NATIONAL INSTITUTE ON ALCOHOL
ABUSE AND ALCOHOLISM

Strategic Plan
2017–2021

National Institute
on Alcohol Abuse
and Alcoholism

Director's Message

Alcohol-related problems touch virtually everyone. I, personally, have lost several colleagues to alcohol use disorder and seen it wreak havoc in many families. The cost of alcohol misuse to society is enormous, and the public is hungry for information about alcohol and its effects on health. As National Institute on Alcohol Abuse and Alcoholism (NIAAA) Director, I regularly get appeals from people desperate to help loved ones find treatment. Colleges and universities call seeking information about how to address binge drinking on their campuses. This is what motivates me as NIAAA Director and a neuroscientist.

NIAAA's mission is to generate and disseminate fundamental knowledge about the effects of alcohol on health and well-being and apply that knowledge to improve the diagnosis, prevention, and treatment of alcohol-related problems, including alcohol use disorder, across the lifespan. For nearly 50 years, NIAAA has been at the forefront of cutting-edge alcohol research. This work has significantly expanded our understanding of how alcohol affects the brain and body and has led to better interventions to prevent and treat alcohol misuse and related conditions.

Yet more needs to be done. Alcohol misuse still claims the lives of 88,000 Americans each year, making it the fourth-leading preventable cause of death in the United States. Far too many young people see binge and extreme binge drinking—dangerous practices that can have deadly consequences—as rites of passage. And, sadly, alcohol use disorder is still viewed by many as a moral failing or character flaw, rather than a chronic brain disease from which people can, and do, recover. Many people are not aware that there are effective treatments for alcohol use disorder; and personalized treatments are an exciting, attainable goal.

NIAAA's strategic plan charts our course for the next five years as we seek to address these challenges, recognizing that flexibility will be needed to capitalize on emerging research opportunities, and that collaboration with our stakeholders is key to achieving our goals. Preventing alcohol misuse at all ages; improving the diagnosis of alcohol use disorder and alcohol-induced pathology, such as fetal alcohol spectrum disorders and organ damage; and developing new treatments for these conditions are several of the Institute's most salient goals. I am optimistic that NIAAA-supported research will pave the way for future breakthroughs that will help more Americans live healthier, more productive lives.

George F. Koob, Ph.D.
Director
National Institute on Alcohol Abuse and Alcoholism

Table of Contents

Executive Summary

The National Institute on Alcohol Abuse and Alcoholism (NIAAA) is the lead Federal agency for research on alcohol and health and the largest funder of alcohol research in the world. NIAAA's mission is to generate and disseminate fundamental knowledge about the effects of alcohol on health and well-being, and apply that knowledge to improve the diagnosis, prevention, and treatment of alcohol-related problems, including alcohol use disorder (AUD), across the lifespan.

Alcohol misuse refers to drinking in a manner, situation, amount, or frequency that could cause harm to individuals or those around them. It contributes to poor performance at school and work; family trouble; unprotected sex and sexually transmitted diseases; violence; memory blackouts; unintentional injuries, accidents, and overdoses; and organ damage and disease. It can also lead to AUD, a serious condition that affects nearly 16 million people in the United States. The Centers for Disease Control and Prevention estimates that alcohol misuse costs the United States $249 billion per year due to health care expenses, lost workplace productivity, crime, property damage, and other adverse outcomes.

For nearly five decades, NIAAA has supported cutting-edge research to reduce the toll that alcohol misuse takes on human health and well-being. This work has significantly broadened our understanding of the factors that contribute to alcohol-related problems and the mechanisms by which they develop. Once viewed as a moral failing or character flaw, AUD is now widely regarded as a chronic disease of the brain with potential for recovery and recurrence. This shift in perspective, supported by advances in neurobiological research, has helped reduce the stigma associated with AUD, led to more effective interventions, and provided support for integrating prevention and treatment services into mainstream health care.

This strategic plan serves as a roadmap for optimizing the allocation of NIAAA's resources to areas of alcohol research most likely to benefit from additional support, translating scientific discoveries for the benefit of the public, and continuing to build on NIAAA's position as the nation's key source of evidence-based information on alcohol and health. Over the next five years, NIAAA will prioritize the following goals:

Goal 1: Identify Mechanisms of Alcohol Action, Alcohol-Related Pathology, and Recovery. NIAAA will support preclinical and clinical research to generate a more thorough understanding of the fundamental mechanisms through which alcohol exerts its effects on human health and behavior, how patterns of alcohol use interact with genes and the environment in the development and progression of alcohol-related conditions, and the neurobiological mechanisms underlying recovery from alcohol-related pathology.

Goal 2: Improve Diagnosis and Tracking of Alcohol Misuse, Alcohol Use Disorder, and Alcohol-Related Consequences. NIAAA will support research to improve the diagnosis of alcohol-related diseases, including AUD, fetal alcohol spectrum disorders (FASD), and alcoholic liver disease (ALD). The Institute will also support epidemiological research to track the prevalence, patterns, and trends of alcohol misuse, AUD and co-occurring mental health conditions, and related consequences; elucidate the nature and scope of individual- and population-based differences in substance use and related outcomes; and identify the complex biopsychosocial factors that contribute to these outcomes. This information will be used to guide the development and implementation of interventions for preventing and treating alcohol misuse and its negative repercussions.

Goal 3: Develop and Improve Strategies To Prevent Alcohol Misuse, Alcohol Use Disorder, and Alcohol-Related Consequences. NIAAA will support research to adapt and evaluate adult alcohol screening for a broader range of settings and populations, evaluate the effectiveness of youth alcohol screening, and develop and evaluate methods for administering alcohol screening in combination with screening for tobacco, marijuana, and other drugs. NIAAA will also prioritize the development of culturally appropriate interventions for preventing alcohol misuse and its consequences, including human immunodeficiency virus (HIV), among individuals at all stages of life.

Goal 4: Develop and Improve Treatments for Alcohol Misuse, Alcohol Use Disorder, Co-Occurring Conditions, and Alcohol-Related Consequences. NIAAA will support research to develop new and improved treatments for AUD and co-occurring mental health conditions, FASD, ALD, and other alcohol-related diseases. The Institute will also support studies to identify factors that facilitate or inhibit recovery from AUD and improve the implementation, accessibility, and use of alcohol treatment and recovery services tailored to the needs of individuals.

Goal 5: Enhance the Public Health Impact of NIAAA-Supported Research. NIAAA will continue to develop initiatives to raise public awareness about the effects of alcohol on health and well-being and about options for preventing and treating alcohol-related problems. The Institute will strengthen collaborations with other Federal agencies; with scientific, professional, and advocacy organizations; and with patient and community groups to develop, disseminate, and encourage the adoption of evidence-based and culturally appropriate resources and strategies to reduce the public health burden of alcohol misuse.

There has never been a better time to accelerate progress toward these goals. The Collaborative Research on Addiction at NIH (CRAN) initiative is fostering synergy among NIAAA, the National Institute on Drug Abuse, and the National Cancer Institute to develop a comprehensive, well-integrated understanding of polysubstance use and addiction that considers common and distinctive features among substances and substance use disorders. The Human Connectome Project and the Brain Research through Advancing Innovative Neurotechnologies (BRAIN) Initiative, in which NIAAA is an active participant, are expected to spur an explosion of knowledge about the structure and function of brain circuits and how the brain affects behavior. New technologies for

measuring and modulating brain activity are being developed to translate our understanding of the neurobiology of AUD into new diagnostic and treatment methods. Advances are also being made in the behavioral and social sciences toward understanding the mechanisms of behavior change, and opportunities are ripe for applying this knowledge to the development of interventions for preventing and treating AUD.

Although alcohol-related injury and disease may never be eliminated completely, research has opened new avenues for reducing the adverse consequences of alcohol misuse and AUD. For example, three-dimensional facial imaging technologies hold promise for early identification and treatment of children affected by FASD. Significant progress has also been made in identifying the biological mechanisms by which ALD develops and progresses, and NIAAA is supporting a major initiative to translate these findings into new and improved treatments for alcoholic hepatitis.

Alcohol researchers are beginning to unravel the mysteries of why some people are more likely than others to develop alcohol-related diseases or to respond to behavioral and pharmacological interventions. Continued advances in genomics, along with the Precision Medicine Initiative, a national effort to elucidate how individual variability in genes, environment, and lifestyle contribute to disease, are expected to bring us closer to developing individually tailored interventions for preventing and treating these conditions. Moreover, rapid advances in electronic health technologies are providing opportunities to help individuals monitor their alcohol use and to provide them with personalized resources and support where and when they need it most. Such devices also have the potential to facilitate alcohol research and clinical care.

NIAAA looks forward to working with its partners to capitalize on these and the many other advances being made across the spectrum of alcohol research to reduce the public health burden of alcohol misuse on individuals, families, communities, and society.

Introduction

Alcohol is part of our society. People use it to celebrate, socialize, relax, and enhance the enjoyment of meals. Nearly 90 percent of adults in the United States report that they drank alcohol at some point in their lifetime, and more than half report drinking in the last month.[1] Although most people drink in moderation, nearly 40 percent of U.S. adults drink in excess of the low-risk guidelines established by the National Institute on Alcohol Abuse and Alcoholism (NIAAA).[2] (See "Drinking Patterns and Their Definitions," pages 8–9.)

Alcohol misuse has wide-ranging adverse consequences. In the United States, nearly 88,000 people per year die from alcohol-related causes;[3] globally, alcohol accounts for 3.3 million deaths—5.9 percent of all deaths— each year.[4] Alcohol misuse also contributes to poor performance at school and work; family problems; unprotected sex and sexually transmitted diseases; violence; memory blackouts; unintentional injuries, accidents, and overdoses; and organ damage and disease. It can lead to alcohol use disorder (AUD), a serious chronic condition that affects nearly 16 million people in the United States.[5] (See "What Is Alcohol Use Disorder?" page 11.) The Centers for Disease Control and Prevention estimates that alcohol misuse, including AUD, costs the United States $249 billion per year due to health care expenses, lost workplace productivity, crime, property damage, and other outcomes.[6]

NIAAA, a component of the National Institutes of Health (NIH), is the largest funder of alcohol research in the world. For nearly five decades, NIAAA's extramural research program has supported a diverse portfolio of innovative investigator-initiated research to elucidate the effects of alcohol on health and reduce the burden of alcohol misuse for individuals at all stages of life. This work is complemented by a robust intramural research program that leverages the state-of-the-art resources available at NIH to advance high-risk, high-reward studies in key areas of alcohol science. In addition, through the Collaborative Research on Addiction at NIH (CRAN) initiative, NIAAA is partnering with the National Institute on Drug Abuse and the National Cancer Institute to integrate resources and expertise across NIH to develop a comprehensive, well-integrated understanding of substance use, misuse, and addiction that considers the common and distinctive features of addictive substances and substance use disorders (SUDs).

What Is a Standard Drink?

Many people are surprised to learn what counts as a drink. The amount of liquid in your glass, can, or bottle does not necessarily match how much alcohol is in your drink. Different types of beer, wine, or malt liquor can have very different amounts of alcohol. For example, many light beers have almost as much alcohol as regular beer—about 85 percent as much.

What Is a Standard Drink?

12 fl oz of regular beer	=	8–9 fl oz of malt liquor (shown in a 12 oz glass)	=	5 fl oz of table wine	=	1.5 fl oz shot of distilled spirits (gin, rum, tequila, vodka, whiskey, etc.)
about 5% alcohol		about 7% alcohol		about 12% alcohol		about 40% alcohol

Each beverage portrayed above represents one standard drink of "pure" alcohol, defined in the United States as 0.6 fl oz or 14 grams. The percent of pure alcohol, expressed here as alcohol by volume (alc/vol), varies within and across beverage types. Although the standard drink amounts are helpful for following health guidelines, they may not reflect customary serving sizes.

Moderate Alcohol Consumption

According to the Dietary Guidelines for Americans,[7] which are intended to help individuals improve and maintain overall health and reduce the risk of chronic disease, moderate drinking is up to one drink per day for women and up to two drinks per day for men.

Low-Risk Drinking for Developing Alcohol Use Disorder

As defined by NIAAA, for women, low-risk drinking is no more than three drinks on any single day and no more than seven drinks per week. For men, it is defined as no more than 4 drinks on any single day and no more than 14 drinks per week. NIAAA research shows that only about 2 in 100 people who drink within these limits have alcohol use disorder. Even within these limits, you can have problems if you drink too quickly or have other health issues.

Alcohol Misuse

Alcohol misuse refers to drinking in a manner, situation, amount, or frequency that could cause harm to the users or to those around them. For individuals younger than the legal drinking age of 21, or for pregnant women, any alcohol use constitutes misuse.

Binge Drinking

NIAAA defines binge drinking as a pattern of drinking that brings blood alcohol concentration levels to 0.08 g/dL (0.08 percent) or higher. This typically occurs after a woman consumes four drinks or a man consumes five drinks in a 2-hour time frame.

The Substance Abuse and Mental Health Services Administration (SAMHSA), which conducts the annual National Survey on Drug Use and Health (NSDUH), defines binge drinking for men as drinking five or more alcoholic drinks on the same occasion on at least 1 day in the past 30 days. SAMHSA defines binge drinking for women as drinking four or more alcoholic drinks on the same occasion on at least 1 day in the past 30 days.

Extreme Binge Drinking

Extreme binge drinking, also known as high-intensity drinking, refers to drinking at levels far beyond the binge threshold, resulting in high peak blood alcohol concentrations. Though definitions vary, some studies define extreme binge drinking as 2 or more times the gender-specific binge drinking thresholds (i.e., 10 or more standard drinks for men; 8 or more for women); other studies use a higher threshold that may or may not be gender specific.

Heavy Drinking

SAMHSA defines heavy drinking as binge drinking (based on the SAMHSA binge drinking thresholds described above for men and women) on 5 or more days in the past 30 days.

Certain people should avoid alcohol completely, including those who:

- Are younger than the minimum legal drinking age of 21.
- Are pregnant or trying to become pregnant.
- Have a medical condition that alcohol can aggravate.
- Take medications that interact with alcohol.
- Are driving a vehicle or operating machinery (or plan to do so shortly after drinking).

Research supported by NIAAA has spurred tremendous progress in identifying the factors that contribute to alcohol-related problems and the fundamental biological and behavioral mechanisms by which they develop, and it has paved the way for innovative preventive and treatment interventions. Once viewed as a moral failing or character flaw, AUD is now widely regarded as a chronic but treatable brain disease that develops through complex, dynamic interactions among biological, environmental, and developmental factors. This shift in perspective, bolstered by decades of research on the neurobiology of addiction, has helped reduce the stigma associated with AUD and has underscored the need for a multipronged approach to preventing and treating alcohol-related problems, with interventions designed for individuals, families, communities, and society at large.

