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Review Article

The Opioid Epidemic in the United States: What Worked, What Helped, and What Remains to Be Done

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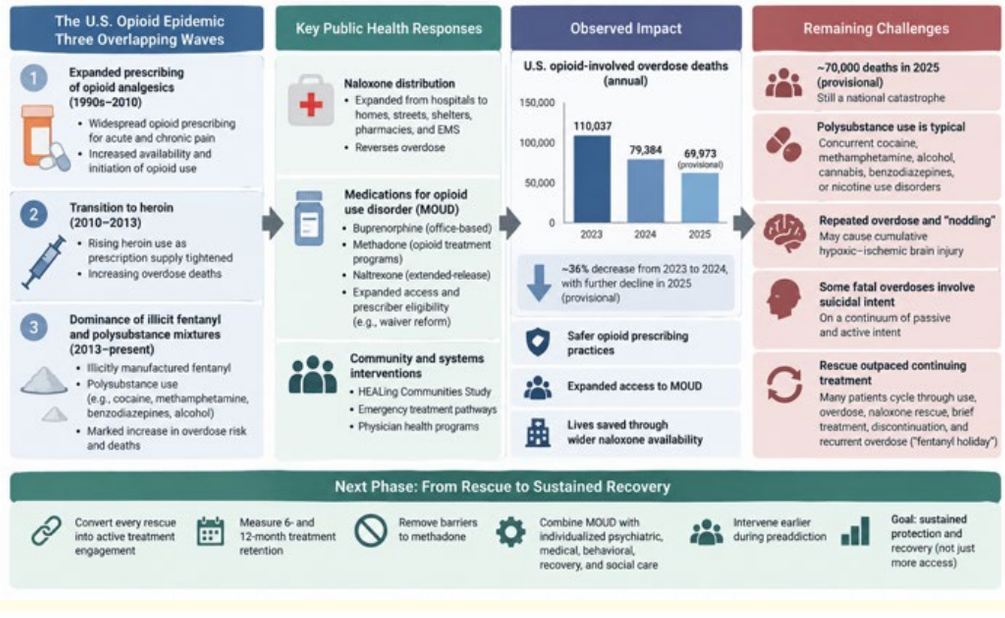
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Graphical Abstract



Abstract

The United States opioid crisis evolved through overlapping waves: expanded prescribing of opioid analgesics, transition to heroin, and then dominance of illicitly manufactured fentanyl and polysubstance mixtures. Public health responses saved lives. Opioid prescribing became safer. Naloxone moved from hospitals into homes, streets, shelters, pharmacies, and emergency medical services. Access to medications for opioid use disorder (MOUD) expanded. Overdose deaths subsequently fell sharply—from 110,037 in 2023 to 79,384 in 2024, with provisional estimates of 69,973 deaths in 2025. This is a major achievement, not a minor statistical fluctuation. Yet nearly 70,000 deaths in one year remain a national catastrophe. Polysubstance use is now typical rather than exceptional; an opioid prescription cannot treat concurrent cocaine, methamphetamine, alcohol, cannabis, benzodiazepine, or nicotine use disorders. Repeated overdose and drug-induced "nodding" may also produce cumulative hypoxic-ischemic brain injury, while some fatal overdoses occur on a continuum of passive and active suicidal intent. The central problem is now visible. Rescue expanded faster than continuing treatment. Prescriber eligibility expanded faster than medication receipt. Treatment initiation expanded faster than retention. Naloxone reverses an overdose; it does not treat opioid addiction. A buprenorphine prescription is not treatment unless it is dispensed, started, taken at an adequate dose, and continued long enough to protect the patient. Too many patients cycle through fentanyl use, overdose, naloxone rescue, brief treatment, discontinuation, and recurrent overdose—a short "fentanyl holiday," not stable recovery. This expert opinion compares policy projections with observed results; examines naloxone, buprenorphine, methadone, naltrexone, waiver reform, emergency treatment, the HEALing Communities Study, and physician health programs; and proposes the next phase. The United States should convert every rescue into active treatment engagement, measure six- and twelve-month retention, remove barriers to methadone, combine MOUD with individualized psychiatric, medical, behavioral, recovery, and social care, and intervene earlier during preaddiction. The next goal is not simply more access. It is sustained protection and recovery.

Keywords: *Opioid Epidemic; Fentanyl; Overdose; Naloxone; Buprenorphine; Methadone; Naltrexone; Medications for Opioid Use Disorder; Treatment Retention; Preaddiction*

Introduction

A success that is not yet victory

The United States has achieved the largest sustained decline in overdose mortality since the contemporary opioid epidemic began. Final data show 79,384 overdose deaths in 2024, 26.2% fewer than in 2023. Provisional data estimate 69,973 deaths in 2025, including 44,564 involving opioids [1-3]. The decline deserves recognition. Tens of thousands of people are alive who might otherwise have died.

But nearly 70,000 annual deaths cannot be called victory. The epidemic has changed faster than the treatment system. Illicitly manufactured fentanyl replaced prescription opioids and much of the heroin market; counterfeit pills and fentanyl-stimulant mixtures widened exposure beyond people who knowingly sought opioids [4-7]. Naloxone became widely available and rescue became increasingly effective. Continuing treatment did not expand at the same rate.

The result is a revolving door: Fentanyl use → overdose → naloxone rescue → failure to start or remain in treatment → recurrent fentanyl use → recurrent overdose.

This paper asks three questions. What worked? What helped but delivered less than expected? What remains to be done? Its premise is straightforward: count survival, medication received, retention, remission, restored health, and restored function—not merely naloxone kits distributed, clinicians authorized, prescriptions written, or first doses administered.

The analysis extends a series of prior clinical commentaries on stigma, fentanyl, methadone, national opioid initiatives, overdose survival, preaddiction, impaired choice, and the goals and limits of medication treatment [59-70]. Those commentaries are used here as a map to the primary evidence; the scientific claims below are anchored principally in peer-reviewed studies and national surveillance.

