Drug Control Programs

Resource Summary

	Budget Authority (in millions)		
	FY 2018 Final[1]	FY 2019 Enacted	FY 2020 Request
Drug Resources by Budget Decision Unit and Function:			
Decision Unit 1: National Institute on Drug Abuse			
Research and Development: Prevention	$533.346	$550.992	$503.079
Research and Development: Treatment	$841.028	$868.852	$793.300
Total, Decision Unit 1	$1,374.374	$1,419.844	$1,296.379
Decision Unit 2: National Institute on Alcohol Abuse and Alcoholism			
Research and Development: Prevention	$49.034	$50.691	$43.635
Research and Development: Treatment	$6.857	$7.089	$6.102
Total, Decision Unit 2	$55.891	$57.780	$49.737
Total Funding	$1,430.265	$1,477.624	$1,346.116
Drug Resources Personnel Summary			
Total FTEs (direct only)	355	382	382
Drug Resources as a Percent of Budget			
Total Agency Discretionary Budget (in billions)[2]	$36.2	$38.0	$33.5
Drug Resources percentage	3.96%	3.89%	4.02%

[1] Total for NIDA includes $213.124 million of Opioid funding not obligated in FY 2018, and carried over into FY 2019.

[2.] Total includes amounts requested in FY 2020 for consolidation 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 NIDA and the NIAAA, two of the 27 Institutes and Centers of the National Institutes of Health (NIH), support research in pursuit of the *National Drug Control Strategy*. NIDA funds research on the prevention and treatment of drug use, addiction, and its harmful consequences. NIAAA supports research on the prevention and treatment of underage drinking and its harmful consequences.

The societal impact of the misuse of illicit drugs in 2007 was estimated at $193 billion in health care, crime-related, and productivity losses.[71] Knowledge is the foundation of the transformative agenda needed to strike at the heart of this stubborn and costly challenge. To provide a comprehensive public health response, NIH-supported research will continue to build on scientific advances from previous and ongoing investments in basic, translational, and clinical research that have led to innovative strategies for preventing and treating substance misuse and substance use disorders (SUDs) in this country and worldwide.

Studying substance misuse, SUDs, and their causes is a complex challenge compounded by societal stigma and misunderstanding that most other illnesses do not face. The landscape of drug addiction in America evolves from year to year; a decades-long prescription drug misuse epidemic has led to a rise in heroin use, and now the use of synthetic opioids such as fentanyl and carfentanil is becoming more widespread. 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 arise as a byproduct of intravenous drug use. In addition, the growing number of states that are legalizing marijuana for recreational and medical use present 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 and brain development in collaboration with NIAAA and other Federal partners; studying the impact of new synthetic drugs; studying the impact of the changing marijuana landscape; and contributing to scientific and public understanding of the brain mechanisms underlying addiction.

Opioid misuse, addiction, and overdose is an ongoing and rapidly evolving public health crisis. Millions of Americans suffer from opioid use disorder (OUD), and millions more suffer from chronic pain. The urgency and scale of this crisis calls for innovative scientific solutions. As part of a government-wide effort to address this crisis, the NIH launched the Helping to End Addiction Long-term (HEAL) Initiative in April 2018. HEAL 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.

Alcohol misuse has profound effects on the health and well-being of individuals, families, and communities, and costs the United States $249 billion per year.[72] Since its creation, NIAAA has supported a diverse portfolio of research to elucidate the effects of alcohol on health and reduce the burden of alcohol misuse for individuals at all stages of life. This research encompasses studies on: the biological and behavioral mechanisms underlying alcohol misuse and alcohol use

[71] U.S. DOJ National Drug Intelligence Center. The Economic Impact of Drug Use in American Society. April 2011.
[72] Sacks, J.J.; Gonzales, K.R.; Bouchery, E.E.; et al. 2010 national and state costs of excessive alcohol consumption. American Journal of Preventive Medicine 49(5):e73–e79, 2015.

disorder (AUD), epidemiological research to track patterns of alcohol use, and the development of interventions to diagnose, prevent, and treat alcohol misuse and its consequences, including among youth. NIAAA also supports efforts to translate and implement research findings into improved health care for individuals with AUD and co-occurring conditions, as well as to disseminate evidence-based information to health care providers, researchers, policy makers, and the public. This work has significantly broadened our understanding of AUD, helping to reduce the stigma associated with it and providing 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 project as relevant to prevention or treatment. This is used to generate the NIAAA drug control budget estimate.

Budget Summary

The FY 2020 request for drug-related activities at NIH is $1,346.1 million ($1,296.4 million for NIDA and $49.7 million for NIAAA), an 8.9% decrease compared with the FY 2019 Enacted level.

