RESOURCE SUMMARY

Drug Control Program
Department of Health and Human Services
NATIONAL INSTITUTES OF HEALTH (NIH)[1]

(Dollars in millions)

	Budget Authority		
	FY 2023 Final[2]	FY 2024 CR[3]	FY 2025 Request
Drug Resources by Function			
Research and Development: Prevention	$492.167	$492.009	$498.300
Research and Development: Harm Reduction	$187.960	$187.730	$190.253
Research and Development: Treatment	$954.055	$954.100	$951.443
Research and Development: Recovery	$104.792	$104.301	$104.246
Total, Drug Resources by Function	**$1,738.974**	**$1,738.140**	**$1,744.241**
Drug Resources by Decision Unit			
National Institute on Alcohol Effects and Alcohol-Associated Disorders (NIAAA)[4]			
Research and Development: Prevention	$64.682	$64.542	$64.930
Research and Development: Treatment	$10.927	$10.903	$10.969
Total, NIAAA	**$75.609**	**$75.445**	**$75.898**
National Institute on Drugs and Addiction (NIDA)[4]			
Research and Development: Prevention	$427.485	$427.467	$433.370
Research and Development: Harm Reduction	$187.960	$187.730	$190.253
Research and Development: Treatment	$943.128	$943.197	$940.474
Research and Development: Recovery	$104.792	$104.301	$104.246
Total, NIDA	**$1,663.365**	**$1,662.695**	**$1,668.343**
Total, Drug Resources by Decision Unit	**$1,738.974**	**$1,738.140**	**$1,744.241**
Drug Resources Personnel Summary			
Total FTEs (direct only)	419	445	470
Drug Resources as a Percent of Budget			
Total Agency Discretionary Budget (in Billions)[5]	$46.125	$45.447	$46.390
Drug Resources Percentage	3.77%	3.82%	3.76%

[1] Detail in this document may not sum to the subtotals and totals due to rounding.
[2] FY 2023 funding levels include HIV/AIDS transfers.
[3] FY 2024 funding levels cited in this document are based on the Continuing Resolution in effect at the time of budget preparation (Public Law 118-35) and do not include HIV/AIDS transfers.
[4] The FY 2025 President's Budget proposes to rename the National Institute on Drug Abuse to the National Institute on Drugs and Addiction and to rename the National Institute on Alcohol Abuse and Alcoholism to the National Institute on Alcohol Effects and Alcohol-Associated Disorders.
[5] Excludes funding for Advanced Research Projects Agency for Health.

PROGRAM SUMMARY

MISSION

The National Institute on Drugs and Addiction (NIDA) and the National Institute on Alcohol Effects and Alcohol-Associated Disorders (NIAAA), 2 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.[489]

NIDA is the lead federal agency supporting scientific research on drug use and addiction, with the mission to apply that knowledge to improve individual and public health. NIDA supports and conducts basic and clinical research on drug use (including nicotine), addiction, overdose, and the neurobiological, behavioral, and social factors that influence drug use patterns and outcomes. 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 overdose, enhance public awareness of addiction as a brain disorder, and reduce stigma toward people with SUD.

In 2022, more than 110,000 Americans died from drug overdoses, driven in large part by synthetic opioids, stimulants, and combination drug use. While these are sobering developments, NIDA-funded research has led to life-saving treatments for SUD. For example, NIDA supported development of the first naloxone nasal spray, approved by the Food and Drug Administration (FDA) in 2015 as an effective medication to reverse opioid overdose. More recent NIDA investments helped lead to a nasal spray formulation of nalmefene, a longer-lasting opioid overdose medication, which received FDA approval in 2023. NIDA's research also has helped establish the safety and efficacy of medications that target the body's opioid signaling pathways to treat opioid use disorder (OUD).

NIDA continues to lead research advances toward additional, wider-reaching therapies for OUD and other types of SUD, and toward primary prevention of harmful substance use. The Institute is also increasing its research investments in harm reduction approaches such as community naloxone distribution, syringe services programs, and drug checking tools; and in recovery services such as residential and school-based programs. Importantly, NIDA also funds a variety of training and career development programs to support an addiction science workforce cross-trained in state-of-the-art disciplines such as data science and artificial intelligence (AI). NIDA also supports a growing number of research programs to leverage AI for understanding addiction, such as programs to characterize how neuronal ensembles encode the rewarding effects of addictive substances and to help identify potential targets for new SUD medications.

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 (AUD), across the lifespan. A major priority within NIAAA's mission is research on the prevention and treatment of underage drinking and its harmful consequences.

[489] The FY 2025 President's Budget proposes to rename the National Institute on Drug Abuse to the National Institute on Drugs and Addiction and to rename the National Institute on Alcohol Abuse and Alcoholism to the National Institute on Alcohol Effects and Alcohol-Associated Disorders.

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, 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.

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 estimates for the drug control budget 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 2025 Request for drug-related activities at NIH is $1,744.2 million ($1,668.3 million for NIDA and $75.9 million for NIAAA), $6.1 million above the FY 2024 CR level.

