Department of Health and Human Services

National Institutes of Health

Drug Control Programs

<table>
<thead>
<tr>
<th>FY 2015 Budget</th>
<th>Page No.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Table</td>
<td>2</td>
</tr>
<tr>
<td>Justification</td>
<td>3</td>
</tr>
</tbody>
</table>
Drug Resources by Function

<table>
<thead>
<tr>
<th>Function</th>
<th>FY 2013 Actual</th>
<th>FY 2014 Enacted</th>
<th>FY 2015 President’s Budget</th>
</tr>
</thead>
<tbody>
<tr>
<td>Research and Development: Prevention</td>
<td>$390.255</td>
<td>$403.667</td>
<td>$406.222</td>
</tr>
<tr>
<td>Research and Development: Treatment</td>
<td>663.748</td>
<td>675.533</td>
<td>680.492</td>
</tr>
<tr>
<td><strong>Total Drug Resources by Function</strong></td>
<td><strong>$1,054.003</strong></td>
<td><strong>$1,079.200</strong></td>
<td><strong>$1,086.714</strong></td>
</tr>
</tbody>
</table>

Drug Resources by Decision Unit

<table>
<thead>
<tr>
<th>Decision Unit</th>
<th>FY 2013 Actual</th>
<th>FY 2014 Enacted</th>
<th>FY 2015 President’s Budget</th>
</tr>
</thead>
<tbody>
<tr>
<td>National Institute on Drug Abuse ¹</td>
<td>$992.225</td>
<td>$1,015.754</td>
<td>$1,023.268</td>
</tr>
<tr>
<td>National Institute on Alcohol Abuse and Alcoholism</td>
<td>61.778</td>
<td>63.446</td>
<td>63.446</td>
</tr>
<tr>
<td><strong>Total Drug Resources by Decision Unit</strong></td>
<td><strong>$1,054.003</strong></td>
<td><strong>$1,079.200</strong></td>
<td><strong>$1,086.714</strong></td>
</tr>
</tbody>
</table>

Drug Resources Personnel Summary

| Total FTEs (direct only) | 394 | 394 | 394 |

Drug Resources as a Percent of Budget

| Total Agency Budget Authority (in Billions) | $29.001 | $30.003 | $30.203 |
| Drug Resources Percentage                   | 3.63%   | 3.60%   | 3.60%   |

¹ Comparable Budget Authority in FY 2013 and FY 2014
Program Summary

MISSION

National Institute on Drug Abuse (NIDA)
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 abuse and addiction in this country and worldwide.

National Institute on Alcohol Abuse and Alcoholism (NIAAA)
Since its creation, NIAAA has led efforts to define alcohol issues as medical in nature and address them using evidence-based findings. The work supported by the Institute has transformed the understanding of alcohol abuse and dependence and their treatment. NIAAA provides leadership in the national effort to reduce alcohol-related problems, including underage drinking by: conducting and supporting research in a wide range of scientific areas including genetics, neuroscience, epidemiology, health risks and benefits of alcohol consumption, prevention, and treatment; coordinating and collaborating with other research institutes and Federal programs on alcohol-related issues; collaborating with international, national, state, and local institutions, organizations, agencies, and programs engaged in alcohol-related work; and translating and disseminating research findings to health care providers, researchers, policymakers, and the public.

Collaborative Research on Addiction at NIH (CRAN)
NIH established the Collaborative Research on Addiction at NIH (CRAN) in FY 2013 to facilitate collaborative research across Institutes on substance use, abuse, addiction, and their related health consequences. The National Institute on Alcohol Abuse and Alcoholism (NIAAA), the National Institute on Drug Abuse (NIDA), and the National Cancer Institute are the lead Institutes; participation by other NIH Institutes/Centers (ICs) is encouraged for relevant initiatives.

METHODOLOGY
NIDA’s entire budget is drug-related and therefore 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, abuse and dependence in minors (children under the legal drinking age of 21). It includes all alcohol related research in minors, including behavioral research, screening and intervention studies and longitudinal studies. Beginning with the reporting of FY 2010 final budget authority, NIAAA’s methodology for developing budget estimates for the Budget and Performance Summary uses the NIH research categorization and

DCP-3
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 2015 Request is $1,086.7 million for NIH’s drug budget related activities, which is an increase of $7.5 million above the FY 2014 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 addiction, 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 problems, HIV, or both, into a network of care, and generate a major public health impact.

