Evidence-Based Treatment for Opioid Use Disorder

MEDICATION

Medication is an essential part of the treatment of opioid use disorder. Medication treatment is effective for two key purposes: for the short term to treat withdrawal symptoms during detoxification (opioid detoxification) and on an ongoing basis to prevent relapse (maintenance).

**Opioid Detoxification**

- Medications may be used to treat withdrawal symptoms for individuals undergoing detoxification. This is often done in inpatient settings where withdrawal symptoms can be closely monitored.

- Medications for opioid detoxification may include opioids (such as buprenorphine) used in a tapering fashion (with successively lower doses given over a period of days/weeks) and/or ancillary medications to treat withdrawal symptoms (e.g., nonopioid pain relievers, antinausea medication).

- Detoxification alone is not a sufficient treatment and actually increases the risk for overdose.
Maintenance Treatment

There are three medications approved by the FDA specifically for the ongoing treatment of opioid use disorder, each of which exerts its effects through the mu opioid receptor system: methadone, buprenorphine, and naltrexone.

**METHADONE**

**ABOUT**

Methadone is a mu opioid agonist. Due to its long duration of action (i.e., half-life of about 24 hours), methadone is able to suppress opioid withdrawal symptoms from emerging and reduce the need/urge to use opioids.

**FORMULATIONS**

Methadone is used orally daily and is available in pills, diskettes, and a liquid formulation that is intended to aid in prevention of diversion.

**WHERE TO GET IT**

In the United States, methadone is a Schedule II drug and can only be used in the context of a special federally licensed opioid treatment program (OTP); it is illegal to prescribe methadone for the treatment of opioid use disorder in any other context with the exception of 3-day emergency treatment within an inpatient hospital setting (methadone can be prescribed as an analgesic in other settings). Patients receiving methadone typically begin treatment by coming every day to a clinic.

**CHALLENGES**

Because methadone can only be prescribed in an OTP, this can present logistical challenges, such as needing to travel to the program daily (or near daily) for dosing. Methadone also has several side effects, such as constipation and sedation, and can be diverted (e.g., selling or giving one’s prescription to others).

**Methadone has a half-life of about 24 hours and is able to suppress opioid withdrawal symptoms from emerging and reduce the need/urge to use opioids.**
BUPRENORPHINE

ABOUT
Buprenorphine is a partial mu opioid agonist and, like methadone, is effective at suppressing opioid withdrawal symptoms and opioid craving. It also produces a functional opioid blockade whereby its occupancy of the mu opioid receptors can prevent other opioids from binding and exerting effects. As a partial opioid agonist, there is a limit to the magnitude of effects that buprenorphine can produce (and these are less than a full agonist); this “ceiling” on the effects of buprenorphine leads to an improved safety profile in contrast to methadone.

OTHER NAMES
Suboxone, Subutex, Sublocade, Probuphine

FORMULATIONS
Buprenorphine is typically taken by mouth (sublingual/transmucosal tablets and films).

WHERE TO GET IT
Buprenorphine may be prescribed by physicians (and, more recently, nurse practitioners and physician assistants, depending on state law) who have received specialized training and fulfilled the requirements to obtain a waiver from the DEA for their DEA license (known as the DEA-x license, because an “x” appears after the provider’s DEA number on their license).

CHALLENGES
Resistance to opioid agonist medications (such as the claim that you are simply “replacing a drug with a drug”) has had a negative impact on the use of buprenorphine. Diversion (e.g., selling or giving one’s prescription to others) also has been documented.

NALTREXONE

ABOUT
Naltrexone works by occupying mu opioid receptors and thereby preventing other opioids (such as heroin) from binding to those receptors and producing their euphoric effects.

OTHER NAMES
Vivitrol, Revia

FORMULATIONS
Naltrexone was initially introduced as an oral formulation to be dosed once daily. A sustained-release formulation of naltrexone was approved by the FDA that provides one month of coverage after a single administration. The formulation is a depot that is injected intramuscularly in the gluteal muscle.

WHERE TO GET IT
Naltrexone is not a scheduled drug, does not exert direct psychoactive effects, and can be prescribed by any licensed physician in a regular office setting.

CHALLENGES
Despite its safety and desirable pharmacological profile, oral naltrexone has had very limited clinical use because it is challenging to initiate treatment and patients are commonly nonadherent to taking the medication. Sustained-release naltrexone (Vivitrol) can increase compliance and has demonstrated comparable outcomes to buprenorphine once successfully initiated. Because naltrexone is an opioid antagonist, individuals who are physically dependent on opioids must first achieve an opioid-free state before they can initiate naltrexone. If they are not completely abstinent, naltrexone will precipitate a robust and sustained withdrawal syndrome. Thus, individuals who are physically dependent but seeking treatment with naltrexone must first undergo detoxification; this is often challenging and sometimes impossible for some individuals. A longer period of abstinence before initiating treatment with naltrexone is more likely to lead to a successful and comfortable transition to naltrexone.

The FDA recently approved a 6-month buprenorphine implant and a monthly subcutaneous injection that produces comparatively high plasma concentrations (≥ 24 mg/day).
BEHAVIORAL THERAPIES

In general, behavioral therapies, when delivered alone, have limited efficacy in addressing the complex symptoms and physical aspects of opioid use disorder. Hence, behavioral therapies for opioid use disorder have been delivered in the context of structured approaches (e.g., residential programs) or after completion of detoxification and stabilization to prevent relapse and, most effectively, in combination with a medication such as methadone, buprenorphine, or naltrexone.

Behavioral therapies in addition to medication treatment can help to:

- Improve adherence to the medication
- Address aspects of the disorder not addressed by medication (e.g., social influences, stress)
- Address specific weaknesses of the medication

The specific types of behavioral therapy that enhance efficacy of medication are somewhat controversial; however, those with the strongest levels of empirical support include:

- Contingency management approaches
- Cognitive behavioral approaches
- Motivational interviewing
- Structured family approaches

Although little research has investigated the efficacy of behavioral therapy for the treatment of co-occurring disorders (e.g., anxiety, depression) in people with opioid use disorder, behavioral therapy is a promising strategy for addressing these conditions.

REFERENCES

