

Advancing Care in Opioid Use Disorder: Evidence-Based Approaches

Hailee Monies, PA-S, Susan McDiarmid, EdD, MS, PA-C

Westfield State University
Physician Assistant Program



Introduction

The opioid epidemic in the United States has evolved over the past two decades, marked by three major waves of overdose deaths. The first wave began in the late 1990s with rising prescription opioid use and overdose. The second wave, around 2010, was driven by heroin, while the third and most devastating wave began in 2013 with the rapid escalation of synthetic opioids such as fentanyl. Together, these waves have fueled a public health crisis that demands comprehensive strategies for prevention and treatment.

Opioid use disorder (OUD) is a chronic, relapsing condition characterized by compulsive opioid use despite harmful consequences. It is driven by complex neurobiological mechanisms, including changes in the brain's reward, stress, and self-control systems. The consequences of OUD are profound, ranging from overdose and infectious diseases to psychiatric comorbidities and significant social and economic burdens. On average, approximately 217 people died every single day from opioid overdose in 2023. Addressing this crisis requires a multifaceted approach that integrates pharmacologic and psychosocial interventions, harm reduction strategies, and expanded access to care.

Key areas of focus include the pathophysiology of OUD, behavioral therapies such as motivational interviewing and contingency management, evidence-based pharmacologic treatments including methadone, buprenorphine, and naltrexone, and the expanding role of physician assistants in medication-assisted treatment (MAT). By combining these strategies, clinicians can improve outcomes, reduce stigma, and ultimately decrease morbidity and mortality associated with opioid use disorder.¹

Three Waves of Opioid Overdose Deaths

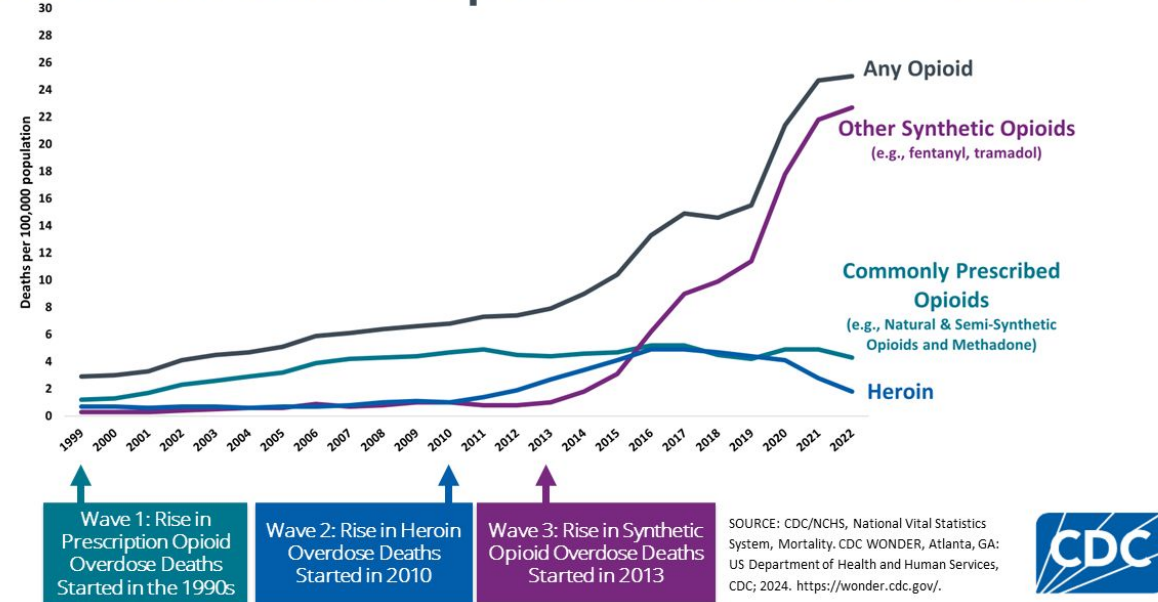


Figure 1. Three waves of opioid overdose deaths in the United States. Reproduced from Centers for Disease Control and Prevention (CDC).¹

Pathophysiology

Opioid Use Disorder is a brain disease involving the dysregulation of reward, stress, and control pathways. Opioids bind to mu-opioid receptors in the brain, leading to dopamine release in the mesolimbic pathway, reinforcing drug use and creating euphoria. Chronic opioid use results in neuroadaptations: receptor downregulation, tolerance, and withdrawal symptoms when use is discontinued. These changes explain why individuals continue using opioids despite harmful consequences.