Author perspective: From detoxification to recovery systems

The author's clinical and research perspective spans the period from the heroin epidemic of the 1970s to the current fentanyl crisis. At Yale, work with David Redmond, Herbert Kleber, and colleagues helped establish the locus-coeruleus/noradrenergic model of opioid withdrawal and translate it into clonidine treatment [71-74]. Clonidine became the first widely adopted nonopioid medication for suppressing major autonomic signs of withdrawal and later informed the use of related α2-adrenergic agonists, including lofexidine. Sequential clonidine-to-naltrexone protocols were developed to move patients through withdrawal and into relapse-prevention treatment [75,87].

That translational success also taught a limiting lesson relevant today: detoxification is not treatment of the full addiction. Suppressing withdrawal can open the door to recovery, but it does not erase craving, conditioned reinforcement, anhedonia, stress reactivity, or relapse vulnerability. The same distinction now applies to naloxone rescue and brief MOUD exposure. Each can be lifesaving; neither should be mistaken for completed treatment.

Later work at the University of Florida helped build the Division of Addiction Medicine, the Florida Recovery Center, one of the first ten ASAM-approved addiction medicine fellowships, and an integrated physician-health research and treatment program. This experience reinforced the value of five-year outcomes, comprehensive assessment, continuing care, monitoring, recovery support, rapid response to recurrence, and restoration of professional function [40,41,68]. It also showed that increasing the number of trained clinicians is not the same as building a treatment system capable of retaining patients.

How the crisis developed

The epidemic is often described as three waves, although the waves overlap [5-7].

Wave 1: Prescription opioid exposure

In the 1990s and early 2000s, opioid prescribing increased for acute and chronic pain. Misleading reassurance about addiction risk, aggressive promotion, pain-as-the-fifth-vital-sign initiatives, permissive prescribing, and fragmented monitoring increased exposure. Some patients developed opioid use disorder (OUD); pills were diverted; high-dose and combined opioid-benzodiazepine prescribing raised fatal risk. Opioid-involved deaths began rising in 1999 [5-8].

The response—prescription drug monitoring programs, formulation changes, enforcement, revised guidelines, and reductions in high-dose prescribing—reduced prescription availability and probably prevented new iatrogenic cases. But supply restriction applied after dependence and addiction were established could not extinguish demand. Some people transitioned to cheaper, more accessible heroin. A policy can reduce one source while leaving the addicted brain, conditioned behavior, pain, psychiatric illness, and drug market intact [9].

Wave 2: Heroin

Heroin deaths rose rapidly beginning around 2010 [5,6]. Heroin supplied the opioid effects no longer obtained as easily from prescribed pills. The transition demonstrated a recurrent error in drug policy: controlling a product is not equivalent to treating the person who has become addicted to it.

Wave 3: Illicit fentanyl and polysubstance death

Beginning around 2013, illicitly manufactured fentanyl transformed the risk environment [4-7]. Fentanyl is potent, inexpensive to manufacture and transport, rapidly acting, and inconsistently mixed. It increasingly appeared in heroin, counterfeit tablets, cocaine, and methamphetamine. By 2023, synthetic opioids other than methadone—principally illicit fentanyl—were involved in nearly 73,000 deaths and approximately 92% of opioid-involved deaths [5].

The fentanyl era is not simply a more severe version of the prescription-opioid era. It is a different treatment environment. Tolerance is high. Withdrawal can be prolonged or atypical. Buprenorphine induction may be more difficult. Multiple naloxone doses may be required. Stimulant co-use, homelessness, trauma, chronic pain, infection, depression, psychosis, and cognitive impairment complicate engagement. A medication remains essential, but a prescription alone cannot reverse every conditioned cue, neuroadaptation, comorbidity, or social determinant sustaining self-administration.

Repeated opioid self-administration also changes decision making. Drug cues and craving increase the immediate value assigned to opioids while devaluing delayed health, family, occupational, and legal consequences. Prefrontal circuits supporting inhibition, salience attribution, and choice become dysfunctional [50]. The first exposure may be voluntary; established addiction is increasingly automatic, compulsive, and poorly explained by a simple failure of will. This is why information and referral alone so often lose to the next fentanyl opportunity.

Polysubstance use is the new normal

The contemporary overdose epidemic is frequently described as an opioid epidemic, but the patient and toxicology increasingly reveal a polysubstance epidemic. Among 309,274 overdose deaths reported from 49 states and the District of Columbia during January 2021-June 2024, 59.0% involved at least one stimulant; 31.2% involved methamphetamine and 30.0% involved cocaine [76]. In many regions fentanyl and stimulants are taken sequentially, intentionally combined, or encountered unknowingly in a variable illicit supply. Alcohol, benzodiazepines, gabapentinoids, xylazine, cannabis, and nicotine add further respiratory, cardiovascular, cognitive, and psychiatric risk.

This changes the meaning of "treatment success." Buprenorphine and methadone treat OUD. They do not treat cocaine use disorder, methamphetamine use disorder, alcohol use disorder, cannabis use disorder, sedative-hypnotic use disorder, or nicotine dependence. Even in a reductionistic medication model, one opioid prescription cannot be expected to treat the other pharmacologies driving intoxication, craving, psychosis, impaired judgment, arrhythmia, respiratory depression, or relapse. A patient whose fentanyl use decreases while severe methamphetamine, cocaine, or alcohol use continues has achieved an important opioid-risk reduction, but not full substance-use remission.

