

DRUG CONTROL PROGRAMS

RESOURCE SUMMARY

	Budget Authority ¹ (in millions)		
	FY 2020 Final	FY 2021 Enacted	FY 2022 Request
Drug Resources by Function			
Research and Development: Prevention	\$488.462	\$496.004	\$609.092
Research and Development: Treatment	\$1,029.853	\$1,045.804	\$1,306.604
Total, Drug Resources by Function	\$1,518.315	\$1,541.808	\$1,915.696
Drug Resources by Decision Unit			
<i>National Institute on Alcohol Abuse and Alcoholism (NIAAA)</i>			
Research and Development: Prevention	\$51.145	\$51.911	\$53.341
Research and Development: Treatment	\$9.446	\$9.588	\$9.852
<i>National Institute on Drug Abuse (NIDA)</i>			
Research and Development: Prevention	\$437.317	\$444.093	\$555.751
Research and Development: Treatment	\$1,020.407	\$1,036.216	\$1,296.752
Total, Drug Resources by Decision Unit	\$1,518.315	\$1,541.808	\$1,915.696
Drug Resources Personnel Summary			
Total FTEs (direct only)	363	388	388
Drug Resources as a Percent of Budget			
Total Agency Discretionary Budget (in Billions)	\$40.3	\$41.5	\$50.5
Drug Resources percentage	3.77%	3.72%	3.79%

¹Reflects regular appropriations for NIH drug control programs. These programs did not receive supplemental funding in FY 2020 or FY 2021.

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 is the lead federal agency supporting scientific research on drug use and its consequences. Its mission is to advance science on drug use and addiction and apply that knowledge to improve individual and public health. This includes basic and clinical research on drug use (including nicotine), addiction, and the underlying neurobiological, behavioral, and social mechanisms involved. NIDA also works to ensure the effective translation, implementation, and dissemination of scientific research findings to improve the prevention and treatment of substance use disorder (SUD) and to enhance public awareness of addiction as a brain disorder. While NIDA's mission broadly encompasses substance use, addressing opioid misuse and addiction is a top priority at NIDA.

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 SUD cost the U.S. more than \$740 billion a year in healthcare, crime, and lost productivity;²⁶¹ 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 2019, more than 20 million Americans had SUD,²⁶² and drug overdose claimed more than 71,000 lives, about 70% of which were from illicit or prescription opioids.²⁶³ For every fatal overdose it is estimated that there are 10 non-fatal overdoses and 20 opioid-related hospitalizations.²⁶⁴

The collision of the overdose crisis with the coronavirus disease 2019 (COVID-19) pandemic puts people with SUD at particular risk. Early data show increases in drug use and overdose since the pandemic began,²⁶⁵ and the highest number of overdose deaths (over 90,000) ever recorded occurred in the 12 months ending in September 2020.²⁶⁶ Individuals with SUD, especially Blacks/African Americans and those with opioid use disorder (OUD), are at higher risk for COVID-19 and its adverse outcomes.²⁶⁷

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 accomplish this goal. 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 identify, 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 alcohol misuse and AUD and have provided support for the integration of 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.

²⁶¹ www.drugabuse.gov/related-topics/trends-statistics

²⁶² 2018 National Survey on Drug Use and Health, 2019. SAMHSA

²⁶³ www.cdc.gov/drugoverdose/index.html#:~:text=The%20number%20of%20drug%20overdose

²⁶⁴ Rudd, R. et al. MMWR Morb. Mortal. Wkly. Rep. 65, 1445-1452, (2016).

²⁶⁵ emergency.cdc.gov/han/2020/han00438.asp

²⁶⁶ www.cdc.gov/nchs/nvss/vsrr/drug-overdose-data.htm

²⁶⁷ pubmed.ncbi.nlm.nih.gov/32929211/

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 2022 Request for drug-related activities at NIH is \$1,915.7 million (\$1,852.5 million for NIDA and \$63.2 million for NIAAA), a 24.2 percent increase compared with the FY 2021 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, 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 studying 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 Opioids²⁶⁸
- Focused Medication Development to Treat Opioid Use Disorder and Prevent/Reverse Overdose²⁶⁹
- Determining strategies to reduce opioid overdose in communities hardest hit by the opioid crisis (the HEALing Communities Study)²⁷⁰