National Institute on Drugs and Addiction
FY 2025 Request: $1,668.3 million
($5.6 million above the FY 2024 CR level)

According to provisional data through March 2023, more than 110,000 Americans are dying from drug overdoses each year. While there are effective treatments that could have prevented many of these deaths, delivering these treatments remains a challenge. Of the 46 million people who had SUD in 2021, only about 6 percent received any treatment.[490] Another challenge is that existing treatments do not work for all people or all types of SUD; in particular, there is a need for effective medications to reduce stimulant use, which plays an increasing role in overdose deaths. Overall, these data speak to the persistent need to improve and disseminate evidence-based treatments for SUD and overdose, and to prevent SUD and harmful substance use from occurring in the first place. To that end, in the coming years, NIDA will strengthen its research investments in prevention, treatment, harm reduction, and recovery services related to substance use, in alignment with the priorities of the Office of National Drug Control Policy and with additional funding made available through the NIH Helping to End Addiction Long-term® (HEAL) Initiative.

In the prevention area, NIDA will continue working to understand risk and protective factors for substance misuse and SUD, which will enable more targeted and effective prevention programs. Research shows that adverse early childhood experiences are associated with early substance misuse, which may in turn alter brain development in ways that increase the risk of SUD in adulthood.[491] Yet, much remains to be learned about how a vast constellation of early-life experiences, combined with a person's genetic makeup, affects vulnerability to SUD and other psychiatric disorders. Led by NIDA, NIAAA, and the National Cancer Institute, the Adolescent Brain Cognitive Development (ABCD) Study is collecting brain imaging, genetic, and environmental data from more than 12,000 children aged 9-10 and following them through adulthood to help fill this knowledge gap. More recently, with funding from various Institutes and the HEAL Initiative®, the HEALthy Brain and Child Development (HBCD) Study was launched to complement the ABCD study by following brain development in thousands of children from birth through their first decade of life.

In the treatment area, it is critical to improve the reach of existing evidence-based treatments for SUD, such as medications for opioid use disorder (MOUD) including methadone, buprenorphine, and naltrexone. While MOUD can reduce opioid craving, use, and risk of overdose, they are vastly under-prescribed, especially among people of color.[492] NIDA-funded research has helped identify barriers to MOUD—such as lack of integration between primary

[490] samhsa.gov/data/release/2022-national-survey-drug-use-and-health-nsduh-releases
[491] pubmed.ncbi.nlm.nih.gov/29690790/
[492] pubmed.ncbi.nlm.nih.gov/31066881; cdc.gov/mmwr/volumes/71/wr/mm7129e2.htm

care and specialized addiction services—and is investigating approaches to overcome them and improve MOUD access. At the same time, saving lives from overdose will also require novel medications. MOUD may be less effective in treating addiction to fentanyl (which is 100 times stronger than morphine)[493] and there are no effective medications to reduce stimulant use, which is now implicated in 50 times as many fentanyl-related deaths as it was in 2010.[494] For this reason, NIDA continues to support development of novel treatments, including long-acting drug formulations, neuromodulation therapies, immunotherapies, and sequestrants designed to stop drugs from entering the brain. Since September 2019, NIDA-supported research has led to more than 50 Investigational New Drug applications and 2 Investigational Device Exemptions submitted to the FDA for evaluation in clinical trials.

NIDA also prioritizes research in harm reduction, which aims to reduce the risk of overdose and other drug-related harms—including transmission of HIV and hepatitis C virus, and risk of infections that can damage the heart. Harm reduction approaches such as syringe service programs and community naloxone distribution have been shown to reduce morbidity and mortality from substance use; drug checking tools can help people detect adulterants in drugs and take safety precautions.[495] Yet, because most harm reduction studies have focused on urban areas hit hard by the opioid crisis, there is a need to investigate these approaches in rural areas and to target unique harms from stimulants. With HEAL Initiative funding in FY 2022, NIDA launched a new research network that focuses on testing new harm reduction strategies, evaluating new ways to deliver existing strategies, and reaching underserved populations. In addition to opioids, the network is examining harm reduction strategies related to other drugs, including stimulants and xylazine—an increasingly common adulterant in fentanyl that the Administration has designated as an emerging drug threat. The network is also funding an observational study of overdose prevention centers, which allow people to consume pre-obtained drugs under the supervision of staff who are trained in addiction and overdose treatment.

Because drug combinations play an increasing role in overdose deaths, NIDA is leading several research efforts to better understand drivers for polysubstance use and to develop multi-pronged effective interventions for it. For example, a HEAL-funded program supports research to define polysubstance use patterns and outcomes, and to improve their prevention and treatment. One project is examining how changes in housing status and other factors affect patterns of combined fentanyl and stimulant use among people experiencing homelessness. Clinical trials funded through the program will investigate interventions for co-use of opioids and stimulants. For example, two trials will focus on contingency management, which typically provides small financial incentives for abstinence or treatment attendance and is the only intervention proven to reduce stimulant use. The trials will examine whether smartphone-based contingency management can be integrated into MOUD treatment programs to reduce polysubstance use and improve MOUD adherence.

