How Medication for Opioid Use Disorder Works in the Brain Empty Opioid Receptor Methadone **Buprenorphine Naltrexone** *The treatment approach shown to be most effective

Full agonates: generates effect

Partial agonates: generates limited effect

Antagonist: blocks effect for long-term management of OUD is a combination of FDA-approved medications with counseling and behavioral therapies tailored to the patient, also known as medication-assisted treatment (MAT).

TREATMENTS

The three FDA approved medications for treating Opioid Use Disorder (OUD) are methadone, buprenorphine, and naltrexone. The decision on which medication to use for each patient is a medical decision made by patients in collaboration with their physician, nurse, and counselor. Methadone and buprenorphine are both opioid agonists, meaning they activate mu-opioid receptors in the brain.

However, unlike other opioids, they do so in a way that provides withdrawal symptom relief and curbs cravings while blocking the high of other opioids. Methadone is a "full agonist" that fully activates to opioid receptors. Buprenorphine, a "partial agonist", only partially activates to opioid receptors creating a ceiling on the medication's effect. In contrast to these opioid agonists, naltrexone is an opioid antagonist that simply blocks opioid receptors rather than activating them. Since opioid antagonist do not activate opioid receptors, they do not provide relief for physical withdrawal symptoms or cravings and require full detoxification before starting treatment.



OPIOID USE DISORDER MEDICATION

| | Methadone | Buprenorphine | Naltrexone |
|---|---------------|---------------|------------|
| Reduces opioid use | ✓ | ✓ | ✓ |
| Reduces opioid craving | ✓ | ✓ | / |
| Keeps people in treatment | ✓ | ✓ | √1-* |
| Prevents opioid withdrawal | ✓ | ✓ | - |
| Reduces alcohol use | - | - | / |
| Reduces alcohol craving | - | - | / |
| Medication is a controlled substance (a narcotic) | ✓ | ✓ | - |
| Can start without needing detoxification first | ✓ | √/-** | - |
| Opioid withdrawal happens if medication is abruptly stopped | ✓ | ✓ | - |
| Used in pregnancy | / /*** | ✓ | - |
| Taken by mouth every day | ✓ | ✓ | - |
| Taken by injection to buttock once a month | - | - | ✓ |

^{*} Naltrexone keeps people in treatment so long as the person has been fully detoxified before coming to the clinic to start the medication. Many people drop out of treatment while being detoxified.

^{**} To start buprenorphine you must be in moderate opioid withdrawal. Because of how it works in the brain, starting buprenorphine too soon after using other opioids can cause severe opioid withdrawal

^{***} Methadone and buprenorphine are both safe for use in pregnancy. However, methadone has been around longer and more is known about it so it is the first choice (or "gold standard") for treating opioid use disorders in pregnancy