²⁶⁸ heal.nih.gov/research/research-to-practice/enhancing-clinical-trials-network

²⁶⁹ heal.nih.gov/research/medication-options/focusing-development

²⁷⁰ 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)²⁷¹
- Preventing At-Risk Adolescents Transitioning into Adulthood from Developing Opioid Use Disorder²⁷²
- Prevention of Progression to Moderate or Severe Opioid Use Disorder ²⁷³
- Optimizing the Duration, Retention, and Discontinuation of Medication Treatment for Opioid Use Disorder²⁷⁴
- 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)²⁷⁵

Stimulants have also emerged as an overdose threat. From 2012 through 2019, the number of deaths involving methamphetamine increased more than 6-fold (from around 2,600 to more than 16,100), and the number involving cocaine more than tripled (from around 4,400 to nearly 16,000).²⁷⁶ Given the urgent need to confront these dramatic increases, NIDA has prioritized the development of medications to treat stimulant use disorders.

National Institute on Drug Abuse
FY 2022 Request: \$1,852.5 million
(\$372.2 million above the FY 2021 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 increased from the FY 2021 Enacted level within NIDA's overall FY 2022 Request.

Neuroscience and Behavioral Research
FY 2022 Request: \$603.8 million
(\$111.0 million above the FY 2021 Enacted Level)

NIDA's Division of Neuroscience and Behavior (DNB) advances knowledge of the basic biological mechanisms that underlie drug use and guide the development of novel prevention strategies and treatments for SUD. This includes identifying the effects of illicit substances on brain structure and function throughout the lifespan and across stages of drug use and SUD.

²⁷¹ heal.nih.gov/research/research-to-practice/jcoin

²⁷² heal.nih.gov/research/new-strategies/at-risk-adolescents

²⁷³ heal.nih.gov/research/new-strategies/prevent-progression

²⁷⁴ heal.nih.gov/research/new-strategies/duration-retention-discontinuation

²⁷⁵ heal.nih.gov/research/in-fants-and-children/healthy-brain

²⁷⁶ www.cdc.gov/nchs/nvss/vsrr/drug-overdose-data.htm

Areas of support include studies to identify genetic variants and epigenetic modifications that influence vulnerability to SUD, the effects of drugs on gene expression and brain development and function; the interaction of genes with environmental conditions, including how they influence brain development; and basic processes underlying vulnerability and resilience to SUD. DNB supports research to elucidate the pharmacology of drugs and to leverage this knowledge towards the development of therapeutics to treat SUD, the adverse consequences of illicit drugs, and pain. One recent DNB-supported study found that prenatal exposure to cannabinoids altered the ways the brains of male, but not female, adolescent rats respond to cannabis, and identified a drug that could normalize those responses.²⁷⁷ The DNB portfolio also includes research on non-pharmacological SUD treatments including transcranial magnetic stimulation, transcranial direct current stimulation, deep brain stimulation, and neurofeedback. Research on the interactions of complex neural circuits that underlie substance use, aversive responses to drugs that can inhibit drug-seeking, and interactions between neural and non-neuronal cells in these circuits is also supported in this portfolio. DNB funds technology development that enables studies of the functional organization of the living brain from cells to circuits to networks, and advanced computational approaches including theoretical modeling and novel methods for analyzing large, diverse data sets. One recent study found that activity in two different brain regions is linked with nicotine addiction severity and nicotine withdrawal, which is of particular interest because current smoking cessation treatments only affect one of those areas.²⁷⁸ Such studies can help inform the creation of new and improved treatments with basic data on neural circuits. Finally, DNB supports mechanistic research to address real-world challenges faced in clinical care of SUD, such as polysubstance use, co-occurring conditions, and sex and gender differences in the development of SUDs.

