

A Brief History of Heroin Use in the United States:

EVOLVING IMPACT ON RX DRUG ABUSE

Phil Walls, RPh

@Phil_Walls_



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Individuals who were addicted to prescription opioids are 40 times more likely to become addicted to heroin.



When heroin was first discovered in 1874 its properties were poorly understood, and as a result, it was grossly overused. This led to significant addiction problems well into the 20th century, and the use of heroin and all of the related opioid analgesics was frowned upon by the medical community. In fact, throughout much of the 20th century, physicians would allow patients to die in pain rather than treat them with opioids. All of that changed in the 1990s, but unfortunately the medical community was misled with regard to the true addiction dangers of opioids—and iatrogenic, or physician-induced, addiction became quite common, resulting in a prescription drug abuse epidemic.

However, several factors have curtailed the use of these prescription drugs in recent years, notably:

- Improved physician and prescriber education
- The Food and Drug Administration's Risk Evaluation and Mitigation Strategy
- State Prescription Drug Monitoring Programs

As a result, recent data indicates the overuse of prescription opioids and resultant accidental deaths are on the decrease. Unfortunately though, the efforts to date have not solved the addiction problem itself, yielding the unintended consequence of the first rise in heroin use in decades. Although not all heroin addicts started with prescription opioids, those who did are finding that street heroin is both easier to find and cheaper to purchase than the prescription opioids that started their addiction.

Workers' compensation is certainly not immune to this consequence, and therefore, the possibility of injured workers becoming addicted to heroin is quite high. In fact, individuals who were addicted to prescription opioids are 40 times more likely to become addicted to heroin. This paper will first place heroin use in a historical context, examine causes for the current epidemic, and then arm the claims professional involved in the management of workers' compensation claims with the tools necessary to help prevent the crisis from continuing.

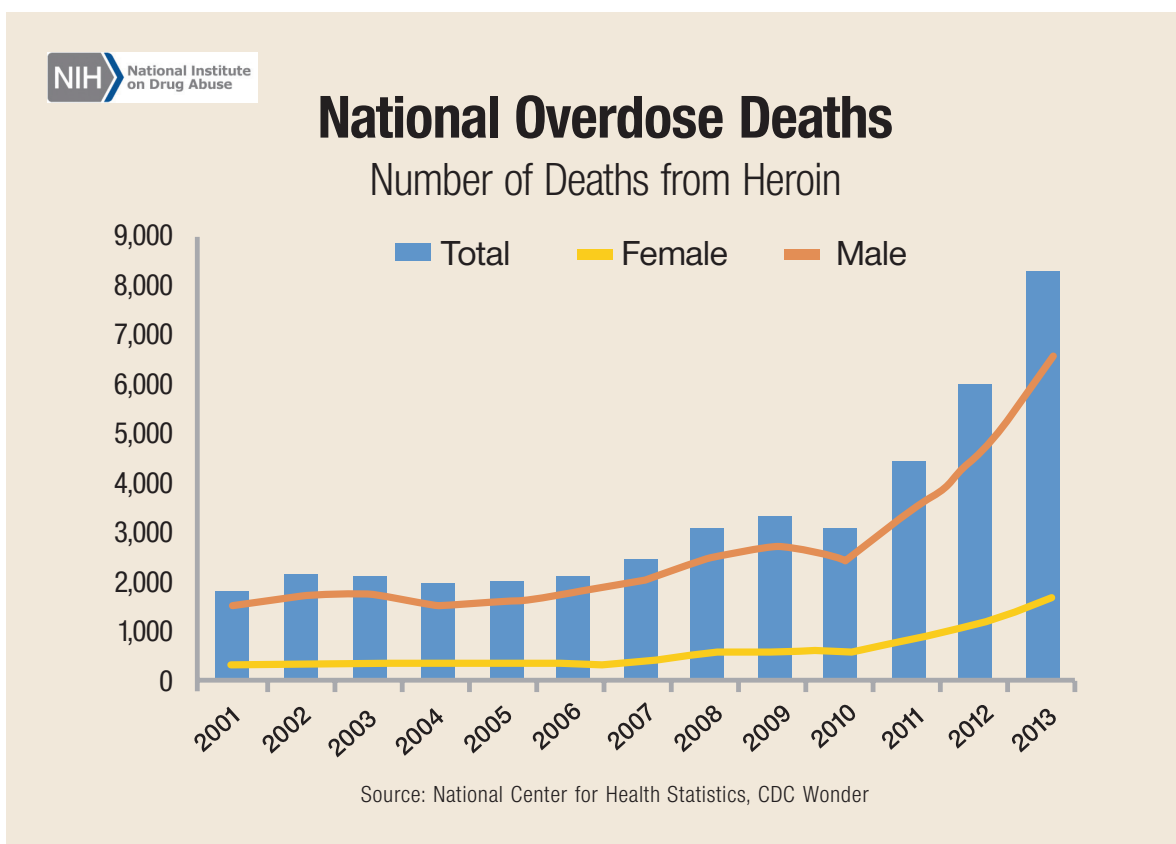
Over the past several years, myMatrixx has considered several drug-related subjects to be hot topics for classes and seminars in workers' compensation. These have included subjects such as the legalization of marijuana, physician dispensing, compounding, and of course, prescription drug abuse especially as it relates to opioids. With regard to the latter, myMatrixx has been receiving frequent questions regarding opioids and heroin, of which a few are listed below:

- Is heroin an opioid?
- Is it true that prescribing opioids is tantamount to giving patients heroin?
- Are physicians culpable for iatrogenic addiction?

This white paper has been written to answer questions such as these and to provide further insight into the current prescription drug epidemic and what the workers' compensation community can do to help prevent addiction and to respond to it appropriately when it does occur.

This white paper is being presented as a historical review of heroin use in the United States in order to give the reader context in which to place the current resurgence in heroin use. Unfortunately, we are witnessing a significant increase in overdose deaths related to heroin as seen in the chart below.¹

The cause for this increase is complex, and there is no single entity responsible, but there have been key events that have contributed to this phenomenon. Likewise, the cure will also be complex. One can only hope that we do not repeat the mistakes of the past.



¹ National Center for Health Statistics, CDC

Heroin was first synthesized in 1874 by an English chemist named Charles Alder Wright.² However, that simple statement does not adequately describe the events leading up to this development; therefore, let's examine an earlier event that has been considered by many to be the first isolation of a drug from a plant source – the isolation of morphine from the opium poppy – along with the genesis of what was to become the modern pharmaceutical industry.

Morphine was first isolated from opium in 1806 by a German pharmacist assistant named Friedrich Seturner. Seturner experimented with the drug on himself, and because of the euphoric effects named it Morphiium after the Greek god of dreams, Morpheus.³ However, widespread use of the drug was not going to occur for several decades and was dependent on another event: the development of the hypodermic needle in 1853.⁴ Regardless of the delay in use, the isolation of morphine represented a significant change in the profession of pharmacy, and a young German entrepreneur named Heinrich Emanuel Merck converted his pharmacy into a full-time commercial producer of morphine in 1827. That pharmacy, located in Darmstadt, Germany was named Engel-Apotheke. That translates to The Angel Pharmacy. Today, that same company is known as Merck and Company⁵ and ranks among the top five pharmaceutical companies in the world.⁶



The first injection of morphine occurred in 1853 by a physician named Alexander Wood, who independently invented the hypodermic syringe at the same time as another physician named Charles Pravaz. Dr. Wood published his findings in a paper entitled “A New Method for Treating Neuralgia by the Direct Application of Opiates to

Painful Points,” published in the Edinburgh Medical and Surgical Journal in 1855. Sadly, his wife “who was injecting morphine to excess” became the first fatality as the result of an injected overdose of morphine.



Alexander Wood
(1817 - 1884)

At that time, neither Dr. Wood nor Dr. Pravaz would have known that their invention would be responsible for increasing the euphoric effect of opioids, which in turn would increase the incidence of addiction. Essentially, the faster an opioid can be introduced into the body, the greater the euphoric effect and the greater the risk of addiction. To this day, the hypodermic syringe is still the fastest way to get a drug into the bloodstream, and that is why many modern day victims of the prescription drug abuse epidemic attempt to grind up and dissolve a prescription tablet in order to inject it.