Polysubstance use is also a retention and outcome problem. National urine-testing data from patients receiving buprenorphine show substantial and changing co-use of cocaine, methamphetamine, and nonprescribed opioids [77]. Prospective treatment data likewise show that polysubstance use frequently persists before and during MOUD, even when its association with short-term retention is not uniform across substances or studies [78]. Programs should not respond by expelling the patient. Continued use is evidence that the treatment plan is incomplete: reassess diagnosis, dose, medication choice, withdrawal, craving, psychiatric symptoms, pain, sleep, cognition, housing, and the function of each drug.

The treatment target is therefore the entire acquired addictive brain state, not a single molecule. Every patient entering OUD care should receive repeated—not one-time—assessment for alcohol, stimulants, cannabis, sedatives, nicotine, gambling and other behavioral addictions, prescribed psychoactive drugs, and emerging adulterants. Toxicology should guide care without becoming a punitive test. Evidence-based treatment should be added for each disorder: contingency management and other behavioral treatment for stimulant use; medications and behavioral care for alcohol and nicotine dependence; and targeted treatment for cannabis, sedative, and co-occurring psychiatric disorders. MOUD remains the mortality-protective foundation, but it is not the whole building.

What modeling predicted would save the most lives

Pitt, Humphreys, and Brandeau used a dynamic compartmental model to compare 11 policy responses over five- and ten-year horizons [9]. The analysis was unusually important because it compared interventions within one framework and accounted for transitions among opioid exposure, misuse, OUD, treatment, and death.

The model predicted that demand-focused interventions would outperform supply-only strategies in the near term. Broad naloxone availability produced the largest estimated mortality reduction—approximately 21,200 fewer deaths over ten years. Expanded medication treatment was projected to prevent approximately 12,500 deaths. Reduced opioid prescribing for acute pain was projected to prevent approximately 8,000 [9,10]. The model also warned that supply restriction could produce substitution toward heroin when demand remained untreated.

The model's central logic proved prescient. Naloxone expansion saved lives. MOUD reduced mortality when patients received and continued it. Safer prescribing reduced exposure but could not by itself control an epidemic already driven by heroin and fentanyl. The unexpected limitation was implementation: the United States expanded the availability of interventions more successfully than their sustained use.

A later dynamic model reached a related conclusion: no single intervention was sufficient, and the largest gains required combinations that expanded naloxone, medications, recovery support, and prevention [51]. Models estimate effects under specified uptake and retention assumptions. Observed policy tests whether the system can achieve those assumptions. The widening distance between modeled availability and real-world continuation is now the central implementation problem.

What worked

Naloxone distribution and overdose rescue

Naloxone is the clearest public health success. It reverses opioid-induced respiratory depression rapidly and can be administered by relatives, peers, police, firefighters, emergency medical technicians, outreach workers, and people who use drugs. Take-home programs reduce fatal overdose, and legal access expanded through standing orders, co-prescribing, community distribution, harm-reduction programs, and over-the-counter approval [11-14].

The HEALing Communities Study showed that a large, community-engaged intervention could increase naloxone distribution by 79% relative to usual-care communities [15]. This is a substantial implementation achievement. Naloxone probably contributed to the recent national mortality decline alongside changes in the illicit supply, reduced fentanyl lethality or purity in some markets, treatment, harm reduction, and other factors [1-3,16].

Naloxone's success must be described precisely. It prevents death from a particular overdose. It neither reduces craving nor blocks conditioned drug seeking after it wears off. It does not diagnose depression, treat infection, stabilize housing, relieve chronic pain, or retain a patient in care. Naloxone buys time. Whether that time becomes recovery depends on what follows.

The period after rescue remains dangerous. In a Massachusetts EMS cohort, 6.5% of naloxone-treated patients died the same day and 9.3% died within one year [52]. An apparently successful reversal is therefore not the end of an episode; it is a sentinel event predicting recurrent overdose, medical complications, and death.

Methadone and buprenorphine

Methadone and buprenorphine are the treatments with the strongest mortality evidence. Among Massachusetts residents who survived a nonfatal opioid overdose, methadone was associated with a 59% reduction in all-cause mortality and buprenorphine with a

38% reduction during the following year [17]. Meta-analysis similarly shows substantially lower all-cause and overdose mortality during opioid agonist treatment than after treatment stops [18].

These medications work through several mechanisms: suppressing withdrawal, reducing craving, stabilizing opioid receptors, reducing illicit opioid use, and increasing tolerance to the destabilizing cycle of intoxication and withdrawal. They create the biological stability in which recovery work becomes possible. Calling them "substituting one addiction for another" is scientifically incorrect and clinically dangerous.

Treatment goals should be staged and explicit: immediate protection from overdose and withdrawal; remission of uncontrolled opioid use and OUD symptoms; and recovery of health, relationships, agency, and function [53]. Medication can accomplish the first goal quickly and powerfully. It supports the second. The third often requires time and additional care. Confusing protection with complete recovery leads clinicians to overclaim early success and patients to conclude prematurely that medication has "failed".

Methadone often retains more patients than buprenorphine, particularly those with high opioid tolerance or unstable fentanyl use [19]. Buprenorphine has a favorable safety profile, can be prescribed in office and telehealth settings, and can be delivered in long-acting formulations. Treatment should not force every patient into the same medication. The correct medication is the one the patient will receive, tolerate, and continue.

Emergency department and prehospital initiation

Waiting for a patient to locate treatment after an overdose is a weak handoff. In the landmark randomized trial by D'Onofrio and colleagues, emergency department (ED)-initiated buprenorphine more than doubled engagement in formal addiction treatment at 30 days compared with referral alone [20]. Later implementation work confirmed that ED systems can increase initiation and follow-up [21].

Yet most naloxone reversals do not necessarily end in an ED. Patients are rescued at home, in public places, shelters, and vehicles. Some refuse transport because of cost, stigma, fear, withdrawal, prior mistreatment, or the belief that the emergency has ended. Prehospital buprenorphine therefore brings treatment to the actual point of rescue. In New Jersey, buprenorphine administered by paramedics after naloxone was associated with nearly six-fold greater odds of treatment engagement within 30 days [22]. Even then, most patients did not engage. The intervention worked; the remaining cascade losses remained large.