One of NIDA's flagship basic science projects is the Adolescent Brain Cognitive Development (ABCD) study, which will follow children over 10 years, beginning at ages 9-10. Scientists are using techniques such as advanced brain imaging, interviews, and behavioral testing to determine how childhood experiences interact to affect brain development and—ultimately—social, behavioral, academic, and health outcomes, including substance use. Understanding how drugs interact with individual genetic, neurobiological, environmental, social, and developmental factors is essential to understanding what puts a person at risk for or confers resilience to addiction. Enrollment is complete with a total of 11,878 youth and their families participating. The study has already released baseline and one-year follow-up data from the full cohort, and more than 70 research papers have been published using these data, leading to a better understanding of the association between certain traits and experiences and brain structure and function, cognitive ability, and mental health. For example, a recent study has found that certain measures of obesity correlate with measurements of the density of an area of the brain responsible for motivation and reward, suggesting a possible neural mechanism for behavioral changes that lead to obesity.²⁷⁹

²⁷⁷ pubmed.ncbi.nlm.nih.gov/31611707/

²⁷⁸ europepmc.org/article/med/22493758

²⁷⁹ pubmed.ncbi.nlm.nih.gov/31816020/

Epidemiology, Services, and Prevention Research
FY 2022 Request: \$418.0 million
(\$76.9 million above the FY 2021 Enacted Level)

NIDA's Division of Epidemiology, Services, and Prevention Research (DESPR) 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, the Population Assessment of Tobacco and Health study, and other studies, DESPR monitors trends in drug use, including marijuana, vaping/e-cigarettes, and other drugs, as well as the potential risks and health outcomes related to these behaviors.

Preventing the initiation of substance use to minimize risks of harmful consequences is an essential part of addressing SUD. To this end, DESPR funds a portfolio of prevention research to understand and intervene upon mechanisms that underlie risk for and resilience to addiction and common comorbidities. This includes studies on how biological, psychosocial, and environmental factors operate to enhance or mitigate an individual's propensity to initiate substance use or to escalate from use to misuse to SUD across different developmental stages. This information, along with rapidly growing knowledge about substance use and addiction, is helping to inform the development of evidence-based prevention strategies.

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 examining efforts to implement evidence-based SUD treatment in jails and prisons, expand the use of effective medications for OUD in primary care settings, develop strategies to reduce transmission of viral infections related to substance use (e.g., HIV and Hepatitis C), and increase uptake and retention in treatment for SUD and HIV. DESPR also funds research into the efficacy of screening, brief intervention, and referral to treatment in primary care settings for reducing drug use and SUD.

Therapeutics and Medical Consequences
FY 2022 Request: \$142.3 million
(\$26.2 million above the FY 2021 Enacted Level)

NIDA's Division of Therapeutics and Medical Consequences (DTMC) supports research to evaluate the safety and efficacy of pharmacotherapies and devices to treat SUD. This work spans all phases of medical product development including synthesis and preclinical evaluation of potential therapeutics, clinical trial design and execution, and preparing regulatory submissions. Through these investments, NIDA helps to mitigate risks of developing new treatments for SUD. 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,²⁸⁰ which was approved by the FDA in May 2018.

²⁸⁰ <http://www.drugabuse.gov/about-nida/noras-blog/2018/05/nida-supported-science-leads-to-first-fda-approved-medication-opioid-withdrawal>

NIDA also supports research to identify promising compounds and make them more feasible for pharmaceutical companies to complete costly clinical studies for SUD indications. As part of the HEAL InitiativeSM, described below, DTMC leads efforts to develop new and repurposed medications to treat OUD.

NIDA is also prioritizing the development of pharmacological treatments for stimulant use disorders. This portfolio includes approaches from repurposing approved medications for other SUDs, to developing a novel monoclonal antibody that could prevent or reduce methamphetamine intoxication (see program portrait “Medications Development for Stimulant Use Disorder”).

Clinical Trials Network

FY 2022 Request: \$48.6 million

(\$8.9 million above the FY 2021 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: 16 research nodes with 31 principal investigators affiliated with academic medical centers and large health care networks; two research coordinating centers; and more than 240 community-anchored treatment programs. This unique partnership enables the CTN to conduct studies of behavioral, pharmacological, and integrated treatment interventions in multisite clinical trials to determine effectiveness across a broad range of settings and populations. It also allows the CTN to ensure the transfer of research results to providers and patients. The network evaluates interventions, implementation strategies, and health system approaches to addressing SUD and co-occurring conditions such as mental illnesses and HIV. Using support from HEAL, the CTN has been able to expand its geographical reach, adding 5 new nodes in 2020 that can develop and test interventions in new populations.

