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Understanding Opioid Use Disorder: Treatment Standards and the Role of Buprenorphine

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Overview

- Opioid Use Disorder: The Scope of the Problem
- Treatment Options for Opioid Use Disorder
- Overview of Buprenorphine

Opioid Use Disorder: The Scope of the Problem

The Opioid Crisis in the United States



8.9 million
Misused an opioid (2023)[1]



5.7 million
People with opioid use disorder (2023)[1]



938,969
Opioid-related ED visits (2024)[2]



54,743
Opioid-related deaths (2024)[3]



48,422
Opioid-related deaths involving synthetic opioids (2024)[3]

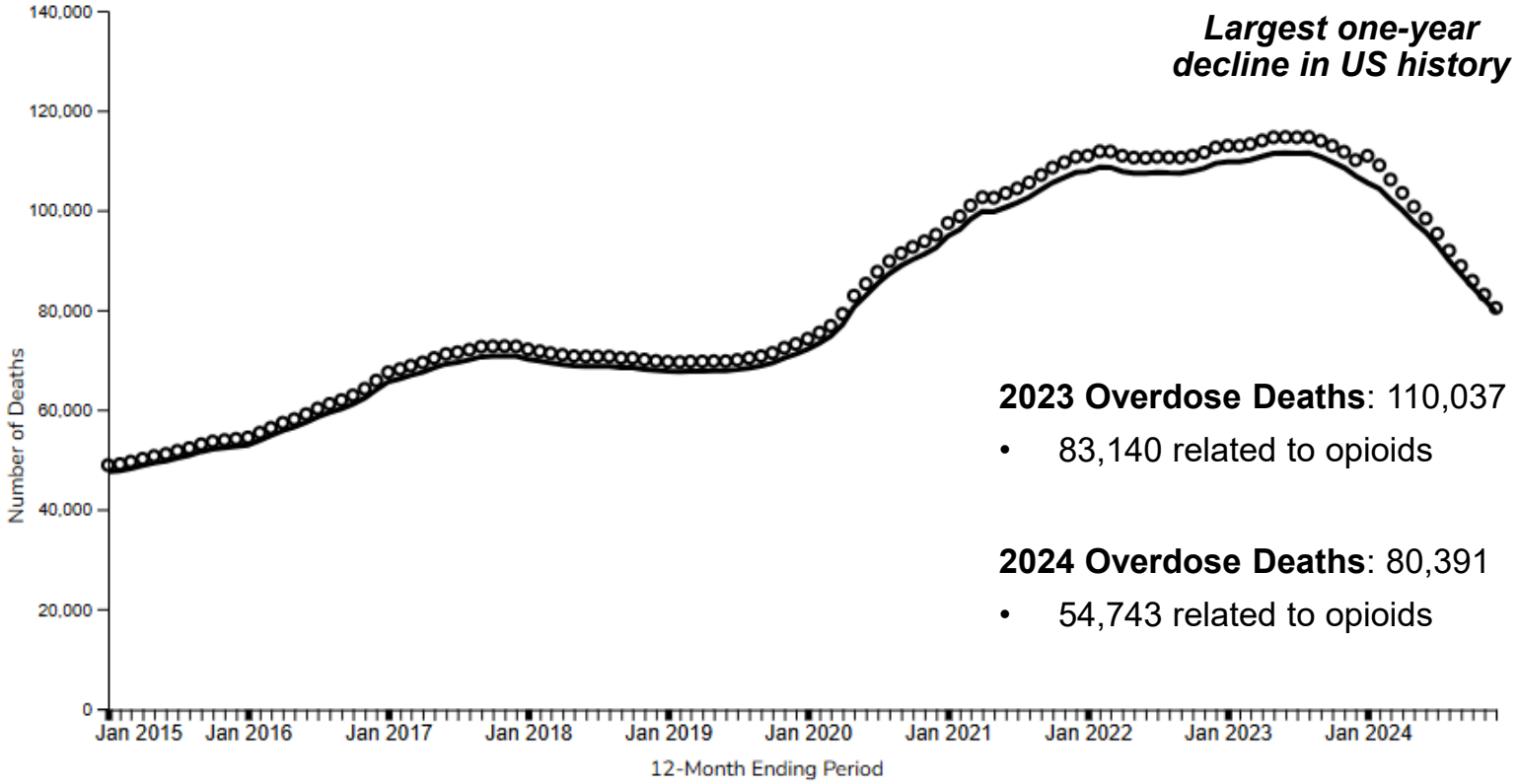


$4 trillion
Total costs related to opioid crisis (2024)[4]