This strategic plan serves as a roadmap for catalyzing continued progress across the spectrum of alcohol research and translating these advances for the benefit of the public. It highlights NIAAA's research goals in five key areas:

- **Goal 1: Identify Mechanisms of Alcohol Action, Alcohol-Related Pathology, and Recovery**

- **Goal 2: Improve Diagnosis and Tracking of Alcohol Misuse, Alcohol Use Disorder, and Alcohol-Related Consequences**

- **Goal 3: Develop and Improve Strategies To Prevent Alcohol Misuse, Alcohol Use Disorder, and Alcohol-Related Consequences**

- **Goal 4: Develop and Improve Treatments for Alcohol Misuse, Alcohol Use Disorder, Co-Occurring Conditions, and Alcohol-Related Consequences**

- **Goal 5: Enhance the Public Health Impact of NIAAA-Supported Research**

Along with the goals outlined above, NIAAA has identified several cross-cutting research themes, which are woven throughout this strategic plan.

Address Alcohol Misuse Across the Lifespan

Human biology and behavior change throughout life; these changes affect drinking patterns and risks for alcohol-related injury and disease. NIAAA has adopted a "lifespan approach" to alcohol research that considers how the emergence and progression of drinking behavior and related outcomes interact with developmental changes and environmental inputs across the lifespan, from the embryonic and fetal stages of development into older adulthood. This perspective guides the identification of life-stage–appropriate strategies for preventing, treating, and facilitating recovery from alcohol problems, as well as tailoring resources to the needs of individuals of all ages.

What Is Alcohol Use Disorder?

Alcohol use disorder (AUD) is a medical condition that doctors diagnose when a patient's drinking causes distress or harm. It ranges from mild to severe and is characterized by clinically significant impairments in health and social function. To be diagnosed with AUD, a person must meet certain diagnostic criteria outlined in the *Diagnostic and Statistical Manual of Mental Disorders* (DSM).[8] The current DSM (DSM-5) integrates the two DSM–IV disorders, alcohol abuse and alcohol dependence, into a single disorder called AUD. Under DSM-5, anyone meeting any 2 of the 11 criteria during the same 12-month period is diagnosed with AUD. The severity of AUD is based on the number of criteria a person meets—mild (2–3), moderate (4–5), or severe (6 or more).
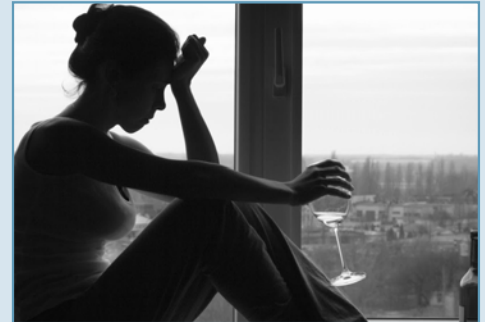
To assess whether someone has AUD, a health care provider may ask him or her some questions. For example, in the past year, have you:

- Had times when you ended up drinking more, or longer, than you intended?
- More than once wanted to cut down or stop drinking, or tried to, but couldn't?
- Spent a lot of time drinking? Or being sick or getting over the aftereffects?
- Experienced craving—a strong need, or urge, to drink?
- Found that drinking—or being sick from drinking—often interfered with taking care of your home or family? Or caused job troubles? Or school problems?
- Continued to drink even though it was causing trouble with your family or friends?
- Given up or cut back on activities that were important or interesting to you, or gave you pleasure, in order to drink?
- More than once gotten into situations while or after drinking that increased your chances of getting hurt (such as driving, swimming, using machinery, walking in a dangerous area, or having unsafe sex)?
- Continued to drink even though it was making you feel depressed or anxious or adding to another health problem? Or after having had a memory blackout (i.e., forgetting, after drinking, where you were or what you did while drinking)?
- Had to drink much more than you once did to get the effect you want? Or found that your usual number of drinks had much less effect than before?
- Found that when the effects of alcohol were wearing off, you had withdrawal symptoms, such as trouble sleeping, shakiness, irritability, anxiety, dysphoria, depression, restlessness, nausea, or sweating? Or sensed things that were not there?

Any of these symptoms may be a cause for concern. The more symptoms one has, the more urgent the need for change.

Address Co-Occurring Conditions

AUD frequently co-occurs with other SUDs and mental health conditions, including major depressive disorder, anxiety disorders, bipolar disorder, antisocial and borderline personality disorders, and post-traumatic stress disorder (PTSD). Individuals suffering from psychiatric comorbidity tend to have a poorer prognosis, higher risk for treatment dropout, less support for sobriety from their families and in the workplace, and a higher risk for suicide. Alcohol misuse also contributes to more than 200 diseases and injury-related health conditions,[9] including alcoholic liver disease. In fact, alcohol is involved in nearly half of all liver disease deaths in the United States each year.[10] Alcohol misuse frequently co-occurs with human immunodeficiency virus (HIV), contributes to HIV transmission, reduces HIV screening, makes it difficult to follow complex HIV medication regimens, and contributes to or exacerbates other health conditions in HIV-infected individuals. NIAAA will continue to support research to investigate the relationships between AUD and co-occurring conditions and to develop interventions to prevent and treat them.

Reduce Health Disparities

Some groups of people may be more vulnerable to alcohol problems than others. For example, although Native Americans are less likely to drink than white Americans, those who do drink are more likely to binge drink,[11] have a higher rate of past-year AUD compared with other racial and ethnic groups,[12] and are approximately twice as likely to die from alcohol-related causes than the general American public.[13] In addition, Hispanics and blacks who drink are more likely to binge drink than whites who drink,[11] but Hispanics with AUD are less likely than whites with AUD to receive alcohol treatment at a specialty facility.[14] The lesbian, gay, bisexual, and transgender communities are also important subpopulations to consider. Lesbian and bisexual women are about seven times more likely than heterosexual women to meet criteria for AUD.[15] Although rates of alcohol use and AUD among men who have sex with men (MSM) are comparable to rates in the general population, alcohol misuse among MSM is an important public health problem. Alcohol misuse is a known risk factor for HIV, and MSM account for more than half of all new HIV infections each year in the United States.[16] NIAAA is committed to ensuring that all people benefit from alcohol research advances and will support studies to better understand health disparities and develop interventions for at-risk groups.

Advance Precision Medicine

Studies investigating how individual variability in genes, environment, and lifestyle contribute to disease are bringing us closer to developing individually tailored interventions for alcohol-related conditions. NIAAA will continue to support research on the factors that contribute to individual variation in alcohol misuse, AUD, and alcohol-related outcomes. The Institute will use that information to guide the development and validation of prognostic and diagnostic biomarkers and personalized interventions for these conditions. These efforts will be aided by the recent expansion of electronic medical records and the development of mobile health technologies, which have the potential to improve the quality and collection of patient data and to provide comprehensive, personalized health care services where and when patients need them.

Strengthen the Biomedical Research Workforce

Cultivating a talented and diverse research workforce is essential to advancing the frontiers of scientific knowledge and to translating research findings into practice. NIAAA promotes alcohol research training through individual pre- and postdoctoral fellowships, institutional training grants, and career development awards that span the breadth of NIAAA's research portfolio. Diverse research teams broaden the scope of scientific inquiry, bring creative solutions to bear on complex scientific problems, and encourage research relevant to the health care needs of underserved populations. Programs to identify, recruit, and train scientists from diverse populations, especially those underrepresented in health research, are an important component of NIAAA's training portfolio.

Serve as a Responsible Steward of Our Nation's Research Resources

Underpinning NIAAA's ability to advance innovative science is an unwavering commitment to responsible research stewardship. NIAAA supports efforts to enhance the rigor and reproducibility of research, including ensuring that sex is incorporated as a biological variable into the design, analysis, and scientific reporting of the studies it funds. This is a critical step toward ensuring that everyone, regardless of sex or gender, benefits from alcohol research advances. NIAAA maximizes the use of research resources by forging strategic partnerships with other NIH Institutes, Centers, and Offices; other Federal agencies; academia; industry; and not-for-profit organizations. Such partnerships provide opportunities to share resources and expertise, and to broaden the dissemination of alcohol research findings. Moreover, by encouraging the use of common research metrics and protocols, as well as the sharing, aggregation, and secondary analysis of data, NIAAA hopes to improve the efficiency of alcohol research and stimulate new insight into preventing and treating alcohol-related conditions.

GOAL 1
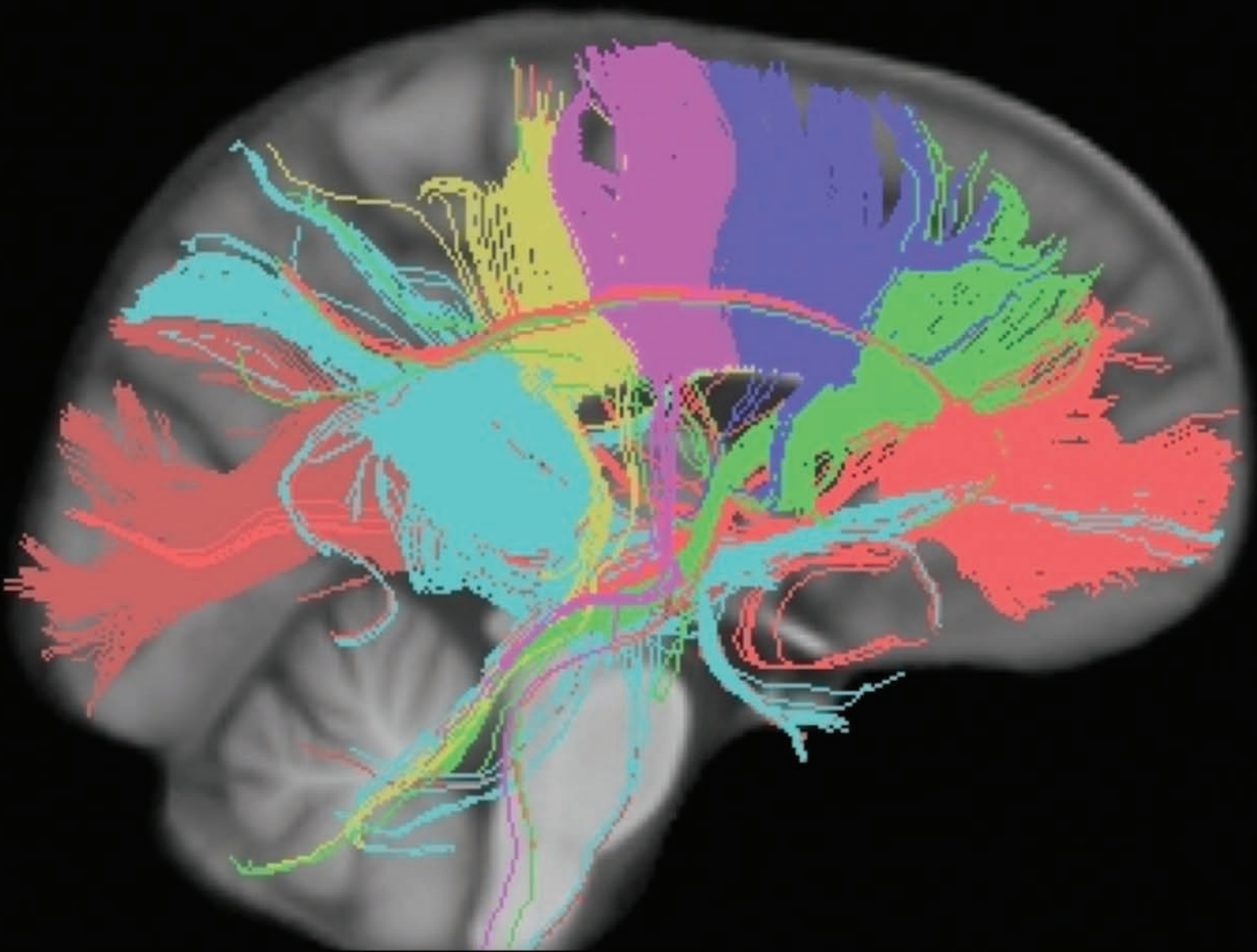
Diffusion tensor imaging of fiber tracks in the brain of a 58-year-old man with alcohol use disorder.
Image courtesy of Drs. Adolf Pfefferbaum and Edith V. Sullivan.

Identify Mechanisms of Alcohol Action, Alcohol-Related Pathology, and Recovery

Basic research is the foundation for medical advancement, and it is integral to NIAAA's mission to reduce the public health burden associated with alcohol misuse. Through research, great strides have been made in understanding the mechanisms by which alcohol exerts its effects on human health and behavior. Breakthroughs in neuroscience have revolutionized our understanding of alcohol use disorder (AUD) and demonstrated that it is a chronic brain disease with the potential for recovery and recurrence. As individuals progress from initial alcohol use to misuse to AUD, changes occur in brain structure and function that drive the transition from occasional, controlled alcohol use to chronic, compulsive drinking. Sophisticated new tools and techniques are enabling researchers to identify these changes with a precision never before possible. Basic research across the biomedical sciences is opening new avenues of investigation for understanding the biological and behavioral mechanisms through which these conditions develop. Studies are beginning to reveal the complex interactions between organ systems, including the gut, liver, and brain, and the immune and endocrine systems. This work indicates that the neurobiological changes induced by alcohol misuse may not be due entirely to the direct actions of alcohol on the brain, but that they may be mediated, in part, by interactions with peripheral systems.

A major focus of NIAAA's work is to generate a more thorough understanding of these processes and to translate this information into innovative interventions for AUD and co-occurring mental health conditions. NIAAA is also committed to defining the mechanisms by which alcohol and its byproducts exert their effects on the body, including how patterns of alcohol consumption interact with genetic and environmental factors to influence health and the development and progression of alcohol-related pathology. NIAAA will continue to support a robust portfolio of basic biological and behavioral alcohol research and identify opportunities to apply the knowledge gained through this work into effective interventions for preventing and treating disease.