Safer opioid prescribing

Reducing unnecessary initiation, high doses, dangerous combinations, and prolonged exposure was appropriate. Prescription monitoring, clinician education, safer pain practice, and opioid stewardship reduced iatrogenic risk [8,9]. But these interventions were most powerful as prevention. For a person with established OUD, reducing the legal supply without immediate treatment can move use to a more lethal illegal supply. Prevention and treatment must be temporally matched to disease stage.

What helped less than anticipated

Expanding prescriber eligibility did not reliably expand treatment receipt

The DATA 2000 waiver was intended to permit office-based buprenorphine treatment but eventually became a barrier and a symbol of stigma. Training requirements were relaxed in 2021 and the waiver was eliminated in 2022 [23]. Removal was rational: clinicians do not need a special federal waiver to prescribe full-agonist opioids for pain, and buprenorphine has an excellent safety profile.

However, authorizing more clinicians did not automatically produce more treated patients. In 33 HEALing Communities sites, relaxed training requirements increased the number of eligible clinicians in three of four states but produced no consistent increase in active

prescribers or patients receiving buprenorphine [24]. Nationally, the number of buprenorphine prescribers increased 27% during 2023 after waiver elimination, while the number of patients filling prescriptions increased only about 2% [25]. A Pennsylvania analysis likewise found no significant dispensing increase attributable to waiver elimination in high-need counties [26].

The correct conclusion is not that deregulation was useless. It removed an unnecessary barrier and increased potential capacity. The mistake was expecting prescriber capacity alone to overcome pharmacy stock, reimbursement, clinical support, stigma, fentanyl-related induction concerns, fragmented referral systems, patient ambivalence, and weak retention.

The same caution applies to training. ASAM education and addiction-specialty expansion improve competence and remain essential. But training a clinician is an input, not an outcome. A trained prescriber who does not initiate treatment—or who writes prescriptions that are not dispensed—does not change population mortality.

A prescription is not treatment

The treatment cascade has a trapdoor between prescribing and medication receipt. In a 2026 cohort of 1,428 adults with a new buprenorphine prescription, 25.8% abandoned the first prescription; annual abandonment increased from 19% in 2020 to 37% in 2024 [27]. "Abandonment" should not be reflexively labeled noncompliance. Pharmacies may not stock buprenorphine. Insurers may delay or deny payment. Deductibles, identification requirements, dosing confusion, stigma, transportation, and administrative errors can prevent dispensing [27,28].

A written prescription should therefore be considered an incomplete clinical event. Treatment begins only when medication is received and taken. Systems should verify dispensing, contact the patient within 24-72 hours, resolve pharmacy problems in real time, and provide bridge medication when appropriate.

Starting MOUD is not the same as remaining protected

MOUD produces its mortality benefit while patients remain in treatment. Risk rises after discontinuation, especially immediately after methadone or buprenorphine stops [18,29]. Yet retention is commonly poor. Definitions and populations vary, but many real-world programs lose most new patients within months. Methadone generally retains more patients than buprenorphine, and higher effective doses improve retention [19,30].

The public health system often counts a first dose as success. For a patient who returns quickly to fentanyl, a few days or weeks of medication may be only a fentanyl holiday. It is better than no treatment and may create a later pathway to recovery, but it is not the outcome the system should claim.

Retention failures are not solely patient failures. Programs may discharge patients for continued opioid or stimulant use, missed visits, or unexpected toxicology results—the manifestations of the disorder they were asked to treat. Dose may be inadequate. Fentanyl induction may be poorly managed. Depression, posttraumatic stress disorder, psychosis, attention-deficit/hyperactivity disorder, chronic pain, hepatitis, HIV, sleep disorders, and cognitive impairment may go untreated. Housing, food, transportation, legal exposure, and intimate-partner violence may be more urgent to the patient than the next appointment.

The HEALing Communities Study: Rescue expanded; treatment did not

The NIH-funded HEALing Communities Study randomized 67 highly affected communities in Kentucky, Massachusetts, New York, and Ohio to a community-engaged package of evidence-based practices or wait-list control [15,31]. Intervention communities had an 8% lower opioid-overdose death rate during the comparison period, but the difference was not statistically significant [31]. The trial occurred during COVID-19 and a national fentanyl surge—conditions that made implementation unusually difficult.

The secondary results are especially instructive. Naloxone distribution increased 79%, but the intervention did not significantly improve MOUD receipt, retention for more than 180 days, or initiation within 31 days of opioid-related emergency care [15,32]. The study did not demonstrate that evidence-based practices are ineffective. It showed that community selection and deployment of evidence-based practices did not reliably penetrate the treatment cascade deeply enough, rapidly enough, during a worsening fentanyl epidemic.

This was not simply a "failed trial". It was a national diagnostic test. The result identified the bottleneck: the United States learned how to distribute rescue more effectively than how to deliver and retain people in continuing treatment.

Naltrexone: Effective after initiation, but a difficult doorway

Extended-release naltrexone is an evidence-based option for selected patients who prefer an antagonist, have completed withdrawal, and can reliably return for injections. It has no opioid agonist effects, no diversion, and can be valuable in structured or safety-sensitive settings. Its development, pharmacology, clinical uses, and future directions have been reviewed by Srivastava and Gold [87]. Its population limitation is induction. Patients must first complete an adequate opioid-free interval, often a substantial obstacle in the fentanyl era. In comparative effectiveness research, inability to initiate naltrexone accounts for much of its disadvantage relative to buprenorphine; among successfully inducted patients, outcomes can be comparable [33].

Naltrexone should remain available, but policy should not mistake theoretical eligibility for practical initiation. The best medication is ineffective if the patient cannot get through its doorway.