NIH-supported research has provided and will continue to provide the scientific basis for budget 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 SUDs, 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 SUDs. 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 medication-assisted treatment (MAT) for OUD, 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 SUDs 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 NIH Helping to End Addiction Long-term (HEAL) Initiative^{SM}, 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 medications for opioid use disorder (OUD).

As part of the NIH HEAL Initiative, NIDA (and to a lesser extent, NIAAA) support 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 to (1) develop new and reformulated medications to treat OUD; (2) determine strategies to reduce opioid overdose in communities hardest hit by the opioid crisis; (3) conduct clinical trials to enhance widespread implementation of evidence-based interventions; and (4) determine ways to improve the effectiveness and adoption of interventions within justice systems.

National Institute on Drug Abuse
FY 2020 Request: $1,296.4 million
($123.5 million below the FY 2019 Enacted level)

NIDA's efforts consist of Neuroscience and Behavioral Research; Epidemiology, Services and Prevention Research; Therapeutics and Medical Consequences; Clinical Trials Network; Responding to the Opioid Crisis; Intramural Research Program (IRP); and Research Management and Support (RMS).

Neuroscience and Behavior Research
FY 2020 Request: $423.4 million
($50.4 million below the FY 2019 Enacted level)

The Neuroscience and Behavior research portfolio seeks to advance knowledge of the fundamental molecular, cellular, genetic/epigenetic, neurological, and behavioral processes that underlie SUDs. Additionally, a goal of this research is to elucidate the effects of drugs of abuse on brain structure and function. Central to these goals are efforts to delineate the multiple neurobiological factors that contribute to drug abuse, physical dependence and addiction risk, with particular emphasis on determining the bases for individual differences in vulnerability and drug sensitivity. NIDA supports research to develop advanced technologies that improve our ability to study the organization of the living brain from cells to networks and elucidate the interactions of complex neural circuits and how they encode reward, craving, compulsive behavior, and related decision making that drive substance use. Ongoing pharmacological research is discovering, developing, and testing new compounds for the treatment of substance abuse, physical dependence, and addiction. NIDA pharmacological research is also involved in the discovery of molecules and mechanisms that can relieve pain without producing adverse effects, including tolerance, dependence, and addiction. NIDA also supports research on the development of novel non-pharmacological strategies such as transcranial magnetic stimulation (TMS), transcranial direct current stimulation (tDCS), deep brain stimulation (DBS), and neurofeedback. Notable projects are investigating the effects of drugs on gene expression and brain development and function; how an individual's genes interact with environmental conditions, such as stress and early exposure to drugs to influence risk for addiction; basic processes underlying resilience against SUDs in childhood and adolescence; and gender-related differences in these effects. NIDA also supports research on the interactions between HIV infection and addiction to understand how this comorbidity influences outcomes for both illnesses. Finally, NIDA is working to support big data science to promote efficient analysis of large, diverse data sets on a scale not previously possible. Collectively, this research will provide new perspectives on the effects of drugs on multiple biological systems and improve our understanding of the basic neural and genetic mechanisms that underlie drug use and addiction, thus guiding the development of novel therapies for treating addiction.

In addition, under the Collaborative Research on Addiction at the NIH (CRAN) initiative, NIDA and NIAAA, along with nine other components of the NIH and the Centers for Disease Control and Prevention (CDC), are supporting a longitudinal study that will not only examine how substance use affects neural development, but also identify risk factors and biomarkers that make adolescents vulnerable to substance use disorder. The Adolescent Brain Cognitive Development (ABCD) study will follow the biological and behavioral development of more than 10,000 children beginning at ages 9-10 through adolescence into early adulthood. Over the course of the next decade, scientists will use 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, health and other outcomes, including both substance use and broader health outcomes. Understanding these

relationships may help reveal the biological and environmental building blocks that contribute to successful and resilient young adults. This enhanced knowledge also may lead to ways to predict potential developmental problems including mental illness and SUD so that they can be prevented or reversed. Families that volunteer will be part of groundbreaking research that promises to inform future substance use prevention strategies, educational priorities, child development innovations, research priorities, and public health interventions. The ABCD study has enrolled more than 11,000 participants and released curated data on the first approximately 4,500 participants to the scientific community in February 2018. Curated baseline data on the full ABCD cohort will be released in early 2019.