The dysregulation extends beyond the reward system, affecting stress pathways in the amygdala and hypothalamus, which heightens negative emotional states during withdrawal. Additionally, the prefrontal cortex—responsible for decision-making and impulse control—becomes impaired, reducing the ability to regulate drug-seeking behaviors. This neurobiological cycle of craving, withdrawal, and impaired control sustains compulsive opioid use and highlights why OUD requires comprehensive medical and behavioral interventions.²

Motivational Interviewing

Motivational interviewing (MI) is a patient-centered, evidence-based counseling approach designed to enhance intrinsic motivation to change by exploring and resolving ambivalence. In the context of opioid use disorder, MI supports patients in recognizing the risks of continued opioid use and encourages engagement with treatment, including medications for OUD. MI is flexible and can be delivered in brief sessions, making it feasible for integration into primary care, behavioral health, and specialty addiction treatment settings. Research shows that MI improves treatment engagement, increases adherence to recovery plans, and can reduce substance use when combined with pharmacologic and psychosocial interventions. By fostering a collaborative, nonjudgmental relationship, MI empowers patients to take an active role in their recovery journey.³

Contingency Management

Contingency management (CM) is a behavioral intervention that provides tangible rewards—such as vouchers, gift cards, or prizes—to patients who achieve specific recovery goals, like submitting opioid-negative urine samples or attending counseling sessions. By reinforcing positive behaviors, CM significantly improves treatment adherence and engagement, with studies showing longer periods of participation in care. CM also reduces substance use, with a medium-to-large effect size for abstinence (Cohen's $d = 0.70$) among patients receiving medication-assisted treatment. In addition to clinical benefits, CM reduces opioid-related morbidity, hospitalizations, and emergency department visits, resulting in a net medical cost savings of approximately \$720 per patient. Despite strong evidence supporting its effectiveness, CM remains underutilized due to concerns about cost, ethical considerations, regulatory restrictions, and stigma. Integrating technology-enabled solutions, such as mobile apps, can make CM more accessible and scalable, allowing it to reach more patients efficiently while maintaining its positive impact on adherence, abstinence, and overall recovery outcomes.⁴

Harm Reduction

Harm reduction is a patient-centered approach that minimizes the negative consequences of opioid use, even when full abstinence is not achieved. It promotes safety, autonomy, and engagement while complementing pharmacologic and psychosocial interventions. Key benefits include reducing overdose risk and infections, improving engagement and retention in care, supporting safer substance use practices, and facilitating access to evidence-based OUD treatment.⁵

Overdose Prevention

- Naloxone distribution: provide kits and training.
- Overdose education: test strips, avoid mixing substances, never use alone.
- Clinic response protocols: staff training, overdose plans, safety measures.

Low-Barrier Access to Treatment

- Same-day medications for OUD (MOUD) initiation and walk-in appts.
- Telemedicine and flexible scheduling.
- Support from peer recovery coaches.

Patient-Centered MOUD Prescribing.

- Offer all FDA-approved MOUD.
- Abstinence not required from other substances.
- Microdosing protocols for safe initiation of MOUD.

Reducing Stigma

- Use inclusive, non-judgemental language.
- Normalize disclosure of substance use and sexual/injection behaviors.
- Apply trauma-informed care principles to build trust.

Infection Prevention and Treatment

- Screen/treat HIV, Hepatitis B and C, STIs, and other infections.
- Provide vaccinations and sterile injection supplies.
- Harm reduction counseling on safe injection, vein care, and substance prep.⁵

Methadone

Overview:

Methadone is a slow-acting opioid agonist used to treat OUD and manage opioid withdrawal. It suppresses withdrawal symptoms, reduces cravings, decreases the reinforcing effects of non-prescribed opioids, and facilitates engagement in psychosocial and nonpharmacologic interventions. Methadone is dispensed through federally approved opioid treatment programs, with take-home doses available for patients demonstrating progress.

Mechanism of Action:

- Full μ -opioid receptor agonist: affects NMDA receptors, contributing to analgesia and potentially reducing opioid tolerance development.

Dosing:

- **Initial dose:** 10–30 mg, administered under supervision in an opioid treatment program
- **Maintenance dose:** Typically 60–120 mg daily; doses of 80–100 mg improve retention.
- Higher doses (above 120 mg) may be needed for patients with high opioid tolerance.

Considerations:

- Risks include QT interval prolongation, cardiac arrhythmias, and drug-drug interactions via CYP450 metabolism; Close monitoring is required for cardiac risk and interactions.
- Methadone is dispensed only through federally approved opioid treatment programs, requiring patients to receive care at these facilities.
- Safe for use during pregnancy.
- Retention and relapse prevention improve with higher doses.