1. Substance Abuse and Mental Health Services Administration. Key substance use and mental health indicators in the United States: Results from the 2023 National Survey on Drug Use and Health. Publication No. PEP24-07-021, July 2024. 2. Substance Abuse and Mental Health Services Administration. Drug Abuse Warning Network: National Estimates From Drug-Related Emergency Department Visits, 2024. Publication No. PEP25-07-005, 2025. 3. Centers for Disease Control and Prevention, National Center for Health Statistics. U.S. Overdose Deaths Decrease Almost 27% in 2024 [press release]. May 14, 2025. 4. Avalere Health. The Cost of Opioid Addiction: Opioid Use Disorder in the United States. May 2025.

Overdose Deaths are Decreasing but Counts are Still Significant

CDC: Provisional Counts of Drug Overdose Deaths in the US[1-3]



- Overdose deaths **decreased by 27%** in 2024 vs 2023[3]
- Overdose deaths involving opioids **decreased by 34%**[3]
- Overdose deaths **still above pre-COVID-19 levels**[2]
- Opioid overdose deaths in 2024 **comparable to US casualties of Vietnam War**[4]

US = United States. 1. Ahmad FB, et al. Provisional drug overdose death counts. National Center for Health Statistics. 2025. DOI: https://dx.doi.org/10.15620/cdc/20250305008.
2. Stobbe M, et al. U.S. Overdose Deaths Fell by 27% Last Year — the Largest One-Year Decline Ever Recorded. PBS News. May 14, 2025. Accessed June 2, 2025. https://www.pbs.org/newshour/nation/us-overdose-deaths-fell-by-27-last-year-the-largest-one-year-decline-ever-recorded. 3. Centers for Disease Control and Prevention, National Center for Health Statistics. U.S. Overdose Deaths Decrease Almost 27% in 2024 [press release]. May 14, 2025. Accessed June 2, 2025. https://www.cdc.gov/nchs/pressroom/nchs_press_releases/2025/20250514.htm. 4. National Archives and Records Administration. Vietnam War U.S. Military Fatal Casualty Statistics. April 29, 2008. Accessed June 2, 2025. https://www.archives.gov/research/military/vietnam-war/casualty-statistics

What is Opioid Use Disorder and How is it Diagnosed?

- **Opioid Use Disorder (OUD)** is a chronic, relapsing brain disease characterized by compulsive drug seeking and use despite adverse life consequences[1]

- OUD is diagnosed and classified based on DSM-5 criteria[2]:
  - *Presence of **at least 2 of the 11 specified symptoms**, occurring within a 12-month period*

Example DSM-5 symptoms:

- *Taking opioids in larger amounts or over a longer period of time than intended*
- *Opioid use causing inability to fulfill work, home, or school responsibilities*
- *Recurrent opioid use in situations in which it is physically hazardous*

OUD Severity Classification

CATEGORY	DESCRIPTION
Mild	Presence of 2-3 symptoms
Moderate	Presence of 4-5 symptoms
Severe	Presence of 6 or more symptoms

DSM-5 = The Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition. 1. NIDA. Drug Misuse and Addiction. National Institute on Drug Abuse website. https://nida.nih.gov/publications/drugs-brains-behavior-science-addiction/drug-misuse-addiction. July 6, 2020. Accessed June 2, 2025. 2. American Psychiatric Association. Diagnostic and Statistical Manual of Mental Disorders. 5th ed. American Psychiatric Publishing; 2013.

Cycle of Addiction for Opioid Use Disorder

3 Craving

Due to changes in the brain, a person experiences an intense desire to use opioids that they cannot control even when faced with harmful consequences as a result of their use



1 Binge/Intoxication

A person uses opioids to feel euphoria, pleasure, or relief. Over time, the brain adjusts by reducing the effects of natural rewards and normalizing the effects of opioids, making it hard to feel pleasure from anything besides opioids

2 Withdrawal/Negative Affect

Without opioids a person experiences negative physical and emotional symptoms like depressed mood and sensitivity to stress and anxiety. A person continues to use opioids to relieve these symptoms and not to get "high"

Volkow ND, et al. *N Engl J Med*. 2016;374(4):363-371.

