DRUG CONTROL PROGRAMS

	Budget Authority (in Millions)		
	FY 2015 Final	FY 2016 Enacted	FY 2017 Request*
Drug Resources by Function			
Research and Development: Prevention	$400.462	$405.880	$405.880
Research and Development: Treatment	$674.767	$698.895	$698.985
Total Drug Resources by Function	**$1,075.229**	**$1,104.775**	**$1,104.775**
Drug Resources by Decision Unit			
National Institute on Drug Abuse	$1,015.695	$1,050.550	$1,050.550
National Institute on Alcohol Abuse and Alcoholism	$59.534	$54.225	$54.225
Total Drug Resources by Decision Unit	**$1,075.229**	**$1,104.775**	**$1,104.775**
Drug Resources Personnel Summary			
Total FTEs (direct only)	396	400	400
Drug Resources as a Percent of Budget			
Total Agency Budget (in Billions)	$30.3	$32.3	$33.1
Drug Resources Percentage	3.4%	3.4%	3.3%

*Includes mandatory financing.

Program Summary

MISSION

The National Institute of Drug Abuse (NIDA) and the National Institute on Alcohol Abuse and Alcoholism (NIAAA), two of the twenty-seven Institutes and Centers of the NIH, support the *Strategy*: NIDA, by funding research on the prevention and treatment of drug use, addiction, and its harmful consequences; and NIAAA, by funding research on the prevention and treatment of underage drinking and its harmful consequences.

The societal impact of substance misuse (alcohol, tobacco, illicit drugs, and nonmedical use of prescription drugs) in this country is daunting, exceeding $700 billion a year in health care, crime-related, and productivity losses. 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, NIDA will continue to build on science advances from our investments in genetics, neuroscience, pharmacotherapy, and behavioral and health services research that have led to innovative strategies for preventing and treating substance use disorders (SUDs) in this country and worldwide.

Studying drug use, 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; we are currently seeing the terrible results of a decades-long epidemic of prescription drug abuse that is leading to a rise in heroin use as well as new HIV and Hepatitis C outbreaks. A growing number of states are legalizing marijuana for medical or recreational use, producing natural experiments whose outcomes cannot yet be

predicted. New synthetic drugs as well as new delivery systems such as e-cigarettes are changing how people use drugs. On the bright side, healthcare reform and parity regulations are poised to deliver effective prevention and treatment interventions to larger numbers of Americans. NIDA is supporting research to address today's drug use-related challenges in several key areas, including supporting the Secretary of Health and Human Services to respond to opioid abuse and overdose; spearheading a landmark longitudinal study of adolescent substance use and brain development; studying the impact of the changing marijuana landscape; studying the impact of new synthetic drugs; and contributing to scientific and public understanding of the brain mechanisms underlying addiction.

Alcohol misuse has profound effects on the health and well-being of individuals, families, and communities, with substantial economic costs. Since its creation, NIAAA has led the national effort to define alcohol problems as medical in nature and address them using evidence-based findings. The research supported by the Institute has transformed understanding and treatment of alcohol misuse and its consequences, including alcohol use disorder (AUD). NIAAA is working to reduce the considerable burden of alcohol misuse for individuals at all stages of life by supporting: research on the neurobiological mechanisms underlying AUD and co-occurring disorders; the development of behavioral therapies and medications that promote recovery; studies on the consequences of alcohol misuse, including fetal alcohol spectrum disorders, effects on the developing adolescent brain, and tissue and organ damage; the development of strategies to prevent and intervene with the short- and long-term consequences of alcohol misuse; the translation and implementation of research findings into improved health care for individuals with AUD alone and with co-occurring conditions; and the dissemination of research-based information to health care providers, researchers, policy makers, and the public.

METHODOLOGY

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

The prevention and treatment components of NIAAA's underage drinking research program are scored 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 the development of AUD. It includes basic research, epidemiological studies, behavioral research, screening and intervention studies, and the development and testing of preventive interventions. NIAAA's methodology for estimating its portion of the national drug control is a two-step process. First, NIAAA identifies all of its underage drinking projects using the NIH's automated, electronic text mining system for research, condition, and disease categorization (RCDC). Once all underage drinking projects are identified through this process, NIAAA conducts a manual review of the project listing and identifies only those projects and amounts that are relevant to prevention and treatment. This is used to generate the NIAAA drug control budget estimate.

BUDGET SUMMARY

In FY 2017, NIH requests $1,104.775 million for drug control activities, flat to the FY 2016 enacted level.

NIH-supported research has 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 drug 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 of therapeutic interventions to treat SUDs, including medications, biologics, 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. 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, thereby enhancing the public health impact of NIH-supported research.

National Institute on Drug Abuse
FY 2017 Request: $1,050.6 million
(Flat to the FY 2016 enacted level)
NIDA's efforts consist of Epidemiology, Services, and Prevention Research, Basic and Clinical Neuroscience Research, Therapeutic and Medical Consequences, Clinical Trials Network, the Intramural Research Program, and Research Management and Support.