The revolving door is a cascade failure

Only a minority of people with OUD receive MOUD. In 2022, approximately one in four adults who needed medication treatment received it; NIDA has used the more conservative estimate of fewer than one in five [34,35]. After nonfatal overdose, treatment rates are even more revealing. In the Massachusetts cohort, only 11% received methadone and 17% received buprenorphine during the following year [17]. A 2026 national Medicaid study found that only 26% received MOUD within six months after overdose [36].

The cascade can fail at every point:

1. Overdose is reversed, but the patient is not transported or engaged.
2. The patient reaches emergency care, but OUD is not diagnosed or medication is not offered.
3. Medication is offered, but the patient declines or induction is delayed.
4. A prescription is written, but the pharmacy does not dispense it.
5. Medication is started, but the dose is inadequate or follow-up fails.
6. Treatment continues briefly, but psychiatric, medical, pain, and social needs remain untreated.
7. The patient returns to fentanyl after tolerance and protection decline, increasing fatal risk.

Naloxone utilization and buprenorphine prescription counts may therefore rise together without closing the revolving door. The proper dashboard is a cascade: overdose survivors contacted; OUD diagnosed; medication offered; medication started; prescription dispensed; retained at 30, 90, 180, and 365 days; recurrent overdose; mortality; remission; and functional recovery.

The neurological burden after overdose and nodding

Overdose survival is usually counted as a binary success: alive or dead. That misses acquired neurological disease. Opioid overdose suppresses ventilation, producing hypoxemia and hypercapnia. The brain regions most vulnerable to oxygen deprivation—including hippocampus, cerebellum, basal ganglia, watershed white matter, and cortex—may be injured before breathing is restored. Naloxone reverses opioid receptor-mediated respiratory depression; it cannot reverse neurons already injured by hypoxia.

A systematic review found reported cognitive impairment and structural brain abnormalities after opioid-related overdose, although the literature was heterogeneous and often lacked premorbid testing [79]. MRI studies have linked prior nonfatal overdose to lower hippocampal volume, supporting the hypothesis that overdose-related hypoxia contributes to memory-system injury [80]. Newer work similarly reports posterior hippocampal vulnerability and substantial neuroanatomical heterogeneity in OUD [81]. Because many overdoses are unwitnessed or never medically documented, the cumulative neurological burden is probably underestimated.

"Nodding" should not be dismissed as sleep. It is a semiconscious opioid-toxic state in which respiratory rate and tidal volume may fall repeatedly, oxygen decreases, and carbon dioxide rises. A patient who cycles through prolonged nodding, apnea, overdose, rescue, and recurrent use may experience multiple hypoxic insults—physiologically analogous in important respects to repeated near-drowning, choking, or cardiac-arrest events. The severity of any one event varies, but repeated events make cumulative injury biologically plausible.

Residual deficits can undermine the very treatment offered after rescue. Impaired new learning may look like failure to remember instructions. Executive dysfunction may look like poor motivation. Slowed processing, apathy, emotional lability, gait disorder, tremor, neuropathy, seizures, sleep disturbance, or impaired judgment may be attributed incorrectly to "addictive personality," intoxication, or noncompliance. Alcohol-related thiamine deficiency, hepatic disease, traumatic brain injury, infections, stroke, stimulant-associated vascular injury, nutritional deficiency, and medication effects can coexist.

Every patient with repeated overdose, prolonged nodding, unexplained functional decline, or treatment failure should receive a focused neurological and cognitive assessment. At minimum this includes overdose and loss-of-consciousness history, collateral history when available, neurological examination, cognitive screening emphasizing memory and executive function, gait and motor assessment, review of oxygen-requiring events, and evaluation for nutritional, hepatic, infectious, traumatic, vascular, and sleep-related causes. Neuropsychological testing, brain imaging, EEG, laboratory evaluation, rehabilitation, occupational therapy, and neurology referral should follow when indicated. Treatment plans must be cognitively accessible: simple dosing, repetition, written and visual reminders, long-acting medication options, family or peer support, transportation help, and active follow-up.

Overdose, suicide, and deaths of despair

Drug overdose, suicide, and alcohol-related disease are commonly grouped as "deaths of despair," a concept introduced to describe rising midlife mortality associated with social and economic deterioration [82]. The categories are epidemiologically distinct, but clinically they overlap. Depression, hopelessness, pain, trauma, social isolation, unemployment, alcohol use, and OUD can increase both recurrent overdose and suicide risk.

Death certificates commonly classify overdose as unintentional, intentional, or undetermined. Intent, however, is not always binary or observable. Some patients report active intent to die; others describe passive intent, indifference to survival, or knowingly using a potentially fatal fentanyl dose while alone. In one study of opioid-overdose survivors, 51% reported some suicidal motivation—44% passive and 7% active [83]. These self-reports cannot be projected directly onto all fatal overdoses, but they show why "accidental" should not automatically mean "without suicidality".

Misclassification adds uncertainty. Poisoning suicides are particularly vulnerable to being recorded as accidental or undetermined when no note or explicit preparatory behavior is found. Epidemiological work has long estimated substantial undercounting of poisoning suicide, with estimates around 30% in some analyses [84,85]. That is an estimate of potential misclassification, not proof that 30% of contemporary fentanyl deaths are suicides. The defensible conclusion is that the true proportion is unknown and almost certainly greater than the number coded as intentional.

OUD itself is associated with markedly elevated suicidal ideation, attempts, and death. Time in opioid agonist treatment appears to reduce suicide risk as well as overdose risk [86]. Therefore every overdose survivor should be screened for depression, hopelessness, active and passive suicidal intent, prior attempts, access to lethal drugs or firearms, recent loss, psychosis, intoxication-related impulsivity, and protective factors. Patients with concerning findings need an integrated suicide-safety plan, lethal-means counseling, psychiatric treatment, close follow-up, and OUD treatment—not referral to separate systems that may each assume the other is responsible.

