

Fact Sheet: Fentanyl and Synthetic Opioids



September 2016

What are synthetic opioids like fentanyl?

Synthetic opioids refer to a category of novel psychoactive substances (NPS) that are either known to be opiates or have opiate-like effects. These non-naturally occurring substances have related effects to the naturally occurring drugs from several species of the opium poppy plant. These plants have been cultivated and used by humans for medicinal and recreational purposes over thousands of years,ⁱ from which well-known opiates like morphine and heroin are derived.

Fentanyl is perhaps the most well-known of the synthetic opioids, since it has been extensively researched and is one of the only substances approved for prescription use. Discovered in the 1960's, fentanyl was only used for surgery, but its clinical use expanded in the 90's when an extended release skin patch was developed as treatment for chronic pain. Though diversion of prescription fentanyl has occurred since it first became available, this has never been a major contributor of the increasing supply of fentanyl on the illicit market.ⁱⁱ

Following the discovery of fentanyl, some of its analogues were developed and brought to market for medical use, but recently many related compounds have been appearing on the illicit market that have no prior use in medicine. Unfortunately, not much is known about the effects of numerous fentanyl analogues like acetyl, butyl, or furanyl fentanyl, and other opiate-like NPS that have begun to appear. Currently, synthetic opioids are being produced in clandestine labs and are often used as cutting agents to heroin or other drugs. Many of these substances are known only by their chemical shorthand, such as W-18, U-47700 and AH-7921. Potency and effects can vary widely among these substances, and short and long term health risks are not always clearly known.

What are the effects of fentanyl and other synthetic opioids?

Opiates are a widely researched class of drugs whose effects are well understood. In general, these effects include pain relief and sedation, but also constipation, nausea, and respiratory depression, including: shallow breathing, lowered blood pressure and reduced heart rate.ⁱⁱⁱ Opiates produce these effects through acting on the mu-opioid receptor brain receptor. Fentanyl is one of the most potent opiate-based painkillers approved for medical use, intended for chronic pain patients who have developed a tolerance to less potent opiates such as oxycodone or morphine and are no longer achieving therapeutic pain relief.

Fentanyl's effects are active at much lower doses (around 1-2 nanograms or less), so careful control over dosage and use frequency must be maintained. However, fentanyl's effects are shorter lasting, and are often not considered as euphoric as heroin among those that have used it.^{iv,v,vi}

Understanding of the effects of other synthetic opioids that have not been as extensively studied is limited. Like fentanyl, other synthetic opioids like W-18 and U-47700 are extremely potent; that is, active at very low doses. People who have used these substances also report effects similar to other opiates, like relaxation and pain relief.

How similar is fentanyl to prescription painkillers or heroin?

Types of opiates differ in a few key ways: what form the drugs are available in (i.e. powder or tar, pill, liquid, etc.), how potent they are, how long their effects last, their potential for addiction, and whether the way they are produced leads to predictable results.

The production of prescription painkillers like oxycodone is regulated and therefore produces consistent effects; for example, quick, short-acting relief for less severe pain in doses as low as 5 milligrams, or treatment of chronic and severe pain in extended release doses of over 120 milligrams.^{vii} Heroin derives from morphine but is active at lower doses, and is unregulated in the United States. Because heroin is unregulated, dose and purity vary widely, but generally doses fall within 5-200 milligrams.^{viii} Many synthetic opioids are unapproved and have very little available research on their effects in humans. What is known about some of the fentanyl analogues and other opiate-like NPS is that many are highly potent, with effects active at much lower doses (around 1-2 nanograms or less) than other opiates.^{ix} This is what can make synthetic opiate-laced heroin misuse more dangerous: the euphoric high that people are often seeking from heroin comes with more sedation when fentanyl is present. Therefore, people may take more than usual in pursuit of that sensation, and risk overdosing. Although this risk is present even in those with a tolerance for heroin, it is greater for opiate-naïve users.^x

How many people are fatally overdosing due to fentanyl? Why?