To advance these goals, NIAAA will pursue the following objectives:

Objective 1a: Identify mechanisms underlying alcohol use disorder and co-occurring mental health conditions

AUD is characterized by a three-stage cycle: a loss of control in limiting alcohol intake (*binge/intoxication stage*), the experience of a negative emotional state in the absence of alcohol (*withdrawal/negative affect stage*), and a compulsion to seek out and consume alcohol (*preoccupation/anticipation stage*).[17] (See "The Three Stages of the Alcohol Use Disorder Cycle," pages 16–17.) These stages are largely mediated by distinct but interacting neurobiological circuits involved in the experience

The Three Stages of the Alcohol Use Disorder Cycle

Alcohol use disorder (AUD) is characterized by a three-stage cycle involving a loss of control over alcohol intake (*binge/intoxication stage*), the experience of a negative emotional state in the absence of alcohol (*withdrawal/negative affect stage*), and a compulsion to seek out and consume alcohol (*preoccupation/anticipation stage*).
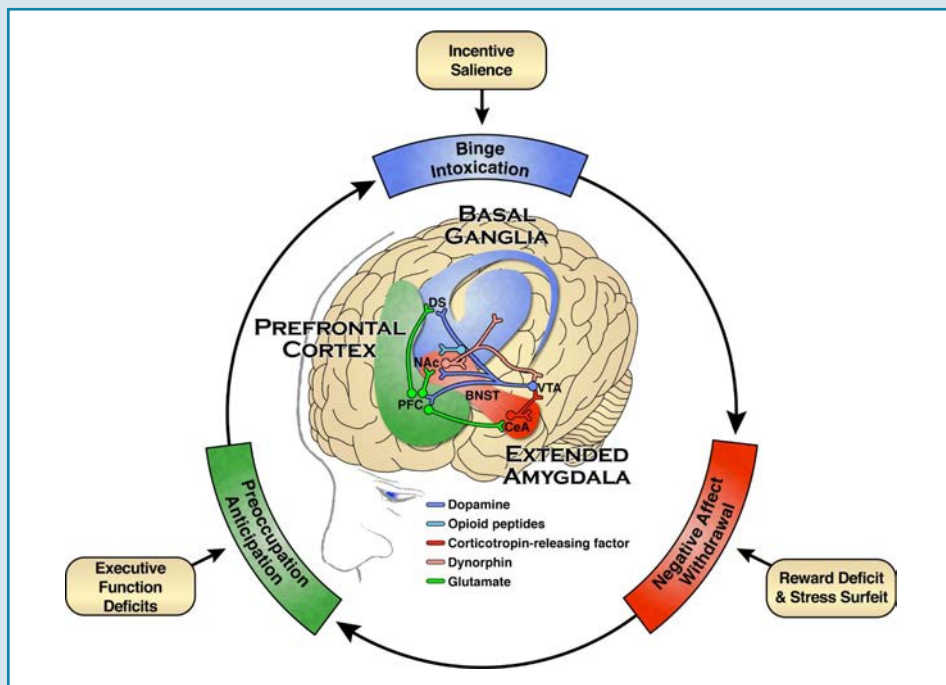
There may be variation in how people progress through the cycle, the intensity with which they experience each of the stages, and the nature of the disruptions to the underlying neurobiological circuits.

The *binge/intoxication* stage primarily involves the nucleus accumbens and the striatum, two structures within the brain's basal ganglia. The nucleus accumbens mediates the rewarding, or pleasurable, effects of alcohol. Repeated activation of this reward system by alcohol can trigger changes in the striatum, an area of the brain responsible for habit formation, and lead to the development of compulsive alcohol seeking. The stimuli present when people drink—including people, places, and even their own internal mood states—can become associated with the rewarding effects of alcohol, and over time these cues may acquire the ability to activate the brain's reward centers even in the absence of alcohol. This associative learning process, a phenomenon called facilitation of *incentive salience*, helps explain the intense desire for alcohol and compulsive alcohol seeking that occurs when some people addicted to alcohol are exposed to cues they have come to associate with drinking.

During the *withdrawal/negative affect* stage, the absence of alcohol leaves the reward neurotransmitter systems in a deficit state, activates stress neurotransmitters in the brain's extended amygdala, and dysregulates the

activity of neurotransmitters that counter stress. These effects contribute to the feelings of unease, anxiety, and irritability that typically accompany alcohol withdrawal. Repeated cycles of alcohol use and withdrawal also disrupt the activity of neurotransmitters in the brain's reward systems and sensitize anti-reward stress systems, making it more difficult for people suffering from AUD to experience the pleasures of daily living. The combination of loss of function in reward systems (i.e., *reward deficit*), heightened activation of brain stress systems (i.e., *stress surfeit*), and conditional responding to environmental stimuli associated with the rewarding effects of alcohol (i.e., *incentive salience*) drive the motivation to drink and are key elements of relapse during the *preoccupation/ anticipation* stage of AUD.

The prefrontal cortex—an area of the brain responsible for *executive function*, including the ability to organize thoughts and activities, prioritize tasks, manage time, and make decisions—plays a key role in the *preoccupation/anticipation* stage of AUD. The prefrontal cortex can be divided into two opposing systems: a "go" system that drives *impulsive* behavior and habitual responding, and a "no-go" system that inhibits these responses and exerts control over activation of brain stress systems, putting the brakes on compulsive behavior. Too much activity in the go system, or too little activity in the no-go system, can lead to binge drinking, as well as increased responsiveness to alcohol-associated cues and heightened stress reactivity, both of which can increase alcohol craving and lead to relapse.

The neuroadaptations that underlie AUD may persist long after a person stops drinking, contributing to the chronic nature of this disease.

of reward and habit formation (the basal ganglia), stress (the extended amygdala), and executive function (the prefrontal cortex).[18] NIAAA supports preclinical and clinical research to examine: how alcohol-induced changes in these circuits contribute to AUD; how they relate to the cognitive, behavioral, and emotional phenotypes observed in individuals with AUD and co-occurring psychiatric conditions such as post-traumatic stress disorder and other substance use disorders (SUDs); and how they may be modified during treatment and recovery.

The role of the neuroimmune system in AUD is an important area of focus. Human and animal studies have revealed a link between alcohol consumption and altered neuroimmune function. Characterizing the pathways by which neuroimmune signaling contributes to functional changes in the brain associated with alcohol misuse could provide a new framework for understanding the development of AUD and lead to the identification of novel molecular targets for treating this disorder.

Studies investigating the effects of low-dose alcohol (i.e., less than 10 mM) on the brain also are of interest. Relatively low concentrations of alcohol are known to adversely affect aspects of cognitive function and behavior, yet little is known about how low-dose alcohol affects brain function, including what molecular and cellular targets mediate its initial rewarding effects. Elucidating how the brain

responds to low-dose alcohol will provide a window into the brain changes that occur in the progression from alcohol use to misuse to AUD and into the neurobiological mechanisms underlying resilience or vulnerability to the disorder.

A major challenge to preventing and treating AUD lies in its heterogeneity. While the mechanisms underlying each stage of the AUD cycle are similar across individuals, there is variation in how people progress through the cycle and in the extent and nature of the disruptions to relevant brain circuits. For example, whereas some people with AUD may have trouble moderating their drinking because of heightened sensitivity to stress, others may drink due to an inability to experience pleasure from once-rewarding experiences, deficits in cognitive function that lead to poor decision-making, or some combination of these or other factors. Developing a better understanding of the neurobiological and behavioral phenotypes associated with AUD, including those relevant to the mental health conditions with which AUD frequently co-occurs, will facilitate the development of precision medicine–based approaches to preventing and treating these disorders.

To better understand mechanisms underlying AUD and co-occurring mental health conditions, including other SUDs, NIAAA will support preclinical and clinical research to:

- **Elucidate mechanisms mediating each of the three stages of the AUD cycle.**

- **Identify mechanisms that confer resistance to AUD and those that influence recovery and relapse.**

- **Study how alcohol affects neural circuits involved in reward, emotional regulation, behavioral control, sleep, and decision-making; assess whether these effects can be remediated by modulating relevant neural pathways.**

- **Identify and classify neurobiological and behavioral phenotypes of AUD, including those relevant to co-occurring mental health conditions, and the mechanisms underlying them.**

- **Examine how mechanisms of learning, memory, and other cognitive functions contribute to the development and maintenance of AUD and co-occurring mental health conditions.**

- **Identify mechanisms through which stress contributes to the development and maintenance of AUD and co-occurring mental health conditions, and identify stress-related biomarkers predictive of relapse.**

- **Investigate mechanisms through which neuroimmune factors contribute to the development and maintenance of AUD.**

- **Define molecular targets and neuropathways that mediate the effects of low-dose alcohol (i.e., 10 mM and below) on the brain.**

- **Encourage the application of computational and "big data" approaches to integrate data on alcohol's effects on the brain across multiple studies and levels of investigation.**

Objective 1b: Identify genomic and nongenomic factors associated with resilience and vulnerability to alcohol misuse, alcohol use disorder, and co-occurring mental health conditions

Whereas the research strategies outlined in Objective 1a are aimed at developing a more thorough understanding of the mechanisms underlying AUD and co-occurring mental health conditions, the strategies outlined in Objective 1b are expected to further elucidate factors that predispose individuals to, or protect them from, these conditions. Over the past several decades, NIAAA has supported a number of large studies to examine the role that genetics play in the development of AUD and the mechanisms through which genes exert their effects. Studies of twins, adopted siblings, and individuals from families with an extensive history of AUD have established that genetic factors account for about half a person's risk of developing AUD.[19]

The genes most strongly implicated in AUD and best characterized are those that code for enzymes involved in the metabolism of alcohol. Other gene variants are thought to influence drinking by affecting the activity of neurotransmitters associated with alcohol use or with impulsivity, reward deficits, stress, or cognitive function, which contribute to alcohol misuse. Still other variants are linked to AUD treatment responses. Environmental factors, such as exposure to childhood trauma and peer and parental influences, also affect AUD risk and resilience; epigenetic changes in gene expression due to environmental influences likely play a role as well. Continued research in this area, facilitated by advances in genomics and large-scale data collection, aggregation, and analysis, offers promise for defining factors associated with AUD risk and resilience and for guiding treatment.

The developmental stage at which an individual begins drinking and at which he or she is exposed to certain risk and protective factors has a profound influence on the development of alcohol-related problems. Adolescence is the stage of life during which most people begin drinking, and it is also a time of considerable social, psychological, and physiological change. The brain, particularly the frontal cortex, continues to develop throughout adolescence and does not fully mature until early adulthood. Adolescent alcohol exposure can impair brain development, compromise short- and long-term cognitive functioning, and increase the likelihood of developing alcohol-related problems during adolescence and later in life. Furthering our understanding of alcohol's effects on the developing brain—as well as how differences in brain structure and function prior to alcohol initiation contribute to later alcohol misuse and AUD—is a high priority for NIAAA. (See "Advancing Research on Alcohol and the Adolescent Brain," page 20.)

Advancing Research on Alcohol and the Adolescent Brain

NIAAA has made a major commitment to research aimed at advancing our understanding of alcohol's effects on the developing brain and how differences in brain structure and function prior to alcohol initiation contribute to later alcohol misuse and alcohol use disorder.

In 2012, NIAAA launched the National Consortium on Alcohol and Neurodevelopment in Adolescence (NCANDA), a nationally representative, accelerated longitudinal study evaluating brain structure and function in more than 800 youth before and after they start to drink. NCANDA has provided important insights into the adverse effects of alcohol on the adolescent brain. It has also laid the methodological foundation for the ongoing Adolescent Brain Cognitive Development (ABCD) Study, the largest long-term study of brain development and child health in the United States.

More than 11,000 9- to 10-year-olds will be recruited to the ABCD Study. Using advanced brain imaging and neuropsychological and behavioral assessments, researchers will track the biological and behavioral development of participating youth over a 10-year period, with the goal of collecting data before and after they start to use alcohol or other addictive substances.

The ABCD Study will yield an unprecedented amount of information about normal adolescent brain development and how it is affected by substance use and other childhood experiences, such as sleeping patterns and sports, social media, and video game engagement. The study is also expected to illuminate neurobiological, cognitive, and behavioral precursors of substance misuse and could ultimately inform preventive and treatment interventions.

Complementing NCANDA and ABCD, NIAAA's Neurobiology of Adolescent Drinking in Adulthood initiative is enabling investigators to examine, in animal models, the molecular-, cellular-, and circuit-level mechanisms by which adolescent drinking affects brain structure and function in the short and long term, and how the changes observed during this critical period persist into adulthood.

An increase in pubertal hormones is a prominent feature of adolescence that shapes adolescent brain development, including sexual differentiation of the brain. Although patterns of alcohol use are similar between boys and girls in early adolescence, sex differences in alcohol use emerge by adulthood, when men tend to drink more than women. Notably, however, the gap between men's and women's drinking patterns has been narrowing. In animal models, individual differences in alcohol-seeking and drinking, as well as in associated behaviors, such as novelty seeking, depression and anxiety, stress reactivity, and cognition, develop during the transition to adulthood. The extent to which sex contributes to these effects and to the broader neurobiological and behavioral changes associated with alcohol misuse, and the mechanisms through which sex exerts its effects, are important areas of investigation with implications for developing sex- and age-appropriate interventions.

To identify additional factors associated with resilience and vulnerability to alcohol misuse, AUD, and co-occurring conditions, NIAAA will support studies that:

- **Capitalize on advances in genomics and studies of twins, adopted siblings, individuals from families with a high density of AUD, and participants in AUD treatment studies to identify additional gene variants, noncoding genomic elements, and gene networks associated with alcohol misuse, AUD, and co-occurring disorders.**

- **Examine the impact of AUD candidate genes on alcohol-related neurobiological and behavioral phenotypes, including factors such as temperament and behavioral control that interact with the environment to affect alcohol-related outcomes.**

- **Examine whether sex affects the development of AUD and co-occurring mental health conditions and the mechanisms through which these effects may occur.**

- **Identify the neurobiological mechanisms that convey risk and resilience for alcohol misuse and AUD.**

- **Use structural and functional brain imaging to examine the effects of adolescent alcohol use on brain structure and function into adulthood and the mechanisms underlying these effects.**

- **Use computational and "big data" approaches to integrate data from multiple studies using different tools and techniques (e.g., genetics, epigenetics, and imaging).**

Objective 1c: Identify mechanisms through which alcohol affects health and disease across the lifespan

Chronic and binge alcohol consumption have wide-ranging, adverse effects on human health. Alcohol is a toxin that can damage tissues and organs directly and indirectly through its metabolic byproducts such as acetaldehyde. Alcohol-metabolizing enzymes have been extensively studied, and researchers have identified multiple pathways through which metabolic byproducts contribute to tissue damage.

Further elucidating the genetic-, epigenetic-, cellular-, organ-, and systems-level mechanisms through which these effects occur would provide new opportunities to prevent and treat alcohol-related diseases.

The prenatal stage of development is characterized by dynamic and highly orchestrated developmental changes that are especially vulnerable to perturbation by alcohol. Alcohol exposure during embryonic and fetal development is a leading preventable cause of birth defects and can result in fetal alcohol spectrum disorders (FASD). (See "Fetal Alcohol Spectrum Disorders," page 25.) Individuals with FASD may experience damage to the brain and other organs, growth retardation, facial abnormalities, and a range of neurobiological deficits that can result in physical, cognitive, behavioral, and social challenges throughout a person's life. While research on FASD has historically focused on the neurobiological deficits associated with the condition, the research community has become increasingly aware that prenatal alcohol exposure has wide-ranging effects on other organ systems, including the kidneys, circulatory system, and immune system.