Epidemiology, Services, and Prevention Research
FY 2017 Request: $323.4 million
($0.8 million below the FY 2016 enacted level)
This portfolio supports integrated approaches to understand and develop strategies to address the interactions between individuals and environments that contribute to drug abuse-related problems. With a focus on research to inform public health, the program includes large surveys – such as the annual Monitoring the Future survey, which tracks drug use and related attitudes among teens – and surveillance networks to monitor drug-related issues and trends locally and nationally. NIDA's National Drug Early Warning System (NDEWS) monitors emerging trends related to illicit drug use including designer synthetic compounds and heroin. NDEWS generates critical information about new drug trends in specific locations around the country so that rapid, informed, and effective public health responses can be developed and implemented precisely where and when they are needed. NIDA also supports research related to treatment of SUDs in the criminal justice system, including studies that pertain to the implementation of medication-assisted treatment (MAT) and the seek, test, treat, and retain (STTR) model of care for people with SUDs at risk for HIV. Program efforts also guide development of preventive interventions for a variety of populations; as well as research to optimize implementation and service delivery in real-world settings. The program also includes research to better understand the impact of policy changes related to substance use including implementation of health reform and parity regulations and changes in state policies related to marijuana. Specifically, current research is examining the impact of health reform on access to quality treatment for persons with

SUDs, as well as associations between changes in State marijuana policies and trends in use, harm perception, health consequences including trauma and car crashes, and educational outcomes, particularly for adolescents and young adults. Such knowledge can be then used to inform policy and to improve prevention and treatment interventions.

Basic and Clinical Neuroscience Research
FY 2017 Request: $350.0 million
($0.9 million below the FY 2016 enacted level)
The Basic and Clinical Neuroscience portfolio seeks to expand understanding of the fundamental neurological, genetic/epigenetic, and behavioral processes that underlie substance use disorders. Central to this goal are efforts to tease apart the multiple factors that contribute to drug abuse and addiction risk, with particular attention to significant individual differences in risk and responses to drugs, while at the same time expanding basic knowledge of the function of the brain from the molecular to the behavioral level. Key projects are investigating the effects of drugs on gene expression and brain development and function, and exploring gender-related differences in these effects. Risk for addiction is profoundly affected by an individual's genes as well as environmental conditions, such as stress and early exposure to drugs of abuse. Additional studies are exploring the mechanisms underlying these effects, including the role of epigenetic changes that can influence long-term patterns of gene expression in specific brain cells (neuron and glia) without changing DNA sequence. Collectively, this research will improve our understanding of the basic neural and genetic mechanisms that underlie drug abuse and addiction and will provide critical insights toward the development of more effective approaches for the prevention and treatment of SUDs. For example, continuing efforts to improve understanding of the endocannabinoid system are opening up new areas of investigation for the development of novel pain and addiction treatments. Other projects are exploring the basic processes underlying resilience against substance use disorders in childhood and adolescence. In addition, and in line with the goals of the President's Brain Research through Advancing Innovative Neurotechnologies (BRAIN) Initiative, NIDA is supporting research to: 1) develop advanced technologies that improve the ability to study the organization and function of the living brain; 2) better understand the interactions of complex neural circuits including those that mediate reward, aversion to drug effects, and related decision-making through development; and 3) develop strategies to therapeutically influence substance use disorder-relevant brain circuits (e.g., transcranial magnetic and deep brain stimulation, neurofeedback, optogenetics). Progress in these combined areas will revolutionize the ability to mitigate or even reverse the deleterious effects of addiction.

Therapeutic and Medical Consequences
FY 2017 Request: $178.4 million
($0.5 million below the FY 2016 enacted level)
Since the pharmaceutical industry has traditionally had limited involvement in the development of medications for SUDs, the responsibility for their development has rested largely with NIDA. NIDA, therefore, has developed a program to develop therapeutics for the treatment of SUDs. To 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 therapeutics through the development pipeline toward Food and Drug Administration approval in a timely manner. NIDA supports research to decrease the risk associated with therapeutics development to make it more appealing for

pharmaceutical companies to complete costly phase IIb and III clinical studies. An example of such a project is a partnership with AstraZeneca to explore a novel medication that modulates the activity of glutamate – an excitatory neurotransmitter – to treat drug addiction. Preclinical studies with this class of molecules indicate that it could be effective for treating abuse of various drugs such as tobacco and cocaine. Another example is the partnership with two biotechnology companies to support the development of an intranasal formulation of naloxone, one of which received FDA-approval in November 2015 (NARCAN® Nasal Spray). In addition, NIDA is collaborating with Teva Pharmaceutical Industries on a clinical trial to test the efficacy and safety of a cholinesterase compound that has shown promise in pre-clinical trials for the treatment of cocaine addiction. NIDA continues to actively seek potential partners in the pharmaceutical and biotechnology sectors to develop novel therapeutics for SUDs. For example, NIDA has invested in research supporting the development of vaccines and antibodies for the treatment of SUDs. One example of NIDA's efforts in this area is an ongoing collaboration with Selecta Biosciences to develop a novel nicotine vaccine. NIDA-supported research is working to address the lingering challenge of developing vaccines that stimulate an immune response powerful enough to neutralize high concentrations of a drug before it enters the brain.