**National Institute on Drug Abuse**

The FY 2015 Request is $1,023.3 million for NIDA, which is an increase of $7.5 million above the FY 2014 level. 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). Each is discussed below.

**Epidemiology, Services and Prevention Research (FY 2015 Request: $253.8 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 (e.g., the Community Epidemiology Work Group) to monitor drug-related issues and trends locally and nationally. Program efforts help identify substance abuse trends locally, nationally, and internationally; guide development of responsive interventions for a variety of populations; and encourage optimal service delivery in real-world settings. For example, factors associated with marijuana use have been undergoing dramatic changes. The potency, sources, availability, public perception, and legal status are significantly different than when marijuana use became a national issue more than 40 years ago. NIDA plans to support research to better understand the longer term outcomes resulting from these changes, such as trends in use, harm perception, clinical/social consequences, brain development, educational outcomes, and market/demographic variables, particularly for
adolescents and young adults. Such knowledge can be then used to inform policy, the public, and to improve prevention and treatment interventions.

**Basic and Clinical Neuroscience Research (FY 2015 Request: $440.7 million)**
The Basic and Clinical Neuroscience programs work together to expand understanding of the neurobiological, genetic/epigenetic, and behavioral factors that underlie drug abuse and addiction. Specifically, they examine which variables influence risk of drug abuse, addiction, and drug-related disorders; how addiction works in the brain, including the effects of drugs on the expression or silencing of genes; and how resultant changes affect brain function and consequent behaviors. Collectively, this research provides critical information to develop and test novel prevention and treatment interventions for drug abuse and addiction. For example, as mentioned above, a pressing research priority that has recently emerged due to the rapidly changing political and legal landscape surrounding marijuana, is the need to improve our understanding of the role of the endocannabinoid system in brain development, function and activity and the impact of marijuana use on these processes (particularly among young people). This Division also supports fundamental research to better understand brain function. For example, our knowledge of the various mechanisms the brain uses to fuel its operations (i.e., brain energetics) is surprisingly limited. Energy utilization patterns in the brain enable and shape all mental and behavioral activities, both normal and pathological. Brain energy utilization (and thus behavior) is profoundly affected by environmental conditions, such as diet, stress and exposure to drugs of abuse. NIDA is, therefore, soliciting grant applications to improve our basic understanding of the molecular mechanisms whereby chronic exposure to drugs of abuse impacts brain energetics. Successful projects are poised to identify new molecular targets that could be harnessed to design novel medications and/or behavioral treatments for addiction.

**Pharmacotherapies and Medical Consequences (FY 2015 Request: $133.0 million)**
This program area is responsible for medications development aimed at helping people recover from drug abuse and addiction and sustain abstinence. For example, this Division is encouraging the formation of strategic alliances to leverage NIDA resources between collaborating organizations (such as academic institutions, pharmaceutical and biotechnology companies) with the common goal of advancing medications through the development pipeline toward Food and Drug Administration (FDA) approval, in a timely manner. This Division also includes programs to address the medical consequences of drug abuse and addiction, including infectious diseases such as Hepatitis C virus (HCV) and HIV. Because of the high co-occurrence of substance abuse and infectious diseases, infectious disease specialists have a role to play in ensuring that their HIV+/HCV+ patients receive treatment for their substance-use disorders. NIDA plans to support research to address this critical gap by understanding both the barriers to and opportunities for engaging infectious disease specialists in implementing screening, brief intervention, and referral to treatment in their practices.

**Clinical Trials Network (FY 2015 Request: $45.5 million)**
NIDA’s National Drug Abuse Treatment Clinical Trials Network (CTN) comprises 13 research nodes and more than 240 individual community treatment programs 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 drug abuse and related disorders, such as comorbid mental health disorders and HIV, with diverse patient populations and
community treatment providers. The CTN is currently at the final stage of completing (1) a multi-site study to evaluate the effect of Screening, Brief Intervention, and Referral to Treatment (SBIRT) in emergency departments on substance use and substance-related outcomes, (2) a trial of the safety and effectiveness of Suboxone (buprenorphine) plus Vivitrol (extended-release naltrexone) for the treatment of cocaine addiction in patients also abusing opioids, and (3) a randomized trial evaluating safety and preliminary efficacy of buspirone for relapse-prevention in patients with cocaine addiction. Ongoing studies are evaluating (1) the effect of contingency management on treatment engagement of HIV-infected drug users, (2) comparison of Vivitrol to Suboxone for patients addicted to heroin or other opioids, including prescription pain relievers, (3) N-acetylcysteine for treatment of marijuana addiction, (4) combination therapy with Vivitrol plus Wellbutrin (bupropion) for treatment of methamphetamine addiction, and (5) Vivitrol for HIV positive opioid users in HIV settings.

