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# A Dissemination and Implementation Science Approach to the Epidemic of Opioid Use Disorder in the United States

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#### Abstract

**Purpose of Review** This review aims to (1) conceptualize the complexity of the opioid use disorder epidemic using a conceptual model grounded in the disease continuum and corresponding levels of prevention and (2) summarize a select set of interventions for the prevention and treatment of opioid use disorder.

Recent Findings Epidemiologic data indicate non-medical prescription and illicit opioid use have reached unprecedented levels, fueling an opioid use disorder epidemic in the USA. A problem of this magnitude is rooted in multiple supply- and demand-side drivers, the combined effect of which outweighs current prevention and treatment efforts. Multiple primary, secondary, and tertiary prevention interventions, both evidence-informed and evidence-based, are available to address each point along the disease continuum—non-use, initiation, dependence, addiction, and death.

**Summary** If interventions grounded in the best available evidence are disseminated and implemented across the disease continuum in a coordinated and collaborative manner, public health systems could be increasingly effective in responding to the epidemic.

Keywords Opioid use disorder · Non-medical use · Addiction · Prevention · Dissemination · Implementation science

### Introduction

Opioid use disorder, often secondary to non-medical use of prescription opioids (NMUPO), is a leading public health issue in the USA, and one of such scale it has been called an epidemic [1–4]. According to the National Institute on Drug Abuse (NIDA), non-medical use refers to "the use of a medication without a prescription, in a way other than as prescribed, or for the experience or feelings elicited" [5]. Since 1979, the

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overdose death rate in the USA has grown exponentially, increasing at a rate of 9% each year and doubling at a rate of every 8 years [6]. In 2014, an estimated 4.3 million individuals 12 years of age or older reported current NMUPO, with 1.9 million individuals meeting the criteria for abuse or dependence in the past year [7]. Moreover, the share of substance abuse treatment admissions for primary non-heroin opiates roughly tripled from 3% in 2003 to 9% in 2013 [8]. Among infants, neonatal abstinence syndrome (NAS), a drugwithdrawal syndrome often resulting from prenatal opioid exposure, has nearly quadrupled from 7 to 27 cases per 1000 neonatal intensive care unit (NICU) admissions from 2004 through 2013 [9]. Given the staggering trends, opioid use disorder and its consequences have rapidly climbed to a level that has alarmed the nation. The current epidemic is the likely result of a surge of marketing, prescribing, dispensing, and consumption of prescription narcotics that began two decades ago, much of which was diverted for non-medical use [2]. To understand interventions for the epidemic, it is first necessary to understand drivers of NMUPO.

**Drivers of Non-Medical Use of Prescription Opioids** NMUPO results from a complex, cumulative interaction of multiple



drivers. At its core, however, is a copious supply of prescription opioids, including those used for the treatment of pain and those, like buprenorphine, used for the treatment of addiction. Prescription opioid sales have quadrupled since 1999, concurrent with increases in prescription opioid-related treatment admissions and overdose deaths [10]. The prescription opioid supply is most immediately a function of the prescribing/ dispensing practices of health care providers. In 2012, health care providers wrote an estimated 259 million prescriptions for opioids, equating to one prescription per American adult [11]. At the state level, opioid prescribing rates vary considerably, ranging from a high of roughly 143 prescriptions per 100 persons to a low of 52 prescriptions per 100 persons [12]. Variability in opioid prescribing has been tied to variability in rates of NMUPO and overdose deaths among states [10]. For example, 21 of 27 (77.8%) states with overdose death rates above the national rate were also found to have prescription opioid sales rates that exceeded the national rate [10].

It is important, however, to make a finer distinction between the "supply" of prescription opioids and the "source." The supply of legitimate prescription opioids, among several classes of controlled substances, is a function of a federally regulated system of quotas obtained and sometimes traded by pharmaceutical manufacturers. These quotas, and thus the supply, have steadily increased with demand, driven by effective marketing of the products to professionals, governmental and non-governmental entities, regulatory bodies, and directly to the public [2, 13, 14]. In turn, an unprecedented supply has been available to be prescribed and dispensed as federally approved safe and effective medications through historically trusted and legitimate sources.