Epidemiology, Services, and Prevention Research
FY 2020 Request: $289.5 million
($34.5 million below the FY 2019 Enacted level)

NIDA's Division of Epidemiology, Services, and Prevention Research (DESPR) supports integrated approaches to understanding and developing strategies to address the interactions between individuals and environments that contribute to drug use, addiction, and related health problems. The Division supports the annual Monitoring the Future survey, which tracks drug use and related attitudes among adolescent students nationwide, and the National Drug Early Warning System (NDEWS), a surveillance network that monitors emerging trends related to illicit drug use around the country so that rapid, informed, and effective public health responses can be developed and implemented when and where they are needed. 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 criminal justice system, including studies on implementation of MAT and seek, test, treat, and retain (STTR) strategies for people with SUDs who are also at risk for HIV. NIDA also funds research into the efficacy of screening brief intervention and referral to treatment (SBIRT) in primary care settings for reducing drug use and SUD. Program efforts also 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 from the 21st Century Cures Act to test approaches for expanding access to MAT for opioid use disorder and naloxone for the reversal of overdose.

NIDA recently partnered with the Appalachian Regional Commission (ARC), the CDC and the Substance Abuse and Mental Health Services Administration (SAMHSA) and have issued nine grants to help communities develop comprehensive approaches to prevent and treat consequences of opioid injection, including substance use disorder, overdose, HIV, hepatitis B and C virus infections, as well as sexually transmitted diseases. Once developed, these projects will 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 2020 Request: $146.6 million
($17.5 million below the FY 2019 Enacted level)

NIDA's Division of Therapeutics and Medical Consequences is focused on developing therapeutics for the treatment of SUDs. Since the pharmaceutical industry has traditionally made limited investment in the development of medications to treat SUDs, the responsibility for supporting their development has rested largely with NIDA. To most effectively leverage NIDA resources, this program encourages the formation of alliances between strategic partners (pharmaceutical and biotechnology companies, as well as academic institutions) with the common goal of advancing medications through the development pipeline toward FDA approval in a timely manner. NIDA supports and conducts pre-clinical and clinical research with new or repurposed compounds with the goal of advancing their development towards FDA approval. This research also supports efforts 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. NIDA also invests in research supporting the development of vaccines and monoclonal antibodies for the treatment of SUDs.

Clinical Trials Network
FY 2020 Request: $37.2 million
($4.4 million below the FY 2019 Enacted level)

The Clinical Trials Network (CTN) comprises 13 research nodes with 25 principal investigators affiliated with academic medical centers and large health care networks, two 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. The overarching mission of the CTN is to allow medical and specialty treatment providers, treatment researchers, participating patients, and NIDA to cooperatively develop, validate, refine, and deliver new treatment options to patients. This unique partnership enables the CTN to conduct studies of behavioral, pharmacological, and integrated behavioral and pharmacological treatment interventions in rigorous, multisite clinical trials to determine effectiveness across a broad range of community-based treatment settings and diversified 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 SUDs and related disorders, such as co-occurring mental health disorders and HIV, in randomized controlled trials (RCTs) and other clinical studies that are conducted in diverse treatment settings and patient populations.

The CTN is conducting studies to evaluate strategies for integrating OUD screening and treatment into emergency departments, pharmacies, primary care clinics, and American Indian communities. The CTN has also supported studies to integrate OUD care into electronic health record (EHR) systems, to capture important data for research on SUD in EHR systems for primary care and emergency departments, and is currently developing and testing a clinical decision support (CDS) tool for OUD care for use in EHR systems. 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 currently developing a variety of studies, including examining the effects of medications for OUD in pregnant women and studying the effects of medical cannabis use via electronic health records.

Responding to the Opioid Crisis
FY 2020 Request: $250.0 million
(Unchanged from the FY 2019 Enacted Level)

As part of the NIH HEAL Initiative, NIDA will continue to expand its support for new research efforts to combat opioid addiction, with several major projects beginning or ramping up in FY 2019 with continued support into FY 2020. Initiatives under consideration include studies to determine the optimal length of medication treatment for OUD; management of subsyndromal and low-severity OUD; preventing OUD in older adolescents and young adults; and understanding consequences of prenatal opioid exposure on brain and behavioral development.

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. HEAL also includes focused development efforts for OUD treatment, such as:

- Repurposing already-approved medications to treat OUD
- Evaluating medications already in use internationally but not in the U.S.
- Discovering and validating novel biological targets
- Developing novel immunotherapies for OUD and overdose
- Reducing drug craving and harm in people with OUD
- Developing devices to prevent and treat OUD and overdose

NIDA also plans to expand the size and scope of research conducted by the CTN to address emergent needs presented by the opioid crisis. The CTN has already generated important findings on the effectiveness and safety of medications to treat OUD and the utility of behavioral interventions for OUD management. By incorporating new research sites and investigators into existing research nodes and centers, the CTN will incorporate OUD-related research questions into studies currently underway, expedite new studies of OUD treatment in general medical and other settings, and enhance clinical and research training opportunities. While MAT is known to be effective to OUD, there is significantly less evidence about how long individuals should remain in treatment, or what the minimum length of MAT should be, given that most patients do not want to take medication for longer than necessary. Starting with buprenorphine, the NIDA CTN will be studying the optimal length of treatment in order to better understand how best to

deploy this highly effective, evidence-based intervention. NIDA is also in the planning stages of using the CTN to build the evidence base for early detection and intervention in individuals with opioid misuse who do not meet diagnostic criteria for severe OUD.