In January 2016 the U.S. Centers for Disease Control and Prevention reported on the increase in drug and opioid overdose deaths in the United States between 2000-2014. In the CDC document, the authors report a 200% increase (between 2000 and 2014) in the rate of overdose deaths involving opioids, including an 80% increase in fatal overdoses involving fentanyl and other synthetic opioids in only one year (2013-2014).^x

People at highest risk of fatal overdose are those who unknowingly take fentanyl.^{xi} Because of the higher potency of fentanyl and other synthetic opioids compared to heroin, their effects are stronger at lower doses than the heroin it is sometimes laced in.^{vi} Thus, if people who stop using heroin then return to heroin use, their tolerance has inevitably been lowered, and they are more susceptible to overdose.^{xii} Moreover, even in people already using heroin, their tolerance to stronger synthetic opioids like fentanyl may be lower,^{xiii} so risk of accidental overdose is higher if they unknowingly take fentanyl-laced heroin, whether through the same method, or their first time trying a new method (i.e. snorting, smoking, or injecting).^{xiv}

How risky are fentanyl and other synthetic opioids?

When fentanyl is prescribed it is a safe and effective pain reliever as long as the recommended dosage and usage frequency is followed, and any side-effects are reported to the medical provider.

Though fatal overdose involving prescribed fentanyl is rare,^{xv} the latest available national data on fentanyl-related deaths from the Centers for Disease Control and Prevention shows an increase of over 700 fatal overdoses between late 2013 and early 2015, but this is mostly from use of non-pharmaceutically produced fentanyl.^{ix} In April 2016, the New York City Department of Health and Mental Hygiene issued an advisory that among the 886 unintentional drug overdoses in 2015, 15% involved fentanyl, compared with fewer than 3% in all of the previous decade.^{xvi}

Fentanyl, its analogues, and other synthetic opioids, though similar in effects to longer-acting opiates like morphine, heroin, or oxycodone, are riskier in use due to their increased potency. Fentanyl has a rapid onset with a shorter duration of effects, so there is some limited evidence that may suggest compulsive use and repeated administration,^{xvii} which increases the risk of fatal overdose. However, the risk of fatal overdose is highest when people unknowingly snort or inject heroin that has been adulterated with a synthetic opiate like fentanyl,^{xii} and not because people who use opiates crave a stronger high from fentanyl.^{xviii}

How do fentanyl and other synthetic opioids get into the heroin supply?

Fentanyl and its analogues have been discovered to be an attractive cutting agent, since their increased sedative potency can be perceived as strengthening a batch of heroin.^{vi} Due to prohibition, there is more incentive for producers and distributors to minimize costs and maximize profits, rather than ensure a safe product.

Sellers in the illicit market are constantly weighing costs and profit against potency. When cutting agents like fentanyl and other synthetic opioids are added, this increases the quantity that can be sold. As long as a particular batch produces noticeable effects, demand will remain.

Are fentanyl and other synthetic opioids more addictive than heroin?

Opiates in general can be habit-forming and continued use can lead to addiction. When considering fentanyl and other synthetic opioids, while their chemical makeup suggests the potential for addiction, we don't yet have much evidence that people are choosing these drugs rather than using them accidentally in pursuit of other opiates. Despite fentanyl and other synthetic opioid's greater potency than heroin, this does not mean people seeking a euphoric high from opiates prefer fentanyl, and actually, the opposite has been reported due to fear of overdose.^{xii} However, limited preliminary evidence suggests preference for fentanyl in heroin-dependent, methadone-stabilized individuals.^{xvii,xviii} Even though fentanyl has not proven addictive, people who have used it should be offered a variety of types of treatment options should they seek to decline or quit use.

How common are fentanyl and other synthetic opioids?

It is hard to tell. In the United States, heroin is typically found in two forms: off-white powder (primarily along the east coast), and black tar (on the west coast), with fentanyl/analogue-laced samples predominantly being found in the powder form.^{xi} Because illicit, clandestinely-produced fentanyl is the same drug as pharmaceutical fentanyl, it is impossible to distinguish the source of the fentanyl involved in fatal overdoses by relying on post-mortem toxicology tests.^{xv} Unlike other pharmaceutical pain relievers, the prevalence of fentanyl and other synthetic opioids does not appear to be tied to supply of prescriptions diverted to the illicit market,^x nor from people using opiates and craving a stronger high.^{xviii}

The most reliable evidence showing the presence of fentanyl laced into the illicit heroin supply comes from reports of seizures by the U.S. Drug Enforcement Administration. In the mid-2000s, the discovery of a single clandestine laboratory operating in Toluca, Mexico, between 2005-2007, reportedly manufactured enough fentanyl that seized samples of heroin during this time contained 20-25% fentanyl. The fentanyl laced from this Mexican lab was believed to be tied to over a thousand confirmed overdose deaths. Following a 2007 raid that shut the operation down, heroin seizures saw a drop in amount of laced-fentanyl (0-6%).^{xi}