The CTN is conducting studies to evaluate strategies for integrating OUD screening and treatment into emergency departments, primary care clinics, and American Indian/Alaska Native communities. The CTN is also conducting a study to examine the effects of medications for OUD in pregnant women. It has supported studies to capture important data for research on SUD in electronic health record (EHR) systems in primary care and emergency departments, and is currently developing and testing a clinical decision support tool that integrates with EHR systems to help doctors diagnose OUD and provide treatment or refer patients to appropriate care. Complementing the work supported through NIDA’s DTMC, CTN studies are investigating the effectiveness and safety of pharmacotherapies (e.g., ADAPT-2), and transcranial magnetic stimulation for methamphetamine and cocaine use disorders.

High-Tech Biomedical Product Development

FY 2022 Request: \$55.9 million

(\$10.3 million above the FY 2021 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. OTIPI manages NIDA's Small Business Innovation Research/Small Business Technology Transfer Programs to advance health applications. It also uses novel fit-for-purpose funding authorities, such as Prizes and Open Competitions, and establishes teaching programs that equip scientists with the competence to translate advances in addiction research into products.

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 2022 Request: \$405.4 million

(\$135.1 million above the FY 2021 Enacted Level)

Through the HEAL InitiativeSM, NIDA continues to expand its support for research to combat opioid addiction. For example, NIDA is supporting a study to prevent the high rate of opioid misuse initiation associated with the transition from adolescence to adulthood. HEAL funds are also being used to accelerate the availability of novel treatments for OUD and overdose, including to develop longer-acting formulations of existing OUD drugs like buprenorphine, repurpose approved drugs for other indications for OUD, and develop novel antibodies to prevent the action of opioids in the brain.

The HEAL InitiativeSM leveraged NIDA's existing CTN to expand the network by adding 5 new nodes that are supporting the development of 26 new research protocols. Two large projects address knowledge gaps around treatment initiation and retention. The first is a study of the efficacy of prevention interventions to halt the progression from risky opioid use to OUD. Researchers will test the efficacy of a Subthreshold Opioid Use Disorder Prevention (STOP) intervention in primary care settings to identify and address early-stage opioid misuse. The second is a study to test strategies to improve retention in medication treatment for OUD, as well as strategies to improve outcomes for patients stabilized on OUD medications who want to stop taking them. This will be the first study of medications to treat OUD to follow prospectively a large sample of patients through discontinuation.

HEAL also supports studies that are developing effective implementation strategies for evidence-based interventions. The Justice Community Opioid Innovation Network (JCOIN) is testing strategies to expand effective OUD treatment and care for people in justice settings in partnership with local and state justice systems and community-based treatment providers, which will fully launch as clinical trials in early 2021. The HEALing Communities Study, a multisite implementation research study, is investigating coordinated approaches for deploying evidence-

based strategies to prevent and treat opioid misuse and OUD tailored to the needs of local communities. The goal of the study is to reduce opioid-related overdose deaths by 40 percent over 3 years. Research sites are partnering with 67 communities highly affected by the opioid crisis in 4 states to measure the impact of these efforts.

Finally, the HEALthy Brain and Child Development Study is a NIDA and HEAL-led, trans-NIH effort to add to our understanding of early brain development trajectories. This study will establish a cohort of pregnant women and follow their children through the first decade of their lives to determine how environmental factors, including maternal drug exposure and genetics, influence early brain development and behavioral and clinical outcomes such as mental illnesses and addiction.

Intramural Research Program

FY 2022 Request: \$105.2 million

(\$3.1 million above the FY 2021 Enacted Level)

NIDA conducts research in high priority areas through its Intramural Research Program (IRP). The IRP portfolio includes research to: 1) elucidate the mechanisms underlying the development of SUDs; 2) evaluate potential new therapies for SUDs, including pharmacological and non-pharmacological interventions; and 3) identify and characterize emerging drugs such as synthetic opioids, stimulants, and cannabinoids.

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 that 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 animal models and people with OUD, and whether it prevents opioid withdrawal with fewer side effects than medications in current use. If 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 suggest 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 potentially for OUD.

Non-pharmacological addiction treatments are also being developed in NIDA's IRP. The on-site treatment-research clinic includes efforts to develop a smartphone app that uses machine learning to detect or predict stress, craving, and drug use within hours—and a parallel project to develop content that the app could deliver “just in time.” Because current apps purporting to serve these functions do not meet scientific standards of evidence, IRP is addressing a 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 unprotected sex in the context of substance use.