While misuse of prescription opioids like Vicodin™ and OxyContin™ and use of heroin are at record low levels among middle and high school students, the prevalence of opioid misuse has risen dramatically among older adolescents and young adults. As part of its efforts to address the opioid crisis, NIDA will focus on preventing OUD during this vulnerable time of transition. The goal of this prevention initiative is to develop and disseminate evidence-based prevention interventions targeting adolescents and young adults ages 16-30 residing in areas that are affected by the opioid crisis. Studies will be conducted to improve our understanding of risk factors to opioid misuse, transition to OUD, and opioid overdose as well as other adverse health consequences. Research grants in this initiative will also support studies to test interventions in a variety of settings in the healthcare, community, and justice systems. Settings selected will encompass those most likely to reach the targeted audience including primary care centers, emergency departments, urgent care centers, HIV/sexually transmitted infection clinics, school-based and community college health centers, the workplace, and the justice system.

It is well established that the first few years of life are a period of exponential brain growth and development. However, there is much to be learned about typical brain development beginning prenatally through early childhood, its variability, 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. This knowledge is critical to help predict and prevent some of the known impacts of pre-/postnatal exposure to certain drugs or adverse environments, including risk for substance use, mental disorders, and other behavioral and developmental problems. Currently, no large prospective cohort study has been conducted to comprehensively assess brain development or the long-term consequences of early adverse experiences or exposure to opioids, other drugs (including prescribed medication), or other substances (e.g., tobacco, alcohol, cannabis). Furthermore, establishing a causal link between substance exposures and specific outcomes is very difficult due to confounding factors such as socioeconomic, environmental, cultural, and genetic influences. To disentangle these factors, the HEALthy Brain and Cognitive Development 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 offspring into early childhood, collecting data in the following domains: pregnancy/fetal development measures; infant and early childhood structural and functional brain imaging; medical history; family history; biospecimens; and social, emotional, and cognitive development. This prospective approach will allow for the investigation of pre-symptomatic changes in brain and behavioral development resulting from early exposure to opioids and other substances, as well as associated adverse conditions that might predict emergence of SUD and other mental illness. It will also identify protective and resiliency factors that may ameliorate the effects of these exposures and inform the development of early interventions

Opioid misuse and addiction is an ongoing and rapidly evolving public health crisis that affects millions of Americans and requires innovative scientific solutions. A great tragedy of the opioid crisis is that so many effective tools already exist but are not being deployed effectively in communities that need them. Only a fraction of people with opioid use disorder (OUD) receive any treatment, and of those, less than half receive the medications that are universally acknowledged to be the standard of care, or they receive treatment for too short a duration. In partnership with the SAMHSA, and as part of the broader NIH HEAL Initiative, NIDA is leading a multisite research effort called the HEALing Communities Study.

This study will develop and test strategies to help communities respond rapidly and effectively to their opioid crisis with a focus on significantly reducing opioid-related overdose fatalities by 40 percent in 3 years and improving other outcomes. More specifically, the funding opportunities released in September 2018, (RFA-DA-19-0164 and its companion RFA-DA-19-0175), call for cooperative agreement applications for a data coordinating center and up to three research sites to measure the impact of integrating evidence-based prevention, treatment, and recovery interventions for opioid misuse, OUD, opioid-related overdose events and fatalities across multiple settings including healthcare, behavioral health, and justice. Each research site will be made up of several counties, towns, or cities within a single state, and will involve community resources such as police departments, faith-based organizations, and schools, with a focus on strong partnerships with state and local governments. The study also aims to decrease the incidence of OUD; increase the number of individuals receiving medications for OUD, staying in treatment beyond six months, and receiving recovery support services; and expand the distribution of naloxone. The lessons learned from this study will allow us to parlay the power of science to tackle one of the worst drug crises our country has ever seen.

Intramural Research Program
FY 2020 Request: $86.6 million
($9.6 million below the FY 2019 Enacted level)

In addition to funding extramural scientists, NIDA also conducts research in high priority areas through its Intramural Research Program (IRP). Intramural research at NIDA focuses on conducting multidisciplinary cutting-edge research to: 1) elucidate the mechanisms underlying the development of addiction; 2) evaluate the potential of emerging new therapies for SUDs, including pharmacological and non-pharmacological interventions (e.g. psychosocial, biofeedback, brain stimulation technologies); 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 street drugs. Two specific examples of current and translational IRP research are described below.