Finally, given that addiction is a chronic relapsing disorder, NIDA is prioritizing research to identify best practices in addiction recovery and relapse prevention. There are a variety of recovery service models—including peer-based mutual aid groups, recovery housing, and youth

[493] pubmed.ncbi.nlm.nih.gov/36055727
[494] pubmed.ncbi.nlm.nih.gov/37705148
[495] pubmed.ncbi.nlm.nih.gov/34686281; pubmed.ncbi.nlm.nih.gov/28061909; pubmed.ncbi.nlm.nih.gov/35255392

programs—but there is little evidence regarding which kind of program works best for different people. Moreover, many such programs focus on short-term medical treatments and may lack support for participants to receive long-term MOUD.[496] In 2020, NIDA established a recovery research networks program to develop tools, resources, and training to grow this area of research. With additional support from the HEAL Initiative®, this program has expanded and is testing new and existing recovery models through clinical trials.

NIDA's research efforts are organized into the following programmatic areas: Neuroscience and Behavior; Epidemiology, Services and Prevention Research; Therapeutics and Medical Consequences; the NIDA Clinical Trials Network; Translational Initiatives and Program Innovations; HEAL Initiative® programs; Intramural Research Program (IRP); and Research Management and Support (RMS). Dollars budgeted to the HEAL Initiative® for the purpose of opioid research are used to supplement base funding for opioid and pain research that are included within other NIDA program areas. Funding for the HEAL Initiative® in NIDA will remain equal to the FY 2024 CR level.

Division of Neuroscience and Behavior
FY 2025 Request: $532.2 million
($44,059 below the FY 2024 CR level)

NIDA's Division of Neuroscience and Behavior (DNB) supports research to understand the biological mechanisms that underlie drug use and addiction, and to inform the development of novel prevention and treatment strategies for SUD. This includes identifying the effects of illicit drugs on brain structure and function throughout the lifespan; and how genes, the environment, and other factors such as sex and gender influence the risk of SUD and its outcomes. DNB also supports research on pharmacology of drugs with addiction potential; data science; foundations of neuromodulation technology; and technology that enables study of the living brain from cells to circuits to networks.

A recent study exemplifies DNB support for research on the genetics of addiction. In that study, researchers combed through genomic data from over 1 million people, including ABCD study participants, and found nearly 20 gene variants associated with SUD, regardless of the substance involved. The researchers then developed a genetic risk score that was able to discern between healthy individuals and people with an SUD diagnosis, with the highest accuracy for those who had polysubstance use disorder.[497] Although genetic approaches like this cannot fully predict who will develop SUD, they could someday aid in SUD risk assessment, lead to more personalized interventions, and inform potential targets for new SUD therapeutics.

Because people who use drugs are at higher risk for HIV infection, DNB also supports fundamental research on HIV. With funding through a data science program, one recent study investigated how HIV manages to persist in some people despite antiretroviral therapy, and found that HIV-infected cells sometimes multiply and continue producing the virus, acting as a viral reservoir.[498] With funding through the NIDA Avante-Garde program, another study

[496] pubmed.ncbi.nlm.nih.gov/34700201
[497] pubmed.ncbi.nlm.nih.gov/37250466
[498] pubmed.ncbi.nlm.nih.gov/35320704

identified genes that are down-regulated during HIV-related brain inflammation, suggesting a potential early step in HIV-associated neurocognitive disorder, which affects up to half of people with HIV.[499] Both of these programs were renewed in FY 2023.

DNB also supports research focused on the intersection of SUD and sleep disorders, which have a strong bidirectional association. Substance use can lead to sleep disturbances, and sleep disturbances can increase the risk of drug withdrawal, craving, and relapse. In fact, a recent DNB-funded study found that SUD and sleep disturbances are linked at a molecular level; compared to healthy individuals, people with OUD had unique daily rhythmic patterns of gene activity in the brain, specifically in brain regions involved in addiction.[500] In FY 2023, DNB announced new funding to explore the mechanisms that link sleep, circadian rhythms, and SUDs.

Division of Epidemiology, Services, and Prevention Research
FY 2025 Request: $391.1 million
($32,380 below the FY 2024 CR level)

NIDA's Division of Epidemiology, Services, and Prevention Research (DESPR) supports studies to understand and address the interactions between individuals and environments that contribute to drug use, addiction, and related health problems. DESPR supports a broad portfolio that informs evidence-based strategies to support prevention, harm reduction, treatment, and recovery for people at risk or with SUDs. This includes two nationally representative studies—the Monitoring the Future (MTF) survey, which measures substance use and related attitudes among adolescents, and the Population Assessment of Tobacco and Health (PATH) Study, which focuses on tobacco use, attitudes, and health outcomes of people aged 12 and older.

DESPR's research is shedding light on e-cigarette use among youth and its relation to smoking and other substance use. For example, many studies suggest that e-cigarette use, or vaping, in adolescence is a gateway to smoking later. New PATH data suggest that vaping also entrenches smoking among teens who have already tried it.[501] Meanwhile, MTF has found that compared to teens who do not use nicotine, odds of cannabis use are higher among those who vape nicotine—about 40 times higher among those who both vape and smoke nicotine.[502] Even accounting for smoking and cannabis use, youth who use e-cigarettes are more likely to experience wheezing, bronchitis, and shortness of breath.[503] These findings highlight the need for interventions to address the health risks of vaping during youth.

