# Resource Summary

<table>
<thead>
<tr>
<th>Drug Resources by Function</th>
<th>FY 2012 Actual</th>
<th>FY 2013 CR</th>
<th>FY 2014 President’s Budget</th>
</tr>
</thead>
<tbody>
<tr>
<td>Research and Development: Prevention</td>
<td>$375.972</td>
<td>$378.525</td>
<td>$383.117</td>
</tr>
<tr>
<td>Research and Development: Treatment</td>
<td>$737.075</td>
<td>$742.054</td>
<td>$750.711</td>
</tr>
<tr>
<td><strong>Total Drug Resources by Function</strong></td>
<td><strong>$1,113.047</strong></td>
<td><strong>$1,120.579</strong></td>
<td><strong>$1,133.828</strong></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Drug Resources by Decision Unit</th>
<th>FY 2012 Actual</th>
<th>FY 2013 CR</th>
<th>FY 2014 President’s Budget</th>
</tr>
</thead>
<tbody>
<tr>
<td>National Institute on Drug Abuse ¹</td>
<td>$1,051.410</td>
<td>$1,058.567</td>
<td>$1,071.612</td>
</tr>
<tr>
<td>National Institute on Alcohol Abuse and Alcoholism</td>
<td>61.636</td>
<td>62.012</td>
<td>62.216</td>
</tr>
<tr>
<td><strong>Total Drug Resources by Decision Unit</strong></td>
<td><strong>$1,113.047</strong></td>
<td><strong>$1,120.579</strong></td>
<td><strong>$1,133.828</strong></td>
</tr>
</tbody>
</table>

## Drug Resources Personnel Summary

| Total FTEs (direct only) | 382 | 411 | 411 |

## Drug Resources as a Percent of Budget

<table>
<thead>
<tr>
<th>Total Agency Budget (in Billions)</th>
<th>2012</th>
<th>2013</th>
<th>2014</th>
</tr>
</thead>
<tbody>
<tr>
<td>Drug Resources Percentage</td>
<td>3.63%</td>
<td>3.63%</td>
<td>3.64%</td>
</tr>
</tbody>
</table>

¹ Comparable Budget Authority in FY 2012 and FY 2013
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. 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. HIV prevention and treatment is another top NIDA research priority including research on integrating treatment for patients with infectious diseases (e.g., HIV, HCV) and substance abuse, and linking vulnerable populations to HIV prevention, testing, and treatment services. We will also pursue a functional integration, that is, a collaborative framework involving other NIH Institutes and Centers (ICs), especially the National Institute on Alcohol Abuse and Alcoholism (NIAAA), continuing to pool resources and expertise, and to work together on a scientific strategic plan. Such approaches will broaden our view of addiction, its precursors and consequences, and strengthen the knowledge base to advance the rapid and broad translation of interventions to prevent and treat addiction.

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.

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 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 2014 President’s Budget request is 1.133.8 million for NIH’s drug budget related activities, which is an increase of 20.8 million above the FY 2012 Actual 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 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 2014 President’s Budget request is 1.072 million for NIDA, which is an increase of 20.2 million above the FY 2012 Actual level. NIDA’s efforts consist of Basic and Clinical Neuroscience Research, Epidemiology, Services and Prevention Research, Pharmacotherapies and Medical Consequences, Clinical Trials Network, the Intramural Research Program (IRP), and Research Management and Support (RM&S). Each is discussed below.