First, a group of IRP investigators has begun a large translational study of a novel biased mu opioid receptor agonist to treat OUD. They have designed cross-species translational studies to test the efficacy of chronic delivery of a proprietary lead compound on oxycodone self-administration and relapse to drug seeking induced by acute exposure to the self-administered

drug and drug-associated cues, in rat and monkey models, developed at the IRP. A human lab study is also planned with prescription opioid addicts on the effect of chronic delivery of the compound on opioid craving induced by acute exposure to the prescription opioid or cues associated with the drug. In both the animal studies and the human study, the efficacy of this novel drug relative to buprenorphine will be compared. The long-term goal is to provide preclinical and clinical evidence to support the use of a biased mu opioid agonist as a novel opioid agonist maintenance treatment for treatment of OUD.

Second, the IRP is furthering OUD research, in partnership with a pharmaceutical company that has recently licensed NIH patents. The lead compounds are dopamine D3 receptor antagonist/partial agonists that show promise in reducing opioid self-administration, reinstatement to drug seeking, and acquisition to drug taking, while having no effect on opioid antinociception, in rodents and nonhuman primates. These novel drugs may prevent the development of dependence in patients who require long-term prescription opioids for the treatment of pain, but also have therapeutic potential for the treatment of OUD.

Research Management and Support
FY 2020 Request: $63.0 million
($7.0 million below the FY 2019 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 are also helping to coordinate NIDA's involvement in the HEAL Initiative, spearheading NIH's response to the opioid overdose epidemic. NIDA currently oversees more than 1,700 research grants and more than 80 research and development contracts. In addition to the infrastructure required to support research and training, NIDA also strives to provide evidence-based resources and educational materials about SUDs and to raise awareness of the science relating to cutting-edge issues such as opioid overdose prevention, marijuana research, synthetic drug trends, and medication-assisted treatment for opioid use and addiction.

The RMS portfolio also incorporates education and outreach activities to inform public health policy and practice by ensuring the institute is the primary trusted source for scientific information on drug use and addiction. NIDA is also committed to being at the forefront of training the next generation of innovative researchers by supporting both pre-doctoral and postdoctoral-level scientists interested in drug use and addiction research. NIDA leads the NIH Pain Consortium Centers of Excellence in Pain Education (CoEPEs); these twelve centers work to enhance patient outcomes by improving the education of healthcare professionals about pain and its treatment. The CoEPEs act as hubs for the development, evaluation, and distribution of pain management curriculum resources for medical, dental, nursing and pharmacy schools to improve how health care professionals are taught about pain and its treatment.

National Institute on Alcohol Abuse and Alcoholism
FY 2020 Request: $49.7 million
($8.0 million below the FY 2019 Enacted level)

NIH's underage drinking portfolio encompasses a broad range of research on the effectiveness and implementation of interventions designed to prevent and treat alcohol use, misuse, and addiction. These include both individual-, family-, school-, community-, and policy-level interventions for underage individuals at large, as well as those designed or adapted for specific populations and settings. Alcohol 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. Yet research indicates that adolescents are not routinely asked about drinking when they interface with the health care system. NIAAA supports research on the implementation of alcohol screening and brief intervention among youth and young adult populations, including those disproportionally affected by alcohol misuse. NIAAA also supports efforts to encourage the adoption of alcohol screening and brief intervention in healthcare and other appropriate settings.

Reducing alcohol misuse among college students, many of whom are underage, continues to be a high priority for NIAAA. Binge drinking[73] and high-intensity drinking (i.e., two or more times the gender-specific binge thresholds) among young people remain a significant concern; these practices are particularly troubling as they increase risks for alcohol-related blackouts, alcohol overdoses, sexual assault, sexually transmitted diseases, AUD, and other detrimental consequences. To assist college and university officials in addressing alcohol misuse on their campuses, NIAAA developed the College Alcohol Intervention Matrix (*CollegeAIM*), a user-friendly guide and website that rates nearly 60 evidence-based alcohol interventions in terms of effectiveness, costs, and other factors. With this tool, school officials can use research-based information to choose wisely among the many potential interventions, including individual- and environmental-level strategies (e.g., policies related to alcohol sales, taxes, and advertising), to address harmful and underage student drinking.

