National Institute on Drug Abuse (NIDA)

Prescription Opioids and Heroin

Last Updated January 2018

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Introduction

Drug overdose deaths involving prescription opioid pain relievers have increased dramatically since 1999. Concerted federal and state efforts have been made to curb this epidemic. In 2011, the White House released an interagency strategy for Responding to America's Prescription Drug Crisis. Enacting this strategy, federal agencies have worked with states to educate providers, pharmacists, patients, parents, and youth about the dangers of prescription drug abuse and the need for proper prescribing, dispensing, use, and disposal; to implement effective prescription drug monitoring programs; to facilitate proper medication disposal through prescription take-back initiatives; and to support aggressive enforcement to address doctor shopping and pill mills and support development of abuse-resistance formulations for opioid pain relievers.

Improvements have been seen in some regions of the country in the form of decreasing availability of prescription opioid drugs and a decline in overdose deaths in states with the most aggressive policies (Johnson et al., 2014). However, since 2007, overdose deaths related to heroin have started to increase. The Centers for Disease Control and Prevention counted 10,574 heroin overdose deaths in 2014, which represents more than a fivefold increase of the heroin death rate from 2002 to 2014 (CDC, 2015).

In an effort to combat the intertwined problems of prescription opioid misuse and heroin use, in March of 2015 the Secretary of Health and Human Services announced the Secretary's Opioid Initiative, which aims to reduce addiction and mortality related to opioid drug abuse by (HHS takes strong steps, 2015):

- reforming opioid prescribing practices
- expanding access to the overdose-reversal drug naloxone
- expanding access to medication-assisted treatment for opioid use disorder

The relationship between prescription opioid abuse and increases in heroin use in the United States is under scrutiny. These substances are all part of the

same opioid drug category and overlap in important ways. Currently available research demonstrates:

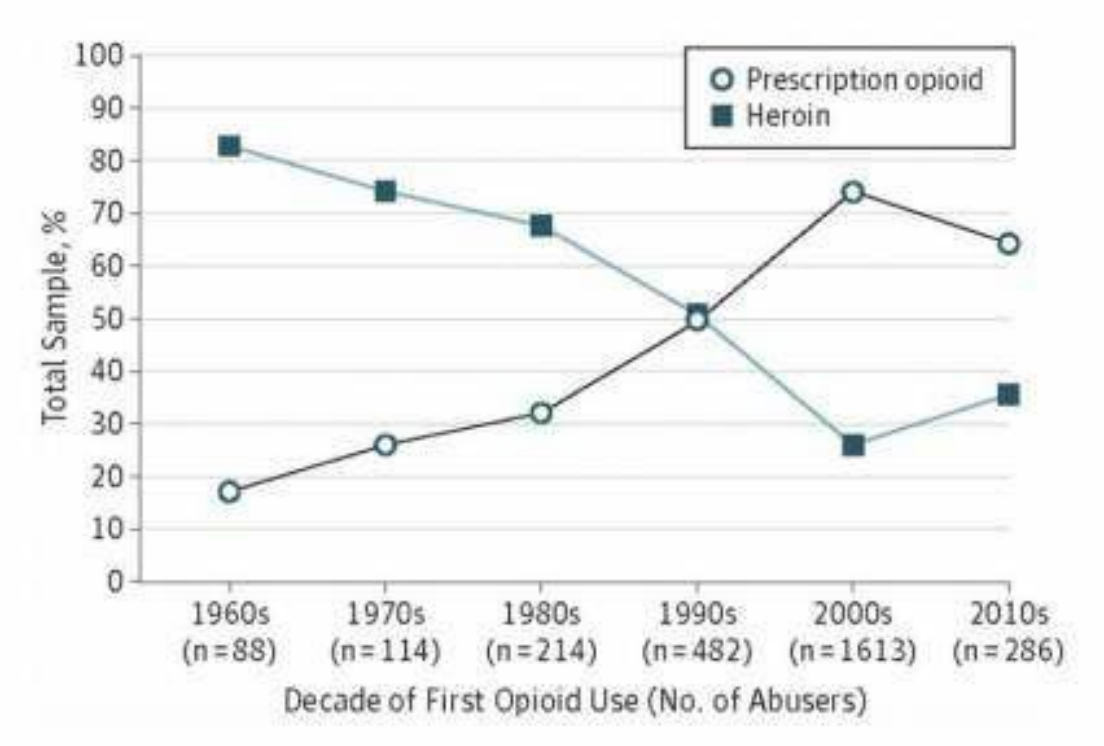
- Prescription opioid use is a risk factor for heroin use.
- Heroin use is rare in prescription drug users.
- Prescription opioids and heroin have similar effects, different risk factors.
- A subset of people who abuse prescription opioids may progress to heroin use.
- Increased drug availability is associated with increased use and overdose.
- Heroin use is driven by its low cost and high availability.
- Emphasis is needed on both prevention and treatment.

References

- Centers for Disease Control and Prevention (CDC). Number and age-adjusted rates of drug-poisoning deaths involving opioid analgesics and heroin: United States, 2000-2014. National Vital Statistics System, Mortality File. http://wonder.cdc.gov/. Reviewed December 9, 2015. Accessed December 10, 2015.
- HHS takes strong steps to address opioid-drug related overdose, death and dependence [news release]. Washington, DC: U.S. Dept. of Health and Human Services; March 26, 2015. http://www.hhs.gov/news/press/2015pres/03/20150326a.html. Accessed October 8, 2015.
- Johnson H, Paulozzi L, Porucznik C, Mack K, Herter B. Decline in drug overdose deaths after state policy changes – Florida, 2010-2012. *Morbidity and Mortality Weekly Report (MMWR)*. Atlanta, GA: Centers for Disease Control and Prevention; 2014.

Prescription opioid use is a risk factor for heroin use

Pooling data from 2002 to 2012, the incidence of heroin initiation was 19 times higher among those who reported prior nonmedical pain reliever use than among those who did not (0.39 vs. 0.02 percent) (Muhuri et al., 2013). A study of young, urban injection drug users interviewed in 2008 and 2009 found that 86 percent had used opioid pain relievers nonmedically prior to using heroin, and their initiation into nonmedical use was characterized by three main sources of opioids: family, friends, or personal prescriptions (Lankenau et al., 2012). This rate represents a shift from historical trends. Of people entering treatment for heroin addiction who began abusing opioids in the 1960s, more than 80 percent started with heroin. Of those who began abusing opioids in the 2000s, 75 percent reported that their first opioid was a prescription drug (Cicero et al., 2014). Examining national-level general population heroin data (including those in and not in treatment), nearly 80 percent of heroin users reported using prescription opioids prior to heroin (Jones, 2013; Muhuri et al., 2013).



Percentage of the total heroin-dependent sample that used heroin or a prescription

opioid as their first opioid of abuse. Data are plotted as a function of the decade in which respondents initiated their opioid abuse. *Source: Cicero et al., 2014*

References

- Cicero TJ, Ellis MS, Surratt HL, Kurtz SP. The changing face of heroin use in the United States: a retrospective analysis of the past 50 years. *JAMA Psychiatry*. 2014;71(7):821-826.
- Jones CM. Heroin use and heroin use risk behaviors among nonmedical users of prescription opioid pain relievers – United States, 2002-2004 and 2008-2010. Drug Alcohol Depend. 2013;132(1-2):95-100.
- Lankenau SE, Teti M, Silva K, Jackson Bloom J, Harocopos A, Treese M. Initiation into prescription opioid misuse amongst young injection drug users. *Int J Drug Policy.* 2012;23(1):37-44.
- Muhuri PK, Gfroerer JC, Davies MC; Substance Abuse and Mental Health Services Administration. Associations of nonmedical pain reliever use and initiation of heroin use in the United States. *CBHSQ Data Review.* http://www.samhsa.gov/data/2k13/DataReview/DR006/nonmedical-pain-reliever-use-2013.pdf. Published August 2013. Accessed October 8, 2015.

Heroin use is rare in prescription drug users

While prescription opioid abuse is a growing risk factor for starting heroin use, only a small fraction of people who abuse pain relievers switch to heroin use. According to general population data from the National Survey on Drug Use and Health, less than 4 percent of people who had abused prescription opioids started using heroin within 5 years (Muhuri et al., 2013). This suggests that prescription opioid abuse is just one factor in the pathway to heroin. Furthermore, analyses suggest that those who transition to heroin use tend to be frequent users of multiple substances (polydrug users) (Jones, et al., 2015). Additional analyses are needed to better characterize the population that abuses prescription opioids who transition to heroin use, including demographic criteria, what other drugs they use, and whether or not they are injection drug users.

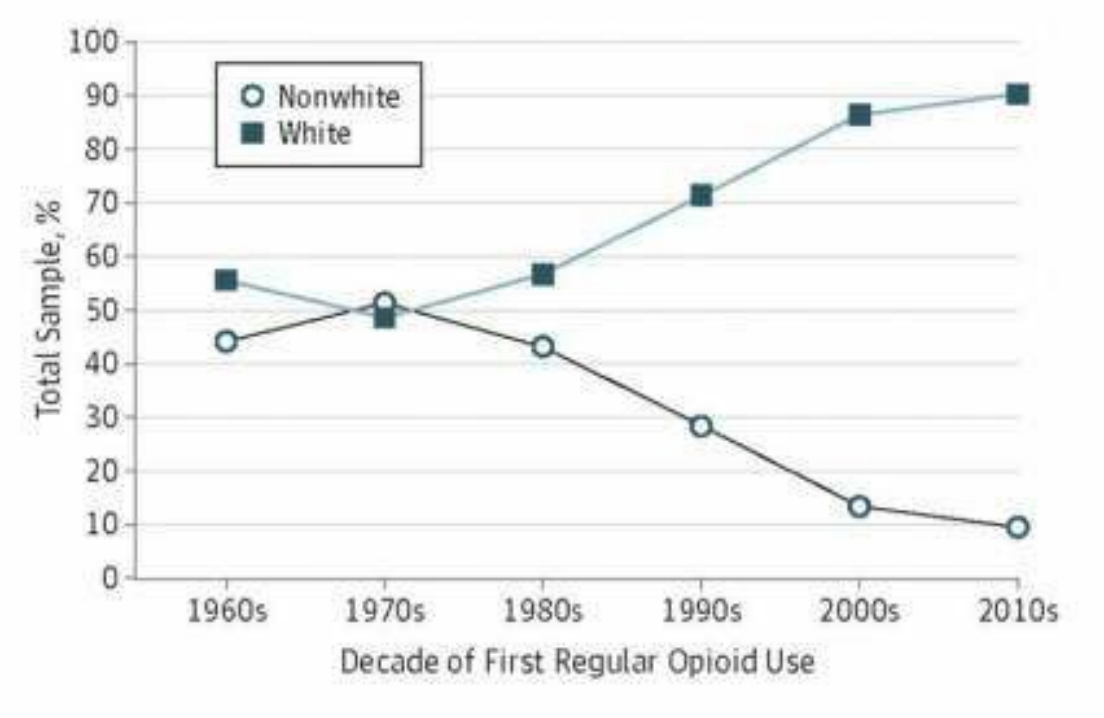
References:

- Jones CM, Logan J, Gladden RM, Bohm MK. Vital signs: demographic and substance use trends among heroin users – United States, 2002-2013. *Morbidity and Mortality Weekly Report (MMWR)*. Atlanta, GA: Centers for Disease Control and Prevention; 2015.
- Muhuri PK, Gfroerer JC, Davies MC; Substance Abuse and Mental Health Services Administration. Associations of nonmedical pain reliever use and initiation of heroin use in the United States. *CBHSQ Data Review.* http://www.samhsa.gov/data/2k13/DataReview/DR006/nonmedical-pain-reliever-use-2013.pdf. Published August 2013. Accessed October 8, 2015.

Prescription opioids and heroin have similar effects, different risk factors

Heroin and prescription opioid pain relievers both belong to the opioid class of drugs, and their euphoric effects are produced by their binding with mu opioid receptors in the brain. Different opioid drugs have different effects that are determined by the way they are taken and by the timing and duration of their activity at mu opioid receptors.

People who began using heroin in the 1960s were predominantly young men from minority groups living in urban areas (82.8 percent; mean age at first opioid use, 16.5 years) whose first opioid of abuse was heroin (80 percent). The epidemic of prescription opioid abuse has been associated with a shifting of the demographic of opioid users toward a population that is somewhat older (mean age at first opioid use, 22.9 years), less minority, more rural/suburban, with few gender differences among those who were introduced to opioids through prescription drugs. Whites and nonwhites were equally represented in those initiating use prior to the 1980s, but nearly 90 percent of respondents who began use in the last decade were white (Cicero et al., 2014).



Racial distribution of respondents expressed as percentage of the total sample of heroin users. Data are plotted as a function of decade in which respondents initiated their opioid abuse. *Source: Cicero et al. 2014.*

Because heroin is often injected, the upsurge in use also has implications for HIV, hepatitis C (HCV), and other injection-related illnesses. Recent studies suggest that having used opioid pain relievers before transitioning to heroin injection is a common trajectory for young injection drug users with HCV infection (Klevens et al., 2012). A study of new HCV infections in Massachusetts found that 95 percent of interview respondents used prescription opioids before initiating heroin (Church et al., 2010).

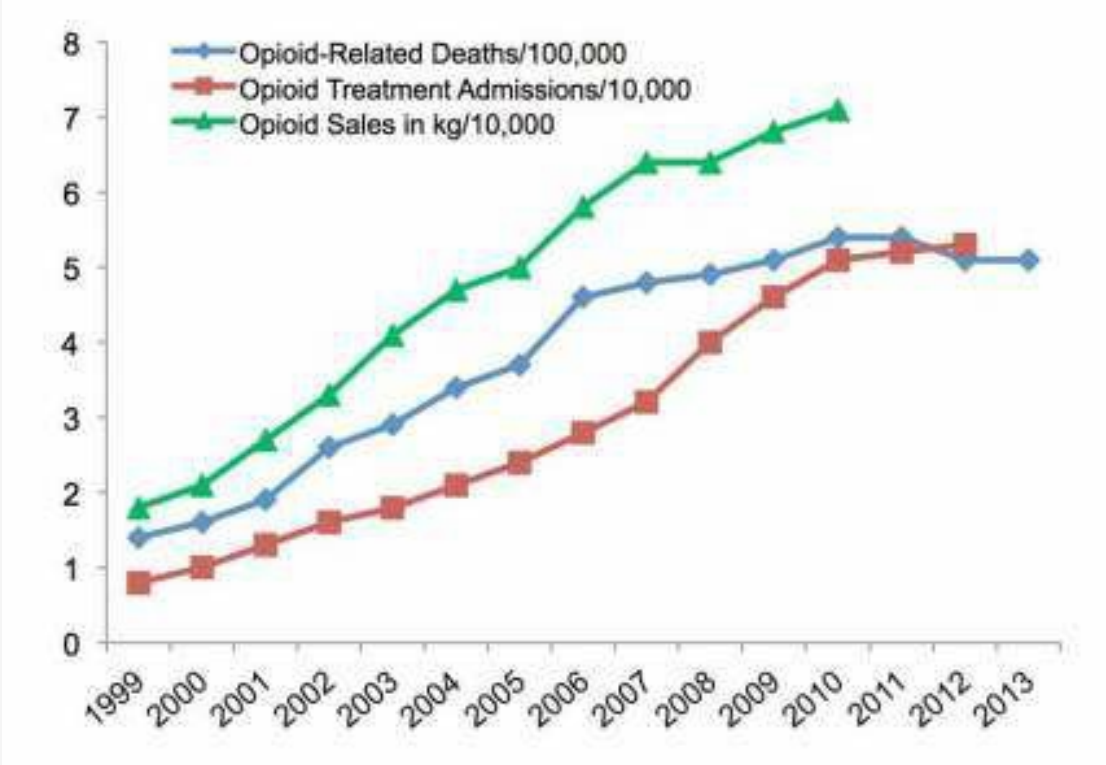
References

- Church D, Barton K, Elson F, DeMaria A, et al. Notes from the field: risk factors for hepatitis C virus infections among young adults – Massachusetts, 2010. *Morbidity and Mortality Weekly Report (MMWR)*. Atlanta, GA: Centers for Disease Control and Prevention; 2011.
- Cicero TJ, Ellis MS, Surratt HL, Kurtz SP. The changing face of heroin use in the United States: a retrospective analysis of the past 50 years. *JAMA Psychiatry*. 2014;71(7):821-826.

- Klevens RM, Hu DJ, Jiles R, Holmberg SD. Evolving epidemiology of hepatitis C virus in the United States. *Clin Infect Dis*. 2012;55(S1):S3-S9.

