DEPARTMENT OF HEALTH AND HUMAN SERVICES
National Institutes of Health

Resource Summary

	Budget Authority (in Millions)		
	FY 2014 Final	FY 2015 Enacted	FY 2016 Request
Drug Resources by Function			
Research and Development: Prevention	$391.620	$389.478	$401.473
Research and Development: Treatment	$685.691	$685.761	$707.143
Total Drug Resources by Function	**$1,077.311**	**$1,075.239**	**$1,108.616**
Drug Resources by Decision Unit			
National Institute on Drug Abuse	$1,017.961	$1,015.705	$1,047.397
National Institute on Alcohol Abuse and Alcoholism	59.350	59.534	61.219
Total Drug Resources by Decision Unit	**$1,077.311**	**$1,075.239**	**$1,108.616**

Drug Resources Personnel Summary			
Total FTEs (direct only)	393	395	395
Drug Resources as a Percent of Budget			
Total Agency Budget (in Billions)	$30.1	$30.1	$31.1
Drug Resources Percentage	3.4%	3.4%	3.4%

Program Summary

MISSION

The National Institute on Drug Abuse (NIDA) and the National Institute on Alcohol Abuse and Alcoholism (NIAAA), two of the twenty-seven Institutes and Centers (ICs) of the National Institutes of Health (NIH), support the National Drug Control Strategy: NIDA, by funding research on the prevention and treatment of substance abuse, 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 abuse (alcohol, tobacco, illicit and nonmedical use of prescription drugs) in this country is daunting, exceeding $600 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 in this country and worldwide.

In addition, NIDA is supporting research to better understand the impact of changes in state policies related to marijuana. Current research is exploring the impact on trends in use, harm perception, health consequences including trauma and death from car accidents, and educational outcomes, particularly for adolescents and young adults. In addition, a significant new initiative is being initiated as part of the Collaborative Research on Addiction (CRAN), a trans-NIH consortium involving NIDA, NIAAA, and the National Cancer Institute (NCI), and in partnership with the *Eunice Kennedy Shriver* National Institute of Child Health and Health Development (NICHD), that will seek to understand the impact of marijuana (and other drug) use during adolescence. This Adolescent Brain Cognitive Development (ABCD) study will be the largest longitudinal brain-imaging study of adolescents ever conducted. It will follow approximately 10,000 U.S. adolescents for 10-12 years to determine whether use of marijuana, alcohol, nicotine, or other drugs is associated with changes in brain function and behavior throughout development. Participants will be recruited prior to any substance use and will periodically undergo a variety of tests such as brain imaging, genetic, psychiatric, and cognitive testing to potentially identify predictors of adolescent substance misuse and to delineate the role of social, psychological, and biological mechanisms.

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 our understanding of alcohol misuse and its consequences, as well as their treatment. 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 alcohol use disorder (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 (FASD), 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 NIAAA prevention and treatment components of its underage drinking research are scored as a part of the National Drug Control Budget. Underage drinking research is defined as research that focuses on alcohol use and binge drinking in minors (children under the legal drinking age of 21), as well as the negative consequences of alcohol use, e.g. alcohol-related injuries, impact on adolescent development, including on the developing brain, and the

development of alcohol use disorder. It includes basic research, epidemiological studies, behavioral research, screening and intervention studies and development and testing of preventive interventions. NIAAA's methodology for developing budget estimates uses the NIH research categorization and disease coding (RCDC) fingerprint for underage drinking that allows for an automated categorization process based on electronic text mining to make this determination. Once all underage drinking projects and associated amounts are determined using this methodology, NIAAA conducts a manual review and identifies just those projects and amounts relating to prevention and treatment. This subset makes up the NIAAA drug control budget estimate.

BUDGET SUMMARY

The FY 2016 Request is $1,108.6 million for NIH's drug-related activities, which is an increase of $33.4 million above the FY 2015 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 influences on drug addiction vulnerability, including genetics and epigenetics, which will allow the development of more targeted and effective prevention approaches. Research reveals that universal prevention programs not only reduce drug abuse, 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 drug use, violence, and mental health problems.

Another top priority continues to be the development of medications to treat substance use disorders, with NIH now poised to capitalize on a greater understanding of the neurobiology underlying addiction and of newly identified candidate systems and molecules as medication targets. NIH is also exploring ways in which health care reform, and the Affordable Care Act (ACA) specifically, can help bring people who have been marginalized, such as those with substance use disorders, HIV, or both, into a network of care and generate a major public health impact.