**Intramural Research Program (IRP) (FY 2015 Request: $88.2 million)**
The Intramural Research Program performs cutting edge research within a coordinated multidisciplinary framework. The IRP attempts to (1) elucidate the nature of the addictive process; (2) determine the potential use of emerging new therapies for substance abuse, 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.

A prime example of the unique role the IRP plays in furthering substance abuse research is the recently established Designer Drug Research Unit (DDRU), created in response to the worldwide epidemic of synthetic drug abuse. Synthetic drugs are marketed as safe, cheap and legal alternatives to illicit drugs like marijuana, cocaine and ecstasy. However, they can produce serious cardiovascular and neurological side-effects that require emergency medical care and 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. The NIDA 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. The IRP also works collaboratively with NIDA’s Extramural Division of Pharmacotherapies and Medical Consequences of Drug Abuse to identify potential targets for addiction medications, an approach that should speed up the progress of selected targets along the NIDA medications development pipeline. In addition, NIDA and NIAAA together have made significant progress at integrating their intramural research programs in substance use, abuse, and addiction, including the appointment of a single Clinical Director for NIAAA and NIDA and the establishment of a joint genetics Intramural Research Program and a common optogenetics lab.

**Research Management and Support (RMS) (FY 2015 Request: $62.0 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 1,800 research grants and more than 190 research and development contracts. In addition to the
infrastructure required to support research and training, NIDA also strives to educate the public about drug abuse and addiction and to raise awareness of the science addressing it.

Adolescents are a key target for NIDA’s outreach efforts. NIDA created National Drug Facts Week (NDFW), a week-long health observance event held annually at the end of January during which teens and scientists connect at local events to discuss the scientific facts about drug abuse and addiction. In 2013, more than 500 events were held reaching all 50 states. Promotional media activities surrounding the week reached more than 71 million people. Another key audience is health care professionals. In October 2012, the Office of National Drug Control Policy (ONDCP) and NIDA launched two online continuing medical education courses—one focused on safe prescribing for pain, the other on managing patients who abuse prescription opioids—in partnership with Medscape. To date, these courses have been completed nearly 75,000 times for credit. In 2014, NIDA will also publish a new NIDA Principles of Effective Treatment for Adolescents, intended to provide parents, referring clinicians, treatment practitioners, youth, and others with an evidence-based resource to the principles of effective substance abuse treatment for youth.

**National Institute of Alcohol Abuse and Alcoholism**
The FY 2015 Request is $63.446 million for NIAAA’s Underage Drinking activities, which equals to the FY 2014 funding level.

**Underage Drinking (FY 2015 Request: $63.446 million)**
NIAAA has a strong focus on preventing and reducing underage drinking, recognizing the pervasive use of alcohol among young people, and 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 disorders in children and adolescents, and to identify risk for alcohol use, especially for younger children. In FY 2012, NIAAA funded four 5-year studies to evaluate the youth alcohol screening guide, one in a network of emergency departments, one in a juvenile justice setting, one in primary care, and one with youth who have a chronic condition (e.g., asthma or diabetes). In FY 2013, two additional five-year studies were funded to evaluate the guide, one in school settings and another study in primary care. The brief, two-question screener is being assessed in youth ages 9 to 18 as a predictor of alcohol risk, alcohol use, and alcohol problems including alcohol-use disorders, and as an initial screen for other behavioral health problems; for example, other drug use, smoking, or conduct disorder. NIAAA also has a significant investment in underage drinking research including seven ongoing projects that comprise the National Consortium on Alcohol and Neurodevelopment in Adolescence (N-CANDA). Collectively, these projects will follow more than 600 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.

**PERFORMANCE**
This section on FY 2013 performance is based on agency GPRA documents and other agency information. NIH’s GPRA 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. Each measure is 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 2013.