A subset of people who abuse prescription opioids may progress to heroin use

A recent study of heroin users in the Chicago metropolitan area identified three main paths to heroin addiction: Prescription opioid abuse to heroin use, cocaine use to heroin use (to "come down"), and polydrug use (i.e., use of multiple substances) to heroin use. Polydrug use to heroin was the most common path in this study (Kane-Willis, et al., n.d.). The estimated 4 percent subset of people who transition from prescription opioid abuse to heroin use (Muhuri et al., 2013) may be predisposed to polydrug use, and the transition may represent a natural progression for them. Examination of new HCV cases in young adults living in rural areas identified a population who reported transition from non-injection drug use to injecting opioid pain relievers before switching to injecting heroin or methamphetamine (Stanley et al., 2012). A study looking at a larger sample found that prescription opioid abuse preceded heroin use by an average of 2 years (Suryaprasad et al., 2014). Frequent prescription opioid users and those diagnosed with dependence or abuse of prescription opioids are more likely to switch to heroin; dependence on or abuse of prescription opioids has been associated with a 40-fold increased risk of dependence on or abuse of heroin (Jones et al., 2015).



Opioid sales, opioid treatment admissions, and opioid-related deaths. *Sources: CDC Wonder, 2015; DEA ARCOS, 2015; TEDS, 2015*

References

- CDC WONDER. Atlanta, GA: Centers for Disease Control and Prevention; 2015. http://wonder.cdc.gov/. Updated September 17, 2015. Accessed September 25, 2015.
- Center for Behavioral Health Statistics and Quality, Substance Abuse and Mental Health Services Administration, Treatment Episode Data Set (TEDS). http://www.samhsa.gov/data/client-level-data-teds. Updated November 19, 2014. Accessed September 25, 2015.
- Jones CM, Logan J, Gladden RM, Bohm MK. Vital signs: demographic and substance use trends among heroin users – United States, 2002-2013. *Morbidity and Mortality Weekly Report (MMWR)*. Atlanta, GA: Centers for Disease Control and Prevention; 2015.
- Kane-Willis K, Schmitz SJ, Bazan M, Narloch, VF, Wallace CB. *Understanding suburban heroin use*. Roosevelt University. https://www.robertcrown.org/files/Understanding_suburban_heroin_use.pdf.

Accessed October 8, 2015.

- Muhuri PK, Gfroerer JC, Davies MC; Substance Abuse and Mental Health Services Administration. Associations of nonmedical pain reliever use and initiation of heroin use in the United States. *CBHSQ Data Review.* http://www.samhsa.gov/data/2k13/DataReview/DR006/nonmedical-pain-reliever-use-2013.pdf. Published August 2013. Accessed October 8, 2015.
- Stanley MM, Guilfoyle S, Vergeront JM, et al. Notes from the field: hepatitis C virus infections among young adults – rural Wisconsin, 2010. *Morbidity and Mortality Weekly Report (MMWR)*. Atlanta, GA: Centers for Disease Control and Prevention; 2012.
- Suryaprasad AG, White JZ, Xu F, et al. Emerging epidemic of hepatitis C virus infections among young nonurban persons who inject drugs in the United States, 2006-2012. *Clin Infect Dis*. 2014;59(10):1411-1419.
- U.S. Drug Enforcement Administration (DEA) ARCOS. Data extracted October 8, 2015.

Increased drug availability is associated with increased use and overdose

From 1991 to 2011, there was a near tripling of opioid prescriptions dispensed by U.S. pharmacies: from 76 million to 219 million prescriptions (IMS Health, 2014a; IMS Health, 2014b). In parallel with this increase, there was also a near tripling of opioid-related deaths over the same time period.

Mexican heroin production increased from an estimated 8 metric tons in 2005 to 50 metric tons in 2009—more than a six-fold increase in just 4 years. Domination of the U.S. market by Mexican and Colombian heroin sources, along with technology transfer between these suppliers, has increased the availability of easily injectable, white powder heroin (National Drug Intelligence Center, 2011). In a recent survey of patients receiving treatment for opioid abuse, accessibility was one of the main factors identified in the decision to start using heroin (Cicero et al., 2014).

References

- Cicero TJ, Ellis MS, Surratt HL, Kurtz SP. The changing face of heroin use in the United States: a retrospective analysis of the past 50 years. *JAMA Psychiatry*. 2014;71(7):821-826.
- IMS Health, National Prescription Audit, Years 1997-2013. Data extracted 2014.
- IMS Health, Vector One: National, Years 1991-1996. Data extracted 2014.
- National Drug Intelligence Center, U.S. Department of Justice. National Drug Threat Assessment 2011. http://www.justice.gov/archive/ndic/pubs44/44849/44849p.pdf. Published August 2011. Accessed October 8, 2015.

Heroin use is driven by its low cost and high availability

One main factor that contributes to the popularity of a drug is availability. One key to prevention is reducing exposure. While efforts to reduce the availability of prescription opioid analgesics have begun to show success, the supply of heroin has been increasing (see Increased drug availability is associated with increased use and overdose). Prescription opioids and heroin have similar chemical properties and physiological impacts; when administered by the same method (i.e., ingested or injected), there is no real difference for the user.

It is not clear whether the increased availability of heroin is causing the upsurge in use or if the increased accessibility of heroin has been caused by increased demand. A number of studies have suggested that people transitioning from abuse of prescription opioids to heroin cite that heroin is cheaper, more available, and provides a better high. Notably, the street price of heroin has been much lower in recent years than in past decades (Unick et al., 2014). In addition to these market forces, some have reported that the transition from opioid pills to heroin was eased by sniffing or smoking heroin before transitioning to injection (Mars et al., 2014). In a recent survey of people in treatment for opioid addiction, almost all—94 percent—said they chose to use heroin because prescription opioids were "far more expensive and harder to obtain" (Cicero et al., 2014).

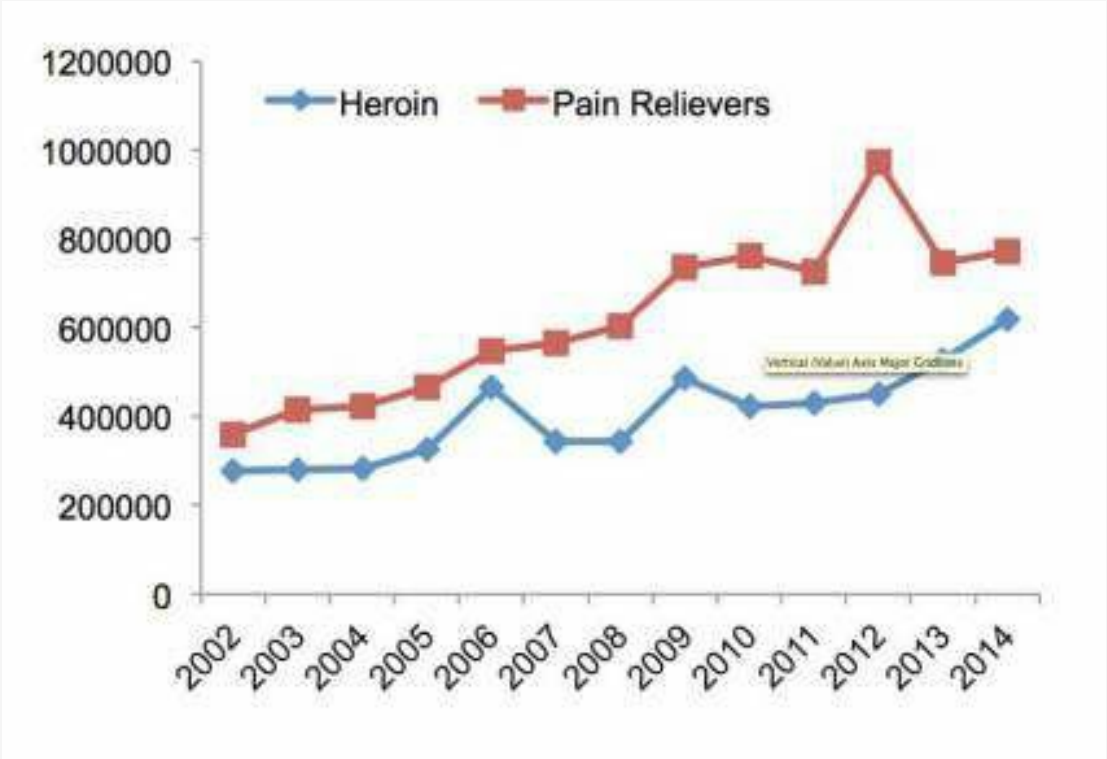
References

- Cicero TJ, Ellis MS, Surratt HL, Kurtz SP. The changing face of heroin use in the United States: a retrospective analysis of the past 50 years. *JAMA Psychiatry*. 2014;71(7):821-826.
- Mars SG, Bourgois P, Karandinos G, Montero F, Ciccarone D. "Every 'never' I ever said came true": transitions from opioid pills to heroin injecting. *Int J Drug Policy*. 2014;25(2)257-266.
- Unick G, Rosenblum D, Mars S, Ciccarone D. The relationship between US heroin market dynamics and heroin-related overdose, 1992-2008.

Addiction. 2014;109(11):1889-1898.

Emphasis is needed on both prevention and treatment

With the increasing use of opioids, there has been a concomitant increase in the number of treatment admissions attributable to prescription opioids and heroin. The number of persons receiving substance use treatment for prescription opioids rose from 360,000 in 2002, representing 10.3 percent of the total treatment population, to 772,000 (18.6 percent) in 2014 (CBHSQ, 2015b). The number of persons receiving treatment for heroin increased from 277,000 in 2002 to 618,000 in 2014 (CBHSQ, 2015b). In addition, the number of heroin users in the United States jumped from about 404,000 in 2002 to 914,000 in 2014, and the number of those with heroin "dependence or abuse" more than doubled from 2002 to 2014, increasing from about 214,000 to 586,000 (CBHSQ, 2015a).



Number of persons 12 years or older who received last or current substance use treatment for heroin or pain relievers. *Source: CBHSQ, 2015b*

In addition to efforts to prevent initiation of abuse of prescription opioids and use of heroin, there is a significant need to identify and treat people who have

already developed an addiction to these substances. The prescription drug monitoring programs are one means by which states are identifying individuals who are doctor shopping. In addition, there are ongoing efforts to encourage health care practitioners to screen patients for potential drug abuse problems. However, identification is only the first step; it is critical to provide evidence-based treatments for these individuals. Treatment should include access to the medication-assisted treatment (MAT) options of methadone, buprenorphine, or extended-release naltrexone, which are effective for both prescription opioid and heroin addiction. In fact, a NIDA study found that once treatment is initiated, both a buprenorphine/naloxone combination and an extended release naltrexone formulation are similarly effective in treating opioid use disorder. Because full detoxification is necessary for treatment with naloxone, initiating treatment among active users was difficult, but once detoxification was complete, both medications had similar effectiveness. Currently, far fewer people receive MAT than could potentially benefit from it. Nearly all U.S. states have higher rates of opioid abuse and dependence than their buprenorphine treatment capacity [(Jones et al., 2015)], and fewer than 1 million of the 2.5 million Americans who abused or were dependent on opioids in 2012 received MAT [(Volkow ND et al., 2014)]. Removing barriers to MAT access and utilization is a top priority for the U.S. Department of Health and Human Services and is a key objective of the Secretary's Opioid Initiative to combat opioid drug-related dependence and overdose.

References

- Center for Behavioral Health Statistics and Quality (CBHSQ). Table 7.50A. *2014 National Survey on Drug Use and Health: Detailed Tables.* Substance Abuse and Mental Health Services Administration, Rockville, MD; 2015.
- Center for Behavioral Health Statistics and Quality (CBHSQ). Table 7.62A. *2014 National Survey on Drug Use and Health: Detailed Tables*. Substance Abuse and Mental Health Services Administration, Rockville, MD; 2015.
- Jones CM, Campopiano M, Baldwin G, McCance-Katz E. National and state treatment need and capacity for opioid agonist medication-assisted treatment. *Am J Public Health*. 2015;105(8):e55-e63.
- Volkow ND, Frieden TR, Hyde PS, and Cha SS. Medication-assisted therapies—tackling the opioid-overdose epidemic. *N Engl J Med*.

2014;370(22):2063-2066.

National Institute on Drug Abuse (NIDA)

Medications to Treat Opioid Addiction

Last Updated January 2018

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Overview

An estimated 2 million people in the United States suffered from substance use disorders related to prescription opioid pain medicines in 2015.[1] Treatment admissions linked to these medications more than quadrupled between 2002 and 2012, although only a fraction of people with prescription opioid use disorders receive specialty treatment (18 percent in 2015).[1] Overdose deaths linked to these medicines nearly quadrupled (from 4,400 to nearly 19,000, or 1.5 to 5.9 per 100,000 persons) from 2000 to 2014.[2] There is now also a rise in heroin use and heroin addiction as some people shift from prescription opioids to their cheaper street relative; 591,000 people had a heroin use disorder in 2015, and nearly 13,000 Americans died of a heroin overdose in 2015.[1,3] Besides overdose, consequences of the opioid crisis include a rising incidence of infants born dependent on opioids because their mothers used these substances during pregnancy[4,5] and increased spread of infectious diseases, including HIV and hepatitis C (HCV), as was seen in 2015 in southern Indiana.[6]

Effective prevention and treatment strategies exist for opioid misuse and addiction but are highly underutilized across the United States. An initiative of the Secretary of Health and Human Services[7] began in 2015 to address the complex problem of prescription opioid and heroin use. This initiative emphasizes improved education of healthcare providers in managing pain and prescribing opioids appropriately; wider availability and adoption of the effective overdose-reversing drug naloxone, which research has shown to be a lifesaver in communities where it has been distributed to people who use opioids, their families, and potential bystanders;[8] and wider implementation of evidence-based treatment strategies.

Effective medications exist to treat opioid use disorders: methadone, buprenorphine, and naltrexone. These medications could help many people recover from opioid addiction, but they remain highly underutilized. Fewer than half of private-sector treatment programs offer medications for opioid use disorders, and of patients in those programs who might benefit, only a third actually receive it.[9] Overcoming the misunderstandings and other barriers that prevent wider adoption of these treatments is crucial for tackling the problem of opioid addiction and the epidemic of opioid overdose in the United States.

How Do Medications to Treat Opioid Addiction Work?

Opioid Agonists and Partial Agonists (Maintenance Medications)

Studies show that people with opioid addiction who follow detoxification with complete abstinence are very likely to return to using the drug (*relapse*).[10] While relapse is a normal step on the path to recovery, it can also be life threatening, raising the risk for a fatal overdose.[11] Thus, an important way to support recovery from heroin or prescription opioid addiction is to maintain abstinence from those drugs using medications that reduce the negative effects of withdrawal and craving without producing the euphoria that the original drug of abuse caused. **Methadone** and **buprenorphine** are medications approved for this purpose.

Methadone is a synthetic *opioid agonist* that eliminates withdrawal symptoms and relieves drug cravings by acting on opioid receptors in the brain—the same receptors that other opioids such as heroin, morphine, and opioid pain medications activate. Although it occupies and activates these opioid receptors, it does so more slowly than other opioids and, in an opioid-dependent person, treatment doses do not produce euphoria. It has been used successfully for more than 40 years to treat opioid addiction and must be dispensed through specialized opioid treatment programs.[12]

Buprenorphine is a *partial opioid agonist*, meaning that it binds to those same opioid receptors but activates them less strongly than full agonists do. Like methadone, it can reduce cravings and withdrawal symptoms in a person with an opioid use disorder without producing euphoria, and patients tolerate it well. Research has found buprenorphine to be similarly effective as methadone for treating opioid use disorders, as long as it is given at a sufficient dose and for sufficient duration.[13] Unlike methadone, buprenorphine can be prescribed by certified physicians in an office setting. It has been available since 2002 as a tablet and since 2010 as a sublingual film,[14] and the U.S. Food and Drug Administration (FDA) approved a 6-month subdermal buprenorphine implant in

May 2016 and a once-monthly buprenorphine injection in November 2017. Both formulations are available to patients stabilized on buprenorphine and will eliminate the treatment barrier of daily dosing for these patients. (Also see "Misconceptions About Maintenance Treatment")

Opioid Antagonists

Naltrexone is an *opioid antagonist*, which means that it works by blocking the activation of opioid receptors. Instead of controlling withdrawal and cravings, it treats addiction by preventing any opioid drug from producing rewarding effects such as euphoria. Its use for ongoing addiction treatment has been somewhat limited because of poor adherence and tolerability by patients. However, in 2010 an injectable, long-acting form of naltrexone (Vivitrol®), originally approved for treating alcohol use disorder, was FDA-approved for treating opioid addiction. Because its effects last for weeks, Vivitrol® is a good option for patients who do not have ready access to healthcare or who struggle with taking their medications regularly.