National Institute on Drug Abuse
FY 2016 Request: $1,047.4 million
(Reflects $31.7 million increase over FY 2015)

NIDA's efforts consist of Epidemiology, Services and Prevention Research, Basic and Clinical Neuroscience Research, Pharmacotherapies and Medical Consequences, Clinical Trials Network, the Intramural Research Program (IRP), and Research Management and Support (RM&S).

Epidemiology, Services and Prevention Research (FY 2016 Request: $265.8 million)

This NIDA Division supports integrated approaches to understand and address the interactions between individuals and environments that contribute to drug abuse-related problems. It supports large surveys (e.g., 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, such as the emergence of synthetic drugs and e-cigarettes. It also supports a large research network for conducting studies related to treatment of substance use disorders (SUDs) in the criminal justice system, including studies that pertain to the

implementation of medication-assisted treatment (MAT) and seek, test, treat, and retain (STTR) for substance abusers at risk for HIV. Program efforts also help identify substance abuse trends locally, nationally, and internationally; guide development of responsive interventions for a variety of populations; and encourage optimal implementation and service delivery in real-world settings. For example, NIDA recently launched an innovative National Drug Early Warning System (NDEWS) to monitor emerging trends related to illicit drug use and to identify increased use of designer synthetic compounds. NDEWS will generate 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 is also supporting research to better understand the impact of policy changes related to substance use including implementation of health reform and changes in state policies related to marijuana. Specifically, current research is evaluating: 1) the impact of health reform on access to quality treatment for persons with SUDs, and 2) the longer-term outcomes resulting from changes in State marijuana policies such as trends in use, harm perception, health consequences including trauma and death from car accidents, 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 2016 Request: $446.6 million)

The Basic and Clinical Neuroscience portfolio seeks to expand our understanding of the fundamental neurological, genetic/epigenetic, and behavioral processes that underlie SUDs. 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 our basic knowledge of the function of the brain from the molecular to the behavioral. 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 our 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 SUDs 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 our 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 SUD-relevant brain circuits (e.g., transcranial magnetic and deep brain stimulation, neurofeedback, optogenetics).

Progress in these combined areas will revolutionize our ability to mitigate or even reverse the deleterious effects of addiction.

Pharmacotherapies and Medical Consequences (FY 2016 Request: $137.5 million)
Since the pharmaceutical industry has 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 that is responsible for medications development for SUDs. To leverage NIDA resources, this program encourages the formation of alliances between strategic partners (such as academic institutions, pharmaceutical and biotechnology companies) with the common goal of advancing medications through the development pipeline toward FDA approval in a timely manner. NIDA conducts research to decrease the risk associated with medications 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 (see program portrait on intranasal naloxone). 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 also hosted a conference bringing together basic and translational researchers along with representatives from the pharmaceutical industry to evaluate emerging targets for stimulant use disorders and to identify ways to accelerate this area of research. NIDA is also continuing to invest in research supporting the development of vaccines and antibodies for the treatment of SUDs. A lingering challenge in this area has been the development of vaccines that stimulate an immune response powerful enough to neutralize high concentrations of a drug before it enters the brain.

Clinical Trials Network (CTN) (FY 2016 Request: $45.9 million)
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. The CTN develops and tests the feasibility and effectiveness of promising medications and behavioral treatment approaches for SUDs and related disorders, such as comorbid mental health disorders and HIV, with diverse patient populations and community treatment providers. 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) N-acetylcysteine for treatment of marijuana addiction; 3) a combination therapy with Vivitrol® plus Wellbutrin XL® (bupropion hydrochloride, Extended-release Tablets) for treatment of methamphetamine addiction; 4) Vivitrol® for HIV-positive opioid users in HIV settings; and 5) and a brief screening and assessment instrument to identify patients with SUDs in general medical settings.

Intramural Research Program (IRP) (FY 2016 Request: $89.0 million)

