

Opioid Use Disorder with Dr. Cummings

Catalina Baas, David Puder, MD

Michael Cummings, M.D., and David Puder, M.D., do not have any conflicts of interest.

This week's episode is on opioid use disorder and is the second in our series on addiction. We are once again joined by Dr. Michael Cummings. Dr. Puder and Dr. Cummings discuss the history of opioids, the neurobiology of addiction, risk factors for opioid use disorder, and treatment options.

This episode will count towards the CME requirements of the new DEA law. This is a one-time, 8-hour training requirement introduced by the Consolidated Appropriations Act of 2023 for all Drug Enforcement Administration (DEA)-registered practitioners. This training focuses on the treatment and management of patients' substance use disorders. Here are some other episodes that meet the requirements (more to come!):

- [Episode 181: Alcohol Use Disorder with Dr. Cummings](#) (1 CME unit)
- [Episode 044: Marijuana and Mental Health](#) (0.5 CME units)
- [Episode 064: Does Cannabis Use Increase Schizophrenia and Psychosis?](#) (0.75 CME units)
- [Episode 066: Fentanyl: The Next Phase in the Opiate Epidemic](#) (0.75 CME units)
- [Episode 030: Ketamine and Psychedelics with Dr. Michael Cummings](#) (0.75 CME units)

Of note, under the section 1262 of the Consolidated Appropriations Act, 2023, there is also no longer a requirement for a special waiver to prescribe buprenorphine, and no longer a limit on the number of patients a provider can prescribe buprenorphine to under federal law.

- See DEA website on this detail: [here](#)
- See SAMHSA summary of changes: [here](#)

History of Opioids

For thousands of years, people have utilized derivatives of the opium poppy for their mellowing and pain-relieving effects. The addictive nature of opioids went largely unrecognized for much of that time. However, a major change occurred in the 19th century when people began to develop increasingly potent opioid medications, starting with the discovery of morphine, which was later modified to make heroin (Rosenblum et al., 2008). As the use of such medications spread, the potential for opioid addiction and dependence became more and more apparent. Heroin was eventually outlawed in 1924, and the use of opioids became tightly regulated from that point on.

Opioid Use Disorder with Dr. Cummings

Catalina Baas, David Puder, MD

In the 1980s, another shift occurred as people became increasingly concerned that chronic pain was being undertreated. A number of influential publications were released arguing that opioids were underutilized due to overblown fears of addiction, and pharmaceutical companies further perpetuated the idea that opioids have a low addictive potential (Meldrum, 2016; Cicero and Ellis, 2017). Additionally, pain was added as a 5th vital sign in many clinical settings. Opioids came into increasing favor and were more liberally prescribed, a trend which ultimately laid the groundwork for today's opioid crisis. The number of annual opioid prescriptions has continued to rise since the 1990s, with a three-fold increase occurring between 2011 and 2021. The increased amount of prescriptions appears to be directly related to the rising incidence of drug diversion and abuse (Cicero and Ellis, 2017). Approximately 4-5% of people prescribed an opioid ultimately become addicted, with some studies generating substantially higher estimates (Minozzi et al., 2013; Fleming et al., 2007; Boscarino et al., 2010).

The Opioid Epidemic

Since 2017, the U.S. Department of Health and Human Services has recognized the opioid crisis as a national health emergency. Preliminary data from the CDC indicates that over 109,000 people died from a drug overdose in 2022. In 2020, the number of overdose deaths attributed to opioids was nearly 75% (Health and Human Services, 2022). Fentanyl, a synthetic opioid 100 times more potent than morphine, is increasingly responsible for such fatalities. The drug is tasteless, odorless, and extremely cheap to manufacture, making it an ideal agent to add to other drugs for increased profits. Unfortunately, those same properties make it easy for people to accidentally overdose if they are unaware the drugs they purchased contain fentanyl. Just two milligrams—roughly the size of a grain of rice—can be a fatal dose.

Opioid Use Disorder

Opioid use disorder (OUD) describes a compulsive pattern of opioid use. The Diagnostic and Statistical Manual of Mental Disorders, 5th Edition (DSM-5) criteria for OUD consists of problematic opioid use with at least two of the following in a 12-month span: using opioids more, or over a longer period, than intended; unsuccessful attempts to cut down; spending a significant amount of time on the drug habit; cravings; failure to fulfill obligations; continued use despite social problems; reducing normal activities; risky use, such as driving under the influence; continued use despite health issues; tolerance; and withdrawal (American Psychiatric Association, 2013).

The development of OUD often follows a sequence which is characteristic of addictive behavior. First, the substance (opioids) may be taken to treat an unpleasant condition (pain); next, it is used for the sake of feeling “high”; and finally, the substance is taken to stave off unpleasant

Opioid Use Disorder with Dr. Cummings

Catalina Baas, David Puder, MD

withdrawal symptoms (Farisco et al., 2018). Importantly, the disorder typically begins as an *unconscious* process where the user is unaware that he/she has transitioned into problematic or compulsive use. At that stage, there is an underlying belief that the opioid is still being used for a legitimate reason, and evidence to the contrary is readily overlooked. The reason for this likely has neurobiological underpinnings. Studies suggest that substance addiction is connected to impairment of the paralimbic network, which is important for self-awareness and self-control (Changeux and Lou, 2011).