The surge in prescribing/dispensing and consumption of prescription opioids has its origin in the 1980s and 1990s, a period characterized by calls to address untreated pain and for greater use of prescription opioids to treat pain, especially non-cancer chronic pain [2, 13]. The American Pain Society put forth "pain as the fifth vital sign," which elevated the importance of pain assessment to equal that of established vital signs and urged physicians to respond to patient pain [2, 15, 16]. Multiple professional organizations, patient advocacy groups, and others also advocated for a more proactive approach to pain management, with an emphasis on prescription opioids as the remedy [2, 16]. Highly intertwined with the shift toward more aggressive use of prescription opioids was the introduction of OxyContin® by Purdue Pharma, an event accompanied by resource-intensive marketing and education to promote it, and prescription opioids in general, to health care providers and patients [2, 13]. The activities of Purdue Pharma and other companies understated the risk of addiction and overstated the advantages of prescription opioids, a tactic that facilitated broad uptake of prescription opioids in the medical community [2, 13]. The pharmaceutical industry has thrived on the uptake, a factor that underlies the epidemic gripping the nation [13, 14].

Compared to illicit drugs like heroin or cocaine, prescription opioids present a distinct, yet dangerous risk to public health [1, 13]. Nevertheless, they have often been considered safer to abuse than their illicit counterparts, in part because they can be legally obtained, possess legitimate medical indications, and are regulated by the Food and Drug Administration [1, 17]. From an epidemiological standpoint, evidence also suggests that low perceptions of risk/harm as well as parental and peer approval, among other risk factors, are associated with non-medical use [18]. Notably, most individuals (53%) obtain prescription opioids for non-medical use free from friends or family, over 80% of whom obtained them from one prescriber [19]. While these risk factors likely represent key drivers of NMUPO, it is also important to recognize that they are amenable to change.

Despite NMUPO reaching epidemic levels, a socio-cultural environment of stigma remains a formidable driver and a barrier to an optimal response. Stigma and discrimination toward individuals with mental illness and addiction are prevalent, a troubling reality as it can hinder help-seeking behaviors, the availability of treatment and other support, and perhaps the implementation of interventions across all levels of prevention [20, 21]. Public views have even been found to be more negative toward individuals with drug addiction as compared to those with mental illness [22]. For example, when compared to other mental illness, individuals have indicated greater acceptance of discriminatory practices against those with addiction, greater skepticism of the effectiveness of addiction treatments, and greater opposition toward policies to assist those with addiction [22]. In addition, misperceptions of addiction as a moral failing, a weakness, or a choice, rather than a chronic, relapsing disease endure [23]. Stigma similarly surrounds evidence-based strategies critical for curbing the growing public health burden of the epidemic. Its association with opioid overdose reversal drugs (e.g., naloxone) and medication-assisted treatment (MAT) for opioid addiction is especially concerning as it challenges adequate access to and use of these life-saving strategies [24, 25]. Thus, stigma, whether toward addiction or toward strategies aimed at alleviating its harms, can foster a socio-cultural environment unsupportive of responding to NMUPO, thereby perpetuating the problem.

These drivers—market forces, misguided policy, perceptions of risk, and stigma—serve as a backdrop to the complexity of addressing NMUPO, and ultimately opioid use disorder, as a public health problem. Presently, prevention and treatment efforts are greatly outweighed by the combined effect of these drivers as evidenced by multiple public health markers: (1) non-heroin opiate-related treatment admissions [8], (2) overdose deaths [27], and (3) progression to heroin among a sub-group of individuals with a history of NMUPO



[26]. In the end, neither a single nor a simple solution will solve such a complex public health problem.

