

## DRUG CONTROL PROGRAMS

## RESOURCE SUMMARY

	Budget Authority (in millions)		
	FY 2019 Final	FY 2020 Enacted	FY 2021 Request
<b>Drug Resources by Function</b>			
Research and Development: Prevention	\$477.151	\$446.883	\$435.063
Research and Development: Treatment	\$988.635	\$1,070.760	\$1,051.215
<b>Total, Drug Resources by Function</b>	<b>\$1,465.786</b>	<b>\$1,517.643</b>	<b>\$1,486.278</b>
<b>Drug Resources by Decision Unit</b>			
<i>National Institute on Alcohol Abuse and Alcoholism (NIAAA)</i>			
Research and Development: Prevention	\$51.208	\$53.298	\$48.485
Research and Development: Treatment	\$6.362	\$6.621	\$6.023
<i>National Institute on Drug Abuse (NIDA)</i>			
Research and Development: Prevention	\$425.943	\$393.585	\$386.578
Research and Development: Treatment	\$982.273	\$1,064.139	\$1,045.192
<b>Total, Drug Resources by Decision Unit</b>	<b>\$1,465.786</b>	<b>\$1,517.643</b>	<b>\$1,486.278</b>
<b>Drug Resources Personnel Summary</b>			
Total FTEs (direct only)	357	382	382
<b>Drug Resources as a Percent of Budget</b>			
Total Agency Discretionary Budget (in Billions) *	\$37.9	\$40.3	\$37.7
Drug Resources percentage	3.87%	3.77%	3.94%

\* The total agency discretionary budget includes amounts requested in FY 2021 for consolidation of activities of the Agency for Healthcare Research and Quality into NIH as the National Institute for Research on Safety and Quality (NIRSQ). NIRSQ does not have any programs classified as part of the National Drug Control Budget.

## PROGRAM SUMMARY

**MISSION**

The National Institute on Drug Abuse (NIDA) and the National Institute on Alcohol Abuse and Alcoholism (NIAAA), two of the 27 Institutes and Centers of the National Institutes of Health (NIH), support research in pursuit of the objectives of the *National Drug Control Strategy*. NIDA funds research on the prevention and treatment of drug use, addiction, and its harmful consequences. NIDA is the lead federal agency supporting scientific research on drug use and its consequences, with a mission to advance science on the causes and consequences of drug use and addiction and to apply that knowledge to improve individual and public health. NIDA accomplishes its mission through strategically supporting and conducting basic and clinical research on drug use (including nicotine), its consequences, and the underlying neurobiological, behavioral, and social mechanisms involved, and ensuring the effective translation, implementation, and dissemination of scientific research findings to improve the prevention and treatment of substance use disorders and enhance public awareness of addiction as a brain disorder. NIAAA's mission is to generate and disseminate fundamental knowledge about the

effects of alcohol on health and well-being, and apply that knowledge to improve diagnosis, prevention, and treatment of alcohol-related problems, including alcohol use disorder, across the lifespan. A major priority within NIAAA's mission is research on the prevention and treatment of underage drinking and its harmful consequences.

Substance use and substance use disorder (SUD) cost the United States more than \$740 billion a year in healthcare, crime, and lost productivity;<sup>162</sup> but dollars cannot capture the devastating human cost of addiction to individuals, families, and communities. Drug overdose is now the leading cause of unintentional fatal injury in our nation. In 2017, more than 19.7 million Americans had substance use disorder (SUD),<sup>163</sup> and drug overdose claimed more than 70,000 lives, about two-thirds of which were from illicit or prescription opioids. For every fatal overdose it is estimated that there are 10 non-fatal overdoses and 20 opioid-related hospitalizations.<sup>164</sup>

Studying substance misuse, SUD, and their causes is a complex challenge compounded by societal stigma and misunderstanding that many other illnesses do not face. The landscape of drug use and addiction in America evolves from year to year; a decades-long prescription opioid overdose epidemic led to a rise in heroin deaths, and now overdose from synthetic opioids such as fentanyl and carfentanil predominates. The rising use of synthetic drugs as well as new drug delivery systems such as electronic cigarettes (e-cigarettes) are changing how people use drugs. New HIV and Hepatitis C outbreaks have arisen as a byproduct of intravenous drug use. In addition, the line between legal and illegal substance use has blurred as a growing number of states are legalizing marijuana for recreational and medical use. This presents an opportunity to study the outcomes of these policy changes as natural experiments.

NIDA is supporting research to address today's drug use-related challenges in several key areas, including supporting the Secretary of HHS in responding to opioid misuse, addiction, and overdose; spearheading a landmark longitudinal study of adolescent substance use (including vaping) and brain development in collaboration with NIAAA and other Federal partners; studying the impact of new synthetic drugs; studying the impact of marijuana use; supporting development of new treatments for stimulant addiction; and contributing to scientific and public understanding of the brain mechanisms underlying addiction. These projects represent a significant contribution to the *National Drug Control Strategy*.

Opioid misuse, addiction, and overdose is an ongoing and rapidly evolving public health crisis. Millions of Americans have an opioid use disorder (OUD), and millions more suffer from chronic pain. The urgency and scale of this crisis call for innovative scientific solutions. As part of a government-wide effort to address the opioid crisis, the NIH launched the NIH HEAL (Helping to End Addiction Long-term<sup>SM</sup>) Initiative in April 2018. The HEAL Initiative is an aggressive effort to speed scientific solutions to stem the national opioid public health crisis, bolstering research to develop and improve treatments for opioid misuse and addiction and to enhance pain management.

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<sup>162</sup> <https://www.drugabuse.gov/related-topics/trends-statistics>

<sup>163</sup> 2017 National Survey on Drug Use and Health, 2018. SAMHSA.

<sup>164</sup> Rudd, R. et al. MMWR Morb. Mortal. Wkly. Rep. 65, 1445-1452, (2016).