Dr. Wood's work preceded the American Civil War by almost a decade, and both morphine and the hypodermic syringe were used to excess during that war. Physicians at that time had little if any experience with the drug especially as an injectable drug, and yet it came at a time of war when there were no alternatives for pain and suffering. Approximately 400,000 soldiers became addicted to the drug. As a result, “the returning veteran could be... identified because he had a leather thong around his neck and a leather bag (with) Morphine Sulfate tablets, along with a syringe and a needle issued to the soldier on his discharge...This was called the “Soldier's Disease” or “Old Soldiers' Disease.”

² <http://www.thelancet.com/pdfs/journals/lancet/PIS0140673698071153.pdf>

³ <http://factsanddetails.com/world/cat54/sub348/item1219.html>

⁴ <http://www.historytoday.com/ian-scott/heroin-hundred-year-habit>

⁵ Heroin: Its History, Pharmacology & Treatment By Humberto Fernandez, Therissa A. Libby (<https://books.google.com/books?id=4ilsUorX6wsC&pg=PT25&lpg=PT25&dq=merck+and+heroin&source=bl&ots=148jSliOrU&sig=9ZTG3S0qpZ0sj8ou6cgNM4YPqFU&hl=en&sa=X&ei=49SaVZ75F8W0ggSDr4HgAw&ved=0CDoQ6AEwBA#v=onepage&q=merck%20and%20heroin&f=false>)

⁶ http://www.pmlive.com/top_pharma_list/global_revenues

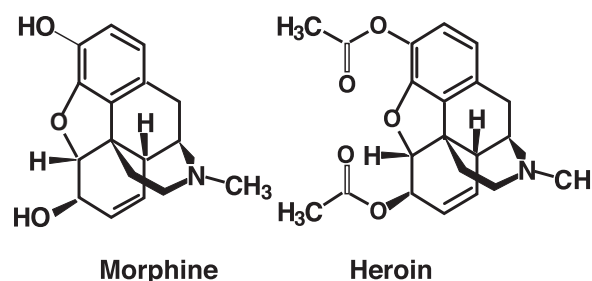
One such veteran was a confederate colonel named John Pemberton. Colonel Pemberton was wounded during the war and like many others became addicted to morphine.⁷ Trained as a pharmacist, Colonel Pemberton produced an elixir that contained both cocaine and the kola nut. In 1886, he marketed this elixir to treat morphine addiction among other things and branded it as Coca Cola. The original formula containing cocaine was available until 1905.⁸

Surprisingly, surveys conducted between 1878 and 1885 revealed that the real crisis was not restricted to war veterans alone. The majority of opium addicts in the United States at that time were middle- to upper-class white women who purchased the drug legally.⁹ Opium was readily available in cough syrups and elixirs, and the addiction went largely unnoticed because the majority of these addicts remained in the home. The use of opium was so widespread that it was recommended to help with teething pain in infants and advertised as “The Mother’s Friend.”



Recall that a young chemist named Charles Alder Wright first synthesized heroin in 1874. The chemical name for heroin is diacetylmorphine, and as the name implies, it is chemically very similar to morphine and as such is indeed an opioid. However, at that time, heroin was not recognized as having any particularly important qualities.

Similarities Between the Chemical Structure of Morphine and Diacetylmorphine (Heroin):



Note the presence of the two acetyl groups in heroin:



When compared to morphine, the structure literally differs by the addition of four carbon atoms, two oxygen atoms and four hydrogen atoms.

The use of opium was so widespread that it was recommended to help with teething pain in infants and advertised as “The Mother’s Friend.”

⁷ Richard Gardiner, “The Civil War Origin of Coca-Cola in Columbus, Georgia,” *Muscogiana: Journal of the Muscogee Genealogical Society* (Spring 2012), Vol. 23: 21–24.

⁸ http://inventors.about.com/od/cstartinventions/a/coca_cola.htm

⁹ Heroin: Its History, Pharmacology & Treatment By Humberto Fernandez, Therissa A. Libby
(<https://books.google.com/books?id=4ilsUorX6wsC&pg=PT25&lpg=PT25&dq=merck+and+heroin&source=bl&ots=148jSli0rU&sig=9ZTG3S0qpZ0sj8ou6cgNM4YPqFU&hl=en&sa=X&ei=49SaVZ75F8W0ggSDr4HgAw&ved=0CDoQ6AEwBA#v=onepage&q=merck%20and%20heroin&f=false>)



Am. J. Ph. J 7 [December, 1901]

BAYER Pharmaceutical Products
HEROIN—HYDROCHLORIDE

is pre-eminently adapted for the manufacture of cough elixirs, cough balsams, cough drops, cough lozenges, and cough medicines of any kind. Price in 1 oz. packages, \$4.85 per ounce; less in larger quantities. The efficient dose being very small (1-48 to 1-24 gr.), it is

The Cheapest Specific for the Relief of Coughs
(In bronchitis, phthisis, whooping cough, etc., etc.)

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Nat. Struct. Biol. 10, 349?356 (2003).

By the mid-1880s, a seemingly unrelated event occurred in Germany: a shortage of raw materials necessary for a once-booming German dye industry developed. A young German entrepreneur named Friedrich Bayer had invested heavily in developing a factory in Elberfeld, Germany to develop new processes to produce these dyes. This shortage prompted him to diversify his company by investing in research and development of medicines.¹⁰ The chemists working for Bayer seized upon the opportunity to take powerful drugs extracted from plants – like morphine – and modify them in hopes of making them more effective or safer – a practice that continues to drive many discoveries in the pharmaceutical industry today. One of their first discoveries was actually the re-discovery of diacetylmorphine by chemist Heinrich Dreser in the late 1890s. Bayer named this drug heroin from the German word *heros* meaning hero.

With the introduction of drugs like heroin, it also became necessary to distinguish between drugs like morphine that were naturally occurring in the opium poppy plant versus those like heroin that are synthetic derivatives. Therefore, the term *opiate* designates the naturally occurring drugs, whereas *opioid* refers to all *opiate-like* drugs and, therefore, includes both morphine and the synthetic derivatives including heroin, oxycodone, hydrocodone, etc. Narcotic is a term that once referred to drugs related to the opium poppy, but that term has fallen in disfavor in the medical community because today it is used by law enforcement

Bayer named this drug heroin from the German word *heros* meaning hero.

as a term synonymous with controlled substances, which includes many dangerous drugs like amphetamine, cocaine and others that are not related to the opium poppy at all.

This discovery was followed a year later by the discovery of acetylsalicylic acid. In a process very similar to the creation of diacetylmorphine from the naturally occurring morphine, acetylsalicylic acid was synthesized from the acetylation of salicylic acid, which is naturally occurring in the bark of the willow tree. Bayer named this new drug aspirin. Ironically, aspirin required a prescription whereas heroin did not.

Bayer, along with Merck, had launched the advent of the modern pharmaceutical industry with the development and mass production of three of the world's most popular analgesics: morphine, heroin and aspirin. Of these three, heroin was promoted as a safe and non-addictive substitute for morphine. In fact, the medical community at this time was so concerned with morphine addiction and withdrawal that physician A. Morel-Lavallée proposed in 1902 that heroin be used in the “demorphinisation” of morphine addicts.¹¹—and thus began the practice of treating addiction to one drug with the use of another drug.

Heroin remained unregulated until 1920.¹²

Ironically, aspirin required a prescription whereas heroin did not.

¹⁰ <http://www.historytoday.com/ian-scott/heroin-hundred-year-habit>

¹¹ <http://www.historytoday.com/ian-scott/heroin-hundred-year-habit>

¹² <http://www.narconon.org/drug-information/heroin-history.html>

Early Attempts to Regulate and Control Heroin

By the early 1900s, drug companies were producing kits that contained a hypodermic syringe and a vial of either an opioid like morphine or heroin or a drug such as cocaine.