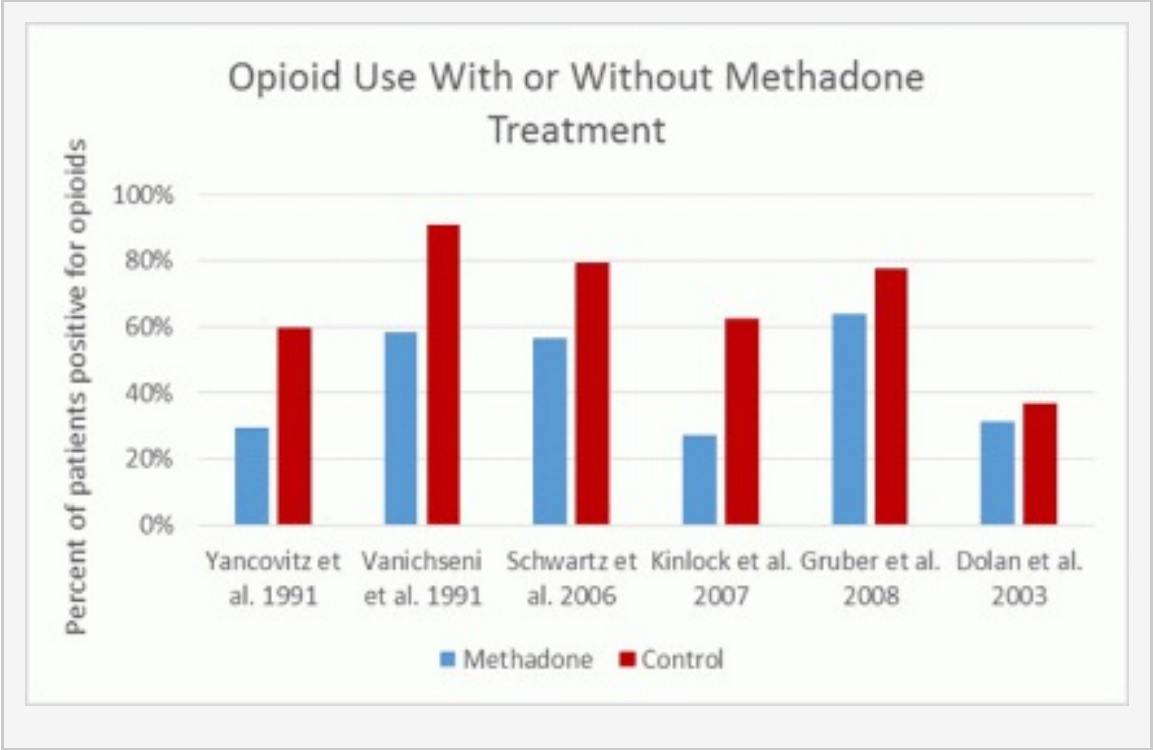
Because each medication works differently, a treatment provider should decide on the optimal medication in consultation with the individual patient and should consider the patient's case unique history and circumstances (see "Efficacy of Medications for Opioid Use Disorder").

Efficacy of Medications for Opioid Use Disorder

Abundant evidence shows that methadone, buprenorphine, and naltrexone all reduce opioid use and opioid use disorder-related symptoms, and they reduce the risk of infectious disease transmission as well as criminal behavior associated with drug use.[15] These medications also increase the likelihood that a person will remain in treatment (*treatment retention*), which itself is associated with lower risk of overdose mortality, reduced risk of HIV and HCV transmission, reduced criminal justice involvement, and greater likelihood of employment.[15]

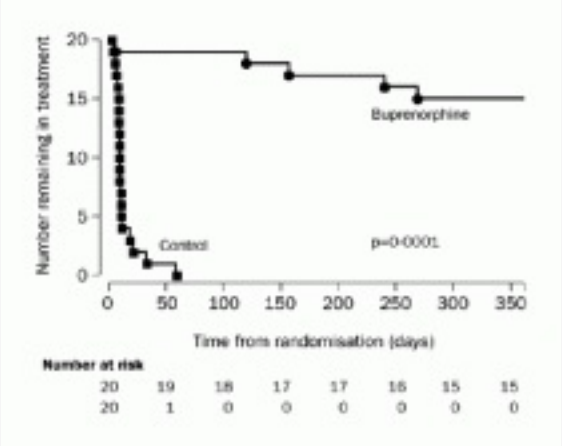
Methadone

Methadone is the medication with the longest history of use for opioid use disorder treatment, having been used since 1947. A large number of studies (some of which are summarized in the graph below) support methadone's effectiveness at reducing opioid use. A comprehensive Cochrane review in 2009 compared methadone-based treatment (methadone plus psychosocial treatment) to placebo with psychosocial treatment and found that methadone treatment was effective in reducing opioid use, opioid use–associated transmission of infectious disease, and crime.[12,16–20] Patients on methadone had 33 percent fewer opioid-positive drug tests and were 4.44 times more likely to stay in treatment compared to controls.[12] Methadone treatment significantly improves outcomes, even when provided in the absence of regular counseling services;[18,19,21] long-term (beyond 6 months) outcomes are better in groups receiving methadone, regardless of the frequency of counseling received.[22,23]



Buprenorphine

Buprenorphine, which was first approved in 2002, is currently available in two forms: alone (Subutex®) and in combination with the opioid receptor antagonist naloxone (Suboxone®). The latter formulation is designed to deter diversion and misuse: the naloxone has no effect so long as the drug is taken orally, as intended; if it is crushed, dissolved, and injected, the naloxone blocks the effect of the buprenorphine. Both formulations of buprenorphine are effective for the treatment of opioid use disorders, though recent studies have shown high recidivism rates among patients tapered off of buprenorphine compared to patients maintained on the drug for a longer period of time.[24]

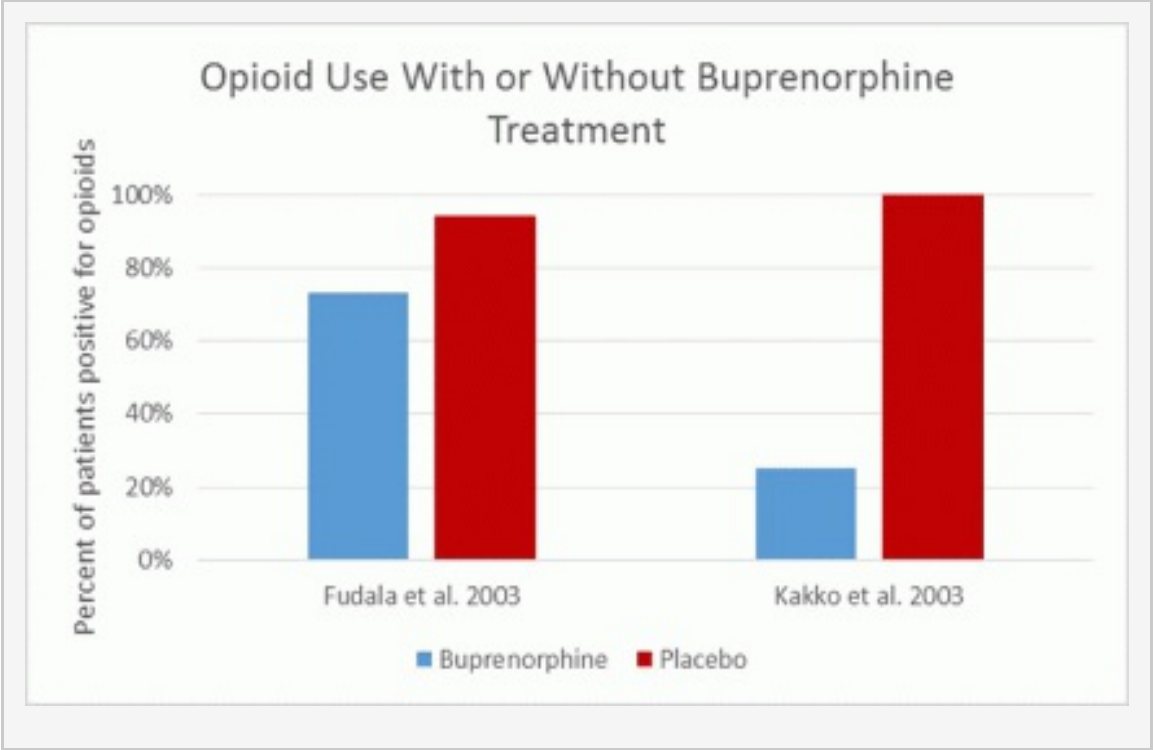


Source: Kakko et al., 2003

A Swedish study compared patients maintained on 16 mg of buprenorphine daily to a control group that received buprenorphine for detoxification (6 days) followed by placebo.[25] All patients received psychosocial supports. In this study, the treatment failure rate for placebo was 100 percent vs. 25 percent for buprenorphine—more than two opioid-positive urine tests within 3 months resulted in cessation of treatment, so treatment retention was closely related to relapse. Of patients not retained in treatment, there was a 20 percent mortality rate.

Meta-analysis determined that patients on doses of buprenorphine of 16 mg per day or more were 1.82 times more likely to stay in treatment than placebo-treated patients, and buprenorphine decreased the number of opioid-positive drug tests by 14.2 to 25 percent (the standardized mean difference was -1.17).[13,25,26]

To be effective, buprenorphine must be given at a sufficiently high dose (generally, 16 mg per day or more). Some treatment providers wary of using opioids have prescribed lower doses for short treatment durations, leading to failure of buprenorphine treatment and the mistaken conclusion that the medication is ineffective.[13,27]



Methadone and Buprenorphine Compared

Methadone and buprenorphine are equally effective at reducing opioid use. A comprehensive Cochrane review comparing buprenorphine, methadone, and placebo found no differences in opioid-positive drug tests or self-reported heroin use when treating with methadone or buprenorphine at medium-to-high doses.[13]

Notably, flexible dose regimens of buprenorphine and doses of buprenorphine of 6 mg or below are less effective than methadone at keeping patients in treatment, highlighting the need for delivery of evidence-based dosing regimens of these medications.[13]

Naltrexone

Naltrexone was initially approved for the treatment of opioid use disorder in a daily pill form. It is an antagonist medication that does not produce tolerance or withdrawal. Poor treatment adherence has primarily limited the real-world effectiveness of this formulation.[28] As a result, there is insufficient evidence that oral naltrexone is an effective treatment for opioid use disorder.[29] Extended-release injectable naltrexone (XR-NTX) is administered once monthly, which

removes the need for daily dosing. While this formulation is the newest form of medication for opioid use disorder, evidence to date suggests that it is effective.[28,30]

The double-blind, placebo-controlled trial that was most influential in getting XR-NTX approved by the FDA in 2010 for opioid use disorder treatment showed that XR-NTX significantly increased opioid abstinence; the XR-NTX group had 90 percent confirmed abstinent weeks compared to 35 percent in the placebo group. Treatment retention was also higher in the XR-NTX group (58 percent vs. 42 percent), while subjective drug craving and relapse (0.8 percent vs. 13.7 percent) were both decreased.[31] Improvement in the XR-NTX group was sustained throughout an open label period out to 76 weeks.[32] These data were collected in Russia, and additional studies are required to determine if effectiveness will be similar in the United States.[33]

Buprenorphine and Naltrexone Compared

A NIDA study shows that once treatment is initiated, a buprenorphine/naloxone combination and an extended release naltrexone formulation are similarly effective in treating opioid use disorder. Because naltrexone requires full detoxification, initiating treatment among active opioid users was more difficult with this medication. However, once detoxification was complete, the naltrexone formulation had a similar effectiveness as the buprenorphine/naloxone combination.

Misconceptions About Maintenance Treatment

Because maintenance medications (methadone and buprenorphine) are themselves opioids and are able to produce euphoria in people who are not dependent on opioids, many people have assumed that this form of treatment just substitutes a new addiction for an old one. This belief has unfortunately hindered the adoption of these effective treatments. In the past, even some inpatient treatment programs that were otherwise evidence based did not allow patients to use these medications, in favor of an "abstinence only" philosophy.

Although it is possible for individuals who do not have an opioid addiction to get high on buprenorphine or methadone (see "Treatment Need vs. Diversion Risk for Opioid Addiction Treatment Medications"), these medications affect people who have developed a high *tolerance* (see "Opioid Tolerance") to opioids differently. At the doses prescribed, and as a result of their *pharmacodynamic* and *pharmacokinetic* properties (the way they act at opioid receptor sites and their slower metabolism in the body), these medications do not produce a euphoric "high" but instead minimize withdrawal symptoms and cravings (see "Mechanisms of Opioid Dependence"). This makes it possible for the patient to function normally, attend school or work, and participate in other forms of treatment or recovery support services to help them become free of their addiction over time.

The ultimate aim can be to wean off the maintenance medication, but the treatment provider should make this decision jointly with the patient, and tapering the medication must be done gradually. It may take months or years in some cases. Just as body tissues require prolonged periods to heal after injury and may require external supports (e.g., a cast and crutches or a wheelchair for a broken leg), brain circuits that have been altered by prolonged drug use and addiction take time to recover and benefit from external supports in the form of medication. In cases of serious and long-term opioid addiction, a patient may need these supports indefinitely.

In 2005, methadone and buprenorphine were added to the World Health

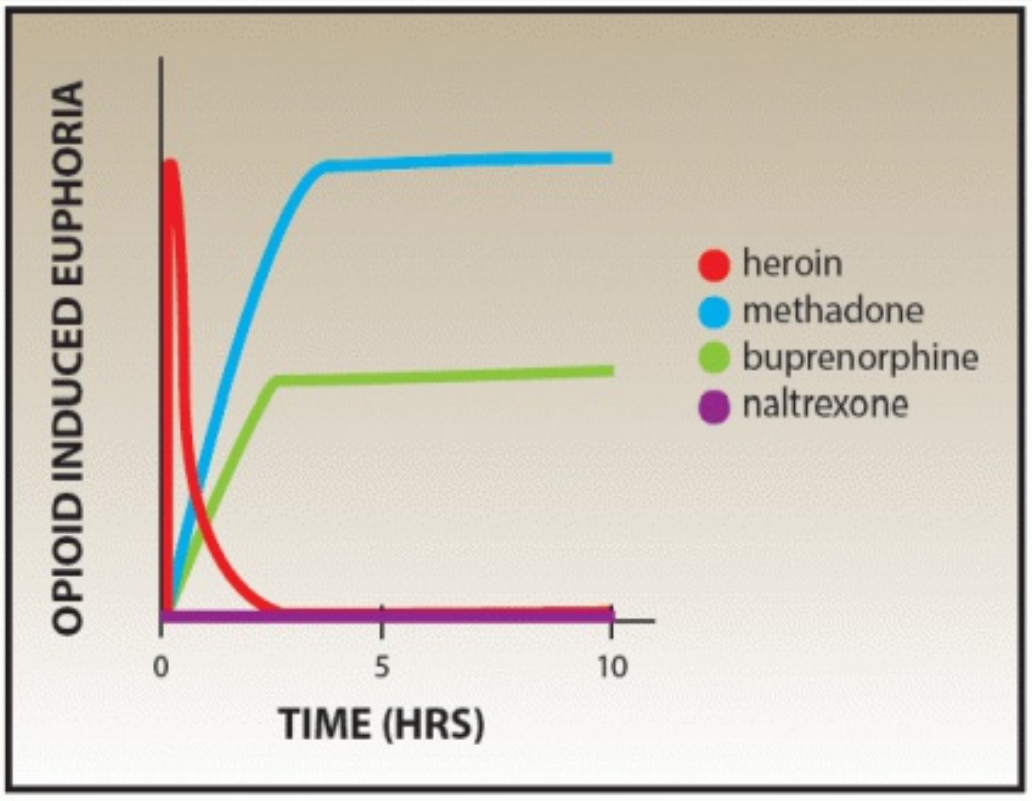
Organization's list of essential medicines, defined as medicines that are "intended to be available within the context of functioning healthcare systems at all times in adequate amounts, in the appropriate dosage forms, with assured quality, and at a price the individual and the community can afford."[34,35]

Opioid Tolerance

People who take opioids for long periods of time typically develop *tolerance*, a state in which more of the drug is needed to produce the same effect. Receptor desensitization and downregulation are molecular processes that cause tolerance. In people with opioid use disorder, the brain is continually exposed to high levels of opioids as well as dopamine, which is released in the reward circuit following opioid receptor activation. Brain cells respond to this by reducing their response to receptor activation and by removing opioid and dopamine receptors from the cell membrane, resulting in fewer receptors that can be activated by the drug.[36,37] These mechanisms result in a lessened response to the drug, so higher doses are required to elicit the same effect. This opioid tolerance is the reason that people with opioid use disorder do not experience euphoric effects from therapeutic doses of buprenorphine or methadone, while people without opioid use disorder do.[38,39] It is also the reason why people are at increased risk of overdose when relapsing to opioid use after a period of abstinence: They lose their tolerance to the drug without realizing it, so they no longer know what dose of the drug they can safely tolerate.