Buprenorphine

Overview:

Buprenorphine is a partial μ -opioid receptor agonist and κ -opioid receptor antagonist. It reduces cravings and withdrawal symptoms while maintaining a high safety profile, because its effects plateau at higher doses, limiting the risk of respiratory depression. Buprenorphine can be prescribed in outpatient settings, increasing access to medication-assisted treatment.

Mechanism of Action:

- Partial μ -opioid receptor agonist: reduces cravings and withdrawal without full euphoria.
- κ -opioid receptor antagonist: may reduce dysphoria and stress-related relapse risk.

Dosing:

- Initiation: 2–4 mg to avoid precipitated withdrawal.
- Maintenance: 16 mg daily or higher, up to FDA limit of 24 mg/day.
- Available as sublingual tablets, films, or extended-release injections.
- Can be combined with naloxone (Suboxone) to deter misuse.

Considerations:

- Safer than methadone regarding overdose.
- Caution when combined with other sedatives.
- Safe in pregnancy, with less severe neonatal abstinence syndrome than methadone.
- Retention improves with higher doses and psychosocial support.
- Group-based or office-based models may enhance access and retention.

Naltrexone

Overview:

Naltrexone is a long-acting μ -opioid receptor antagonist used to prevent relapse in OUD. It blocks the effects of opioids, reduces cravings, and facilitates engagement in psychosocial interventions. Naltrexone can be prescribed in outpatient settings and is also indicated for alcohol use disorder.

Mechanism of Action:

- Full μ -opioid receptor antagonist: prevents opioid effects and reinforcement.

Dosing:

- Oral: 50 mg daily or intermittently (100 mg twice + 150 mg once weekly).
- Extended-release injectable (ER): 380 mg every 3–4 weeks via intramuscular gluteal injection.

Considerations:

- Patients must be opioid-free before initiation to avoid precipitated withdrawal.
- Oral formulation has higher nonadherence rates; ER preferred for better retention.
- Side effects: insomnia, mild liver enzyme elevation, hypertension, upper respiratory symptoms.
- Not recommended in pregnancy or breastfeeding.
- Relapse after treatment may result in overdose due to decreased tolerance.⁶

PAs in MOUD

Physician Assistants (PAs) expand access to medications for opioid use disorder (MOUD). By using screening tools in primary care and ED settings, PAs identify at-risk patients and initiate early intervention. They apply motivational interviewing, contingency management, and harm reduction strategies to improve engagement. PAs can prescribe all three FDA-approved MAT medications—methadone, buprenorphine, and naltrexone—ensuring timely access to pharmacologic care.

Collaborative care models show high effectiveness:

- Massachusetts Nurse Case Manager Model: non-physician clinicians achieved 51% retention at 12 months with 91% opioid-negative urine screens among retained patients.
- Project ECHO (rural primary care): NP/PAs performing evaluation and monitoring increased buprenorphine-waivered providers per capita, expanding access in underserved areas.
- ED-initiated MAT: collaborative teams achieved 78% treatment engagement at 30 days, versus 37–45% for referral-only approaches.

PAs help bridge healthcare gaps, particularly in rural and underserved areas, integrating care with social work, psychiatry, and addiction medicine. By increasing the number of trained MAT providers, PAs improve retention, reduce barriers, and lower opioid-related morbidity and mortality, ultimately enhancing outcomes for individuals with OUD.⁷

Conclusion

Opioid use disorder (OUD) is a chronic, relapsing condition characterized by compulsive opioid use, physical dependence, and high risk of overdose and infectious complications. The opioid epidemic has progressed in waves driven by prescription opioids, heroin, and synthetic opioids, causing substantial morbidity and mortality in the U.S.

Understanding OUD's pathophysiology—dysregulation of reward, stress, and executive control systems—is essential for designing effective interventions. Evidence-based treatment combines pharmacologic and psychosocial approaches. Psychosocial strategies, including motivational interviewing and contingency management, enhance engagement, readiness for change, and adherence, while harm reduction principles reduce immediate risks and promote access to care. Medications for OUD—methadone, buprenorphine, and naltrexone—address neurobiological mechanisms, lower overdose risk, and improve long-term outcomes.

Physician Assistants play a critical role by screening patients, applying psychosocial interventions, incorporating harm reduction, and prescribing MOUD, expanding access and supporting patient-centered recovery. Together, these interventions provide a comprehensive approach that promotes retention in care, recovery, and long-term health.

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