The deficits observed in people with FASD and the severity of those deficits depend on the dose, pattern, and timing of prenatal alcohol exposure. In addition, FASD can be influenced by maternal hormones, nutrition, age, number of previous pregnancies, years of drinking, and genetic factors. Alcohol exerts its injurious effects through multiple mechanisms. These include alterations in gene expression patterns, cellular responses to growth factors, and cell death; impairments in the molecular mechanisms involved in moving brain cells to their correct locations during development; and cell damage from chemically reactive molecules.

To further characterize the biological mechanisms involved in the development of FASD, NIAAA will support research to:

- **Investigate the diverse neurobehavioral consequences of prenatal alcohol exposure in individuals with FASD in relation to the activities of daily living, including its effects on sensory, motor, cognitive, and emotional function.**

- **Further characterize neural mechanisms through which prenatal alcohol exposure adversely affects neurodevelopment and sensory, motor, cognitive, and emotional function.**

- **Identify when, and at which doses of alcohol exposure, these neural mechanisms are activated during prenatal development and how they contribute to the diverse phenotypes associated with FASD.**

- **Identify biological and environmental factors that impact susceptibility to FASD and contribute to diverse phenotypes associated with it.**

- **Examine biological mechanisms by which prenatal alcohol exposure contributes to other chronic diseases and health conditions later in life.**

As the primary site of alcohol metabolism, the liver is particularly vulnerable to damage from drinking. Alcohol misuse can lead to alcoholic liver disease (ALD), a serious and potentially fatal disease that includes steatosis (fatty liver), alcoholic hepatitis (AH), cirrhosis, and hepatocellular carcinoma. (See "Alcoholic Liver Disease," pages 28–29.) It is not clear why some people progress from fatty liver to more severe forms of ALD, but factors such as gender, body mass, genes, diet, race and ethnicity, and smoking status are thought to play a role. AH, which has a mortality rate of more than 50 percent within the first 60 days of diagnosis in severe cases,[20] is a particularly important area of focus for NIAAA. Activation of liver immune mechanisms, alcohol and lipid metabolism, oxidative stress, and the production of reactive oxygen species are all known to contribute to AH (see "Pathogenesis of Alcoholic Liver Disease," page 27); however, the complexity of the liver and a lack of animal models that reflect the severity of human disease and relevant pathological endpoints have made it challenging to develop a comprehensive understanding of disease pathogenesis. NIAAA will continue to support research on ALD, including through translational research consortia aimed at improving our understanding of the mechanisms underlying AH and translating this knowledge into novel therapies.

The gastrointestinal system is the primary site at which alcohol is absorbed into the blood stream, and accumulating evidence indicates that processes occurring in this system contribute to alcohol's adverse effects on other organs, including the liver and brain. A single episode of binge drinking can increase intestinal permeability, causing bacterial toxins to escape into the blood stream and induce inflammation in peripheral organs. Chronic alcohol misuse can also affect the composition of the microbiome, exacerbating the problem. Inflammation is implicated in much of the downstream organ damage associated with alcohol misuse, including liver damage, and it is emerging as an important factor in the development of many other diseases, including AUD.

Nutrition is a factor in some alcohol-related diseases. Individuals with severe AUD may consume a significant portion of their daily calories from alcohol, depriving their bodies of essential nutrients. Drinking to excess can impair absorption and digestion of nutrients from food, as well as the liver's ability to use them. Nutrition also plays a role in preventing and treating cardiovascular and liver diseases, two potential consequences of alcohol misuse, and it is an important factor in FASD.

Although considerable progress has been made toward understanding the effects of alcohol on human health and disease, the complex mechanisms through which alcohol exerts its effects are not fully understood. Moreover, while considerable attention has been focused on the adverse health effects of alcohol, some studies have found benefits associated with moderate alcohol consumption, particularly for cardiovascular disease. NIAAA encourages research that integrates genetic-, molecular-, cellular-, and systems-level approaches to investigating how alcohol affects tissue and

organ function, how one dysregulated physiological system may perturb others, as well as the common and unique aspects of alcohol-induced pathology at multiple organ sites.

To identify new pathways for preventing, diagnosing, and treating alcohol-related disease, NIAAA will support research to:

■ **Identify physiological mechanisms through which alcohol contributes to chronic diseases and conditions, including ALD, pancreatitis, cancer, neurodegeneration, and cardiovascular disease; through which moderate alcohol consumption may protect against disease; and through which alcohol interacts with biological and environmental factors to affect health and disease states.**

■ **Support a prospective clinical trial to examine the effects of moderate alcohol use on health outcomes.**

■ **Further elucidate mechanisms by which alcohol affects interactions among the gut, liver, and brain, including through changes in the composition of gut microbiota and its metabolomes, increased intestinal permeability, and inflammation.**

■ **Develop and validate new animal models to explore mechanisms by which genetics, sex, nutrition, drinking patterns, aging, and obesity contribute to ALD.**

■ **Identify new endogenous stem cell populations in organs susceptible to alcohol damage, and use new and existing stem cell lines to develop alcohol-related disease models.**

■ **Identify new molecular targets for treating ALD by conducting functional studies of the physiology dysregulated in AH, cirrhosis, and hepatocellular carcinoma and determining the association of these physiological changes with disease severity and mortality.**

Extraordinary progress has been made in preventing and treating human immunodeficiency virus (HIV) and improving the lives of the millions of people affected by it. Nonetheless, HIV remains a serious public health concern. Approximately 40,000 people are diagnosed with HIV infection each year in the United States alone;[21] worldwide the number is considerably higher. In the United States, a substantial proportion of people living with HIV consume alcohol, and the prevalence of unhealthy alcohol use in this group ranges from 8 to 42 percent.[22] As noted above, chronic drinking facilitates HIV infection, accelerates disease progression, and hastens the death of those who have progressed to AIDS, but the mechanisms for these interactions are not well understood. Alcohol may interfere with the metabolism of medications to treat HIV, an effect that could account for the increased frequency of adverse medical events and increased mortality among HIV-infected individuals who take antiretroviral medications and drink. In addition, little is known about how alcohol affects the effectiveness of medications taken to prevent HIV infection (i.e., pre-exposure prophylaxis). Alcohol can exacerbate HIV-associated comorbid conditions such as tuberculosis and hepatitis C virus, and it has been linked to the development of other diseases in HIV-infected individuals. People with HIV and hepatitis C virus are especially likely to develop liver disease if they drink, and alcohol has been

Fetal Alcohol Spectrum Disorders

Prenatal alcohol exposure occurs when the embryo or fetus is exposed to alcohol. Alcohol can disrupt prenatal development at any stage during pregnancy—including at the earliest stages, often before a woman knows that she is pregnant. Fetal alcohol spectrum disorders (FASD) is an umbrella term for a range of physical, cognitive, and behavioral abnormalities caused by prenatal alcohol exposure. The medical disorders labeled as FASD include the following:

Fetal Alcohol Syndrome (FAS): FAS is characterized by structural or functional central nervous system (CNS) abnormalities, growth deficits, skeletal abnormalities, and facial anomalies, which may include narrow eye openings, a smooth area between the lip and the nose, and a thin upper lip.

Partial Fetal Alcohol Syndrome (pFAS): pFAS is characterized by some, but not all, of the features of FAS. For example, individuals with pFAS may not experience growth deficits.

Alcohol-Related Neurodevelopmental Disorder (ARND): Individuals with ARND do not exhibit the full range of physical deficits that characterize FAS or pFAS; they do have the CNS, cognitive, and behavioral deficits.

Alcohol-Related Birth Defects (ARBD): ARBD is characterized by physical abnormalities, such as heart, kidney, and skeletal problems. ARBD is rarely seen alone but rather as a secondary disorder accompanying other forms of FASD.
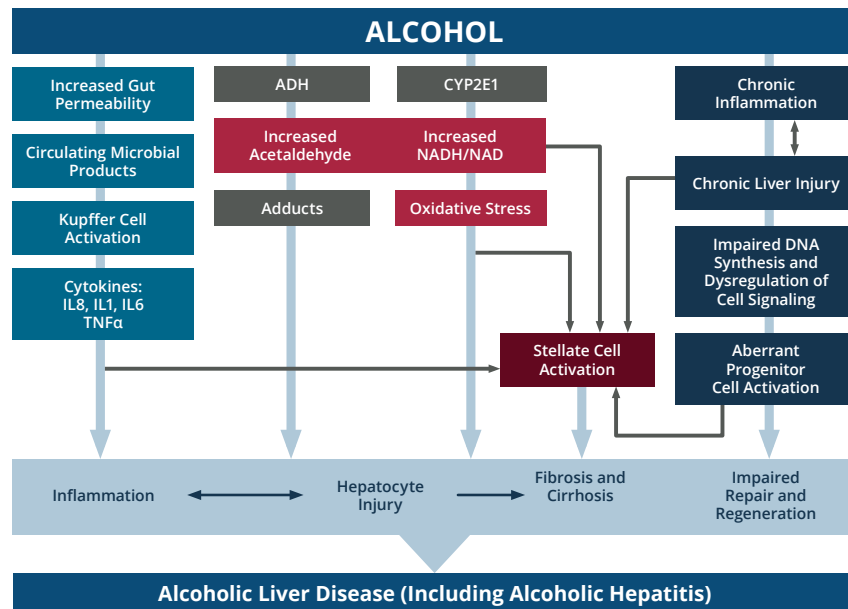
Neurobehavioral Disorder Associated with Prenatal Alcohol Exposure (ND-PAE): ND-PAE is defined only by cognitive and behavioral features and is characterized specifically by impairments in neurocognition, self-regulation, and adaptive functioning.

identified as a key factor in increased liver mortality among people with HIV. Alcohol also contributes to age-related medical problems including cardiovascular dysfunction, peripheral neuropathies, and neurocognitive impairments in HIV-positive individuals.

Considering the serious adverse consequences associated with alcohol misuse by people with HIV, NIAAA will support research to:

- **Determine how current and past alcohol use in the context of HIV infection and other co-infections affects development and progression of organ and tissue injury with a focus on the gut, liver, lung, and brain, and translate these findings into strategies for limiting alcohol-related organ and tissue injury in HIV-positive individuals.**

- **Improve understanding of how alcohol affects disease progression and tissue and organ injury in HIV-positive individuals taking antiretroviral medications.**

- **Identify and model mechanisms through which alcohol contributes to infectious and noninfectious diseases and mental health conditions among HIV-positive individuals, as well as to frailty among HIV-infected older adults.**

- **Elucidate how the interaction of HIV, HIV medications, and alcohol affects brain development and function, and identify neurobiological mechanisms underlying the persistence of neuronal injury and dysfunction in HIV-infected individuals with varying patterns of viral suppression and immune competence.**

PATHOGENESIS OF ALCOHOLIC LIVER DISEASE

ALCOHOL

Increased Gut Permeability	ADH	CYP2E1		Chronic Inflammation
Circulating Microbial Products	Increased Acetaldehyde	Increased NADH/NAD		Chronic Liver Injury
Kupffer Cell Activation	Adducts	Oxidative Stress		Impaired DNA Synthesis and Dysregulation of Cell Signaling
Cytokines: IL8, IL1, IL6 TNFα			Stellate Cell Activation	Aberrant Progenitor Cell Activation

Inflammation ⟷ Hepatocyte Injury ⟶ Fibrosis and Cirrhosis   Impaired Repair and Regeneration

**Alcoholic Liver Disease (Including Alcoholic Hepatitis)**

Repeated exposure to alcohol contributes to liver damage through several parallel processes. Alcohol exposure increases gut permeability, leading to leakage of microbes and microbial products, including lipopolysaccharides, into the liver and into circulation. These and other bacterial products trigger the activation of Kupffer cells (resident liver macrophages) to produce the pro-inflammatory cytokines interleukin 8 (IL8), interleukin 6 (IL6), interleukin 1 (IL1), and tumor necrosis factor alpha (TNFα). A sustained inflammatory state damages the host tissue. In parallel, alcohol is metabolized in the liver by the enzymes alcohol dehydrogenase (ADH) and cytochrome P450 oxidase 2E1 (CYP2E1), leading to the production of acetaldehyde and the reduced form of nicotinamide adenine dinucleotide (NADH). The altered balance between NADH and the oxidized form of nicotinamide adenine dinucleotide (NAD) results in oxidative stress that also damages host tissue. Excess acetaldehyde leads to the formation of protein adducts that contribute to inflammation and DNA adducts that interfere with DNA synthesis. Pro-inflammatory cytokines, acetaldehyde, and oxidative stress activate hepatic stellate cells, a specialized cell population whose activation triggers fibrosis. Chronic inflammation caused by excessive alcohol intake leads to chronic liver injury and impairs tissue repair. Progenitor cells normally support liver repair and regeneration. However, aberrant activation of progenitor cells by alcohol interferes with the liver's capacity to repair damage and further promotes fibrosis by hepatic stellate cell stimulation. *Figure adapted and modified from Haber et al. Pathogenesis and management of alcoholic hepatitis.* J Gastroenterol Hepatol. *2003;18:1332–1344.*

Alcoholic Liver Disease

Alcoholic liver disease (ALD) comprises a broad spectrum of liver disease, which can include asymptomatic fatty liver, steatohepatitis, fibrosis, cirrhosis, and hepatocellular carcinoma. A particularly severe form of ALD, with an especially high mortality rate, is alcoholic hepatitis. ALD development is not necessarily linear; the main determinants of its progression are still the subject of debate in the alcohol research community. What is clear is that there are multiple stages of ALD varying in severity. The images below show human liver tissue in various healthy and diseased states.

Healthy Liver
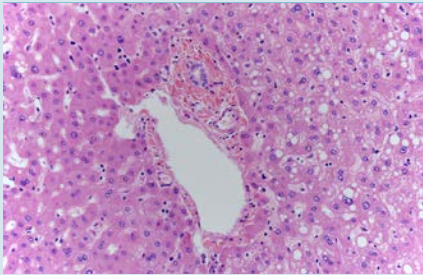
The liver helps digest food, store energy, and break down (or metabolize) and remove toxins from the body. It is the chief organ responsible for metabolizing alcohol and is especially vulnerable to alcohol-related injury.

Alcoholic Steatosis (Fatty Liver Disease)
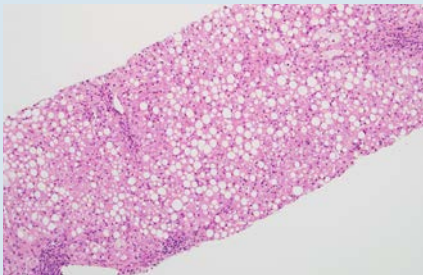
It has been estimated that up to 90 percent of patients with heavy alcohol intake have alcoholic steatosis, or fatty liver, which is the least serious form of ALD and clinically asymptomatic. Abstaining from drinking will reverse this damage.