Mechanisms of Opioid Dependence

The sustained activation of opioid receptors that results from opioid use disorder and causes tolerance also causes withdrawal symptoms when the opioid drugs leave the body. Drug withdrawal symptoms are opposite to the symptoms caused by drug taking. In the case of opioids, they include anxiety, jitters, and diarrhea.[40] Avoidance of these negative symptoms is one reason that people keep taking opioids, and in the early stages of treatment, medications such as methadone and buprenorphine reduce withdrawal symptoms.



Opioid receptor activity. Heroin (red line) activates opioid receptors fully and quickly. Methadone (blue) is also a full agonist, but the activation is much slower and longer lasting. Buprenorphine (green) activates the receptors partially, with a similar time course to methadone. Naltrexone (purple) is an opioid receptor antagonist and therefore prevents receptor activation.[41,42]

Sources: Cruciani & Knotkova, 2013; Goodman et al., 2006

Treatment Need vs. Diversion Risk for Opioid Addiction Treatment Medications

Like other opioid medications, buprenorphine and methadone are sometimes diverted and misused. However, most data suggest that the majority of buprenorphine and methadone misuse (use without a prescription) is for the purpose of controlling withdrawal and cravings for other opioids and not to get high. Among all opioid agonist medications, methadone and buprenorphine together make up 15 percent of diversion reports, while oxycodone and hydrocodone are responsible for 67 percent.[43] Naltrexone, the third medication used to treat opioid addiction, is an opioid antagonist, which means it does not cause euphoric effects and is not a diversion risk.

Both buprenorphine and buprenorphine/naloxone formulations can interfere with the effects of full opioid agonists such as heroin and can precipitate withdrawal in individuals with opioid dependence. Two U.S. surveys of people with opioid use disorders found that a majority of those who used illicit buprenorphine reported that they used it for therapeutic purposes (i.e., to reduce withdrawal symptoms, reduce heroin use, etc.).[44,45] Ninety-seven percent reported using to prevent cravings, 90 percent to prevent withdrawal, and 29 percent to save money.[45] Illicit use of buprenorphine decreased as individuals had access to treatment.[45] The minority proportion of people who use buprenorphine illicitly to get high (ranging from 8 to 25 percent)[45,46] has been shown to decrease over time, which could suggest that people abandon this goal after they experience the drug's blunted rewarding effects.[46] Indeed, patients in treatment for opioid use disorder rarely endorse buprenorphine as the primary drug of abuse.[47]

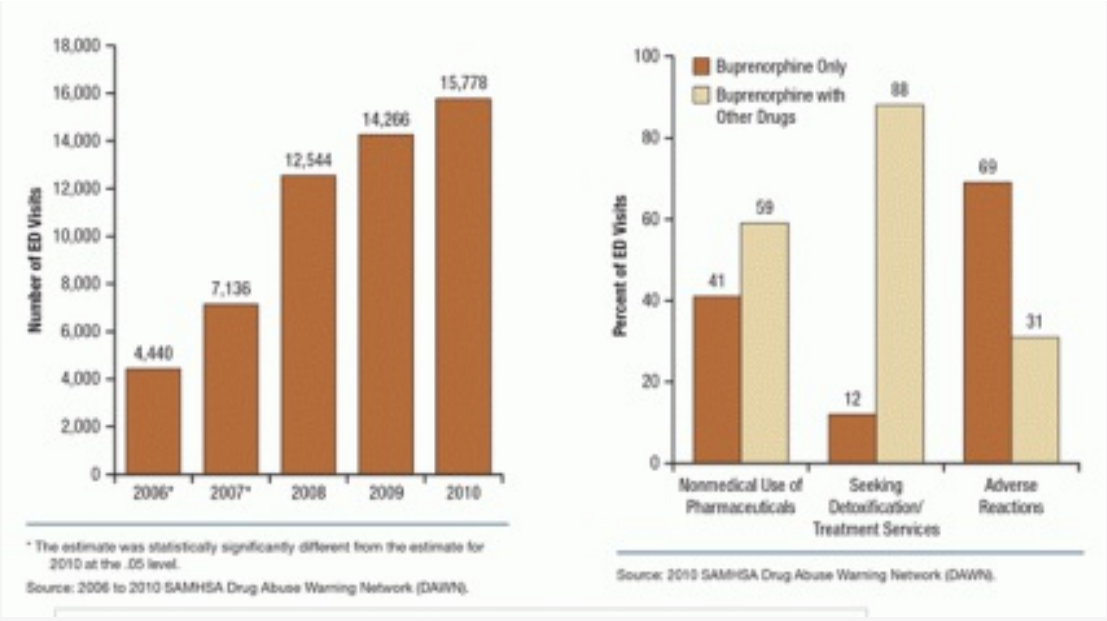
Methadone diversion is primarily associated with methadone prescribed for the treatment of pain, and not for the treatment of opioid use disorders. Opioid treatment programs are required to maintain and implement a diversion control plan; they typically require patients to come in daily to receive their medication and strictly monitor take-home doses. In addition, evidence suggests that the

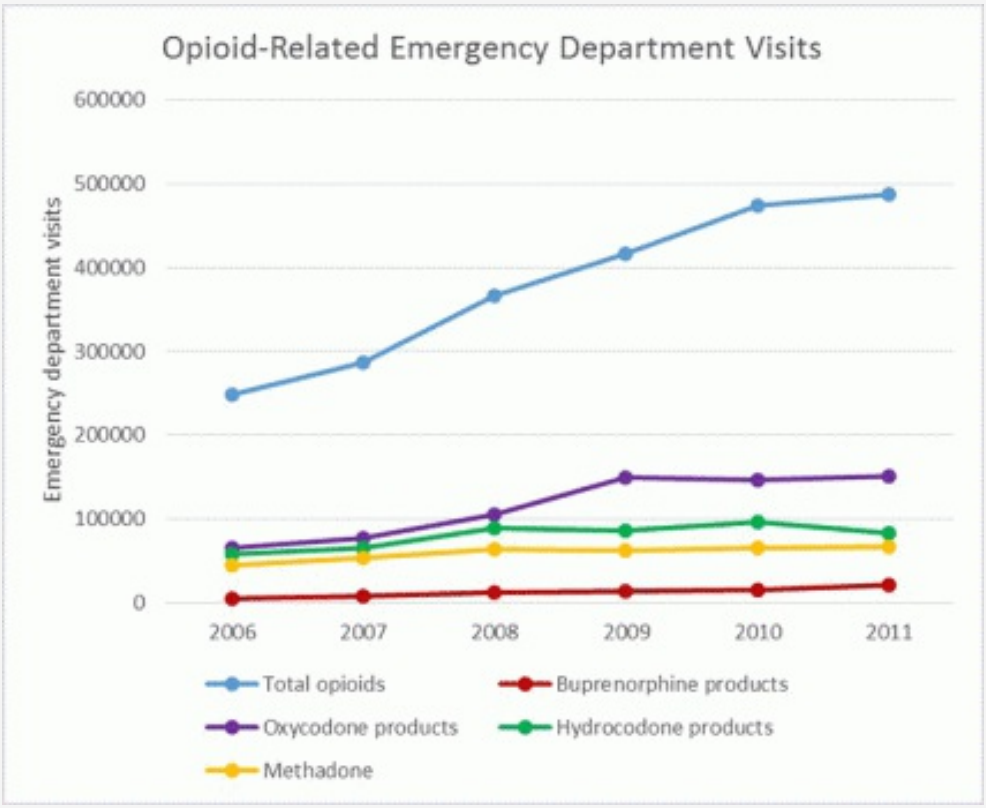
diversion that does occur is associated with a lack of access to medication.[48] In one survey, giving methadone away was identified as the most common form of methadone diversion,[49] which aligns with other findings that 80 percent of people who report diverting methadone did so to help others who misused substances.[48,50] Among those using illicit methadone, the most common reason was a missed medication pick-up.[50]

While there is some risk associated with misuse of buprenorphine, the risk of harms, such as fatal overdose, are significantly lower than those of full agonist opioids (oxycodone, hydrocodone, heroin).[39,51] Overdoses and related deaths do occur but are usually the result of combination with other respiratory depressant drugs such as benzodiazepines or alcohol. Emergency department (ED) visits involving buprenorphine increased from 3,161 in 2005 to 30,135 visits in 2010 as availability of the drug increased (buprenorphine was first approved in 2002); but ED visits for buprenorphine remain significantly less common than those for other opioids.[52] Fifty-two percent, or 15,778 visits (see left bar chart below), were related to nonmedical use in 2010; 59 percent of these visits involved additional drugs (see right bar chart below).[53,54]

Methadone, as a full opioid agonist that is metabolized slowly, poses a greater risk of overdose than buprenorphine. In 2010, 65,945 ED visits involved nonmedical use of methadone.[53] However, methadone that is dispensed for use as a pain reliever, not as an addiction medication, is the main source of the methadone involved in overdose deaths.[55]

Emergency department (ED) visits involving buprenorphine increased as drug availability increased, but ED visits for buprenorphine are far less common than those for other opioids.





Source: CBHSQ, 2011

Impact of Medication for Addiction Treatment on HIV/HCV Outcomes

Injection drug use is still a primary driver of the HIV/AIDS epidemic across the world.[56] A recent example is the small community of Austin, Indiana, where 170 new HIV infections occurred in the 8 months between November 2014 and June 2015 among people misusing the prescription opioid pain reliever oxymorphone (Opana®) via injection.[6] People who inject drugs frequently share their needles and other injection equipment, enabling viruses such as HIV and hepatitis C (HCV) to spread between people.

Medications for addiction treatment can reduce transmission of HIV and HCV by reducing risk behaviors in people who inject drugs and can improve HIV- and HCV-related outcomes by treating those not engaged in injection opioid use who might otherwise transition to injection, linking those with HIV/HCV infection to appropriate treatment[57,58] and improving adherence to HIV/HCV treatment.[59,60] These improvements depend on accessibility of medications for opioid use disorders to people who need it and coordinating medication delivery with HCV/HIV screening and treatment.

Treatment with methadone or buprenorphine is associated with reduced injection drug use risk behaviors. Meta-analyses have shown a reduction in risk behaviors including a 32 to 69 percent reduction in illicit opioid use, a 20 to 60 percent reduction in injection drug use, and a 25 to 86 percent reduction in sharing of injection equipment.[61,62] Treatment with extended-release naltrexone also reduced HIV risk behaviors compared to placebo.[31]

Methadone and buprenorphine treatment are also associated with lower HCV infection rates in young adults who injects drugs, while other treatments and detoxification alone are not.[63] Methadone treatment is associated with low rates of contracting HCV overall,[64] with mathematical modeling suggesting that it can prevent 22.6 new HCV infections per 100 treated people who engaged in injection drug use, per year.[65,66] Methadone treatment also reduces both HIV risk behaviors and HIV infection, with better outcomes for people who inject drugs who are in treatment (3.5 percent contracting HIV vs. 22 percent), and

better outcomes for longer treatment duration and for continuous (vs. interrupted) treatment.[67–69]

A study comparing the effects of methadone and buprenorphine treatment on HIV risk from injection behaviors and HIV risk from sexual behaviors showed equal and significant reductions in risky injection behaviors. Risky sexual behaviors were reduced in both male and female methadone patients but were higher in male patients on buprenorphine.[70]

Mitigating Factors

There are several known interactions between medications used to treat HIV or HCV and both methadone and buprenorphine.[71,72] These could require an adjustment of dosage or revision of the treatment plan, and highlight the need for integrated care. For example, some patients are reluctant to begin highly active antiretroviral therapy (HAART) because of worries that it will interfere with their methadone treatment, so treatment providers should consider revised methadone doses for these patients.[72]

Contracting HCV while on methadone is associated with continued injection drug use.[73] Some studies have shown methadone detoxification alone to be associated with increased rates of contracting HIV, so ongoing treatment with this medication is key to reducing transmission of viral infection.[74]

Possibility of Dual Therapeutic Potential

One recent report demonstrates the potential of buprenorphine to counteract a neuroinflammatory process that is involved in HIV-associated neurocognitive disorders, suggesting that buprenorphine could potentially be simultaneously therapeutic for opioid addiction and HIV.[75,76] Opioid use disorder medications are also associated with increased adherence to HAART for the treatment of HIV.[59,60] Some providers hesitate to treat HCV in people who inject drugs, but a naltrexone implantation clinic showed rates of sustained virologic response in their patients that were comparable to clinics treating non-injection drug-using patients.[77]

Treatment of Opioid Use Disorder in the Criminal Justice System

Opioid use disorders are highly prevalent among criminal justice populations. According to data from the U.S. Department of Justice, approximately half of state and federal prisoners meet criteria for substance use disorder.[78] Even so, there has been reticence in criminal justice settings to using medications (methadone, buprenorphine, naltrexone) to treat opioid use disorders. In national surveys, utilization of these medications is very low in criminal justice settings, including drug courts,[79] jails,[80] and prisons.[81] Thus, opioid use disorder goes largely untreated during periods of incarceration, and opioid use often resumes after release.

A former inmate's risk of death within the first 2 weeks of release is more than 12 times that of other individuals, with the leading cause of death being a fatal overdose.[82] Overdoses are more common when a person relapses to drug use after a period of abstinence due to loss of tolerance to the drug. Untreated opioid use disorders also contribute to a return to criminal activity, reincarceration, and risky behavior contributing to the spread of HIV and hepatitis B and C infections (see "Impact of Medication for Addiction Treatment on HIV/HCV outcomes").[83]

The World Health Organization's *Guidelines for the Psychosocially Assisted Pharmacological Treatment of Opioid Dependence* states: "Prisoners should not be denied adequate health care because of their imprisonment . . . Opioid withdrawal, agonist maintenance and naltrexone treatment should all be available in prison settings, and prisoners should not be forced to accept any particular treatment."[84]

Many states currently do not offer appropriate access to or utilize medications to treat opioid use disorders among arrestees or inmates,[80,85] even though research has shown many benefits of incorporating medication-assisted treatment into criminal justice treatment programs. Inmates who receive buprenorphine treatment prior to release are more likely to engage in treatment after their release than inmates who only participate in counseling.[86]

Participants who engage in methadone treatment and counseling in prison are more likely to enter community-based methadone treatment centers after their release (68.6 percent) than those receiving only counseling (7.8 percent) or those in counseling and referred to a treatment center (50 percent).[19]

In one study, inmates who began buprenorphine treatment while incarcerated engaged in post-release treatment sooner, averaging 3.9 days after release, compared to 9.2 days for participants referred to treatment post-release.[83] They were also likely to stay in treatment longer if they were initiated in treatment prior to release (20.3 weeks on average) than if they began treatment after their release (13.2 weeks).[83]

Inmates who participate in methadone treatment and counseling while in prison are less likely to test positive for illicit opioids at one month following their release (27.6 percent) compared to those who only receive counseling (62.9 percent) and those who receive counseling and a referral to a treatment center (41 percent).[19]

A randomized controlled trial was published in 2016, comparing prison-initiated extended-release naltrexone (XR-NTX) treatment to standard counseling protocols for prevention of opioid relapse. During the treatment phase, relapse was significantly lower in the group receiving XR-NTX (43 percent vs. 64 percent). The XR-NTX group also experienced no overdose events, while there were seven overdose events in the control group.[87]

A survey of community correction agents' views on using medications to treat opioid addiction showed that more favorable attitudes toward medication use are associated with greater knowledge about the evidence base for these medications and greater understanding of addiction as a medical disorder.[88] Organizational linkage between correctional stakeholders and community treatment providers, along with training sessions, can be an effective way to change perceptions and increase knowledge about the efficacy of these medications and can increase the intent within correctional facilities to refer individuals with opioid use disorder to treatment that incorporates medications.[85]

A mechanism to reduce recidivism and divert nonviolent offenders from traditional jail and prison settings is the drug treatment court model, which provides treatment services in combination with judicial supervision.[89] Still, resistance to medications persists even in this area of the criminal justice system; a survey published in 2013 reported that 50 percent of drug courts did not allow agonist treatment for opioid use disorder under any circumstances.[79] In 2015, the Office of National Drug Control Policy announced that state drug courts receiving federal grants must not: 1) deny any appropriate and eligible client for the treatment drug court access to the program because of their use of FDA-approved medications (methadone, injectable naltrexone, non-injectable naltrexone, disulfiram, acamprosate calcium, buprenorphine, etc.) that is in accordance with an appropriately authorized [physician's prescription]; or 2) mandate that a drug court client no longer use medications as part of the conditions of the drug court if such a mandate is inconsistent with a physician's recommendation or prescription.[90]

