

# 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. More recently, rates of drug overdose involving opioids are highest for synthetic opioids such as illicitly manufactured fentanyl<sup>1</sup> and the rise in overdose deaths involving stimulants, primarily methamphetamine and cocaine,<sup>2</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>3,4</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 and reduce stigma

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

- Address key drivers of health inequities – including a focus on improving our understanding of the social determinants of health and people experiencing a disproportionate burden of substance use disorders and overdose<sup>1</sup> – and developing or evaluating tailored and culturally appropriate prevention interventions.
- 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, while ensuring we address health disparities to achieve equitable health outcomes. Detailed below are a set of research priorities that provide a 3 -to-5-year road map for future applied research that will address key gaps in our current understanding of the drug overdose epidemic and supporting strategies.

<sup>1</sup>Persons experiencing a disproportionate burden of substance use disorders and overdose may include but are not limited, to those people in certain socio-demographic groups (e.g. non-English speaking populations, tribal populations, rural communities, racial/ethnic minority groups, sexual and gender minority groups), people experiencing certain social determinants of health (e.g., reduced economic stability; limited educational attainment, access or quality; limited healthcare access or quality including those who have been historically underserved or are uninsured; limited access to substance use treatment; limited health literacy; those in geographically underserved areas), and people experiencing certain social or physical health conditions or experiences (e.g., homelessness, a mental health condition, chronic pain, incarceration or recent release from incarceration, a disability, adverse childhood experiences, a history of suicidal ideation or suicide attempt, a history of substance use disorders and/or overdose).

## 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 epidemic 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 disorders, and overdose. Integral to this work is understanding how long-standing structural barriers and systemic inequities, including racism, introduce additional or worsen other risk factors. Similarly, community strengths, assets, and solutions that aim to address inequities are key protective factors to explore. Furthermore, understanding norms and behaviors surrounding drug use and related behaviors and outcomes that incorporate diverse cultural contexts and lived experiences 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 disorders, 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 or without the knowledge of the person using the 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**?
- How do risk and protective factors and trajectories related to drug use, misuse, substance use disorders, and overdose vary among **populations experiencing a disproportionate burden of substance use disorders and overdose** and **intersectional<sup>ii</sup> social identities**?
- What are risk and protective factors for early drug use initiation and escalation of use? How do these vary among **populations experiencing a disproportionate burden of substance use disorders and overdose**?
- What are risk and protective factors for **early drug use initiation** and **escalation of use**? How do these vary among populations experiencing a disproportionate burden of substance use disorders and overdose?
- What are the **associations among ACEs, prescription opioid misuse and/or illicit drug use, and chronic pain**, as well as moderators of these associations, including social determinants of health?
- What are **norms and behaviors** surrounding prescription opioid misuse, illicit drug use, overdose, and related health and behavioral outcomes. What are norms and behaviors among people experiencing a disproportionate burden of substance use disorders and overdose and/or groups that are at greater risk of experiencing adverse outcomes related to substance use due to social determinants of health? What are the best **strategies to tailor communication about risk** such that messages related to these outcomes resonate with all members of the public, particularly those disproportionately affected by overdose?

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 and equitable 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.

<sup>ii</sup>Intersectional means that individuals belong to more than one group and, therefore, may experience overlapping health and social inequities, as well as overlapping strengths and assets (please see: [Using a Health Equity Lens](#) | [Gateway to Health Communication](#) | CDC for more information).



## 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 and retention in 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. To achieve health equity, evaluation of these strategies must incorporate how access to and provision of care differs among diverse population groups and identify options for adapting strategies to address systemic inequities among people experiencing a disproportionate burden of substance use disorders and overdose through institutional changes and culturally appropriate interventions. Such interventions include incorporating CDC's [Clinical Practice Guideline for Prescribing Opioids for 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). It is important that research and evaluation in this area not only focus on the potential benefits but also consider potential unintended consequences of interventions, including implications for patients with pain. Additionally, intervention impacts may differ for people experiencing a disproportionate burden of substance use disorders and overdose, in particular people who are uninsured; and people who have been historically underserved by health systems or lack access to care.