DESPR also supports the ABCD study, which is advancing knowledge about the impacts of social determinants of health on brain development. In one analysis, researchers found that Black children ages 9-10 faced greater adversity than white children—including lower parental education and income, living in disadvantaged neighborhoods, and more exposure to trauma such as vehicle accidents and assault—and that this adversity was associated with differences in brain structure. When the differences in adversity were controlled statistically, the brain

[499] pubmed.ncbi.nlm.nih.gov/36525955
[500] pubmed.ncbi.nlm.nih.gov/35347109
[501] pubmed.ncbi.nlm.nih.gov/37072167
[502] pubmed.ncbi.nlm.nih.gov/37198725
[503] pubmed.ncbi.nlm.nih.gov/37582630

differences largely evaporated.[504] Another analysis found that compared to children from high-income families, those from low-income families were likely to have structural brain differences as well as symptoms of anxiety and depression. More importantly, those disparities narrowed significantly among children living in states with robust antipoverty programs.[505] These studies provide real-world evidence that intervening on social determinants of health can help ensure healthy brain development.

DESPR also supports implementation science to identify and address gaps in translating evidence-based interventions into practice. For instance, a study of national Medicare data found that adults who received buprenorphine (BUP) following an overdose had a 62 percent lower risk of fatal overdose over the next year. However, fewer than 1 in 20 patients received it, and most recipients waited more than 30 days.[506] DESPR is funding research on innovative solutions to this challenge, such as collaborative care models that bring together BUP providers and pharmacists. A pilot trial in which the pharmacist handled BUP management including adjustments for withdrawal, in consultation with the provider, found that this model significantly boosts retention in treatment compared to usual provider-based care.[507]

Division of Therapeutics and Medical Consequences
FY 2025 Request: $109.8 million
($9,095 below the FY 2024 CR level)

NIDA's Division of Therapeutics and Medical Consequences (DTMC) supports research to evaluate the safety and efficacy of pharmacotherapies, behavioral interventions, and medical devices to prevent and treat SUDs and drug overdose. 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.

DTMC supports research on a diverse array of pharmacotherapies, including repurposing of drugs used for other conditions and developing new compounds with novel molecular targets. For example, diabetes drugs like semaglutide, which are based on the hormone glucagon-like peptide-1 (GLP-1), may hold potential for treating SUD. GLP-1 analogs help control food cravings, and anecdotal reports from people taking these drugs for diabetes or weight loss suggest they might help reduce drug cravings, too. NIDA is supporting preclinical studies of GLP-1 analogs for alcohol and opioid addiction and a small clinical trial for smoking cessation. While stimulants generally work by increasing dopamine signals in the brain, methamphetamine and cocaine use disorder (MtUD and CcUD) also involve changes in glutamate signaling. A phase I clinical trial is underway to investigate treating CcUD with a small-molecule inhibitor of the glutamate receptor mGluR5.

DTMC also supports research on therapies involving psychedelic and dissociative drugs. For example, a large randomized controlled trial is investigating whether psilocybin in combination

[504] pubmed.ncbi.nlm.nih.gov/36722118
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[506] pubmed.ncbi.nlm.nih.gov/36906496
[507] pubmed.ncbi.nlm.nih.gov/36630629

with psychotherapy can improve smoking cessation. Other trials are investigating ketamine-assisted therapy for CcUD and MtUD, and as a bridge to start MOUD.

Another focus of DTMC's portfolio is neuromodulation, which involves stimulating the brain to reset the circuitry underlying brain disorders. Deep brain stimulation— which involves inserting electrodes into the brain and is FDA-approved for treating Parkinson's disease and epilepsy—is in clinical trials for refractory OUD. DTMC also supports research on non-invasive neuromodulation therapies, including low-intensity focused ultrasound and transcranial magnetic stimulation (TMS). TMS is FDA-approved as an adjunct therapy for smoking cessation, in part due to NIDA-funded research, and is now being investigated for other SUDs.

DTMC has a growing portfolio of research to address OUD and other co-occurring mental health disorders. For example, 40-60 percent of people with OUD suffer from chronic pain and depression, which can increase their risk of opioid misuse. To improve health outcomes for these patients, researchers are evaluating an approach in which primary providers and behavioral health specialists provide collaborative care. In FY 2023, DTMC announced new funding to develop pharmacotherapies, behavioral therapies, and devices for co-occurring OUD and mental illness.

Center for Clinical Trials Network
FY 2025 Request: $35.7 million
($2,955 below the FY 2024 CR level)

The Center for Clinical Trials Network (CCTN) manages NIDA's National Drug Abuse Treatment Clinical Trials Network (CTN), which provides a collaborative framework for healthcare providers, researchers, and patients to conduct clinical trials on the safety and efficacy of SUD interventions. The CTN includes 16 research nodes across the country and more than 240 community-anchored treatment programs. This unique structure enables the CTN to investigate behavioral, pharmacological, and integrated therapies across diverse settings and populations, and to develop implementation strategies that help bring research results into practice. Active protocols focus on a variety of areas, including primary prevention of SUD; increasing patient access and adherence to MOUD, especially in rural and underserved populations; evaluating potential medications for stimulant use disorder; and addressing stigma and other barriers to SUD treatment. Some examples are highlighted below.