Alcohol misuse has profound effects on the health and well-being of individuals, families, and communities, costing the United States an estimated \$249 billion per year. NIAAA is committed to reducing the burden of alcohol misuse for individuals at all stages of life and supports a diverse portfolio of research to elucidate the effects of alcohol on health. Research areas include biological and behavioral mechanisms underlying alcohol misuse, alcohol use disorder (AUD), and alcohol-related health conditions; epidemiological assessments of patterns and trends in alcohol use; and the development and evaluation of interventions to diagnose, prevent, and treat alcohol misuse and its consequences, including among youth. NIAAA also supports efforts to translate research findings to improve prevention and treatment of alcohol-related problems and co-occurring conditions and to disseminate evidence-based information to health care providers, researchers, policy makers, and the public. These ongoing efforts have significantly broadened our understanding of AUD, helping to reduce stigma, and provided support for integrating alcohol prevention and treatment services into mainstream health care.

## **METHODOLOGY**

NIDA's entire budget is drug-related and classified as a part of the National Drug Control Budget.

The prevention and treatment components of NIAAA's underage drinking research program are classified as a part of the National Drug Control Budget. Underage drinking research is defined as research that focuses on alcohol use by youth (individuals under the legal drinking age of 21), as well as the negative consequences of underage alcohol use (e.g., alcohol-related injuries, impact on adolescent development including on the developing brain, and risk for AUD). It includes basic biological and behavioral research, epidemiological research, screening studies, the development and testing of preventive and treatment interventions, and efforts to disseminate evidence-based information. NIAAA's methodology for developing budget estimates for the Budget and Performance Summary is a two-step process. First, NIAAA identifies its underage drinking projects using NIH's automated, electronic text mining system for research, condition, and disease categorization. Once these projects are verified as underage drinking projects, NIAAA conducts a manual review of the project listing and codes each verified project as relevant to prevention or treatment.

## BUDGET SUMMARY

The FY 2021 request for drug-related activities at NIH is \$1,486.3 million (\$1,431.8 million for NIDA and \$54.5 million for NIAAA), a 2.1 percent decrease compared with the FY 2020 Enacted level.

NIH-supported research has provided and will continue to provide the scientific basis for drug control policy. For example, NIH continues to explore the many biological, behavioral, and environmental influences on substance misuse and addiction vulnerability, which will allow the development of more targeted and effective prevention approaches. Research reveals that universal prevention programs not only reduce drug use, underage drinking, and other risky behaviors that can lead to HIV and other adverse outcomes, but can also promote other positive outcomes, such as strengthening young people’s sense of community or “connection” to school—key to reducing substance misuse, violence, and mental health problems.

Another top priority continues to be the development and deployment of therapeutic interventions to treat SUD, including medications, biologics, behavioral interventions, and non-pharmacological interventions such as transcranial magnetic stimulation or neurofeedback. NIH is now poised to capitalize on a greater understanding of the neurobiology underlying addiction, and of newly identified candidate molecules and brain circuits that show promise as potential targets for the treatment of SUD. However, discovering new therapies is not sufficient to combat SUD if these therapies do not reach the people who need them. In many cases, such as medications for the treatment of OUD (MOUD), studies suggest that effective treatments are under-utilized despite strong evidence of their effectiveness. To address this issue, NIH is also exploring ways of improving the dissemination and implementation of evidence-based practices (implementation science) in real world settings to improve the prevention and treatment of SUD and co-occurring conditions such as HIV and psychiatric disorders, thereby enhancing the public health impact of NIH-supported research.

In April 2018, NIH launched the HEAL Initiative (see above), an aggressive, trans-agency effort to speed scientific solutions to stem the national opioid public health crisis. This Initiative will build on extensive, well-established NIH research, including basic science of the complex neurological pathways involved in pain and addiction, implementation science to develop and test treatment models, and research to integrate behavioral interventions with MOUD.

As part of the NIH HEAL Initiative, NIDA (and to a lesser extent, NIAAA) supports a variety of projects aimed at advancing our understanding of how to prevent and treat opioid misuse and addiction and reverse opioid overdose. This includes research studies focused on:

- Enhancing the NIDA Clinical Trials Network to Address Opioids<sup>165</sup>
- Focused Medication Development to Treat Opioid Use Disorder and Prevent/Reverse Overdose<sup>166</sup>
- Determining strategies to reduce opioid overdose in communities hardest hit by the opioid crisis (the HEALing Communities Study)<sup>167</sup>

<sup>165</sup> <https://heal.nih.gov/research/research-to-practice/enhancing-clinical-trials-network>

<sup>166</sup> <https://heal.nih.gov/research/medication-options/focusing-development>

<sup>167</sup> <https://heal.nih.gov/research/research-to-practice/healing-communities>

- Determining ways to improve the effectiveness and adoption of interventions within justice systems. (The Justice Community Opioid Innovation Network)<sup>168</sup>
- Preventing At-Risk Adolescents Transitioning into Adulthood from Developing Opioid Use Disorder<sup>169</sup>
- Prevention of Progression to Moderate or Severe Opioid Use Disorder<sup>170</sup>
- Optimizing the Duration, Retention, and Discontinuation of Medication Treatment for Opioid Use Disorder<sup>171</sup>
- Studying the effects of environmental factors, including opioids and other substance use, on early brain development from pregnancy through early childhood (HEALthy Brain and Child Development Study)<sup>172</sup>

**National Institute on Drug Abuse**  
**FY 2021 Request: \$1,431.8 million**  
**(\$26.0 million below the FY 2020 Enacted Level)**

NIDA’s efforts consist of Neuroscience and Behavioral Research; Epidemiology, Services and Prevention Research; Therapeutics and Medical Consequences; Clinical Trials Network; High-Tech Biomedical Product Development; Responding to the Opioid Crisis; Intramural Research Program (IRP); and Research Management and Support (RMS). The section entitled “Responding to the Opioid Crisis” details how NIDA is using dollars budgeted to the HEAL Initiative for the purpose of opioid research, but those dollars supplement base funding for opioid and pain research that are included within other NIDA program areas. Funding for both the HEAL initiative and other opioid and pain research will be held flat at the FY 2020 Enacted level within NIDA’s overall FY 2021 request. In addition, FY 2021 funding includes \$50.0 million for research to develop medication-assisted treatment and evidence-based psychosocial treatment to support the strategy to reduce the use of methamphetamines.