**National Institute on Drug Abuse**

NIDA continues to contribute to a number of trans-NIH scientific research outcomes (SROs). One of these, indicative of NIDA’s contribution to the prevention of substance abuse and addiction, is SRO-3.5: “By 2013, identify and characterize at least two human candidate genes that have been shown to influence risk for substance use disorders and risk for psychiatric disorders using high-risk family, twin, and special population studies.” By identifying genetic factors involved in the various stages of the addiction process, this outcome aids in the development of improved primary (stop drug use before it starts) and secondary (prevent relapse) prevention programs. Please note that NIH is completing SRO-3.5 in FY 2013. In FY 2014, NIH will replace SRO-3.5 with SRO-5.15, which states “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.” Like SRO-3.5, this new measure is indicative of NIDA’s efforts to support prevention research related to substance abuse and addiction.

NIDA also contributes 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

<table>
<thead>
<tr>
<th>Measure</th>
<th>FY 2013 Target</th>
<th>FY 2013 Achieved</th>
</tr>
</thead>
<tbody>
<tr>
<td>SRO-3.5</td>
<td>Continue to characterize functional genetic variations associated with substance abuse disorder and risk for psychiatric disorders using high-risk family, twin, and special population studies.</td>
<td>NIH researchers characterized additional gene variants associated with drug dependence and smoking cessation as well as developed new resources to help interpret the functional significance of identified variants.</td>
</tr>
<tr>
<td>SRO-8.7</td>
<td>Continue ongoing data collection in 2 studies designed to test 3 implementation strategies for incorporating research-supported treatment interventions in the criminal justice system using collaborative implementation protocols.</td>
<td>The CJ-DATS research protocols MATICCE and HIV-STIC completed data collection in FY 2013.</td>
</tr>
</tbody>
</table>

Discussion

Prevention – SRO-3.5

NIDA contributes to NIH’s scientific research goal of identifying and characterizing human candidate genes that influence risk for substance use disorders and risk of psychiatric disorders, by funding research to further characterize the functional roles of genetic variations associated with substance abuse.

From 2007 to 2013, multiple genome-wide and targeted association studies have revealed significant associations between genetic variants and substance abuse and addiction. NIDA supported deep sequencing and functional analyses to understand the relationships and mechanisms of how those genetic variants contribute to addiction and its treatment.

Recent work by NIDA-supported researchers has identified new variants associated with opioid addiction. Xie et al. (2013) sequenced 1,520 subjects with co-occurring alcohol, cocaine, and opioid dependence and identified 11 rare variants that showed an association with opioid dependence in an African American sample. Although rare variants were identified in several genes, the bulk of them were identified in DISC1 and GRIN2B genes. This targeted sequencing approach, i.e., repeatedly sequencing a known region, is particularly valuable for substance abuse phenotypes because of what we already know about the genes involved in the metabolism of the substance or major biologic systems that are affected.

---

In other work, NIDA researchers built upon work reported last year on variations in the nicotinic subunit receptor cluster on chromosome 15 that may be associated with response to smoking cessation medications. Bergen et al. evaluated nicotinic receptor subunit polymorphisms in an analysis of 8 separate, but similar, randomized clinical trials. The data show that the abstinence rates at the end of treatment and at 6 months post treatment were influenced by CHRNA5 variants. Another study examined whether these genes predict efficacy of the smoking cessation medications varenicline and bupropion. Continuous abstinence (weeks 9–12) with varenicline treatment was associated with multiple nAChR subunit genes (including CHRNA5, CHRNA5, and CHRNA4); whereas abstinence associated with bupropion treatment was associated with the CYP2B6 gene. Thus, different loci are associated with varenicline vs. bupropion response, suggesting that additional research may identify clinically useful markers to guide treatment decisions.

Another genetic variant of interest, CYP2A6, has been shown to affect how quickly nicotine is metabolized, which in turn influences nicotine use and the efficacy of smoking cessation medications. For example, a recent NIDA-funded study showed that differences in the CYP2A6 gene can predict whether nicotine replacement therapies (nicotine lozenge and/or nicotine patch) will be effective in helping a person quit smoking. The effectiveness of bupropion, a non-nicotine based medication often prescribed to quit smoking, was not affected by differences in this gene. This study adds to previous findings with the CHRNA5 gene, showing that screening for genetic variation may better guide personalized treatments to quit smoking. However, before moving these findings to the clinic, additional data are needed to assess long term outcomes, and generalizability to diverse populations.