Because adolescence is a critical time for susceptibility to SUD and responsiveness to interventions, the CTN prioritizes development and testing of screening tools tailored to this age range. A recent study tested three brief SUD screening tools in a large, diverse adolescent population and found that they performed well compared to an in-depth diagnostic interview.[508] Through the ongoing Subthreshold OUD Prevention (STOP) trial, the CTN seeks to determine if screening and intervention for low-severity OUD in primary care can reduce OUD progression and overdose risk.

The CTN is also testing strategies to identify OUD patients and start MOUD treatment in emergency departments (EDs)—at the frontline of the overdose epidemic. In one approach, the

[508] pubmed.ncbi.nlm.nih.gov/37213103

CTN designated champions to educate ED and community clinicians on BUP treatment and how to overcome stigma and other barriers to its use. Implementing this approach for six months led to higher rates of standard oral BUP initiation in the ED and referral to ongoing OUD treatment in the community, and was feasible even in rural and low-resource EDs.[509] The CTN is now conducting a similar implementation trial, called ED-INNOVATION, to compare initiation with oral BUP vs. a longer-lasting injectable form, which could help keep patients stable while providers address any barriers to referral.

The CTN also recently leveraged the ED-INNOVATION trial to address concerns about precipitated withdrawal—debilitating withdrawal symptoms that can occur within hours of receiving BUP. For patients who use potent opioids such as fentanyl, some clinicians prescribe BUP at lower doses to avoid precipitated withdrawal, but that practice may not adequately curb opioid craving and subsequent relapse. An interim analysis of trial data found that while most patients had used fentanyl, only one percent experienced precipitated withdrawal after BUP initiation, similar to rates seen for patients using less potent opioids.[510]

The CTN is developing and evaluating potential treatments for MtUD and CcUD, for which there are no FDA-approved therapies. A recent CTN trial found that a combination of injectable naltrexone and oral bupropion, a commonly prescribed medication for depression and nicotine cessation, was effective in helping people with MtUD reduce their use. A secondary analysis focused on men who have sex with men—who are at higher risk for MtUD and harmful outcomes, including HIV infection—and found they had higher response rates to this treatment than heterosexual men.[511] Two other CTN trials will examine whether patients with MtUD or CcUD and opioid co-use will benefit from injectable naltrexone and monthly injectable BUP.

Office of Translational Initiatives and Program Innovations
FY 2025 Request: $43.2 million
($3,580 below the FY 2024 CR level)

NIDA's Office of Translational Initiatives and Program Innovations (OTIPI) translates discoveries in addiction research into candidate health applications. OTIPI supports translational research through NIDA's Small Business Innovation Research/Technology Transfer (SBIR/STTR) programs, as well as Challenge competitions. OTIPI also develops training programs that help scientists move their discoveries from the lab to the real world.

In FY 2023, OTIPI issued a Primary Care Challenge competition to propose models for how primary care providers can more effectively identify people at risk for substance use and deliver interventions to reduce this risk. Three winning projects were selected. One project will focus on recently incarcerated adults, who are at high risk for drug use and overdose, with community health workers leading patient outreach, substance use screening, and linkages to preventive care. Another project will screen teens with a mental health diagnosis for substance use risk, and the third will use AI to identify high-risk pre-teens based on their electronic health records.

[509] pubmed.ncbi.nlm.nih.gov/37017967; pubmed.ncbi.nlm.nih.gov/37140493
[510] pubmed.ncbi.nlm.nih.gov/36995717
[511] pubmed.ncbi.nlm.nih.gov/33497547; pubmed.ncbi.nlm.nih.gov/37478502

OTIPI supports medical device development, including devices to treat neonatal opioid withdrawal syndrome (NOWS), which can affect infants exposed to opioids in the womb. For example, an SBIR project has developed a vibrating crib mattress to soothe infants with NOWS. In a large trial, infants who slept on this mattress needed less medication to manage withdrawal symptoms and left the hospital three days earlier on average than infants who received only usual care.[512] Another SBIR project focuses on treating NOWS by retooling an FDA-approved technology for opioid withdrawal in adults, called transcutaneous auricular neurostimulation. This technology uses an earpiece to painlessly stimulate nerves near the ears, transmitting signals that are believed to cause release of the brain's own endogenous opioids and help control withdrawal. A safety trial found that this technology was well-tolerated by infants with NOWS, and efficacy trials are planned.[513]

OTIPI also supports development of SUD treatment modalities that are powered by AI. One example is Woebot, a conversational smartphone app originally designed to help people struggling with depression. SBIR-funded researchers have modified Woebot to help people with SUD track their mood and drug cravings, and to provide coaching in behavior change. In a pilot study, after using Woebot-SUD for eight weeks, participants reported increased ability to resist craving and had improved scores on SUD screening tests.[514] Results from a larger trial are expected soon. Other researchers are working on a wrist-worn device for MOUD patients that would record biometric data, including mobility and skin temperature; use AI to read those data for signs of opioid withdrawal or relapse; and alert providers so that they can adjust treatment.