Medication is essential—but medication alone is not always sufficient

Two errors should be avoided. The first is withholding MOUD until a patient accepts counseling, abstinence, or residential care. That increases mortality and is not evidence based. The second is assuming that access to medication automatically supplies everything needed for durable recovery.

The brain changes and conditioning produced by repeated opioid self-administration do not disappear when a prescription is printed. Drug cues, stress, negative affect, anhedonia, pain, sleep disturbance, impaired executive control, social networks, and learned routines continue to drive use. MOUD stabilizes opioid neurobiology and reduces death; it creates an opportunity for recovery. Some patients do well with medication and limited additional services. Others require intensive, integrated care.

Some OUD is treatment refractory—not because MOUD is ineffective, but because protection is incomplete, adherence is intermittent, dose or medication is poorly matched, polysubstance use persists, or comorbid illness and environmental reinforcement overwhelm the treatment delivered [54]. Such patients need treatment intensification, not therapeutic nihilism.

Psychosocial treatment should therefore be offered but not used as a barrier to medication. Evidence suggests that structured behavioral services can improve retention for some populations, but mandatory counseling requirements can reduce access [37,38]. The clinical question is not medication versus treatment. It is how much additional treatment this patient needs to remain alive and recover.

For methadone specifically, meta-analysis indicates that combined psychosocial treatment can improve several outcomes compared with methadone alone [55]. The implication is additive, not exclusionary: start medication promptly, then build the behavioral and recovery platform around it.

High-quality office-based opioid treatment and opioid treatment programs can provide more than medication: rapid access, adequate dosing, contingency management, group treatment, cognitive-behavioral and trauma-focused therapy, peer recovery support, family involvement, pain care, psychiatric treatment, infectious-disease care, vocational support, housing navigation, and assertive re-engagement after missed visits.

What physician health programs teach—and what they do not

Physician health programs (PHPs) demonstrate that sustained remission is possible when treatment is long, structured, actively monitored, and linked to powerful recovery contingencies. Cohort studies report favorable five-year outcomes for approximately three quarters of participating physicians; one study found 78% had no positive alcohol or drug test during five years and 72% continued practicing medicine [39-41]. A systematic review of monitoring programs for health professionals estimated pooled abstinence success of 72% and work retention of 77% [42].

PHPs usually include comprehensive evaluation, extended treatment, frequent random testing, recovery-group participation, workplace coordination, rapid response to recurrence, and monitoring measured in years rather than weeks. The “carrot” is unusually powerful: preservation or restoration of a medical license, career, identity, and livelihood. The consequence of recurrence is also immediate and credible.

These outcomes cannot simply be generalized to every person with OUD. Physicians are selected, educated, occupationally anchored, and offered resources unavailable to many patients. Coercion can cause harm, and abstinence-only requirements may conflict with appropriate MOUD. The transferable lesson is not that every patient should be treated like an impaired physician. It is that duration, structure, monitoring, contingency management, rapid re-intervention, comprehensive care, and a meaningful recovery incentive matter. The ordinary patient deserves an equally serious longitudinal system—adapted ethically and voluntarily to the patient's life.

Lessons from Lexington and therapeutic communities

The federal narcotic hospital at Lexington and later therapeutic communities such as Daytop treated addiction as more than drug exposure. They offered separation from the drug environment, time, work, groups, community roles, and an identity organized around recovery. Their outcomes were mixed, relapse after discharge was common, and the Lexington model also supported ethically troubling research. Synanon's early therapeutic-community innovations were later overwhelmed by authoritarian control, coercion, violence, and abuse; it should not be rehabilitated as a treatment model [43,44].

The useful historical lesson is narrower. Medication without time, relationships, structure, and a recovery environment may be insufficient for some patients. Modern residential and recovery-housing programs should retain these therapeutic elements while using evidence-based MOUD, protecting civil rights, measuring outcomes, and avoiding coercive or anti-medication ideology.

Methadone expansion was too slow

The United States restricts methadone for OUD to federally certified opioid treatment programs (OTPs), even though clinicians prescribe methadone for pain in other settings. The OTP system provides valuable structure and services but is geographically sparse, burdensome for daily attendance, and unevenly patient centered. In 2022, 19% of U.S. counties had neither an OTP nor an office-based buprenorphine provider [45].

COVID-era take-home flexibilities demonstrated that methadone could be delivered more flexibly without a corresponding increase in methadone-involved overdose deaths [46]. Federal rules finalized in 2024 expanded take-home dosing and mobile access [47]. These changes were overdue.

Methadone should be available sooner when buprenorphine induction fails, cravings persist, illicit fentanyl use continues, or higher structure is desired. Expansion can include mobile units, hospital and jail initiation with direct OTP transfer, guest dosing, pharmacy dispensing under regulated models, and office-based methadone pilots with appropriate safeguards. Not expanding methadone access earlier likely cost lives.

Primary-care methadone reform has been proposed for years [56]. The continued exception—physicians can prescribe methadone for pain but generally cannot prescribe it for OUD—reflects history and stigma more than a coherent comparison of current risks. Expansion must be monitored, but fentanyl has changed the risk-benefit calculation decisively.

What remains to be done

Make every rescue a treatment activation

Every naloxone reversal should trigger a protocol, not a pamphlet. Provide another naloxone supply; assess OUD and withdrawal; offer buprenorphine immediately when appropriate; arrange methadone linkage when preferred or indicated; use peers and navigators; verify the first treatment encounter; and recontact the patient after refusal. EMS, EDs, shelters, syringe-service programs, correctional facilities, and mobile teams must become treatment doors [20-22].

Replace referral with a closed-loop handoff

"Here is a phone number" is not a handoff. The receiving program should accept same-day contact, confirm arrival, and notify the referring team if linkage fails. Bridge clinics should provide medication until longitudinal care is established. The system—not the recently resuscitated patient—should carry the administrative burden.