Treatment Options for Opioid Use Disorder

Treatment of Opioid Use Disorder

Once a patient is diagnosed with OUD and is determined to be medically and psychiatrically stable, the next step is to determine treatment

Treatment options include medications and psychosocial therapy

Treatment choice should be a shared decision between the clinician and patient	Evidence suggests that treatment with medications for OUD is superior to withdrawal management alone	Medication combined with psychosocial treatment is generally associated with the best clinical results

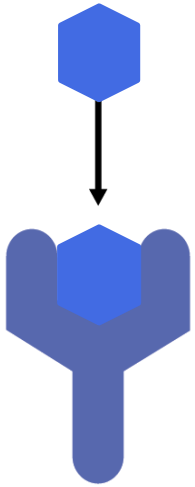
OUD = opioid use disorder. American Society of Addiction Medicine. The ASAM National Practice Guideline for the Treatment of Opioid Use Disorder: 2020 Focused Update. 2020. https://sitefinitystorage.blob.core.windows.net/sitefinity-production-blobs/docs/default-source/guidelines/npg-jam-supplement.pdf?sfvrsn=a00a52c2_2

FDA-approved Medications for the Treatment of Opioid Use Disorder

Methadone

Dosage Form:

- Oral (daily)

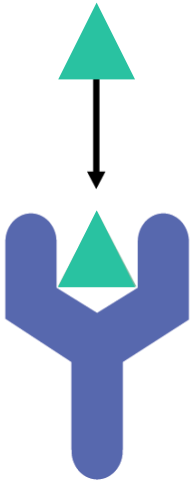


Full Agonist

Buprenorphine

Dosage Form:

- Transmucosal (daily)
- Subcutaneous injection (weekly or monthly)

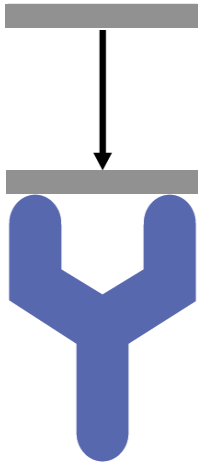


Partial Agonist

Naltrexone

Dosage Form:

- Intramuscular injection (monthly)



Antagonist

American Society of Addiction Medicine. The ASAM National Practice Guideline for the Treatment of Opioid Use Disorder: 2020 Focused Update. 2020. https://sitefinitystorage.blob.core.windows.net/sitefinity-production-blobs/docs/default-source/guidelines/npg-jam-supplement.pdf?sfvrsn=a00a52c2_2

Psychosocial Treatment for Opioid Use Disorder

Psychosocial treatment: "*Any nonpharmacological, professionally administered interventions carried out in a therapeutic context at an individual, family, or group level*"

–American Society of Addiction Medicine (ASAM)

Therapeutic goals of psychosocial treatment are generally to:

1. Modify underlying processes that reinforce use behavior
2. Encourage adherence to treatment plan; and
3. Treat any concomitant psychiatric disorders that either complicate OUD or act as a trigger for relapse

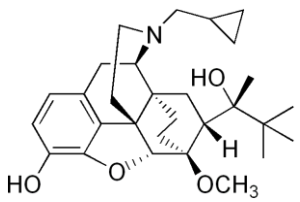
A patient's decision to decline psychosocial treatment or the absence of available psychosocial treatment **should not preclude or delay MOUD**



MOUD = medications for opioid use disorder; OUD = opioid use disorder. American Society of Addiction Medicine. The ASAM National Practice Guideline for the Treatment of Opioid Use Disorder: 2020 Focused Update. 2020. https://sitefinitystorage.blob.core.windows.net/sitefinity-production-blobs/docs/default-source/guidelines/npg-jam-supplement.pdf?sfvrsn=a00a52c2_2

Overview of Buprenorphine

Buprenorphine Regulatory History and Legislation[1,2]



1966 — Buprenorphine discovered and first synthesized

2000 — Drug Addiction Treatment Act (DATA)

Allowed physicians to obtain X-waiver to prescribe Schedule III-V medications for OUD outside of opioid treatment program (OTP)

