

# **The American Opioid Crisis and the Future of Drug Policies**

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## ABSTRACT

The U.S. opioid crisis has resulted in the deaths of several hundred thousand people since the early 2000s. It is therefore a major public health crisis. It started on the legal market with massive prescriptions of oxycodone and then developed on the black market with fentanyloids. Who is affected? How can this epidemic be stopped? Could it develop in Europe? What is its significance? These questions are addressed in the article.

**Keywords:** Opioids, crisis, United States, legal market, underground market, oxycodone, fentanyloids

# **La crisis estadounidense de los opioides y el futuro de las políticas de drogas**

## RESUMEN

La crisis de los opioides en EE. UU. ha provocado la muerte de varios cientos de miles de personas desde principios de la década de 2000. Por lo tanto, es una gran crisis de salud pública. Comenzó en el mercado legal con prescripciones masivas de oxicodona y luego se desarrolló en el mercado negro con fentaniloide. ¿Quién está afectado? ¿Cómo se puede detener esta epidemia? ¿Podría desarrollarse en Europa? ¿Cuál es su significado? Estas preguntas se abordan en el artículo.

Palabras clave: Opioides, crisis, Estados Unidos, mercado legal, mercado clandestino, oxicodona, fentaniloide

# **美国阿片类药物危机与毒品政策的未来**

## 摘要

自2000年代初以来，美国的阿片类药物危机已导致数十万人

死亡。因此，这是一场重大的公共卫生危机。这一危机始于合法市场大量的羟考酮处方药，然后在芬太尼类药物黑市上发展起来。谁受到危机的影响？如何才能阻止该危机？危机能在欧洲发展起来吗？危机的意义是什么？本文研究了这些问题。

关键词：阿片类药物，危机，美国，合法市场，地下市场，羟考酮，芬太尼类药物

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“92% of the world’s morphine supply is consumed by only 17% of the population, with consumption concentrated in the North, and 75% of the world’s population has no access to any analgesic medication. The reasons have little to do with cost or scarcity of supply and everything to do with global drug prohibition and repression.”<sup>1</sup> (Global Commission on Drug Policy, 2015).

## **The prehistory of the opioid crisis**

In the United States, the Harrison Act, which preceded the “Volstead Act” of 1919 by five years, prohibited alcohol for fifteen years. It aimed to prohibit the production, importation, and distribution of opiates (opium, morphine, heroin) and cocaine. In principle, it did not prevent doctors from prescribing. But provided, the law specified, that it was “in the exercise of their profession” and “for legitimate medical purposes.” What are legitimate medical purposes?

“Maintenance,” i.e., long-term prescribing for morphine and heroin addicts, was not considered legitimate. In a country where the medical and pharmaceutical world was much less structured than in Europe, and later on the application of the Harrison Act gave rise to a struggle.

Between 1914 and 1920, 44 *narcotic clinics* opened, some of which practiced maintenance.<sup>2</sup> Most of these clinics were harassed by federal agents of the Narcotic Bureau who used, in the words of David Musto, “*threats and intimidation*.”<sup>3</sup> Finally, between 1914 and 1938, twenty-five thousand doctors were prosecuted for selling narcotics, three thousand were imprisoned and thousands more were disbarred.<sup>4</sup> Prescription is now the exclusive jurisdiction of the federal government. In the United States, as in most of the Western world, the medical use of morphine collapsed from the 1920s to the 1970s and 1980s.

In this young country where, seventy years earlier, thousands of doctors were incarcerated for abusive opioid prescriptions, the largest epidemic of fatal opioid overdoses ever seen in the world started with ... massive prescriptions written by doctors!

## **The U.S. Opioid Crisis: An Unprecedented Event**

As of late 2019, we learned that for the first time since 1990, the number of fatal overdoses in the U.S. has decreased, in this case by 5%. But the year 2020 saw deaths rise again. Since 1990, in fact, the number of primarily opioid-related overdoses has increased by 500%. It was about 8,500 25 years ago, 52,000 in 2015, and that number continues to grow with an estimated 60,000 opioid-related deaths in 2017. This makes it the leading cause of death in the United States for those under 50, ahead of car accidents, homicides, suicides, or AIDS deaths.<sup>5</sup> What happened? It all began, starting in the 1970s and 1980s, with a new (and welcome) societal sensitivity to the issue of pain in the Western world.