**Basic and Clinical Neuroscience Research (FY 2014 Request: $465.3 million)**
The NIDA Basic and Clinical Neuroscience programs together enlarge our understanding of the neurobiological, genetic/epigenetic, and behavioral factors underlying drug abuse and addiction. This research lays the groundwork for developing effective prevention and treatment interventions. Basic and Clinical divisions at NIDA support research to investigate the molecular and cellular correlates and consequences of substance abuse, HIV infection, and their interactions. For example, new research is building on the growing recognition of the many essential roles played by non-neuronal cells (collectively referred to as glia) in neurotransmission, inflammation, neuroprotection, and energy management in the brain. Recent findings suggest that glia can influence behavioral responses to drugs, including their rewarding/aversive effects. Additionally, viral and host responses to HIV infection are known to usurp and alter glial cell function, undermining their vital role as supporters of neuronal physiology.
Epidemiology, Services and Prevention Research (FY 2014 Request: $264.4 million)
This program area promotes integrated approaches to understand and address the interactions between individuals and environments that contribute to drug abuse and related problems. Program efforts help identify substance abuse trends locally, nationally, and internationally to guide development of responsive interventions for a variety of real-world populations and settings. For example, runaways and other homeless young people are a highly vulnerable population at increased risk for HIV infection and substance abuse. To address this critical public health gap, NIDA plans to support research to better understand the extent of HIV infection among homeless youth, the factors driving it, and how optimally to link these youth to HIV prevention, testing, care and treatment services. Other exemplary studies assess prescription drug abuse trends and the impact of “medical” marijuana laws on attitudes and corresponding use across different age groups. In addition, this NIDA Division oversees partnering initiatives, including the first large-scale NIH-FDA collaboration on tobacco regulatory research since Congress granted FDA the authority to regulate tobacco products. The Population Assessment of Tobacco and Health (PATH) Study, a national, longitudinal cohort study, will follow an estimated 59,000 adults and youth (12 to 18 years old) to assess susceptibility to tobacco use, patterns of use, risk perceptions, and resultant health impacts. Data collection is slated to begin in the fall of 2013, with plans for four or more annual data collection waves. Outcomes will inform current and future regulatory options for the FDA to protect public health, including setting tobacco product standards and communicating the risks of tobacco use to the general public.

Pharmacotherapies and Medical Consequences (FY 2014 Request: $141.5 million)
This program area is responsible for medications development aimed at helping people recover from drug abuse and addiction and sustain abstinence. NIDA is using a new funding paradigm (e.g., “GO-MD” grants) aimed at “de-risking” medications in the early stages of discovery. This approach provides greater up-front support to closely monitored grantees for a shorter period of time, so that they can produce results quicker—whether for new compounds or repurposed medications—or change direction as needed. This Division also supports innovative technological approaches to medication monitoring and delivery. For example, studies are being sought to develop and validate a reliable remote, real-time monitoring system to detect and measure cocaine ingestion in cocaine-dependent people participating in clinical trials. Such technology will be valuable for researchers testing and verifying treatments for cocaine addiction. Finally, this Division 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 2014 Request: $49.6 million)
NIDA’s National Drug Abuse Treatment Clinical Trials Network (CTN) comprises 13 research nodes and more than 240 individual community treatment programs nationwide. The CTN develops and tests treatment protocols for drug abuse and related disorders, such as comorbid mental health disorders and HIV, testing the feasibility and effectiveness of promising medication and behavioral approaches 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 web-delivery of evidence-based psychosocial treatment for substance use disorders, (2) a trial of the safety and effectiveness of buprenorphine plus naltrexone for the treatment of cocaine addiction in patients also dependent on or abusing opioids, and (3) a trial evaluating the impact of adding smoking-cessation to standard treatment for stimulant addiction. Ongoing studies are evaluating the effect of Screening, Brief Intervention, and Referral to Treatment (SBIRT) in emergency departments on substance use and substance-related outcomes, and a new study is comparing extended-release naltrexone (Vivitrol) to buprenorphine for patients addicted to heroin or other opioids, including prescription pain relievers.

Intramural Research Program (IRP) (FY 2014 Request: $88.6 million)
The Intramural 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 emphasis on the brain and its development, maturation, function, and structure. In addition, the IRP supports an HIV/AIDS Pathophysiology and Addiction Medications Discovery Program. IRP investigators are working on varied potential targets for addiction medications, many of which are being pursued through collaborative efforts with NIDA’s extramural medications development program, an approach that should speed up the progress of selected targets along the NIDA medications development pipeline. In addition, NIDA and NIAAA have together made significant progress at integrating our 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 2014 Request: $62.1 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, RMS functions encompass strategic planning, coordination, and evaluation of NIDA's programs, regulatory compliance, international coordination, and liaison with other Federal agencies, Congress, and the public. 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 behind it. Physicians are a key target for NIDA’s outreach efforts. In October 2012, ONDCP and NIDA launched two online continuing medical education courses, using the “test-and-teach” model—one focused on safe prescribing for pain, the other on managing patients who abuse prescription opioids—in
partnership with Medscape, a web resource for health professionals. After just two months, nearly 25,000 clinicians have completed these courses. Parents are another key target. In 2012, as part of National Substance Abuse Prevention Month, NIDA launched “Family Checkup,” an online resource that equips parents with research-based skills to help keep their children drug-free. NIDA-funded research has shown the critical role parents play in preventing their children from using drugs. Family Checkup poses questions for parents to consider as they interact with their children, highlighting parenting skills that are important in preventing the initiation and progression of drug use among youth. The resource incorporates video examples that show parents how and how not to emulate each skill with their own children. The tools were developed by the Child and Family Center at the University of Oregon.

