal in the U.S. and is typically cheaper to obtain than opioid painkillers, so it is sometimes used as a substitute by people who began their addictions with painkillers.

**Opioid Overdose Deaths**

Between 2000 and 2016, rates of U.S. drug poisoning deaths related to all three types of opioids increased significantly. Drug overdose deaths from natural and semi-synthetic opioids grew more than four times, from 1.0 to 4.4 per 100,000 people (Figure 1). Deaths from heroin increased more than seven times, from 0.7 to 4.9 per 100,000 people. And deaths from synthetic opioids climbed more than 22 times, from 0.3 to 6.2 per 100,000 people.

Although deaths from all three forms of opioids have increased since 2000, their trends have differed. Deaths from natural and semi-synthetic opioids increased gradually but continuously from 2000 to 2010 in a pattern that mirrors legal sales of prescription painkillers. They then dropped slightly for a few years beginning in 2011, likely due to efforts to curb abuse of prescription painkillers through a variety of interventions, such as pharmaceutical companies’ introduction of new tamper-resistant formulations, law enforcement efforts to shut down “pill mills,” and more-stringent prescribing practices by health care providers. Around the same time that deaths from natural and semi-synthetic opioids slowed, deaths from heroin began increasing dramatically, growing from 1.0 per 100,000 people in 2010 to 4.9 deaths per 100,000 people just six years later. That increase may be due to people seeking heroin as a substitute for prescription painkillers as they have become harder to obtain. More recently, deaths from synthetic opioids have increased precipitously, from 1.0 per 100,000 people in 2013 to 6.2 per 100,000 people just three years later. That rise is likely due to fentanyl and similar drugs that are illegally manufactured and trafficked, then commonly mixed with heroin and counterfeit painkillers.

Some research is available to support the hypothesis that the increase in heroin death rates since 2010 may be due, at least in part, to people switching from prescription painkillers to heroin. For example, studies have found that most people who use heroin began by abusing prescription painkillers and that rates of heroin use have increased in recent years among people who use prescription opioids for non-medical purposes. Other studies also have found evidence that a reformulation of the popular prescription opioid OxyContin, designed to make the medication abuse-resistant, may have caused some people to adopt heroin as a substitute.

---

**Figure 1: U.S. Opioid Death Rates Per 100,000 People, 2000-2016**

* Statistically significant at 95% level.

Source: SHADAC analysis of vital statistics data from the CDC WONDER system.
**Opioid deaths by age**

Since 2000, U.S. deaths from opioids have increased measurably across nearly all ages of adolescents and adults, but we focus on non-elderly adults, because they have the highest rates of overdose deaths.\(^{31}\) However, the death rate totals include people of all ages (i.e., children, non-elderly adults, and elderly adults). These increases across age sub-groups largely mirror the overall trends in overdose deaths among the U.S. population as a whole—steep increases in heroin deaths since 2010 and synthetic opioids since 2013, and more gradual but consistent increases in deaths from natural and semi-synthetic opioids since 2000.

Even though opioid death rates for most age groups moved in similar directions over time, actual opioid death rates differed between age groups. In 2016, three age groups had synthetic opioid death rates that were significantly higher than the overall rate for all ages (6.0 per 100,000):\(^{32}\) Adults ages 25-34 had the highest rate for synthetic opioid deaths (13.6 per 100,000), followed by ages 35-44 (11.9 per 100,000) and ages 45-54 (9.0 per 100,000) (Figure 2).\(^{33}\) Adults ages 55-64 had rates that were significantly lower than the overall rate (5.4 per 100,000), and young adults ages 18-24 had a rate that was not significantly different from the overall rate (6.2 per 100,000).

The pattern for heroin deaths was similar to synthetic opioids. Four age groups experiencing heroin overdose death rates higher than the overall rate for all ages (4.8 per 100,000). Adults ages 25-34 had the highest rate for heroin deaths (11.3 per 100,000), followed by ages 35-44 (9.0 per 100,000), ages 45-54 (7.0 per 100,000), and ages 18-24 (5.5 per 100,000). Adults ages 55-64 had rates that were significantly lower than the overall rate (4.3 per 100,000).

The pattern for natural and semi-synthetic opioids differed from heroin and synthetic opioids, skewing toward older adults. In this case, four age groups had death rates higher than the overall rate (4.5 per 100,000): Adults ages 45-54 had the highest rate (8.7 per 100,000), followed by ages 35-44 (7.7 per 100,000), ages 55-64 (7.2 per 100,000), and ages 25-34 (6.3 per 100,000). Young adults ages 18-24 had rates that were significantly lower than the overall rate (3.1 per 100,000).