Neurobiology of Opioid Addiction

The mu and delta opioid receptors play a major role in promoting opioid addiction and dependence. Both receptors are present throughout the nucleus accumbens, which is a structure involved in motivated behaviors and is a component of the brain's reward circuitry (Wright & Wesson, 2021). Mu receptors are responsible for the euphoria of taking opioids, while delta receptors appear to increase drug-seeking behaviors by influencing learning, memory, and habit formation (Klenowski et al., 2015; Valentino and Volkow, 2018). Delta receptors also contribute to formation of cues and contexts for drug use, which perpetuates continued use and increases the risk of relapse.

Risk Factors for Opioid Use Disorder

The development of addiction involves a complex interplay between genetics, personality, and social factors such as family environment, peers, life stressors, and culture (Kreek et al., 2012). It is well established in the literature that having a family history of substance abuse is a strong risk factor. The reason for this may be partially genetic, and partially a consequence of childhood influences on mindset, ethical rules, and behavior (Farisco et al., 2018).

Young age is another strong risk factor for addiction. The reward pathway in the brain develops earlier than the prefrontal cortex, which facilitates planning and decision-making. Because of this, younger individuals are more susceptible to reward-seeking behaviors without fully considering the consequences. Additionally, many psychiatric disorders make their first appearance in adolescence and are themselves strongly comorbid with substance abuse (*Common Comorbidities with Substance Use Disorders Research Report*, 2020).

Additional risk factors include male sex, personal history of substance abuse, lower education level, unemployment, and lower income (Blanco & Volkow, 2019; Webster, 2017).

Opioid Use Disorder with Dr. Cummings

Catalina Baas, David Puder, MD

Overdose

Death from opioid overdose occurs due to respiratory depression. Under normal circumstances, if breathing is inadequate, neurons in the brain detect the rising CO₂ concentration and increase respiratory drive. Opioid overdose impairs this feedback mechanism, which can lead to suffocation.

Opioid Detoxification

Opioid withdrawal generally lasts 3-4 days, but can take up to a week to resolve. Symptoms are unpleasant and can include nausea, vomiting, diarrhea, insomnia, photophobia, piloerection, myalgias, and autonomic hyperactivity. If not monitored, dangerous dehydration and electrolyte disturbances secondary to vomiting and diarrhea can occur.

There are two options for helping patients with opioid detoxification: opioid substitution or symptom management. Substitution involves placing patients on opioid agonists, such as methadone or buprenorphine, and gradually tapering the dose to zero. This route tends to be slower but helps avoid unpleasant withdrawal symptoms. Symptom management involves removing all opioids and treating withdrawal symptoms as they arise. Clonidine, antiemetics, antidiarrheals, sedative hypnotics, and antiepileptics have been utilized for this purpose. Another technique is to place patients under general anesthesia and administer an opioid antagonist so they rapidly undergo detoxification without experiencing withdrawals. However, the safety of this technique has been called into question and is less commonly utilized.

When the withdrawal period ends, patients are no longer physically dependent on opioids. However, they typically still experience drug cravings and can benefit from additional medications and treatment programs (like partial or day treatment programs) to maintain recovery and treat underlying psychiatric issues.

Medication Overview

Naloxone

Mechanism: Rapid-acting mu-opioid receptor antagonist.

Use: Blocks the effects of opioids within 2-3 minutes. Especially useful for reversing overdose.

Naltrexone

Mechanism: Mu, kappa, and delta opioid receptor antagonist.

Opioid Use Disorder with Dr. Cummings

Catalina Baas, David Puder, MD

Use: Helps establish and maintain abstinence by reducing cravings and blocking the effects of any opioids taken. Available as a daily pill or a once-per-month injection.

Clonidine or Guanfacine

Mechanism: Alpha-2-adrenergic agonists.

Use: Reduces sympathetic nervous system activity to decrease withdrawal symptoms.

Hydroxyzine

Mechanism: Pure H1 histamine receptor antagonist.

Use: Decreases cortical activity in the brain to produce sedation and reduce withdrawal symptoms of anxiety.

Buprenorphine

Mechanism: Partial mu receptor agonist.

Use: Substitute for illicit opioids which staves off withdrawal symptoms. Patients are often gradually tapered off, but individuals who have had multiple unsuccessful attempts to stop opioids may be kept on a maintenance dose indefinitely to prevent relapse. Unlike methadone, which must be administered in federally licensed clinics, this drug may be prescribed by any provider with a current DEA registration. Per 2023 DEA guidance, an X-waiver is no longer required.

Suboxone (buprenorphine/naloxone)

Mechanism: Combination of buprenorphine and naloxone.

Use: Functions the same as buprenorphine alone, with epidemiologic studies showing the addition of the naloxone reduces parenteral misuse.

Methadone

Mechanism: Full opioid agonist.

Use: Substitute for illicit opioids. Less commonly used than buprenorphine since it is a full agonist.

Probuphine

Mechanism: Buprenorphine implant.

Use: Each implant is good for six months. Especially useful for patients who struggle with nonadherence.

Opioid Use Disorder with Dr. Cummings

Catalina Baas, David Puder, MD

Additional Recommendations

- Recommend psychotherapy to help patients learn to process stressors without relying on substances, as well as to heal from past trauma.
- Consider family therapy to help families reconnect, heal, and learn how to support patients in their recovery.
- Encourage patients to maintain strong social support, regularly engage in enjoyable activities, and avoid situations/environments that may tempt them to relapse.
- Treat any underlying mood disorders to further reduce the risk of relapse.