More recently, in April 2016, the New York City Department of Health and Mental Hygiene issued an advisory that among the 886 unintentional drug overdoses in 2015, 15% involved fentanyl, compared with fewer than 3% in all of the previous decade.^{xvixvi} In addition, in 2016, Illinois became the first state to declare two drug overdoses involving what may be a synthetic opioid known only as W-18,^{xix} though authorities in Canada have discovered W-18 in seizures of counterfeit "fentanyl" tablets since 2015,^{xx} and carfentanil has been confirmed in at least one case involving seizure of illicit blotter paper.^{xxi} For the most up to date resource on monitoring of synthetic opioid and other NPS related news, the University of Maryland coordinates the National Drug Early Warning System, for communication between health officials, law enforcement, media, and disseminating information to the general public.^{xxii}

Are synthetic opioids legal?

In the United States, fentanyl is classified as a Schedule II controlled substance, meaning there is a potential for misuse and dependence, but it does have an accepted medical use and can be prescribed for restricted use. Though prescribed synthetic opioids are sometimes diverted to the illicit market, the main reason for the surge in high purity synthetic opioids are from the increase in manufacturing from clandestine labs, which are either pressed into pills and sold as fentanyl, or left in powder form and mixed with heroin.^{xi}

In 2016, following the high profile case of music legend Prince's fentanyl-related death and increasing seizures of synthetic opioid-laced heroin by law enforcement, calls from politicians^{xxiii} to increase punishment for possession and/or sale of illicit fentanyl included escalating mandatory minimum sentencing, and even capital punishment for sale of heroin.^{xxiv} Similar to enforcement efforts toward other NPS, individual states and the federal government's^{xxv} efforts are centered around placing individual synthetic opioids and opiate-like NPS into Schedule I of the Controlled Substances Act (CSA). There is no evidence that escalating criminal punishment will have any effect on reducing risk of overdose or use in general.^{xxvi} These policies will fail to address the issues involving fentanyl and will continue the harmful trend of mass incarceration in the US.^{xxvii}

What's a harm reduction approach to the use of fentanyl and other synthetic opioids?

The first, most important step is to increase access to, and continue to develop accurate, non-judgmental education programs on drug use, misuse, and how to prevent and decrease the probabilities of overdose by teaching practices such as not combining opioids with other depressants like alcohol and benzodiazepines.

Beyond education, there are already a number of evidenced-based options that can help save lives and minimize harms associated with misuse of fentanyl and other synthetic opioids. These include: drug checking to detect fentanyl-laced drugs,^{xxviii} medication-assisted therapy for opiate dependence with methadone and buprenorphine, heroin prescribing if that's what patients are already taking (a long-accepted practice in Europe, and recently adopted in Canada)^{xxix}, expanding access to the opiate overdose antidote naloxone, enacting 911 Good Samaritan immunity laws to protect overdose witnesses from arrest, and opening supervised injection facilities that are proven to reduce fatal opiate-related overdoses.^{xxx}

DPA has put together recommendations for a comprehensive response to the opiate overdose crisis that includes these harm reduction initiatives as well as others.^{xxxi} DPA also works to ensure these life-saving strategies don't meet with political resistance. When it comes to fentanyl and other synthetic opioids, we must ensure that any new laws do not imitate ineffective drug war tactics by relying on criminal punishment rather than a public health approach.

ⁱ "Erowid Opiates Vault : Opium Timeline." Erowid Opiates Vault : Opium Timeline. Accessed June 09, 2016. https://www.erowid.org/chemicals/opiates/opiates_timeline.php.

ⁱⁱ U. S. Department of Justice, Drug Enforcement Administration, DEA Investigative Reporting, January 2015

ⁱⁱⁱ Stott, D. G., and B. J. Pleuvry. "Relationship Between Analgesia And Respiratory Depression For Mu Opioid Receptor Agonists In Mice." *Br J Anaesth BJA: British Journal of Anaesthesia* 67, no. 5 (1991): 603-07. doi:10.1093/bja/67.5.603.