Marketing of these drugs promised cures for all sorts of conditions including alcohol withdrawal, cancer, depression, sluggishness, coughs, colds, tuberculosis and even old age. Snake oil salesmen almost always included one of these drugs in their elixirs.¹³ As the United States entered the twentieth century, between 250,000 and 300,000 of its citizens were addicted to one of these drugs. On a per capita basis, this appears to be more serious than heroin addiction today, with an estimated 467,000 heroin addicts in 2012. However, when one factors in an additional 2.1 million individuals diagnosed with substance abuse disorders related to prescription opioids that appearance changes drastically.¹⁴ A later section will evaluate the differences and similarities between the various opioids, but consider for now the fact that heroin and morphine differ by only a few carbon, oxygen and hydrogen atoms and the distinction between an illicit drug like heroin and a prescription drug like morphine fades dramatically.

As a result, attempts to regulate these drugs were met with considerable resistance by the manufacturers. Indeed, these companies now possessed significant financial power and were among the largest advertisers in print publications. Therefore, newspapers were disdain to publicize the dangers of addiction associated with their best clients.¹⁵ The U.S. was also lagging way behind Britain and Germany, which had both enacted pharmacy laws by the end of the previous century to curtail the use of these drugs. However, in the United States, medical regulation was handled only at the state level. Reminiscent of today's concerns over differences in state laws regarding legalized marijuana, physician dispensing, or the use of a prescription drug monitoring program, individuals could simply cross state lines to obtain whatever they wanted.



Syringe Hypodermic Set, 1800s

One of the first changes at the federal level came in 1906 with passage of the Pure Food and Drug Act. Not surprisingly, this act was met with much resistance because it required the manufacturers of these so-called “patent” medications to accurately label the contents of their products, and therefore the public could readily identify ingredients such as opium, cocaine or cannabis. Interestingly, one of the few products that survived this era was Coca Cola.

Following the Pure Food and Drug Act by almost a decade was passage of the Harrison Narcotic Act, which was signed into law by President Woodrow Wilson in 1914. At best, the Harrison Narcotic Act represented a compromise between the drug companies that made significant profits from the sale of narcotics and the reformers led by Dr. Hamilton Wright, who erroneously fueled the notion that addiction was increasing at a pace faster than population growth. Neither side was completely honest, and the compromise position simply created a tax to be paid by entities involved in the sale of these drugs, including physicians, druggists, manufacturers and importers.

¹³ <http://www.narconon.org/drug-information/heroin-history.html>

¹⁴ <http://www.drugabuse.gov/about-nida/legislative-activities/testimony-to-congress/2014/americas-addiction-to-opioids-heroin-prescription-drug-abuse>

¹⁵ Heroin: Its History, Pharmacology & Treatment By Humberto Fernandez, Therissa A. Libby
(<https://books.google.com/books?id=4ilsUorX6wsC&pg=PT25&lp=PT25&dq=merck+and+heroin&source=bl&ots=148jSli0rU&sig=9ZTG3S0qpZ0sj8ou6cgNM4YPqFU&hl=en&sa=X&ei=49SaVZ75F8W0ggSDr4HgAw&ved=0CD0Q6AEwBA#v=onepage&q=merck%20and%20heroin&f=false>)

However, more significant possibly than the tax itself were two seemingly innocuous components of the law. First, the law defined narcotics as both opium- and coca-based drugs, thus combining drugs like heroin and cocaine into a single category. This was completely contrary to medical practice which defined narcotics as drugs that induce sleep or stupor and was in no way related to a stimulant like cocaine. This contradiction still leads to confusion today as law enforcement and medical practitioners use the same term for two different purposes. Secondly, the law did not reference whether or not it was legal to allow an addict to continue to receive a supply of narcotics on an indefinite basis. Therefore, the act was reviewed by the Supreme Court. Initially, the court ruled that it was unconstitutional for the act to stop physicians from prescribing narcotics for addicts, but then it reversed that decision in 1919, setting the stage for opinions – both medical and lay – with regard to narcotics usage for decades to come.¹⁶

This reversal of opinion was narrowly supported, and the defendant Alexander Ameris was described as a ‘dope fiend.’ Furthermore, the physician involved profited by prescribing large doses of heroin to Mr. Ameris and others. He averaged more than 80 morphine prescriptions a week at 50 cents each – a sizeable income at that time. Because of the characterization of the patient and the questionable ethics of the physician, this court ruling likely set the stage for conservative attitudes for years or even decades to come. Over twenty years later, a letter to the editor of the Journal of the American Medical Association summed up the attitude of the first half of the twentieth century by blasting the medical community with the following statement: “The use of narcotics in the terminal cancer patient is to be condemned . . . due to undesirable side effects . . . dominant in the list of these . . . is addiction.”¹⁷



The 1960s represented a decade of turbulence and change. America's involvement in the Vietnam War became substantial in 1961. Outrage over this war, combined with skepticism over perceived misinformation from authorities about marijuana use, helped create a youth counterculture that was very willing to experiment with marijuana and other drugs, including heroin. The decade was also marred by a series of assassinations starting with Ngo Dinh Diem, the President of South Vietnam on November 2, 1963. This event was followed by the assassination of President John F. Kennedy less than three weeks later. Malcom X was assassinated in 1965, and in 1968 civil rights leaders Dr. Martin Luther King, Jr., and Senator Robert F. Kennedy were assassinated. During this same era, the impact of the drug culture became very apparent with the accidental overdose deaths of two highly visible pop culture icons: Jimi Hendrix, rock guitar legend, died on September 18, 1970, as the result of an excess dose of sleeping pills, followed by rock singer Janis Joplin who died from a heroin overdose on October 4, 1970.

The following May, Congressman Robert Steele and Congressman Morgan Murphy traveled to Vietnam for an official visit. One of their most memorable conclusions from that visit was that an estimated 15% of U.S. servicemen in Vietnam were addicted to heroin. Although the military disputed that claim by placing the estimate at closer to 2%, the placement of heroin at the top of the most dangerous drugs list was once again implanted in the collective mind

¹⁶ http://www.ncbi.nlm.nih.gov/books/NBK234750/pdf/Bookshelf_NBK234750.pdf
pp 7-9

¹⁷ Lee LE Jr. Medication in the control of pain in terminal cancer. JAMA 1941;116:216-219

of the American public.^{18 19} The debate, however, should not have been about whether or not heroin was dangerous, but rather on the causes of addiction, along with recognition once again that there are many dangerous drugs available to those individuals with a propensity – genetic or otherwise – toward addiction.

All of this activity came about almost simultaneously with implementation of the Comprehensive Drug Abuse Prevention and Control Act of 1970 on May 1, 1971. This act invoked severe penalties against the drug pushers while extending leniency toward the drug users. This act also included the Controlled Substances Act (CSA), which among other things created the five schedules that rank drugs according to their potential for abuse and addiction. Please see the section on the next page entitled *Controlled Substance Act of 1970*.

In addition, the report from Congressmen Steele and Murphy had a direct impact on then-President Richard M. Nixon. On June 17, 1971, in a special message to Congress on drug abuse prevention and control, President Nixon stated that “[drug abuse] has assumed the dimensions of a national emergency.” Several key components were outlined in his message:

- The president created a new office dedicated to fighting the drug abuse problem: the Special Action Office of Drug Abuse Prevention
- He pointed out that drug abuse could no longer be considered a “class problem”
- Focus was placed on rehabilitation with special attention given to returning veterans
- He asked Congress to amend the Narcotic Addict Rehabilitation Act of 1966 to increase access to methadone maintenance programs.²⁰

¹⁸ <http://www.ncbi.nlm.nih.gov/books/NBK234755/>

¹⁹ www.npr.org/sections/health-shots/2012/01/02/144431794/what-vietnam-taught-us-about-breaking-bad-habits

²⁰ www.presidency.ucsb.edu/ws/?pid=3048#axzz1hwOalbU1

²¹ Crime, Justice, and Society. Calvin J Larson and Gerald R Garrett

America's War on Drugs OVERVIEW

America's War on Drugs had begun, but the war would be long-lived, and every president since Nixon has grappled with this issue. Early battles yielded apparent success with the break-up of the infamous *French Connection*, which involved a trafficking operation that moved heroin from Marseilles in southern France to New York City and resulted in shortages of heroin on the east coast in 1972. However, Mexico quickly replaced France as a major supplier of heroin to the United States.²¹ This operation was followed in 1973 with the creation of the Drug Enforcement Administration (DEA) by President Nixon – heralded as a *super agency*.