**Neuroscience and Behavioral Research**  
**FY 2021 Request: \$456.4 million**  
**(\$10.1 million below the FY 2020 Enacted Level)**

NIDA’s Division of Neuroscience and Behavior (DNB) funds a research portfolio focused on advancing knowledge of the fundamental molecular, genetic/epigenetic, cellular, neurological, pharmacological, cognitive and behavioral processes that underlie SUD and its co-occurring conditions such as HIV. This includes identifying the effects of addictive substances on brain structure and function throughout the lifespan and across stages of drug use and SUD, from first exposure through abstinence, relapse, and recovery. Central to these goals are efforts to delineate the multiple biological (e.g., genes, epigenetic modifications, neural substrates, development) and environmental (e.g., stress, social, childhood adversity) factors that contribute to drug use, physical dependence, and SUD risk. Areas of emphasis include studies to identify genetic variants and epigenetic modifications that influence vulnerability to SUD, the effects of

<sup>168</sup> <https://heal.nih.gov/research/research-to-practice/jcoin>

<sup>169</sup> <https://heal.nih.gov/research/new-strategies/at-risk-adolescents>

<sup>170</sup> <https://heal.nih.gov/research/new-strategies/prevent-progression>

<sup>171</sup> <https://heal.nih.gov/research/new-strategies/duration-retention-discontinuation>

<sup>172</sup> <https://heal.nih.gov/research/infants-and-children/healthy-brain>

addictive substances on gene expression and brain development and function; the interaction of genes with environmental conditions, such as stress and early exposure to drugs that influence risk for SUD; and basic processes underlying resilience against SUD. DNB supports research to elucidate the pharmacology of drugs with respect to their molecular interactions with receptors, ion channels and other proteins and intracellular signaling pathways and to leverage this knowledge towards the development of therapeutics to treat SUD, the adverse consequences of addictive substances, and pain. The DNB portfolio also includes research on non-pharmacological SUD treatments including transcranial magnetic stimulation, transcranial direct current stimulation, deep brain stimulation, and neurofeedback. DNB funds technology development that enables studies of the functional organization of the living brain—from cells to networks. This includes the interactions of complex neural circuits, the encoding of reward, craving, compulsive behavior, decision-making that may drive substance use, as well as the aversive responses to drugs that can inhibit drug-seeking. Advanced computational approaches, including theoretical modeling and novel methods for analyzing large, diverse data sets that enable the integration and simultaneous analysis of experimental data to better understand the neurobiological and behavioral consequences of drug use and SUD, are supported by DNB. Finally, DNB supports mechanistic research towards addressing real-world challenges faced in clinical care of SUD, such as polysubstance use and comorbid psychiatric disorders. Spanning these areas of interest is research into how sex/gender and individual differences affect the SUD trajectory, including risk, resilience, and recovery and the basic neurobiology underlying SUD. Collectively, the research supported by DNB shapes perspectives on the effects of drugs on multiple biological systems and advances knowledge of the basic biological mechanisms that underlie drug use, thus guiding the development of novel prevention strategies and therapies for SUD.

NIDA's portfolio also includes basic research to understand trajectories of substance use and its effects across the lifespan, funded by the Division of Extramural Research. Under the Collaborative Research on Addiction at the NIH (CRAN) partnership, NIDA, NIAAA, and the National Cancer Institute, along with other components of the NIH and the Centers for Disease Control and Prevention (CDC), are supporting a longitudinal study to examine how substance use affects neural development and identify factors that make adolescents vulnerable to SUD. The Adolescent Brain Cognitive Development (ABCD) study will follow the development of more than 10,000 children over 10 years beginning at ages 9-10. Scientists will use techniques including advanced brain imaging, interviews, and behavioral testing to determine how childhood experiences interact with each other and with a child's changing biology to affect brain development and—ultimately—social, behavioral, academic, and health outcomes, including substance use and SUD. The ABCD study has enrolled 11,878 participants, meeting its recruitment target. Data on the first roughly 4,500 participants were released to the scientific community in February 2018; a comprehensive baseline dataset was released in April 2019.

**Epidemiology, Services, and Prevention Research**

***FY 2021 Request: \$326.2 million***

**(\$7.3 million below the FY 2020 Enacted Level)**

NIDA's Division of Epidemiology, Services, and Prevention Research (DESPR or the Division) supports integrated approaches to understanding and addressing the interactions between

individuals and environments that contribute to drug use, addiction, and related health problems. Through Monitoring the Future and other studies, DESPR is also monitoring trends in vaping and e-cigarette use, and the potential risks and health outcomes related to these behaviors. DESPR also supports research on integrating prevention and treatment services into healthcare and community systems to reduce the burden of drug problems across the lifespan. For example, ongoing research is exploring SUD treatment in the justice system, including studies on implementation of medications for opioid use disorder and strategies for finding and screening people with SUD who are also at risk for HIV, as well as strategies for retaining them in treatment. NIDA also funds research into the efficacy of screening, brief intervention, and referral to treatment in primary care settings for reducing drug use and SUD. Other program efforts focus on research to optimize implementation of evidence-based prevention interventions and treatment services in real-world settings. For instance, NIDA is funding researchers to partner with states as they use the State Targeted Response funding provided to the Substance Abuse and Mental Health Services Administration (SAMHSA) in the 21st Century Cures Act to test approaches for expanding access to MOUD and naloxone for the reversal of overdose.