### **Relieve pain**

For decades, from the 1920s to the 1980s, physicians were very reluctant to prescribe opiates for pain. Morphine was only used in cancer patients, often at the end of life, so much so that, the general opinion was that morphine meant imminent or near death.

This morphinophobia can be explained in good part by the period that preceded it, from the 1870s to the 1920s, when morphine and heroin (diacetylmorphine) were widely prescribed for both physical and mental pain. It was not known, or only discovered, that these substances could provoke a “hunger” that drove the patient to increase the doses while becoming physically dependent: thus, morphine addiction was born. The opiophilia of the 1870s/1920s was therefore followed by a period of opiophobia in the 1920s/1980s. However, from the 1970s and 1980s onwards, there was a real change in the way our societies conceived suffering. From then on, it was the doctor’s duty to “relieve pain.”

### **An explosion in the supply of opioids on the legal market**

If pain is to be managed, the opiophobic mentality of physicians must be addressed. The medical press, both in Europe and the United States, is full of scholarly articles explaining that when an opiate is prescribed for a patient in pain, addiction is rare. Slowly, doctors began to prescribe again. The medicine of pain, algology, took off and pain consultations were created in many hospitals. Administrative obstacles, such as the “carnet à souches” in France, were removed.

Taking advantage of this new sensitivity, most of the opiate laboratories that manufacture opiates and have access to the American market have knowingly lied. One substance sums up these lies: oxycodone.

## **The new youth of oxycodone**

Like heroin, oxycodone is a semi-synthetic opiate. However, while heroin is derived from morphine, itself extracted from *papaver somniferum*, oxycodone is derived from thebaine, the main alkaloid extracted from *papaver bracteatum* or Persian poppy.

Synthesized in 1916, oxycodone began to be used as an analgesic in 1917, “the year of initial enthusiasm.”<sup>6</sup> As early as 1919, cases of iatrogenic addiction to Eucodal, its first commercial name, were described. At the time of the Geneva Limitation Convention in 1931, oxycodone was one of the first fourteen drugs classified in Group 1. And, in 1939, the Health Organization of the SDN regarded “the danger of contracting an addiction by taking Eucodal should not be considered less than the risk of morphinomaniac.”<sup>7</sup> Let us add that after the war, Eubine suppositories enjoyed great “popularity.” How can we imagine for a moment that the Food and Drug Administration (FDA) was unaware of this issue?

In 1995, Purdue Pharma launched OxyContin® on the American market, with a sustained-release formulation that theoretically allows for two doses of analgesia covering the entire 24 hours. The oxycodone file, in which information has been accumulating for more than seventy years, makes it possible to affirm that it does indeed cause physical dependence and the risk of overdose. Nevertheless, Purdue will deny this for the next ten years, while reaping huge profits.

The Food and Drug Administration (FDA) quickly agreed to extend the indications of OxyContin, marketed in 1995, to all severe pain, whether cancerous or not, especially pain of rheumatological origin. The removal of the legal obstacle related to cancer was an opportunity that was immediately seized by the most enterprising laboratories, starting with the one that, as of 2015, is being singled out by all of America: Purdue Pharma. The FDA also accepted dosages of 40, then 80 and finally 160 mg.

In the United States, unlike in Europe, it is possible to advertise many prescription drugs in the mainstream media. Purdue then embarked on an intense television promotional campaign, initially targeting the 70 million Americans with lower back pain. The marketing campaigns were as aggressive as ever and sales exploded.

## **When certain laboratories buy “opinion leaders”**

We know today, after investigations carried out by the most important American newspapers (*The New York Times*, *The Washington Post*, *The New Yorker*, etc.), that certain laboratories have been able to buy many, sometimes prestigious opinion leaders from the medical world. They are responsible for convincing their colleagues to prescribe oxycodone and other opioids such as hydromorphone or

fentanyl in increasingly broad indications. The laboratories have also hired, with comfortable salaries, experts from the administrations with a predilection for the FDA and even the Drug Enforcement Administration (DEA). Moreover, oxycodone has been associated with aspirin since the 1950s, then with paracetamol, which makes its prescription completely commonplace.