OTIPI is also supporting the development of tools to remove barriers to methadone treatment for OUD, which is available only from federally regulated opioid treatment programs (OTPs). Continuing flexibilities implemented during the COVID-19 pandemic allow OTPs to dispense up to 28 days of take-home methadone for stable patients, but clinicians have significant discretion—and difficult decisions—regarding take-home doses for less stable patients. In a pilot study, an OTP in Washington enabled patients to submit video confirmation that they were using their take-home methadone as prescribed. Compared to regular OTP clients, pilot participants had more days of observed dosing and were more often approved for increased take-home doses.[515] Other researchers are developing a wearable biosensor to remotely monitor patients' adherence to their take-home methadone, and a new OTIPI-led program calls for further research on low-cost point-of-need approaches to lower barriers to SUD care.

NIH HEAL Initiative®
FY 2025 Request: $355.3 million[516]
(Equal to the FY 2024 CR level)

The HEAL Initiative, which is co-led by NIDA and the National Institute of Neurological Disorders and Stroke (NINDS), aims to accelerate scientific solutions to the opioid crisis. One of its major focus areas has been research on how to implement effective prevention and

[512] pubmed.ncbi.nlm.nih.gov/37184872
[513] pubmed.ncbi.nlm.nih.gov/33762918
[514] pubmed.ncbi.nlm.nih.gov/33755028
[515] pubmed.ncbi.nlm.nih.gov/36215911
[516] Includes funding for RMS to support the HEAL Initiative.

treatment interventions for OUD and overdose across healthcare and non-healthcare settings. The HEALing Communities Study (HCS), led by NIDA in collaboration with the Substance Abuse and Mental Health Services Administration (SAMHSA), is testing the impact of integrating evidence-based interventions for OUD and overdose in 67 communities spanning 4 states. HCS communities have deployed over 1,000 evidence-based strategies to expand access to MOUD, implement overdose education and naloxone distribution, and reduce high risk prescribing. Lessons learned from the HCS have been captured in two practice guides to help providers, public health agencies, and others assemble community coalitions and implement effective approaches to reduce overdose deaths.

The Justice Community Opioid Innovation Network (JCOIN) is studying approaches to improve evidence-based treatment for people with OUD in criminal-legal settings. JCOIN has found that MOUD access during incarceration not only saves lives but is also associated with 32 percent lower recidivism after release.[517] JCOIN recently disseminated a first-of-its-kind MOUD Budget Impact tool to helps jail and prison administrators estimate the cost of providing MOUD services.[518] NIDA plans to extend JCOIN through at least FY 2030, with a focus on research to scale up MOUD and other evidence-based interventions across justice settings and where they intersect with community-based treatment.

The HEAL Harm Reduction Research Network is developing and testing strategies to prevent overdose, transmission of HIV and hepatitis C virus, and other harms associated with drug use. Current projects are studying delivery of harm reduction services during emergency care, and via mobile vans and smartphones for hard-to-reach patients. The network is also examining the impact of state and local harm reduction policies. In the first study of its kind in the United States, the network is examining outcomes associated with overdose prevention centers that are operating in New York and Rhode Island.

With HEAL funding, NIDA's Recovery Research Networks are working to build an evidence base for effective recovery support services. While such services have strong foundations in the lived experiences of people with SUD, most have not been formally evaluated. These networks are engaging recovery service providers and people with lived experience in research to examine what types of recovery services work best for different people and to help link recovery services with established standards of care including MOUD.

A new HEAL program funded in FY 2023—Research to Foster an OUD Treatment System Patients Can Count On—is supporting four projects in which researchers are working with providers, patients, payors, and public health agencies to develop quality measures to improve patient outcomes in OTPs and other settings.

Intramural Research Program
FY 2025 Request: $120.9 million
($2.4 million above the FY 2024 CR level)

[517] pubmed.ncbi.nlm.nih.gov/35063323
[518] pubmed.ncbi.nlm.nih.gov/36880906; www.jcoinctc.org/resources/budget-impact-tool

The NIDA Intramural Research Program (IRP) conducts research to inform strategies for prevention and treatment of SUD and related health outcomes. The IRP portfolio includes research to elucidate the mechanisms underlying development of SUDs, evaluate potential new therapies, and identify and characterize emerging drugs such as synthetic opioids, stimulants, and cannabinoids.

IRP researchers who study how opioids affect brain and respiratory functions were able to pivot quickly to study the additive effects of xylazine. In preclinical studies, they found that fentanyl exposure causes respiratory suppression, which produces a rapid, robust decrease in oxygen flow to the brain, followed by a gradual rebound. Adding xylazine to fentanyl eliminated this rebound, prolonging the brain's oxygen deficit—which could contribute to the increasing involvement of xylazine in opioid overdose deaths.[519]

The IRP Designer Drug Research Unit focuses on emerging synthetic drugs with addiction potential, including stimulants called synthetic cathinones. Like other stimulants, cathinones increase dopamine levels at synapses, sometimes by blocking the activity of transporters that clean up excess dopamine. Illicit synthetic cathinones, also called "bath salts," can be extremely potent, with longer lasting effects than cocaine. IRP researchers found that this is due to unusually long-lasting inhibition of dopamine transporters.[520] These researchers are also investigating cathinone derivatives that act preferentially on serotonin transporters as an alternative to selective serotonin reuptake inhibitors (like Prozac) for depression and anxiety.[521]

IRP researchers also are examining the neurobiological basis for opioid withdrawal symptoms, which contribute to relapse risk. One recent study investigated brain pathways responsible for increased pain sensitivity (or hyperalgesia) during opioid withdrawal. Through a combination of brain imaging and chemogenetics—the use of designer drugs and receptors to control neuronal activity—researchers identified a cell type in the mouse brainstem that contributes to hyperalgesia (see cover image).[522] Future neuromodulation therapies or other approaches could target those cells to reduce hyperalgesia and relapse risk.

