

# OVERDOSE PREVENTION RESEARCH PRIORITIES

## PROBLEM DESCRIPTION

The [drug overdose epidemic](#) in the United States continues to evolve and substantially impact individuals, families, and communities across the nation. The first wave of the opioid overdose epidemic began with deaths involving prescription opioids starting in the 1990s.<sup>1</sup> Since 2013, deaths involving illicitly manufactured fentanyl and fentanyl analogs have been increasing each year.<sup>2-4</sup> More recently, the rise in overdose deaths involving stimulants, primarily methamphetamine and cocaine,<sup>5</sup> often in combination with opioids, highlights the importance of polydrug use and the complexity of developing and implementing prevention and response interventions to reduce overdose deaths and related harms.<sup>6,7</sup>

▼ **Preventing drug overdose, including opioid overdose, in the United States requires a comprehensive public health approach. To this end, CDC's efforts focus on the following areas:**

1. Conducting surveillance and research to monitor emerging trends, identify risk factors, and inform prevention activities
2. Strengthening state, local, territorial, and tribal capacity to improve data collection and implement evidence-based prevention strategies
3. Working with providers, health systems, and payers to support safer and more effective opioid prescribing and pain management
4. Coordinating with public safety and community-based partners to rapidly identify and respond to overdose threats
5. Increasing public awareness about the risks of opioids and other drug overdoses and related harms

▼ **Fundamental to CDC's Injury Center overdose prevention efforts are rigorous applied research and evaluation projects that:**

- Identify risk and protective factors at the societal, community, family, and individual levels that contribute to or protect against overdose, including adverse childhood experiences (ACEs), another Injury Center priority
- Evaluate the impacts of policies, programs, or practices designed to reduce overdose or antecedents to overdose, with a focus on health system and public health-public safety innovations
- Identify barriers and strategies to translate and scale-up effective interventions to different communities, populations, or settings

As part of addressing the drug overdose epidemic, the Injury Center also aims to reduce cross-cutting negative health outcomes and related behaviors, including suicide and drug impaired driving. Detailed below are a set of research priorities that provide a road map for future applied research that will address key gaps in our current understanding of the drug overdose epidemic and supporting strategies.



## RESEARCH GAPS AND PRIORITIES

### Identify **risk and protective** factors for drug overdose, with a focus on overdoses involving opioids, emerging drugs, and polydrug combinations.<sup>1</sup>

Risk and protective factors for drug overdose exist at multiple levels of the social ecology. Our understanding of the risk and protective factors for drug overdose is complicated by the complex and evolving nature of the drug overdose epidemic. Changes in the illicit drug supply, mixing of drugs with or without the knowledge of the person using those drugs, and polydrug use are factors that contribute to the complexity of the drug overdose landscape and challenge our ability to identify and address risk and protective factors for drug use and overdose. These factors also create challenges for developing and implementing response and intervention strategies. Addressing the drug overdose epidemic will require a better understanding of the unique risk and protective factors for the multiple trajectories and combinations of illicit drug use and prescription opioid and other prescription drug misuse, substance use disorder, and overdose. Furthermore, understanding norms and behaviors surrounding drug use and related behaviors and outcomes will help inform prevention and response strategies as well as communication strategies for increasing public awareness about the risks of opioids and other drugs.

Key research questions under this priority include:

- How do risk and protective factors and trajectories for use, misuse, substance use disorder, and overdose differ for **prescription opioids, illicit opioids, and other emerging drug threats** such as resurging methamphetamine and cocaine?
- What are risk and protective factors and trajectories related to **polydrug use and overdose**, including co-use of opioid and non-opioid drugs, with a focus on methamphetamine, cocaine, and benzodiazepines?
- How do these risk and protective factors and trajectories vary by sociodemographic and geographic characteristics at **all levels of the social ecology**?
- What are risk and protective factors for **early drug use initiation** and **escalation of use**?
- What are the **associations among ACEs, prescription opioid misuse and/or illicit drug use, and chronic pain**, as well as moderators of these associations?
- What are **norms and behaviors** surrounding prescription opioid misuse, illicit drug use, overdose, and related health and behavioral outcomes? What are the best **strategies to communicate about risk** for these outcomes to the public?

The identification of risk and protective factors can lead to the development of behavioral and communication interventions that may reduce prescription opioid misuse, illicit drug use, and overdose and provide a more nuanced understanding of the complex nature of opioid, polydrug, and emerging drug use trends in order to develop and implement effective policies, practices, and programs.

<sup>1</sup> **2015 Priority:** Identify factors that increase risk for prescription drug-related mortality, and identify risk and protective factors related to the co-use of prescription opioid pain relievers and heroin.