### **Oxycodone? A delicious opiate ...**

Still, it's hard to understand why OxyContin has been so successful. Marketing doesn't explain everything. There is a secret: like heroin, oxycodone is a "delicious" opiate. It provides a sweet euphoria to which most people are rarely immune. Almost everyone falls under its spell, both drug users and patients, who discover this drug because they are in pain.

However, this is not the case for all opioids, and the euphoria that an opioid produces is often confused with the weight of the addiction it generates. Take methadone. It is physically highly addictive. Yet it plays a minor role in the current opioid crisis in the United States, even though it has a dual indication in that country: as an OST (opioid replacement therapy) and as a painkiller (level 3). The most likely explanation? Methadone is a "heavy" opiate which is very effective in erasing the signs of withdrawal, but it has very little euphoria. The opioid crisis should encourage us to have a consensus scale.

### **From the legal market to the underground market**

Faced with the increase in overdoses, several American administrations became concerned in the early 2000s and asked the laboratories that market these opioids to take action. The response was the development of *abuse* deterrent galenicals ("*abuse deterrent*") through the combination of oxycodone/naloxone<sup>8</sup> and *tamper resistant galenicals*. This was due to the hardness of the tablet that could not be crushed to make a powder or dissolved in water. In both cases, the aim is to discourage misuse by sniffing or injection. The FDA accepted to validate these new galenic forms, resulting in disastrous effects. Far from solving the crisis, they pushed prescription opiate users into the underground market.<sup>9</sup>

### **Non-Pharmaceutical Fentanyls (NPF) on the underground market**

Up to that point, much has been said about oxycodone, but another opioid, or rather a group of opioids, plays a key role in the crisis: fentanyls. Synthesized in 1959, the first fentanyl was originally used in anesthesiology under the self-explanatory trade name of Sublimaze. It was then prescribed for pain in many forms, including patches (Durogésic), transmucosal tablets (Actiq) and sprays (Instanyl). Fentanyl has many derivatives of which at least three (alfentanil, remifentanil—which is very short acting, and the potent sufentanil) are used in human medicine. Carfen-

tanyl, the most potent opioid ever synthesized, is used only in veterinary medicine. Non-pharmaceutical fentanyls (NPF) or fentanyloids, including carfentanyl, are sold on the underground market or on the Internet and are responsible for thousands of deaths. Produced in China, they are brought to the American black market by Mexican cartels.

Short-acting and euphoric, even if less so than oxycodone or heroin, their potency opens a completely new page in the two-hundred-year history of modern opiates. The legal fentanyls, thus prescribed, certainly held a place in the heap of the corpses. But it is on the clandestine market that they cause carnage. Especially since in 1974 carfentanyl was synthesized. Its analgesic power is ten thousand times that of morphine. It became a kind of myth since it is said that two grains of salt of carfentanyl can take a person from life to death. This does not prevent some users from enjoying fentanyloids, sometimes combined with methamphetamine, and injecting it all together, thus relegating the “good old” speedball (heroin and cocaine) to the status of a remedy for the elderly.

### **Poor whites: first victims**

Finally, this crisis has a specificity: for the first time in decades, it is an epidemic that affects mainly whites. Not just any whites, however: men who live in the countryside or on the outskirts of medium-sized cities, in regions that have been hard hit by deindustrialization and the ravages of globalization. In the northeastern United States, the *Rust Belt* is a symbol of this. It is among these “little whites” that the majority of the 60,000 deaths in 2016 were counted. The great heroin epidemic of the 60s and 70s and the cocaine/crack epidemic of the 80s and 90s primarily affected “visible minorities,” starting with African Americans. Now it is the “deaths by despair” of whites (alcohol, overdoses, suicides) that dominate the picture.<sup>10</sup>

“Since the early 1990s, among whites who died of accidental overdoses, the proportion with a master’s degree has held steady at 9 percent. Two-thirds of the victims had no more than a bachelor’s degree. Blacks and Hispanics were virtually unaffected until the advent of illegal fentanyl in 2013, after which they too experienced a sharp rise in overdose deaths.”<sup>11</sup>

What is happening in the underground market at the same time? Heroin consumption is on the rise again. Mexican cartels quickly realized that demand was increasing. But, starting in 2010, this heroin is frequently cut to NPF. They most often come from China. The precursors to make NPF are fairly easy to find, while the synthesis is relatively simple. The over-prescription of opioids (including pharmaceutical fentanyl) and the dynamism of the underground market are acting in synergy.