**National Institute of Alcohol Abuse and Alcoholism**

The FY 2014 President’s Budget request is $62.2 million for NIAAA Underage Drinking activities, which is an increase of $0.6 million above the FY 2012 Actual level.

**Underage Drinking (FY 2014 Request: $62.2 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, diabetes). The brief, two question screener is being assessed in youth ages 9 to 18. It is both a predictor of alcohol risk, alcohol use, and alcohol problems including alcohol use disorders and 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 projects funded in FY 2012 which are part of a multisite longitudinal study to address the short and long term effects of alcohol exposure on the developing adolescent brain.

**PERFORMANCE**

This section on FY 2012 performance is based on agency GPRA performance reports and other 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 Institutes and Center (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 2012.

**National Institute on Drug Abuse**

NIDA continues to contribute to a number of trans-NIH scientific research outcomes (SRO). 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 2015, identify three key factors influencing the scaling up of research-tested interventions across large networks of service systems such as primary care, specialty care, and community practice.” By studying treatment implementation, this outcome improves the translation of research into practice.
## 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.

Multiple genome-wide and targeted association studies have revealed significant associations between nicotine dependence and variants in the CHRNA5-CHRNA3-CHRNB4 (CHRNA5/A3/B4) gene cluster in subjects of European origin, with a recent study also demonstrating such associations among Korean smokers. A recent meta-analysis of 27 datasets, including those of European, Asian, and African American ancestry (sample size = 32,587) extends the involvement of this specific gene cluster across all three populations, narrowing the region of association. Of the variants tested, only rs16969968 was associated with smoking in these three populations and was a marker of a larger “high risk” haplotype (a set of alleles of linked genes). The observed consistent association of rs16969968 with heavy smoking across multiple populations, combined with its known biological significance, suggests rs16969968 is most likely a functional variant that alters risk for heavy smoking. Additional studies have demonstrated novel associations between other gene variants in this cluster with various smoking-related phenotypes, such as nicotine dependence symptoms, nicotine tolerance, smoking initiation, and comorbid conditions (e.g., regular drinking and depression), these vulnerabilities being heightened in early onset smokers. Another study demonstrated that carriers of the high-risk haplotype were three times more likely to respond to smoking cessation medications, making this haplotype of interest for personalized cessation therapies. An editorial on this report adds that the chances of successfully quitting increase

### Table: Selected Measures of Performance

<table>
<thead>
<tr>
<th>Selected Measures of Performance</th>
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</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>Characterize the functional genetic variations associated with substance abuse</td>
<td>NIH researchers characterized the functional roles of genes previously identified as being associated with addiction to tobacco and other drugs, including those within the CHRNA5/A3/B4 gene cluster and A11G of the human mu opioid receptor gene.</td>
</tr>
<tr>
<td>SRO-8.7, by 2015, identify three key factors influencing the scaling up of research-tested interventions across large networks of service systems such as primary care, specialty care and community practice.</td>
<td>Collect data in two studies designed to test three 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 (Medication-Assisted Treatment Implementation in Community Correctional Environments), and HIV-STIC (HIV Services and Treatment Implementation in Corrections) - were implemented and collected data in FY 2012.</td>
</tr>
</tbody>
</table>
two-fold in patients with the high-risk variant if they are treated with nicotine replacement, bupropion, or a combination.