Lastly, an important part of functional characterization is using computational approaches to integrate information from a variety of sources. To this end, NIDA has supported several studies to facilitate the discovery and possible functional significance of genetic or chromosomal changes corresponding to disease status. NIDA has supported methods to more robustly identify contributing (or causal) single nucleotide polymorphisms related to addiction. (Single nucleotide polymorphisms, or SNPs, are DNA sequence variations that occur when a single nucleotide (A, T, C, or G) in the genome sequence is altered.) In addition, NIDA supported the development of a resource to explore long-range genomic interactions using the WashU Epigenome Browser to gain deeper insights to genomic changes.

---


DCP-10
**Treatment - SRO-8.7**

NIDA also contributes to NIH’s scientific research goal of identifying effective implementation strategies that enhance the uptake of research-tested interventions in service systems such as primary care, specialty care, and community practice. NIDA recognizes that despite major strides in treatment research, only limited improvements have occurred in non-research settings. For example, the rates of drug abuse among people involved with the criminal justice system are very high (e.g., 70-85 percent of state inmates) yet few receive treatment while incarcerated (approximately 13 percent), jeopardizing both public health and public safety. To improve drug treatment within the criminal justice system, NIDA continues to support a national multisite research program, the Criminal Justice-Drug Abuse Treatment Studies (CJ–DATS), which tests strategies for how best to implement effective treatment within the criminal justice system.

The CJ-DATS protocol completed data collection in FY 2013; research protocols are described in the FY 2010 target description. Specifically, the **MATICCE (Medication-Assisted Treatment Implementation in Community Correctional Environments)** protocol is testing implementation approaches aimed at improving service coordination between community correctional agencies and local treatment agencies; to increase the number of persons in corrections who are provided medication-assisted treatment (MAT); and improving community corrections agents’ knowledge and perceptions about MAT and intent to refer appropriate individuals to community-based MAT services. The interventions to be tested are the Knowledge, Perception, and Information (KPI) intervention and the KPI + organizational linkage (OL) intervention. The KPI intervention consists of professional training for correctional staff on use of medications in addiction treatment. The KPI + OL intervention is intended to improve correctional staff knowledge, perceptions, and capacity for interorganizational relationships to improve referral to, utilization of, and support for medication-assisted treatment appropriate for individuals with substance use disorders.

In FY 2013, all nine research centers completed the active implementation protocol—that is, the strategic planning intervention with the Pharmacotherapy Exchange Council (PEC). To date, in each experimental site, the PEC has completed all assigned protocol activities: an assessment/walkthrough process to identify agency needs, a collaborative strategic planning process to identify key goals for improving offender referrals, the implementation of activities needed to achieve those goals, the production of written summary reports and sustainability plans, and the disengagement from the research teams as planned. All research centers implemented the same study protocol and associated measures.

In FY 2013, the research teams completed end-of-intervention and follow-up data collection at all sites. This included records abstraction from offender case reports at the end of the intervention and at 6 months post-intervention to determine the extent to which offenders are referred to treatment and gains are sustained over time. These data can be compared to referral rates documented at baseline (collected in FY 2011). The second half of FY 2013 was devoted to intensive data cleaning and analysis activities. One paper was submitted for publication⁸, and

---

four main findings papers are being prepared for publication. Research teams presented preliminary findings at several national conferences, including the American Association for the Treatment of Opioid Dependence (AATOD), the Association for Medical Education and Research (AMERSA), and the Academic and Health Policy Conference on Correctional Health. FY 2014 is entirely devoted to data analysis, and reporting of study findings.

**HIV Services and Treatment Implementation in Corrections (HIV-STIC)** protocol is testing an organizational intervention strategy for more effectively implementing improvements in HIV services for preventing, detecting, and treating HIV in offenders under correctional supervision. The interventions to be tested are an HIV Training for corrections intervention and Local Change Team (LCT) Process Improvement intervention. The HIV training includes basic training on the fundamentals of HIV infection, prevention, testing, and treatment, as well as information about the HIV services continuum and its implications. The process improvement using LCT guides the team through a structured series of quality improvement techniques intended to identify key change targets and to make incremental organizational changes that will improve the quality and coordination of HIV services across correctional and community agencies.