Verify dispensing

Electronic prescribing creates an illusion of completion. Health systems and payers should detect unfilled initial prescriptions within 24 hours, contact the pharmacy and patient, identify stock or coverage problems, and route the prescription to a dispensing site. Pharmacies should maintain adequate inventory, and regulators should distinguish legitimate OUD care from diversion without intimidating pharmacists [27,28].

Make retention the primary treatment metric

Programs should report 30-, 90-, 180-, and 365-day retention, recurrent overdose, ED use, mortality, and patient-reported recovery. Payment should reward sustained engagement, rapid re-entry, and clinical improvement—not visits completed or prescriptions written. A missed visit should trigger outreach. Continued opioid use should trigger dose reassessment, more support, or transition to methadone—not discharge [18,19,29].

Treat fentanyl-era OUD at adequate intensity

Fentanyl exposure may require higher buprenorphine doses, alternative induction strategies, long-acting injectable buprenorphine, or methadone [30,48]. Long-acting formulations can reduce pharmacy gaps and missed daily doses, but they should be offered as choices rather than punishment or surveillance. Treatment should remain available for years or indefinitely when clinically indicated.

Expand methadone and preserve all medication choices

Buprenorphine cannot be the only scalable answer. Expand OTP capacity, mobile methadone, take-home flexibility, correctional access, hospital initiation, and carefully evaluated office or pharmacy models. Maintain extended-release naltrexone for patients who can and wish to complete induction. No program should define recovery by discontinuation of an effective medication.

Integrate psychiatric, medical, pain, and social care

Concurrent care matters—but it can work only after contact is made. Screen and treat depression, suicidality, trauma, psychosis, stimulant use disorder, alcohol use disorder, cannabis use disorder, sedative use disorder, tobacco use, chronic pain, sleep disorders, HIV, viral hepatitis, endocarditis, wounds, pregnancy-related needs, and cognitive impairment. Stabilize housing, transportation, benefits, and legal problems. Integration should reduce burden, not add appointments that become new failure points.

Treat the entire polysubstance disorder

Do not define success by opioid reduction alone. Reassess all substance use throughout care, determine the function and risk of each drug, and add disorder-specific treatment. Continued cocaine, methamphetamine, alcohol, cannabis, benzodiazepine, or nicotine use should lead to treatment intensification rather than discharge. Remission should describe the patient's actual clinical state, not the single prescription issued [76-78].

Evaluate acquired brain injury and adapt treatment

Repeated overdose, naloxone rescue, prolonged nodding, memory complaints, gait change, behavioral change, or unexplained treatment failure should prompt neurological and cognitive evaluation. Identify hypoxic-ischemic injury, traumatic brain injury, stroke,

seizure, infection, hepatic dysfunction, sleep-disordered breathing, and nutritional deficiencies. Adapt treatment to the patient's cognitive capacity and provide rehabilitation when needed [79-81].

Use recovery supports without making them medication barriers

Narcotics Anonymous and other mutual-help groups, recovery coaches, family treatment, contingency management, outpatient programs, recovery housing, and residential care can add belonging, structure, accountability, and hope. They should welcome patients receiving methadone, buprenorphine, or naltrexone. Treatment culture must stop forcing patients to choose between medication and a recovery community.

Intervene before severe OUD: Preaddiction

Most resources arrive late—after severe OUD, fentanyl exposure, arrest, hospitalization, pregnancy complication, or overdose. Addiction medicine needs the equivalent of prediabetes: identification and active treatment of hazardous use and early disorder before catastrophic progression [49]. Warning signs include escalating dose or route, using alone, counterfeit pill exposure, nonfatal overdose, recurrent withdrawal, craving, loss of control, polysubstance use, deteriorating function, and psychiatric destabilization.

Intervention can include motivational treatment, family engagement, pain reassessment, naloxone, fentanyl test education, lower-threshold MOUD when diagnostic criteria are met, treatment of depression and trauma, and close follow-up. Prevention is most effective before conditioned behavior and neuroadaptation become severe.

Assess suicide risk after every overdose

Do not presume that survival proves an overdose was accidental. Ask about active intent, passive desire not to wake up, hopelessness, use while alone, prior attempts, and access to lethal means. Integrate suicide prevention with MOUD, psychiatric care, follow-up after rescue, and family or peer involvement when appropriate [82-86].

Build meaningful, ethical contingencies

PHPs remind us that recovery is aided by something valuable to regain and protect [39-42]. For other patients, the "carrot" might be housing, family reunification, employment, education, relief from criminal-legal supervision, or restoration of health. Contingency management is one of the most effective behavioral interventions in addiction care and should be expanded, particularly for stimulant co-use. Incentives should support autonomy and recovery—not threaten abandonment or basic human needs.

A new scorecard

The next national scorecard should include:

- Overdose deaths and recurrent nonfatal overdoses.
- Naloxone availability and reversals.
- Percentage of overdose survivors contacted within 24 hours.
- Percentage offered buprenorphine or methadone at the point of care.
- Percentage receiving the medication—not only a prescription.
- Time from rescue to first dose.
- Retention at 30, 90, 180, and 365 days.

- Adequate dosing and access to long-acting formulations.
- Rapid re-entry after treatment interruption.
- Methadone geographic access and take-home availability.
- Psychiatric, medical, pain, and social needs identified and treated.
- Concurrent alcohol, stimulant, cannabis, sedative, and nicotine disorders identified and treated.
- Neurological and cognitive screening after repeated overdose or nodding.
- Active and passive suicidal intent assessed after every overdose.
- Remission, quality of life, housing, employment, and restored family function.

Counting naloxone units without treatment linkage measures rescue activity. Counting prescribers without dispensing measures theoretical capacity. Counting first doses without retention measures starts. None alone measures recovery.