Clinical Trials Network
FY 2017 Request: $43.2 million
($0.1 million below the FY 2016 enacted level)
The Clinical Trials Network (CTN) comprises 13 research nodes and more than 240 community treatment programs and/or medical settings in 38 states plus the District of Columbia and Puerto Rico. Current initiatives are emphasizing research to develop and test strategies for the integration of SUD treatment into mainstream general medical settings, embedding research in clinical practice, and enhancing capacity to leverage electronic health record data in research studies. Through collaborations with clinical investigators, the CTN generates research-based strategies needed for the integrated management of patients with substance misuse/SUD in general medical settings and linked specialty care treatment settings. The CTN develops and tests the feasibility and effectiveness of interventions and health system approaches for SUDs and related disorders, such as co-occurring mental health disorders and HIV, in diverse patient populations. The CTN is currently conducting studies evaluating: 1) a comparison of Vivitrol (naltrexone for extended-release injectable suspension) to Suboxone (buprenorphine and naloxone) Sublingual Film for patients addicted to heroin or other opioids, including prescription pain relievers; 2) a combination therapy with Vivitrol plus Wellbutrin XL (bupropion hydrochloride, extended-release tablets) for treatment of methamphetamine addiction; 3) Vivitrol for HIV-positive opioid users in HIV settings; and 4) and a brief screening and assessment instrument to identify patients with substance use disorders in general medical settings. Research under development includes several studies which will utilize electronic health record data from large healthcare systems to enable larger, more efficient research trials.

Intramural Research Program
FY 2017 Request: $91.7 million
($1.4 million above the FY 2016 enacted level)
NIDA's Intramural Research Program (IRP) performs cutting-edge research within a coordinated multidisciplinary framework to: 1) elucidate the nature of the addictive process; 2) evaluate the potential use of emerging new therapies for substance use disorders, both

pharmacological and psychosocial; and 3) describe the long-term consequences of drugs of abuse on systems and organs, with particular emphasis on the brain and its development, maturation, function, and structure. For example, the IRP is collaborating with pharmaceutical industry partners to study a potential medication that can decrease methamphetamine craving. In addition, the IRP is working to understand the impact of long-lasting deficits in the prefrontal cortex – an area of the brain that mediates decision-making – caused by cocaine and heroin use. In an animal model, scientists can reverse this deficit by hyper-stimulating the prefrontal cortex for brief periods. This intervention is being developed as a possible therapy for addiction. The IRP is also working to develop clinically useful indicators (biomarkers) of nicotine addiction severity or treatment efficacy. Scientists are using brain imaging along with genetic and epigenetic data to develop quantitative addiction markers that will support the development of more efficacious treatments and discovery of novel treatment targets. IRP scientists are also working to better understand factors that contribute to cravings and relapse. Memories of items, people, or environments that are present when addicted individuals take drugs become powerful cues that trigger them to relapse again and again. Scientists have shown that these memories are stored in specific patterns of neurons called neuronal ensembles in the brain. Researchers have successfully inactivated these drug-related ensembles and memories in animal models, and are developing similar procedures that might be used in humans to selectively impair harmful addiction memories. In addition, IRP scientists are developing a mobile health toolbox to collect data on the daily-life reality of addiction. These tools can support intensive assessments to help identify individual and environmental influences on drug craving and use to understand when people are most vulnerable to relapse. One of the goals of this research is to deploy a mobile intervention that will automatically predict imminent drug use and deliver help just when a person needs it.

Research Management and Support
FY 2017 Request: $63.9 million
($0.9 million above the FY 2016 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. NIDA currently oversees more than 1,600 research grants and more than 100 research and development contracts. In addition to the infrastructure required to support research and training, NIDA also strives to provide evidence-based resource and educational materials about substance use disorders 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 treatments.

In addition, NIDA's Office of Science Policy and Communication leads strategic efforts to inform public health policy and practice by ensuring the institute is the primary trusted source for scientific information on drug abuse and addiction. Healthcare providers are a key target audience for NIDA's outreach efforts. NIDA leads the NIH Pain Consortium Centers of Excellence in Pain Education; these eleven centers work to enhance patient outcomes by improving the education of healthcare professionals about pain and its treatment. The NIH Pain Consortium Centers of Excellence in Pain Education 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 2017 Request: $54.2 million
(Flat to the FY 2016 enacted level)

A key priority for NIAAA is preventing and reducing underage drinking. NIAAA recognizes the pervasive use of alcohol among young people and its negative consequences, as well as the association between early initiation of alcohol use and future alcohol problems. NIAAA's investment in underage drinking research includes the National Consortium on Alcohol and Neurodevelopment in Adolescence, a longitudinal study that is following more than 800 participants through adolescence, using state-of-the-art structural and functional brain imaging and extensive behavioral and clinical assessments to identify the short and long-term effects of alcohol exposure on the developing adolescent brain. The program provided the foundation for the recently launched Adolescent Brain Cognitive Development study, a more extensive longitudinal study conducted under the Collaborative Research on Addiction at NIH (CRAN). This initiative will follow approximately 10,000 U.S. adolescents for 10 years to assess the neurodevelopmental consequences of substance use in youth. NIAAA will continue to support complementary studies with animals under the Neurobiology of Adolescent Drinking in Adulthood initiative which investigates the underlying neurobiological mechanisms by which adolescent alcohol exposure affects adult brain function and behavior. Given that many college students who consume alcohol are underage, efforts to prevent and intervene with drinking by college students will continue to be an NIAAA priority in FY 2017.