Although these associations and related predictive treatment models show promise, biochemical analyses and further characterization are needed to understand the mechanism of action. To explore the effect of the rs16969968 SNP, the D398—or the N398 variant—of the nicotinic α5 receptor subunit—was examined in a cell line containing the nicotinic receptor α3α4*complex. The N398 showed diminished response to nicotinic agonists when extracellular calcium was high, suggesting signaling differences at downstream targets. Further research is needed to better understand these differences and their implications. In other work, virus-induced expression of the α5 subunit risk allele in the medial habenula-interpeduncular nucleus, a brain region associated with nicotine withdrawal, resulted in reduced aversion to nicotine and, consequently, greater consumption of the drug.

Another genetic variant, A118G in the human mu opioid receptor gene (MOR), has been associated with opioid, alcohol, and other drug addictions and with the need for higher morphine doses to achieve adequate analgesia. Recent work using animal- and human-cultured cell lines found that the G-allele (asparagine) reduced N-linked glycosylation more than the aspartic acid form. This difference in glycosylation status causes protein instability and may account for the reduction of the MOR protein in certain brain regions. Other work has examined this genetic variant’s effects on dopamine release after tobacco smoking. One study shows that carriers of the G-allele had more dopamine release in response to smoking than homozygous A-allele carriers. In addition, plasma cortisol levels were lower in G-allele carriers. These studies are consistent with literature on the association of MOR A11G with drug abuse and stress, yet continued research is needed to explore the implications of these findings and to link these mechanisms to drug abusing behaviors.

**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. In the past year, CJ-DATS research protocols (described in the FY 2010 performance discussion) began data collection. 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 2012, all nine research centers completed the active implementation protocol—that is, the strategic planning intervention with the Pharmacotherapy Exchange Council (PEC). All sites completed the KPI training and collected follow-up data from participants three months later. 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.

The research teams are currently engaged in end-of-intervention and follow-up data collection at all sites. This ongoing data collection includes 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. Both will be compared to referral rates documented at baseline (collected in FY 2011). Data collection also includes a repeated assessment of staff opinions about MAT, to determine lasting impacts of the KPI training at 12 months post-training; measures of interorganizational relationships, to assess improvements in referral relationships over time from the collaborative strategic planning process; and monthly counts of the number of treatment referrals made by parole/probation officers in each study site.

While the final data collection activities continue, research centers (RCs) are actively engaged in cleaning and analyzing baseline data. FY 2013 is entirely devoted to final data collection, analysis, and reporting of study findings.

**The HIV Services and Treatment Implementation in Corrections (HIV-STIC) protocol** will test 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 2012, all nine research centers began the active implementation protocol, that is, the HIV training and Local Change Team Intervention. In FY 2012, all sites (experimental and control) at all RCs completed baseline data collection, baseline HIV trainings, and site randomization. The experimental sites (those sites implementing HIV training + LCT) at all nine RCs have completed their LCT process improvement training. Three RCs have completed the implementation phase of the intervention. The nine month LCT implementation phase is in progress at five RCs. One RC is in the planning phase of the intervention. While the final data collection activities continue, all RCs are actively engaged in cleaning and analyzing baseline data. FY 2013 is devoted entirely to final data collection, analysis, and reporting of study findings.

Research Highlights

Long-term marijuana use begun in adolescence linked to drop in IQ

The first long-term prospective study to test young people before their first use of marijuana and again after 20+ years of age showed an association between use and impaired intellectual functioning—especially if use began in the teen years. The new research is part of a large-scale study of health and development conducted in New Zealand and co-funded by NIDA and NIMH. Researchers administered IQ tests to over 1,000 individuals at age 13 (born in 1972 and 1973) and assessed their patterns of cannabis use at several points as they aged. Participants were again tested for IQ at age 38, and their two scores were compared as a function of their marijuana use. The results were striking: participants who used cannabis heavily in their teens and continued through adulthood showed a significant drop in IQ between the ages of 13 and 38—an average of eight points for those who met criteria for cannabis dependence. (For context, a loss of eight IQ points could drop a person of average intelligence into the lowest third of the intelligence range.) Those who started using marijuana regularly or heavily after age 18 showed minor declines. By comparison, those who never used marijuana showed no declines in IQ.