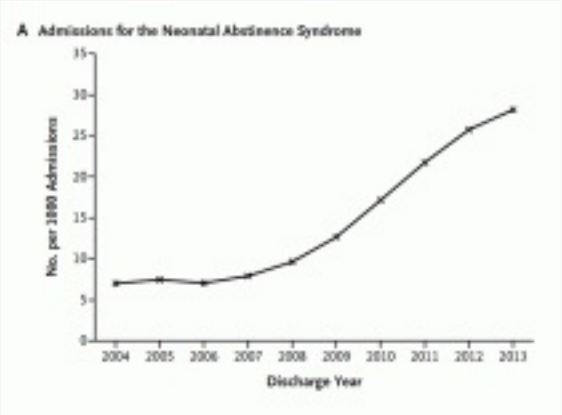
Opioid Addiction Medication in the Military

Rates of prescription opioid misuse are higher among service members than among civilians.[91] Survey results suggest drug use among returning soldiers is often a coping strategy to treat arousal symptoms of post-traumatic stress disorder.[92] Returning military personnel also experience higher rates of chronic pain and related medical use of opioid pain relievers compared to the civilian population. These data collectively suggest an unmet need for the assessment, management, and treatment of both chronic pain and opioid use disorders in this population.[93]

The Veterans Health Administration (VHA) acknowledges that treatment with opioid agonists (methadone or buprenorphine) is the first-line treatment for opioid addiction and recommends it for all opioid-dependent patients. Notably, a 2015 revision of treatment guidelines for the U.S. Department of Veteran Affairs and U.S. Department of Defense shifted toward allowing these medications as a treatment option for active duty military members.[94] Still, only about a quarter of patients with an opioid addiction treated at VHA facilities receive medication.[95] Barriers to opioid agonist medication among VHA providers include: lack of perceived patient interest, stigma toward the patient population, and lack of education about opioid agonist treatment.[96]

In the past, lack of insurance coverage for opioid agonist medications was a barrier for use among active duty military; however, as of 2013, TRICARE included coverage for these medications, and a 2016 modification of TRICARE regulation included provisions for expanded coverage of opioid use disorder treatment.[97] This expanded coverage removed annual and lifetime limitations on substance use disorder treatment, allowed for office-based opioid treatment and established opioid treatment programs as a newly recognized category of institutional provider under TRICARE.

Treatment for Pregnant Mothers and Babies



Source: Tolia et al., 2015

Paralleling the large recent increases in opioid use, use disorders, and overdose, the incidence of babies born dependent on opioids (neonatal abstinence syndrome, or NAS) as a result of the mother's opioid use during pregnancy has also greatly increased.[5] Incidence of NAS rose nearly fivefold between 2000 and 2012;[4] this increase was associated with increases in the prescription of opioids to pregnant women for pain, which doubled between 1995 and 2009.[98,99]

Untreated opioid addiction during pregnancy can have devastating effects on the fetus. The fluctuating levels of opioids in the blood of mothers misusing opioids expose the fetus to repeated periods of withdrawal,[100] which can also harm the function of the placenta and increase the risk of:

- fetal growth restriction
- placental abruption
- preterm labor
- fetal convulsions
- fetal death[101]

- intrauterine passage of meconium

In addition to these direct physical effects, other risks to the fetus include:

- untreated maternal infections such as HIV[102]
- malnutrition and poor prenatal care[103]
- dangers conferred by drug-seeking lifestyle, including violence and incarceration[101,103]

Methadone and Buprenorphine As the Standard of Care for Opioid Use Disorder in Pregnancy

To lessen the negative effects of opioid dependence on the fetus, treatment with methadone has been used for pregnant women with opioid use disorder since the 1970s and has been recognized as the standard of care since 1998.[101,102] Recent evidence, however, suggests that buprenorphine may be an even better treatment option.[104]

Both methadone and buprenorphine treatment during pregnancy:

- stabilize fetal levels of opioids, reducing repeated prenatal withdrawal[100,105]
- improve neonatal outcomes
- increase maternal HIV treatment to reduce the likelihood of transmitting the virus to the fetus[101–103]
- link mothers to better prenatal care[101,103]

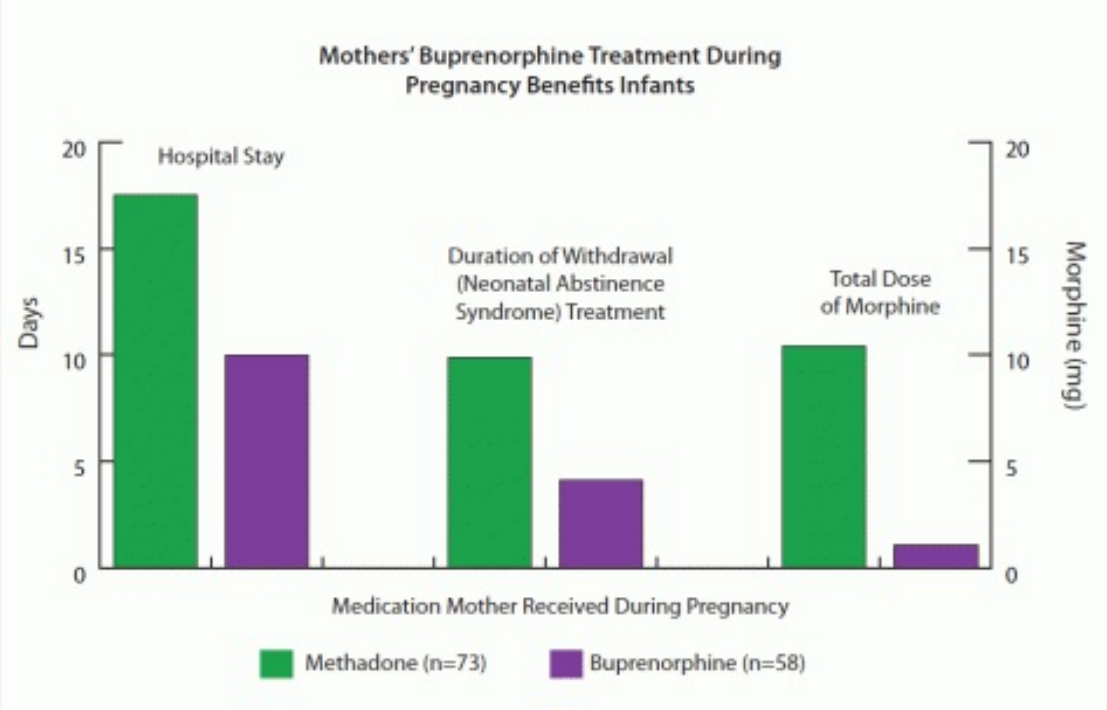
A meta-analysis showed that, compared to single-dose methadone treatment, buprenorphine resulted in:

- 10 percent lower incidence of NAS
- shorter neonatal treatment time (an average of 8.4 days shorter)

- lower amount of morphine used for NAS treatment (an average of 3.6 mg lower)
- higher gestational age, weight, and head circumference at birth[104]

Data from the NIDA-funded *Maternal Opioid Treatment: Human Experimental Research* study show similar benefits of buprenorphine.[106] Still, methadone is associated with higher treatment retention than buprenorphine.[104] Divided dosing with methadone has been explored as a way to reduce fetal exposure to withdrawal periods, and recent data show low levels of NAS in babies born to mothers treated with divided doses of methadone.[107] Larger comparison studies are needed to determine if split methadone dosing for opioid use disorders in pregnancy is associated with better outcomes.

NAS still occurs in babies whose mothers have received buprenorphine or methadone, but it is less severe than it would be in the absence of treatment.[108] Research does not support reducing maternal methadone dose to avoid NAS, as this may promote increased illicit drug use, resulting in increased risk to the fetus.[100]



Source: Jones et al., 2010

How Much Does Opioid Treatment Cost?

Although the price for opioid treatment may vary based on a number of factors, recent preliminary cost estimates from the U.S. Department of Defense for treatment in a certified opioid treatment program (OTP) provide a reasonable basis for comparison:[97]

- methadone treatment, including medication, and integrated psychosocial and medical support services (assumes daily visits): $126.00 per week or $6,552.00 per year
- buprenorphine for a stable patient provided in a certified OTP including medication and twice-weekly visits: $115.00 per week or $5,980.00 per year
- naltrexone provided in an OTP, including drug, drug administration, and related services: $1,176.50 per month or $14,112.00 per year

To put these costs into context, it is useful to compare them with the costs of other conditions. According to the Agency for Healthcare Research and Quality, annual expenditures for individuals who received healthcare are $3,560.00 for those with diabetes mellitus and $5,624.00 for kidney disease.[109]

It is also important to remember the costs associated with untreated opioid use disorders, including costs associated with:

- criminal justice
- treating babies born dependent on opioids
- greater transmission of infectious diseases
- treating overdoses
- injuries associated with intoxication (e.g., drugged driving)
- lost productivity

The amount paid for treatment of substance use disorders is only a small portion of the costs these disorders impose on society. A recent analysis suggested that the total costs of prescription opioid use disorders and overdoses in the United States was $78 billion in 2013. Of that, only 3.6 percent, or about $2.8 billion, was for treatment.[110]

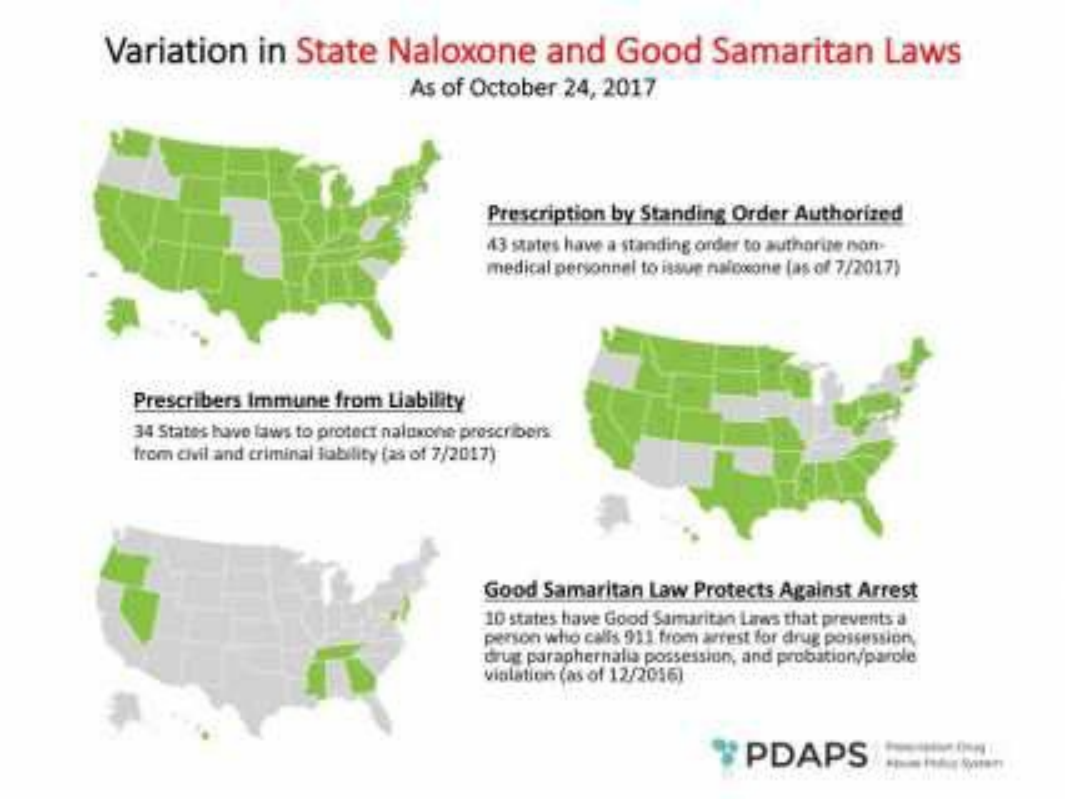
Access to Naloxone

Naloxone is an opioid antagonist that can reverse an opioid overdose. Naloxone access increased between 2010 and 2014, with:[8]

- more than three times the number of local sites providing naloxone (from 188 to 644)
- nearly three times the number of laypersons provided naloxone kits (from 53,032 to 152,283)
- a 94 percent increase in states (from 16 to 30), including Washington, DC, with at least one organization providing naloxone
- more than 2.5 times the number of overdose reversals reported (from 10,171 to 26,463)

Naloxone prescriptions dispensed from retail pharmacies increased nearly twelvefold between the fourth quarter of 2013 and the second quarter of 2015.[111]

Many states have passed laws to widen the availability to naloxone for family, friends, and other potential bystanders of overdose.



Naloxone has become widely used by emergency medical providers, with all 50 states and the District of Columbia, Guam, and Puerto Rico certifying and approving emergency medical service personnel at the paramedic level to administer naloxone. One step further, emergency medical technicians (EMTs) were explicitly permitted to administer naloxone in 12 of these 53 jurisdictions (23 percent—California, Colorado, District of Columbia, Massachusetts, Maryland, New Mexico, North Carolina, Ohio, Oklahoma, Rhode Island, Virginia, and Vermont) as of November 2013. Because nonparamedic EMTs are typically the first and sometimes only source of emergency care, providing authorization and training for them to administer naloxone is a promising strategy to reduce overdose deaths.[112]

After a naloxone training session, a majority of police officers reported that it would not be difficult to use naloxone at the scene of an overdose (89.7 percent) and that it was important that other officers be trained to use naloxone (82.9 percent).[113]

Effects of Naloxone Distribution

Overdose education and naloxone distribution (OEND) has been shown to increase the reversal of potentially fatal overdoses; one study showed opioid overdose death rates to be 27 to 46 percent lower in communities where OEND was implemented.[114] Among 4,926 people who used substances and participated in OEND in Massachusetts, 373 (7.6 percent) reported administering naloxone during an overdose rescue, with few differences in behavior between trained and untrained overdose rescuers.[115] A naloxone distribution study in San Francisco reported that 11 percent of participants used naloxone during an overdose; of 399 overdose events where naloxone was used, 89 percent were reversed.[116] Brief education is sufficient to improve comfort and competence in recognizing and managing overdose.[117] Prospective studies are needed to determine the optimal level of training and whether naloxone rescue kits can meet the standard for becoming available over the counter.[115]

In a probabilistic analysis, naloxone distribution programs were shown to prevent overdose deaths, increase quality-adjusted life years (QALYs) and be highly cost-effective. Naloxone distribution was predicted to prevent 6 percent of overdose deaths, 1 for every 227 naloxone kits distributed. Cost effectiveness, under markedly conservative predictions, was measured to be $14,000.00 per QALY, well within the standard favorable range of cost-benefit ratios (under $50,000.00 per QALY).[118]

Critics of naloxone distribution have claimed that it could lead to an increase in risky opioid use, but a study in Massachusetts showed rates of opioid-related visits to an emergency department and hospital admission were not significantly different in communities with low or high implementation of OEND programs.[114]

References

1. Substance Abuse Center for Behavioral Health Statistics and Quality. Results from the 2015 National Survey on Drug Use and Health: Detailed Tables. SAMHSA. https://www.samhsa.gov/data/sites/default/files/NSDUH-DetTabs-2015/NSDUH-DetTabs-2015/NSDUH-DetTabs-2015.pdf. Published September 8, 2016. Accessed January 18, 2017.

2. Rudd RA, Aleshire N, Zibbell JE, Gladden RM. Increases in Drug and Opioid Overdose Deaths--United States, 2000-2014. *MMWR Morb Mortal Wkly Rep*. 2016;64(50-51):1378-1382. doi:10.15585/mmwr.mm6450a3.

3. Rudd RA, Seth P, David F, Scholl L. Increases in Drug and Opioid-Involved Overdose Deaths - United States, 2010-2015. *MMWR Morb Mortal Wkly Rep*. 2016;65(5051):1445-1452. doi:10.15585/mmwr.mm655051e1.

4. Patrick SW, Davis MM, Lehmann CU, Lehman CU, Cooper WO. Increasing incidence and geographic distribution of neonatal abstinence syndrome: United States 2009 to 2012. *J Perinatol Off J Calif Perinat Assoc*. 2015;35(8):650-655. doi:10.1038/jp.2015.36.

5. Tolia VN, Patrick SW, Bennett MM, et al. Increasing incidence of the neonatal abstinence syndrome in U.S. neonatal ICUs. *N Engl J Med*. 2015;372(22):2118-2126. doi:10.1056/NEJMsa1500439.