Opioid use disorder, and other substance use disorder that results in injection drug use, has always been a key factor in transmission of human immunodeficiency virus (HIV), hepatitis C virus, hepatitis B virus, and other blood borne pathogens. Lack of availability of safe syringes to use for injection, and an ever-increasing demand and use of prescribed and illicit opioids, has resulted in a new surge in needle sharing among those with opioid use disorder. There are recent rapid increases in hepatitis C and at least one alarming spike in HIV has been reported in the rural Midwest [28]. The Centers for Disease Control and Prevention (CDC), in collaboration with state and local organizations in the state, successfully deployed a rapid intervention to halt the epidemic. They learned that the more than 200 new cases of HIV were largely the result of sharing needles to inject diverted or prescribed opioids among a large network of users, many sharing needles that were re-used dozens of times between users [28, 29]. Best practices for syringe services programs are reviewed elsewhere in this issue and will not be reviewed herein. The purpose of this work is to conceptualize the opioid use disorder epidemic and frame it against promising and proven interventions.

### **Methods**

To identify the targeted strategies, we examined the English language literature for evidence to support the intervention strategies recommended herein, with an emphasis on randomized controlled trials, systematic reviews, and reviews of reviews when possible. Many of the identified studies and reviews were conducted in the past 15 years. The recommended intervention strategies are thus not only current, but many are supported by at least the quality of evidence consistent with randomized controlled trials. Nevertheless, there are other potential interventions that could be recommended to address the epidemic. We, however, restricted the set of interventions described herein for brevity and parsimony.

Fig. 1 Conceptual model of evidence-informed and evidencebased strategies to address the opioid use disorder epidemic

### Results

A Conceptual Model to Guide a Comprehensive Response Below, we propose a conceptual model that simultaneously illustrates the complexity of the problem and offers a roadmap of evidence-informed and evidence-based strategies to address it (Fig. 1). The continuum of the disease of addiction, from non-use to dependence, addiction, and ultimately, premature death, is central to the model. Targeted public health strategies need to be brought to bear against different points all along the disease continuum for measurable progress to be made against the epidemic.

The three levels of prevention—primary, secondary, and tertiary—are placed along the disease continuum. Eight evidence-informed and evidence-based strategies encompassing all three levels of prevention have then been strategically positioned along the disease continuum (summary in Table 1.). By engaging in these strategies at once, disseminating and implementing best practices in high-risk communities and target populations, we posit that public health systems will be increasingly effective in combating the problem. In addition to the disease continuum being central to the model, we also advocate for an approach grounded in dissemination and implementation science. In other words, there are promising and evidence-based tools available to address each point along the disease continuum, leaving no time to spare in disseminating, implementing, and evaluating them.

## **Primary Prevention**

# Dissemination and Implementation of Prevention Programs

Primary prevention aims to prevent the development of a disease, and addiction is a preventable disease [23, 96]. Preventing the initiation of NMUPO or any illicit opioid should be the highest goal. The dissemination and implementation of effective, evidence-based prevention programs to decrease risk factors and increase protective factors for NMUPO across developmental periods is critical [30]. They can be delivered in various settings (e.g., homes and schools)

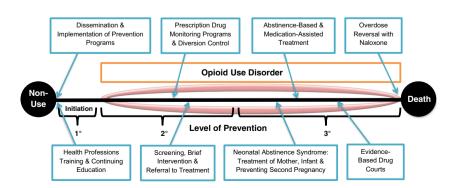




Table 1 Summary of conceptual model strategies to address the opioid use disorder epidemic