NIDA partnered with the Appalachian Regional Commission, the CDC, and SAMHSA to issue nine grants to help communities develop comprehensive approaches to prevent and treat consequences of opioid injection, including SUD, overdose, HIV, hepatitis B and C viral infections, as well as sexually transmitted infections. Funded in FY 2017, these projects work with state and local communities to develop best practice responses that can be implemented by public health systems in the nation's rural regions.

### **Therapeutics and Medical Consequences**

***FY 2021 Request: \$134.8 million***

**(\$3.0 million below the FY 2020 Enacted Level)**

NIDA's Division of Therapeutics and Medical Consequences (DTMC) supports preclinical and clinical research focused on developing treatments for SUD. Since the pharmaceutical industry has traditionally made limited investments in this area, the responsibility for supporting the development of therapeutics has rested largely with NIDA. To most effectively leverage NIDA resources, DTMC encourages the formation of partnerships among pharmaceutical and biotechnology companies, academic institutions, and other stakeholders with the common goal of expeditiously advancing new and repurposed compounds through the medications development pipeline toward FDA approval. For example, in collaboration with US WorldMeds, DTMC supported clinical trials on LUCEMYRA™, the first medication targeted specifically to treat the physical symptoms associated with opioid withdrawal. Having been shown to be safe and effective at managing withdrawal in patients discontinuing opioid use under medical supervision, LUCEMYRA™ was approved by the FDA in May 2018. NIDA also supports research to reduce the medical risks of compounds and to make them more feasible for pharmaceutical companies to complete costly phase IIb and III clinical studies for SUD indications.

**Clinical Trials Network*****FY 2021 Request: \$40.1 million*****(\$0.9 million below the FY 2020 Enacted Level)**

The overarching mission of the NIDA Clinical Trials Network (CTN) is to allow medical and specialty treatment providers, treatment researchers, patients, and NIDA to cooperatively develop, validate, refine, and deliver new treatment options to patients. The CTN comprises: 18 research nodes with 34 principal investigators affiliated with academic medical centers and large health care networks; 2 research coordinating centers; and more than 240 community-anchored treatment programs and/or medical settings in over 40 States plus the District of Columbia and Puerto Rico. This unique partnership enables the CTN to conduct studies of behavioral, pharmacological, and integrated treatment interventions in rigorous, multisite clinical trials to determine effectiveness across a broad range of settings and patient populations. It also allows the CTN to ensure the transfer of research results to physicians, clinicians, providers, and patients. The network evaluates interventions, implementation strategies, and health system approaches to addressing SUD and related disorders, such as co-occurring mental health disorders and HIV.

The CTN is conducting studies to evaluate strategies for integrating OUD screening and treatment into emergency departments, pharmacies, primary care clinics, and American Indian/Alaska Native communities. It has also supported studies to capture important data for research on SUD in electronic health record (EHR) systems in primary care and emergency departments. The CTN is currently developing and testing a clinical decision support tool that integrates with EHR systems to help doctors diagnose OUD and either provide treatment or refer patients to appropriate treatment. Additional studies are investigating the effectiveness and safety of a combination pharmacotherapy for treatment of methamphetamine use disorder, assessing the effectiveness of OUD treatments for HIV-positive individuals with OUD, and improving the ability of healthcare providers to detect and address cocaine use using smartwatch technology. The CTN is also developing studies to examine the effects of medications for OUD in pregnant women and the effects of medical cannabis use using EHR data.

**High-Tech Biomedical Product Development*****FY 2021 Request: \$38.3 million*****(\$0.9 million below the FY 2020 Enacted Level)**

NIDA's Office of Translational Initiatives and Program Innovations (OTIPI) takes research discoveries in prevention, detection, and treatment of SUD into candidate health applications for commercialization. Addiction (moderate to severe SUD) represents an underserved market, and OTIPI works to support early-stage commercialization of products in this area. OTIPI manages NIDA's Small Business Innovation Research/Small Business Technology Transfer (SBIR/STTR) Programs, utilizing novel fit-for-purpose funding authorities such as Prizes and Open Competitions, and establishing teaching programs that equip scientists with the competence to translate advances in addiction research into tangible solutions that our society needs.

Many of these efforts take the form of innovative new technology applications, from mobile apps that help patients find open beds in addiction treatment facilities or connect to support communities, to more sophisticated medical devices. Among OTIPI-funded technologies are: hospital bassinets delivering calming signals to infants with neonatal abstinence syndrome; alarms for detecting the early signs of a drug overdose; and virtual reality systems to manage pain and reduce opioid analgesic use.

### **Responding to the Opioid Crisis**

***FY 2021 Request: \$266.3 million***

**(Unchanged from the FY 2020 Enacted Level)**

As part of HEAL, NIDA will continue to expand its support for new research efforts to combat opioid addiction with several major projects which began or ramped up in FY 2019 with continued support into FY 2020 and FY 2021.

NIDA supports research to accelerate the development of novel medications and devices to treat all aspects of the opioid addiction cycle, including progression to chronic use, withdrawal symptoms, craving, relapse, and overdose. This includes developing longer-acting formulations of existing addiction medications to promote adherence to treatment while preventing medication misuse, as well as developing stronger, longer-acting formulations of opioid antagonists (including longer-lasting naloxone formulations and novel compounds) to reverse opioid overdose. The following projects are currently underway:

#### **Enhancing the NIDA Clinical Trials Network to Address Opioids**

To expand NIH research to more communities in areas of the country that are severely impacted by the opioid crisis, NIH is expanding the National Drug Abuse Treatment Clinical Trials Network (CTN). The Network facilitates collaboration between government researchers, scientists at universities, and treatment providers in local communities with the aim of developing, testing, and implementing new addiction treatments. Through its work to date, the Network has contributed to broad-reaching changes in medical practice, including the development of the OUD treatment medication buprenorphine.