## **The long inertia of the Food and Drug Administration**

Today, the “opioid crisis” has received and continues to receive impressive media coverage.<sup>12</sup> This situation has evolved significantly and there is something mysterious about the delay in the recognition of the drama by specialists and then by American society as a whole. Since the mid-1990s, the prescription of opiates for pain has increased, and since the 2000s the death figures have become alarming. Twenty years later, the Food and Drug Administration (FDA) is in the dock: the early extension of the indications for OxyContin to non-cancerous chronic pain (NCCP) opened up a huge market. This included the validation of high doses per unit of intake, and the validation of “*abuse deterrent*” formulations. The main consequence of this was to accelerate the flight of patients to heroin on the underground market. The FDA’s slowness in taking measure of the catastrophe has permanently tarnished its image, while rumors of corruption are circulating.

Further, by an ironic paradox, only the Drug Enforcement Administration (DEA), the armed wing of the “war on drugs,” hated by all the enemies of “punitive prohibition” in the United States, tried, without success, to calm the “prescriptive” madness that had spread to a large part of the medical world and to force the pharmaceutical laboratories to stop pushing doctors to prescribe Oxycontin by all means. They also tried to calm down the “prescriptive” madness which had taken over a good part of the medical world and to oblige the pharmaceutical laboratories to stop pushing doctors to prescribe Oxycontin in the famous “*pills mills*” and in boxes of 100 tablets.

## **When reformers are indicted**

The “*drug warriors*” point the finger at those who have fought for relief for suffering patients. These supporters of “punitive prohibition” gloat and say: “The American crisis gives a small idea of the catastrophe that would be the legalization of drugs! You were told that they were all dangerous, but you preferred to listen to irresponsible demagogues who spend their time explaining that they are not. And here we are!”

This speech is clever, too clever. For the “iron law” of prohibition is at the heart of the current crisis. It is formulated as follows: make and sell on the underground market the most potent substance in the smallest volume.<sup>13</sup> During alcohol prohibition, between 1919 and 1934, the underground market offered neither wine nor beer but only distilled (and often adulterated) spirits with very high alcohol content. Today, fentanyloids are the equivalent of those distilled spirits from the time of the dry law that prohibited alcohol. Since the beginning of the second wave of the epidemic, i.e., in the last ten years, they have killed tens of thousands of people.

Moreover, the opacity of the clandestine market favors overdoses (OD): how can one know if a product is cut with fentanyl? More generally, no one today is able to measure what consequences the American opioid crisis will have on drug policy in America and in the world. Will it put a stop to pain management, to the development of OSTs and, more generally, to drug policy reform based on public health, harm reduction and human rights? Are we going to see essential achievements called into question? We must not hide the fact that the crisis raises these questions.

The United States and Canada now must deal with several million opioid addicts, which requires the mobilization of considerable budgets and the training of professionals. But they also have to find a solution to many outstanding problems: is it reasonable to continue to allow consumer advertising for prescription drugs? Who should check that a laboratory's discourse on its product respects, at the very least, the facts? What credible information should patients have? Who will have access to methadone or buprenorphine substitution treatments?

To face this epidemic in the long term, the authorities will have to mobilize impressive sums of money. Indeed, millions of Americans who have become addicted must be helped to manage their addiction as best they can, thanks to substitution treatments, often using buprenorphine (which, when not combined with psychotropic drugs and/or alcohol, makes OD practically impossible), while needle exchange programs, the creation of low-risk consumption rooms (SCMR), the widest possible access to naloxone, and simple, inexpensive tests to determine if there is NPF in heroin bought on the street or on the Internet should be multiplied. This will take years, the most pessimistic say decades.