IRP performs cutting-edge research within a coordinated multidisciplinary framework to: 1) elucidate the nature of the addictive process; 2) determine the potential use of emerging new therapies for SUDs, both pharmacological and psychosocial; and 3) establish 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, IRP is furthering substance abuse research through the recently established Designer Drug Research Unit (DDRU), which was created in response to the worldwide epidemic of synthetic drug use. Synthetic drugs are marketed as safe, cheap, and legal alternatives to illicit drugs like marijuana, cocaine, and MDMA (a.k.a. Ecstasy). However, they can produce serious cardiovascular and neurological consequences that can be fatal. Many popular designer drugs have been rendered illegal by regulatory control, but new replacement analogs are flooding the marketplace at an alarming rate. IRP is uniquely poised to respond to this public health crisis by collecting, analyzing, and disseminating current information about the pharmacology and toxicology of newly emerging designer drugs. Similarly, IRP is working to develop and evaluate quicker, more reliable, and more accurate roadside tests for drug-related intoxication. With the legalization of recreational or medical marijuana use in some states, this is a critically needed tool for enforcing drug-impaired driving laws. IRP has also established a Medications Development Program that works with NIDA's Extramural Division of Pharmacotherapies and Medical Consequences of Drug Abuse, NIAAA, the National Center for Advancing Translational Sciences (NCATS), and the Brain Science Institute, Johns Hopkins University School of Medicine, to identify potential targets for addiction medication development. In addition, IRP is working to develop advanced new technologies to genetically manipulate and study the organization and function of brain circuits involved in SUDs.

Research Management and Support (RMS) (FY 2016 Request: $62.6 million)
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 130 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 SUDs and to raise awareness of the science relating to cutting-edge issues such as marijuana research, opioid overdose prevention, and Medication Assisted Treatments.

In addition, NIDA's Office of Science Policy and Communication (OSPC) 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 (CoEPEs); these twelve centers work to enhance patient outcomes by improving the education of healthcare professionals about pain and its treatment. The CoEPEs act as hubs for the development, evaluation, and distribution of pain management

curriculum resources for medical, dental, nursing and pharmacy schools to improve how health care professionals are taught about pain and its treatment.

National Institute of Alcohol Abuse and Alcoholism

FY 2016 Request: $61.2 million

(Reflects $1.7 million increase over FY 2015)

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. In FY 2012, NIAAA released an alcohol screening guide for health care providers to identify alcohol use and alcohol use disorder in children and adolescents, and to identify risk for alcohol use, especially for younger children. NIAAA launched an initiative to evaluate the guide in practice and is supporting six studies that are evaluating the guide in a range of settings: one in a network of emergency departments; one in a juvenile justice setting; two in primary care; one with youth who have a chronic condition (e.g., asthma, diabetes); and one in a school setting The brief, two-question screener is being assessed in youth ages 9-18 as a predictor of alcohol risk, alcohol use, and alcohol problems including alcohol use disorder, and as an initial screen for other behavioral health problems; for example, other drug use, smoking, or conduct disorder. NIAAA's investment in underage drinking research also includes the National Consortium on Alcohol and Neurodevelopment in Adolescence (NCANDA), 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. NIAAA's NCANDA program has created the foundation for a more extensive longitudinal study under the CRAN initiative 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 effects of adolescent alcohol exposure on subsequent brain function and behavior into adulthood. Given that many college students who consume alcohol are underage, efforts to prevent and intervene with drinking by college students will continue to be a major NIAAA priority in FY 2016.

PERFORMANCE

Information regarding the performance of the drug control efforts of NIH is based on the agency's performance reporting in support of the budget process 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 ICs. This approach reflects NIH's commitment to supporting the best possible research and coordination of research efforts across ICs. All performance results reported were achieved in FY 2014.

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 taking drugs or becoming addicted.

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." By studying treatment implementation, this outcome improves the translation of research into practice.

National Institute on Drug Abuse		
Selected Measures of Performance	**FY 2014 Target**	**FY 2014 Achieved**
» SRO-5.15 (started in FY 2014): 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.	Develop and assess at least two interventions to prevent drug use, drug use problems, and risk behaviors.	NIH funded research tested multiple 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.	Undertake analyses to examine the effects of implementation strategies used in MATICCE and HIV-STIC protocols.	Eight peer-reviewed publications analyzing the effects of implementation of the MATICCE and HIV-STIC protocols have been published. Several more manuscripts are in progress.

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 2014 to the present (FY 2015), multiple studies have been funded to develop and test interventions to prevent drug use, drug use problems, and risk behaviors. NIDA is currently supporting studies to test culturally and developmentally appropriate strategies to prevent substance use and abuse across the lifespan: for all developmental stages, from birth through adulthood and older age; for diverse racial/ethnic populations, targeted to diverse settings such as family, school, community, and health care settings; and for diverse special populations and/or high risk populations, such LGBT, homeless, child welfare involved, juvenile justice system involved, criminal justice involved, individuals comorbid conditions, populations at risk for HIV/AIDS.