NIAAA's investment in underage drinking research also includes studies to understand how alcohol affects the developing brain. For example, NIAAA supports the National Consortium on Alcohol and Neurodevelopment in Adolescence (NCANDA), an accelerated longitudinal study of more than 800 youth ages 12-21 to assess the vulnerability of the adolescent brain to alcohol exposure. NCANDA has laid the methodological foundation for the NIH Adolescent Brain Cognitive Development (ABCD) study, the largest long-term study of brain development and child health in the United States. 11,874 youth, ages 9-10, have been enrolled in the ABCD study which will use brain imaging and neuropsychological and behavioral assessments to track the development of youth before and after they start to use alcohol and/or other addictive substances. These two studies are expected to illuminate the neurobiological, cognitive, and behavioral precursors of alcohol and other drug misuse and ultimately inform preventive and treatment strategies. Complementing NCANDA and ABCD, NIAAA's Neurobiology of

[73] 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.

Adolescent Drinking in Adulthood initiative is enabling investigators to examine, in animal models, the molecular, cellular, and circuit-level mechanisms by which adolescent drinking affects brain structure and function in the short and long term, and how the changes observed during this critical period persist into 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 (GPRMA) 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 NIDA's and 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.

NIDA created and leads SRO-7.3: "By 2020, develop and/or evaluate two treatment interventions using health information technology (HIT) to improve patient identification, treatment delivery and adherence for substance use disorders and related health consequences." This measure began in FY 2014 and has been updated to reflect NIDA's current focus in exploring and leveraging technological advances to improve the efficiency and quality of health care delivery for SUDs.

In addition to developing and leading SRO-5.15, NIAAA contributed to SRO-8.7: "By 2018, identify three effective system interventions generating the implementation, sustainability, and

ongoing improvement of research-tested interventions across health care systems." This measure, which began in FY 2008 and was updated over time, reflects NIH's ongoing commitment to supporting research on the implementation of preventive and treatment interventions and improving the translation of research into practice. NIAAA's contribution to SRO-8.7 ended in FY 2018, and a replacement measure – SRO: 4.15: "By 2021, evaluate three interventions for facilitating treatment of alcohol misuse in underage populations" – has been developed for future reporting.

National Institute on Drug Abuse		
Selected Measures of Performance	**FY 2018 Target**	**FY 2018 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 substance use disorders and their consequences in underage populations.	Assess the efficacy or effectiveness of at least two strategies or interventions to prevent prescription drug abuse in youth and young adult populations.	The effect of an intervention to prevent prescription drug abuse in youth and young adult populations was tested, and several ongoing studies are assessing the efficacy or effectiveness of strategies to prevent prescription drug abuse in this target population.
» Scientific Research Outcome-7.3: By 2020, develop and/or evaluate two treatment interventions using health information technology (HIT) to improve patient identification, treatment delivery and adherence for substance use disorders and related health consequences.	Develop and/or test 1-2 technology-based treatments for substance use disorders and common comorbidities.	Research testing the feasibility and efficacy of 2 technology-based strategies to improve substance use disorder treatments and adherence was conducted, including (1) reSET-O which is under expedited review by FDA and (2) a web-delivered cognitive behavior therapy for veterans who screen positive for PTSD and SUD.

Prevention – Scientific Research Outcome-5.15

The FY 2018 target was partially achieved. NIDA tested the effect of one intervention to prevent prescription drug abuse in youth and young adult populations as part of its ongoing portfolio of research. NIDA funds research to assess the Partnership Model for Diffusion of Proven Prevention (PROSPER), which is a partnership-based delivery system to support the implementation of effective universal family and youth preventive interventions (e.g., Strengthening Families Program, Life Skills Training, Project ALERT, All Stars) in communities targeting known risk and protective factors. Substance misuse, antisocial behavior and health-risk taking sexual behavior are increasingly prevalent in young adulthood. The environments in

which adolescents socialize (e.g., school, family, peers) can exert substantial influence on both risk and protective factors for substance use and progression to misuse. As such, universal prevention interventions have been developed and tested to influence the family-, school-, and peer related risk and protective factors.

With a family-based prevention intervention delivered in 6th grade and school-based prevention intervention in 7th grade, NIDA-funded studies of PROSPER have demonstrated the model's sustained impact on substance use outcomes, including prescription drug use. A paper published in FY 2018[74] reported the long-term impact of PROSPER on a 'Prescription Drug Misuse Index' which measured overall prescription drug misuse and included three items addressing lifetime non-prescribed use of narcotics (e.g., Vicodin, Oxycontin, Percocet) and barbiturates. When study participants were re-assessed at age 19, they were 20 percent less likely to report having misused prescription narcotics. These and other related findings provide support for the potential public health impact of the PROSPER delivery system on reducing the initiation of substance use into emerging adulthood.