Abuse of prescription pain relievers treated with sustained buprenorphine/naloxone

A NIDA study suggests that patients addicted to prescription opioid painkillers can be effectively treated in primary care settings using Suboxone (buprenorphine + naloxone). This combination was specifically designed to prevent abuse and diversion of buprenorphine and was one of the first to be eligible for prescribing under the Drug Addiction Treatment Act, which permits specially trained physicians to prescribe certain FDA-approved medications for the treatment of opioid addiction. The study, which was the first randomized large scale clinical trial using a medication for the treatment of prescription opioid abuse, also showed that the addition of intensive opioid dependence counseling provided no added benefit. However, more research is needed to determine how to sustain recovery among these patients.

Study provides clues for designing new anti-addiction medications

Scientists are now one step closer to developing anti-addiction medications, thanks to new research that provides a better understanding of the properties of the only member of the opioid receptor family whose activation counteracts the rewarding effects of addictive drugs. The kappa opioid receptor (KOR) is not associated with the development of physical dependence or the abuse potential of opiate drugs (e.g., heroin, morphine). Therefore, medications that act at the KOR could have broad therapeutic
potential for addressing addiction, pain, as well as other mental disorders. In this new study, supported by NIDA, NIGMS, and NIMH, scientists mapped all the points of contact between JDTic, a drug that specifically blocks activity at the KOR, and the human KOR, producing a high-resolution 3-D image that enabled researchers to see how the two fit together. This advance opens the door to the development of compounds targeting the KOR with improved therapeutic profiles, including that of non-addictive pain medications.

Onsite HIV testing increases life expectancy in substance abusers and is cost-effective
NIDA's Drug Abuse Treatment Clinical Trials Network (CTN) has shown that rapid HIV testing can be implemented in community-based drug abuse treatment centers, thus contributing to more comprehensive health care for patients with substance use disorders. A September 2012 study, co-funded by NIDA, NIAID, and NIMH, shows that on-site rapid HIV testing can increase life expectancy for substance abuse treatment patients newly diagnosed with HIV in a cost effective way. Using modeling, this study estimated that life expectancy would be increased from 17.1 years (no on-site test) to 20.8 years (on-site testing with information on the testing procedure). The cost-effectiveness of providing onsite rapid HIV testing was calculated using a model that took into account patient information (CD4 cell counts, viral burden, anti-retroviral therapy regimen, presence of an acute AIDS-defining illness, etc.), costs for medical treatment, and quality-adjusted life year (QALY) – a measure of both the length and quality of life that accounts for the burden of illness.

Bath Salts: more dangerous than thought
Recent NIDA research shows that MDPV, a synthetic chemical commonly found in the drugs referred to as “bath salts,” is potentially more dangerous than cocaine when tested in rodents. In this study, MDPV prolonged the effects of two neurotransmitters, dopamine and norepinephrine (by blocking reuptake at brain nerve cells) and produced hyperactivity, rapid heart rate and increased blood pressure. Through an animal study, results could help explain why these substances are addictive and highly dangerous in humans, as indicated by reports that MDPV is the chief substance found in the blood and urine of emergency room patients who have overdosed on “bath salts.”

National Institute of Alcohol Abuse and Alcoholism
NIAAA continues to contribute to a number of trans-NIH scientific research outcomes (SRO). 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 2015, identify three key factors influencing the scaling up of research-tested interventions across large networks of service systems such as primary care, specialty care and community practice.” 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.
National Institute on Alcohol Abuse and Alcoholism

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<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>Initiate replication and refinement of genome wide association and functional analysis data.</td>
<td>The genetic association of ADH1B-Arg48His with reduced risk for alcohol dependence in East Asian populations was replicated in European Americans and African Americans. The association was extended to reduced alcohol consumption in both populations.</td>
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<tr>
<td>» SRO-8.7, by 2015, identify three key factors influencing the scaling up of research-tested interventions across large networks of service systems such as primary care, specialty care and community practice.</td>
<td>Develop strategies for dissemination of the underage drinking screening guide and begin dissemination for use in primary care settings.</td>
<td>NIAAA developed strategies for dissemination of the underage drinking screening guide and began dissemination for use in primary care settings.</td>
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Discussion

Prevention – SRO-3.5

NIAAA 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.