In FY 2014 multiple publications were released related to this target by NIDA-funded researchers who conducted studies that tested interventions to prevent drug use, drug use problems, and risk behaviors. One recent study explored the effect of a Multidimensional Treatment Foster Care (MTFC) in at-risk female youth who had been referred for out-of-home placement due to chronic delinquency.[1] Previous studies have shown that juvenile justice girls have high rates of co-occurring risk behaviors including substance abuse. The current research showed that women with prior juvenile justice involvement who were assigned to the MTFC intervention during adolescence showed greater decreases in drug use than girls assigned to treatment as usual. In addition, women who participated in MTFC were found to be more resilient to partner drug use than women in the treatment as usual condition.

Another recent publication demonstrated that girls who participated in the Middle School Success (MSS) Intervention, a program to promote healthy adjustment in foster girls, showed lower levels of health risk-taking behaviors.[2] The analysis demonstrated that the effect of the intervention on health-risking sexual behavior was mediated through its effect on tobacco and marijuana use. These finding demonstrate that the MSS prevention intervention delivered during adolescence improves young adult drug use trajectories (7-9 years after the study began). These findings add to a growing body of evidence of the longer term impacts of early prevention interventions delivered during adolescence to a high risk population.

Another ongoing study is looking at the feasibility and effectiveness of using web-based tools for screening college students for marijuana use and providing brief interventions.[3] Students who use marijuana have an increased likelihood of poor academic performance, as well as physical health and relationships problems. Despite the availability of efficacious interventions,

[1] Rhoades KA et al. Drug Use Trajectories After a Randomized Controlled Trial of MTFC: Associations with Partner Drug Use. J Res Adolesc. 2014 Mar 1;24(1):40-54. PubMed PMID: 24729667

[2] Kim HK, et al. Intervention Effects on Health-Risking Sexual Behavior Among Girls in Foster Care: The Role of Placement Disruption and Tobacco and Marijuana Use. J Child Adolesc Subst Abuse. 2013 Nov 1;22(5):370-387. PubMed PMID: 24043921

[3] Palfai TP, et al. Web-based screening and brief intervention for student marijuana use in a university health center: pilot study to examine the implementation of eCHECKUP TO GO in different contexts. Addict Behav. 2014 Sep;39(9):1346-52.

few students identify their marijuana use as problematic or seek treatment to reduce their use. Recent developments in health technology have expanded the range of tools available to engage students in screening and to deliver interventions. A pilot study was conducted to explore the efficacy of a web-based screening and brief intervention tool that delivers personalized feedback in an easily utilized and confidential manner to students presenting their marijuana use to a university health center. The researchers found that while the intervention did not reduce frequency of marijuana use the intervention significantly altered perceived norms regarding marijuana use. The findings demonstrated that it is feasible to screen and identify marijuana users in a college student health center and deliver a web-based intervention. The study suggests that these types of technology based intervention can be useful for correcting misperceptions of norms and reducing related consequences.

Collectively these findings 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. 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 rapidly move more promising science-based addiction treatments into community settings, to improve existing drug treatment for criminal justice populations, and to inform the development of integrated treatment models. The CJ-DATS program included testing of *Medication-Assisted Treatment Implementation in Community Correctional Environments (MATICCE) and HIV Services and Treatment Implementation in Corrections (HIV-STIC).* The MATICCE protocol tested implementation approaches aimed at improving service coordination between community correctional agencies and local treatment agencies. The HIV-STIC protocol tested an organizational intervention strategy targeting effective implementation of quality improvements in HIV services for preventing, detecting, and treating HIV in offenders under correctional supervision. 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, quality improvement, and of drug abuse treatment programs for criminal justice populations.

The CJ-DATS research protocols developed in FY 2010 to test the two implementation models – MATTICCE and HIV-STIC – completed data collection in FY 2014. Across the two protocols

described below, 8 peer-reviewed publications have been published to date[4,5,6,7,8,9,10,11]. More than a dozen additional manuscripts are in progress.

MATICCE was a collaborative study involving nine academic research centers (RCs), each with two community corrections partner agencies. The MATICCE protocol tested implementation approaches aimed at improving service coordination between community correctional agencies and local treatment agencies. The goals were to increase the number of persons in corrections who are given access to medication-assisted treatment (MAT) and to improve community corrections agents' knowledge and perceptions about MAT and increase their intent to refer individuals to appropriate community-based MAT services. The study randomized correctional agencies to one of two implementation strategies: 1) a KPI (Knowledge, Perception, and Information) intervention where correctional staff received structured training on use of medications in addiction treatment, including the effectiveness of MAT for reducing drug use and crime, for overcoming negative perceptions about MAT, and for providing information about local healthcare providers offering MAT; or 2) the KPI training plus an Organizational Linkage (OL) intervention, which engages key representatives from the corrections and treatment agencies in a strategic planning process designed to facilitate inter-organizational referral relationships, thereby improving the flow of offenders from community corrections to community-based treatment.