**Table 2:** U.S. Opioid Death Rates Per 100,000 People by Age, 2016

<table>
<thead>
<tr>
<th>Age Group</th>
<th>Natural and semi-synthetic</th>
<th>Heroin</th>
<th>Synthetic</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total</td>
<td>4.5</td>
<td>11.3*</td>
<td>13.6*</td>
</tr>
<tr>
<td>18-24 years</td>
<td>3.1*</td>
<td>4.3*</td>
<td>5.4*</td>
</tr>
<tr>
<td>25-34 years</td>
<td>6.3*</td>
<td>5.5*</td>
<td>6.2</td>
</tr>
<tr>
<td>35-44 years</td>
<td>7.7*</td>
<td>7.0*</td>
<td>9.0*</td>
</tr>
<tr>
<td>45-54 years</td>
<td>8.7*</td>
<td>9.0*</td>
<td>11.9*</td>
</tr>
<tr>
<td>55-64 years</td>
<td></td>
<td>6.0</td>
<td></td>
</tr>
</tbody>
</table>

* Statistically significant difference from total rate at 95% level.  
Source: SHADAC analysis of vital statistics data from the CDC WONDER system.

**Opioid deaths by race and ethnicity**

Death rates from all types of opioids have increased significantly since 2000 for most races and ethnicities—blacks, whites, and Hispanics/Latinos. Death rates from natural and semi-synthetic opioids also increased significantly among American Indians and Alaska Natives, but statistical testing for increases since 2000 wasn’t possible among this group for heroin and synthetic opioids, and testing since 2000 also wasn’t possible among Asians and Pacific Islanders for any opioid types.\(^{34}\)

In 2016, whites had the highest rates of death for all three types of opioids. The death rate for whites was significantly higher than the overall rate for synthetic opioids (8.2 versus 6.2 per 100,000), heroin (6.3 versus 4.9 per 100,000), and natural and semi-synthetic opioids (6.0 versus 4.4 per 100,000) (Figure 3). American Indians and Alaska Natives were the only other group...
to have an opioid overdose death rate above the overall rate. Their rate for natural and semi-synthetic opioids was significantly higher than the overall rate (5.5 versus 4.4 per 100,000), their rate for heroin was not significantly different from the overall rate (5.0 versus 4.9 per 100,000), and their rate for synthetic opioids was significantly lower than the overall rate. Among Asians and Pacific Islanders, Hispanics/Latinos, and blacks, overdose death rates were significantly lower than the overall rate for synthetic opioids, natural and semi-synthetic opioids, and heroin.

**Figure 3: U.S. Opioid Death Rates Per 100,000 People by Race/Ethnicity, 2016**

* Statistically significant difference from total rate at 95% level.
Source: SHADAC analysis of vital statistics data from the CDC WONDER system.

**Figure 4: U.S. Opioid Death Rates Per 100,000 People by Sex, 2016**

* Statistically significant difference from total rate at 95% level.
Source: SHADAC analysis of vital statistics data from the CDC WONDER system.

**Opioid deaths by sex**

Death rates from synthetic opioids, natural and semi-synthetic opioids, and heroin have increased significantly among both males and females since 2000, but males have consistently had higher rates of overdose deaths for all opioids. However, the gap between overdose death rates varies by type of opioid.

For heroin-related overdoses, females’ death rate in 2016 was less than one-third the rate of males (2.4 versus 7.5 per 100,000). For synthetic opioids, females’ death rate was slightly more than one-third the rate of males (3.5 versus 8.9 per 100,000). But for natural and semi-synthetic opioids, the overdose death rate for females was more than two-thirds the rate of males (3.6 versus 5.2 per 100,000).
The Opioid Epidemic: National Trends, 2000 to 2016

Opioid deaths by urbanization
Death rates from synthetic opioids, natural and semi-synthetic opioids, and heroin have increased significantly since 2000 in all categories of urbanization: large metro, small/medium metro, and non-metro (i.e., rural) areas of the U.S. However, the types of opioids associated with deaths vary across these settings.

In 2016, overdose death rates from synthetic opioids were significantly higher in large metros (6.8 per 100,000) than the overall rate of 6.2 per 100,000 (Figure 5). The rate for non-metro areas was significantly lower at 4.6 per 100,000, and the rate for small/medium metros was also significantly lower (5.8 per 100,000).

For heroin, the pattern was similar. Overdose death rates from heroin were significantly higher in large metros (5.6 per 100,000) than the overall rate of 4.9 per 100,000. The rate for non-metro areas was significantly lower at 3.2 per 100,000, and the rate for small/medium metros was also significantly lower (4.5 per 100,000).

Death rates from natural and semi-synthetic opioids followed an opposite pattern. Non-metro and small/medium metro areas had rates that were significantly higher (5.0 and 4.9 per 100,000, respectively) compared to the overall rate of 4.4 per 100,000, while the rate for large metro areas was significantly lower than the overall rate (4.1 per 100,000).