^{iv} "Erowid Experience Vaults: Fentanyl (Patch) - Effective, but Not Euphoric - 52688." Erowid Experience Vaults: Fentanyl (Patch) - Effective, but Not Euphoric - 52688. Accessed June 09, 2016. <https://www.erowid.org/experiences/exp.php?ID=52688>.

^v "Will a 50 Mcg/hr Mylan Fentanyl Patch Produce Euphoria? Or Just That Warm All over Feeling? • /r/opiates." Reddit. Accessed June 09, 2016.

https://www.reddit.com/r/opiates/comments/3eabro/will_a_50_mcg_hr_mylan_fentanyl_patch_produce/.

^{vi} Comer, Sandra D., Maria A. Sullivan, Robert A. Whittington, Suzanne K. Vosburg, and William J. Kowalczyk. "Abuse Liability of Prescription Opioids Compared to Heroin in Morphine-Maintained Heroin Abusers." *Neuropsychopharmacology* 33, no. 5 (2007): 1179-191. doi:10.1038/sj.npp.1301479.

^{vii} Marcus, Dawn A., and Ronald M. Glick. "Sustained-Release Oxycodone Dosing Survey of Chronic Pain Patients." *The Clinical Journal of Pain* 20, no. 5 (2004): 363-66. doi:10.1097/00002508-200409000-00012.

^{viii} "Erowid Heroin Vault : Dosage." Erowid Heroin Vault : Dosage. Accessed June 09, 2016. https://www.erowid.org/chemicals/heroin/heroin_dose.shtml.

^{ix} Peng, Philip W. H., and Alan N. Sandler. "A Review of the Use of Fentanyl Analgesia in the Management of Acute Pain in Adults." *Anesthesiology* 90, no. 2 (1999): 576-99. doi:10.1097/00000542-199902000-00034.

^x "Increases in Fentanyl Drug Confiscations and Fentanyl-related Overdose Fatalities." HAN Archive. Accessed June 09, 2016. <http://emergency.cdc.gov/han/han00384.asp>.

^{xi} "National Heroin Threat Assessment Summary." Drug Enforcement Administration. April 2015. Accessed June 9, 2016. https://www.dea.gov/divisions/hq/2015/hq052215_National_Heroin_Threat_Assessment_Summary.pdf.

^{xii} Strang, John. "Death Matters: Understanding Heroin/opiate Overdose Risk and Testing Potential to Prevent Deaths." *Addiction* 110 (2015): 27-35. doi:10.1111/add.12904.

^{xiii} Kriván, Márta, Gyula Szabó, Zoltán Sarnyai, Gábor L. Kovács, and Gyula Telegdy. "Oxytocin Blocks the Development of Heroin-fentanyl Cross-tolerance in Mice." *Pharmacology Biochemistry and Behavior* 52, no. 3 (1995): 591-94. doi:10.1016/0091-3057(95)00145-m.

^{xiv} Hall, Aron J. "Patterns of Abuse Among Unintentional Pharmaceutical Overdose Fatalities." *Jama* 300, no. 22 (2008): 2613. doi:10.1001/jama.2008.802.

^{xv} Gill JR, Lin PT, Nelson L. Reliability of Postmortem Fentanyl Concentrations in Determining the Cause of Death. *Journal of Medical Toxicology*. 2013;9(1):34-41. doi:10.1007/s13181-012-0253-z.

^{xvi} "Increase in Drug Overdoses Deaths and Increased Presence of Fentanyl in New York City." NEW YORK CITY DEPARTMENT OF HEALTH AND MENTAL HYGIENE. April 21, 2016. Accessed June 9, 2016. <https://a816-health30ssl.nyc.gov/sites/nychan/Lists/AlertUpdateAdvisoryDocuments/Fentanyl-HAN-advisory.pdf>.

^{xvii} Greenwald, Mark K., and Timothy A. Roehrs. "Mu-opioid Self-Administration vs Passive Administration in Heroin Abusers Produces Differential EEG Activation." *Neuropsychopharmacology* 30, no. 1 (2004): 212-21. doi:10.1038/sj.npp.1300596.

^{xxviii} Cicero, Theodore J., Matthew S. Ellis, Alethea Paradis, and Zachary Ortbal. "Determinants of Fentanyl and Other Potent μ Opioid Agonist Misuse in Opioid-dependent Individuals." *Pharmacoepidemiology and Drug Safety* *Pharmacoepidem. Drug Safe.* 19, no. 10 (2010): 1057-063. doi:10.1002/pds.1989.