In FY 2013, all nine research centers continued to collect data associated with the active implementation protocol; that is, the HIV training and Local Change Team Intervention. In FY 2013, all sites (experimental and control) have completed the implementation and data collection phases of the study. CJ-DATS investigators submitted three publications to peer-reviewed journal outlets related to the HIV-STIC study during FY 2013. FY 2014 is devoted entirely to data analysis and continued reporting of study findings.

**Research Highlights**

**Long-term effects of universal preventive intervention on prescription drug abuse.**

Brief prevention interventions delivered during middle school are effective at reducing students’ abuse of prescription drugs throughout adolescence and into young adulthood, according to a new NIDA-funded study. Three randomized controlled trials tested the effects of brief universal interventions (i.e., those targeting all kids) aimed at reducing youth risky behaviors and substance use: (1) the Iowa Strengthening Families Program (ISFP); (2) a modified version of the ISFP called the Strengthening Families Program: For Parents and Youth 10-14 (SFP) coupled with Life Skills Training; and (3) the SFP paired with one of three school-based interventions. All tested interventions were associated with significantly lower prescription opioid abuse and lower lifetime prescription drug abuse overall, and the interventions either were equally or more effective for higher-risk subgroups as for lower-risk groups. This study is the first to examine the long-term effectiveness (6-14 years following the intervention) of brief universal prevention programs on reducing prescription drug abuse throughout adolescence and into young adulthood.

**Research suggests that targeted stimulation of the brain’s prefrontal cortex is a promising treatment for addiction.**

Compulsive drug-taking, despite negative health and social consequences, has been the most difficult challenge in human drug addiction. NIDA researchers used an animal model of cocaine addiction, in which some rats exhibited addictive behavior by pushing levers to get cocaine even when followed by a mild electric shock to the foot. Other rats did not exhibit addictive...
responses. The NIDA scientists compared nerve cell firing patterns in both groups of rats by examining cells from the prefrontal cortex. They determined that cocaine produced greater functional brain deficits in the addicted rats. Scientists then used optogenetic techniques on both groups of rats—essentially shining a light onto modified cells to increase or lessen activity in that part of the brain. In the addicted rats, activating the brain cells (thereby removing the deficits) reduced cocaine-seeking. In the non-addicted rats, deactivating the brain cells (thereby creating the deficits) increased compulsive cocaine seeking. This is the first study to show a cause-and-effect relationship between cocaine-induced brain deficits in the prefrontal cortex and compulsive cocaine-seeking.

**New breath test may detect recent marijuana use.**
Marijuana causes serious impairment in motor skills, judgment, and perception, which are necessary for operating a vehicle safely. In the past, testing drivers for recent marijuana use has not been as simple as testing for alcohol, but preliminary research on the detection of THC (tetrahydrocannabinol)—the main psychoactive chemical in marijuana—in the breath of marijuana smokers may change that. According to NIDA scientists who published their work in September, a new breath test they have developed can, in most cases, detect whether a person used marijuana within the previous ½ hour to 2.5 hours, depending on the frequency of use. This could be a valuable tool for workplace or roadside marijuana testing.

**Drug overdose is the leading cause of death in former prisoners.**
A new study identifies drug overdose as the leading cause of death in former prisoners, with prescription opioids most commonly involved in these deaths. In addition, women leaving prison had higher mortality rates from opioids, cocaine, and antidepressants than men.

These findings highlight the vulnerability of former prisoners as they transition from prison to the community, suggesting the need for more effective overdose education, monitoring for medical problems, and drug treatment in prison- and community-based mental and health care systems.

**National Institute of Alcohol Abuse and Alcoholism**
NIAAA continues to contribute to a number of trans-NIH scientific research outcomes (SROs). One which is indicative of NIAAA’s contribution to the prevention of substance abuse and addiction is SRO-3.5: “By 2013, identify and characterize at least two human candidate genes that have been shown to influence risk for substance use disorders and risk for psychiatric disorders using high-risk family, twin, and special population studies.” By identifying genetic factors involved in the various stages of the addiction process, this outcome aids in the development of improved primary (stop drug use before it starts) and secondary (prevent relapse) prevention programs. In FY 2014, NIH will replace SRO-3.5 with SRO-5.15, which states “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.” Like SRO-3.5, this new measure is indicative of NIAAA’s efforts to support prevention research related to underage alcohol abuse and addiction.
In addition NIAAA contributes 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 focusing on treatment implementation, this outcome improves the translation of research into practice. SRO-8.7 is indicative of NIAAA’s efforts to more broadly bring evidence-based treatments for substance addiction to the people who need them.