Strategy	Potential public health impact	Examples of supportive literature
Primary prevention		
Dissemination and implementation of prevention programs	Evidence indicates prevention and promotion programs can significantly decrease multiple problem outcomes, including substance use, among children and young people. For prescription drugs specifically, data highlight the potential long-term effectiveness of universal preventive interventions delivered in early adolescence for addressing prescription drug misuse. Primary prevention initiatives focused on promoting safe storage and disposal of prescription drugs also hold promise.	[1, 30, 31, 32••, 33–39]
Health profession training and continuing education	Literature suggests that training and continuing education can improve outcomes (e.g., knowledge and skills) among health professionals. The incorporation of multiple exposures and interactive techniques, for example, may be beneficial.	[40•, 41–47]
Secondary prevention		
Prescription drug monitoring programs and diversion control	Findings suggest that prescription drug monitoring programs (PDMPs) could contribute to positive outcomes, such as reductions in use of multiple providers and opioid prescribing, diversion, and overdose deaths. Evidence suggests that state legislation and other enforcement initiatives are also promising strategies.	[48–51, 52•53–58]
Screening, brief intervention, and referral to treatment	Literature supports the effectiveness and cost-effectiveness of screening, brief intervention, and referral to treatment (SBIRT), particularly screening and brief intervention, for risky alcohol use. A comparatively smaller evidence base suggests that SBIRT may be effective for risky drug use, but mixed results have been reported.	[59–65]
Tertiary prevention	and and, our mined results have even reported	
Abstinence-based and medication-assisted treatment	Evidence demonstrates the effectiveness and cost-effectiveness of medication-assisted treatment (MAT) for opioid use disorder. MAT has been found to improve treatment retention and reduce illicit opioid use, among other positive impacts. Evidence also suggests that psychosocial interventions can be beneficial in the treatment of substance use disorders, including when added to pharmacological treatment.	[66, 67, 68••, 69–75]
Neonatal abstinence syndrome: treatment of mother, infant, and preventing second pregnancy	Literature supports the effectiveness of MAT among pregnant women with opioid use disorder. For infants, evidence suggests that pharmacological and non-pharmacological interventions can be beneficial in managing neonatal abstinence syndrome (NAS); however, current treatment approaches vary. For preventing unintended pregnancies, and in turn NAS, evidence supports the effectiveness and cost-effectiveness of voluntary, long-acting reversible contraception.	[67, 68, 76–82]
Evidence-based drug courts	Evidence suggests that drug courts can decrease recidivism and substance abuse and can be cost-effective.	[83, 84••, 85–89]
Overdose reversal with naloxone	Literature indicates that community-based overdose prevention and naloxone distribution programs can result in opioid overdose reversals.	[90–95, 101]

and target diverse populations. On a population level, risk for substance abuse can be used to stratify target populations and to deliver prevention strategies that more effectively meet their needs [30]. Moreover, prevention programs can be conceptualized by a three-tiered typology—universal, selected, and indicated—reflecting increasing levels of risk [30, 31]. Tailoring prevention programs to the attributes of target populations and making them culturally relevant could also augment their effectiveness and facilitate acceptance, implementation, and sustainability in community settings [31, 97]. For maximum public health impact, prevention programs seeking to prevent or delay the initiation of substance abuse among

children and youth may be especially important since individuals with a substance use disorder often initiate before they are 18 years of age [31, 98].

Evidence demonstrating the effectiveness and costeffectiveness of prevention programs continues to grow.
Prevention and promotion programs can generate significant,
sustainable reductions in multiple problem outcomes, including substance use, among children and young people [32••].
With regard to prescription drugs specifically, evidence suggests that prevention programs can reduce non-medical use.
For example, findings from three randomized controlled trials
indicate that brief, universal prevention interventions



implemented in early adolescence can decrease non-medical use, including NMUPO, in late adolescence and young adult-hood [33]. As for the economic implications, effective school-based programs implemented nationwide, for example, could result in an estimated 18 dollars saved for each dollar invested [99]. Simply put, "prevention works" and is a high value proposition [100].

A fundamental risk factor for NMUPO centers on access to prescription opioids, whether through retail outlets, social sources, or other avenues. National data indicate social access is particularly problematic since most individuals obtain prescription opioids for non-medical use from friends or family [19]. Consequently, primary prevention initiatives focused on safe storage and disposal of prescription opioids are one strategy for reducing social access [1], though one for which randomized controlled trials of effectiveness do not yet exist. In Utah, for example, a statewide media campaign targeted adults to promote safe use, storage, and disposal [34]. In a post-campaign survey, 18% of respondents reported medication disposal because of the campaign, and those reporting use of a drop box or collection event for disposal increased from < 1 to 5.4% [34, 101]. In Tennessee, an analysis of permanent drug donation box collections found that 4.9% of the collected pharmaceutical waste were controlled substances, which suggests that permanent drug donation boxes can effectively eliminate controlled substances from community settings [35]. Thus, a variety of primary prevention initiatives hold significant promise for lessening the volume of prescription opioids accessible for non-medical use.