Alcoholic Steatohepatitis*
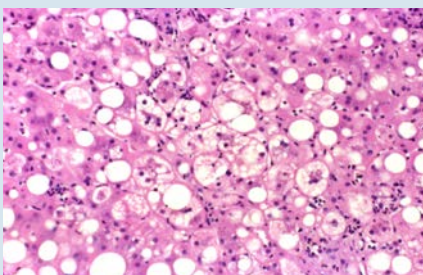
Alcoholic steatohepatitis is a histological representation of an inflammatory condition in the liver caused by continued drinking and characterized by fat accumulation in the hepatocytes, neutrophil infiltration, and cellular damage.

The alcoholic liver disease field has yet to reach consensus on the terms alcoholic hepatitis and alcoholic steatohepatitis.

Alcoholic Hepatitis*†

Alcoholic hepatitis is a severe and acute form of ALD defined clinically and characterized clinically by rapid elevation in serum bilirubin levels, jaundice, and liver-related complication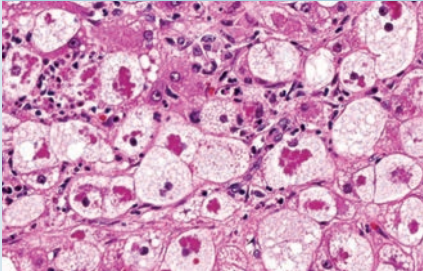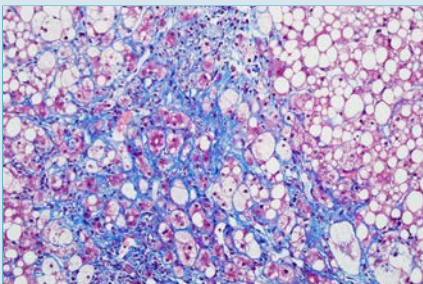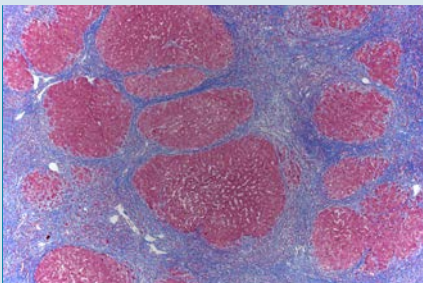s after prolonged, heavy alcohol use. Many alcoholic hepatitis patients also have underlying severe fibrosis or cirrhosis.

Fibrosis

Liver fibrosis is characterized by an accumulation of fibrous connective tissue around cells in the liver, forming a chicken-wire pattern. Fibrosis distorts normal liver architecture and function.

Cirrhosis

The most severe form of fibrosis is cirrhosis, or scarring of the liver.[23] Cirrhosis increases risk of ALD complications such as abdominal fluid accumulation, bleeding in the gastrointestinal tract, loss of brain function, kidney failure, and bacterial infections. Several longitudinal studies indicate that 11–18 percent of patients with alcoholic fatty liver who continue to drink develop cirrhosis over a period of 4–13 years.

Hepatocellular Carcinoma
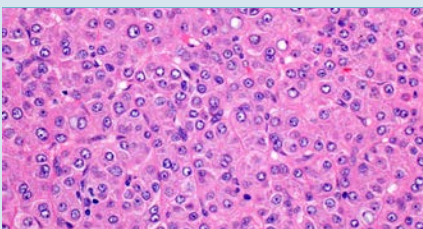
A large cross-sectional study shows that 10 percent of patients with alcoholic cirrhosis have hepatocellular carcinoma (HCC), or malignant liver cancer, whereas longitudinal studies suggest that patients with alcoholic cirrhosis have a rate of developing HCC at 0.2–1.8 incidence per year per 100 persons.[24] The risk remains even after cirrhosis patients have stopped drinking.

†The thresholds for amount and duration of alcohol use causing alcoholic hepatitis are not known, although a pattern of drinking more than three drinks per day for women and four drinks per day for men for more than five years is typical.

All images provided courtesy of Drs. Vijay Shah, Dhanpat Jain, and Taofic Mounajjed, except the alcoholic hepatitis image, which was provided courtesy of Drs. John Woosley and Ramon Bataller.

GOAL 2

Improve Diagnosis and Tracking of Alcohol Misuse, Alcohol Use Disorder, and Alcohol-Related Consequences

Alcohol misuse remains a formidable public health problem. It is the fourth-leading preventable cause of death in the United States and the fifth-leading risk factor for death and disability worldwide.[25] In addition to its adverse effects on individual health and well-being, alcohol misuse takes an enormous toll on families, communities, and society. Efforts to prevent and treat alcohol-related problems must be designed for each of these domains.

Changing patterns of alcohol consumption, shifts in the burden of alcohol-related disease, and shifts in the demographic composition of the United States pose new challenges for alcohol prevention and treatment. A recent study found an increase in mortality among white, middle-aged Americans primarily due to drug and alcohol overdoses, suicide, and cirrhosis and other chronic liver diseases. Although men are still more likely than women to drink alcohol and to drink more when they do, the magnitude of these differences is diminishing as binge and extreme binge alcohol use by women increases. This is particularly alarming, because women who drink are at higher risk for certain alcohol-related diseases, including alcoholic liver disease (ALD) and alcohol-related heart and muscle diseases, compared with men who drink. Moreover, drinking during pregnancy introduces a risk that a child will be born with a fetal alcohol spectrum disorder. By 2030, more than half of all Americans are projected to belong to racial or ethnic minority groups, and one in five Americans is projected to be age 65 or older.[26] As noted above, some minority groups bear a disproportionate burden of alcohol-related problems, and older adults are at higher risk of unintentional alcohol-related injuries, are more likely to experience health problems exacerbated by drinking, and are more likely to take medications, many of which can have adverse interactions with alcohol. The ongoing military conflicts in Iraq and Afghanistan have also influenced patterns of alcohol-related disease: more than 2.1 million service members have been deployed since 2001,[27] and those returning from combat duty face a dramatically increased risk of alcohol use disorder (AUD) and other mental health conditions.

To reduce the burden associated with alcohol misuse in these, and indeed in all, populations, it is essential to define the scope and magnitude of the problems and the factors that contribute to them. Therefore, NIAAA will continue to support research to identify behavioral and biological markers

of alcohol use and alcohol-related conditions, develop and optimize methods for assessing these markers, and establish precise estimates of alcohol use, misuse, and related conditions.

To advance these goals, NIAAA will support the following objectives:

Objective 2a: Improve the diagnosis of alcohol use disorder

The fifth and current edition of the American Psychiatric Association's *Diagnostic and Statistical Manual of Mental Disorders* (DSM-5) provides clinicians with a basis for diagnosing AUD as mild, moderate, or severe based on how many of 11 equally weighted symptoms a patient experiences.[8] These symptoms are largely associated with adverse consequences of substance use, as well as indicators of alcohol tolerance, withdrawal, and escalating or uncontrolled use. When properly assessed, the DSM is a statistically reliable and valid tool for diagnosing substance use disorders (SUDs). Of note, the DSM criteria for AUD were derived from clinical experience and research with adults. Although clinicians do use these criteria to diagnose AUD in adolescents, concerns have been raised about applying them to this population.

Even among adults, the DSM-5 criteria do not reflect the complex and heterogeneous pathophysiology underlying AUD. A patient develops AUD based on a combination of his or her unique biological makeup and life experiences, and there is considerable variation in the way the disorder is expressed among individuals. Developing diagnostic measures that reflect the variation in AUD phenotypes may lead to new and improved treatments and better matching of treatments to patient needs.

NIAAA has proposed developing the Addictions Neuroclinical Assessment as a framework for classifying individual differences in AUD based on the genetic, neurobiological, and behavioral phenotypes corresponding to an individual's disorder. (See "Addictions Neuroclinical Assessment," page 33.) The Institute will support research to identify these phenotypes, or functional domains, and the biological mechanisms that give rise to them. Preclinical studies employing animal models of addiction will continue to be an important avenue for identifying these functional domains. Together with clinical studies, this work will provide a deeper understanding of the biological underpinnings of AUD. It will also provide a basis for identifying AUD biomarkers and specifying a panel of assessments that can be used to identify clinically relevant AUD subtypes, leading to tailored AUD treatment interventions and better outcomes for more people.

To advance these goals, NIAAA will pursue research and related initiatives to:

- **Develop a clinical assessment system using cognitive, behavioral, and biological (e.g., genetic, neuroimaging, and neuropsychological) measures to diagnose and classify individuals of all ages with AUD and other SUDs.**

- **Evaluate this clinical assessment against other frameworks for diagnosing AUD, tailoring treatment to the individual, and assessing recovery.**

ADDICTIONS NEUROCLINICAL ASSESSMENT
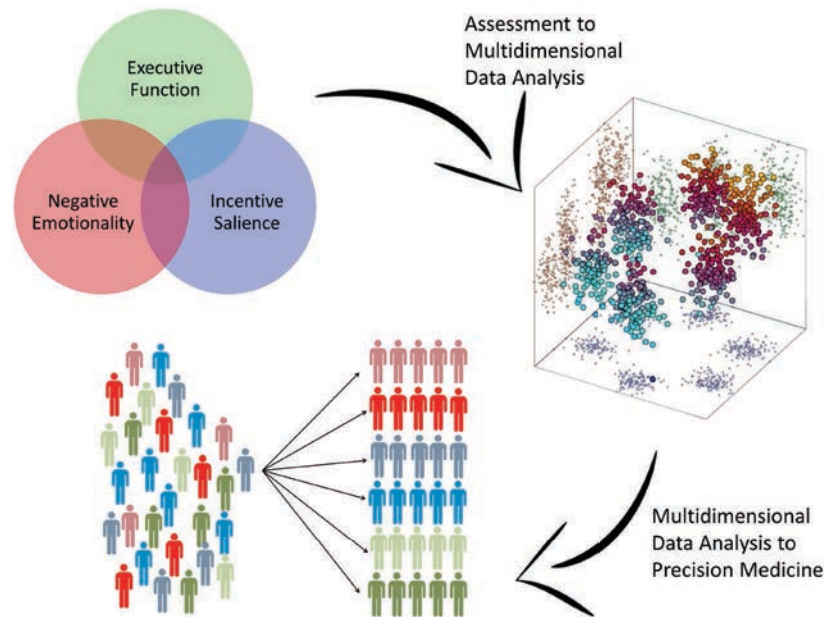
Source: Kwako, Momenan, Litten, Koob, and Goldman. *Biological Psychiatry*, August 1, 2016, 179–189.

NIAAA has proposed developing an Addictions Neuroclinical Assessment (ANA) for assessing and classifying individual differences in key functional domains involved in alcohol use disorder (AUD): incentive salience, negative emotionality, and executive function. The ANA will include a multidimensional battery of tests, including genetic and other "omics" analyses, neuroimaging, and cognitive and behavioral assessments, designed to assess individual variation in each of these domains. The results of these assessments will be used to identify clinically relevant AUD subtypes and guide the provision of individually tailored AUD treatment strategies.

Objective 2b: Develop new approaches for diagnosing fetal alcohol spectrum disorders, enabling early interventions

The prevalence of fetal alcohol spectrum disorders (FASD) in the U.S. general population is estimated to be between 20 and 50 per 1,000 live births.[28] Establishing more precise estimates of FASD is complex due to challenges assessing prenatal alcohol exposure and FASD. Although various alcohol biomarkers exist, they are not reliable enough to use as assays for prenatal alcohol exposure in everyday clinical practice. Work to identify and validate such markers continues. In addition, NIAAA

supports research to improve FASD diagnosis. Many individuals with FASD have cognitive and behavioral problems that are also associated with other developmental disorders. Moreover, whereas people with fetal alcohol syndrome, the most clinically recognizable form of fetal alcohol spectrum disorder, typically have hallmark facial characteristics that facilitate its diagnosis, the facial features associated with other forms of FASD are often very subtle and may even be absent. Recently, NIAAA-funded researchers developed three-dimensional photography and computerized image analysis techniques that can enhance the detection of a broad range of alcohol-induced facial characteristics in children who were prenatally exposed to alcohol. This technology makes it possible to provide more accurate diagnoses of FASD and at an earlier age. It employs three-dimensional cameras routinely used in medical care and photographic images that could be sent for analysis to diagnostic centers anywhere in the world. This technology has the potential to enable widespread FASD screening and early intervention, including for children who do not have access to a clinician with the expertise to diagnose FASD. (See "Three-Dimensional Facial Imaging.")

THREE-DIMENSIONAL FACIAL IMAGING

Researchers funded by NIAAA have developed three-dimensional photography and computerized image analysis techniques that can enhance the detection of alcohol-induced facial features in children who were prenatally exposed to alcohol. Facial signatures captured through this method can be visualized as heat maps, such as the one shown here, which depicts differences in facial features between an individual with fetal alcohol syndrome (FAS) and age-matched control individuals. Red indicates where facial features are contracted, blue is where they are expanded, and green is where they are similar, in the individual with FAS compared to age-matched controls. *Image developed by Drs. Peter Hammond and Michael Suttie, Collaborative Initiative on Fetal Alcohol Spectrum Disorders.*
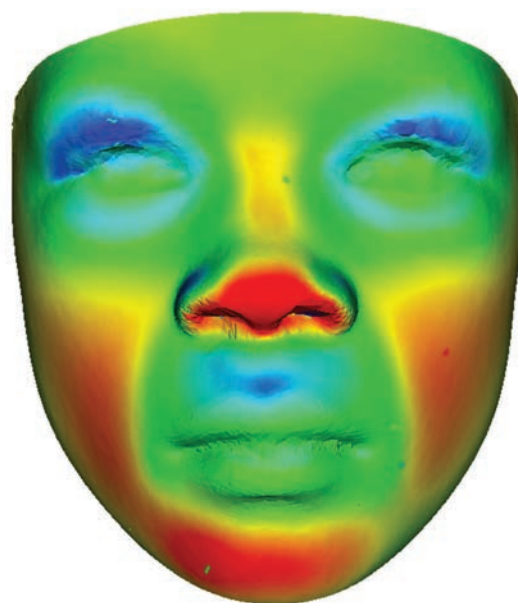
To improve the identification of prenatal alcohol exposure, the diagnosis of FASD, and early intervention with individuals affected by FASD, NIAAA will support studies to:

- **Develop and evaluate pre- and postnatal assays to detect prenatal alcohol exposure and injury—including assays using metabolic and epigenetic biomarkers, in utero sonography, and neuroimaging—to facilitate early intervention and improve outcomes for individuals affected by prenatal alcohol exposure.**

- **Improve the sensitivity of three-dimensional photography and computerized image analysis and evaluate the use of this technology for detecting FASD in individuals of varying age, race, and ethnicity in a wider range of settings.**