Notable events in the war on drugs included:

1975: the Ford administration names marijuana a low priority drug

1976: Carter campaigns for decriminalization of marijuana

1978: the Comprehensive Drug Abuse Prevention and Control Act is amended to allow law enforcement to seize “all things of value” involved in and exchange for controlled substances

1981 - 1982: rise of the Medellín Cartel in Colombia and creation of a bilateral extradition treaty between the governments of Colombia and the United States

1984: Nancy Reagan launches her “Just Say No” campaign, which becomes a focal point of President Reagan’s anti-drug campaign

1989: President Bush creates the Office of National Drug Control Policy (ONDCP) and campaigns to “make drug abuse socially unacceptable.” Spending for treatment and law enforcement increases under the ONDCP, but the budget for treatment is less than one-third that of law enforcement.

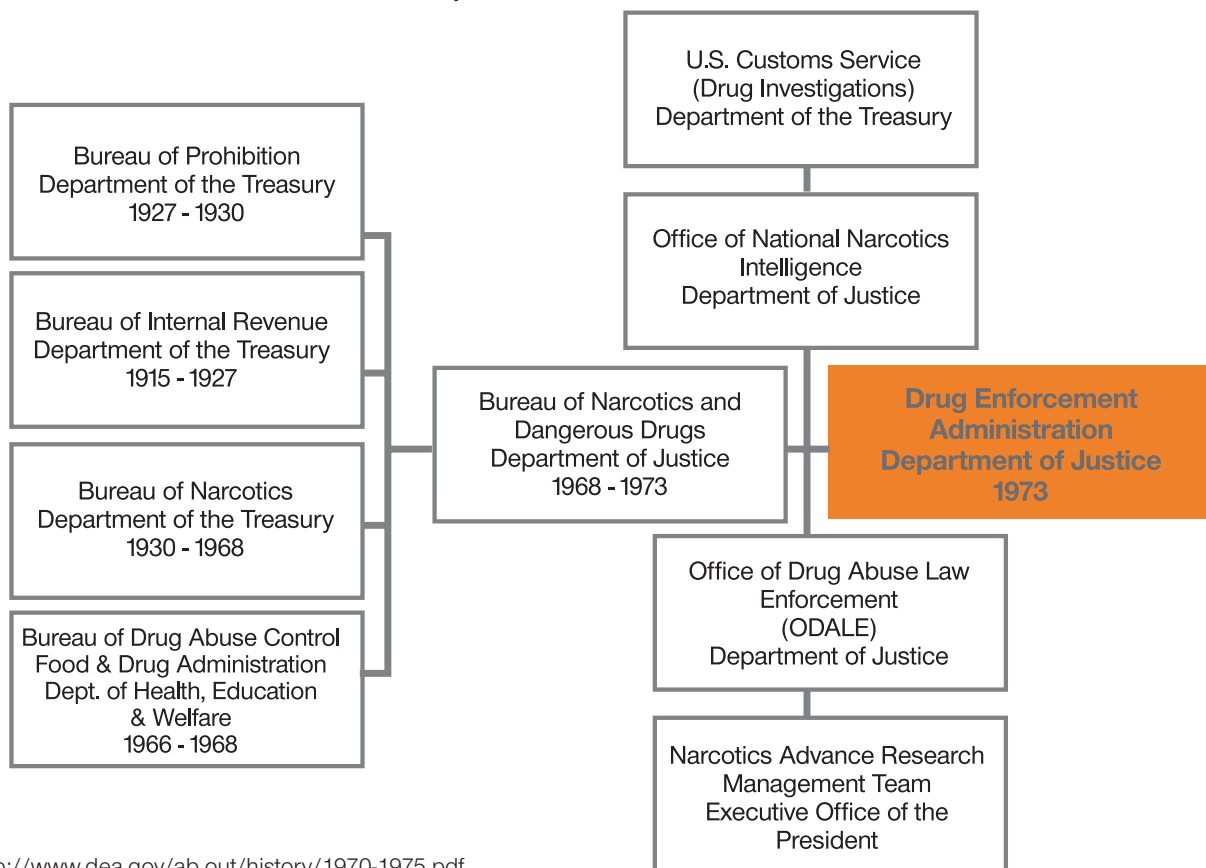
1993: President Clinton signs the North American Free Trade Agreement (NAFTA). This agreement results in a significant increase in legitimate trade shipments across the Mexican-U.S. border but has the unintended consequence of making it difficult for U.S. Customs agents to find contraband narcotics in these shipments.

2000: President Clinton commits \$1.3 billion in aid to Colombia to fight drug trafficking.

Controlled Substance Act of 1970:

Evolution of Federal Agencies Involved with Narcotics Control

The Prohibition Unit was created in 1920 as part of the Bureau of Internal Revenue to enforce the National Prohibition Act of 1919, which forbade the manufacture, sale and transportation of alcoholic beverages. In 1927, this unit was converted into the Bureau of Prohibition as part of the Department of the Treasury. In 1930, with the repeal of prohibition, the Bureau of Narcotics was created and remained part of the Department of the Treasury through 1968. At that time, the recognition of the existence of dangerous drugs other than narcotics led to the creation of the Bureau of Narcotics and Dangerous Drugs. Also at this time, responsibility for the Bureau shifted from the Department of the Treasury to the Department of Justice. President Nixon then created the DEA as we know it today.²²



<http://www.dea.gov/ab,out/history/1970-1975.pdf>

The Controlled Substance Act of 1970 laid the foundation for the enforcement activities of the DEA.

²² <http://www.dea.gov/ab,out/history/1970-1975.pdf>

Drugs of Abuse | Uses and Effects

Narcotics								
	Drugs	Heroin	Morphine	Hydrocodone	Hydromorphone	Oxycodone	Codeine	Other Narcotics
	CSA Schedules	Substance I	Substance II	Substance II, Product III, V	Substance II	Substance II	Substance II, Product III, V	Substance II, III, IV
	Trade or Other Names	Diamorphine, Horse, Smack, Black Tar, Chiva, Negra (Black Tar)	MS Contin, Roxanol, Oramorph SR, MSR	Hydrocodone w/ Acetaminophen, Vicodin, Vicoprofen, Tussionex, Lortab	Dilaudid	Roxicet, Oxycodone w/ Acetaminophen, OxyContin, Endocet, Percocet, Percodan	Acetaminophen, Guaifenesin or Promethazine w/Codine, Fiorinal, Tylenol w/Codine	Fentanyl, Demerol, Methadone, Darvon, Stadol, Talwin, Paregoric, Buprenex
	Medical Uses	None in U.S., Analgesic, Antitussive	Analgesic	Analgesic, Antitussive	Analgesic	Analgesic	Analgesic, Antitussive	Analgesic, Antitussive, Antidiarrheal
Dependence	Physical:	High	High	High	High	High	Moderate	High-Low
	Psychological:	High	High	High	High	High	Moderate	High-Low
	Tolerance:	Yes	Yes	Yes	Yes	Yes	Yes	Yes
	Duration (Hours)	3-4	3-12	3-6	3-4	3-12	3-4	Variable
	Usual Method	Injected, Snorted, Smoked	Oral, Injected	Oral	Oral, Injected	Oral	Oral Injected	Oral, Injected, Snorted, Smoked
	Possible Effects	Euphoria, drowsiness, respiratory depression, constricted pupils, nausea						
	Effects of Overdose	Slow and shallow breathing, clammy skin, convulsions, coma, possible death						
	Withdrawal Symptoms	Watery eyes, runny nose, yawning, loss of appetite, irritability, tremors, panic, cramps, nausea, chills and sweating						
Depressants					Stimulants			
	Drugs	gamma Hydroxybutyric Acid	Benzodiazepines	Other Depressants	Cocaine	Amphetamine/ Methamphetamine	Methylphenidate	Other Stimulants
	CSA Schedules	Substance I, Product III	Substance IV	Substance I, II, III, IV	Substance II	Substance II	Substance II	Substance III, IV
	Trade or Other Names	GHB, Liquid Ecstasy, Liquid X, Sodium Oxybate, Xyrem	Valium, Xanax, Halcion, Ativan, Restoril, Rohypnol, Roofies, Klonopin	Ambien, Sonata, Mephedrone, Chlorale Hydrate, Barbiturates, Methaqualone (Quaaludes)	Coke, Flake, Snow, Crack, Coca, Perico, Nora, Soda	Crack, Ice, Crystal Meth, Speed, Adderall, Dexedrine, Desoxyn	Ritalin, Concerta, Focalin, Metadate	Adipex P, Prelu-2, Didrex, Provigil
	Medical Uses	None in U.S., Analgesic, Antitussive	Antianxiety, Sedative, Anticonvulsant, Hypnotic, Muscle Relaxant	Antianxiety, Sedative, Hypnotic	Local Anesthetic	Attention deficit, hyperactivity disorder, narcolepsy, weight control	Attention deficit, hyperactivity disorder	Varicostriction
Dependence	Physical:	Moderate	Moderate	Moderate	Possible	Possible	Possible	Possible
	Psychological:	Moderate	Moderate	Moderate	High	High	High	Moderate
	Tolerance:	Yes	Yes	Yes	Yes	Yes	Yes	Yes
	Duration (Hours)	3-6	1-8	2-6	1-2	2-4	2-4	2-4
	Usual Method	Oral	Oral, Injected	Oral	Snorted, smoked, injected	Oral, smoked, injected	Oral, snorted, smoked	Oral
	Possible Effects	Slurred Speech, disorientation, drunken behavior without aid of alcohol, impaired memory of events, interacts with alcohol				Increased alertness, excitation, euphoria, increased pulse rate and blood pressure, insomnia, loss of appetite		
	Effects of Overdose	Shallow respiration, clammy skin, dilated pupils, weak and rapid pulse, coma, possible death				Agitation, increased body temperature, hallucinations, convulsions, possible death		
	Withdrawal Symptoms	Anxiety, insomnia, delirium, tremors, convulsions, possible death				Apathy, long periods of sleep, irritability, depression, disorientation		