#### **Focused Medication Development to Treat Opioid Use Disorder and Prevent/Reverse Overdose**

More flexible treatment options for opioid use disorder (OUD) are needed to promote long-term recovery in more patients. Methadone, buprenorphine, and naltrexone are approved by the FDA to treat OUD, and lofexidine is approved to treat opioid withdrawal, but many people do not receive these medications or take them for only a short time, making it difficult to achieve long-term recovery. Naloxone can effectively reverse opioid overdose, but multiple doses can be required to reverse respiratory arrest caused by drug combinations or powerful synthetic opioids. NIDA is conducting a series of targeted studies with the goal of producing approximately 15 Investigational New Drugs (INDs) and 5 New Drug Applications (NDAs) submitted to the FDA. This project will accelerate the development of novel medications and devices to treat all aspects of the opioid addiction cycle, including progression to chronic use, withdrawal symptoms, craving, relapse, and overdose.

Determining strategies to reduce opioid overdose in communities hardest hit by the opioid crisis (the HEALing Communities Study)

The HEALing Communities Study will generate evidence about how tools for preventing and treating opioid addiction are most effective at the local level. NIH, together with SAMHSA, has launched this multisite implementation research study to test the impact of an integrated set of evidence-based interventions across healthcare, behavioral health, justice, and other community-based settings. The goal is to prevent and treat opioid misuse and opioid use disorder (OUD) within highly affected communities in 4 states and reduce opioid related deaths by 40 percent over 3 years. Each site is partnering with at least 15 communities to measure the impact of these efforts.

The Study will also look at the effectiveness of coordinated systems of care designed to reduce overdose fatalities and events; decrease the incidence of OUD; increase the number of individuals receiving medication to treat OUD, retained in treatment, and receiving post-treatment recovery support services; and increase the distribution of naloxone. The HEALing Communities Study provides funding to four academic institutions, in partnership with local community-based organizations.

Determining ways to improve the effectiveness and adoption of interventions within justice systems. (The Justice Community Opioid Innovation Network)

Many individuals with OUD pass through the criminal justice system over the course of their life. Improved access to high-quality, evidence-based addiction treatment in justice settings will be critical to addressing the opioid crisis. Through the Justice Community Opioid Innovation Network (JCOIN), NIH will study approaches to increase high-quality care for people with opioid misuse and OUD in justice populations. The Network will test strategies to expand effective treatment and care in partnership with local and state justice systems and community-based treatment providers.

Preventing At-Risk Adolescents Transitioning into Adulthood from Developing Opioid Use Disorder

Older adolescents and young adults (ages 16-30) are the group at highest risk for initiation of opioid use, opioid misuse, OUD, and death from overdose. Building on successful research models to prevent alcohol consumption among adolescents and young adults, NIH is supporting a series of studies to identify and test effective prevention strategies targeted to young adults in geographic areas most affected by the opioid crisis. The studies will focus on older adolescents and young adults in a variety of health care settings, including primary care, emergency departments, urgent care, infectious disease clinics, school-based and community college health centers, workplaces, and justice settings.

Prevention of Progression to Moderate or Severe Opioid Use Disorder

There are currently multiple evidence-based strategies for the treatment of OUD. And yet, OUD develops over time, beginning with opioid use and misuse below the threshold for the clinical diagnosis for OUD. Historically, low severity opioid misuse, especially in the context of co-occurring pain and psychiatric disorders, has been poorly identified in clinical settings. To understand how to prevent the transition from opioid misuse to more severe opioid use disorder,

NIH will develop and test effective intervention strategies for persons with low severity opioid misuse, including patients with pain.

This study will recruit individuals with sub-threshold and low-severity opioid use disorder in general medical settings such as primary or integrated care settings to define, identify, and intervene in the management of opioid misuse. The study will test a model including (1) a practice-embedded nurse care manager who provides patient education and supports the primary care provider (PCP) in engaging and monitoring patients who have unhealthy opioid use; (2) brief advice delivered to patients by their PCP; and (3) counseling of patients by health coaches and mental health providers to motivate and support behavior change.

#### Optimizing the Duration, Retention, and Discontinuation of Medication Treatment for Opioid Use Disorder

Effective medications for treating OUD exist; patients have better outcomes with longer periods of treatment, and risk of relapse increases when patients stop taking medication. Better strategies are needed to retain patients in treatment, and little is known about when it may be safe to discontinue medications. This study will test strategies to improve retention in medication-based treatment for OUD as well as strategies to improve outcomes among patients who have been stabilized on OUD medications and want to stop taking medication. The research will also identify patient characteristics associated with relapse after discontinuation and develop a predictive risk model for relapse.

#### Studying the effects of environmental factors, including opioids and other substance use, on early brain development from pregnancy through early childhood (HEALthy Brain and Child Development Study) (<https://heal.nih.gov/research/infants-and-children/healthy-brain>)

The first few years of life is a period of exponential brain growth and development. It is not currently known how infant and childhood development is affected by early exposure to opioids. To address this question, NIH is working to better understand typical brain development, beginning in the prenatal period through early childhood, including variability in development and how it contributes to cognitive, behavioral, social, and emotional function. Knowledge of normative brain trajectories is critical to understanding how brain development may be affected by exposure to opioids and other substances (e.g., alcohol, tobacco, cannabis), stressors, trauma and other significant environmental influences.

The HEALthy Brain and Child Development (HBCD) Study will establish a large cohort of pregnant women from regions of the country significantly affected by the opioid crisis, and follow them and their children for at least 10 years. Research from this cohort will help researchers understand normative childhood brain development as well as the long-term impact of pre- and postnatal opioid and other drug and adverse environmental exposures. The study will collect data on pregnancy and fetal measures; infant and early childhood structural and functional brain imaging; anthropometrics; medical history; family history; biospecimens; and data on social, emotional, and cognitive development. This knowledge will be critical to help predict and prevent some of the known impacts of pre- and postnatal exposure to certain drugs or adverse environments, including risk for future substance use, mental disorders, and other behavioral and developmental problems.

