

DEPARTMENT OF HEALTH AND HUMAN SERVICES
NATIONAL INSTITUTES OF HEALTH
NATIONAL INSTITUTE ON DRUG ABUSE

What Science Tells us About Opioid Abuse and Addiction

Testimony before the House Committee on Energy and Commerce
Subcommittee on Oversight and Investigations

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Good Morning, Mr. Chairman, Ranking Member DeGette, and Members of the Subcommittee. Thank you for inviting the National Institute on Drug Abuse (NIDA), a component of the National Institutes of Health (NIH), to participate in this important hearing and provide an overview of what science tells us about the growing and intertwined problems of non-medical use of prescription pain medicines and use of heroin in our Nation.

Background

The misuse of and addiction to opioids such as heroin, morphine, and other prescription pain medicines is a serious national problem that affects public health as well as social and economic welfare. An estimated 1.9 million people in the United States suffered from substance use disorders related to prescription opioid pain medicines in 2013 and 517,000 suffered from a heroin use disorder.¹ This issue has become a public health epidemic with devastating consequences including not just opioid use disorders and related overdoses, but also the rising incidence of newborns who experience neonatal abstinence syndrome because their mothers used these substances during pregnancy; and increased spread of infectious diseases including HIV and hepatitis C (HCV).

Existing evidence based prevention and treatment strategies are highly underutilized across the United States. The recently announced initiative of the Secretary of Health and Human Services to address the complex problem of prescription opioid and heroin abuse in this country emphasizes the implementation of these evidence based prevention and treatment strategies which include not only better prescription practices but also deployment of medication to combat overdoses and medication-assisted treatment (MAT) to treat opioid use disorders. NIDA is an active partner in this initiative and will focus on supporting research and disseminating findings to improve opioid prescribing practices, to expand the use of the opioid overdose reversal drug naloxone, to improve the integration of pharmacotherapies into treatment services in specialty care and primary care, and to develop pain treatments with reduced potential for misuse and diversion.

disorders, and related public health outcomes. This research has demonstrated the efficacy of multiple types of interventions including:

Educational initiatives delivered in school and community settings (primary prevention)^{xi}

Supporting consistent use of prescription drug monitoring programs (PDMPs)^{xii}

Implementation of overdose education and naloxone distribution programs to issue naloxone directly to opioid users and potential bystanders^{xiii}

Aggressive law enforcement efforts to address doctor shopping and pill mills^{xiv}

Diverting individuals with substance use disorders to Drug Courts^{xv}

Expansion of access to MAT^{xvi}

Abuse-deterrent formulations for opioid analgesics^{xvii}

In states with the most comprehensive initiatives to reduce opioid overprescribing, the results have been encouraging. Washington State's implementation of evidence-based dosing and best-practice guidelines and enhanced funding for the state's PDMP helped reduce opioid deaths by 27 percent between 2008 and 2012.^{xviii} In Florida, new restrictions were imposed on pain clinics, new policies were implemented requiring more consistent use of the state PDMP, and the Drug Enforcement Administration worked with state law enforcement to conduct widespread raids on pill mills, which resulted in a dramatic decrease in overdose deaths between 2010 and 2012.^{xix} These examples show that state and

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medically started using heroin within five years of their initiation of non-medical use of pain medication.^{xviii}

Heroin and prescription opioid pain relievers belong to a single class of drugs—but each are associated with distinct risks. The risk of overdose and negative consequences is even greater with heroin due to the lack of control over the purity of the drug and its possible contamination with other drugs (such as fentanyl, originally a potent prescription opioid but now variants of which are often produced in clandestine labs). All of these factors increase the risk for overdose since users have no way of assessing the potency of the drug before taking it and because in the case of fentanyl contamination, users typically have no opportunity to become tolerant.

There also has been a shift in the demographic of opioid users over the last few decades. In the 1960s, more than 80 percent of people who began using opioids initiated with heroin; in the 2000s, 75 percent of opioid users reported that their first regular opioid was a prescription pain reliever.^{xxii} It also has been reported that current heroin users are more likely to be white, middle-class, and live in more suburban and rural areas; this is consistent with the population of people who report the largest increases in non-medical use of opioid pain relievers over the last decade.^{xxi}

The transition from misusing prescription opioids to using heroin may be part of the natural progression of disease in a subset of users. Evidence from interviews with individuals with heroin use disorder suggest that market forces, including the accessibility, cost, and high potency of heroin are driving increased use of and transition from prescription opioids.^{xxii}, ^{xxiii}

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pain, leveraging NIDA funds with the strengths and resources of outside organizations, including academic institutions, pharmaceutical and biotechnology companies, private and public foundations, and small businesses. This includes research to identify new pain medicines with reduced abuse, tolerance, and dependence risk, as well as devising alternative delivery systems and formulations for existing drugs that minimize diversion and non-medical use (*e.g.*, by preventing tampering) and reduce the risk of overdose deaths. For example, a partnership with Signature Therapeutics is working to develop an abuse deterrent formulation of oxycodone that uses prodrug technology—attaching an extension to the opioid molecule that renders it inactive if injected, snorted, or smoked; instead it must pass through the digestive system to begin the process of releasing the opioid. Early phase trials have supported safety, dose proportionality, and a clinically beneficial extended release profile.