Drugs of Abuse | Uses and Effects *continued*

Hallucinogens									Cannabis		
	Drugs	MDMA and Analogs	LSD	Phencyclidine and Analogs	Other Hallucinogens	Marijuana	Tetrahydrocannabinol	Hashish and Hashish Oil			
	CSA Schedules	Substance I	Substance I	Substance I, II, III	Substance I	Substance I	Substance I, Product III	Substance I			
	Trade or Other Names	Ecstasy, XTC, Adam, MDA (Love Drug), MDEA (EVE), MBCB	Acid, Microdots, Sunshine, Blotters	PHP, Angel Dust, Hog, Loveboat, Nymphetamine (Special K), PCK, PCPy, TCP	Psychedelic Mushrooms, Mescaline, Peyote Cacti, Ayahuasca, DMT, Dextromethorphan "DXO" not regulated	Pot, Grass, Sintetica, Blunts, Moca, Refer, Ganja	THC, Marinol	Hash Hash Oil			
	Medical Uses	None	None	Anesthetic	None	None	Antidepressant, Appetite stimulant	None			
Dependence	Physical:	None	None	Possible	None	Unknown	Yes	Unknown			
	Psychological:	Moderate	Unknown	High	None	Moderate	Moderate	Moderate			
	Tolerance:	Yes	Yes	Yes	Possible	Yes	Yes	Yes			
	Duration (Hours)	4-6	8-12	1-12	4-8	2-4	2-4	2-4			
	Usual Method	Oral, Snorted, Smoked	Oral	Oral, injected, smoked, snorted	Oral	Smoked, Oral	Smoked, Oral	Smoked, Oral			
	Possible Effects	Heightened senses, teeth grinding, and dehydration		Illusions and Hallucinations, altered perception of time and distance			Euphoria, relaxed inhibitions, increased appetite, disorientation				
	Effects of Overdose	Increased body temperature, electrolyte imbalance, cardiac arrest	LSD- longer more intense "trip," episodes	Unable to direct movement, feel pain or remember			Fatigue, paranoia, possible psychosis				
	Withdrawal Symptoms	Muscle aches, drowsiness, depression, acne	None	Drug seeking behavior			Occasional reports of insomnia, decreased appetite, hyperactivity				
Anabolic Steroids				Inhalants			Alcohol				
	Drugs	Testosterone	Other Anabolic Steroids	Amyl Nitrate and Butyl Nitrates	Nitrous Oxide	Other Inhalants	—				
	CSA Schedules	Substance III	Substance III	None	None	None	None				
	Trade or Other Names	Depo Testosterone, Saponin, Sten, Crypt	Parabolan, Winstrol, Equipoise, Anadrol, Dianabol, Primobolan-Depo, D-Ball	Pearls, Poppers, Rush, Locker Room	Laughing Gas, Whippets, Balloons	Adhesives, Spray Paint, Hair Spray, dry cleaning fluid, spot remover, lighter fluid	Liquor, Beer, Wine				
	Medical Uses	Hypogonadism	Anuria, Breast cancer	Angina (Amyl)	Anesthetic	None	None				
Dependence	Physical:	Unknown	Unknown	Unknown	Unknown	Unknown	High				
	Psychological:	Unknown	Yes	Unknown	Low	High	High				
	Tolerance:	Unknown	Unknown	No	No	No	Yes				
	Duration (Hours)	14-28 days	Variable	1	0.5	0.5-2	1-3				
	Usual Method	Injected	Oral, Injected	Inhaled	Inhaled	Inhaled	Oral				
	Possible Effects	Virilization, edema, testicular atrophy, gynecomastia, acne, aggressive behavior		Flushing, Hypotension, Headache	Impaired memory, slurred speech, drunken behavior, slow onset vitamin deficiency, organ damage						
	Effects of Overdose	Unknown		Methemoglobinemia	Vomiting, respiratory depression, loss of consciousness, possible death						
	Withdrawal Symptoms	Possible Depression		Agitation	Trembling, anxiety, insomnia, vitamin deficiency, confusion, hallucinations, convulsions						

Schedule of Controlled Substances			
Schedule	Description	Restrictions	Examples
I	High potential for abuse. No currently accepted medical use in the U.S. Lack of accepted safety for use of the drug.	No legal use.	heroin, LSD, marijuana, crystal meth
II	High potential for abuse. Currently accepted medical use in the U.S. Abuse may lead to severe psychological or physical dependence.	Prescription cannot be refilled. Requires an original signed order from the prescriber.	morphine, oxycodone, fentanyl, cocaine, amphetamine
III	Potential for abuse less than Schedule I and II. Currently accepted medical use in the U.S. Abuse may lead to moderate or low physical dependence or high psychological dependence.	Prescription can be phoned or faxed. Refills limited to 6 times within 6 months from the date of the Rx.	buprenorphine, Marinol®
IV	Lower potential for abuse than Schedule III. Currently accepted medical use in the U.S. Abuse may lead to limited psychological or physical dependence relative to Schedule III substances.	Prescription can be phoned or faxed. Refills limited to 6 times within 6 months from the date of the Rx.	lorazepam, alprazolam, carisoprodol, tramadol
V	Low potential for abuse relative to Schedule IV drugs. Currently accepted medical use in the U.S. Abuse may lead to limited psychological or physical dependence relative to Schedule IV substances.	Exempt narcotics	Diphenoxylate, cough syrups containing codeine

It is important to note in the War on Drugs that the DEA announced just this past May the most successful enforcement action in its history: Known as *Operation Pilluted*, this operation resulted in 280 arrests, including 22 doctors and pharmacists. This operation lasted fifteen months, involved thousands of law enforcement officers and spanned Arkansas, Alabama, Louisiana and Mississippi.

Twenty-one search warrants were executed across Arkansas, Alabama, Louisiana, and Mississippi. Fifty-one vehicles, 202 weapons and \$404,828 in cash were seized in the operation. Seventy-three seizure warrants were executed that resulted in the seizure of \$11,651,565 in U.S. currency and \$6,745,800 in real property.