PERFORMANCE

Information regarding the performance of the drug control efforts of NIH is based on agency GPRAMA documents 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. Most measures are trans-NIH, encompassing lead and contributory 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. All performance results reported were achieved in FY 2015.

NIDA and NIAAA 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 support activities, two measures best reflect the breadth of their portfolios, specifically, efforts in the prevention and treatment of substance abuse, addiction, and its consequences.

One of these measures is SRO-5.15: "By 2018, develop, refine and evaluate evidence-based intervention strategies and promote their use to prevent substance use, abuse, addiction and their consequences in underage populations." This measure 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 abuse and addiction. SRO-5.15 began in FY 2014 and replaces the previous prevention measure, SRO-3.5, which was completed in FY 2013. 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 abuse 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 substance use disorders.

NIDA and NIAAA also contribute 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 reflects NIH's commitment to supporting research on the implementation of preventive and treatment interventions and improving the translation of research into practice.

National Institute on Drug Abuse		
Selected Measures of Performance	**FY 2015 Target**	**FY 2015 Achieved**
» SRO-5.15, by 2018, develop, refine and evaluate evidence-based intervention strategies and promote their use to prevent substance use, abuse, addiction and their consequences in underage populations.	Assess the effectiveness of at least two strategies for dissemination and implementation of tested, efficacious interventions to prevent youth and young adult drug use, drug use problems, and risk behaviors.	NIH-funded research tested over twenty strategies for improving the dissemination and implementation of evidence-based interventions to prevent drug use, drug use problems, and drug-related risky behaviors including HIV risk behaviors.
» 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.	Establish cooperative partnership with at least 3 juvenile justice agencies across the United States to participate with NIH investigators in studies intended to develop and test models that facilitate uptake of evidence-based drug abuse prevention and treatment interventions. The level of achievement from this target is conditional on receiving applications of sufficient scientific merit.	A cooperative partnership has been established with 39 juvenile justice agencies across the US to test two different implementation models designed to facilitate the uptake of evidence-based substance use services.

Prevention – SRO-5.15

NIDA continues to fund a robust theory-based prevention portfolio that builds upon solid epidemiological findings and insights from genetics and neuroscience and applies this knowledge to development of effective strategies to prevent initiation of drug use and escalation of use to addiction in underage youth.

From FY 2015 to the present (FY 2016), multiple studies have been funded to develop and test interventions to prevent drug use, drug use problems, and risk behaviors and to improve the

implementation of these evidence-based interventions. NIDA is supporting research to test culturally and developmentally appropriate strategies to prevent drug use and addiction across the lifespan: for all developmental stages, from birth through adulthood and older age; for diverse racial/ethnic populations, targeted to various settings such as family, school, community, and health care settings; and for high risk populations, such as LGBT, homeless, child welfare involved, juvenile justice system involved, criminal justice involved, individuals with comorbid conditions, and populations at risk for HIV/AIDS.

In FY 2015 multiple publications were released related to this target by NIDA-funded researchers who conducted studies that tested implementation of interventions to prevent drug use, drug use related problems, and risk behaviors. A recent study examined the long-term effects of a partnership-based intervention delivery model called PROSPER (PROmoting School/community-university Partnerships to Enhance Resilience) on adolescent conduct problem behaviors such as substance misuse behaviors, anti-social behaviors and sexual risk behavior.[61] Previous studies have established the effectiveness of PROSPER, with positive effects on young adolescent competencies (e.g., peer refusal skills); parenting effectiveness and family functioning; adolescent conduct problems; and misuse of a wide range of substances through the end of high school. The current research compared adolescents in school districts randomly assigned to PROSPER or to a control condition. Community-based teams in school districts delivering PROSPER utilized selected evidence-based interventions including a family-focused intervention in 6th grade and a school-based intervention the next year; follow-up assessments were conducted through 12th grade. The intervention group exhibited significantly lower levels of conduct problems than controls at each time point from 9th to 12th grade. In addition, the control group reached a reference level of conduct problem behaviors sooner than the intervention group. These results demonstrate the long-term effects of early preventive interventions and establish effective community based implementation strategies.

Another recent publication demonstrated how nonparticipants may benefit from indirect exposure to an intervention as attitudes, knowledge, and behaviors diffuse through friendship networks.[62] Specifically, researchers tested whether the effects of the Strengthening Families Program for Youth 10–14 (SFP10-14) – an evidence-based prevention program – diffused from intervention participants to their friends. They also tested which program effects accounted for this diffusion. Students identified up to seven friends and self-reported past month drunkenness and cigarette use, substance use attitudes, parenting practices, and unsupervised time spent with friends. Three years post-intervention, the odds of getting drunk (odds ratio = 1.4) and using cigarettes (odds ratio = 2.7) were higher among nonparticipants with zero SFP-attending friends compared with nonparticipants with three or more SFP-attending friends. The study also found that nonparticipants with a higher cumulative proportion of SFP-attending friends were less likely than their peers to use drugs. Effects from SFP10-14 primarily diffused through friendship networks by reducing the amount of unstructured socializing (unsupervised time that nonparticipants spent with friends), changing friends' substance use attitudes, and then changing nonparticipants' own substance use attitudes. The results of this study suggest that effects from

[61] Spoth, Richard L., et al. "PROSPER partnership delivery system: Effects on adolescent conduct problem behavior outcomes through 6.5 years past baseline." *Journal of adolescence* 45 (2015): 44-55.
[62] Rulison, Kelly L., et al. "Diffusion of intervention effects: the impact of a family-based substance use prevention program on friends of participants." Journal of Adolescent Health 57.4 (2015): 433-440.

implementation of a family-based prevention program can impact nonparticipating adolescents by diffusing through school-based friendship networks.