**Intramural Research Program*****FY 2021 Request: \$98.0 million*****(\$2.2 million below the FY 2020 Enacted Level)**

In addition to funding extramural scientists, NIDA conducts research in high priority areas through its Intramural Research Program (IRP). The IRP conducts multidisciplinary cutting-edge research to: 1) elucidate the mechanisms underlying the development of SUD; 2) evaluate potential new therapies for SUD, including pharmacological and non-pharmacological interventions (e.g., psychosocial, neurofeedback, brain stimulation technologies, mobile health tools); and 3) identify and pharmacologically characterize emerging designer drugs such as synthetic opioids, stimulants, and cannabinoids, providing data-based evidence to the public on the dangers of these drugs.

One example of treatment evaluation at the IRP is a bench-to-bedside project in which IRP investigators are testing a novel compound to treat OUD. The compound activates the same receptors as traditional opioids, but has only a subset of their cellular actions. IRP investigators are testing whether the compound reduces self-administration of opioids in a variety of animal models and, in parallel studies in people with OUD, whether it prevents opioid withdrawal with fewer side effects than treatment drugs in current use. If trials prove successful, this compound could be a new medication for OUD.

The IRP is also working with the National Center for Advancing Translational Sciences on a dopamine D3 receptor antagonist that could be taken together with opioid pain relievers to reduce the chance of developing OUD. Preliminary animal studies have suggested that the compound reduces opioid self-administration and drug-seeking behavior without reducing the pain-relieving effects of opioids. This compound holds promise as an adjunct to opioid treatment for pain, and evidence suggests it could also be useful as a treatment for OUD.

Non-pharmacological addiction treatments are also being developed at NIDA. Research at the IRP's on-site treatment-research clinic includes efforts to develop a smartphone app that detects or predicts stress, craving, and drug use via machine learning, on a time scale of hours—and a parallel project to develop the content that the app should deliver in a “just in time” fashion. Currently marketed apps purporting to serve these functions do not meet scientific standards of evidence for either their content or their risk-detection methods. The IRP is addressing that major gap in mobile health. Using passive measurement and digital phenotyping techniques, the IRP is also developing interventions and big data methodologies to prevent HIV transmission associated with high-risk sexual behavior in the context of substance use.

**Research Management and Support*****FY 2021 Request: \$71.5 million*****(\$1.6 million below the FY 2020 Enacted Level)**

Research Management and Support (RMS) activities provide administrative, budgetary, logistical, and scientific support in the review, award, and monitoring of research grants, training awards, and research and development contracts. Additionally, the functions of RMS encompass strategic planning, coordination, and evaluation of NIDA's programs, regulatory compliance,

international coordination, and liaison with other Federal agencies, Congress, and the public. RMS staff at NIDA play leadership roles in helping to coordinate NIDA's involvement in the NIH HEAL Initiative, spearheading NIH's response to the opioid overdose epidemic. In addition to the infrastructure required to support research and training, NIDA strives to provide evidence-based resources and educational materials about substance use and addiction, including information about timely public health topics such as opioid overdose prevention, marijuana research, use and consequences of vaping, synthetic drug trends, and medications for treatment of SUD including OUD.

The RMS portfolio also incorporates education and outreach activities to inform public health policy and practice by ensuring that NIDA is the primary trusted source for scientific information on drug use and addiction. Staff supported by NIDA's RMS budget coordinate key activities that help to train the next generation of scientists and clinicians in the science of addiction and evidence-based approaches to treatment and prevention. In addition, NIDA's RMS portfolio includes the NIDAMED initiative, which is aimed at engaging and educating clinicians in training and in practice in the latest science related to drug use and addiction.

### **National Institute on Alcohol Abuse and Alcoholism**

***FY 2021 Request: \$54.5 million***

**(\$5.4 million below the FY 2020 Enacted Level)**

NIAAA's underage drinking portfolio includes studies to develop, evaluate, and implement evidence-based prevention programs for underage and college drinking. These include individual-, family-, school-, community-, and environmental-level interventions for underage individuals at large, as well as those designed or adapted for specific populations and settings. The college environment remains a high priority target for reducing underage drinking. NIAAA developed the College Alcohol Intervention Matrix (CollegeAIM) to assist college and university officials in addressing alcohol misuse on their campuses. CollegeAIM is a user-friendly guide and website that rates nearly 60 evidence-based alcohol interventions in terms of effectiveness, cost, and other factors, allowing school officials to select among the many potential interventions to address harmful and underage student drinking.

Although the prevalence of alcohol use among 8th, 10th, and 12th graders has declined by one-third over the past decade, alcohol remains the most widely used substance among U.S. youth. Binge drinking<sup>173</sup> and high intensity drinking (i.e., two or more times the gender-specific binge drinking thresholds) among young people remain significant concerns; these practices are particularly troubling as they increase risks for poor academic performance, alcohol-related blackouts, injuries, overdoses, sexual assault, unsafe sexual behavior, AUD, and other detrimental consequences. NIAAA recently convened an expert panel to better understand the biological and social determinants of high-intensity drinking to inform NIAAA efforts in moving this area of research forward.