Policy: From rescue to recovery: A proposed policy for accountable, individualized opioid use disorder care

Opioid policy should connect overdose prevention and rescue with sustained, individualized treatment. Expanding access remains essential, but accountability should extend to whether patients receive medication, remain engaged in care, and experience improvements in survival, health, and function. Public investment and reimbursement should support the clinical work required to achieve these outcomes.

Establish an accountable transition after overdose

Every overdose encounter should activate a defined pathway from stabilization to continuing care. Emergency departments, emergency medical services, hospitals, and community programs should identify a clinician or team responsible for offering treatment, arranging timely follow-up, and confirming that the patient reaches the next point of care. When clinically appropriate and accepted by the patient, medication initiation should occur at the earliest feasible opportunity. Discharge planning should address medication availability, pharmacy access, transportation, and a reliable means of contact. An unsuccessful referral should prompt renewed outreach. Accountability means responsibility for offering and coordinating care while respecting the patient's informed choices.

Fund the work required to deliver treatment

Public and private payers should reimburse the assessment, medication management, care coordination, outreach, and follow-up required to sustain treatment. Payment should recognize professional judgment and time spent resolving barriers, including prescriptions that cannot be filled, interrupted coverage, missed appointments, and transitions between settings. Financing should support collaboration among clinicians, pharmacists, behavioral health professionals, and peer recovery workers, with clear responsibilities for each. Coverage policies should minimize avoidable delays and administrative burdens that interrupt clinically indicated care. Payment adequacy should be evaluated alongside access so that practices serving patients with complex needs can maintain these services.

Preserve medication choice and individualized duration

Coverage should support selection among approved medications according to clinical needs, treatment history, patient preference, and practical access. Policies should facilitate timely access to methadone, buprenorphine, and naltrexone, including appropriate formulations, without imposing a uniform treatment sequence. Treatment duration should follow continuing clinical assessment rather than arbitrary coverage limits or mandatory tapering schedules. Counseling and recovery services should be readily available, but participation should not become a prerequisite that delays medication. Recurrence of substance use or interruption of care should trigger reassessment and an accessible route back into treatment.

Make continuing care responsive to the whole patient

Treatment systems should assess and address co-occurring substance use, psychiatric illness, suicide risk, pain, medical disease, cognitive difficulties, and social circumstances that affect engagement. Services should be coordinated around an individualized plan, with referral completion and follow-up assigned to an accountable team. Patients should have access to appropriate behavioral treatment, peer support, and recovery resources, including voluntary family or spiritual support when desired. Continued substance use should prompt adjustment of care rather than automatic discharge. Housing, employment, and other supports should help patients sustain recovery without making basic needs contingent on perfect adherence.

Measure the complete care pathway

Program evaluation should follow patients from treatment offer through medication receipt, initiation, continuation, and re-engagement after interruption. Measures should include time to treatment, retention at clinically meaningful intervals—including six and twelve months—recurrent overdose, mortality, quality of life, and patient-defined functional goals. Reporting should distinguish a prescription written from medication obtained and treatment actually begun. Outcomes should be interpreted in light of clinical complexity and social barriers, with safeguards against rewarding programs for avoiding patients at greatest risk. Measurement should guide improvement while keeping reporting burdens proportionate to their clinical value.

Connect earlier intervention with individualized care

Earlier intervention should recognize that addiction vulnerability may extend across substances and behaviors, with implications for assessment and continuing care. A research agenda grounded in reward-system biology should examine whether addressing this broader vulnerability improves sustained recovery beyond substance-specific treatment alone.

Policy should also connect earlier identification of addiction vulnerability with the financing of sustained, individualized care. A research agenda should examine whether genetic, neurobehavioral, and clinical measures of reward-related vulnerability improve prediction, treatment selection, or outcomes beyond established assessment. Mechanistic plausibility alone should not establish clinical utility or justify routine reimbursement. At the same time, payment systems should support professional judgment, coordination, and longitudinal services required to translate validated evidence into care. The objective is to identify risk earlier, match treatment more effectively, and make sustained recovery a practical possibility.

Implementation and accountability

Federal and state agencies, public and private payers, and healthcare organizations should translate these priorities into defined responsibilities, adequate financing, and measurable implementation targets. Initial efforts should address transitions after overdose, interruptions in medication access, and loss of follow-up. Evaluation should examine clinical outcomes, patient experience, equitable access, and total costs, with transparent reporting and adjustment when programs fall short. Funding should support both delivery and independent evaluation, while avoiding incentives to exclude patients with complex needs [43-87].

The governing principle is continuity: responsibility for care should extend from rescue through treatment and into sustained recovery.

Conclusion

The United States predicted and implemented several of the correct responses. Naloxone distribution saved lives. Methadone and buprenorphine reduced mortality. Safer prescribing reduced new exposure. Emergency and prehospital initiation improved engagement. The recent fall in overdose deaths is a tremendous public health achievement.

But success exposed the next problem. Rescue expanded; treatment did not expand enough. Prescriber eligibility increased; medication receipt barely changed. Patients started MOUD; too many stopped. A prescription is not treatment, and a brief medication episode is not durable recovery. For some patients it becomes only a short fentanyl holiday before the revolving door turns again.

The next phase must begin where rescue occurs, verify medication receipt, retain patients for as long as needed, expand methadone, treat polysubstance use, evaluate acquired neurological injury, assess suicide risk, integrate medical and psychiatric care, add recovery structure without withholding MOUD, and intervene earlier during preaddiction. Naloxone saves a person today. Methadone or buprenorphine can help keep that person alive tomorrow. Comprehensive, sustained treatment can help rebuild a life.

Our responsibility does not end when breathing returns—or when the prescription is written.

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KB owns all rights and titles to GARS and KB220.

Author Contribution

MSG and KB developed the original manuscript. All co-authors approved the final manuscript.

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