**Health Professions Training and Continuing Education** Health care providers occupy a central role in the epidemic of opioid use disorder given their roles in prescribing/ dispensing prescription opioids and providing care for patients with pain and addiction. As a result, they are uniquely positioned for primary prevention. Unfortunately, their capacity to engage in primary prevention is hindered by the minimal training they receive on pain management, substance abuse and addiction, and safe and timely opioid-prescribing/dispensing practices [1, 102]. Rectifying these shortcomings, both in post-graduate and professional training, must be a priority. Medical, nursing, physician assistant, and pharmacy school curricula, residency training programs, and continuing education should be enhanced to equip health care providers with the knowledge and skills to address NMUPO and addiction in clinical settings. To bolster the clinical benefits of any content and procedural training, efforts should concurrently aim to strengthen dyadic patient and interprofessional communication skills concerning pain management, risks and benefits of prescription opioids, and addiction. The training modality could vary; the incorporation of multiple exposures and interactive techniques, for example, could be beneficial [40•, 41–44, 101].

# **Secondary Prevention**

Prescription Drug Monitoring Programs and Diversion **Control** Secondary prevention involves the early detection of a disease to decrease its severity and consequences [96]. For opioid use disorder, it can involve identifying non-medical use and diversion as a means of averting progression to addiction and the sequelae of untreated addiction. A central tool for doing so is prescription drug monitoring programs (PDMPs), which are state-level, electronic databases used to monitor controlled substances prescribed/dispensed to patients [103]. Often overseen by state Departments of Health or Boards of Pharmacy, PDMPs can be used to identify potential abuse or diversion of controlled substances, obtain data on the controlled substance history of a patient, and detect problematic prescribing/dispensing practices [103, 104]. Nearly all states have PDMPs actively gathering data from dispensing pharmacies and reporting it to authorized users [104]. Promising literature suggests that PDMP use could contribute to a number of desirable outcomes, such as reduced opioid diversion, use/misuse, and overdose deaths as well as improved prescribing/dispensing practices [48–51, 52•, 101]. The CDC further concludes that "PDMPs continue to be among the most promising state-level interventions to improve opioid prescribing, inform clinical practice, and protect patients at risk" [103].

Besides PDMPs, additional state-level diversion control strategies can support the secondary prevention of opioid use disorder, especially since states are largely responsible for regulating and enforcing practices concerning prescription drugs [105]. Specifically, state legislation and enforcement initiatives could decrease diversion and other adverse events stemming from NMUPO. The regulation of pain management clinics is a promising strategy from a legislative perspective. Such regulations can target inappropriate, high volume prescribing, a practice commonly associated with "pill mills," thereby reducing a significant source of prescription opioids for diversion and non-medical use [105]. While pain management clinic regulations vary, they may impose constraints on clinic ownership, operation, and prescribing/dispensing practices, and allow for oversight/regulatory opportunities, among other actions [106]. Tactics and investigations implemented by law enforcement to decrease diversion can also align with secondary prevention. Florida's response to increasing overdose deaths and pill mills offers evidence of the potential effect of concurrent state actions. In 2010–2012, the state implemented multiple initiatives directed at pill mills and unsound prescribing practices, including legislation and law enforcement operations [51, 53, 54]. Overall, they have been associated with promising effects, such as reductions in opioid diversion, prescribing and use, and overdose deaths [49, 51, 53, 54].

Screening, Brief Intervention, and Referral to Treatment A strategy that maps squarely onto the secondary prevention of



addiction is screening, brief intervention, and referral to treatment (SBIRT). It is a public health approach to substance use and abuse prevention and treatment that incorporates universal screening, detection of risky or hazardous substance use, early intervention, and referral to treatment for individuals identified with substance use disorder within a single, evidence-based model [59]. Advantages of SBIRT include its brevity, the potential to target multiple problematic behaviors, and the flexibility for multi-setting implementation (e.g., clinics and schools) [59]. Evidence supports the effectiveness and cost-effectiveness of SBIRT, particularly screening and brief intervention, for risky alcohol use [59, 60]. While the evidence base for its effectiveness in addressing risky drug use is comparatively smaller, and at times mixed, it is growing [59].