Other IRP researchers are studying the addiction potential of S-ketamine. While S-ketamine is FDA-approved for treating severe depression, it has addiction potential that is thought to occur through opioid signaling. IRP researchers with expertise in functional brain imaging partnered with other NIH researchers to investigate this idea. They found that in rats, S-ketamine acts on opioid receptors to stimulate activity in the nucleus accumbens—a brain region associated with addiction—and that self-administration of S-ketamine leads to opioid tolerance.[523] Those findings have implications for monitoring the safety of S-ketamine therapy—both its current use for depression and emergent uses for opioid and stimulant addiction.

[519] pubmed.ncbi.nlm.nih.gov/37340247
[520] pubmed.ncbi.nlm.nih.gov/36730201
[521] pubmed.ncbi.nlm.nih.gov/36352123
[522] pubmed.ncbi.nlm.nih.gov/35728954
[523] pubmed.ncbi.nlm.nih.gov/36841701

Research Management and Support
FY 2025 Request: $80.1 million[524]
($3.4 million above the FY 2024 CR level)

NIDA 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. Staff supported by NIDA's RMS budget also coordinate training and career development programs to sustain a talented, diverse workforce of addiction scientists. Other RMS functions include strategic planning, coordination, dissemination of latest research findings and funding opportunities, program evaluation, regulatory compliance, international coordination, and liaison with other Federal agencies, Congress, and the public. NIDA RMS funding also supports evidence-based education and outreach about substance use and addiction to inform public health policy, and to provide the public with timely, accessible, trustworthy information about drug research in English and Spanish.

National Institute on Alcohol Effects and Alcohol-Associated Disorders
FY 2025 Request: $75.9 million
($0.5 million above the FY 2024 CR level)

Although the rate of underage drinking in the United States has declined over the past several decades, alcohol remains the most widely used substance among youth. Binge drinking[525] and high intensity drinking[526] 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, alcohol use disorder (AUD), and other detrimental consequences. NIAAA supports a broad range of basic, translational, and clinical research to improve our understanding of the impact of alcohol exposure on adolescent health and to improve interventions for alcohol-related problems among youth in community and healthcare settings. NIAAA also disseminates information about evidence-based interventions through the development of resources for the public.

Basic research is key to informing the development of innovative prevention and treatment strategies for underage drinking. A key initiative within NIAAA's adolescent brain research portfolio is the National Consortium on Alcohol and Neurodevelopment in Adolescence (NCANDA), a multi-site longitudinal study to identify brain characteristics in humans that may predict alcohol misuse or occur because of adolescent alcohol exposure. Established in 2012, NCANDA investigators are now following the initial adolescent cohort into young adulthood and examining the sex-specific relationships between brain maturation, alcohol misuse, mental health, and sleep. Data from NCANDA, for example, has demonstrated that adolescent binge drinking is associated with accelerated decline of gray matter volume in the brain, with the most significant effects observed in the frontal regions that are important for executive functioning, such as performing complex tasks and decision-making. Using NCANDA data, a recent study

[524] Excludes funding for RMS to support the HEAL Initiative.
[525] 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.
[526] NIAAA defines high intensity drinking two or more times the gender-specific binge drinking thresholds.

showed that alcohol use in adolescence was negatively associated with the volumes of subcortical (deep) regions of the brain, including structures that are important in movement, learning, memory, emotion, and motivation and reward. Both males and females showed a negative association between alcohol use and volume of the hippocampus. However, in females alcohol use was negatively associated with the volumes of two additional regions (caudate and thalamus). These findings suggest a potential vulnerability to alcohol use in females based on brain structure and morphometry.[527]

Another major program within NIAAA's portfolio on adolescent brain research is the Neurobiology of Adolescent Drinking in Adulthood (NADIA) consortium to examine, using animal models, the mechanisms by which adolescent drinking leads to changes in brain structure and function that persist into adulthood. NADIA researchers recently tested the effects of chronic adolescent alcohol exposure on pain-related behavior and brain function. They found that chronic adolescent alcohol exposure caused an abnormally heightened sensitivity to pain during adolescence and into adulthood, even after abstinence, in males but not females. In addition, chronic adolescent alcohol exposure resulted in alterations in a pain-related brain neurocircuit in adult males, but not adult females. This study suggests that there are sex-dependent effects of chronic adolescent alcohol exposure on pain-related behaviors and neurocircuitry that persist into adulthood.[528] These results are important given previous research demonstrating that alcohol consumption and coping with pain are linked, and that chronic alcohol misuse increases pain sensitivity and makes pain worse over the long-term.