<table>
<thead>
<tr>
<th>National Institute on Alcohol Abuse and Alcoholism</th>
<th>Selected Measures of Performance</th>
<th>FY 2013 Target</th>
<th>FY 2013 Achieved</th>
</tr>
</thead>
<tbody>
<tr>
<td>SRO-3.5, by 2013, identify and characterize at least two human candidate genes that have been shown to influence risk for substance use disorders and risk for psychiatric disorders using high-risk family, twin, and special population studies.</td>
<td>Complete genome wide association and functional studies and identify potential genomic variants associated with risk for substance use and/or psychiatric disorders.</td>
<td>NIH researchers identified genomic variants that were associated with risk for alcohol dependence.</td>
<td></td>
</tr>
<tr>
<td>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.</td>
<td>Refine the underage drinking screening guide based on feedback from primary care providers and develop strategies to encourage widespread adoption of the guide.</td>
<td>NIH supported two additional studies to evaluate its youth alcohol screening guide and developed CME training through Medscape for physicians, nurses and physicians’ assistants.</td>
<td></td>
</tr>
</tbody>
</table>

**Discussion**

**Prevention – SRO-3.5**

NIH researchers conducted genetic association studies within families in which alcohol dependence is prevalent and identified gene variants associated with alcohol dependence.

For more than two decades NIAAA has supported the Collaborative Studies on Genetics of Alcoholism (COGA), a large-scale national, multi-ethnic, high-risk family study, with the goal of identifying specific genes that can influence a person’s likelihood of developing alcohol dependence. This has resulted in a very rich dataset and repository of phenotypic and neurophysiological data, cell lines, and DNA for current and future studies within COGA. A current focus of COGA is the study of adolescents and young adults from these families, to examine genetic effects across development and to understand the environmental factors that modulate genetic risk in this critical age range. Studies on youth from families with a high density of alcohol dependence will enable researchers to examine how genetic variants identified in one generation influence risk in the next generation and how this risk is influenced by various environmental factors. The research will also further explore if exposure to alcohol during key developmental stages causes epigenetic modifications, defined as changes to DNA structure without changes to the DNA sequence that alter gene expression, which may affect the long-term
risk for alcohol dependence and its sequelae. Analyses will also examine the potential association between these epigenetic changes and patterns of alcohol use initiation.

COGA researchers recently completed a genome wide association study (GWAS) and identified gene variants that are potentially associated with risk for alcohol dependence. According to the Diagnostic and Statistical Manual of Mental Disorders (DSM-IV), the diagnosis of alcohol dependence is based on endorsement of at least 3 of 7 diagnostic criteria. Rather than focusing on the presence or absence of alcohol dependence as the primary outcome, the investigators in this study used the overall number of alcohol dependence criteria met (from 0 to 7), which some studies have indicated is a good diagnostic tool that may reflect the severity of dependence. This approach expanded the sample population. For example, information on older adolescents who may have begun to experiment with alcohol, but who met only one or two alcohol dependence criteria, was included in the analysis. The GWAS was conducted on more than 2,000 subjects from 118 extended families severely affected by alcohol dependence. The genomic variants that showed the strongest association with the number of alcohol dependence criteria endorsed were located in C15orf53, a gene of unknown function. Other genomic variants in C15orf53 that were previously found to affect risk for bipolar disorder also showed a strong association with alcohol dependence risk in the current study, suggesting shared genetic factors may contribute to both disorders. The investigators attempted to replicate the alcohol dependence findings using data from two other addiction-related studies that did not select participants based on a strong family history of alcohol dependence. In these two studies, the associations were weaker. This suggests that severely affected families may have a concentration of genetic variants that influence risk for alcohol dependence but that has less effect on alcohol dependence in the general population. An alternate explanation is that the small effect size seen in this study may be difficult to replicate in other types of samples, especially those of limited size.9

Treatment – SRO-8.7
To encourage use of NIAAA’s youth alcohol screening guide, NIAAA developed an online course with Medscape to provide continuing medical education (CME) credits for physicians, nurses, and physician assistants. To date, nearly 8,000 health care providers have been Medscape certified. Previously, NIAAA issued a request for research applications (RFA) to evaluate the youth alcohol screening guide in practice and funded four projects: one in a network of emergency departments, one in a juvenile justice setting, one in primary care, and one with youth who have a chronic condition (e.g., asthma, diabetes). In FY 2013, NIAAA funded two additional five-year studies under the RFA, another one in primary care and one in a school setting. 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.