In addition, new compounds are being developed that exhibit novel properties as a result of their combined activity on two different opioid receptors (*i.e.*, mu and delta). Preclinical studies show that these compounds can induce strong analgesia without producing tolerance or dependence.^{xxv} Researchers are also getting closer to developing a new generation of non-opioid-based medications for severe pain that would circumvent the brain reward pathways, thereby greatly reducing abuse potential. This includes compounds that work through a type of cannabinoid receptor found primarily in the peripheral nervous system.

Education is another critical component of any effort to curb the abuse of prescription medications and must target every segment of society, including healthcare providers (doctors, nurses, dentists, pharmacists). NIDA is advancing addiction awareness, prevention, and treatment in primary care practices through four Centers of Excellence for Physician Information. Intended to serve as national models, these Centers target physicians-in-training, including medical students and resident physicians in primary care specialties (*e.g.* internal medicine, family practice, and pediatrics). NIDA also has developed, in partnership with the Office of National Drug Control Policy, two online continuing medical education courses on safe prescribing for pain and managing patients who abuse prescription opioids. To date, these courses have been completed by over 100,000 clinicians combined.

Developing More Effective Means for Preventing Overdose Deaths

The opioid overdose-reversal drug naloxone can rapidly restore normal respiration to a person who has stopped breathing as a result of overdose from heroin or prescription opioids. Naloxone is widely used by emergency medical personnel and some first responders. Beyond first responders, some communities have established overdose education and naloxone distribution programs that issue naloxone directly to opioid users and their friends or loved ones, or other potential bystanders, along with brief training in how to use these emergency kits. Such programs have been shown to be effective, as well as cost-effective, ways of saving lives. CDC reported that, as of 2010, lay-distributed naloxone had resulted in more than 10,000 overdose reversals nationwide since 1996.^{xxvi}

For many years, naloxone was available only in an injectable formulation that was generally carried only

methadone, buprenorphine, and injectable naltrexone (*e.g.*, Vivitrol), when administered in the context of an addiction treatment program, all effectively help maintain abstinence from other opioids, reduce opioid use disorder-related symptoms, and reduce the risk of infectious disease and crime.^{xxvii} Two comprehensive Cochrane reviews, one analyzing data from 11 randomized clinical trials that compared the effectiveness of methadone to placebo and another analyzing data from 31 trials comparing buprenorphine or methadone treatment to placebo,^{xxviii,xxix} found that:

Patients on methadone were over four times more likely to stay in treatment and had 33 percent fewer opioid-positive drug tests compared to patients treated with placebo;

Methadone treatment significantly improves treatment outcomes alone and when added to counseling; long-term (beyond six months) outcomes are better for patients receiving methadone, regardless of counseling received;

Buprenorphine treatment significantly decreased the number of opioid-positive drug tests, multiple studies found a 75-80 percent reduction in the number of patients testing positive for opioid use;

Methadone and buprenorphine are equally effective at reducing opioid use; no differences were found in opioid-positive drug tests or self-reported heroin use when treating with these medications.

To be clear, the evidence supports long term maintenance with these medicines in the context of behavioral treatment and recovery support, not short term detoxification programs aimed at abstinence.^{xxx} Abstinence from all medicines may be a particular patient's goal and that goal should be discussed between patients and providers. However the scientific evidence suggests the relapse rates are high when tapering off of these medications and treatment programs with an abstinence focus generally do not facilitate patients' long term, stable recovery. It is often the case that patients with good long-term outcomes are the ones who engaged in MAT although cycling in and out of treatment is not unusual in the path to a stable recovery.^{xxxi} Maintenance treatments have also been shown to be protective against injecting and overdose.^{xxxii, xxxiii}

Ongoing NIDA research is working to develop improved strategies for the implementation of these evidence-based interventions. This includes research to better

ⁱ Substance Abuse and Mental Health Services Administration. Results from the 2013 National Survey on Drug Use and Health: Summary of National Findings. (2014)

ⁱⁱ Williams, J. T. *et al.* Regulation of μ -opioid receptors: desensitization, phosphorylation, internalization, and tolerance. *Pharmacol. Rev.* **65**, 223–254 (2013).

ⁱⁱⁱ Jones, C. M. *et al.* Alcohol involvement in opioid pain reliever and benzodiazepine drug abuse-related emergency department visits and drug-related deaths - United States, 2010. *MMWR.* 2014 Oct 10;63(40):881-5.

^{iv} Federation of State Medical Boards Model Policy on the Use of Opioid Analgesics in the Treatment of Chronic