Research Management and Support***FY 2022 Request: \$73.3 million*****(\$0.7 million above the FY 2021 Enacted Level)**

Research Management and Support 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 InitiativeSM, 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. To this end, the RMS portfolio incorporates education and outreach activities to inform public health policy and practice with the goal of 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 addiction scientists. In addition, NIDA's RMS portfolio includes the NIDAMED initiative,²⁸¹ 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 2022 Request: \$63.2 million*****(\$1.7 million above the FY 2021 Enacted Level)**

Although the prevalence of alcohol consumption 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 drinking²⁸² and high intensity drinking (i.e., two or more times the gender-specific binge drinking thresholds) among young people remain significant concerns. These drinking patterns 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.

Characterizing the effects of alcohol exposure on the developing adolescent brain

Basic research is key to informing the development of innovative prevention and treatment strategies for underage drinking. NIAAA's Neurobiology of Adolescent Drinking in Adulthood

²⁸¹ www.drugabuse.gov/nidamed-medical-health-professionals

²⁸² 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. Research suggests that fewer drinks in the same timeframe result in the same blood alcohol concentration in youth.

(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. For example, preclinical research conducted through NADIA established a link between adolescent alcohol exposure and specific molecular changes in the brain that contribute to increased anxiety in adulthood. Building on basic research, NIAAA funds collaborative research to assess the impact of adolescent drinking on brain development in longitudinal studies in humans. 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 research has characterized the alterations in brain development that occur after adolescent alcohol exposure, including weakened connections between brain networks involved in the regulation of emotional and cognitive functioning. Recent studies have linked childhood trauma with future alcohol misuse in adolescence, suggesting potential benefits of targeted alcohol interventions among trauma-exposed youth. NCANDA laid the methodological foundation for NIH's ABCD study, the largest longitudinal study of brain development and child health in the United States.

Preventing underage drinking

NIAAA's underage drinking portfolio includes studies to develop, evaluate, and implement evidence-based prevention programs for youth. These programs include individual-, family-, school-, community-, and environmental-level interventions for underage individuals at large, as well as those designed or adapted for underserved populations and specific settings, including the college setting. 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 over 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. NIAAA is also interested in addressing alcohol misuse in young adults who are not enrolled in college, and challenges remain for targeting this population.

Promoting implementation of alcohol screening and brief intervention among youth and young adult populations

Increasing implementation of alcohol screening and brief intervention among youth and young adult populations in health care and other appropriate settings is a priority area for NIAAA. Alcohol screening and brief intervention in primary care has been recognized as a leading preventive service for reducing alcohol misuse in adults, and a growing body of evidence demonstrates its effectiveness in preventing and reducing alcohol misuse in youth. NIAAA-supported research has found that, relative to usual care, adolescent patients (ages 12-18) subjected to screening, brief intervention, and referral to treatment in pediatric primary care settings had improved substance use, mental health, and health outcomes over a three-year follow up period. To facilitate the integration of screening and brief intervention into primary care, NIAAA developed a youth alcohol screening tool, Alcohol Screening and Brief Intervention for Youth: A Practitioner's Guide, to enable pediatric and adolescent health

practitioners to identify patients at risk for underage drinking and associated problems. This screening tool has been validated among youth in pediatric emergency room settings, in school settings, in primary care settings (including among racially and ethnically diverse youth), and among youth with chronic health conditions.

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 and Center 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- or Center-specific. Some 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, created by NIDA, is SRO-5.2: "By 2025, develop or evaluate the efficacy or effectiveness of new or adapted prevention interventions for substance use disorders." This new measure, which began reporting in FY 2020, is indicative of NIDA's portfolio of efforts to support the development and testing of prevention interventions for SUD. The annual targets for this goal reflect targeted investments in particular areas of need or opportunity, including vulnerable periods during critical life transitions for OUD, and reduction of vaping in teens. This measure replaces NIDA's reporting for SRO-5.15, which focused on SUD and prescription misuse in adolescent populations. NIDA's contribution to SRO-5.15 ended in FY 2019 as planned.

NIDA also created SRO-4.9: "By 2023, evaluate the efficacy of new or refined interventions to treat opioid use disorders." 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. Originally scheduled to be discontinued beginning in FY 2021, this measure has been extended through FY 2023 to reflect the five-year time horizon of FY 2018 investments in the development and evaluation of OUD interventions within HEAL.

SRO-5.15, created by NIAAA, aims to: "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 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.