Abstinence-Based and Medication-Assisted Treatment

# **Tertiary Prevention**

Tertiary prevention focuses on decreasing the complications of a disease through treatment and other support [96]. For the disease of addiction, facilitating access to and use of evidencebased treatment is a key element of tertiary prevention. Treatment options include medication-assisted treatment (MAT) and psychosocial approaches, such as residential treatment and 12-step models [2, 66]. MAT uses pharmacotherapy (e.g., methadone, buprenorphine, and naltrexone) in combination with psychosocial interventions and support to treat opioid addiction [66, 67]. A large body of evidence indicates that it is a safe, effective, and cost-effective treatment for opioid addiction [67, 68., 107]. It has been shown to improve treatment retention, minimize illicit opioid use, and is promising for gains in social functioning and reducing mortality, transmission of infectious diseases, and criminal activity [67, 68. 108]. As for psychosocial interventions, evidence suggests that they can be beneficial in the treatment of substance use disorders when used alone and in conjunction with pharmacological treatment [66, 69, 70]. For example, a moderate level of evidence indicates that residential treatment can be effective for some patients, while aspects of membership in the 12-step fellowship of Narcotics Anonymous (NA) may have a role in long-term recovery [109, 110]. Treatment with methadone or buprenorphine, though, has been found to be more effective and less expensive than other forms of non-MAT behavioral health treatment [111]. Further, a longitudinal study of treatment

Ultimately, there is no one treatment approach that is effective for all individuals with addiction [71]. Treatment approaches and settings should be selected, and tailored as

for prescription opioid addiction suggested that participa-

tion in MAT was related to a higher likelihood of absti-

nence from illicit opioids [112].

necessary, to meet the needs of each individual [71]. Nevertheless, opioid addiction is a treatable disease, underscoring the importance of facilitating access to all forms of evidence-based treatment as a means of curbing potential complications from untreated opioid addiction.

Neonatal Abstinence Syndrome: Treatment of Mother, Infant, and Preventing Second Pregnancy Neonatal abstinence syndrome (NAS) is another serious consequence of the disease of addiction. Tragically, infants are born physiologically dependent on opioids and go through withdrawal after separation from the mothers' blood supply, resulting in a NAS diagnosis. A tertiary prevention approach to mitigating NAS as a complication of maternal addiction is two-fold. First, evidence-based treatment should be delivered to mothers and infants. For pregnant women with opioid addiction, MAT is the standard of care [113]. Clinical practice guidance is being evaluated on an urgent and ongoing basis to lessen infant suffering and to prevent long-term developmental consequences, many of which are unknown at this point. After delivery, pharmacological and nonpharmacological (e.g., breastfeeding) interventions have demonstrated promise in managing NAS [76, 77]. Second, the prevention of unintended pregnancies among mothers of infants diagnosed with NAS is important for reducing additional cases of NAS [114]. It has been estimated that nearly nine out of ten pregnancies among women abusing opioids are unintended, which highlights the value of prevention [115]. Specifically, voluntary reversible longacting contraception (VRLAC) is a safe and highly effective method to prevent unintended pregnancy, thereby preventing NAS [78]. Its use should therefore be promoted.

Evidence-Based Drug Courts Drug abuse, criminal activity, and involvement in the criminal justice system are often intertwined. Approximately half of incarcerated individuals (i.e., inmates) meet the diagnostic criteria for drug abuse or dependence, yet only a minority receive treatment [83, 116]. Substance use is also prevalent among detained juveniles, with almost half of detained youth estimated to have one or more substance use disorders according to one study [117]. There can be a cyclical relationship between crime and drug abuse, a potential factor contributing to the characterization of prisons and jails as the largest establishments to house individuals with mental illness [83, 116]. The interface of treatment with the criminal justice system holds significant potential for "breaking the cycle" and supporting individuals in leading full and productive lives [83, 118].