NIAAA also supports research on the implementation of alcohol screening and brief intervention among youth and young adult populations in health care and other appropriate settings. Alcohol

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<sup>173</sup> NIAAA defines binge drinking as a pattern of drinking that increases an individual's blood alcohol concentration to 0.08 percent or higher. This typically occurs after 4 drinks for women and 5 drinks for men – in about 2 hours.

screening and brief intervention in primary care has been recognized as a leading preventive service for reducing harmful alcohol use in adults, and a growing body of evidence demonstrates its effectiveness in preventing and reducing alcohol misuse in youth. However, adolescents are not routinely asked about drinking when they interface with the health care system. To facilitate the integration of this practice into primary care, NIAAA developed a youth alcohol screening tool to enable pediatric and adolescent health practitioners to identify patients who may benefit from intervention. This screening tool has been validated among youth in pediatric emergency room settings, in school settings, in primary care settings with racially and ethnically diverse youth, and among youth with chronic health conditions.

Basic research is key to informing the development of innovative prevention and treatment strategies for underage drinking. NIAAA funds collaborative research to assess the impact of adolescent drinking on brain development. For example, the National Consortium on Alcohol and Neurodevelopment in Adolescence (NCANDA), a longitudinal study of approximately 800 youth ages 12-21, was designed to identify brain characteristics that may predict alcohol-misuse and to elucidate the neurodevelopmental effects that occur as a consequence of alcohol exposure. NCANDA researchers have demonstrated that youth with a history of alcohol use exhibit weakened connections between brain networks involved in the regulation of emotional and cognitive functioning. NCANDA laid the methodological foundation for NIH's Adolescent Brain Cognitive Development (ABCD) study, the largest longitudinal study of brain development and child health in the United States. Complementing NCANDA and ABCD, NIAAA's Neurobiology of Adolescent Drinking In Adulthood (NADIA) consortium enables investigators to examine, using animal models, the mechanisms by which adolescent drinking leads to changes in brain structure and function that persist into adulthood. Recent preclinical research conducted through NADIA elucidated a link between adolescent alcohol exposure and specific molecular changes in the brain that contribute to increased anxiety in adulthood.

## PERFORMANCE

Information regarding the performance of the drug control efforts of NIH is based on agency documents related to the Government Performance and Results Modernization Act and other information that measures the agency's contribution to the *Strategy*. NIH's performance measures are representative of Institute contributions to NIH's priorities regarding specific scientific opportunities, identified public health needs, and Presidential priorities. Such measures, reflecting NIH's broad and balanced research portfolio, are not Institute-specific. Many measures are trans-NIH, encompassing lead and contributing Institutes and Centers. This approach reflects NIH's commitment to supporting the best possible research and coordination of research efforts across its Institutes and Centers.

NIDA and NIAAA lead and support a number of trans-NIH measures in the Scientific Research Outcome (SRO) functional area. While NIDA and NIAAA engage in many research and related activities, four measures best reflect the breadth of their efforts in the prevention and treatment of substance use, misuse, addiction, and its consequences.

One of these measures, led by NIAAA and supported by NIDA, is SRO-5.15: "By 2025, develop, refine and evaluate evidence-based intervention strategies and promote their use to prevent substance misuse and substance use disorders and their consequences in underage populations." This measure, which began in FY 2014, is indicative of NIAAA's and NIDA's efforts to support research to foster the development and implementation of prevention-based strategies for reducing substance misuse and addiction. NIH's prevention portfolio encompasses a broad range of research on the efficacy and cost effectiveness of primary prevention programs—designed to prevent substance use before it starts, or prevent escalation to misuse or addiction—and how these programs can be enhanced by targeting prevention efforts toward populations with specific vulnerabilities (genetic, psychosocial, or environmental) that affect their likelihood of substance use or SUDs.

NIDA created and leads SRO-4.9: "By 2020, evaluate the efficacy of new or refined interventions to treat opioid use disorders (OUD)." This measure began in FY 2018, and reflects NIDA's increasing focus on finding solutions to the current crisis of opioid overdose and addiction. As part of the NIH HEAL Initiative, NIDA has been supporting a variety of focused medications development research at varying stages of the clinical pipeline.

In addition to developing and leading SRO-5.15, NIAAA created SRO-4.15: "By 2021, evaluate three interventions for facilitating treatment of alcohol misuse in underage populations." This measure began in FY 2019 and reflects NIH's ongoing commitment to research on the development of interventions to improve treatment of alcohol-related problems among youth.

<b>National Institute on Drug Abuse</b>		
<b>Selected Measures of Performance</b>	<b>FY 2019 Target</b>	<b>FY 2019 Achieved</b>
Scientific Research Outcome-5.15: By 2025, develop, refine and evaluate evidence-based intervention strategies and promote their use to prevent substance misuse and substance use disorders and their consequences in underage populations.	Develop, adapt or tailor at least one intervention or strategy to prevent prescription drug misuse and/or OUD in older adolescent and young adult populations.	NIDA supported at least three projects focused on developing, tailoring and/or adapting interventions to prevent prescription drug misuse and/or OUD in older adolescent and young adult populations.
Scientific Research Outcome-4.9: By 2020, evaluate the efficacy of new or refined interventions to treat opioid use disorders (OUD).	Conduct 1 pre-clinical study and 1 clinical trial to develop non-opioid based medications to treat OUD that may avoid the risks of opioid dependence and overdose.	A pre-clinical study of a novel opiate withdrawal therapy was conducted, and a clinical trial of a therapy for both opioid withdrawal and associated insomnia was also conducted.

### **Prevention – Scientific Research Outcome-5.15**

The FY 2019 target was met. In FY 2019 NIDA supported at least three projects focused on developing, tailoring and/or adapting interventions to prevent prescription drug misuse and/or OUD in older adolescent and young adult populations.

NIDA supported a project<sup>174</sup> which intervenes at the level of the patient, aiming to improve opioid risk understanding and analgesic decision-making and to enhance analgesic self-efficacy, analgesic use, storage behaviors and pain outcome. The project tests the effectiveness of targeting parents of children who have been prescribed opioids for acute pain with new strategies to help parents learn about opioid risks, make safe and effective analgesic decisions, and develop and demonstrate safe drug management behaviors.