In addition to 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.

National Institute on Drug Abuse		
Selected Measures of Performance	FY 2020 Target	FY 2020 Achieved
Scientific Research Outcome-5.2: Conduct 3-5 pilot studies to By 2025, develop or evaluate the efficacy or effectiveness of new or adapted prevention interventions for substance use disorders (SUD).	test the efficacy of promising prevention interventions for SUD.	Nine prevention pilot studies were conducted as part of the Helping to End Addiction Long-term (HEAL SM) Initiative.
Scientific Research Outcome-4.9: Conduct 1 pre-clinical and 1 By 2023, evaluate the efficacy of new or refined interventions to treat opioid use disorders (OUD).	conduct 1 pre-clinical and 1 clinical study of a longer acting formulation of a medication for the treatment of opioid use disorders or opioid overdose.	NIH conducted a pre-clinical development study of a novel long-acting formulation of nalmefene for treating OUD, and a clinical study of a novel long-acting implant that delivers naltrexone, an effective treatment for OUD.

Prevention – Scientific Research Outcome-5.2

The FY 2020 target was met. NIH funded nine prevention pilot studies that were conducted in FY 2020, under the auspices of the Helping to End Addiction Long-term (HEALSM) Initiative. These grants used the two-phase, milestone-based UG3-UH3 grant mechanism, which allows for grants that successfully complete pilot-study progress milestones to apply to advance into larger clinical studies. Of those nine pilot studies, seven completed their pilots and were eligible for transition. (Two of the studies had planned for two-year pilot phases, so were not eligible for transition.) Three of the seven transitioning studies are highlighted as examples below.

One transitioning study involves modifying an existing alcohol and drug prevention intervention designed for American Indian/Alaska Native youth to be appropriate for opioid prevention in young adults. The study conducted focus groups to determine how best to engage the target population, adapted and enhanced the intervention to specifically address opioid use, and pilot-tested the intervention. The scaled-up study will test the intervention in larger groups over a 12-month period, examine the mechanisms by which it produces change, and explore approaches to making it sustainable over time.

Another transitioning study is focused on preventing OUD among adolescents/young adults ages 18-24 years experiencing homelessness and explores whether providing housing in addition to opioid and related risk reduction services could improve outcomes. The pilot study demonstrated feasibility of recruitment, locating housing and placement into housing, and delivery of prevention services through strengths-based outreach and advocacy. Partnerships with community-based homeless youth service providers and landlords have been established for the post-pilot phase, housing has been identified, and Institutional Review Board (IRB) approval has been obtained. The scaled-up study will compare individuals randomly assigned to receive housing alongside opioid and related risk prevention services to individuals who receive those services alone.

A third study developed a plan to leverage technology that is appealing to adolescents and young adults to facilitate delivery of an emergency department-based intervention via health coaches. In their transitioning pilot, researchers were able to adapt promising health coach-delivered intervention and pilot test feasibility/acceptability in adolescents and young adults, as well as actively engage hospital administration leadership in the study. As the project transitions to the next phase, it will begin testing the intervention in a sample of over 1,000 adolescents and young adults in emergency department settings.

Treatment – Scientific Research Outcome-4.9

The FY 2020 target was met. NIH funded the pre-clinical development of a new implant that will deliver nalmefene, a drug that blocks opioid signaling, over a six-month period. The goal is to advance this compound to be tested in humans for the prevention of relapse to opioid addiction in patients following opioid detoxification. This long-acting formulation will use the Proneura® technology that has been successful in an FDA-approved long-acting formulation of buprenorphine. This long-acting nalmefene is completing the necessary nonclinical safety, toxicology, pharmacokinetic and manufacturing activities to start studies in humans (clinical trials) and begin the process of applying for FDA approval.

In FY 2020, NIH also funded a clinical trial to evaluate the safety and efficacy of GM0017, an implant that delivers the opioid antagonist naltrexone for six months. This compound is being developed for prevention of opioid relapse in individuals with OUD who have been detoxified. Recruitment for this study has been delayed due to the COVID-19 pandemic, but it is expected that clinical results will soon be presented to the FDA.

National Institute on Alcohol Abuse and Alcoholism		
Selected Measures of Performance	FY 2020 Target	FY 2020 Achieved
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	Develop a digital technology-based intervention to prevent or reduce alcohol misuse in underage individuals.	Researchers developed and tested technology-based interventions to prevent and reduce underage drinking.

consequences in underage populations.