- **Refine the understanding of the neurobehavioral phenotypes associated with FASD to improve diagnosis and distinguish individuals with FASD from those with other neurodevelopmental conditions.**

- **Establish more precise estimates of the prevalence of FASD in the United States to improve health outcomes for individuals with these disorders.**

Objective 2c: Develop and evaluate measures to improve the diagnosis of alcohol-related organ damage, especially alcoholic liver disease, and assess its progression

Although the liver breaks down most of the alcohol a person consumes, this process generates dangerous metabolites and byproducts that can damage liver cells, promote inflammation, and weaken the body's natural defenses. Advances in biomarker research and the development of technologies such as liver elastography, a noninvasive, ultrasound-based method of assessing liver disease, may facilitate earlier detection of alcohol-induced liver injury. Additional research is needed to refine these and other methods for diagnosing ALD and preventing its progression to more serious and potentially fatal conditions. In addition to ALD, chronic alcohol misuse is associated with damage to other organ systems and with other serious medical conditions. Attribution of a causative role for alcohol in many of these conditions is, however, often subject to considerable uncertainty, since the organ damage may occur with or without alcohol misuse. Nonetheless, organ damage is often exacerbated in those individuals with a history of problem drinking.
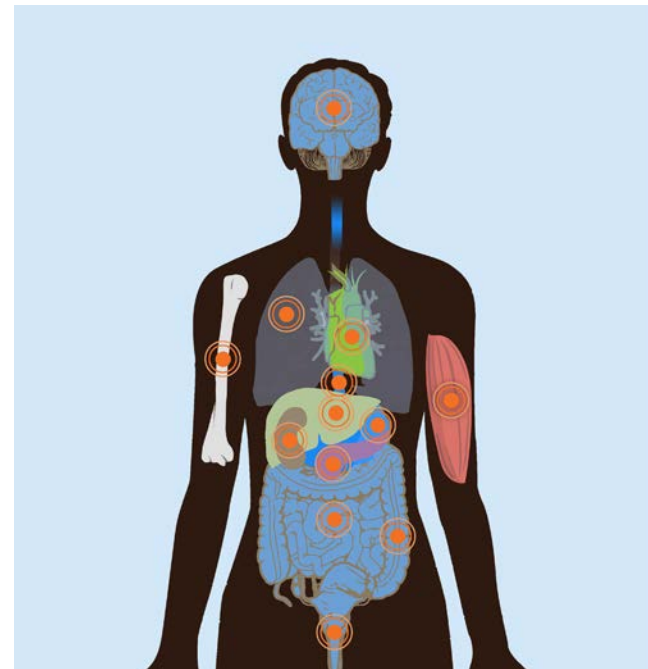
To improve the diagnosis of alcohol-related diseases and generate appropriate therapeutic strategies for them, NIAAA will support studies to:

■ **Develop and validate noninvasive methods of assessing organ injury to improve detection, and assess the status, of ALD.**

■ **Identify biomarkers to distinguish alcoholic and nonalcoholic causes for disease and to monitor the progression of alcohol-related diseases and the effectiveness of treatments.**

Objective 2d: Track the prevalence, patterns, and trends of alcohol use, misuse, and alcohol use disorder; co-occurring conditions; and alcohol-related consequences across the lifespan

NIAAA has a long history of supporting rigorous epidemiological research to identify and track patterns of alcohol use and misuse, drinking-related outcomes, and individual and environmental variables that confer risk or resilience to these outcomes. NIAAA's National Epidemiologic Survey on Alcohol and Related Conditions (NESARC) is the largest and most comprehensive national survey conducted on patterns of alcohol use, AUD, and co-occurring mental and physical disabilities. First conducted in 2001, with subsequent surveys administered in 2004 and 2012, data collected through NESARC has had a profound impact on alcohol research and public health. Analyses of NESARC data showed that people who begin to drink at a young age are more likely to develop AUD later in life and at a younger age, experience more and longer episodes of AUD, and meet more diagnostic AUD criteria. Data from the most recent survey demonstrate that extreme binge drinking—drinking beyond the binge threshold—is increasing, and there has been a significant increase in AUD over the past decade.[29]

In addition to providing data on the distribution and determinants of alcohol-related consequences, epidemiologic research can inform interventions. Studies have demonstrated that alcohol policy interventions can have significant effects on public health outcomes. Every state has established a law against driving with a blood alcohol concentration (BAC) of 0.08 percent or above, and all states have adopted "zero tolerance" laws that mandate lower BAC levels for drivers younger than age 21. These laws, combined with other policies designed to deter driving after drinking, have helped reduce rates of alcohol-related traffic fatalities in the United States by 67 percent since 1982.[30] (See "Alcohol- vs. Non–Alcohol-Related Traffic Fatalities in the United States," page 37.) Among the policies with the best evidence of effectiveness is the minimum legal drinking age of 21. Since the early 1980s, 16- to 20-year-olds have experienced the greatest reduction in alcohol-related crashes, and the percent of high school seniors who engage in binge drinking has been cut in half.[31] Research on how policy changes affect alcohol use and related outcomes continues to be important, particularly as new policies relevant to substance use are implemented. NIAAA's Alcohol Policy Information System

(APIS), a database that tracks alcohol-related policies at the State and Federal levels, facilitates research on the impact and effectiveness of these policies. APIS was recently expanded to include policies related to the recreational use of marijuana and drugged-driving laws.

To better understand the nature and scope of individual- and population-based differences in alcohol and other substance use, the outcomes associated with substance use, and the complex biopsychosocial factors that contribute to these outcomes, NIAAA will:

- **Support epidemiologic research on patterns of alcohol use, alcohol misuse (including extreme binge drinking), and AUD; alcohol-related consequences; and treatment.**

- **Use epidemiologic data to identify and track populations that are differentially vulnerable to alcohol misuse, AUD, and other alcohol-related consequences.**

- **Support epidemiologic and systems science research to elucidate how biological and environmental determinants interact to impact alcohol misuse and related consequences.**

- **Support research to examine how substance use policies, including those relevant to substance use treatment and the changing legal status of marijuana, affect alcohol and other drug use and their consequences.**

ALCOHOL VS. NON-ALCOHOL-RELATED TRAFFIC FATALITIES IN THE UNITED STATES
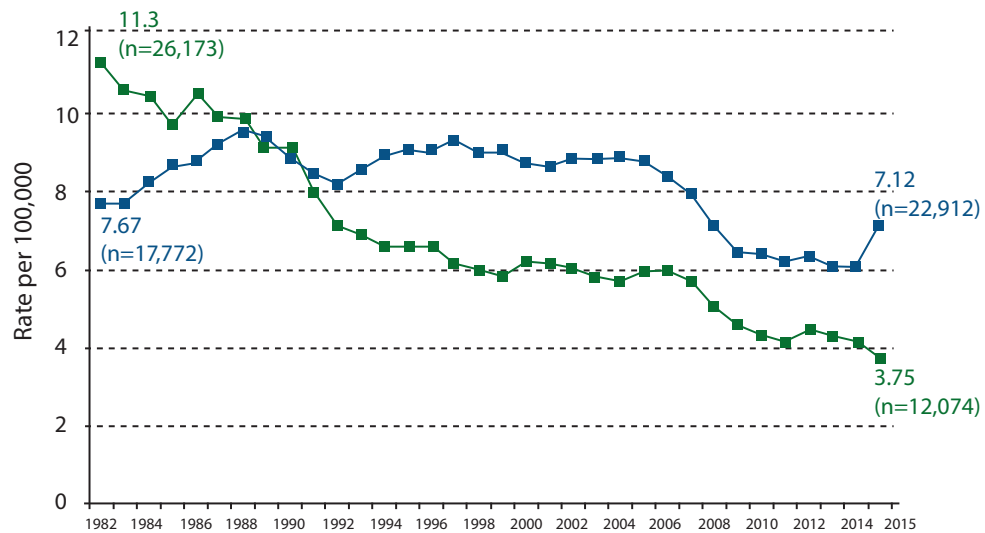
Sources: National Highway Traffic Safety Administration;[32] U.S. Census Bureau.[33]

■ Alcohol Related   ■ Non–Alcohol Related

GOAL 3

Develop and Improve Strategies To Prevent Alcohol Misuse, Alcohol Use Disorder, and Alcohol-Related Consequences

People begin drinking for different reasons and at different points in their lives, have different risk and protective factors, and vary in their susceptibility to the negative effects that may result from drinking too much. The stage of life at which a person is exposed to alcohol is an important moderator of alcohol misuse and the consequences associated with it, and it is a key consideration in designing and implementing preventive interventions.
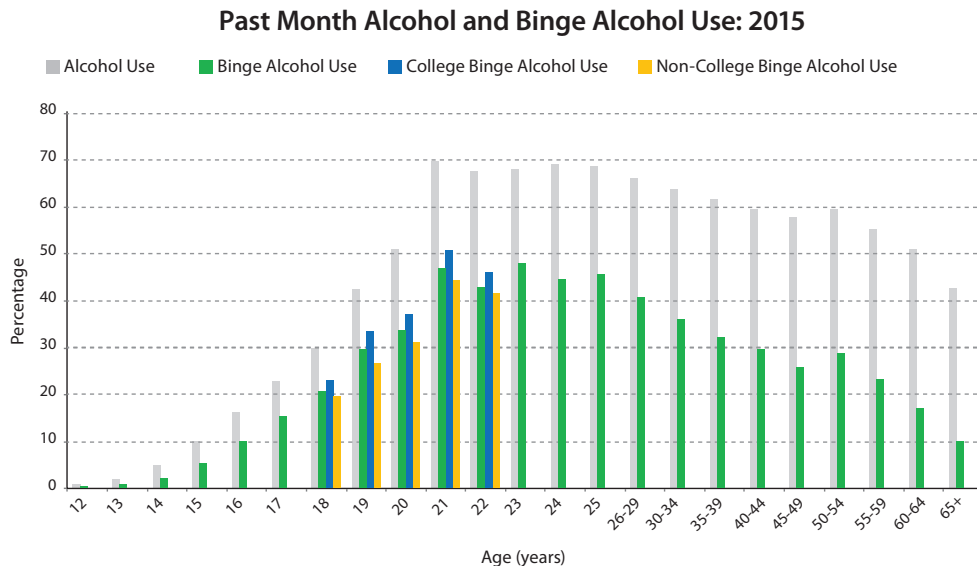
Many people first begin using alcohol during adolescence, and the prevalence of drinking and binge drinking increases dramatically during this time, peaking in the early 20s. (See "Alcohol Use Across the Lifespan," page 40.) Not only are adolescents at increased risk of injuries and accidents while under the influence, but those who begin drinking before age 15 are four times more likely to report symptoms of alcohol use disorder (AUD) at some point in their lives compared to those who wait until they are 21 or older.[34] Moreover, preclinical and clinical research indicates that alcohol exposure during adolescence can affect brain development and compromise cognitive function in both the short and long term. In light of the adverse consequences associated with adolescent drinking, a key objective is to prevent, or at least delay, the onset of drinking among youth.

Young adults are also vulnerable to alcohol misuse and its consequences. This time of life is marked by burgeoning independence and a transition into more adult roles, including, for many, the pursuit of a college degree or the beginning of a career in the military or civilian workforce. Each year, more than 5,000 18- to 24-year-olds die from unintentional injuries related to alcohol.[35] Binge and extreme binge drinking are particularly troubling, as they increase risks for blackouts, alcohol poisoning, sexual assault and sexually transmitted diseases, poor academic performance, and developing AUD.

There are special considerations facing older adults who drink. Midlife is the time when individuals with AUD are most likely to seek alcohol treatment, and when many of the pathological health consequences associated with chronic alcohol misuse emerge, including alcoholic liver disease, alcoholic cardiomyopathy, neurodegeneration, acute and chronic pancreatitis, and kidney failure. Older adults are more sensitive than younger people to the sedative effects of alcohol, as well as to the effects of alcohol on reaction time, balance, attention, and driving skills. Adults older than age 65 are more likely than younger people to take medications, and combining alcohol with certain

ALCOHOL USE ACROSS THE LIFESPAN

Past Month Alcohol and Binge Alcohol Use: 2015

Legend: ▪ Alcohol Use ▪ Binge Alcohol Use ▪ College Binge Alcohol Use ▪ Non-College Binge Alcohol Use

Y-axis: Percentage (0–80). X-axis: Age (years) — 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26-29, 30-34, 35-39, 40-44, 45-49, 50-54, 55-59, 60-64, 65+

Source: SAMHSA, Center for Behavioral Health Statistics and Quality, National Survey on Drug Use and Health, 2015.

The percentage of individuals who report using any alcohol (light grey) or binge drinking (green) in the past month increases during adolescence and peaks in the early 20s. Among 18- to 22-year-olds, full-time college students (blue) are more likely to report binge drinking than individuals who are not full-time college students (orange).

medications increases the potential for injuries and other adverse health effects. Alcohol-interactive medications are also metabolized more slowly as one ages, creating a larger window of time for potential negative interactions. Many older adults also have poor dietary intake due to a multitude of problems, including depression, problems chewing, and poor appetite, which can result in higher blood alcohol content when they do drink.

Developmental factors are not the only consideration in designing preventive interventions. A person's genetic makeup, health status, demographic and cultural background, and individual life experiences are also important factors, as is the broader sociocultural context in which one lives. This may include alcohol-related policies, community attitudes toward alcohol use, and exposure to social media. Such individual and environmental determinants, as well as interactions among them, affect the likelihood that a person will misuse alcohol, develop AUD, or suffer adverse alcohol-related outcomes.

NIAAA will continue to support research to translate basic behavioral science findings into individual-, family-, and community-level interventions to prevent alcohol misuse and its myriad

adverse consequences. NIAAA is particularly interested in supporting the development of culturally appropriate interventions for at-risk groups; interventions to reduce alcohol-related violence, sexually transmitted diseases, overdose, and adverse medication interactions; and interventions that capitalize on electronic health technologies as a means of broadening their reach.

To advance these goals, NIAAA will pursue the following objectives:

Objective 3a: Promote universal screening and brief intervention for alcohol and other substance use

Regular screening for alcohol misuse is a key prevention strategy, and the U.S. Preventive Services Task Force recommends that primary care clinicians screen adults for alcohol use. Studies show that most patients do not object to being screened, that they are open to hearing advice, and that those who screen positive for heavy drinking or AUD show some motivational readiness to change. Moreover, adult screening in primary care is effective at reducing alcohol misuse, though additional research is needed to evaluate its effectiveness in other settings and with diverse populations. Screening is also an important tool for delaying the onset of drinking among youth. To facilitate youth alcohol screening, NIAAA developed *Alcohol Screening and Brief Intervention for Youth: A Practitioner's Guide*. The guide is designed to help primary care providers identify 9- to 18-year-olds who are at risk for alcohol use, are using alcohol, or have AUD, and to intervene as appropriate. It introduces a two-question screening tool and an innovative youth alcohol risk estimator to help clinicians overcome time constraints and other common barriers to alcohol screening and brief interventions.