2002 — FDA approves oral buprenorphine for the treatment of OUD

2016 — Comprehensive Addiction and Recovery Act (CARA)

Allowed NPs and PAs to obtain temporary X-waiver to prescribe buprenorphine for OUD; increased the number of patients prescribers could treat

2017 — FDA approves first injectable buprenorphine

2018 — The SUPPORT for Patients and Communities Act

Made CARA permanent; allowed other specialized nurses to obtain X-waiver to prescribe buprenorphine for OUD

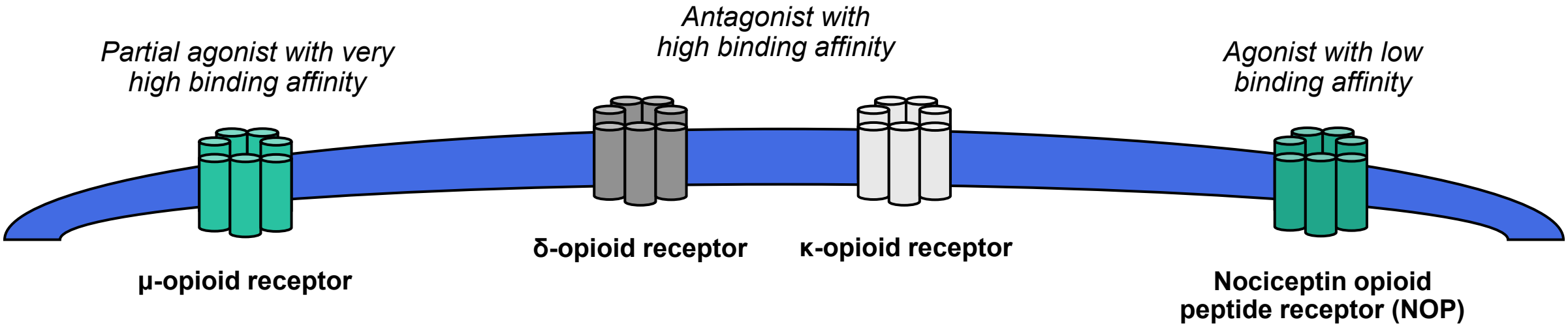
2022 — The Mainstreaming Addiction Treatment (MAT) Act

Eliminated X-waiver requirement and patient limits for prescribing buprenorphine for OUD

2023 — FDA approves second injectable buprenorphine

NP = nurse practitioner; OUD = opioid use disorder; PA = physician assistant. 1. Heidbreder C, et al. *Drug Alcohol Depend Rep*. 2023;6:100133. 2. Silwal A, et al. *Drug Alcohol Depend Rep*. 2023;7:100164.

Buprenorphine Mechanism of Action for Opioid Use Disorder



As a partial agonist, buprenorphine activates the μ-opioid receptor enough to relieve cravings and withdrawal, but is less likely to cause euphoria and respiratory depression than full agonists (*ceiling effect*)

Because of its high affinity, buprenorphine can displace other opioids from the receptor, thereby blocking their effects

The clinical relevance of antagonism at δ-opioid receptor is not well understood

By blocking the κ-opioid receptor, buprenorphine may reduce dysphoria, stress reactivity, and drug-seeking behavior

The clinical relevance of agonism at NOP receptor is not well understood

Hale M, et al. *J Pain Res*. 2021;14:1359-1369.