NIDA also supported two projects that are examining interventions at the level of the provider testing strategies to change prescribing behavior. One project<sup>175</sup> focuses on a behavioral intervention for providers that alters the default settings for prescribing opioids to children and young adults after common childhood surgical procedures like tonsillectomy. Another study<sup>176</sup> seeks to reduce the number of opioids prescribed after caesarian section, in order to reduce the prescription of unused opioids and reduce the potential for friends and family members to obtain and misuse such opioids.

<sup>174</sup> “Scenario tailored opioid messaging program: An interactive intervention to prevent analgesic-related adverse drug events in children and adolescents”, R01-[DA044245](#)

<sup>175</sup> “Using default opioid prescription settings to limit excessive opioid prescribing to adolescents and young adults” [K08DA048110](#)

<sup>176</sup> “Reducing unused prescribed opioids after Cesarean Birth” [K23DA047476](#)

While it is too early for these studies to have produced published findings, each represents a NIDA’s commitment to finding novel approaches to prevent opioid misuse prevention.

**Treatment – Scientific Research Outcome-4.9**

The FY 2019 target was met. In FY 2019, NIDA funded the preclinical development of ITI-333. This is a novel compound with high affinity activity at mu opioid (MOP), 5-HT2A, and D1 receptors. The pre-clinical profile of ITI-333 suggests a promising medication, lacking addiction liability, for treatment of opioid withdrawal in individuals with OUD. ITI is currently completing Investigational New Drug (IND)-enabling nonclinical safety, toxicology, pharmacokinetic and manufacturing activities to start studies in humans (clinical trials).

NIDA also funded a clinical trial to evaluate the safety and efficacy of suvorexant for treatment of insomnia and opioid withdrawal in patients with OUDs. Suvorexant is an orexin-1 antagonist that is approved by the FDA for treatment of insomnia because it improves sleep architecture without producing drug dependence. In addition, the orexin system has been involved in the pathophysiology of OUD. Therefore, suvorexant is promising medication to treat the sleep problems of OUD and OUD itself.

<b>National Institute on Alcohol Abuse and Alcoholism</b>		
<b>Selected Measures of Performance</b>	<b>FY 2019 Target</b>	<b>FY 2019 Achieved</b>
<b>Scientific Research Outcome 5.15: By 2025, develop, refine and evaluate evidence-based intervention strategies and promote their use to prevent substance misuse and SUDs and their consequences in underage populations.</b>	Develop an intervention to prevent or reduce alcohol misuse among college age individuals.	Researchers demonstrated the efficacy of interventions involving brief motivational interviewing and a supplemental activity for reducing alcohol misuse among college age individuals.
<b>Scientific Research Outcome 4.15: By 2021, evaluate three interventions for facilitating treatment of alcohol misuse in underage populations.</b>	Test a screening and brief alcohol intervention in an underage population.	Researchers tested NIAAA’s Alcohol Screening and Brief Intervention for Youth: A Practitioner's Guide’s two-question screening tool to determine its predictive ability in identifying future risk for alcohol-related problems in an underage population.

**Prevention – Scientific Research Outcome-5.15**

The FY 2019 target was met. Brief Motivational Interviewing (BMI) is a cost-effective preventive intervention for alcohol misuse that involves providing individualized feedback on drinking behavior and associated risks. Feedback may include goal-setting strategies for cutting back on drinking or reducing risks of harm. Although BMI is considered an effective

intervention for college-age populations, the magnitude of the effect is typically moderate or small. For this reason, researchers have studied the utility of adding additional intervention elements to enhance the effects of BMI on reducing alcohol consumption and resulting harms among college students. NIAAA-supported researchers conducted a two-site randomized controlled clinical trial in a college student population to evaluate BMI efficacy when supplemented by a substance-free activity session or relaxation training session. Outcomes were evaluated up to 16 months after the intervention. Compared to the control condition, BMI combined with either an activity session or relaxation training was associated with reductions in alcohol use and related problems across the 16-month follow-up period. The combined approach resulted in effects greater in magnitude when compared to previous reports of BMI alone. The same research group conducted an analysis of existing data from three randomized controlled trials specifically to examine the effects of BMI with a supplemental intervention on alcohol-induced blackouts in college-age individuals. Their analyses indicated that, compared to a control group, participants who received BMI in conjunction with either a substance-free activity session or relaxation training were less likely to report a blackout up to six months later. Together, these two studies demonstrate the efficacy of BMI supplemented with an additional intervention session for reducing alcohol misuse and related problems, including alcohol-induced blackouts, and suggest that supplemental activities enhance the impact of BMI effects.

#### **Treatment – Scientific Research Outcome-4.15**

The FY 2019 target was met. Several studies have demonstrated the utility of NIAAA's youth alcohol screening guide in identifying youth who are at current risk for alcohol-related problems, but no studies had been performed to test whether it can predict risk for future alcohol problems. A multi-site study conducted at 16 pediatric emergency departments by NIAAA-supported researchers evaluated the two-question screening tool's predictive validity for future alcohol use disorder (AUD). They found that the two-question screening tool has acceptable predictive validity with respect to risk for AUD at one, two, and three years after the initial screening. These findings demonstrate that the youth screening guide is effective for identifying current and future risk for alcohol-related problems in youth.

Additionally, in a recent NIAAA-supported study, researchers examined the effects of screening, brief intervention, and referral to treatment (SBIRT) delivered in pediatric primary care settings on health care use and health outcomes over time. The investigators used electronic health data from a randomized clinical trial of adolescents aged 12-18 years that compared SBIRT delivered either by a pediatrician or behavioral health clinician to usual care. They found that patients who received SBIRT had fewer medical and mental health comorbidities, fewer psychiatry visits after one year, and fewer substance use diagnoses, as well as lower outpatient use over three years. These findings suggest that providing SBIRT in primary care may reduce health care use and improve adolescent health.