NIDA's portfolio of prescription drug abuse prevention is in the early stages of expansion, in response to the Nation's opioid crisis. As part of this expansion, several ongoing studies testing strategies and interventions are underway, but have yet to publish findings on effectiveness, though there have been qualitative reports of the possible impact of novel approaches to prevent prescription drug abuse. One such report, Young et al.,[75] demonstrated both the acceptability and potential benefit of an online social media intervention, Harnessing Online Peer Education (HOPE), to prevent addiction and overdose among individuals receiving opioid therapy for chronic non-cancer pain. Now that acceptability and potential benefit have been demonstrated, the researchers are moving forward with additional testing.

NIDA believes that as its prevention portfolio continues to make progress, the FY 2018 target will be fully met in FY 2019 as studies are completed and their findings published.

Treatment – Scientific Research Outcome-7.3

The FY 2018 target was met. Research testing the feasibility and efficacy of two technology-based strategies to improve SUD treatments and adherence was conducted in FY 2018. An additional byproduct of ongoing efforts in this area is a funding opportunity announcement designed to test technology-based treatments to increase adherence to FDA-approved

[74] Spoth R, Redmond C, Shin C, Greenberg MT, Feinberg ME, Trudeau L. PROSPER delivery of universal preventive interventions with young adolescents: long-term effects on emerging adult substance misuse and associated risk behaviors. Psychol Med. 2017;47(13):2246-2259. doi: 10.1017/S0033291717000691.
[75] Young SD, Heinzerling K. The Harnessing Online Peer Education (HOPE) Intervention for Reducing Prescription Drug Abuse: A Qualitative Study. J Subst Use. 2017;22(6):592-596. doi: 10.1080/14659891.2016.1271039. Epub 2017 Jan 31.

pharmacotherapies for SUD (https://grants.nih.gov/grants/guide/rfa-files/RFA-DA-19-015.html). Funding has been allocated to support 3-4 technology-based treatments.

The research findings leveraging technology-based treatments to address NIDA's research priority areas and the FY 2018 target are summarized below.

- *Approval of the ReSET and ReSET-O mobile application for SUD Treatment* – A major development in mHealth (mobile health) was the 2017 FDA approval of the reSET mobile app. ReSET – previously known as the Therapeutic Education System (TES) – is a mobile app that is approved for use in outpatient treatment for SUD related to cocaine, other stimulants, cannabis, and alcohol. This treatment tool was created through NIDA's behavior-therapy development program and validated through a major nationwide multi-site trial conducted in the NIDA Clinical Trials Network (CTN) program. In the clinical trial, the 12-week abstinence rate from drugs and alcohol for users of the app was 40 percent, more than twice the abstinence rate for individuals who received standard care such as medication-assisted treatment with buprenorphine (18 percent). Pear Therapeutics, Inc. acquired the right to rebrand TES as reSET and used the CTN trial results as pivotal evidence to gain approval from the FDA as the first prescription digital therapeutic to improve clinical outcomes in a disease.

  The reSET app was not approved for treating OUD, but with a Small Business Innovation Research grant from NIDA in FY 2018, a new version of the app called reSET-O was developed and tested for use as an adjunct to buprenorphine and standard treatment for patients with OUD. reset-O, along with the evidence from the earlier CTN studies, was reviewed by FDA under a process known as Breakthrough Therapy Designation, which is designed to expedite the development and review of products that are intended to treat a serious condition and preliminary clinical evidence indicates that the products may demonstrate substantial improvement over available therapy. reSET-O was approved by the FDA on December 10, 2018.

  reSET-O delivers cognitive behavioral therapy, which aims to change behavior by changing an individual's cognitive processes. The app is composed of digital multimedia modules delivering validated cognitive behavioral therapy and contingency management to promote recovery from OUD. The app rewards users for continuing with therapy with various incentives, which can improve adherence. When adopted widely, evidence-based advances in digital therapeutics will broaden the spectrum of SUD treatment options, particularly in rural and underserved communities.

- *Web-Delivered CBT in Veterans with SUD and PTSD* – The primary aim of this study was to test a web-based self-management intervention based on cognitive behavioral therapy (CBT), targeting post-traumatic stress disorder (PTSD) symptoms and hazardous substance use in a group of symptomatic combat veterans enrolled in VA primary care. Veterans with PTSD/subthreshold PTSD and hazardous substance use were randomized to primary care treatment as usual (TAU; $n = 81$) or to TAU plus a web-based CBT intervention called Thinking Forward ($n = 81$). Thinking Forward consisted of 24 sections (approximately 20

minutes each), accessible over 12 weeks. Participants completed baseline and 4-, 8-, 12-, 16- and 24-week follow-up assessments. Three primary outcomes of PTSD, alcohol and other drug use, and quality of life were examined. Significant treatment effects were found for heavy drinking, but not for PTSD symptoms or quality of life. The effect of the intervention on heavy drinking was mediated by intervening increases in coping, social support, self-efficacy, and hope for the future. These results demonstrate the promise of a web-based, self-management intervention for difficult-to-engage OEF (Operation Enduring Freedom) and OIF (Operation Iraqi Freedom) veterans with behavioral health and substance use concerns.[76]