Figure 5: U.S. Opioid Death Rates Per 100,000 People by Metro Size, 2016

Conclusions
Since 2000, the U.S. has experienced statistically significant increases in opioid-related overdose deaths. This trend began earlier for natural and semi-synthetic opioids, such as prescription painkillers, with increases in overdoses dating to at least the early 2000s. During the past several years, however, the opioid crisis has evolved rapidly. Beginning around 2010, the growth in deaths from natural and semi-synthetic opioids began to slow, replaced with a steeper increase in heroin overdose deaths. Then again around 2014, deaths related to synthetic opioids, such as fentanyl, began an even more-dramatic climb. By 2016, deaths from synthetic opioid overdoses—which used to comprise a small fraction of opioid-related overdoses—now outnumber overdoses from heroin and natural and semi-synthetic opioids.

Our examination of opioid overdose deaths across different segments of the U.S. population shows that, while the epidemic has affected a broad swath of people, certain groups have been harder hit. Among age groups, adults in prime working years—ages 25-54—had the highest opioid-related death rates. Overdoses from heroin and synthetic opioids were particularly high among those age 25-34, while overdoses from natural and semi-synthetic opioids were highest among ages 45-54. The prevalence of overdoses among older working-age adults is somewhat surprising, because other research finds that younger adults (ages 18-25) typically report the highest rates of substance abuse, while adults over age 25 typically report lower rates of substance abuse.35
Our analysis by race/ethnicity found that non-Hispanic whites had the highest rates of overdose deaths for all three types of opioids we examined. But American Indians/Alaska Natives also had relatively high rates of death from natural and semi-synthetic opioids and heroin. In comparison, blacks, Hispanics/Latinos and Asians/Pacific Islanders had opioid death rates that were significantly lower than the overall population.

The epidemic also has affected people in both rural and urban areas across the country, with significant increases in opioid-related deaths across large metro, small/medium metro and non-metro areas. However, there were differences between these groups: Deaths from heroin and synthetic opioids were highest in large metro areas, while deaths from natural and semi-synthetic opioids were highest in non-metro and small/medium metro areas.

Our analysis also found that males consistently have higher rates of opioid overdose deaths than females, but the size of the difference varies by opioid type. Females’ death rates from heroin and synthetic opioids are only approximately one-third the rates for males, but females’ death rates from natural and semi-synthetic opioids are a closer two-thirds the rates of males.

Our findings include insights into the evolving opioid crisis that are important for policymakers to consider as they take steps to address the problem. For example, these data show how the opioid crisis affects various groups of people differently and isn’t predominantly an urban or a rural problem. They also suggest the need for a multi-pronged approach to intervening in the crisis. Efforts to limit prescribing of opioid painkillers cannot eliminate the growth in opioid overdose deaths unless supplies of illegally trafficked heroin and synthetic opioids are also curtailed. The evolution of the opioid epidemic from prescription painkillers (i.e., natural and semi-synthetic opioids) also indicates that unless people with opioid use disorders receive treatment for their addictions, they are likely to simply shift to obtaining opioids from new—and potentially more-dangerous—sources. However, access to needed resources and services, such as opioid addiction treatment and the medication used to reverse opioid overdoses (naloxone), is not equally available to all people. For example, rural areas have known gaps in access to naloxone and treatment for opioid use disorder.\textsuperscript{36,37,38} As policymakers consider solutions to curb opioid overdose deaths, they should also consider differences in need across different sub-populations and the existing barriers that those groups face.
References


4. The issue of legal status of opioid drugs is complex. Heroin, as a Schedule 1 controlled substance, is treated as an “illegal” drug with a high risk for abuse and no medicinal value. Most other opioids, such as oxycodone and hydrocodone, are considered Schedule 2 controlled substances, meaning they have substantial potential for abuse but also have medicinal value. The legality of Schedule 2 opioids depends on how they are manufactured and distributed. If a person takes an opioid painkiller that was properly prescribed and dispensed by licensed health care provider, then that would generally be legal. However, opioid painkillers are sometimes fraudulently prescribed or diverted from their intended patients, which is illegal. Additionally, criminal drug traffickers also manufacture counterfeit opioids that are chemically similar to prescription painkillers (e.g., fentanyl) and sell them illegally on the black market.


32 The death rate totals in the age section may not match the death rate totals in other sections of this brief (e.g., race/ethnicity, gender, metro/non-metro) because this section examines death rates by age groups, which cannot be age-adjusted like in other sections of this brief.

33 Our analysis does not correct for overlap between specific sub-groups (e.g., age, gender) and the total overdose death rates. This results in a more-conservative estimate of statistical significance (i.e., less likely to find a statistically significant difference).

34 Statistical testing from 2000-2016 wasn’t possible for Asians and Pacific Islanders in heroin, natural and semi-synthetic opioids, and synthetic opioids because data are suppressed by the CDC when rates are based on especially small numbers of deaths. That was also the case among American Indians for heroin and synthetic opioids. However, because none of these rates were suppressed by the CDC in 2016, that suggests that death rates for these groups also have increased substantially.