To further encourage alcohol screening and brief intervention, NIAAA will support research and related initiatives to:

- **Evaluate NIAAA's youth alcohol screening guide in primary care settings, emergency departments, juvenile justice settings, and schools, and for youth who have chronic health conditions.**

- **Adapt and evaluate adult alcohol screening and brief intervention for various settings and populations, including underrepresented minorities, pregnant women, seniors, individuals engaged with the justice system, and individuals with chronic illnesses.**

- **Develop and evaluate methods for administering alcohol screening and brief intervention along with screening and brief intervention for other addictive substances, including tobacco and marijuana.**

Objective 3b: Develop, evaluate, and promote effective strategies for preventing alcohol misuse, alcohol use disorder, and related consequences for individuals at all stages of life

Individuals operate within many different social systems, including families, peer groups, schools, workplaces, community groups, and broader sociocultural environments. Each of these systems exposes a person to numerous influences that may confer risk for or protection from alcohol problems. A large body of evidence shows that both individual and environmental interventions can be effective at preventing alcohol-related harm. For example, among college students, a group to which considerable attention has been devoted, some of the most effective individual-level strategies include providing students with personalized feedback about their alcohol use in comparison with use by their peers, and training students to monitor and assess their alcohol consumption, identify personal drinking cues, develop alcohol refusal skills, and manage stress. Effective environmental interventions for college students include restricting happy hours and alcohol price promotions, banning Sunday alcohol sales, enforcing minimum drinking age laws, and increasing the cost of alcohol.

To help colleges and universities identify interventions appropriate for their campuses, NIAAA created CollegeAIM—the College Alcohol Intervention Matrix—in conjunction with leading college alcohol researchers. CollegeAIM is a comprehensive, easy-to-use tool that rates nearly 60 individual- and environmental-level interventions based on factors such as effectiveness, cost, and ease of implementation. It allows officials to identify strategies most likely to reduce drinking and its harmful consequences; see how their current strategies compare with other options; find new, research-based strategies to consider; and select a combination of approaches that meets the needs of their students and campus.

Despite the availability of effective preventive strategies, the prevalence of alcohol misuse remains unacceptably high. Existing interventions do not work for—nor do they reach—every individual. For example, interventions designed for college students may not be effective for young adults who are not in school—a group for which few preventive interventions have been specifically designed.

Likewise, those designed for working-age adults may not be effective for retirees. The desired outcomes of prevention programs may also vary by group. Whereas maintaining alcohol levels at or below the low-risk guidelines established by NIAAA may be an appropriate outcome for many healthy adults, those with chronic diseases, such as human immunodeficiency virus (HIV), or those at risk for adverse alcohol medication interactions may be advised to drink less or not at all. These examples point to the need for a broader menu of preventive interventions. They also underscore the importance of designing evaluations to assess whether an intervention is equally effective for different groups, identifying the variables mediating and moderating subgroup effects, and adapting evidence-based interventions—or designing new ones—for the groups and communities in which they will be delivered.

To prevent alcohol misuse, including binge and extreme binge drinking, and its consequences for diverse populations across the lifespan, NIAAA will support research to:

- **Develop and evaluate strategies to prevent and reduce alcohol misuse among young adults, including those in the military, the civilian workforce, and college.**

- **Assess the impact of NIAAA's CollegeAIM in preventing and reducing alcohol misuse in college students.**

- **Use CollegeAIM as a model for disseminating evidence-based information on preventing and treating alcohol-related harms for noncollege populations.**

- **Develop and evaluate interventions to prevent and reduce alcohol misuse during pregnancy.**

- **Develop and evaluate interventions to prevent and reduce alcohol misuse by older adults.**

- **Develop and evaluate culturally appropriate, evidence-based interventions for preventing alcohol misuse in diverse communities.**

- **Evaluate the effectiveness and implementation of interventions to reduce HIV transmission and improve HIV medication compliance and overall health outcomes by reducing alcohol misuse among people with HIV.**

- **Evaluate the effectiveness and implementation of new policies and other environmental interventions for preventing alcohol misuse and related problems.**

GOAL 4

Develop and Improve Treatments for Alcohol Misuse, Alcohol Use Disorder, Co-Occurring Conditions, and Alcohol-Related Consequences

Considering the serious adverse consequences associated with alcohol misuse noted above, treating alcohol use disorder (AUD) and ameliorating the negative health effects associated with it are crucial. A variety of effective interventions are available to treat AUD. These include professionally led behavioral treatments to help people identify and change behaviors that contribute to alcohol misuse, three U.S. Food and Drug Administration (FDA)–approved medications, and mutual support groups, such as Alcoholics Anonymous and other peer-led groups. Research shows that behavioral and pharmacological therapies are most effective when used in combination, and that most people with AUD who get some form of treatment benefit from it.

Unfortunately, however, many of the people who might benefit from alcohol treatment never receive it: less than 10 percent of people in the United States who had AUD in the past year received treatment or help,[36] and less than 4 percent of those who had AUD in the past year received an FDA-approved alcohol treatment medication.[37] Numerous barriers prevent individuals from seeking treatment. They may be deterred by the stigma associated with alcohol misuse and alcohol-related disease, financial constraints, or logistical challenges that prevent them from attending treatment, such as lack of transportation or childcare. Still others, including many clinicians, are not aware of the full range of alcohol treatment options. The barriers to seeking and using preventive and treatment services—and the outcomes of those services—are not necessarily uniform across demographic groups. Improving the identification of high-risk alcohol users and expanding access to a diverse, high-quality, and culturally and age-appropriate range of health services is critical to reducing the public health burden of alcohol misuse.

Treatment for alcohol misuse has largely been administered in specialty treatment facilities. However, the quality and accessibility of care could be improved by integrating alcohol services into general medical care. Primary care settings, for example, provide opportunities for regular screening, engaging patients who may be unwilling or unable to seek specialty care, treating the physical and mental health conditions that commonly co-occur with AUD, and monitoring recovery. Integrated care models, facilitated by electronic medical records, are beginning to emerge, but these models and approaches for implementing and sustaining them must be evaluated.

Mobile health technologies hold promise for improving upon and expanding access to evidence-based interventions for problem drinking. Smart phones, text messaging, social media applications, biological sensors, and other devices are being used to engage patients outside of usual care settings, assist them in monitoring their alcohol consumption, and provide personalized resources and support where and when they need it most, such as at times or places they tend to use

alcohol. (See "NIAAA Wearable Alcohol Biosensor Challenge," page 47.) Although there are significant challenges to optimizing and facilitating uptake of electronic health technologies, research in this area has the potential to increase the number of people with access to effective, personalized treatment interventions and continuing care.

NIAAA will continue to pave a path to healthier lives for the millions of people affected by alcohol-related disease by supporting a diverse portfolio of treatment and recovery research, with a focus on the following objectives:

Objective 4a: Improve existing behavioral treatments for alcohol use disorder and co-occurring conditions, and develop new behavioral treatments based on advances in neuroscience and basic behavioral research

Cognitive behavioral therapy, motivational therapy, community reinforcement, family and couples therapy, and brief interventions have consistently been found to reduce rates of heavy drinking. Such behavioral treatments for AUD share features, such as having health care professionals work with people to set attainable alcohol reduction goals, build a strong social support system, and develop skills to cope with or avoid triggers that might contribute to relapse. Behavioral treatments also differ in certain ways. For example, cognitive behavioral therapy is aimed at changing the thought processes that contribute to drinking and teaching coping skills directed at managing risky situations. Motivational enhancement therapy, on the other hand, seeks to facilitate and strengthen internal motivation to change drinking behavior by aligning changes in behavior with life goals.

As with pharmacological treatments, particular behavioral strategies are not effective for every patient, and individuals diagnosed with AUD and co-occurring psychiatric conditions often have poorer treatment outcomes. Developing a better understanding of mechanisms through which behavioral interventions exert their effects (i.e., the active ingredients of these therapeutic approaches) will enable health care providers to optimize care by emphasizing the treatment features that have the greatest and longest-lasting impact on outcomes. Research has already identified several possible psychological mechanisms, including eliciting change/commitment talk, therapeutic alliance, client self-efficacy, therapist empathy, coping skills, motivation to change, and attributions of change. Researchers are also examining how patterns of brain activity may be used to predict treatment outcomes, and even whether altering activity in brain networks involved in AUD can influence drinking. Additional research is needed to identify novel mechanisms of behavior change, further elucidate those that have empirical support, and translate this knowledge into new and improved treatments.

NIAAA Wearable Alcohol Biosensor Challenge

In March 2015, NIAAA held a competition to create a better wearable alcohol biosensor device that could aid researchers, clinicians, therapists, and individuals by providing more accurate data on how much an individual is drinking. Current technologies for continuous alcohol monitoring, which are commonly used in the criminal justice system, are effective but cumbersome. Moreover, they only take readings every 30 minutes, and they reflect blood alcohol content (BAC) as it was 60–90 minutes prior to assessment—not in real time.

NIAAA's challenge was designed to stimulate development of a sleek, unobtrusive sensor that could improve upon this interval and more closely approximate real-time BAC. The device was also expected to be able to interpret and securely store BAC data or transmit the data to a smartphone.

NIAAA announced the winner of the Alcohol Biosensor Challenge in May 2016. The winning prototype was submitted by BACtrack, a company known nationally for designing and selling portable breath alcohol testers for consumer and professional use. Their entry, the BACtrack Skyn, is worn on the wrist and, like existing continuous alcohol monitoring devices, detects alcohol through a person's sweat. Significantly, it advances real-time alcohol monitoring by reflecting BAC as it was as little as 40 minutes prior to assessment.

Building on the success of the challenge, NIAAA issued a new challenge to stimulate inventors to develop a wearable biosensor that can detect alcohol directly in blood or the interstitial fluid that surrounds the body's cells, rather than alcohol exuded in sweat. This method would measure a person's current BAC.

To advance behavioral treatments for AUD and co-occurring conditions, NIAAA will:

- Promote research to enhance the effectiveness of current, evidence-based behavioral therapies for a wider range of patients across a wider range of treatment settings.

- Examine the effectiveness of novel behavioral interventions for AUD and co-occurring psychiatric conditions, such as interventions that target reward systems, emotional regulation, stress responsivity, cognitive function, and sleep.

- Characterize changes in neural circuits that accompany responses to behavioral treatments for AUD, use this information to optimize and validate AUD interventions, and determine which type of behavioral therapy works best for which patient.

- Investigate the use of noninvasive devices capable of altering brain activity, such as transcranial direct current stimulation, as AUD treatments or adjuncts to treatment.

- Use electronic health technologies, including mobile devices, to improve the effectiveness, accessibility, and use of behavioral interventions for AUD and co-occurring disorders, including human immunodeficiency virus (HIV).

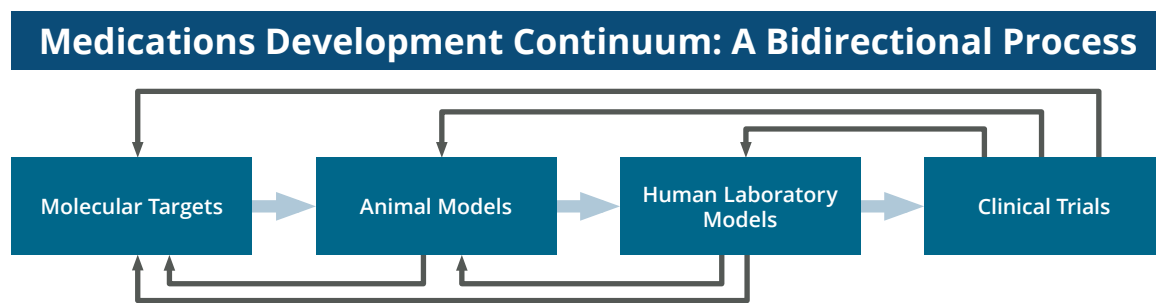## Objective 4b: Develop novel medications for treating alcohol use disorder and co-occurring conditions

Medications are an important component of the AUD treatment toolbox, and they are often used in combination with behavioral interventions for AUD. There are currently three medications approved by the FDA for treating AUD: disulfiram, naltrexone, and acamprosate. Disulfiram blocks an enzyme in the body involved in metabolizing acetaldehyde, a toxic byproduct of alcohol metabolism. It causes unpleasant side effects such as nausea, vomiting, and flushing of the skin when alcohol is consumed, which helps to deter people who are taking disulfiram from drinking. Naltrexone, which is available in oral and extended-release injectable formulations, diminishes the rewarding effects of alcohol to help reduce heavy drinking. Acamprosate reduces the negative emotional state associated with protracted abstinence from alcohol and may also reduce craving, making it easier to maintain abstinence once it is achieved.

Additional AUD treatments are needed, including for people with co-occurring health conditions, such as post-traumatic stress disorder (PTSD), HIV, and alcoholic liver disease (ALD), as well as other substance use disorders. Research is also needed on the safety and efficacy of AUD medications in adolescents, who tend not to be represented in clinical trials. Through its intramural and extramural research programs, NIAAA supports studies across the drug development continuum, from target identification to clinical trials, with the goals of developing a wider variety of safe and effective pharmacotherapies and giving clinicians a menu of options for individualized AUD treatment. At present, researchers have identified more than 30 molecular targets that appear to alter drinking behavior. However, much work is needed to determine the precise role of these

targets in the development and maintenance of AUD. Once a promising target has been selected, it is necessary to identify and screen compounds capable of modulating it. Only a small percentage of candidate compounds are ever approved for use. In fact, to take a central nervous system compound from discovery to market takes approximately 18 years and more than $1.8 billion.[38, 39] To make this process more efficient and less costly, NIAAA is pursuing new approaches to identify drug targets using network biology analyses to examine relationships among candidate compounds, gene expression profiles, and protein and metabolite products associated with AUD. Such approaches reflect a shift toward developing compounds or combinations of compounds that can simultaneously modulate multiple biological targets with a role in AUD. The Institute also continues to support the development and validation of standardized animal screening models with which to evaluate the preclinical efficacy of compounds.

Another particularly challenging barrier to medications development is moving promising compounds from animal studies into human testing. NIAAA is working to bridge the gap between basic and clinical research via its Human Laboratory Program (HLAB) and through the Small Business Innovation Research (SBIR) and Small Business Technology Transfer (STTR) programs. Through the HLAB, NIAAA aims to standardize clinical laboratory paradigms for screening experimental AUD medications for efficacy and safety. Under the SBIR and STTR programs, NIAAA assists small businesses with early-stage compounds to conduct pre-Investigational New Drug (IND) studies intended to result in the submission of an IND application to the FDA. This program also supports Phase I clinical studies to ensure the safety, tolerability, and proper dosing of compounds approved for experimental use in people.