Comparative μ-Opioid Receptor Binding Affinity

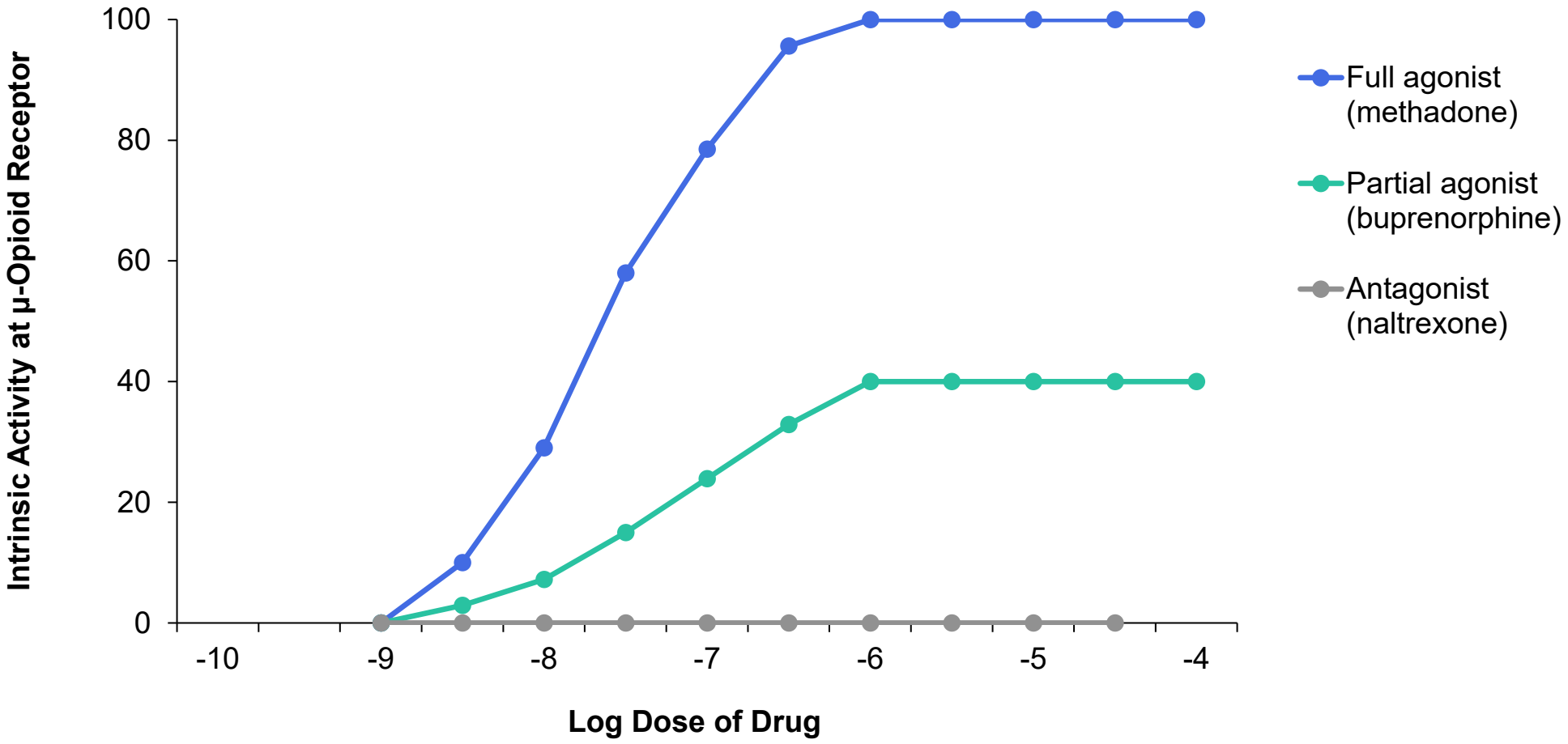
- Binding affinity is measured using K_i value; a low K_i value corresponds to greater binding affinity (separate from receptor activity)
- Buprenorphine exhibits a higher binding affinity at the μ-opioid receptor than full opioid agonists

Opioid	μOR Binding Affinity (K_i, nM)
Buprenorphine	0.22
Hydromorphone	0.37
Morphine	1.17
Fentanyl	1.35
Methadone	3.38
Oxycodone	25.87



μOR = μ-opioid receptor. Volpe DA, et al. *Regul Toxicol Pharmacol*. 2011;59(3):385-390.