Drug courts are an effective strategy for integrating evidence-based addiction treatment into the criminal justice system. Typically operated by a multidisciplinary team, these specialized court programs target eligible criminal defendants and offenders, juvenile offenders, and parents with pending



child welfare cases [119]. While drug courts can differ, a comprehensive drug court model may consist of screening and assessment, judicial interaction, monitoring and supervision, sanctions and incentives, and treatment and rehabilitation [119]. Evidence suggests that drug courts are cost-effective and can reduce recidivism and substance abuse among adults and potentially juveniles [83, 84••, 85, 86, 120].

Overdose Reversal With Naloxone Overdose deaths involving prescription and illicit opioids have reached unprecedented levels. Naloxone, an opioid antagonist without abuse potential, can safely and effectively reverse opioid overdose and is the standard of care for possibly deadly respiratory depression from an opioid overdose [90, 121]. For decades, it has been used by emergency medical personnel, and now, it is increasingly being distributed to and administered by trained laypersons and health professionals through community-based overdose prevention programs [91, 121, 122]. Findings suggest that such programs can lead to opioid overdose reversals and potentially decrease opioid overdose death rates, which align with national, state, and local initiatives to improve access to naloxone [90–92]. Notably, multiple programs across the USA (e.g., Chicago, Los Angeles, and New York City) have specifically targeted people who use drugs and their social networks [93–95, 123–132]. Growing evidence illustrates positive impacts from programs that aim to equip people who use drugs with the resources to prevent and respond to an opioid overdose. Studies on such programs have documented not only improvements in overdose knowledge and response skills but also successful overdose reversals involving peer-administered naloxone and few adverse consequences [93–95, 123–132]. In a study of a pilot overdose prevention and management program in San Francisco, for example, 24 people who inject drugs were trained in heroin overdose prevention, cardiopulmonary resuscitation (CPR), and naloxone administration and provided a naloxone kit [93]. During a 6-month follow-up period, they reported successful resuscitations in 20 cases of heroin overdose, performing CPR in response to 16 cases (80%) and administering naloxone in response to 15 cases (75%) [93]. Moreover, according to a survey of organizations across the USA that distribute naloxone kits to laypersons, people who use drugs comprise the majority of laypersons who both receive naloxone kits and perform reported overdose reversals [122]. Despite its potential life-saving implications, some may perceive there to be a risk in the provision of a "safety net" of this type; that people will not see the risk for overdose death as a likely outcome, thereby setting the conditions for riskier behavior. Anecdotal accounts of multiple overdose reversals involving the same person have been reported in the media. Regardless, naloxone has saved thousands of lives and must be propagated as an evidence-based solution [122]. Some may also perceive broad dissemination of naloxone as evidence of failure of the public health system, but it is hopefully a temporary situation that will be remedied with system-wide implementation of promising and evidence-based strategies across the disease continuum of addiction.

# Conclusion

NMUPO and illicit use of opioids are both inflicting a growing burden of opioid use disorder and other adverse outcomes on the nation. As illustrated by our conceptual model, a comprehensive response comprised of multiple strategies and grounded in the best available evidence is critical for mitigating the problem. Implemented in isolation, each strategy described herein will have minimal impact because it will only target a single point along the disease continuum of addiction. Single strategy approaches may also exacerbate the risk of propagating the problem by detracting from its overall complexity.

In short, there is a pressing public health need for a multifaceted response of sufficient scale and intensity to address opioid use disorder and its consequences on a population level. Responsive actions should be balanced with protecting access to prescription opioids for pain management as appropriate [1, 102]. It is thus imperative that strategies be implemented in a concurrent and coordinated manner to reduce the likelihood of unintended consequences and to maximize the impact of the resources invested in them. To make a response of this magnitude a reality, it will require clear communication and committed collaboration among diverse, multi-sector stakeholders. It will be important to align funding priorities and policies, both state and federal, in such a way as to foster the cross-cutting communication and collaboration that is needed. Finally, a response should be coupled with rigorous evaluation, with the aim of advancing the fields of substance abuse prevention and treatment and informing future public health initiatives [101].

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### **Compliance with Ethical Standards**

**Conflict of Interest** The authors declare that they have no competing interests.

**Human and Animal Rights and Informed Consent** This article does not contain any studies with human or animal subjects performed by any of the authors.



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