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, medication 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?
- How do **health system strategies and approaches** address health disparities, social determinants of health, and social and systemic inequities?
- How do the health **impacts of health system strategies and approaches** vary among people experiencing a disproportionate burden of substance use disorders and overdose and/or groups that are at greater risk of experiencing adverse outcomes related to substance use due to social determinants of health?
- What are the **unintended consequences and benefits** of health system interventions and policies to address prescription opioid misuse and overdose especially among people experiencing a disproportionate burden of substance use disorders and overdose and/or groups that are at greater risk of experiencing adverse outcomes related to substance use due to the social determinants of health?
- What are the attitudes, beliefs, knowledge gaps, and health system structural factors related to health disparities, including among program implementors and populations for whom the interventions were designed, 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 of these interventions, and the benefits of existing and new health care system efforts can assist in identifying evidence-based practices for further adoption and implementation while addressing health disparities to help achieve health equity.

<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 and institutional changes aimed at reducing disparities in drug-related morbidity, mortality, and associated harms (e.g., suicidal behavior, ACEs). Essential to the reduction of disparities is the elimination of the longstanding impact of social and structural inequities, including systemic racism. Examples of such strategies include trauma-informed<sup>iii</sup> training, linkage to programs to directly connect individuals with substance use disorders to healthcare and other support services aimed at increasing access to and use of naloxone to prevent opioid overdose deaths and increasing access to substance use disorder treatment. Other support services include pre-arrest diversion programs, post-release linkage to care, first responder-led overdose outreach, coordinated continuity of care for patients impacted by provider closures, and linkage to care from harm reduction programs such as syringe services programs. 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 and other social determinants of health 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, especially among racial and ethnic minority populations, that enhance **linkage** of individuals with substance use disorder to **evidence-based treatment**, including medications for opioid use disorder and cognitive and behavioral approaches. What is the effectiveness in different contexts (e.g., criminal justice settings, post-release, community settings) 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 of people of various racial and ethnic populations 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 among groups experiencing disproportionate burden of overdose and/or groups that are at greater risk of experiencing adverse outcomes related to substance use due to social determinants of health, especially racial and ethnic minority populations?
- 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? In particular, what is the effectiveness among groups experiencing disproportionate burden of overdose and/or groups that are at greater risk of experiencing adverse outcomes related to substance use due to social determinants of health, especially among racial and ethnic minority populations?
- What are the most salient **risk and protective factors** (e.g., ACEs) and **prevention strategies** (e.g., youth-focused programs, overdose response protocols) among groups experiencing disproportionate burden of overdose and/or groups that are at greater risk of experiencing adverse outcomes related to substance use due to social determinants of health? What factors are most salient among racial and ethnic minority populations, that 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, **including among program implementors and program recipients**, that serve as **barriers and facilitators** to public health-public safety collaboration and intervention uptake? In particular, what are these factors among groups experiencing disproportionate burden of overdose and/or groups that are at greater risk of experiencing adverse outcomes related to substance use due to social determinants of health, especially racial and ethnic minority populations, 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.

<sup>iii</sup>Trauma-informed services incorporate the belief that trauma can impact a person's physical and mental health and stress the importance of treating the client individually instead of providing general treatment approaches.<sup>5</sup>



## 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, harm reduction strategies (e.g., fentanyl test strips, syringe service programs) and naloxone standing order and 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 as well as the effect of these strategies on reducing or worsening existing disparities in medical care and health outcomes. 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 among groups experiencing disproportionate burden of overdose and/or groups that are at greater risk of experiencing adverse outcomes related to substance use due to social determinants of health. Additionally, it is important to assess potential unintended consequences of such policies, including whether these policies worsen existing health disparities and systemic inequities.