One peer-reviewed publication reporting on results of the MATICCE program is currently in press. This publication reports that the KPI staff training coupled with the facilitated OL strategic planning intervention was more effective than staff training alone in improving probation and parole officers' acceptance of MAT and willingness to refer clients to treatment. There are currently two additional publications related to the MATICCE study undergoing peer review and five being prepared for submission.

HIV-STIC was a collaborative study involving 9 academic research centers (RCs) and 30 community corrections partner agencies. The HIV-STIC protocol tested an organizational intervention strategy targeting effective implementation of quality improvements in HIV

[4] Pearson, F., et al. (2014).Efficacy of a process improvement intervention on delivery of HIV services: A multi-site trial. American Journal of Public Health.
[5] Visher, C., et al. (2014). The effect of a local change team intervention on staff attitudes toward HIV service delivery in correctional settings: A randomized trial. AIDS Education and Prevention, 25:5, 411-428.
[6] Gordon, M., et al. (2014). Buprenorphine treatment for probationers and parolees. Substance Abuse. DOI: 10.1080/08897077.2014.902787
[7] Swan, H., et al. (In press, 2015). Improvements in correctional HIV services: A case study in Delaware. Journal of Correctional Health Care. Special Issue 21(2).
[8] Belenko, S., et al. (2013). Policies and practices in the delivery of HIV services in correctional agencies and facilities: Results from a multi-site survey. Journal of Correctional Health Care, 19(4), 293-310.
[9] Ducharme, L.J., et al. (2013). Implementing drug abuse treatment services in criminal justice settings: Introduction to the CJ-DATS study protocol series. Health & Justice, 1:5.
[10] Friedmann, P.D., et al. (2013). A cluster randomized trial of an organizational linkage intervention for offenders with substance use disorders: Study protocol. Health & Justice, 1:6.
[11] Belenko, S., et al. (2013). A cluster randomized trial of utilizing a local change team approach to improve the delivery of HIV services in correctional settings: Study protocol. Health & Justice, 1:8.

services for preventing, detecting, and treating HIV in offenders under correctional supervision. The study randomized correctional facilities to one of two conditions. A control received basic training on the fundamentals of HIV infection, prevention, testing, and treatment, as well as information about the HIV services continuum. The experimental group implemented a process improvement approach to guide a Local Change Team (LCT) through a structured series of steps to improve HIV services. Such models have been found to improve health services implementation in other settings, but had not previously been tested in correctional settings or with HIV services.

Multiple peer-reviewed publications were released in 2014 demonstrating that the modified NIATx (Network for Improvement of Addiction Treatment) process improvement model used by the HIV-STIC protocol was successful in increasing the likelihood that a correctional facility would successfully deliver HIV services to their inmates as compared to facilities that only received training on HIV services.[12] The process improvement model also resulted in more positive attitudes toward HIV service delivery among correctional staff.[13] A survey of sites participating in the CJ-DATS HIV-STIC protocol prior to study commencement indicated that there was wide variation in the degree to which these correctional facilities adhered to national guidelines around HIV prevention, detection and care.[14] Gaps in HIV service delivery were primarily attributed to limited resources. Five additional publications related to HIV-STIC are currently in development.

In July 2013 NIDA launched the Juvenile Justice Translational Research on Interventions for Adolescents in the Legal System (JJ-TRIALS) program. JJ-TRIALS 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. This research program will provide insight 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 service delivery for at-risk youth. The cooperative will also conduct a nationally representative survey of the juvenile justice system that will provide information about policies and practices related to substance use assessment and service delivery in these settings across the United States.