Scientific Research Outcome 4.15: By 2021, evaluate three interventions for facilitating treatment of alcohol misuse in underage populations.	Test a behavioral therapy for intervening with alcohol misuse in an underage population.	Researchers tested the effectiveness of multiple behavioral interventions for reducing alcohol use and other harmful behaviors in underaged incarcerated and homeless youth.
--	--	--

Prevention – Scientific Research Outcome-5.15

The FY 2020 target was met. NIAAA-funded investigators developed and evaluated digital technology-based interventions to prevent or reduce alcohol misuse among underage college and high school students.

Research indicates that perceived norms about alcohol use are a strong correlate of alcohol misuse that predict alcohol consumption over time. Perceived norms among college students tend to be exaggerated relative to actual drinking norms and may have adverse effects on both individuals and the community. NIAAA-supported researchers recently created a text messaging intervention for heavy drinking, underage college students that was designed to realign perceived drinking norms with actual drinking norms of their campus peers. Heavy drinking in the study was defined as more than four drinks per day or more than 14 drinks per week for males, and more than three drinks per day or more than seven drinks per week for females in the past 30 days. Participants were assigned to either an experimental or control condition. The experimental group received text messages containing information about campus-specific drinking norms while the control group received text messages containing unique facts unrelated to alcohol. Text messages were sent daily to participants over a period of 10 weeks. The intervention was shown to be effective at reducing peak alcohol consumption and alcohol-related consequences three months after the beginning of the study. These intervention effects, however, were not maintained another three months later. This study demonstrates the feasibility of text-based norms interventions in reducing alcohol use and its consequences around the time of engagement with the intervention.

In FY 2020, NIAAA also supported research to develop and test digital, school-based interventions aimed at preventing and reducing alcohol use among high school students. One ongoing study focuses on developing and testing the efficacy of an e-learning intervention to improve school staff's knowledge, skills, and self-efficacy in supporting sexual minority youth and protecting them from bullying victimization. Prior research has demonstrated that sexual minority youth have an increased risk of future alcohol and other substance use and supportive school environments can help reduce substance use.

Another school-based study recently demonstrated that eCHECKUP TO GO is effective in reducing alcohol-related cognitive risk factors and alcohol use in both male and female high school seniors. eCHECKUP TO GO is a brief, web-based personalized feedback intervention

designed to reduce alcohol use by targeting cognitive risk factors (e.g., perceived drinking norms among peers) and protective behavioral strategies (e.g., behaviors that minimize the risk of alcohol-related consequences).

In combination with the FY 2019 actual performance which demonstrated the efficacy of interventions designed to prevent alcohol misuse among college-age individuals, the digital interventions described above contribute to the Institute's goal of evaluating and promoting evidence-based intervention strategies to prevent substance misuse in underage populations.

Treatment – Scientific Research Outcome-4.15

The FY 2020 target was met. NIAAA-supported investigators evaluated a treatment invention in an underage, incarcerated population. Research suggests that combining evidence-based behavioral interventions – e.g., motivational interviewing plus cognitive behavior therapy (MI/CBT) – that focus on motivation, problem-solving, communication, mental health, and substance use may be useful in improving outcomes for incarcerated youth. In the current study, NIH-supported researchers conducted a randomized controlled clinical trial to evaluate the effectiveness of MI/CBT in mitigating alcohol and marijuana use and aggression among incarcerated youth. The control condition, RT/SET, was a combined intervention consisting of relaxation training (a mindfulness approach) and treatment as usual (substance-education and twelve step programming). Eligibility criteria included using alcohol or marijuana at least monthly; heavy drinking (defined as more than five standard drinks for boys, more than four standard drinks for girls) at least once; or alcohol or marijuana use in the four weeks before either the offense for which they were incarcerated, or before they were incarcerated. The researchers found RT/SET to be slightly more effective than MI/CBT in reducing percent of heavy drinking days and significantly more effective in reducing alcohol-related aggression after the youths' release from incarceration. RT/SET and MI/CBT both reduced aggression after release but neither showed significant effects on marijuana-related behavioral outcomes. These results suggest that RT/SET may be a viable, lower-cost intervention for delivery in youth correctional settings; however, additional research on RT/SET is needed.