As stated by DEA Special Agent in Charge Keith Brown: "DEA is committed to reducing the destruction brought on by the trafficking and abuse of prescription drugs through aggressive criminal enforcement, robust administrative oversight, and strong relationships with other law enforcement agencies, the public, and the medical

community. The doctors and pharmacists arrested in *Operation Pilluted* are nothing more than drug traffickers who prey on the addiction of others while abandoning the Hippocratic Oath adhered to faithfully by thousands of doctors and pharmacists each day across this country."²³



"As part of Operation Pilluted, DEA Little Rock arrested drug suspects at KJ Medical Clinic. This case is the largest single pharmaceutical operation in law enforcement history. Operation Pilluted resulted in the seizure of drugs and weapons and targeted pill mills, doctors prescribing for non-medical purposes, and illicit pharmacies."²³

²³ <http://www.dea.gov/divisions/no/2015/no052015.shtml>

Misguided Efforts to Stop Undertreatment of Pain During the 1990s

While American society and government agencies like the DEA are grappling with the problems of illicit drug abuse, the conservative approach to the use of opioids in the management of pain has led to an entirely different problem for the medical community: the undertreatment of pain. Although there was a very real and valid concern regarding the undertreatment of pain, the efforts to address this situation were at best misguided and resulted in several factors that eventually led to a resurgence in heroin use in the 21st century.

The first of these efforts became apparent in 1986 with the publication of an article in *Pain* titled “Chronic Use of Opioid Analgesics in Non-malignant Pain: Report of 38 Cases” by Drs. Russell K. Portenoy and K. M. Foley.²⁴ This article set the stage for chronic opioid therapy to be a safe alternative to surgery for patients with intractable pain and no history of drug abuse. Dr. Portenoy continued his campaign into the 1990s to establish opioid therapy as safe and reasonable. Ironically, he portrayed the undertreatment of pain as an *epidemic*. As president of the American Pain Society at that time, Dr. Portenoy was a visible spokesperson to lead the campaign to make pain the “fifth vital sign.” In hindsight, the fallacy of this campaign is all too clear: vital signs have always been objective measures that include heart rate, respiratory rate, blood pressure and temperature. Introduction of pain as a vital sign created a dilemma for clinicians in that a measure that was entirely subjective now had to be considered along with the other objective measures. However, Dr. Portenoy, who had considerable influence among his colleagues, also made statements during this time that less than 1% of chronic pain patients treated with opioids would become addicted.



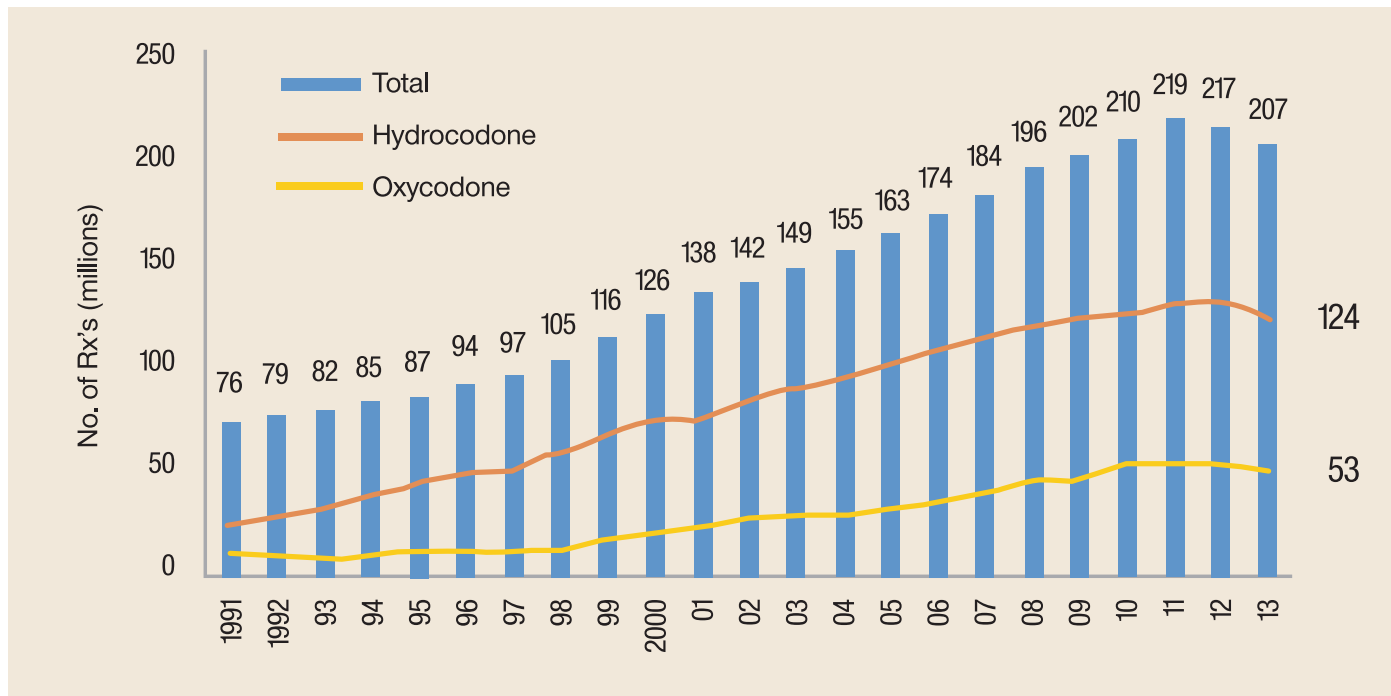
Dr. Portenoy finally came forward in December of 2012 in an article entitled “A Pain-Drug Champion Has Second Thoughts” published in the *Wall Street Journal*.²⁵ In that article, Dr. Portenoy is quoted as stating, “I gave innumerable lectures in the late 1980s and ‘90s about addiction that weren’t true.” To further taint his credibility, the article also disclosed that Dr. Portenoy’s program received millions of dollars in funding from makers of prescription opioid products from companies like Endo (manufacturer of Percocet[®]), Cephalon (manufacturer of Actiq[®]), and Purdue Pharma (manufacturer of OxyContin[®]).

In addition to its influence on Dr. Portenoy, the role of Purdue Pharma may also be tied to the second factor that has contributed to the overuse of prescription opioid products: illegal marketing of drug products. Purdue Pharma produced a marketing video in 1998 titled “I Got My Life Back: Patients in Pain Tell Their Story” and distributed it to 15,000 physicians nationwide. This video espoused the virtues of Purdue’s flagship product, OxyContin, by having patients in pain describe how OxyContin had greatly improved their quality of life. In 2007, Purdue Pharma agreed to pay \$600 million in fines and other payments to resolve criminal and civil charges related to the “misbranding” of OxyContin. In addition, three of its executives pled guilty to misbranding and paid a total of \$34.5 million in fines.²⁶ In spite of this, OxyContin, which was launched in 1996, had already reached \$1 billion per year in sales.

²⁴ Chronic use of opioid analgesics in non-malignant pain: report of 38 cases. *Pain* 1986 May, 25 (2): 171-86. Portenoy, RK and Foley, KM.

²⁵ www.wsj.com/SB10001424127887324478304578173342657044604

²⁶ www.nytimes.com/2007/05/10/business/11dreug-web.html?_r=0



Opioid Prescriptions Dispensed by US Retail Pharmacies IMS Health, Vector One: National, years 1991-1996, Data Extracted 2011. IMS Health, National Prescription Audit, years 1997-2013, Data Extracted 2014.

Although Purdue Pharma certainly played a role in the influence of Dr. Portenoy and thousands of other prescribers throughout the country, OxyContin is not the only prescription drug involved in the prescription drug abuse epidemic that had its origins in the 1990s. Other opioids included Actiq and Fentora, both very rapid onset fentanyl citrate products, Opana ER, Duragesic, and methadone. In addition to the opioid category of drugs, other controlled substances that were used to treat side effects of opioids also caused drug abuse problems. In fact, the prescribing of amphetamines or Ritalin® (methylphenidate) to counter the drowsiness caused by opioids created a cascade effect that led to the overuse of other dangerous drugs like Ambien® to allow sleep in these patients who were now receiving a stimulant. As physicians and other prescribers embraced the message that pain was undertreated, they essentially tripled the number of prescriptions written for opioids in the past 25 years. As demonstrated in the chart above, prescriptions for opioids increased from 76 million in 1991 to 207 million in 2013:²⁷

As physicians and other prescribers embraced the message that pain was undertreated, they essentially tripled the number of prescriptions written for opioids in the past 25 years.