Another ongoing study is looking at the long-term effects of the Communities that Care (CTC) prevention system on young adult substance use and misuse; crime, violence, and incarceration. CTC helps communities select and implement tested and effective prevention programs and policies based on a given community's risks and strengths. This research is examining the impacts of CTC 11 and 13 years following initial implementation. Early findings from this study have found that CTC is a cost-effective community-based approach to preventing initiation of delinquency and drug use.[63] This study has the potential to increase knowledge about effective implementation of community prevention programs and their impact on health-risking behaviors among youth from small towns (an understudied and underserved population) during the transition to adulthood.

Collectively these findings demonstrate strategies for effective dissemination and implementation of evidence-based substance use prevention programs and further support key prevention lessons and principles that have emerged from NIDA-funded studies: prevention interventions implemented in early childhood have effects in later developmental stages and into young adulthood; universal interventions can have strong effects in higher risk youth; universal substance use prevention interventions can have effects on other behavioral outcomes, beyond those specifically targeted by the intervention (e.g., social services utilization).

Treatment - SRO-8.7

NIDA funds a broad portfolio of research addressing drug abuse in the context of the criminal justice system. Two of NIDA's signature projects in this area are the Juvenile Justice Translational Research on Interventions for Adolescents in the Legal System (JJ-TRIALS) program and the Seek, Test, Treat, and Retain (STTR) Initiative.

NIDA's JJ-TRIALS initiative was launched in 2013 and is a seven-site cooperative research program designed to identify and test strategies for improving the delivery of evidence-based substance abuse and HIV prevention and treatment services for justice-involved youth. Many evidence-based interventions targeting adolescent substance abuse and HIV screening, assessment, prevention, and treatment currently exist. Unfortunately, implementation of these interventions within juvenile justice settings is variable, incomplete, and non-systematic at best. The JJ-TRIALS initiative features three studies to address these issues.

The first study is a nationally representative survey of the juvenile justice system to ascertain current policies and practices related to substance use assessment and service delivery in juvenile justice settings across the United States. The first wave of this survey was completed in 2015. Juvenile probation departments, judges, and behavioral health providers from over 200 localities responded to this survey, with a >90% response rate. These data are currently being analyzed and we expect findings to be released in 2016.

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[63] Kuklinski, Margaret R., et al. "Benefit–cost analysis of a randomized evaluation of Communities That Care: monetizing intervention effects on the initiation of delinquency and substance use through grade 12." Journal of Experimental Criminology (2015): 1-2 .

The second study is an organizational level intervention that will be field-tested in 36 juvenile justice systems across the country. An additional three systems participated as pilot sites. These systems are being trained on evidence-based practices to target youth substance use, data driven decision making, and goal setting. Data collection began in 2015 and over the next two years, JJ-TRIALS will track the progress of these 36 systems in improving the delivery of evidence-based substance use services to justice-involved youth.
A third study is currently under development to assist an additional six juvenile justice systems improve the delivery of HIV screening and prevention to justice-involved youth. Through these studies, the JJ-TRIALS research program will provide insights into the process by which juvenile justice and other service settings can successfully adopt and adapt existing evidence-based programs and strategies to improve drug abuse and HIV related service delivery for at-risk youth.

Since 2010, NIDA has supported the Seek, Test, Treat, and Retain (STTR) Initiative to empirically test the STTR paradigm with drug abusers in criminal justice populations. Researchers are developing, implementing, and testing strategies to increase HIV testing and the provision of highly active antiretroviral therapy (HAART) to HIV-positive individuals involved with the criminal justice system, with particular focus on continuity of HAART during and after community re-entry following incarceration. During 2015, 15 peer-reviewed journal articles were published reporting on findings from the STTR initiative. Key findings include: linkage to and retention in care are the two most critical elements in engaging patients in the HIV care continuum; an unexpectedly high mortality rates in some studies due to the recruiting of participants at a late stage in their illness; high prevalence of comorbid health conditions such as HCV; structural barriers in the criminal justice setting often hindered research; and the dearth of medication assisted treatments (or even basic substance abuse care) in settings with relatively high HIV prevalence.[64,65,66,67,68,69,70,7172,73,74,75,76,77,78]