## Evaluate the impact, implementation, and adoption of **health system interventions** designed to reduce drug overdose and other drug-related harms.<sup>2,3</sup>

Health systems provide opportunities to implement interventions that can change prescribing and other clinician behaviors and reduce negative outcomes associated with prescription opioid and other prescription drug misuse and illicit drug use. Strategies employed through health systems may include the following: linkage to and provision of substance use disorder treatment, including medications for opioid use disorder; the use of nonopioid therapies for pain management; collaboration with patients on tapering plans; access to naloxone; emergency department overdose protocols; and linkage of patients and families to additional health and social services that are needed to improve health outcomes. Such interventions include incorporating CDC's [Guideline for Prescribing Opioids for Chronic Pain](#) into clinical decision support tools, utilizing prescription drug monitoring program data, employing technology such as telehealth, and implementing insurer mechanisms (e.g., drug utilization review, coverage policies). In addition to preventing overdose, these interventions can aid in retaining patients in treatment, improve patient functional status and quality of life, potentially mitigate related negative health outcomes such as suicidal behavior, and foster resilience through improving family functioning (e.g., mitigate consequences such as ACEs). Research and evaluation in this area should not only focus on the potential benefits but also consider potential unintended consequences of interventions, including implications for patients with pain.

Key research questions under this priority include:

- What is the impact of **insurer, pharmacy benefit manager, and pharmacy-related** strategies on changing prescribing behavior and the use of nonopioid therapies for pain management, reducing misuse of prescription medications, reducing co-prescribing of opioids and benzodiazepines, and increasing access to and the provision of naloxone, and expanding access to, provision of, and retention in evidence-based treatment for substance use disorder, in particular, medications for opioid use disorder?
- What is the impact of **provider and health system-based approaches** across the full continuum from prevention of prescription opioid or other prescription drug misuse or illicit drug use and related harms to treatment of opioid and other substance use disorders, prevention of overdose, and overdose response?
- What are the **unintended consequences and benefits** of health system interventions and policies to address prescription opioid misuse and overdose?
- What are the attitudes, beliefs, knowledge gaps, and health system structural factors that serve as **barriers and facilitators** to adopting health system interventions, and how can they best be addressed?

In recent years, health systems have implemented a variety of policies, programs, and practices to prevent prescription opioid misuse, opioid use disorder, and overdose and respond to overdose, yet many of these interventions remain unstudied. Understanding the impact and unintended consequences and benefits of existing and new health care system efforts can assist in identifying evidence-based practices for further adoption and implementation.

<sup>2</sup> **2015 Priority:** Evaluate the impact of insurer mechanisms and pharmacy benefit manager strategies to change prescribing behavior, inappropriate use of controlled substances, and patient outcomes.

<sup>3</sup> **2015 Priority:** Evaluate the adoption, implementation, and impact of clinical practice guidelines, clinical decision supports, and coordinated care plans within primary care practices in health systems.



## Evaluate programs, practices, and policies that enhance **public health and public safety collaborations** to prevent and respond to overdose, and increase linkage to and retention in care, with a focus on health outcomes.

Public safety partners—such as police, courts and corrections, EMS, firefighters, and other first responders—frequently interact with people who use drugs and play a critical role in responding to drug overdoses and other drug use-related harms. Recognizing the opportunity to intervene to prevent drug overdoses and related harms, public safety partners are engaging in prevention strategies aimed at reducing drug-related morbidity, mortality, and associated harms (e.g., suicidal behavior, ACEs). Examples of such strategies include linkage to programs to directly connect individuals with substance use disorders to healthcare and other support services (e.g., pre-arrest diversion programs, post-release linkage to care, police-led overdose outreach, and linkage to care from harm reduction programs such as syringe services programs) aimed at increasing access to and use of naloxone to prevent opioid overdose deaths and increasing access to substance use disorder treatment. However, approaches vary widely, and evidence on the efficacy, effectiveness, and scalability of these programs is limited. Moreover, development of these programs requires establishing and maintaining partnerships between public health and public safety, along with other stakeholders, while simultaneously addressing stigma surrounding substance use disorder, overdose, treatment, and use of naloxone. The resurgence of stimulant use and related harms, often in combination with opioids, further underscores the importance of public health and public safety partnerships and the need for evidence-based strategies to prevent and respond to overdose.

Key research questions under this priority include:

- What is the effectiveness of programs, practices, and policies that enhance **linkage** of individuals with substance use disorder **to evidence-based treatment**, including medications for opioid use disorder and cognitive and behavioral approaches, in different contexts (e.g., criminal justice settings, post-release, harm reduction programs) on drug use, treatment engagement, treatment retention, overdose, and other health outcomes?
- What is the effectiveness of programs, practices, and policies that incorporate **referrals to trauma-informed substance use treatment for people who have experienced ACEs** who also have substance use disorders on drug use, treatment engagement, treatment retention, overdose, and other health outcomes?
- How does provision of other **social and behavioral services** impact the effectiveness of linkage to care programs, practices, and policies and impact retention in care?
- What is the effectiveness of programs, practices, and policies that increase access to and use of **naloxone** in different contexts and settings on opioid overdose and related harms?
- Which **risk and protective factors** (e.g., ACEs) and **prevention strategies** (e.g., youth-focused programs, overdose response protocols) are best addressed through public health and public safety partnerships at the state and local level?
- What are the attitudes, beliefs, knowledge gaps, and structural factors that serve as **barriers and facilitators** to public health-public safety collaboration and intervention uptake, and how can they best be addressed?