²⁷ <http://www.drugabuse.gov/about-nida/legislative-activities/testimony-to-congress/2014/americas-addiction-to-opioids-heroin-prescription-drug-abuse>

Although prescriptions for opioids have tripled over the past 25 years, the number of “past-year heroin users” doubled in just 7 years from approximately 380,000 in 2007 to 670,000 in 2012. Furthermore, heroin-related deaths more than doubled in just 2 years from 2011 to 2013, with 8200 deaths in 2013 alone. A recent report from the Centers for Disease Control and Prevention (CDC) finds a clear link between addiction to prescription opioids and heroin addiction:²⁸

However, to understand the reasons for the increase in heroin use, one must look at the potential unintended consequences of efforts designed to curb prescription drug abuse, namely:

- Increased awareness among physicians and other prescribers that opioids are indeed dangerous and highly addictive.
- Access to controlled substance prescribing data through various state Prescription Drug Monitoring Databases (PDMPs). These databases are now available to prescribers in 49 states, although their use is mandated in only 10 states.

Street heroin is readily available
and actually less expensive than
prescription opioids.

- Development of abuse-deterrent formulations for long-acting opioids. This development is a key component of the FDA's Risk Evaluation and Mitigation Strategy (REMS) and in essence makes it more difficult for an individual to intentionally misuse or abuse prescription opioids.

Taken altogether, individuals who became addicted to prescription opioids are having a more difficult time obtaining prescription opioids and/or a more difficult time in abusing them. On the other hand, street heroin is readily available and actually less expensive than prescription opioids.

Heroin use is part of a larger substance abuse problem.

Nearly all people who
used heroin also used
at least 1 other drug

Most used at least
3 other drugs.

Heroin

is a highly addictive
opioid drug with a high
risk of overdose and
death
for users.

People who are addicted to...



2x

3x

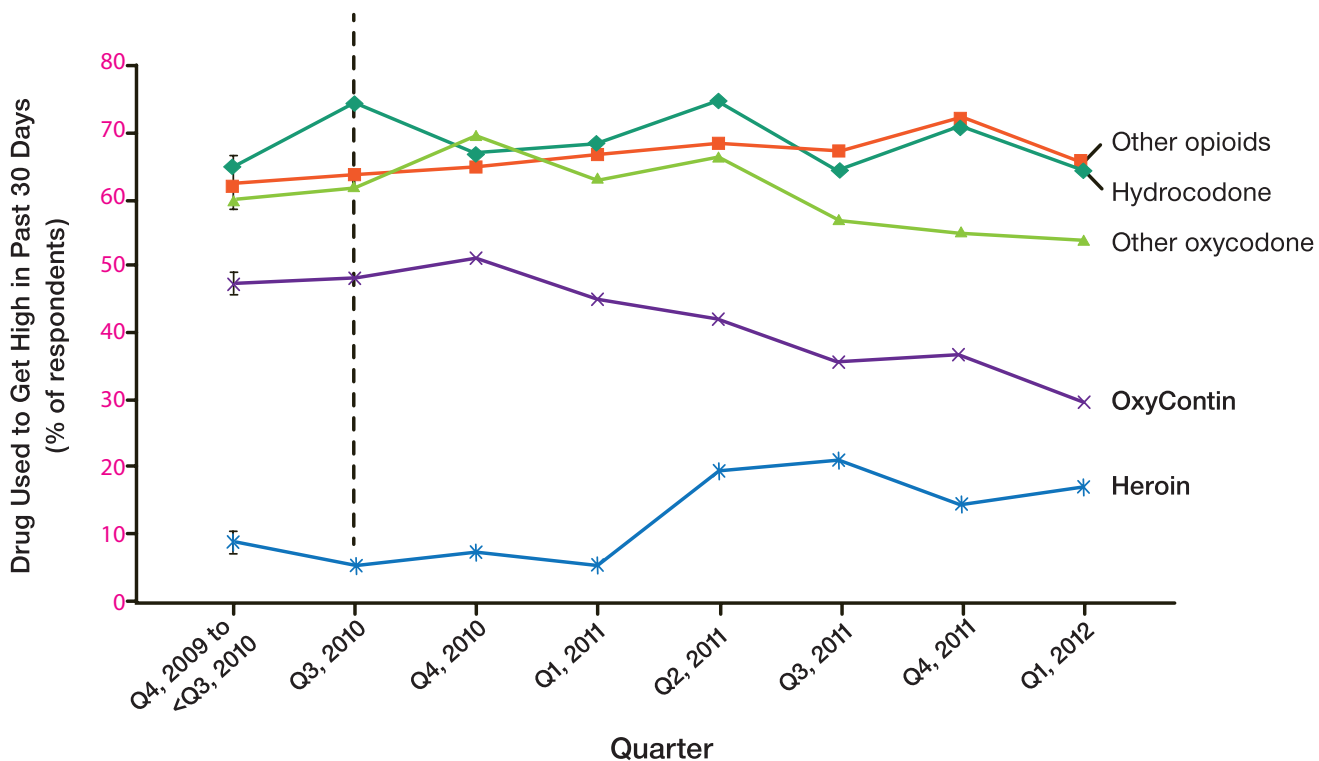
15x

40x

...more likely to be addicted to heroin.

SOURCE: National Survey on Drug Use and Health (NSDUH), 2011-2013

²⁸ <http://www.cdc.gov/media/releases/2015/p0707-heroin-epidemic.html>



Growing evidence suggests that abusers of prescription opioids are shifting to heroin as prescription drugs become less available or harder to abuse. For example, a recent increase in heroin use accompanied a downward trend in OxyContin abuse following the introduction of an abuse-deterrent formulation of that medication (dashed vertical line)

A recent report from the Centers for Disease Control and Prevention (CDC) finds a clear link between addiction to prescription opioids and heroin addiction.

The CDC is recommending a three-pronged approach:

1) Prevent people from starting heroin.

Because of the strong link between prescription opioid addiction and heroin addiction, reducing the misuse and overprescribing of prescription opioids is the logical first step toward reducing heroin addiction. Improving prescribing practices by strong adherence to pain management guidelines such as ACOEM and ODG is critical. myMatrixx tracks and reports on the following indicators of potential high-risk behavior:

- Excessive morphine equivalent (MED) doses
- Use of more than one long-acting opioid or more than a single long-acting and a single short-acting opioid
- Using opioids for excessive periods of time

- Combining opioids with drugs such as Soma® (carisoprodol) and benzodiazepines such as Xanax® (alprazolam)
- Early refills
- Seeing more than one physician for controlled substances
- Receiving controlled substances from more than one pharmacy
- Use of controlled substances with a past diagnosis of substance abuse

In addition, both claims and healthcare professionals involved in the care of injured patients can watch for and report high-risk individuals.

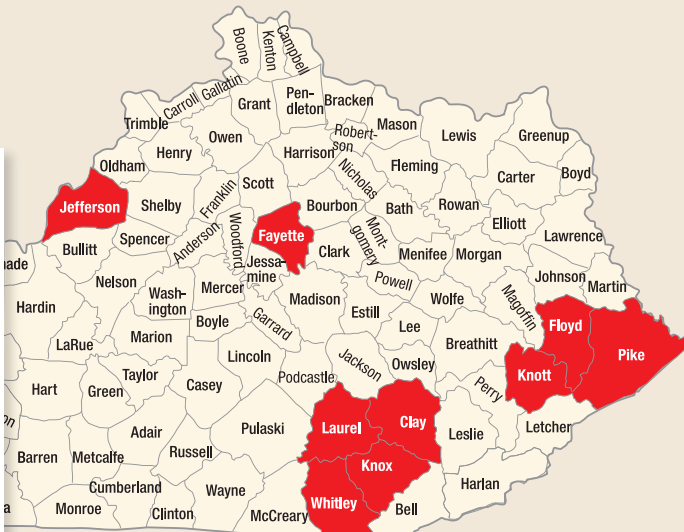
Top 10 counties

The Kentucky Board of Medical Licensure and the state are enforcing new regulations for prescribing Suboxone and other buprenorphine products. Officials say a surge in abuse of those drugs is an unintended consequence of efforts to curb heroin and other opiate use.