Key research questions under this priority include:

- What is the impact of **PDMP-focused policy** interventions on reducing overdose, including among populations that are disproportionately affected by substance use disorders or have inequitable medical care?
- What is the impact of federal, state, and local policies designed to **improve prescribing practices** for treatment of pain? What is the impact among groups experiencing disproportionate burden of overdose and/or groups that are at greater risk of experiencing adverse outcomes related to substance use due to social determinants of health?
- What is the impact of federal, state, and local policies designed to **expand access to and increase provision of medications for opioid use disorder** among groups experiencing disproportionate burden of overdose and/or groups that are at greater risk of experiencing adverse outcomes related to substance use due to social determinants of health?
- What is the impact of federal, state, and local policies designed to **improve overdose response** for groups experiencing disproportionate burden of overdose and/or groups that are at greater risk of experiencing adverse outcomes related to substance use due to social determinants of health?
- What are the **unintended consequences and benefits** of federal, state, and local policies to address drug overdose and related harms? How do these policies worsen or reduce existing disparities and inequities in medical care or health outcomes?
- What are the key factors (e.g., attitudes, implementation, and resources) that **mediate** the effect of policy interventions in particular among groups experiencing disproportionate burden of overdose and/or groups that are at greater risk of experiencing adverse outcomes related to substance use due to social determinants of health?

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 equitable 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, systemic or institutional inequities, 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 address social determinants of health and be culturally appropriate, trauma-informed, and tailored for populations disproportionately affected by drug use and overdose. 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 relation to drug overdose outcomes. 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 communities and diverse population groups, through a culturally responsive and equitable lens, while maintaining effectiveness.

Key research questions under this priority include:

- What is the **effectiveness** of new or innovative prevention approaches designed for populations experiencing a disproportionate burden of substance use disorders and overdose and/or groups that are at greater risk of experiencing adverse outcomes related to substance use due to social determinants of health.
- How can these approaches be **adapted to ensure effectiveness** among groups experiencing disproportionate burden of overdose and/or groups that are at greater risk of experiencing adverse outcomes related to substance use due to social determinants of health?
- 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 **modify and evaluate interventions** from other settings and for other outcomes, including drug use more broadly? What contextual factors involving social determinants of health are important to consider when adapting interventions for use in other settings or for other outcomes?
- 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**, including among program implementors and recipients, 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 intersectional social identities and social determinants of health interact to affect implementation of prevention strategies?
- How do we effectively **tailor prevention and treatment approaches** to address unique risks associated with factors such as social and systemic inequities, ACEs, and 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

1. Merianne Rose Spencer, M.P.H., Arialdi M. Miniño, M.P.H., and Margaret Warner, Ph.D. Drug Overdose Deaths in the United States, 2001–2021. NCHS Data Brief No. 457, December 2022.
2. Kariisa M, Scholl L, Wilson N, Seth P, B H. Drug Overdose Deaths involving Cocaine and Psychostimulants with Abuse Potential – United States, 2003-2017. *MMWR Morb Mortal Wkly Rep.* 2019;68(17):41-43.
3. O'Donnell JK, Gladden RM, Mattson CL, Hunter CT, Davis N. Vital Signs: Characteristics of Drug Overdose Deaths Involving Opioids and Stimulants — 24 States and the District of Columbia, January–June 2019. *MMWR Morb Mortal Wkly Rep.* 2020;69(35):1189-1197.
4. Liu S, Scholl L, Hoot B, Seth P. Nonfatal Drug and Polydrug Overdoses Treated in Emergency Departments — 29 States, 2018–2019. *MMWR Morb Mortal Wkly Rep.* 2020;69(34):1149-1155.
5. Substance Abuse and Mental Health Services Administration TIP 57: Trauma-informed Care in Behavioral Health Services Treatment Improvement Protocol (TIP) Series, No. 57. Center for Substance Abuse Treatment (US). Rockville (MD): Substance Abuse and Mental Health Services Administration (US), 2014.