Now it's time for the lawsuits. Purdue is bankrupt while Johnson & Johnson and three major distributors have negotiated a \$26 billion settlement in exchange for a stay of proceedings. In the meantime, European countries should ponder these lessons and understand that drug education, education based on facts and not lies, that stands at equal distance from apology and demonization, is indispensable. Doctors need to learn how to prescribe opiates and give their patients relevant information. As for "Big Pharma," its campaigns should be supervised. Men must be a little less helpless to tame the opioid dragon. It would be disastrous if this crisis were to result in a pure and simple reversal and if a triumphant opioid phobia were to deprive us of the benefits of opioids.



## Endnotes

- 1 The Global Commission on Drug Policy. “The Negative Impact of Drug Control on Public Health: The Global Crisis of Avoidable Pain.” 2015. <http://www.globalcommissionondrugs.org/reports/the-negative-impact-of-drug-control-on-public-health-the-global-crisis-of-avoidable-pain>
- 2 Annie Mino: “Analyse de la littérature sur la remise contrôlée d’héroïne et de morphine,” Office fédéral de santé publique, Confédération Helvétique, 1990, and Annie Mino and Sylvie Arsever, *Jaccuse les mensonges qui tuent le drogués*, Calmann-Lévy, 1996.
- 3 David Musto, *The American disease, origins of narcotic control*, Oxford University Press, 1987, p. 184.
- 4 Anne Coppel and Christian Bachmann, *Le Dragon domestique, deux siècles de relations étranges entre l’Occident et les drogues*, Albin Michel, 1989, p. 374.
- 5 Josh Katz, “You draw it: how bad is the Drug Overdose Epidemic?” *The New York Times*, April 14, 2017.
- 6 Dr. G. Varenne, *L’Abus des drogues*, Dessart, 1971, p. 136-141.
- 7 *Ibid.*, p. 137.
- 8 This combination is supposed to discourage misuse by injection or sniffing because, unlike the oral route, naloxone can then act and cause a temporary state of withdrawal. Suboxone, a combination of high-dose buprenorphine and naloxone, follows the same logic.
- 9 See in particular William N. Evans, Ethan Lieber, and Patrick Power, “How the reformulation of OxyContin ignited the heroin epidemic,” The National Bureau of Economic Research, April 2018, and Briony Larance, Timothy Dobbins, Amy Peacock, Robert Ali, Raimondo Bruno, Nicholas Lintzeris, Michael Farrel, and Louisa Degenhardt, “The effect of a potentially tamper-resistant oxycodone formulation on opioid use and harm: main findings of the National Opioid Medications Abuse Deterrence (NOMAD) study,” *The Lancet psychiatry*, January 10, 2018.
- 10 Anne Case and Angus Deaton, “Morbidity and mortality in the 21<sup>st</sup> century,” *Brookings papers on Economic Activity*, Spring 2017.
- 11 Anne Case and Angus Deaton, *Deaths of Despair, the Future of Capitalism*, Paris, PUF, 2021, pp. 155–156. It should be noted that numerous other studies tend to show that in the United States, from 1990 to 2013/2014, poor whites are overrepresented among opioid overdose deaths. Chapter 5 of *Deaths of Despair* (pp. 89–99) is thus titled “Black Deaths and White Deaths.”
- 12 For example, *The New Yorker* of October 30, 2017, published Patrick Radden Keefe’s major investigation, “The family that built an empire on bread” on the Sackler family, while *Time* magazine devoted its entire March 5, 2018, issue to a photographic report

on this crisis, but focused almost exclusively on the injectors.

- 13 Leo Beletsky and Corey S. Davis, "Today's fentanyl crisis: Prohibition's Iron Law revisited," *International Journal of Drug Policy* 46 (2017): 156–159. The "iron law of prohibition" is a term coined by Richard Cowan and argues that "the stronger the repression, the more potent the prohibited substances." (Richard Cowan, "How the Narcs Created Crack," *National Review*, December 5, 1986, pp. 30–31).