6. Conrad C, Bradley HM, Broz D, et al. Community Outbreak of HIV Infection Linked to Injection Drug Use of Oxymorphone--Indiana, 2015. *MMWR Morb Mortal Wkly Rep*. 2015;64(16):443-444.

7. U.S. Department of Health and Human Services, Office of the Assistant Secretary for Planning and Evaluation. Opioid Abuse in the U.S. and HHS Actions to Address Opioid-Drug Related Overdoses and Deaths. ASPE. https://aspe.hhs.gov/pdf-report/opioid-abuse-us-and-hhs-actions-address-opioid-drug-related-overdoses-and-deaths. Published November 23, 2015. Accessed May 11, 2017.

8. Wheeler E, Jones TS, Gilbert MK, Davidson PJ, Centers for Disease Control and Prevention (CDC). Opioid Overdose Prevention Programs Providing Naloxone to Laypersons - United States, 2014. *MMWR Morb Mortal Wkly Rep*. 2015;64(23):631-635.

9. Knudsen HK, Abraham AJ, Roman PM. Adoption and implementation of medications in addiction treatment programs. *J Addict Med*. 2011;5(1):21-27. doi:10.1097/ADM.0b013e3181d41ddb.

10. Bart G. Maintenance medication for opiate addiction: the foundation of recovery. *J Addict Dis*. 2012;31(3):207-225. doi:10.1080/10550887.2012.694598.

11. Davoli M, Bargagli AM, Perucci CA, et al. Risk of fatal overdose during and after specialist drug treatment: the VEdeTTE study, a national multi-site prospective cohort study. *Addict Abingdon Engl*. 2007;102(12):1954-1959. doi:10.1111/j.1360-0443.2007.02025.x.

12. Mattick RP, Breen C, Kimber J, Davoli M. Methadone maintenance therapy versus no opioid replacement therapy for opioid dependence. *Cochrane Database Syst Rev*. 2009;(3):CD002209. doi:10.1002/14651858.CD002209.pub2.

13. Mattick RP, Breen C, Kimber J, Davoli M. Buprenorphine maintenance versus placebo or methadone maintenance for opioid dependence. *Cochrane Database Syst Rev*. 2014;(2):CD002207. doi:10.1002/14651858.CD002207.pub4.

14. Substance Abuse and Mental Health Services Administration. *Clinical Guidelines for the Use of Buprenorphine in the Treatment of Opioid Addiction: A Treatment Improvement Protocol TIP 40*. Substance Abuse and Mental Health Services Administration; 2004. https://www.ncbi.nlm.nih.gov/books/NBK64245/pdf/Bookshelf_NBK64245.pdf. Accessed May 11, 2017.

15. The American Society of Addiction Medicine. *Advancing Access to Addiction Medications*. http://www.asam.org/docs/default-source/advocacy/aaam_implications-for-opioid-addiction-treatment_final. Accessed May 11, 2017.

16. Yancovitz SR, Des Jarlais DC, Peyser NP, et al. A randomized trial of an interim methadone maintenance clinic. *Am J Public Health*. 1991;81(9):1185-1191.

17. Vanichseni S, Wongsuwan B, Choopanya K, Wongpanich K. A controlled trial of methadone maintenance in a population of intravenous drug users in Bangkok: implications for prevention of HIV. *Int J Addict*. 1991;26(12):1313-

1320.

18. Schwartz RP, Highfield DA, Jaffe JH, et al. A randomized controlled trial of interim methadone maintenance. *Arch Gen Psychiatry*. 2006;63(1):102-109. doi:10.1001/archpsyc.63.1.102.

19. Kinlock TW, Gordon MS, Schwartz RP, O'Grady K, Fitzgerald TT, Wilson M. A randomized clinical trial of methadone maintenance for prisoners: results at 1-month post-release. *Drug Alcohol Depend*. 2007;91(2-3):220-227. doi:10.1016/j.drugalcdep.2007.05.022.

20. Dolan KA, Shearer J, MacDonald M, Mattick RP, Hall W, Wodak AD. A randomised controlled trial of methadone maintenance treatment versus wait list control in an Australian prison system. *Drug Alcohol Depend*. 2003;72(1):59-65.

21. Schwartz RP, Kelly SM, O'Grady KE, Gandhi D, Jaffe JH. Randomized trial of standard methadone treatment compared to initiating methadone without counseling: 12-month findings. *Addict Abingdon Engl*. 2012;107(5):943-952. doi:10.1111/j.1360-0443.2011.03700.x.

22. Sees KL, Delucchi KL, Masson C, et al. Methadone maintenance vs 180-day psychosocially enriched detoxification for treatment of opioid dependence: a randomized controlled trial. *JAMA*. 2000;283(10):1303-1310.

23. Gruber VA, Delucchi KL, Kielstein A, Batki SL. A randomized trial of 6-month methadone maintenance with standard or minimal counseling versus 21-day methadone detoxification. *Drug Alcohol Depend*. 2008;94(1-3):199-206. doi:10.1016/j.drugalcdep.2007.11.021.

24. Fiellin DA, Schottenfeld RS, Cutter CJ, Moore BA, Barry DT, O'Connor PG. Primary care-based buprenorphine taper vs maintenance therapy for prescription opioid dependence: a randomized clinical trial. *JAMA Intern Med*. 2014;174(12):1947-1954. doi:10.1001/jamainternmed.2014.5302.

25. Kakko J, Svanborg KD, Kreek MJ, Heilig M. 1-year retention and social function after buprenorphine-assisted relapse prevention treatment for heroin dependence in Sweden: a randomised, placebo-controlled trial. *Lancet Lond Engl*. 2003;361(9358):662-668. doi:10.1016/S0140-6736(03)12600-1.

26. Fudala PJ, Bridge TP, Herbert S, et al. Office-based treatment of opiate addiction with a sublingual-tablet formulation of buprenorphine and naloxone. *N Engl J Med*. 2003;349(10):949-958. doi:10.1056/NEJMoa022164.

27. MacDonald K, Lamb K, Thomas ML, Khentigan W. Buprenorphine Maintenance Treatment of Opiate Dependence: Correlations Between Prescriber Beliefs and Practices. *Subst Use Misuse*. 2016;51(1):85-90. doi:10.3109/10826084.2015.1089905.

28. Nunes EV, Krupitsky E, Ling W, et al. Treating Opioid Dependence With Injectable Extended-Release Naltrexone (XR-NTX): Who Will Respond? *J Addict Med*. 2015;9(3):238-243. doi:10.1097/ADM.0000000000000125.

29. Minozzi S, Amato L, Vecchi S, Davoli M, Kirchmayer U, Verster A. Oral naltrexone maintenance treatment for opioid dependence. *Cochrane Database Syst Rev*. 2011;(4):CD001333. doi:10.1002/14651858.CD001333.pub4.

30. Krupitsky E, Nunes EV, Ling W, Gastfriend DR, Memisoglu A, Silverman BL. Injectable extended-release naltrexone (XR-NTX) for opioid dependence: long-term safety and effectiveness. *Addict Abingdon Engl*. 2013;108(9):1628-1637. doi:10.1111/add.12208.

31. Krupitsky E, Nunes EV, Ling W, Illeperuma A, Gastfriend DR, Silverman BL. Injectable extended-release naltrexone for opioid dependence: a double-blind, placebo-controlled, multicentre randomised trial. *Lancet Lond Engl*. 2011;377(9776):1506-1513. doi:10.1016/S0140-6736(11)60358-9.

32. Syed YY, Keating GM. Extended-release intramuscular naltrexone (VIVITROL®): a review of its use in the prevention of relapse to opioid dependence in detoxified patients. *CNS Drugs*. 2013;27(10):851-861. doi:10.1007/s40263-013-0110-x.

33. Jackson H, Mandell K, Johnson K, Chatterjee D, Vanness DJ. Cost-Effectiveness of Injectable Extended-Release Naltrexone Compared With Methadone Maintenance and Buprenorphine Maintenance Treatment for Opioid Dependence. *Subst Abuse*. 2015;36(2):226-231. doi:10.1080/08897077.2015.1010031.

34. World Health Organization. *Proposal for the Inclusion of Buprenorphine in the WHO Model List of Essential Medicines*.; 2004.

http://www.who.int/substance_abuse/activities/buprenorphine_essential_medicines.pd
Accessed May 11, 2017.

35. World Health Organization. *Proposal for the Inclusion of Methadone in the WHO Model List of Essential Medicines*. World Health Organization; 2004. http://www.who.int/substance_abuse/activities/methadone_essential_medicines.pdf. Accessed May 11, 2017.

36. Williams JT, Ingram SL, Henderson G, et al. Regulation of μ-opioid receptors: desensitization, phosphorylation, internalization, and tolerance. *Pharmacol Rev*. 2013;65(1):223-254. doi:10.1124/pr.112.005942.

37. Allouche S, Noble F, Marie N. Opioid receptor desensitization: mechanisms and its link to tolerance. *Front Pharmacol*. 2014;5:280. doi:10.3389/fphar.2014.00280.

38. Walsh SL, June HL, Schuh KJ, Preston KL, Bigelow GE, Stitzer ML. Effects of buprenorphine and methadone in methadone-maintained subjects. *Psychopharmacology (Berl)*. 1995;119(3):268-276.

39. Highlights of Prescribing Information: SUBOXONE®. February 2017. https://www.suboxone.com/content/pdfs/prescribing-information.pdf. Accessed May 11, 2017.

40. Kosten TR, George TP. The neurobiology of opioid dependence: implications for treatment. *Sci Pract Perspect*. 2002;1(1):13-20.

41. Cruciani RA, Knotkova H, eds. *Handbook of Methadone Prescribing and Buprenorphine Therapy*. New York: Springer-Verlag; 2013.

42. Brunton LL, Lazo JS, Parker KL, eds. *Goodman & Gilman's The Pharmacological Basis of Therapeutics*. 11th ed.

43. U.S. Department of Justice Drug Enforcement Administration, Office of Diversion Control. *National Forensic Laboratory Information System (NFLIS) 2013 Annual Report*. https://www.nflis.deadiversion.usdoj.gov/DesktopModules/ReportDownloads/Reports/N Accessed May 11, 2017.

44. Bazazi AR, Yokell M, Fu JJ, Rich JD, Zaller ND. Illicit use of buprenorphine/naloxone among injecting and noninjecting opioid users. *J Addict Med*. 2011;5(3):175-180. doi:10.1097/ADM.0b013e3182034e31.

45. Schuman-Olivier Z, Albanese M, Nelson SE, et al. Self-treatment: illicit buprenorphine use by opioid-dependent treatment seekers. *J Subst Abuse Treat*. 2010;39(1):41-50. doi:10.1016/j.jsat.2010.03.014.

46. Cicero TJ, Surratt HL, Inciardi J. Use and misuse of buprenorphine in the management of opioid addiction. *J Opioid Manag*. 2007;3(6):302-308.

47. Cicero TJ, Ellis MS, Surratt HL, Kurtz SP. Factors contributing to the rise of buprenorphine misuse: 2008-2013. *Drug Alcohol Depend*. 2014;142:98-104. doi:10.1016/j.drugalcdep.2014.06.005.

48. Johnson B, Richert T. Diversion of methadone and buprenorphine from opioid substitution treatment: a staff perspective. *J Psychoactive Drugs*. 2014;46(5):427-435. doi:10.1080/02791072.2014.960109.

49. Johnson B, Richert T. Diversion of methadone and buprenorphine by patients in opioid substitution treatment in Sweden: prevalence estimates and risk factors. *Int J Drug Policy*. 2015;26(2):183-190. doi:10.1016/j.drugpo.2014.10.003.

50. Duffy P, Mackridge AJ. Use and diversion of illicit methadone – under what circumstances does it occur, and potential risks associated with continued use of other substances. *J Subst Use*. 2014;19(1-2):48-55. doi:10.3109/14659891.2012.734539.

51. Soyka M. New developments in the management of opioid dependence: focus on sublingual buprenorphine-naloxone. *Subst Abuse Rehabil*. 2015;6:1-14. doi:10.2147/SAR.S45585.

52. Center for Behavioral Health Statistics and Quality (CBHSQ). *Drug Abuse Warning Network: 2011: Selected Tables of National Estimates of Drug-Related Emergency Department Visits*. Rockville, MD: Substance Abuse and Mental Health Services Administration; 2013.

53. Substance Abuse and Mental Health Services Administration. Drug Abuse Warning Network, 2011: National Estimates of Drug-Related Emergency Department Visits. https://www.samhsa.gov/data/sites/default/files/DAWN2k11ED/DAWN2k11ED/DAWN2 Published May 2013. Accessed May 12, 2017.

54. Substance Abuse and Mental Health Services Administration, Center for Behavioral Health Statistics and Quality (CBHSQ). *The DAWN Report:*

Emergency Department Visits Involving Buprenorphine. Substance Abuse and Mental Health Services Administration; 2013. http://archive.samhsa.gov/data/2k13/DAWN106/sr106-buprenorphine.pdf. Accessed May 12, 2017.

55. Centers for Disease Control and Prevention (CDC). Vital signs: risk for overdose from methadone used for pain relief - United States, 1999-2010. *MMWR Morb Mortal Wkly Rep*. 2012;61(26):493-497.

56. Metzger DS, Donnell D, Celentano DD, et al. Expanding substance use treatment options for HIV prevention with buprenorphine-naloxone: HIV Prevention Trials Network 058. *J Acquir Immune Defic Syndr 1999*. 2015;68(5):554-561. doi:10.1097/QAI.0000000000000510.

57. Perlman DC, Jordan AE, Uuskula A, et al. An international perspective on using opioid substitution treatment to improve hepatitis C prevention and care for people who inject drugs: Structural barriers and public health potential. *Int J Drug Policy*. 2015;26(11):1056-1063. doi:10.1016/j.drugpo.2015.04.015.

58. Otiashvili D, Piralishvili G, Sikharulidze Z, Kamkamidze G, Poole S, Woody GE. Methadone and buprenorphine-naloxone are effective in reducing illicit buprenorphine and other opioid use, and reducing HIV risk behavior--outcomes of a randomized trial. *Drug Alcohol Depend*. 2013;133(2):376-382. doi:10.1016/j.drugalcdep.2013.06.024.

59. Malta M, Strathdee SA, Magnanini MMF, Bastos FI. Adherence to antiretroviral therapy for human immunodeficiency virus/acquired immune deficiency syndrome among drug users: a systematic review. *Addict Abingdon Engl*. 2008;103(8):1242-1257. doi:10.1111/j.1360-0443.2008.02269.x.

60. Batki SL, Gruber VA, Bradley JM, Bradley M, Delucchi K. A controlled trial of methadone treatment combined with directly observed isoniazid for tuberculosis prevention in injection drug users. *Drug Alcohol Depend*. 2002;66(3):283-293.

61. Gowing L, Farrell MF, Bornemann R, Sullivan LE, Ali R. Oral substitution treatment of injecting opioid users for prevention of HIV infection. *Cochrane Database Syst Rev*. 2011;(8):CD004145. doi:10.1002/14651858.CD004145.pub4.

62. Gowing LR, Hickman M, Degenhardt L. Mitigating the risk of HIV infection with opioid substitution treatment. *Bull World Health Organ*. 2013;91(2):148-149. doi:10.2471/BLT.12.109553.

63. Tsui JI, Evans JL, Lum PJ, Hahn JA, Page K. Association of opioid agonist therapy with lower incidence of hepatitis C virus infection in young adult injection drug users. *JAMA Intern Med*. 2014;174(12):1974-1981. doi:10.1001/jamainternmed.2014.5416.

64. Nolan S, Dias Lima V, Fairbairn N, et al. The impact of methadone maintenance therapy on hepatitis C incidence among illicit drug users. *Addict Abingdon Engl*. 2014;109(12):2053-2059. doi:10.1111/add.12682.

65. Peles E, Schreiber S, Rados V, Adelson M. Low risk for hepatitis C seroconversion in methadone maintenance treatment. *J Addict Med*. 2011;5(3):214-220. doi:10.1097/ADM.0b013e31820e13dd.

66. Alavian SM, Mirahmadizadeh A, Javanbakht M, et al. Effectiveness of Methadone Maintenance Treatment in Prevention of Hepatitis C Virus Transmission among Injecting Drug Users. *Hepat Mon*. 2013;13(8):e12411. doi:10.5812/hepatmon.12411.

67. Hallinan R, Byrne A, Amin J, Dore GJ. Hepatitis C virus incidence among injecting drug users on opioid replacement therapy. *Aust N Z J Public Health*. 2004;28(6):576-578.