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[64] Chandler RK., et al. Data Collection and Harmonization in HIV Research: The Seek, Test, Treat, and Retain Initiative at the National Institute on Drug Abuse. Am J Public Health, 10-15-2015. pp. e1-e7.
[65] Beckwith CG., et al. A pilot study of rapid hepatitis C virus testing in the Rhode Island Department of Corrections. J Public Health (Oxf), Mar. 2, 2015.
[66] Beckwith CG., et al. Survey of US Correctional Institutions for Routine HCV Testing. Am J Public Health, Jan., 2015. Vol. 105, issue 1, pp. 68-71.
[67] Comfort, M. A Twenty Hour a Day Job: The Repercussive Effects of Frequent Low-Level Criminal Justice Involvement on Family Life. The Annals of the American Academy of Political and Social Science. (in press).
[68] Comfort, M.,et al. How Institutions Deprive: Ethnography, Social Work, and Interventionist Ethics Among the Hypermarginalized. Russell Sage Foundation Journal of the Social Sciences, Special Issue entitled “Severe Deprivation in America.” (in press).
[69] Dennis AC., et al. "You're in a World of Chaos": Experiences Accessing HIV Care and Adhering to Medications After Incarceration. J Assoc Nurses AIDS Care. 2015 Jun 14. pii: S1055-3290(15)00139-9. doi: 10.1016/j.jana.2015.06.001. [Epub ahead of print].
[70] Gwadz M., et al. Strategies to uncover undiagnosed HIV infection among heterosexuals at high risk and link them to HIV care with high retention: a "seek, test, treat, and retain" study. BMC Public Health, May 10, 2015. Vol. 15, issue 1, pp. 481.
[71] Gwadz M., et. al. Strategies to uncover undiagnosed HIV infection among heterosexuals at high risk and link them to HIV care with high retention: a "seek, test, treat, and retain" study. BMC Public Health, May 10, 2015. Vol. 15, issue 1, pp. 481.
[72] Hammett TM.,et. al. Transitions to Care in the Community for Prison Releasees with HIV: a Qualitative Study of Facilitators and Challenges in Two States. J Urban Health, 2015. Vol. 92, issue 4, pp. 650-666.
[73] Kurth AE. et. al. HIV prevalence, estimated incidence, and risk behaviors among people who inject drugs in Kenya. J Acquir Immune Defic Syndr. 2015 Jul 28. [Epub ahead of print].
[74] Lorvick J. et. al. Heath service use and social vulnerability in a community-based sample of women on probation and parole, 2011-2013. Health and Justice. 19 Jun 2015 vol3, issue 13. doi:10.1186/s40352-015-0024-4.

In addition, from 2002-2014, NIDA funded the Criminal Justice Drug Abuse Treatment Studies (CJ-DATS) program, a multisite research cooperative. The CJ-DATS program aligned with NIDA's multi-pronged approach to improve existing drug treatment for criminal justice populations, and to inform the development of integrated treatment models. This initiative concluded in 2014, but continued to produce publications in 2015. To date, 14 peer-reviewed publications have been published. [79,80,81,82,83,84,85,86,87,88,89,90,91,92] Through these studies CJ-DATS contributed to a significant body of research describing existing treatment practices in the criminal justice system, developing and testing the effectiveness of specific interventions, and exploring strategies for implementation and quality improvement of drug abuse treatment programs for criminal justice populations.

Research Highlights

Researchers identify new complexities within the brain's reward circuitry that involves two major chemicals involved in drug addiction – dopamine and glutamate. [93] In a recent study, researchers used rodent models to better understand a specific brain circuit where dopamine and glutamate are both released from the same brain cells. They found that dopamine and glutamate were typically stored separately from one another and released from different synapses of the

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nerve cell. This finding reveals a greater layer of complexity in signaling within brain reward circuits than had previously been recognized. Deficits in brain reward pathways can produce an inability to derive pleasure from natural stimuli, causing the substance user to focus on obtaining drugs at the expense of work, school, or relationships. A better understanding of these circuits will help drive the development of more targeted and effective prevention and treatment interventions for substance use disorders.

Medication plus ongoing care provided in emergency departments is a promising approach for opioid dependence.[94] Emergency department (ED) and primary care screening, brief intervention, and referral to treatment (SBIRT) can reduce unhealthy alcohol and tobacco use, however, this approach has not been applied to patients with opioid use disorder. In a recent study, researchers applied SBIRT to opioid patients who were randomly assigned to one of three intervention groups: 1) screening and referral to treatment; 2) screening, brief intervention and referral; or 3) screening, brief intervention, ED-initiated treatment with buprenorphine/naloxone, and referral. After 30 days, patients in the ED who initiated buprenorphine/naloxone treatment were more likely to participate in specialty substance use disorder treatment, were less likely to need inpatient treatment services and had reduced self-reported illicit opioid use. This adds to the growing body of literature suggesting that opioid-dependent patients may benefit from immediate initiation of medication while awaiting more comprehensive substance use disorder treatment.