Counties where patients live who fill most buprenorphine prescriptions:

County	Quantity*
1. Pike	163,938
2. Harlan	105,764
3. Floyd	101,093
4. Jefferson	100,124
5. Whitley	92,579
6. Clay	92,177
7. Knox	90,269
8. Fayette	84,447
9. Perry	83,322
10. Laurel	79,582

*Represents doses dispensed to Medicaid members



2) Reduce heroin addiction

The CDC recommends that individuals addicted to heroin or prescription opioids have access to medication-assisted treatment, which combines therapy with drugs like methadone, buprenorphine or naltrexone with counseling and behavioral therapy.

However, as valuable as these treatments are, one must consider the dangers of their misuse as well. All three of these drugs have the potential for misuse and abuse. One tragic report comes from Kentucky where a state that has been struggling to deal with a prescription opioid epidemic is now also dealing with a heroin epidemic.

Source: Kentucky Cabinet for Health and Family Services

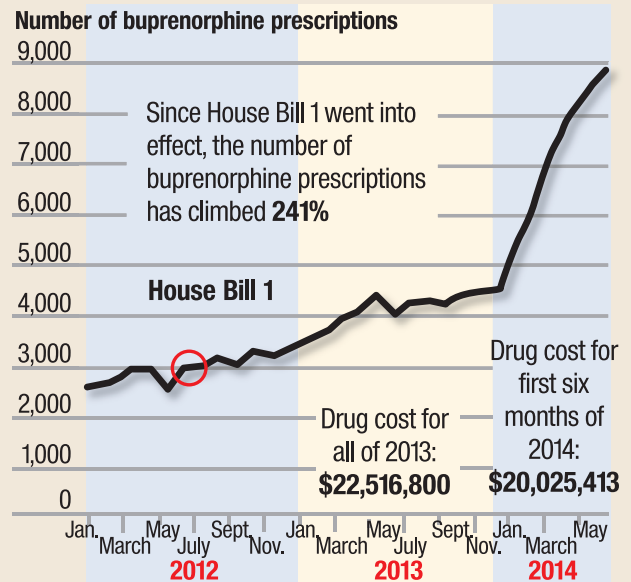
CHRIS WARE | cware@heraldleader.com

One of the first efforts was the passage of House Bill 1 in 2012 by the Kentucky legislature.²⁹ This legislation, designed to control pill mills and the overprescribing of opioids, achieved one goal: prescriptions for these drugs declined. However, the legislation did not put similar restrictions on prescriptions for buprenorphine prescriptions. Buprenorphine is the active ingredient in drugs like Suboxone® and Subutex®. When used properly, these drugs can help an addict quit using heroin without going through horrible withdrawal. However, one addict was quoted as saying, “It was just a great substitute for heroin. It was like doing the same thing, really.”

The initial impact of HB 1 was to cause the state’s pill mills to turn into facilities that provided buprenorphine to addicts without any of the oversight necessary to truly help the patient. The two charts sourced from Kentucky Cabinet for Health and Family Services provide clear insight into both the overuse of this drug as well as the cost to taxpayers. New regulations since the passage of HB 1 now restrict the use of buprenorphine products.³⁰ Other states would be wise to pay attention.

High cost of a proposed cure

As more people got insurance under the Affordable Care Act the number of prescriptions for Suboxone and other drugs with buprenorphine skyrocketed as did the cost to taxpayers footing the bill. The increase is also tied to the passage of House Bill 1 which aimed to stem abuse of heroin and prescription opiates.



Source: Kentucky Cabinet for Health and Family Services

CHRIS WARE | cware@herald-leader.com

3) Reverse heroin overdoses

The CDC also recommends that the use of naloxone be expanded. Naloxone has the ability to reverse the effects of an opioid overdose if it is administered in time.

Naloxone was first discovered in the 1960s, and it has been available under the brand name Narcan® as an injectable drug. It has been the mainstay treatment for opioid overdose for over three decades. Its AWP (average wholesale price) is typically \$3.58 per vial. However, California-based Amphastar, which manufactures a generic version of naloxone, quickly pushed the AWP per unit past \$10.00 in response to the increased demand. The attorney general of Massachusetts recently announced that Amphastar has agreed to donate \$325,000 to that state to assist with its purchase of the drug.³¹ Other states should take note.

Evzio® was introduced last year as an auto-injector version of naloxone to treat opioid overdose. It is not intended to be a self-injector; therefore, a family member or caregiver must administer the injection. It has an AWP of \$862.50 for a kit containing two syringes.

²⁹ <http://kbml.ky.gov/hb1/Pages/default.aspx>

³⁰ http://www.kentucky.com/welcome_page/?shf=/2015/06/20/3910362_the-drug-that-was-supposed-to.html

³¹ <http://www.insurancefraud.org/downloads/drugDiversion.pdf>

Evzio has been recommended by the myMatrixx P&T Committee to be a non-formulary drug for two reasons:

- 1) Evzio is expensive. However, as a life-saving drug, the high cost is not the most important factor.
- 2) The primary reason for recommending that Evzio be designated as a non-formulary drug is that Evzio will not be dispensed through a retail pharmacy in an emergency situation—there is not enough time. Therefore, patients at risk of overdose must be identified by the physician and prescribed Evzio in advance. In a non-emergency situation, there is sufficient time for Evzio to go through our clients' authorization process.



Most of the legislation surrounding naloxone has been aimed at first responders and their need to have immediate access to naloxone. Many municipalities are creating their own “naloxone kits” for less than \$50.³²

Responding to the Heroin Epidemic



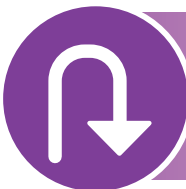
PREVENT People From Starting Heroin

Reduce prescription opioid painkiller abuse.
Improve opioid painkiller prescribing practices and identify high-risk individuals early.



REDUCE Heroin Addiction

Ensure access to Medication-Assisted Treatment (MAT).
Treat people addicted to heroin or prescription opioid painkillers with MAT which combines the use of medications (methadone, buprenorphine, or naltrexone) with counseling and behavioral therapies



REVERSE Heroin Overdose

Expand the use of naloxone.
Use naloxone, a life-saving drug that can reverse the effects of an opioid overdose when administered in time.

³² <http://harmreduction.org/issues/overdose-prevention/tools-best-practices/od-kit-materials/>

Just as there are multiple factors contributing to the recent increase in heroin addiction, there must also be multiple strategies developed to fight drug abuse and, equally important, to treat the causes of addiction. Liability associated with the cases of addiction will likely play out in a court of law. The Coalition Against Insurance Fraud published a white paper in 2007 entitled Prescription for Peril in which an excellent case is presented for the liability that physicians, pharmacists and other healthcare professionals may ultimately face. Indeed, that paper also points out that ultimately insurers may face such liability as well because in many ways the insurance industry has funded the prescription drug abuse epidemic. One may also argue that with that liability comes a need to be able to take advantage of the tools available to fight fraud and abuse such as the PDMP databases. A report that is pertinent to this discussion comes from the Brandeis University Center of Excellence and is entitled PDMPs and Third Party Payers Meeting.³³ Brandeis makes an excellent case for increasing access to the PDMPs beyond law enforcement, treating physicians and dispensing pharmacists.

Until these types of scenarios play themselves out in either the courts or the regulatory process, there are steps that can be taken at the claims professional level:

- Be aware of the signs of potential drug abuse
- Take advantage of tools to identify at-risk individuals
- Refer patients for a drug regimen review
- Engage a clinical pharmacist to consult with the treating physician

Unfortunately, there is no magic bullet to solve the prescription drug abuse epidemic or the heroin crisis. Each patient must be treated individually. Therefore, the value of early recognition and prevention cannot be emphasized enough.

The value of early recognition
and prevention cannot be
emphasized enough.

³³http://www.pdmpexcellence.org/sites/all/pdfs/Brandeis_COE_PDMP_3rd_pty_payer_mtg_rpt.pdf

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