NIDA is also supporting the Seek, Test, Treat, and Retain (STTR) Initiative to empirically test the STTR paradigm with drug abusers in criminal justice populations. Researchers are developing,

[12] Pearson, F., et al. (2014). Efficacy of a process improvement intervention on delivery of HIV services: A multi-site trial. American Journal of Public Health.
[13] Visher, C., et al (2014). The effect of a local change team intervention on staff attitudes toward HIV service delivery in correctional settings: A randomized trial. AIDS Education and Prevention, 25:5, 411-428
[14] Belenko, S., et al. (2013). Policies and practices in the delivery of HIV services in correctional agencies and facilities: Results from a multi-site survey. Journal of Correctional Health Care, 19(4), 293-310.

implementing, and testing strategies to increase HIV testing and the provision of 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. (HAART, or highly active antiretroviral therapy, is a customized combination of different classes of medications that a physician prescribes based on such factors as the patient's viral load (how much virus is in the blood), the particular strain of the virus, the CD4+ cell count, and other considerations (e.g., disease symptoms).)

Research Highlights

Decreased dopamine signaling in the striatum leads to escalation of cocaine use in rats

Drug addiction is a neuropsychiatric disorder marked by escalating drug use. Dopamine neurotransmission in the ventromedial striatum (VMS) (part of the brain reward system) mediates the acute reinforcing effects of abused drugs, but with prolonged use the dorsolateral striatum is thought to assume control over drug seeking. NIDA supported researchers[15] measured dopamine release in these brain regions during a cocaine self-administration experiment that produced escalation of drug-taking in rats. Surprisingly, they found that the typical rapid, phasic bursts of dopamine decreased in both regions as the rate of cocaine intake increased. The decrement in dopamine in the VMS was significantly correlated with the rate of escalation of drug use. Administration of a drug that replenished dopamine signaling, the dopamine precursor L-DOPA, in the VMS reversed escalation of drug use demonstrating a causal relationship between lower dopamine release and excessive drug use. These data provide new mechanistic and therapeutic insights into the excessive drug intake that occurs following chronic use.

Baseline cognitive inhibitory task performance predicts subsequent substance use behaviors

Adolescent substance use has been associated with poorer neuropsychological functioning, but it is unclear if deficits predate or follow the onset of use. A recent prospective study[16] sought to understand how neuropsychological functioning during early adolescence could predict substance use by late adolescence. Participants included 175 substance-use-naïve healthy 12- to 14-year-olds recruited from local schools who completed extensive interviews and neuropsychological tests. Each year, participants' substance use was assessed. By late adolescence (ages 17 to 18), 105 participants transitioned into substance use and 75 remained substance-naïve. The study examined how baseline cognitive performance predicted subsequent substance use, controlling for common substance use risk factors (i.e., family history, externalizing behaviors, gender, pubertal development, and age). Poorer baseline performance on tests of cognitive inhibition-interference predicted higher measures of drinking and marijuana use by ages 17 to 18. Performances on short-term memory, sustained attention,

[15] Willuhn et al. Excessive cocaine use results from decreased phasic dopamine signaling In the striatum. Nat Neurosci. 17(5):704-9 (2014).

[16] Squeglia LM. Et al. Inhibition during Early Adolescence Predicts Alcohol and Marijuana Use by Late Adolescence. Neuropsychology 28(5):782-90 (2014).

verbal learning and memory, visuospatial functioning and spatial planning did not predict subsequent substance use behavior. Inhibitory functioning measures could help identify teens at risk for initiating heavy substance use during adolescence, and potentially could be modified to improve outcome.

Early onset marijuana use associated with white matter abnormalities and higher impulsivity

Adolescence is a critical period of active brain development, teens and emerging adults are at greater risk for experiencing the negative effects of marijuana (MJ) on the brain. A recent study[17] examined the relationship between age of onset of MJ use, white matter microstructure, and reported impulsivity in chronic, heavy MJ smokers. Twenty-five MJ smokers and 18 healthy controls underwent diffusion tensor imaging and completed a standard Impulsiveness Scale (Barratt). MJ smokers were also divided into early onset (regular use prior to age 16) and late onset (age 16 or later) groups in order to clarify the impact of age of onset of MJ use on these variables. MJ smokers exhibited alterations in white matter microstructure (significantly reduced 15 fractional anisotropy (FA) relative to controls) as well as higher levels of impulsivity. Earlier MJ onset was associated with greater white matter alterations. Interestingly, within the early onset group, higher impulsivity scores were correlated with lower FA, a relationship that was not observed in the late onset smokers. MJ use is associated with altered white matter development and reported impulsivity, particularly in early onset smokers.