A preliminary study shows cocaine abstinence and reduced use are associated with lowered marker of heart disease risk.[95] Previous studies have demonstrated that the protein endothelin-1 (ET-1) is associated with endothelial dysfunction, and that ET-1 levels change with cocaine use. ET-1 is higher in cocaine users than in those who do not use cocaine, and abstinence from cocaine can reduce levels of ET-1. This correlation raises the possibility that ET-1 could function as a biomarker for cocaine use and for cocaine-induced risk of heart disease. A recent study examined ET-1 levels and coronary plaques in a group of African American cocaine users participating in an incentive-based program to reduce cocaine use. In addition to confirming the finding that abstinence from cocaine lowers ET-1, the study found that more mild reductions in cocaine use also lowered levels of ET-1. This change in ET-1 provides evidence that both total abstinence and reduction in cocaine use could protect against endothelial dysfunction. Additionally, the responsiveness of ET-1 to changes in cocaine use could make it a useful biomarker to measure harm-reduction outcomes when developing treatments for cocaine use disorder.

Students who have used electronic cigarettes by the time they start ninth grade are more likely than others to start smoking tobacco products.[96] E-cigarettes deliver nicotine to the lungs by heating a liquid solution that contains nicotine and other chemicals to produce an aerosol that the user inhales. A recently published study compared tobacco use initiation among 222 students

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who had used e-cigarettes, but not combustible tobacco products, and 2,308 who had neither used e-cigarettes or combustible tobacco products when initially surveyed at the start of ninth grade. During the first six months after being surveyed, 30.7 percent of those who had used e-cigarettes started using combustible tobacco products, such as cigarettes, cigars, and hookahs, compared to only 8.1 percent of those who had never used e-cigarettes. Over the following six months leading into the start of 10th grade, 25.2 percent of e-cigarette users had used combustible tobacco products, compared to just 9.3 percent of nonusers.

Animal study suggests marijuana may affect future offspring's susceptibility to heroin.[97] Drugs of abuse have been shown to have epigenetic effects – they influence cross-generational transmission of complex traits without altering the genome sequence. A recent study looked at the effect of adolescent exposure to THC, the main psychoactive compound in marijuana, on susceptibility to heroin self-administration in the next generation. Adolescent male and female rats were administered THC for 3 weeks on an intermittent schedule that corresponded to the amounts consumed by typical recreational marijuana users. Researchers then looked at heroin self-administration in their offspring, conceived after a period of abstinence when the THC could no longer be detected in the rats' bodies and raised by mothers who had not been exposed to THC. When the offspring of these matings reached adulthood, the researchers presented them with a lever that, when pressed, delivered heroin. The offspring of THC-exposed parents were willing to work significantly harder to self-administer heroin. This difference was associated with altered neuronal functioning in the dorsal striatum – a brain region involved in reward and addiction. Neurons in this region were less responsive to stimulation and showed altered expression of N-methyl-D-aspartate (NMDA)-type glutamate receptors. While these results have not yet been replicated, they suggest potential mechanisms involved in determining susceptibility to addiction and highlight the importance of prevention efforts aimed at youth.

Methadone maintenance in prison results in treatment retention and lower drug use following release.[98] A recent NIDA-funded study shows that, among people incarcerated for six months or less, those who received ongoing methadone maintenance while imprisoned were more likely to obtain follow-up drug treatment than those who underwent detoxification from methadone while in jail. The findings show that one month after release, participants who continued to receive doses of methadone while incarcerated were more than twice as likely to continue treatment at a community methadone clinic after their release, compared to those who went through tapered methadone withdrawal. In addition, in the month following their release, opioid use was lower among the methadone maintenance patients, versus the tapered withdrawal group. Because of the high risk of relapse and fatal overdose that often occurs among inmates following release from prison, the study results emphasize the importance of continuing methadone treatment while incarcerated and connecting this population to follow-up treatment upon release.

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National Institute on Alcohol Abuse and Alcoholism		
Selected Measures of Performance	**FY 2015 Target**	**FY 2015 Achieved**
» SRO-5.15: By 2018, develop, refine and evaluate evidence-based intervention strategies and promote their use to prevent substance use, abuse, addiction and their consequences in underage populations.	Evaluate the effectiveness of screening and brief intervention for alcohol and other drug use in a variety of settings.	NIH supported six studies to evaluate the effectiveness of its youth guide for alcohol screening and brief intervention in a variety of settings.
» 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.	Penetrate primary care to increase alcohol screening and brief intervention by providing online continuing medical education (CME) for the underage drinking guide and by supporting efforts to enhance medical training curricula.	NIH promoted alcohol screening and brief intervention in primary care by offering online continuing medical education (CME) on the underage guide to primary care providers, and by collaborating with federal and non-federal stakeholders to facilitate integration of prevention and early intervention of alcohol misuse in primary care training and practice.

Prevention – SRO-5.15

NIAAA supported six studies to evaluate the effectiveness of its youth guide for alcohol screening and brief intervention in a variety of settings.

These ongoing studies are evaluating the *Alcohol Screening and Brief Intervention for Youth: A Practitioner's Guide* in practice in various settings: one in a juvenile justice setting, one in a school setting, two in primary care, one in a network of emergency departments, and one with youth who have a chronic health condition (e.g., asthma, diabetes). These studies are also evaluating the effectiveness of the guide as an initial screen for drug use and other behavioral health problems. Released by NIAAA in 2011, this youth alcohol screening guide was designed to help pediatricians and other health care providers quickly identify children at elevated risk for using alcohol, children and adolescents who have already begun to experiment with alcohol, and those who are more heavily involved with alcohol. While this tool was developed for use in the primary care setting, it may also be useful in other settings, which could expand the venues in which at-risk youth can access prevention and intervention services.