NIH researchers replicated and extended the results of previous association studies in East Asian populations to populations of European and African ancestry. Numerous gene variants have been associated with risk for alcohol dependence in different racial and ethnic populations using genome wide association (GWAS) and other approaches. Although many variants identified to date have been associated with increased risk for alcohol dependence and problem drinking, other variants have been associated with protection against alcohol use disorders. A variant in the alcohol dehydrogenase 1B gene, ADH1B-Arg48His, is common in East Asian populations, increases alcohol metabolism leading to elevated acetaldehyde levels and reduces risk for alcohol dependence. Because this variant is uncommon in populations of European or African descent, researchers combined datasets from three large case-control studies that focused on either alcohol dependence, nicotine dependence, or cocaine dependence to assess potential protective effects of ADH1B-Arg48His in these populations. Samples from more than
5,600 individuals with and without alcohol dependence were analyzed. The results indicated that ADH1B-Arg48His was significantly associated with reduced risk of alcohol dependence and also associated with reduced alcohol consumption in both European Americans and African Americans. In addition to the adult sample described above, ADH1B-Arg48His was analyzed in an independent sample of 2,039 European American adolescents and young adults age 12-25, and was also found to be associated with reduced risk for developing future alcohol dependence in this group.

**Treatment - SRO-8.7**
The integration of alcohol screening, brief intervention and referral to treatment (SBIRT) as a routine procedure in primary care has the potential to reach a large number of individuals who are either experiencing or are at risk for alcohol-related problems who may not be identified elsewhere. Alcohol SBIRT has been recognized as a top preventive measure in primary care and standard alcohol screening guidelines are now available for both youth and adults; however, integrating routine alcohol SBIRT into primary care still poses challenges for many practices. Research to inform the implementation of SBIRT in primary care and other clinical settings for underage and adult populations continues to be a priority of NIAAA.

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 in the same health care system mentioned in the study above 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.) In the usual care condition, screening and intervention is optional. Also, physicians in this mode of the study do not receive training on SBIRT and they do not have access to a behavioral medicine specialist.

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 collaboration with the American Academy of Pediatrics, the guide was distributed to the organization’s entire membership; a total of 168,494 guides were requested from NIAAA in FY 2012. To encourage use of the guide, NIAAA also began discussions with Medscape about developing an online course to provide continuing medical education (CME) credits for physicians, nurses, and physician assistants. In addition, NIAAA issued a request for research applications to evaluate the guide in practice and funded four of these projects in FY 2012. These studies will determine appropriate settings for effective use of the guide and inform dissemination strategies in these settings.

**Research Highlights**
**New Youth Alcohol Screening Guidelines for Health Practitioners**
National surveys have shown that 71 percent of high school seniors have used alcohol in their lifetime and that past month alcohol use increases from 14 percent to 41 percent between 8th and 12th grades. By 12th grade, 27 percent of those surveyed report having been drunk in the past month and 23 percent
report having an episode of binge drinking in the past two weeks. Although alcohol use in youth continues to be of great concern, it often goes undetected. To encourage alcohol screening of youth, NIAAA recently released *Alcohol Screening and Brief Intervention for Youth: A Practitioner’s Guide*. NIAAA is currently funding projects to evaluate the effectiveness of the two-question screener as a predictor of alcohol risk/use/problems including alcohol use disorders and as an initial screen for other behavioral health problems such as other drug use, smoking, or conduct disorder. In 2012 NIAAA funded four five year studies to evaluate the youth alcohol screening guide: in a network of emergency departments, in a juvenile justice setting, in primary care, and with youth who have a chronic condition (e.g. asthma, diabetes). A fifth study was funded in early FY 2013 to evaluate the guide in public school settings. CME training will also be developed to further encourage use of the guide.

**Underage drinking: Impact on brain development**

We now know that the brain continues to develop through late adolescence into early adulthood. Whereas a number of studies in both humans and animals have shown deficits associated with heavy adolescent alcohol use, most human studies to date have been cross-sectional in nature and involved heavy binge drinking adolescents with or without alcohol use disorders. It is not clear whether the structural and functional deficits observed in these individuals predated the onset of alcohol use or occurred as a consequence of it. To further elucidate how alcohol impacts the developing adolescent brain in both the short and long term, NIAAA recently funded seven projects which are part of a multisite longitudinal study of youth ages 12-21, capturing them before they begin to drink. The studies are using advanced neuroimaging technology as well as neuropsychological and behavioral measures to assess alcohol’s effects on brain development and the associated cognitive, affective and behavioral processes.