Impact of marijuana legalization in Colorado on perceived risk of marijuana's harms

In 2009, policy changes were accompanied by a rapid increase in the number of medical marijuana cardholders in Colorado. A recent study[18] using the National Survey on Drug Use and Health tested for temporal changes in marijuana attitudes and marijuana use related outcomes in Colorado (2003-11) and differences between Colorado and thirty-four non-medical marijuana states (NMMS). The authors of this study tested whether patterns seen in Colorado prior to (2006-8) and during (2009-11) marijuana commercialization differed from patterns in NMMS while controlling for demographics. Within Colorado the percentage of individuals perceiving "great-risk" to using marijuana 1-2 times per week dropped significantly in all age groups studied between 2007-8 and 2010-11 (from 45% to 31% among those 26 years and older). By 2010-11 past-year marijuana abuse and dependence had become more prevalent in Colorado for 12-17 year olds (5% vs 3% in NMMS) and 18-25 year olds (9% vs. 5%). Analyses demonstrated significantly greater reductions in perceived risk among those 26 years and older and marijuana abuse/dependence among 12-17 year olds in Colorado compared to NMMS in more recent years (2009-11 vs. 2006-8). These results show that commercialization of marijuana in Colorado has been associated with lower risk perception. Evidence is suggestive of an association with increased marijuana abuse/dependence. Analyses including subsequent years, once available, will help determine whether such changes represent momentary vs. sustained effects.

[17] Gruber SA et al. Worth the wait: effects of age of onset of marijuana use on white matter and impulsivity. Psychopharmacology. 231(8):1455–1465 (2014)

[18] Schuermeyer J. et al. Temporal trends in marijuana attitudes, availability and use in Colorado compared to non-medical Marijuana States: 2003-11.Drug Alcohol Depend. 140:145-55 (2014).

Buprenorphine taper is less effective than maintenance in treatment of opioid use disorders

Prescription drug abuse in the United States and elsewhere in the world is increasing at an alarming rate with non-medical opioid use increasing to epidemic proportions over the past two decades. It is imperative to identify and effectively treat individuals with opioid use disorders, however evidence-based medication assisted treatment strategies are often not provided or are restricted in ways that decrease their efficacy. A recent investigation[19] explored outcomes associated with tapering patients off of buprenorphine, a partial opioid agonist, over a nine-week period of time (after six weeks of stabilization) compares to patients maintained on the medication. The study concluded that maintenance buprenorphine therapy is more effective than tapering and discontinuation of the medication in treating prescription opioid-dependent patients in primary care settings. The results suggest that buprenorphine taper should be used only when it is clinically indicated in the treatment of patients dependent on prescription opioids. Additional research is needed to help identify factors associated with successful tapering and maintenance therapy.

National Institute on Alcohol Abuse and Alcoholism		
Selected Measures of Performance	**FY 2014 Target**	**FY 2014 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	Develop materials for dissemination to academic officials that help them address underage and harmful drinking and other substance use by their students.	NIH developed a research-based decision tool, the NIAAA College Alcohol Interventions Matrix (CollegeAIM), to help colleges and universities select appropriate strategies to meet their alcohol intervention goals.
» 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.	Support research to evaluate the effectiveness of the underage drinking screening guide as a predictor of alcohol risk, alcohol use, and related problems, including alcohol use disorders to improve service and treatment options for at-risk youth.	NIH continued to support research to evaluate NIAAA's *Alcohol Screening and Brief Intervention for Youth: A Practitioner's Guide* in emergency department, juvenile justice, school, and primary care settings, and for youth with chronic conditions.

Prevention – SRO-5.15

NIAAA developed a research-based decision tool to help colleges and universities select appropriate strategies to reduce underage and excessive drinking and their consequences.

[19] Fiellin DA. et al. Primary Care–Based Buprenorphine Taper vs Maintenance Therapy for Prescription Opioid Dependence. JAMA Intern Med. 2014;174(12):1947-1954.

The extent of binge drinking and related consequences such as blackouts, assaults and sexual assaults, alcohol poisonings, injuries, and deaths, on college campuses is alarming. Efforts to alter drinking trajectories at this stage have life-changing potential and can significantly reduce the burden of illness resulting from alcohol-related problems. 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 a research-based decision tool to help colleges and universities select appropriate strategies to meet their alcohol intervention goals. The user-friendly decision tool will form the basis of a guide which will allow college presidents and administrators to review the strategies they are currently using as well as explore others that may serve them better. This tool and guide, the NIAAA College Alcohol Interventions Matrix (CollegeAIM), will allow users to search for strategies according to intervention level (e.g., individual, group, campus-wide, community) and evaluate factors such as effectiveness, cost, and ease of implementation. The NIAAA CollegeAIM is being finalized and will be released in 2015. An interactive online version of the decision tool is envisioned.