Treatment – SRO-8.7

NIAAA continued to provide the online continuing medical education (CME) course, *Alcohol Screening and Brief Intervention for Youth: A Practitioner's Guide*, to primary care and other health care providers. As of September 2015, more than 35,500 health care providers had earned CME credit for completing the course. Recognizing the importance of training health care providers in identifying, preventing, and addressing alcohol misuse and the associated consequences, NIAAA is collaborating with professional organizations and federal stakeholders in efforts to integrate prevention, early intervention, and treatment of alcohol misuse in primary care and preventive medicine training, certification, and practice. In 2015, NIAAA also

sponsored a series of symposia, lectures, workshops, and forums at the American Psychiatric Association annual meeting to update psychiatrists on the latest advances in research on alcohol misuse and AUD, and promote the development of clinical knowledge and skills in identifying and managing alcohol problems.

Research Highlights

Assessing the Impact of Adolescent Alcohol Exposure on the Developing Brain. Adolescence is a period of significant brain maturation and also the time when many individuals initiate and escalate alcohol consumption. Human brain imaging studies have shown that over the course of adolescence, the volume of gray matter in the brain decreases, likely reflecting the normal process of synaptic pruning, whereas the volume of white matter increases, presumably reflecting enhanced brain connectivity. The nature of these rapid changes makes the developing adolescent brain particularly vulnerable to the adverse effects of alcohol. In 2012, NIAAA launched the National Consortium on Alcohol and Neurodevelopment in Adolescence (NCANDA), an ongoing multi-site longitudinal study to address alcohol's effects on normal brain development. The five NCANDA sites have collectively enrolled more than 800 adolescents ages 12 to 21, and are using advanced brain imaging as well as other psychological and behavioral research tools to evaluate brain structure and function, beginning before the participants start to drink. NCANDA's overall objectives are to elucidate the short- and long-term effects of alcohol exposure on the developing brain and to identify the brain characteristics that may predict AUD. In a recent study supported through NCANDA,[99] researchers used neuroimaging to assess the developmental trajectory of 134 adolescents, ages 12-24, over 8 years. Of these youth, 75 transitioned to heavy drinking during a 3.5 year period. The results showed that heavy drinking adolescents had accelerated reductions in gray matter and attenuated increases in white matter compared to non-drinking adolescents, providing additional evidence that heavy drinking during adolescence alters the trajectory of brain development.

Improving implementation of youth alcohol SBIRT in primary care. Screening, brief intervention and referral to treatment (SBIRT) by primary care providers has been shown effective in reducing alcohol misuse and related problems in adults, and a mounting body of evidence has supported the use of SBIRT in preventing the initiation and escalation of substance use by adolescents. However, physicians often face barriers to providing these services, including time constraints and a lack of training in SBIRT. Recently, NIAAA-funded researchers examined SBIRT implementation in a large pediatric clinic.[100] In the study, pediatricians participated in one of three study groups: 1) a pediatrician-only group that received three hours of SBIRT training and then conducted screening and brief interventions by themselves; 2) a second group that received less SBIRT training, screened patients, and referred them to behavioral health care clinicians "embedded" in the practices to conduct the interventions; and 3) a control group of pediatricians who received no SBIRT training and performed usual care only. The researchers found that the pediatrician-only group was about 10 times more likely (16 percent) to conduct brief interventions with at-risk patients than "usual

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care" pediatricians (1.5 percent). The intervention rate was even higher (24.5 percent) in the pediatrician group that worked in coordination with embedded behavioral health care clinicians. These results suggest that training pediatricians in SBIRT can significantly increase their use of techniques for identifying and treating young people with potential alcohol, substance use, and mental health problems. The results also show that pediatric practices can improve support for patients who need these services by adding behavioral health clinicians to their teams.

Promoting effective interventions to reduce college drinking. The extent of binge drinking and related consequences such as blackouts, physical and sexual assaults, alcohol poisonings, injuries, and deaths on college campuses is alarming. NIAAA-supported research has shown that both individual and environmental approaches to prevention can effectively reduce harmful drinking and its consequences for college students. Working with researchers with expertise in college drinking interventions, NIAAA developed and released the *College Alcohol Intervention Matrix (CollegeAIM*), an easy-to-use, comprehensive tool and website designed to help higher education officials identify effective alcohol interventions.[101] CollegeAIM allows users to compare individual- and environmental-level strategies based on factors such as cost, effectiveness, and ease of implementation, helping them choose those interventions that best fit the needs of their campus. As part of the dissemination effort, CollegeAIM developers and NIAAA staff will present on the tool at meetings of higher education administrators and college health professionals. NIAAA, in collaboration with its College Presidents Working Group, will also be organizing regional workshops to present CollegeAIM to institutional officials and show them how to use it. The interventions highlighted in CollegeAIM are divided into tiers of effectiveness, based on an extensive research and evaluation process. The highest tier – *higher effectiveness* – contains 8 individual level strategies and 5 environmental level strategies; in general, they represent a range of counseling options and policies related to sales and access.

[101] http://www.collegedrinkingprevention.gov/collegeaim/