68. Gibson DR, Flynn NM, McCarthy JJ. Effectiveness of methadone treatment in reducing HIV risk behavior and HIV seroconversion among injecting drug users. *AIDS Lond Engl*. 1999;13(14):1807-1818.

69. Metzger DS, Woody GE, McLellan AT, et al. Human immunodeficiency virus seroconversion among intravenous drug users in- and out-of-treatment: an 18-month prospective follow-up. *J Acquir Immune Defic Syndr*. 1993;6(9):1049-1056.

70. Woody GE, Bruce D, Korthuis PT, et al. HIV risk reduction with buprenorphine-naloxone or methadone: findings from a randomized trial. *J Acquir Immune Defic Syndr 1999*. 2014;66(3):288-293. doi:10.1097/QAI.0000000000000165.

71. Bruce RD, Moody DE, Altice FL, Gourevitch MN, Friedland GH. A review of pharmacological interactions between HIV or hepatitis C virus medications

and opioid agonist therapy: implications and management for clinical practice. *Expert Rev Clin Pharmacol*. 2013;6(3):249-269. doi:10.1586/ecp.13.18.

72. Maas B, Kerr T, Fairbairn N, Montaner J, Wood E. Pharmacokinetic interactions between HIV antiretroviral therapy and drugs used to treat opioid dependence. *Expert Opin Drug Metab Toxicol*. 2006;2(4):533-543. doi:10.1517/17425255.2.4.533.

73. Zhou W, Wang X, Zhou S, et al. Hepatitis C seroconversion in methadone maintenance treatment programs in Wuhan, China. *Addict Abingdon Engl*. 2015;110(5):796-802. doi:10.1111/add.12836.

74. MacArthur GJ, Minozzi S, Martin N, et al. Opiate substitution treatment and HIV transmission in people who inject drugs: systematic review and meta-analysis. *BMJ*. 2012;345:e5945.

75. Carvallo L, Lopez L, Che F-Y, et al. Buprenorphine decreases the CCL2-mediated chemotactic response of monocytes. *J Immunol Baltim Md 1950*. 2015;194(7):3246-3258. doi:10.4049/jimmunol.1302647.

76. Fitting S, Zou S, El-Hage N, et al. Opiate addiction therapies and HIV-1 Tat: interactive effects on glial $[Ca^{2+}]i$, oxyradical and neuroinflammatory chemokine production and correlative neurotoxicity. *Curr HIV Res*. 2014;12(6):424-434.

77. Jeffrey GP, MacQuillan G, Chua F, et al. Hepatitis C virus eradication in intravenous drug users maintained with subcutaneous naltrexone implants. *Hepatol Baltim Md*. 2007;45(1):111-117. doi:10.1002/hep.21470.

78. Mumola CJ, Karberg JC. *Bureau of Justice Statistics Special Report: Drug Use and Dependence, State and Federal Prisoners, 2004*. U.S. Department of Justice, Office of Justice Programs; 2006. https://www.bjs.gov/content/pub/pdf/dudsfp04.pdf. Accessed May 11, 2017.

79. Matusow H, Dickman SL, Rich JD, et al. Medication assisted treatment in US drug courts: results from a nationwide survey of availability, barriers and attitudes. *J Subst Abuse Treat*. 2013;44(5):473-480. doi:10.1016/j.jsat.2012.10.004.

80. Fiscella K, Moore A, Engerman J, Meldrum S. Jail management of arrestees/inmates enrolled in community methadone maintenance

programs. *J Urban Health Bull N Y Acad Med*. 2004;81(4):645-654. doi:10.1093/jurban/jth147.

81. Nunn A, Zaller N, Dickman S, Trimbur C, Nijhawan A, Rich JD. Methadone and buprenorphine prescribing and referral practices in US prison systems: results from a nationwide survey. *Drug Alcohol Depend*. 2009;105(1-2):83-88. doi:10.1016/j.drugalcdep.2009.06.015.

82. Binswanger IA, Stern MF, Deyo RA, et al. Release from prison–a high risk of death for former inmates. *N Engl J Med*. 2007;356(2):157-165. doi:10.1056/NEJMsa064115.

83. Zaller N, McKenzie M, Friedmann PD, Green TC, McGowan S, Rich JD. Initiation of buprenorphine during incarceration and retention in treatment upon release. *J Subst Abuse Treat*. 2013;45(2):222-226. doi:10.1016/j.jsat.2013.02.005.

84. World Health Organization. *Guidelines for the Psychosocially Assisted Pharmacological Treatment of Opioid Dependence*. World Health Organization; 2009. http://www.who.int/substance_abuse/publications/opioid_dependence_guidelines.pdf. Accessed May 11, 2017.

85. Friedmann PD, Wilson D, Knudsen HK, et al. Effect of an organizational linkage intervention on staff perceptions of medication-assisted treatment and referral intentions in community corrections. *J Subst Abuse Treat*. 2015;50:50-58. doi:10.1016/j.jsat.2014.10.001.

86. Gordon MS, Kinlock TW, Schwartz RP, Fitzgerald TT, O'Grady KE, Vocci FJ. A randomized controlled trial of prison-initiated buprenorphine: prison outcomes and community treatment entry. *Drug Alcohol Depend*. 2014;142:33-40. doi:10.1016/j.drugalcdep.2014.05.011.

87. Lee JD, Friedmann PD, Boney TY, et al. Extended-release naltrexone to prevent relapse among opioid dependent, criminal justice system involved adults: rationale and design of a randomized controlled effectiveness trial. *Contemp Clin Trials*. 2015;41:110-117. doi:10.1016/j.cct.2015.01.005.

88. Mitchell SG, Willet J, Monico LB, et al. Community correctional agents' views of medication-assisted treatment: Examining their influence on treatment referrals and community supervision practices. *Subst Abuse*. 2016;37(1):127-133. doi:10.1080/08897077.2015.1129389.

89. Brown RT. Systematic review of the impact of adult drug-treatment courts. *Transl Res J Lab Clin Med*. 2010;155(6):263-274. doi:10.1016/j.trsl.2010.03.001.

90. Substance Abuse and Mental Health Services Administration. Grants to Expand Substance Abuse Treatment Capacity in Adult and Family Drug Courts: Request for Applications (RFA) No. TI-15-002. 2015. http://www.samhsa.gov/sites/default/files/grants/doc/ti-15-002.doc.

91. National Institute on Drug Abuse. Substance Abuse in the Military. https://www.drugabuse.gov/publications/drugfacts/substance-abuse-in-military. Published March 1, 2013. Accessed May 11, 2017.

92. Shipherd JC, Stafford J, Tanner LR. Predicting alcohol and drug abuse in Persian Gulf War veterans: what role do PTSD symptoms play? *Addict Behav*. 2005;30(3):595-599. doi:10.1016/j.addbeh.2004.07.004.

93. Toblin RL, Quartana PJ, Riviere LA, Walper KC, Hoge CW. Chronic pain and opioid use in US soldiers after combat deployment. *JAMA Intern Med*. 2014;174(8):1400-1401. doi:10.1001/jamainternmed.2014.2726.

94. U.S. Department of Veteran Affairs. A/DoD Clinical Practice Guideline for the Management of Substance Use Disorders. 2015. https://www.healthquality.va.gov/guidelines/MH/sud/VADoDSUDCPGRevised22216.p Accessed May 11, 2017.

95. Oliva EM, Trafton JA, Harris AHS, Gordon AJ. Trends in opioid agonist therapy in the Veterans Health Administration: is supply keeping up with demand? *Am J Drug Alcohol Abuse*. 2013;39(2):103-107. doi:10.3109/00952990.2012.741167.

96. Gordon AJ, Kavanagh G, Krumm M, et al. Facilitators and barriers in implementing buprenorphine in the Veterans Health Administration. *Psychol Addict Behav J Soc Psychol Addict Behav*. 2011;25(2):215-224. doi:10.1037/a0022776.

97. U.S. Department of Defense, Office of the Secretary. TRICARE; Mental Health and Substance Use Disorder Treatment. Federal Register. https://www.federalregister.gov/documents/2016/09/02/2016-21125/tricare-mental-health-and-substance-use-disorder-treatment. Published September 2, 2016. Accessed May 11, 2017.

98. Epstein RA, Bobo WV, Martin PR, et al. Increasing pregnancy-related use of prescribed opioid analgesics. *Ann Epidemiol*. 2013;23(8):498-503. doi:10.1016/j.annepidem.2013.05.017.

99. Patrick SW, Dudley J, Martin PR, et al. Prescription opioid epidemic and infant outcomes. *Pediatrics*. 2015;135(5):842-850. doi:10.1542/peds.2014-3299.

100. Kaltenbach K, Berghella V, Finnegan L. Opioid dependence during pregnancy. Effects and management. *Obstet Gynecol Clin North Am*. 1998;25(1):139-151.

101. The American College of Obstetricians and Gynecologists, The American Society of Addiction Medicine. *Opioid Abuse, Dependence, and Addiction in Pregnancy*. The American College of Obstetricians and Gynecologists; 2012. http://www.acog.org/-/media/Committee-Opinions/Committee-on-Health-Care-for-Underserved-Women/co524.pdf?dmc=1&ts=20150429T1228129639. Accessed May 11, 2017.

102. Effective medical treatment of opiate addiction. National Consensus Development Panel on Effective Medical Treatment of Opiate Addiction. *JAMA*. 1998;280(22):1936-1943.

103. Substance Abuse and Mental Health Services Administration. *Medication-Assisted Treatment for Opioid Addiction in Opioid Treatment Programs. Treatment Improvement Protocol (TIP) Series 43*. Substance Abuse and Mental Health Services Administration; 2005. https://www.ncbi.nlm.nih.gov/books/NBK64164/pdf/Bookshelf_NBK64164.pdf. Accessed May 11, 2017.

104. Brogly SB, Saia KA, Walley AY, Du HM, Sebastiani P. Prenatal buprenorphine versus methadone exposure and neonatal outcomes: systematic review and meta-analysis. *Am J Epidemiol*. 2014;180(7):673-686. doi:10.1093/aje/kwu190.

105. Kandall SR, Doberczak TM, Jantunen M, Stein J. The methadone-maintained pregnancy. *Clin Perinatol*. 1999;26(1):173-183.

106. Jones HE, Kaltenbach K, Heil SH, et al. Neonatal abstinence syndrome after methadone or buprenorphine exposure. *N Engl J Med*. 2010;363(24):2320-2331. doi:10.1056/NEJMoa1005359.

107. McCarthy JJ, Leamon MH, Willits NH, Salo R. The effect of methadone dose regimen on neonatal abstinence syndrome. *J Addict Med*. 2015;9(2):105-110. doi:10.1097/ADM.0000000000000099.

108. Fajemirokun-Odudeyi O, Sinha C, Tutty S, et al. Pregnancy outcome in women who use opiates. *Eur J Obstet Gynecol Reprod Biol*. 2006;126(2):170-175. doi:10.1016/j.ejogrb.2005.08.010.

109. Agency for Healthcare Research and Quality. Mean Expenses per Person with Care for Selected Conditions by Type of Service: United States, 2014. Medical Expenditure Panel Survey Household Component Data. 2016. https://meps.ahrq.gov/mepsweb/survey_comp/household.jsp. Accessed May 11, 2017.

110. Florence CS, Zhou C, Luo F, Xu L. The Economic Burden of Prescription Opioid Overdose, Abuse, and Dependence in the United States, 2013. *Med Care*. 2016;54(10):901-906. doi:10.1097/MLR.0000000000000625.

111. Jones CM, Lurie PG, Compton WM. Increase in Naloxone Prescriptions Dispensed in US Retail Pharmacies Since 2013. *Am J Public Health*. 2016;106(4):689-690. doi:10.2105/AJPH.2016.303062.

112. Davis CS, Southwell JK, Niehaus VR, Walley AY, Dailey MW. Emergency medical services naloxone access: a national systematic legal review. *Acad Emerg Med Off J Soc Acad Emerg Med*. 2014;21(10):1173-1177. doi:10.1111/acem.12485.

113. Ray B, O'Donnell D, Kahre K. Police officer attitudes towards intranasal naloxone training. *Drug Alcohol Depend*. 2015;146:107-110. doi:10.1016/j.drugalcdep.2014.10.026.

114. Walley AY, Xuan Z, Hackman HH, et al. Opioid overdose rates and implementation of overdose education and nasal naloxone distribution in Massachusetts: interrupted time series analysis. *BMJ*. 2013;346:f174.

115. Doe-Simkins M, Quinn E, Xuan Z, et al. Overdose rescues by trained and untrained participants and change in opioid use among substance-using participants in overdose education and naloxone distribution programs: a retrospective cohort study. *BMC Public Health*. 2014;14:297. doi:10.1186/1471-2458-14-297.

116. Enteen L, Bauer J, McLean R, et al. Overdose prevention and naloxone

prescription for opioid users in San Francisco. *J Urban Health Bull N Y Acad Med*. 2010;87(6):931-941. doi:10.1007/s11524-010-9495-8.

117. Behar E, Santos G-M, Wheeler E, Rowe C, Coffin PO. Brief overdose education is sufficient for naloxone distribution to opioid users. *Drug Alcohol Depend*. 2015;148:209-212. doi:10.1016/j.drugalcdep.2014.12.009.

118. Coffin PO, Sullivan SD. Cost-effectiveness of distributing naloxone to heroin users for lay overdose reversal. *Ann Intern Med*. 2013;158(1):1-9. doi:10.7326/0003-4819-158-1-201301010-00003.

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Prescription Opioids

What are prescription opioids?

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Opioids are a class of drugs naturally found in the opium poppy plant. Some prescription opioids are made from the plant directly, and others are made by scientists in labs using the same chemical structure. Opioids are often used as medicines because they contain chemicals that relax the body and can relieve pain. Prescription opioids are used mostly to treat moderate to severe pain, though some opioids can be used to treat coughing and diarrhea. Opioids can also make people feel very relaxed and "high" – which is why they are sometimes used for non-medical reasons. This can be dangerous because opioids can be highly addictive, and overdoses and death are common. Heroin is one of the world's most dangerous opioids, and is never used as a medicine in the United States.

Popular slang terms for opioids include Oxy, Percs, and Vikes.

What are common prescription opioids?

- hydrocodone (Vicodin®) oxycodone (OxyContin®, Percocet®)
- oxymorphone (Opana®)
- morphine (Kadian®, Avinza®)
- codeine
- fentanyl

How do people misuse prescription opioids?

Prescription opioids used for pain relief are generally safe when taken for a short time and as prescribed by a doctor, but they can be misused. People misuse prescription opioids by:

- taking the medicine in a way or dose other than prescribed
- taking someone else's prescription medicine
- taking the medicine for the effect it causes—to get high

When misusing a prescription opioid, a person can swallow the medicine in its normal form. Sometimes people crush pills or open capsules, dissolve the powder in water, and inject the liquid into a vein. Some also snort the powder.

How do prescription opioids affect the brain?

Opioids bind to and activate opioid receptors on cells located in many areas of the brain, spinal cord, and other organs in the body, especially those involved in feelings of pain and pleasure. When opioids attach to these receptors, they block pain signals sent from the brain to the body and release large amounts of dopamine throughout the body. This release can strongly reinforce the act of taking the drug, making the user want to repeat the experience.

What are some possible effects of prescription opioids on the brain and body?

In the short term, opioids can relieve pain and make people feel relaxed and happy. However, opioids can also have harmful effects, including:

- drowsiness
- confusion
- nausea
- constipation
- euphoria
- slowed breathing

Opioid misuse can cause slowed breathing, which can cause hypoxia, a condition that results when too little oxygen reaches the brain. Hypoxia can have short- and long-term psychological and neurological effects, including coma, permanent brain damage, or death.

Researchers are also investigating the long-term effects of opioid addiction on the brain, including whether damage can be reversed.

What are the other health effects of opioid medications?

Older adults are at higher risk of accidental misuse or abuse because they typically have multiple prescriptions and chronic diseases, increasing the risk of drug-drug and drug-disease interactions, as well as a slowed metabolism that affects the breakdown of drugs.

Sharing drug injection equipment and having impaired judgment from drug use can increase the risk of contracting infectious diseases such as HIV and from unprotected sex.

Prescription Opioids and Heroin

Prescription opioids and heroin are chemically similar and can produce a similar high. In some places, heroin is cheaper and easier to get than prescription opioids, so some people switch to using heroin instead. Nearly 80 percent of Americans using heroin (including those in treatment) reported misusing prescription opioids prior to using heroin.[1,2]

However, while prescription opioid misuse is a risk factor for starting heroin use, only a small fraction of people who misuse pain relievers switch to heroin. This suggests that prescription opioid misuse is just one factor leading to heroin use. Read more about this intertwined problem in our *Prescription Opioids and Heroin Research Report*.