Intrinsic Activity of Opioid Use Disorder Medications



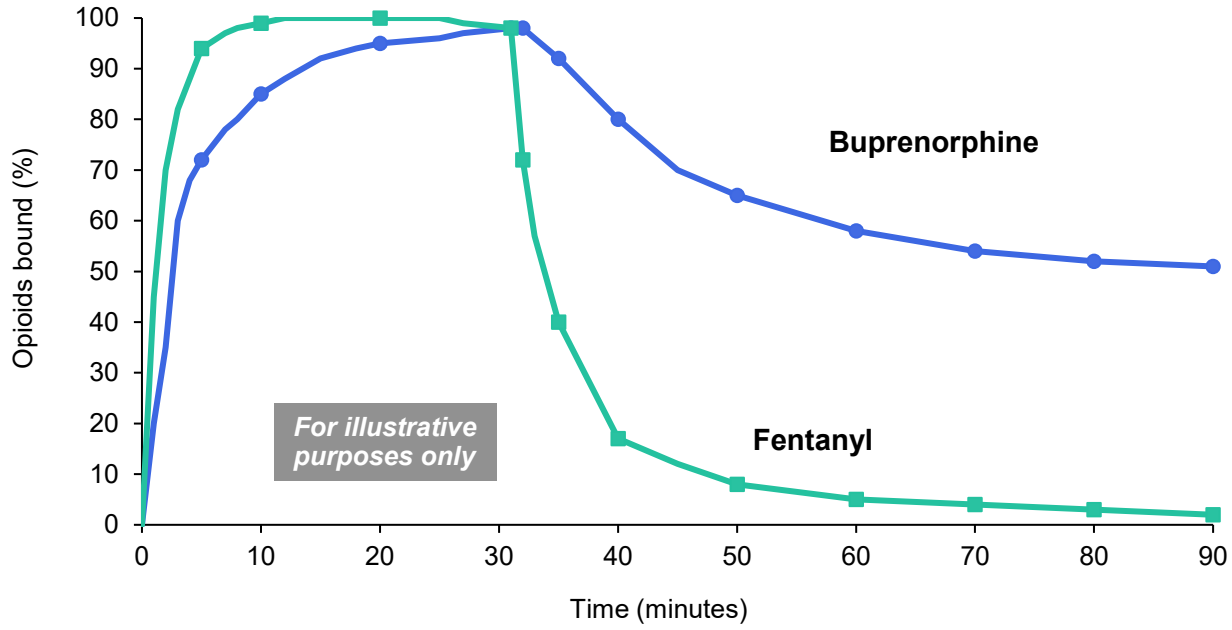
Adapted from Substance Abuse and Mental Health Services Administration. Medications for Opioid Use Disorder. Treatment Improvement Protocol (TIP) Series 63. Publication No. PEP20-02-01-006. Rockville, MD: Substance Abuse and Mental Health Services Administration, 2020.

Dissociation of Buprenorphine from the Opioid Receptor[1-4]

- Buprenorphine has slow dissociation from the μ-opioid receptor, meaning once it is bound, it stays bound for a longer period relative to other opioids, such as fentanyl

- Slower dissociation results in a longer therapeutic effect, milder withdrawal, and less frequent dosing

Association and Dissociation of Buprenorphine and Fentanyl from μ-Opioid Receptor



Adapted from Boas RA, et al. *Br J Anaesth*. 1985;57(2):192-196.

1. Boas RA, et al. Br J Anaesth. 1985;57(2):192-196. 2. Dunn KE, et al. *Drug Alcohol Depend*. 2015;151:47-55. 3. Cohen SM, et al. *J Addict Med*. 2022;16(4):399-406. 4. Greenwald M, et al. *Biol Psychiatry*. 2007;61(1):101-110.

Buprenorphine Formulations for Opioid Use Disorder[1-5]

Sublingual tablet (daily)

- Buprenorphine alone
- Buprenorphine combined with naloxone

Sublingual film (daily)

- Buprenorphine combined with naloxone

Subcutaneous injection (weekly or monthly)

Why Naloxone?

To deter misuse of sublingual buprenorphine, some products are formulated with naloxone which has negligible effect when taken sublingually, but if inhaled or injected, would blunt the effects of buprenorphine and may precipitate opioid withdrawal

1. Indivior Inc. SUBUTEX® (buprenorphine sublingual tablets) [prescribing information]. North Chesterfield, VA; February 2018. 2. Indivior Inc. SUBOXONE® (buprenorphine and naloxone) sublingual tablets [prescribing information]. North Chesterfield, VA; June 2022. 3. Indivior Inc. SUBOXONE® (buprenorphine and naloxone) sublingual films [prescribing information]. North Chesterfield, VA; May 2025. 4. Indivior Inc. SUBLOCADE® (buprenorphine extended-release injection) [prescribing information]. North Chesterfield, VA; February 2025. 5. Braeburn Inc. BRIXADI® (buprenorphine extended-release injection) [prescribing information]. Plymouth Meeting, PA; December 2023.