Treatment – SRO-8.7

Extramural researchers continued to evaluate NIAAA's Alcohol Screening and Brief Intervention for Youth: A Practitioner's Guide in emergency department, juvenile justice, school, and primary care settings, and for youth with chronic conditions.

To expand the venues in which at-risk youth can be screened and referred to treatment when appropriate, NIAAA is supporting six five-year studies that are evaluating the youth alcohol screening guide in practice: one in a network of emergency departments, one in a juvenile justice setting, one in a school setting, two in primary care, and one with youth who have a chronic condition (e.g., asthma, diabetes). In addition to evaluating the effectiveness of the screening guide as a predictor of alcohol risk, alcohol use, and related problems, including alcohol use disorder, these studies are also evaluating the effectiveness of the guide as an initial screen for drug use and other behavioral health problems. These studies will provide feedback to NIAAA that will facilitate refinement of the guide and help identify settings where use of the guide is appropriate and effective, thereby informing strategies for more widespread dissemination. In FY 2014, NIAAA also continued efforts to increase clinicians' use of the youth alcohol screening guide in primary care and other health care settings by offering an online course developed with Medscape to provide continuing medical education (CME) credits for health care providers. To date, more than 24,000 health care providers have been Medscape certified, and almost 200,000 copies of the youth guide have been distributed.

Research Highlights

<u>Assessing the Impact of Adolescent Alcohol Exposure on the Developing Brain</u>

Adolescence is a period of significant brain maturation and also the time when many individuals initiate and escalate alcohol consumption. Previous studies have shown an association between excessive drinking during adolescence and deficits in brain structure and function; however, it is

not clear whether the deficits predated the onset of alcohol use or occurred as a consequence of it. 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 800 adolescents ages 12 to 21, and are using advanced brain imaging as well as 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 alcohol use disorder. In a recent study supported through NCANDA, researchers used high resolution magnetic resonance imaging to assess the brain structure of 40 healthy adolescents, ages 12-17, half of whom initiated heavy drinking during a three year follow up. The researchers found that youth who transitioned from no or minimal substance use to heavy drinking had structural abnormalities prior to the initiation of alcohol use. These abnormalities included smaller brain volumes in specific regions of the frontal cortex, an area important for executive functioning. They also showed that youth who transitioned to heavy drinking had significant reductions in brain volumes after alcohol use was initiated, compared to non-drinking youth. These reductions occurred in regions important for sensory integration, feedback processing, motor control, habit learning, visual object recognition, and language comprehension. Whereas both heavy drinking and non-drinking groups showed reductions in brain volumes as a result of normal developmental pruning, those who transitioned to heavy drinking during the study showed accelerated reductions in brain volumes.[20]

Binge drinking during adolescence reduces white matter in specific regions of rat brains with effects that persist into adulthood

Previous studies have demonstrated that heavy binge drinking is associated with reduced white matter integrity in various brain structures, including the corpus callosum, in both adolescents and alcohol dependent adults. In a recent study, researchers used rodent models of adolescent binge drinking and adult alcohol dependence to gain insight into how alcohol affects white matter integrity in the frontal cortex of the brain. They found that adolescent binge drinking reduced the size of anterior branches of the corpus callosum and this neuropathology correlated with higher relapse to drinking in adulthood. The researchers also demonstrated that adolescent binge drinking was associated with damaged myelin, the insulating sheath that forms around the nerve cells that comprise white matter, in the medial prefrontal cortex in adulthood, as well as reduced density of myelin in the medial prefrontal cortex in adolescence. Heavier drinking in adolescence also predicted worse performance on a working memory task in adulthood. These results suggest that adolescent binge drinking may affect white matter integrity in the medial prefrontal cortex through reduction of myelin and these changes may contribute to deficits in executive function in adulthood.[21]

[20] Squeglia LM, Rinker DA, Bartsch H, Castro N, Chung Y, Dale AM, Jernigan TL, Tapert SF. Brain volume reductions in adolescent heavy drinkers. Dev Cogn Neurosci. 2014 Jul;9:117-25. doi: 10.1016/j.dcn.2014.02.005. Epub 2014 Feb 22.

[21] Vargas WM, Bengston L, Gilpin NW, Whitcomb BW, Richardson HN. Alcohol Binge Drinking during Adolescence or Dependence during Adulthood Reduces Prefrontal Myelin in Male Rats. J Neurosci. 2014 Oct 29;34(44):14777-82. doi: 10.1523/JNEUROSCI.3189-13.2014.