Prevention of underage drinking has long been one of NIAAA's top priorities. NIAAA's portfolio in this area 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. NIAAA also supports research to better understand trends in alcohol use among youth to improve interventions based on that knowledge. For example, researchers recently found that students who begin high-intensity drinking, defined as 10 or more drinks on a single occasion, by grade 11 instead of later on are more likely to have a higher average weekly alcohol consumption, a higher frequency of high-intensity drinking, and an increased risk for AUD at age 20 years.[529] These findings emphasize the importance of prevention strategies that specifically prevent or delay high-intensity drinking among young people. For college settings, NIAAA provides the College Alcohol Intervention Matrix (CollegeAIM), an online resource 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 also supports research to address alcohol misuse among young adults outside of college settings. In an ongoing clinical study, NIAAA-funded researchers are testing the efficacy of two intervention approaches for non-college emerging adults that report heavy drinking.[530] One approach is a combined multi-session brief alcohol intervention (BAI) with a Substance Free

[527] www.sciencedirect.com/science/article/pii/S1878929323000993?via%3Dihub
[528] pubmed.ncbi.nlm.nih.gov/37717844/
[529] pubmed.ncbi.nlm.nih.gov/36716022/
[530] reporter.nih.gov/search/VqssJkar4k68M5kN23V5Mw/project-details/10157726

Activity Session (SFAS) to reduce drinking. The SFAS attempts to increase engagement in goal-directed activities that might provide alternatives to alcohol use. It also provides tools to reduce stress and develop mood-enhancing behavioral substitutes to drinking (or substance use). The researchers are also testing a second intervention, Relaxation Training (RT), in combination with SFAS to determine if this intervention approach better addresses risk factors for alcohol misuse by enhancing wellness, managing stress, and increasing positive activities with the goal of increasing effectiveness of intervention and the potential for dissemination.

Prevention interventions tailored for underserved youth is another important area within NIAAA's prevention research portfolio. For example, NIAAA-funded researchers conducted a pilot study of the Chukka Auchaffi' Natana: the Weaving Healthy Families (WHF) Program, a culturally-informed, family-based program designed to promote parenting practices, family resilience, and wellness, and as a result, prevent substance misuse among Native American families.[531] The researchers found that participation in the WHF program was associated with improvements in parenting quality, family resilience, community resilience that have been shown to serve as primary factors against substance misuse.

Increasing implementation of alcohol screening and brief intervention in primary care and developing evidence-based behavioral therapies to reduce underage drinking is another priority area for NIAAA. For example, NIAAA developed the Alcohol Screening and Brief Intervention for Youth: A Practitioner's Guide to assist pediatric and adolescent health practitioners in identifying patients at risk for underage drinking and associated problems. This screening resource has been validated among youth in pediatric emergency room settings, school settings, primary care settings (including among racially and ethnically diverse youth), and among youth with chronic health conditions.

Equity

Equity is a vital consideration in NIDA and NIAAA efforts to support the objectives of the National Drug Control Strategy. Both NIDA and NIAAA support the NIH UNITE initiative that was established to identify and address structural racism within the NIH-supported and greater scientific community. Both Institutes are also part of NIH's broader efforts to advance health equity research by improving minority health, reducing health disparities, and removing barriers to advancing health disparities research, as well as the agency's efforts to expand, sustain, and promote scientific workforce diversity.

NIDA's Racial Equity Initiative (REI) aligns with NIH's UNITE Initiative by promoting racial equity in NIDA's workplace, workforce, and research portfolio. In FY 2022, the REI released a suite of nine funding opportunities that are supporting research and research training efforts focused on increasing equity in the addiction science community, addressing racial-ethnic health disparities in substance use and addiction outcomes, and understanding how structural racism affects the risk of substance use and SUD. With HEAL funding and in close partnership with other NIH Institutes, Centers, and Offices, NIDA and NINDS are also supporting a new program focused on American Indian, Alaska Native, and Native Hawaiian health called the Native Collective Research Effort to Enhance Wellness (N CREW). N CREW researchers will work in

[531] pubmed.ncbi.nlm.nih.gov/36710265/

partnership with Tribes and Native American-serving organizations to identify community-based priorities related to overdose, substance use, mental health, and pain in Native communities; collaborate in research toward culturally grounded interventions; and build local capacity as needed for this research. The initiative has the potential to slow the rate of overdose deaths in American Indian and Alaska Native communities, which is higher than for any other racial-ethnic group.[532]

NIAAA supports a range of efforts aimed at reducing health disparities and promoting health equity. One area of interest is the social determinants of health that influence the initiation of underage alcohol use. Underserved populations bear a greater burden of alcohol misuse and its adverse effects. Current studies are exploring factors that drive alcohol misuse—including sleep quality, adverse childhood experiences, and family or peer stress—among underserved adolescent populations. Understanding the social and environmental factors that influence alcohol misuse can inform targeted prevention approaches. NIAAA also supports the development of culturally adapted interventions to reduce underage drinking.

[532] www.cdc.gov/nchs/products/databriefs/db457.htm