Answering these questions will provide states and communities with the information they need to implement effective public health-public safety partnerships to link individuals to treatment, facilitate retention and recovery, and prevent overdose and related harms.



## Evaluate **federal, state, and local laws, regulations, and policies** with potential to address risk factors for and prevent prescription opioid and other prescription drug misuse, illicit drug use, overdose, and related harms.<sup>4</sup>

Federal, state, and local jurisdictions have enacted statutes and regulations to facilitate prescription drug monitoring program (PDMP) use, improve prescribing practices, and facilitate treatment and overdose response. Examples of state-level laws and policies include those governing PDMPs (e.g., mandated registration and use, interoperability), Good Samaritan laws, pain clinic regulations, and naloxone standing order and co-prescribing laws. Evidence is needed to understand which of these strategies are effective at reducing prescription opioid and other prescription drug misuse and illicit drug use and preventing overdose. Equally important to quantifying the impacts of these policies on health outcomes is understanding their implementation and how implementation affects achieving the intended outcomes of the policy. Additionally, it is important to assess potential unintended consequences of such policies.

Key research questions under this priority include:

- What is the impact of **PDMP-focused policy** interventions on reducing overdose?
- What is the impact of federal, state, and local policies designed to **improve prescribing practices** for treatment of pain?
- What is the impact of federal, state, and local policies designed to **expand access to and increase provision of medications for opioid use disorder**?
- What is the impact of federal, state, and local policies designed to **improve overdose response**?
- What are the **unintended consequences and benefits** of federal, state, and local policies to address drug overdose and related harms?
- What are the key factors (e.g., attitudes, implementation, and resources) that **mediate** the effect of policy interventions?

Understanding the impact, unintended consequences, and benefits of existing federal, state and local statutes and regulations will provide evidence about these strategies at multiple levels of government to inform implementation and decision-making.

<sup>4</sup> **2015 Priority:** Evaluate the impact of state policies and strategies that facilitate Prescription Drug Monitoring Program (PDMP) use, improve prescribing practices, educate patients, and encourage treatment and overdose response.



## Develop and evaluate **innovative prevention strategies** designed to prevent overdose, including among those at greatest risk.

Reducing the burden of drug overdose requires addressing drug use from multiple fronts, including preventing initiation or continuation or escalation of use (e.g., via improved prescribing, addressing ACEs or other risk factors across the social ecology, and increasing early intervention and treatment uptake and access) and preventing nonfatal and fatal overdose through harm reduction strategies (e.g., via comprehensive syringe service programs and naloxone provision). Moreover, to improve health equity, prevention strategies need to be tailored for populations at greatest risk or with least access to services and address other social determinants of health. State and local communities are implementing a variety of innovative strategies to address known risk factors and/or prevent drug use and overdose, but there is limited knowledge on the impact or cost-effectiveness of these strategies. Moreover, shared risk factors for poor health outcomes suggest that programs intended to address another risk factor or health outcome (e.g., youth skill development programs that reduce risk for interpersonal violence and suicide and community economic development programs) may also be effective for reducing drug use and overdose. However, additional research is needed to understand these interventions in this context. Finally, there is a need to evaluate approaches to scaling up existing effective community-wide strategies to address drug overdose across the continuum from prevention to treatment and recovery, in multiple systems and in different contexts, while maintaining effectiveness.

Key research questions under this priority include:

- What is the **effectiveness** of new or innovative prevention approaches for drug use and overdose that have not been evaluated, including those designed to address populations at greatest risk?
- What is the effectiveness of new or innovative approaches to **prevent youth initiation of drug use**, including those that engage multiple sectors within the community?
- How can we **translate and evaluate interventions** from other settings and for other outcomes, including drug use more broadly?
- What are other possible **settings** to address risk and protective factors, including within the school setting and through faith-based and other community settings.
- What are the **attitudes, beliefs, or knowledge gaps** that serve as barriers and facilitators to the implementation of strategies to address opioid and other drug overdose?
- What are the **social inequities**, including the **social determinants of health**, that serve as barriers and facilitators to the implementation of strategies to address opioid and other drug overdose?
- How do we effectively **tailor prevention and treatment approaches** to address unique risks associated with emerging drugs or drug combinations (e.g., synthetic opioids and co-use of cocaine or methamphetamine) to reduce morbidity and mortality and improve other outcomes (e.g., suicidal behavior, family functioning)?
- What is the effect of strategies designed to prevent overdose on **related injury outcomes**, such as suicide, ACEs, and drug-impaired driving?

Answering these questions will provide states and communities with the information they need to implement effective programs to reduce overdose and related harms.

## References

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