^{xix} Logan, B. (2016, May 9). W18 Confirmed in two fatalities in Illinois. Email communication to the National Drug Early Warning System (NDEWS) Network Listserv

^{xx} "CCENDU Bulletin: Novel Synthetic Opioids in Counterfeit Pharmaceuticals and Other Illicit Street Drugs." Canadian Centre on Substance Abuse. June 2016. Accessed September 19, 2016. <http://www.ccsa.ca/ResourceLibrary/CCSA-CCENDU-Novels-Synthetic-Opioids-Bulletin-2016-en.pdf>.

^{xxi} Winnipeg, City Of. "Drug Investigation Arrest – Follow-up: C16-190364." : Newsroom : September 29, 2016 Media Release. September 29, 2016. Accessed October 11, 2016. http://www.winnipeg.ca/police/press/2016/09Sep/2016_09_29.aspx.

^{xxii} "NDEWS L National Drug Early Warning System L University of Maryland." NDEWS L National Drug Early Warning System L University of Maryland. Accessed October 11, 2016. <https://ndews.umd.edu/>.

^{xxiii} "S.Amdt.4101 to S.2943 - 114th Congress (2015-2016) - Amendment Text." Congress.gov. Accessed June 09, 2016. <https://www.congress.gov/amendment/114th-congress/senate-amendment/4101/text>.

^{xxiv} REED:, By Mr. "H.R.6158 - 114th Congress (2015-2016): HELP Act of 2016." Congress.gov. Accessed September 30, 2016. <https://www.congress.gov/bill/114th-congress/house-bill/6158>.

^{xxv} "Rules - 2016." Federal Register Notices -. Accessed September 30, 2016. https://www.deadiversion.usdoj.gov/fed_regs/rules/2016/index.html.

^{xxvi} Samuel R. Friedman et al., Drug Arrests and Injection Drug Deterrence, 101(2) American Journal of Public Health 344, 347 (2011) ("Changes in hard drug arrest rates did not predict changes in [injection drug use] population rates. These results are inconsistent with criminal deterrence theory and raise questions about whether arresting people for hard drug use contributes to public health."); Valerie Wright, Deterrence in Criminal Justice Evaluating Certainty vs. Severity of Punishment, The Sentencing Project (November 2010) ("Existing evidence does not support any significant public safety benefit of the practice of increasing the severity of sentences by imposing longer prison terms. In fact, research findings imply that increasingly lengthy prison terms are counterproductive. Overall, the evidence indicates that the deterrent effect of lengthy prison sentences would not be substantially diminished if punishments were reduced from their current levels.")

^{xxvii} "Prince, Gone 2 Soon, Spotlights the Complexities of Opioid Use." Drug Policy Alliance. Accessed June 09, 2016. <http://www.drugpolicy.org/blog/prince-gone-2-soon-spotlights-complexities-opioid-use>.

^{xxviii} Diep, Francie. "The Instant Test That Can Tell Whether Users' Drugs Are Cut With a Deadly Chemical." *Pacific Standard*. September 08, 2016. Accessed October 07, 2016. <https://psmag.com/the-instant-test-that-can-tell-whether-users-drugs-are-cut-with-a-deadly-chemical-8feed9ce8a0d#.dgctsheo1>.

^{xxix} Wheeler, Anna. "Regulations Amending Certain Regulations Made Under the Controlled Drugs and Substances Act (Access to Diacetylmorphine for Emergency Treatment)." Government of Canada, Public Works and Government Services Canada, Public Services and Procurement Canada, Integrated Services Branch, Canada Gazette. September 7, 2016. Accessed October 07, 2016. <http://www.gazette.gc.ca/rp-pr/p2/2016/2016-09-07/html/sor-dors239-eng.php>.

^{xxx} Potier, C., et al., Supervised injection services: what has been demonstrated? A systematic literature review. *Drug Alcohol Depend*, 2014. 145: p. 48-68.

^{xxxi} "Opioid Overdose: Addressing a National Crisis of Preventable Deaths." Opioid Overdose: Addressing a National Crisis of Preventable Deaths | Drug Policy Alliance. February 10, 2016. <http://www.drugpolicy.org/resource/opioid-overdose-addressing-national-crisis-preventable-deaths>.