National Institute on Alcohol Abuse and Alcoholism		
Selected Measures of Performance	**FY 2018 Target**	**FY 2018 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 substance use disorders and their consequences in underage populations.	Develop and/or implement additional preventive interventions to address underage alcohol use among specific underserved populations (i.e., American Indian, Alaska Native).	Researchers developed and evaluated the effects of combined individual- and community-level interventions to reduce underage drinking by Native American youth on rural California Indian reservations.
» Scientific Research Outcome-8.7: By 2018, identify three effective system interventions generating the implementation, sustainability and ongoing improvement of research-tested interventions across health care systems.	Disseminate findings from studies evaluating the effectiveness of alcohol screening and brief intervention.	Investigators published research findings from an evaluation of NIAAA's Youth Guide, and NIAAA staff disseminated information about studies evaluating the effectiveness of alcohol screening and brief intervention.

[76] Acosta et al. (2017). Web-Delivered CBT Reduces Heavy Drinking in OEF-OIF Veterans in Primary Care with Symptomatic Substance Use and PTSD. *Behavior Therapy, 42(2), 262-276.*

Prevention – Scientific Research Outcome-5.15

The FY 2018 target was met. Researchers supported by NIAAA developed and evaluated the effects of combining individual- and community-level interventions to reduce underage drinking by American Indian youth living on rural California reservations.

In the individual-level intervention, eligible youth aged 13-20 years were assigned to receive either a culturally-tailored brief motivational interviewing intervention (a type of therapist-delivered counseling strategy for changing behavior) or an educational intervention that provided information about the consequences of drinking. Participation in either the motivational interviewing or educational intervention was associated with significant reductions in drinking and problem behaviors when assessed at a six-month follow up appointment.

The community-level intervention included a "recognition and reminder" program wherein shoppers aged 21 or older who posed as minors attempted to purchase alcoholic beverages from convenience stores on or near the reservations assigned to the intervention. Clerks who asked for identification were rewarded with gift cards and congratulatory letters; those who did not were reminded of the law regarding sales to minors. The community intervention also included outreach activities to raise awareness about the risks of underage drinking and to mobilize community support for the interventions.

To evaluate the impact of the overall intervention program, the researchers analyzed data from the California Healthy Kids Survey, specifically data that was collected from ninth- and eleventh-grade American Indian and non-American-Indian students who attended schools in the intervention area. This data was compared to survey data collected from American Indian students living outside the intervention area. Among current drinkers, researchers found significant reductions in the frequency of past-month alcohol use and heavy alcohol use (defined as drinking five or more drinks on an occasion within the past 30 days) in American Indian youth exposed to the combined interventions relative to the comparison groups.[77]

Treatment – Scientific Research Outcome-8.7

The FY 2018 target was met. NIAAA-supported investigators published the results of a study to evaluate NIAAA's *Alcohol Screening and Brief Intervention for Youth: A Practitioner's Guide*. The study, one of six NIAAA-funded studies to evaluate the *Guide* independently, validated the *Guide's* utility in appropriately identifying youth at risk for AUD in primary care clinics serving racially and ethnically diverse patients. In the study, the researchers performed alcohol screening of youth aged 12-18 years and used statistical analyses to determine the optimal drinking threshold (number of reported days of drinking in the past year) for identifying those with AUD. The thresholds found varied by age and grade in school and were consistent with the

[77] Moore RS, Gilder DA, Grube JW, Lee JP, Geisler JA, Friese B, Calac DJ, Finan LJ, Ehlers CL. Prevention of Underage Drinking on California Indian Reservations Using Individual- and Community-Level Approaches. Am J Public Health. 2018 Aug;108(8):1035-1041. Epub 2018 Jun 21.

risk thresholds presented in the *Guide*, with the exception of 18-year-olds for whom a lower drinking threshold was recommended.[78]

In FY 2018, NIAAA staff disseminated information about studies evaluating the effectiveness of alcohol screening and brief intervention to the public. For example, findings from youth alcohol screening and brief intervention studies were disseminated in presentations to the Community Anti-Drug Coalitions of America's National Leadership Forum and its Mid-Year Training Institute and to the Institute for Public Strategies.

[78] Parast L, Meredith LS, Stein BD, Shadel WG, D'Amico EJ. Identifying adolescents with alcohol use disorder: Optimal screening using the National Institute on Alcohol Abuse and Alcoholism screening guide. Psychol Addict Behav. 2018 Aug;32(5):508-516.