Can I take prescription opioids if I'm pregnant?

If a woman uses prescription opioids when she's pregnant, the baby could develop dependence and have withdrawal symptoms after birth. This is called neonatal abstinence syndrome, which can be treated with medicines. Use during pregnancy can also lead to miscarriage and low birth weight. Read more in the *Substance Use in Women Research Report*.

It can be difficult for a person with an opioid addiction to quit, but pregnant women who seek treatment have better outcomes than those who quit abruptly. Methadone and buprenorphine are the standard of care to treat opioid-dependent pregnant women. Methadone or buprenorphine maintenance combined with prenatal care and a comprehensive drug treatment program can improve many of the adverse outcomes associated with untreated opioid addiction. If a woman is unable to quit before becoming pregnant, treatment with methadone or buprenorphine during pregnancy improves the chances of having a healthier baby at birth.

In general, it is important to closely monitor women who are trying to quit drug use during pregnancy and to provide treatment as needed.

Can a person overdose on prescription opioids?

Yes, a person can overdose on prescription opioids. An opioid overdose occurs when a person uses enough of the drug to produce life-threatening symptoms or death. When people overdose on an opioid medication, their breathing often slows or stops. This can decrease the amount of oxygen that reaches the brain, which can result in coma, permanent brain damage, or death.

How can an opioid overdose be treated?

If you suspect someone has overdosed, the most important step to take is to call 911 so he or she can receive immediate medical attention. Once medical personnel arrive, they will administer naloxone. Naloxone is a medicine that can treat an opioid overdose when given right away. It works by rapidly binding to opioid receptors and blocking the effects of opioid drugs. Naloxone is available as an injectable (needle) solution, a hand-held auto-injector (EVZIO®), and a nasal spray (NARCAN® Nasal Spray).

Some states have passed laws that allow pharmacists to dispense naloxone without a personal prescription. This allows friends, family, and others in the community to use the auto-injector and nasal spray versions of naloxone to save someone who is overdosing.

Read more on our Naloxone webpage.

Tolerance vs. Dependence vs. Addiction

Long-term use of prescription opioids, even as prescribed by a doctor, can cause some people to develop **a tolerance**, which means that they need higher and/or more frequent doses of the drug to get the desired effects.

Drug **dependence** occurs with repeated use, causing the neurons to adapt so they only function normally in the presence of the drug. The absence of the drug causes several physiological reactions, ranging from mild in the case of caffeine, to potentially life threatening, such as with heroin. Some chronic pain patients are dependent on opioids and require medical support to stop taking the drug.

Drug **addiction** is a chronic disease characterized by compulsive, or uncontrollable, drug seeking and use despite harmful consequences and long-lasting changes in the brain. The changes can result in harmful behaviors by those who misuse drugs, whether prescription or illicit drugs.

Can use of prescription opioids lead to addiction?

Yes, repeated misuse of prescription opioids can lead to a substance use disorder (SUD), a medical illness which ranges from mild to severe and from temporary to chronic. Addiction is the most severe form of an SUD. An SUD develops when continued misuse of the drug changes the brain and causes health problems and failure to meet responsibilities at work, school, or home.

People addicted to an opioid medication who stop using the drug can have severe withdrawal symptoms that begin as early as a few hours after the drug was last taken. These symptoms include:

- muscle and bone pain
- sleep problems
- diarrhea and vomiting
- cold flashes with goose bumps
- uncontrollable leg movements
- severe cravings

These symptoms can be extremely uncomfortable and are the reason many people find it so difficult to stop using opioids. There are medicines being developed to help with the withdrawal process, and the U.S. Food and Drug Administration recently approved sale of a device, NSS-2 Bridge, that can help ease withdrawal symptoms. The NSS-2 Bridge device is a small electrical nerve stimulator placed behind the person's ear, that can be used for up to five days during the acute withdrawal phase.

What type of treatment can people get for addiction to prescription opioids?

A range of treatments including medicines and behavioral therapies are effective in helping people with opioid addiction.

Two medicines, buprenorphine and methadone, work by binding to the same opioid receptors in the brain as the opioid medicines, reducing cravings and withdrawal symptoms. Another medicine, naltrexone, blocks opioid receptors and prevents opioid drugs from having an effect.

Behavioral therapies for addiction to prescription opioids help people modify their attitudes and behaviors related to drug use, increase healthy life skills, and persist with other forms of treatment, such as medication. Some examples include, cognitive behavioral therapy which helps modify the patient's drug use expectations and behaviors, and also effectively manage triggers and stress. Multidimensional family therapy, developed for adolescents with drug use problems, addresses a range of personal and family influences on one's drug use patterns and is designed to improve overall functioning. These behavioral treatment approaches have proven effective, especially when used along with medicines. Read more about drug addiction treatment in our *Treatment Approaches for Drug Addiction DrugFacts*.

Points to Remember

- Prescription opioids are used mostly to treat moderate to severe pain, though some opioids can be used to treat coughing and diarrhea.
- People misuse prescription opioids by taking the medicine in a way other than prescribed, taking someone else's prescription, or taking the medicine to get high. When misusing a prescription opioid, a person may swallow, inject, or snort the drug.
- Opioids bind to and activate opioid receptors on cells located in the brain, spinal cord, and other organs in the body, especially those involved in feelings of pain and pleasure, and can strongly reinforce the act of taking the drug, making the user want to repeat the experience.
- People who use prescription opioids can feel relaxed and happy, but also experience drowsiness, confusion, nausea, constipation, and slowed breathing.
- Prescription opioids have effects similar to heroin. While prescription opioid misuse is a risk factor for starting heroin use, only a small fraction of people who misuse opioid pain relievers switch to heroin.
- A person can overdose on prescription opioids. Naloxone is a medicine that can treat an opioid overdose when given right away.
- Prescription opioid use, even when used as prescribed by a doctor can lead to a substance use disorder, which takes the form of addiction in severe cases. Withdrawal symptoms include muscle and bone pain, sleep problems, diarrhea and vomiting, and severe cravings.
- A range of treatments including medicines and behavioral therapies are effective in helping people with an opioid use disorder.

Learn More

For more information about opioid medications, see our:

- Commonly Abused Drugs chart
- *Misuse of Prescription Drugs Research Report*

Updated January 2018

References

1. Muhuri PK, Gfroerer JC, Davies MC. *Associations of Nonmedical Pain Reliever Use and Initiation of Heroin Use in the United States*. Rockville, MD: Substance Abuse and Mental Health Services Administration; 2013. http://archive.samhsa.gov/data/2k13/DataReview/DR006/nonmedical-pain-reliever-use-2013.pdf. Accessed May 13, 2016.

2. Jones CM. Heroin use and heroin use risk behaviors among nonmedical users of prescription opioid pain relievers - United States, 2002-2004 and 2008-2010. *Drug Alcohol Depend*. 2013;132(1-2):95-100. doi:10.1016/j.drugalcdep.2013.01.007.

National Institute on Drug Abuse
DrugFacts
www.drugabuse.gov

Heroin

What is heroin?

Heroin is an opioid drug made from morphine, a natural substance taken from the seed pod of the various opium poppy plants grown in Southeast and Southwest Asia, Mexico, and Colombia. Heroin can be a white or brown powder, or a black sticky substance known as black tar heroin. Other common names for heroin include *big H*, *horse*, *hell dust,* and *smack*.

Photo by DEA/1.usa.gov/1TaKtdj

How do people use heroin?

People inject, sniff, snort, or smoke heroin. Some people mix heroin with crack cocaine, a practice called *speedballing*.

What are the effects of heroin?

Heroin enters the brain rapidly and binds to opioid receptors on cells located in many areas, especially those involved in feelings of pain and pleasure and in controlling heart rate, sleeping, and breathing.

Prescription Opioids and Heroin

Prescription opioid pain medicines such as OxyContin® and Vicodin® have effects similar to heroin. Research suggests that misuse of these drugs may open the door to heroin use. Nearly 80 percent of Americans using heroin (including those in treatment) reported misusing prescription opioids first.[1,2]

While prescription opioid misuse is a risk factor for starting heroin use, only a small fraction of people who misuse pain relievers switch to heroin. According to a national survey, less than 4 percent of people who had misused prescription pain medicines started using heroin within 5 years.[1] This suggests that prescription opioid misuse is just one factor leading to heroin use. Read more about this intertwined problem in our *Prescription Opioids and Heroin Research Report*.

Short-Term Effects

People who use heroin report feeling a "rush" (a surge of pleasure, or euphoria). However, there are other common effects, including:

- dry mouth
- warm flushing of the skin
- heavy feeling in the arms and legs
- nausea and vomiting
- severe itching
- clouded mental functioning
- going "on the nod," a back-and-forth state of being conscious and semiconscious

Long-Term Effects

People who use heroin over the long term may develop:

- insomnia
- collapsed veins for people who inject the drug
- damaged tissue inside the nose for people who sniff or snort it
- infection of the heart lining and valves
- abscesses (swollen tissue filled with pus)
- constipation and stomach cramping
- liver and kidney disease
- lung complications, including pneumonia
- mental disorders such as depression and antisocial personality disorder
- sexual dysfunction for men
- irregular menstrual cycles for women

Other Potential Effects

Heroin often contains additives, such as sugar, starch, or powdered milk, that can clog blood vessels leading to the lungs, liver, kidneys, or brain, causing permanent damage. Also, sharing drug injection equipment and having impaired judgment from drug use can increase the risk of contracting infectious diseases such as HIV and hepatitis (see "Injection Drug Use, HIV, and Hepatitis").

Injection Drug Use, HIV, and Hepatitis

People who inject drugs such as heroin are at high risk of contracting the HIV and hepatitis C (HCV) virus. These diseases are transmitted through contact with blood or other bodily fluids, which can occur when sharing needles or other injection drug use equipment. HCV is the most common bloodborne infection in the Unites States. HIV (and less often HCV) can also be contracted during unprotected sex, which drug use makes more likely.

Read more about the connection between heroin and these diseases in our *Heroin Research Report*.

Can a person overdose on heroin?

Yes, a person can overdose on heroin. A heroin overdose occurs when a person uses enough of the drug to produce a life-threatening reaction or death. Heroin overdoses have increased in recent years.[3]

When people overdose on heroin, their breathing often slows or stops. This can decrease the amount of oxygen that reaches the brain, a condition called *hypoxia*. Hypoxia can have short- and long-term mental effects and effects on the nervous system, including coma and permanent brain damage.

How can a heroin overdose be treated?

Naloxone is a medicine that can treat an opioid overdose when given right away. It works by rapidly binding to opioid receptors and blocking the effects of heroin and other opioid drugs. Sometimes more than one dose may be needed to help a person start breathing again, which is why it's important to get the person to an emergency department or a doctor to receive additional support if needed. Read more in the Substance Abuse and Mental Health Services Administration's Opioid Overdose Prevention Toolkit.

Naloxone is available as an injectable (needle) solution, a handheld auto-injector (EVZIO®), and a nasal spray (NARCAN® Nasal Spray). Friends, family, and others in the community can use the auto-injector and nasal spray versions of naloxone to save someone who is overdosing.

The rising number of opioid overdose deaths has led to an increase in public health efforts to make naloxone available to at-risk persons and their families, as well as first responders and others in the community. Some states have passed laws that allow pharmacists to dispense naloxone without a prescription from a person's personal doctor.

Read more about naloxone at our Naloxone webpage.

Is heroin addictive?

Heroin is highly addictive. People who regularly use heroin often develop a tolerance, which means that they need higher and/or more frequent doses of the drug to get the desired effects. A *substance use disorder* (SUD) is when continued use of the drug causes issues, such as health problems and failure to meet responsibilities at work, school, or home. An SUD can range from mild to severe, the most severe form being addiction.

Those who are addicted to heroin and stop using the drug abruptly may have severe withdrawal. Withdrawal symptoms—which can begin as early as a few hours after the drug was last taken—include:

- restlessness
- severe muscle and bone pain
- sleep problems
- diarrhea and vomiting
- cold flashes with goose bumps ("cold turkey")
- uncontrollable leg movements ("kicking the habit")
- severe heroin cravings

Photo by ©iStock.com/KatarzynaBialasiewicz/ istockpho.to/2dPp5bU

Researchers are studying the long-term effects of opioid addiction on the brain. Studies have shown some loss of the brain's white matter associated with heroin use, which may affect decision-making, behavior control, and responses to stressful situations.[4–6]

How is heroin addiction treated?

A range of treatments including medicines and behavioral therapies are effective in helping people stop heroin use. It's important to match the best treatment approach to meet the particular needs of each individual patient.

Medicines include buprenorphine and methadone. They work by binding to the same opioid receptors in the brain as heroin, but more weakly, reducing cravings and withdrawal symptoms. Another treatment is naltrexone, which blocks opioid receptors and prevents opioid drugs from having an effect. A NIDA study found that once treatment is initiated, both a buprenorphine/naloxone combination and an extended release naltrexone formulation are similarly effective in addiction. Because full detoxification is necessary for treatment with naloxone, initiating treatment among active users was difficult, but once detoxification was complete, both medications had similar effectiveness.

Behavioral therapies for heroin addiction include methods called cognitive-behavioral therapy and contingency management. Cognitive-behavioral therapy helps modify the patient's drug-use expectations and behaviors, and helps effectively manage triggers and stress. Contingency management provides motivational incentives, such as vouchers or small cash rewards for positive behaviors such as staying drug-free. These behavioral treatment approaches are especially effective when used along with medicines. Read more about drug addiction treatment in our *Treatment Approaches for Drug Addiction DrugFacts*.

Points to Remember

- Heroin is an opioid drug made from morphine, a natural substance taken from the seed pod of various opium poppy plants.
- Heroin can be a white or brown powder, or a black sticky substance known as black tar heroin.
- People inject, sniff, snort, or smoke heroin. Some people mix heroin with crack cocaine, called *speedballing*.
- Heroin enters the brain rapidly and binds to opioid receptors on cells located in many areas, especially those involved in feelings of pain and pleasure and in controlling heart rate, sleeping, and breathing.
- People who use heroin report feeling a "rush" (or euphoria). Other common effects include dry mouth, heavy feelings in the arms and legs, and clouded mental functioning.
- Long-term effects may include collapsed veins, infection of the heart lining and valves, abscesses, and lung complications.
- Research suggests that misuse of prescription opioid pain medicine is a risk factor for starting heroin use.
- A person can overdose on heroin. Naloxone is a medicine that can treat a heroin overdose when given right away, though more than one dose may be needed.
- Heroin can lead to addiction, a form of substance use disorder. Withdrawal symptoms include severe muscle and bone pain, sleep problems, diarrhea and vomiting, and severe heroin cravings.
- A range of treatments including medicines and behavioral therapies are effective in helping people stop heroin use. However, treatment plans should be individualized to meet the needs of the patient.

Learn More

For more information about heroin, visit our:

- Heroin webpage (drugabuse.gov/drugs-abuse/heroin)
- Opioids webpage (drugabuse.gov/drugs-abuse/opioids)
- Commonly Abused Drugs chart
- *Medications to Treat Opioid Addiction Research Report*

Updated January 2018

References

1. Muhuri PK, Gfroerer JC, Davies MC. *Associations of Nonmedical Pain Reliever Use and Initiation of Heroin Use in the United States*. Rockville, MD: Substance Abuse and Mental Health Services Administration; 2013. http://archive.samhsa.gov/data/2k13/DataReview/DR006/nonmedical-pain-reliever-use-2013.pdf. Accessed May 13, 2016.

2. Jones CM. Heroin use and heroin use risk behaviors among nonmedical users of prescription opioid pain relievers - United States, 2002-2004 and 2008-2010. *Drug Alcohol Depend*. 2013;132(1-2):95-100. doi:10.1016/j.drugalcdep.2013.01.007.

3. Centers for Disease Control and Prevention (CDC). Multiple Cause of Death, 1999-2015. CDC WONDER Online Database. https://wonder.cdc.gov/mcd-icd10.html. Accessed April 4, 2017.

4. Li W, Li Q, Zhu J, et al. White matter impairment in chronic heroin dependence: a quantitative DTI study. *Brain Res*. 2013;1531:58-64. doi:10.1016/j.brainres.2013.07.036.

5. Liu J, Qin W, Yuan K, et al. Interaction between dysfunctional connectivity at rest and heroin cues-induced brain responses in male abstinent heroin-dependent individuals. *PloS One*. 2011;6(10):e23098. doi:10.1371/journal.pone.0023098.

6. Qiu Y, Jiang G, Su H, et al. Progressive white matter microstructure damage in male chronic heroin dependent individuals: a DTI and TBSS study. *PloS One*. 2013;8(5):e63212. doi:10.1371/journal.pone.0063212.