An NIAAA-supported study is being conducted in one of the nation’s largest private health care organizations to examine the implementation, effectiveness and cost-effectiveness of SBIRT in reducing adolescent alcohol and other drug use in pediatric care. In this study pediatric practices are randomized to three conditions, i.e., usual care, SBIRT delivered by primary care physicians, and SBIRT delivered by behavioral medicine specialists. SBIRT in this study is based on the CRAFFT screening tool plus referral to treatment. (CRAFFT is a mnemonic acronym based on the first letters of key words in the six screening questions.)

Research Highlights

Study finds missed opportunities for underage alcohol screening.
Although drinking is prevalent among adolescents, doctors often fail to ask and counsel their young patients about drinking. In a random survey of more than 2,500 10th grade students with an average age of 16 years, researchers from NIAAA and the Eunice Kennedy Shriver National Institute of Child Health and Human Development found that 34 percent reported drinking alcohol in the past month. Twenty-six percent said they had binged, defined as five or more drinks per occasion for males, and four or more for females. While more than 80 percent of 10th graders said they had seen a doctor in the past year, just 54 percent of that group were asked about drinking, and 40 percent were advised about alcohol harms. Furthermore, among students who had been seen by a doctor in the past year and who reported drinking in the past month, only 23 percent said they were advised to reduce or stop drinking. Among the 43 students who said that they were drunk six times or more in the past month and who said they had been asked about their drinking by a doctor, about 30 percent were not advised about drinking risks, and two-thirds were not advised to reduce or stop drinking. The researchers caution that in the survey students were asked about past-month drinking, not what they may have told their physicians about their drinking. Studies have shown that screening and brief interventions by health care providers – asking patients about alcohol use and advising them to reduce risky drinking – can promote significant, lasting reductions in drinking levels and alcohol-related problems among adults. Accumulating evidence supports the use of alcohol screening among adolescents.

Genetic influences on alcohol use across stages of development.
COGA researchers performed a longitudinal analysis to understand how genetic risk for alcohol dependence evolves during the transition from adolescence to young adulthood. There is a substantial body of evidence that has demonstrated genetic associations with alcohol dependence in adults; however, there is limited evidence about genetic associations with alcohol dependence symptoms at much younger ages as well as how genetic risk for problem drinking may change over time. Using a sample of 1,070 adolescents and young adults ages 14-25 from COGA families, the researchers tested whether variants in GABRA2, a gene previously associated with adult alcohol dependence, was associated with risky drinking behavior. In this study, drunkenness during the past 12 months was used as a measure of risky drinking behavior because, at earlier ages, genetic influences may be more evident for patterns of problem drinking than for the classical symptoms used to diagnose alcohol dependence. A significant association was observed between each of the six GABRA2 variants tested and a sudden, substantial increase in drunkenness during the transition from adolescence to young adulthood (age 18 to 19). Although males overall exhibited higher levels of drunkenness in the sample studied, the genetic influence of the GABRA2 variants on the increase during age 18 to 19 was more evident in females. For many individuals, this transitional period is marked by multiple milestones such
as attending college, acquiring greater autonomy and forming new social networks. These findings illustrate that genetic effects differ across development from adolescence to adulthood and gender differences are important in understanding these effects.10

Genetic correlates of the age of onset of alcohol use disorders in adolescents and young adults. Research has shown that those who begin to drink at an early age are at greater risk of developing alcohol dependence and early drinking may be influenced by genetic factors. COGA investigators looked at a sample of 2,938 adolescents and young adults ages 12-25 to test if variants in the CHRM2 gene that were previously shown to be associated with adult alcohol dependence could predict the onset of alcohol dependence in adolescents and young adults. The researchers found a significant association with CHRM2 variants and onset of alcohol dependence in adolescents under 16 years of age, including those who also reported ever using an illicit drug. An important difference between this data and the previous adult data was that the CHRM2 variant with the strongest association out of the ones tested was different for the under age 16 group compared to adults.11