Medications Development Continuum: A Bidirectional Process

Molecular Targets → Animal Models → Human Laboratory Models → Clinical Trials

Although human laboratory studies can provide preliminary evidence for a compound's efficacy, randomized, placebo-controlled, Phase II proof-of-concept (POC) trials are required to validate these findings. NIAAA has a long history of supporting state-of-the-art POC trials of promising AUD medications, including trials in AUD patients with co-occurring conditions. To expedite such studies, NIAAA's Clinical Investigations Group (NCIG) uses a network of sites to conduct "fast success/fast fail" trials in less than two years in collaboration with the pharmaceutical industry and the National Center for Advancing Translational Sciences.

NIAAA seeks to engage and partner with the pharmaceutical industry to conduct Phase III (pivotal trials) on compounds with promising POC data. NIAAA also supports secondary analyses of trial data that can inform regulatory decision-making and the development of evidence-based research guidelines. For example, studies supported by NIAAA led the FDA to allow "percent of subjects with no heavy drinking days" to be used as an alternative to abstinence as the primary endpoint in trials of drugs evaluated as AUD treatments. NIAAA hopes these efforts will further stimulate the development of treatments that provide meaningful clinical benefits to patients.

NIAAA will continue to prioritize the development of a wider array of medications to treat individuals diagnosed with AUD alone or with other diseases and conditions. To further this goal, NIAAA will support research to:

- **Explore, with secondary analyses and in consultation with the FDA, new, clinically meaningful endpoints for clinical trials of medications for treating AUD.**

- **Use new approaches, such as drug-target networks and connectivity mapping, to expedite the identification of neurobiological drug targets involved in each stage of the AUD cycle, and to identify and optimize compounds that act on those targets as potential treatments for AUD.**

- **Continue to develop human laboratory paradigms as screening models to test compounds for treating AUD.**

- **Conduct clinical trials on novel and repurposed compounds with potential for treating AUD.**

- **Reverse-validate preclinical models and human laboratory models with effective medications as they are developed.**

- **Identify and evaluate candidate therapeutics for treating AUD in patients with co-occurring mental health conditions, alcohol-related organ damage, and HIV, as well as in adolescents.**

Objective 4c: Identify factors that facilitate or inhibit sustained recovery from alcohol use disorder

Though definitions vary, one conceptualization of recovery from AUD is the disappearance of AUD symptoms accompanied by a state of well-being that builds resilience to relapse. Recovery is possible and is associated with parallel neuropsychological and neurobiological changes. However, the process is not the same for everyone. Some people need longer or more intense treatments, whereas others recover more quickly and with minimal intervention. Relapse is often a part of the process; it may take several attempts before someone can stop or reduce drinking over the longer term. A return to drinking after a period of abstinence is especially likely during times of stress or when individuals are exposed to people or places they associate with drinking. Currently, little is known about the factors that facilitate or inhibit long-term recovery, including why some people can recover without some form of assistance. Developing a better understanding of the recovery process, including the factors that enable people to maintain changes in their drinking behavior and promote resilience to relapse, will inform the development of additional effective treatment interventions.

To further this goal, NIAAA will:

- **Collaborate with stakeholders to develop operational definitions of recovery and relapse.**

- **Support observational, epidemiological, and natural history studies that lay the foundation for understanding mediators and moderators of recovery, such as stress and peer and family support, in subgroups of individuals with AUD.**

- **Support research on the use of biomarkers and behavioral and neuropsychological assessments validated by neuroimaging to monitor the recovery process and inform follow-up intervention. (See also Objective 1a.)**

- **Evaluate the effectiveness of the full range of recovery support services, including those that are particularly successful at recruiting understudied populations, such as women and racial and ethnic minorities.**

- **Explore the optimal timing and dose of AUD interventions, including pharmacotherapies, behavioral treatments, and mutual help groups, needed to maximize and sustain recovery.**

Objective 4d: Advance precision medicine by evaluating which treatments for alcohol use disorder and related conditions work best for which individuals

Precision medicine is an emerging approach for preventing and treating disease that considers individual variability in genes, environment, and lifestyle. It is an important focus of the NIH and a guiding framework for NIAAA's work to treat alcohol misuse and AUD. NIAAA's Addictions Neuroclinical Assessment will provide a framework for diagnosing AUD based on neurobiological, behavioral, and genetic phenotypes. (See "Addictions Neuroclinical Assessment," page 33.) NIAAA also supports research to identify patient cohorts most likely to benefit from existing treatments and to develop new interventions based on the unique characteristics of a person's disease. For example, because relapse is frequently triggered by stress, NIAAA is evaluating compounds that target brain stress systems as treatments for people who are particularly susceptible to stress-related drinking. Researchers are also investigating whether patterns of brain activation can be used to identify people who are likely to relapse when exposed to certain stimuli, as well as whether particular AUD treatments are more effective in people with certain gene variants.

Identifying subpopulations that are most likely to respond to certain treatments may help augment the effect sizes found in studies of candidate AUD medications. So far, effect sizes for compounds that act on the central nervous system for conditions such as addiction, depression, and schizophrenia have tended to be modest. Improving effect sizes may encourage greater pharmaceutical interest in developing AUD medications and expedite the production of a broader menu of effective treatments. Together, these efforts hold promise for a future in which clinicians will be able to use brain imaging, genetic testing, biomarker profiling, psychological assessments, and other diagnostic techniques to identify patients most likely to benefit from a given therapy and monitor their progress over the course of treatment and recovery.

To fulfill the promise that precision medicine holds for improving AUD treatment, NIAAA will pursue research and related initiatives to:

- **Identify and evaluate biological, cognitive, and behavioral markers that can be used to predict a patient's response to AUD treatments and treatment combinations, and evaluate their progress throughout recovery.**

- **Identify which preventive and treatment interventions work best for whom by creating DNA, RNA, and protein databases with samples from NIAAA research participants and making these data available to the broader research community.**

Objective 4e: Develop and evaluate interventions to treat fetal alcohol spectrum disorders, alcoholic liver disease, and other negative health outcomes caused by alcohol misuse

Fetal alcohol spectrum disorders (FASD) are among the many devastating negative health outcomes that can result from alcohol misuse. Although there is no cure for FASD, there are interventions that can improve outcomes for individuals affected by these conditions. For example, school-based interventions, which include specialized teaching strategies that provide a consistent routine and numerous opportunities to practice new skills, can help children learn more effectively. Researchers are investigating other approaches to improving cognitive and behavioral function in people with FASD, including game-based interventions to improve attention and working memory; training in metacognition, literacy, problem solving, social skills, and personal safety; and pre- and postnatal nutritional supplements. The use of family support groups and classes to help parents better care for children with FASD are also being investigated as potential strategies for improving behavioral outcomes in affected children.

NIAAA will continue to support research to mitigate the developmental, cognitive, and behavioral challenges faced by people with FASD, including studies to:

- **Identify and evaluate nutritional and pharmacological agents that could lessen alcohol's adverse effects on prenatal development or ameliorate these effects after birth.**

- **Develop and evaluate novel, developmentally relevant behavioral interventions to lessen the sensory, motor, cognitive, and emotional challenges experienced by children and adults with FASD.**

Alcoholic liver disease (ALD) is a serious and potentially fatal consequence of alcohol misuse for which there is a dire need for new treatments. Advanced stages of ALD are very difficult to treat, and many patients do not respond to the pharmacotherapies that are currently available. Indeed, more than 50 percent of patients with a severe case of alcoholic hepatitis die within the first month of being diagnosed.[20] NIAAA has a major ongoing initiative to fund multiple translational research consortia dedicated to developing more effective treatments for alcoholic hepatitis.

Researchers have made advances in understanding the mechanisms by which alcohol misuse leads to liver fibrosis and cirrhosis. This is opening new avenues for the investigation of compounds to reverse these conditions, which were previously considered untreatable. There is growing optimism

that compounds that target multiple pathological mechanisms responsible for ALD may provide better clinical outcomes than current treatments. Additional research is needed to capitalize on these advances and ensure continued progress against ALD. (See Objective 4b to learn more about NIAAA's work in medications development.) The use of liver transplantation in ALD patients is also an important area of inquiry. Although this procedure is the only effective treatment for end-stage liver disease, only a minority of ALD patients are referred for liver transplant, and there is insufficient information on clinical outcomes of liver transplantation in this population.

To improve treatment outcomes for patients with ALD, NIAAA will support research and related activities to:

- **Identify and evaluate novel nutritional and pharmacological agents for treating ALD.**

- **Develop and integrate pharmacological and behavioral AUD treatments for individuals undergoing ALD treatment.**

Objective 4f: Evaluate the effectiveness, accessibility, affordability, and appeal of alcohol use disorder treatments and recovery models, and test strategies to increase their adoption in real-world settings

Although numerous effective alcohol interventions exist, there is a lack of data on their comparative effectiveness, how to optimize their dissemination and implementation among diverse groups and in multiple settings, and how to better integrate them with general medical care. There are concerted Federal efforts to facilitate health services research, and NIH has been at the forefront of supporting hypothesis-driven research on these topics and promoting effective, scalable implementation strategies to broaden health care access and use. NIAAA supports health services research designed to broaden the delivery of the full menu of evidence-based alcohol prevention and treatment services, such that individuals have greater access to interventions that address their specific alcohol-related issues in a wide array of care delivery settings. Innovations in collecting and aggregating clinical data collected within and outside health care settings, along with advances in research methods, have the potential to improve outcomes for individual patients, lower health care expenditures, and reduce the public health burden of alcohol misuse.

To identify and evaluate treatments and treatment delivery models that are appealing, affordable, accessible, and effective for different types of drinkers and for populations with special health care service needs, NIAAA will:

- **Apply innovative clinical and health services research methods, such as adaptive research designs, pragmatic trials, and cluster randomized trials, to the development and evaluation of improved models for delivering alcohol-related care.**

- **Develop and evaluate strategies to reduce barriers that prevent people from seeking and receiving appropriate care for alcohol misuse and AUD and that enhance treatment adherence and retention.**

- **Develop and evaluate strategies to enhance the dissemination, implementation, and adoption of evidence-based treatment practices across the spectrum of services for at-risk and high-risk drinkers, as well as those with AUD and co-occurring conditions.**

- **Develop and evaluate AUD treatment and recovery models, including models tailored for nonmedical settings and medical nonspecialty settings, and models of care coordination between specialty treatment and general medical care settings.**

- **Develop and evaluate models for providing ongoing, comprehensive care for individuals with chronic AUD and other alcohol-related conditions within the health care system.**

GOAL 5

Enhance the Public Health Impact of NIAAA-Supported Research

The research supported by NIAAA has benefited people around the world by propelling advances in the diagnosis, prevention, and treatment of alcohol-related problems. While these achievements are notable, alcohol remains a leading contributor to death and disability. Although many people know that drinking too much can be bad for their health, they may not be aware of the full range of consequences associated with alcohol misuse, how alcohol exerts its adverse effects on the body, or how to prevent and treat alcohol-related problems. Likewise, although there is widespread acceptance among researchers and health care professionals that alcohol use disorder (AUD) is a chronic disease of the brain, this perspective may not be as widely accepted among members of the general public. A critical component of NIAAA's mission, therefore, is to disseminate evidence-based information about alcohol and health to the public, health care providers, educators, researchers, and policymakers.

To improve understanding of the effects of alcohol on health in the United States and globally, NIAAA will pursue the following objectives:

Objective 5a: Improve public awareness of the effects of alcohol on health and well-being and of the options for preventing and treating alcohol misuse, alcohol use disorder, and alcohol-related problems for individuals at all stages of life

NIAAA has developed a robust communications and outreach program aimed at translating alcohol research findings for the benefit of public health. This is done through print publications for diverse populations, news media outreach, and an increasing focus on multimedia products and social media efforts. Each year, the Institute distributes approximately 600,000 alcohol-related publications to diverse audiences (see "NIAAA Print and Multimedia Products," page 58), and more than 6.5 million people visit the NIAAA website. NIAAA's *Rethinking Drinking*, a Web-based resource and accompanying booklet, is designed to help individuals who use alcohol assess their drinking habits and determine if they need to make a change. It also provides evidence-based information, tools, and support for cutting back on or quitting drinking. *Treatment for Alcohol Problems: Finding and Getting Help*, another resource developed for people interested in changing their drinking behavior, outlines behavioral and medication treatment options for AUD and provides tips for selecting among these options and sustaining recovery.

NIAAA PRINT AND MULTIMEDIA PRODUCTS

Youth Screening Guide
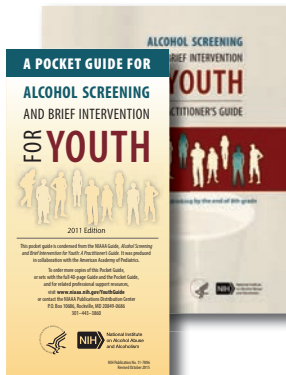
pubs.niaaa.nih.gov/publications/
Practitioner/YouthGuide/YouthGuide.pdf

Rethinking Drinking

rethinkingdrinking.niaaa.nih.gov

NIAAA Spectrum

www.spectrum.niaaa.nih.gov

CollegeAIM (Alcohol Intervention Matrix)

www.collegedrinkingprevention.gov/collegeaim

Clinician's Guide

www.niaaa.nih.gov/guide

NIAAA News Releases

www.niaaa.nih.gov/news-events

Social Media

@NIAAAnews

Spanish-Language Publications

www.niaaa.nih.gov/publications/
publicaciones-en-espanol

The Cool Spot

thecoolspot.gov

NIAAA develops resources tailored to specific populations. For example, to raise awareness of the effects of alcohol on women's health and safety, NIAAA developed the brochure *Alcohol: A Women's Health Issue* and its Women and Alcohol fact sheet. The Institute has also developed materials for adolescents, young adults, older adults, individuals with a family history of AUD, and parents, among others. To engage the nation's growing population of Spanish speakers, NIAAA continues to expand its Spanish-language print products and social media efforts. The Institute is exploring opportunities to develop culturally appropriate products for other audiences as well, which will continue to be important as the demographic composition of the United States changes.

News media coverage of NIAAA research and related initiatives, which encompasses print publications, radio, television, and the Web, allows the Institute to expand its reach to the public. As such, media engagement remains a key component of NIAAA's outreach strategy. The Institute serves as a credible source of scientific information and engages the media on alcohol-related issues through compelling news media packages that include images, infographics, and video and that provide opportunities to showcase the work of our scientific experts. These efforts are designed to increase media interest in—and dissemination of—the research and other initiatives that the Institute supports. To keep pace with changes in the way people seek and consume information, NIAAA will develop a broader array of multimedia products for multiple platforms that emphasize visual learning, the innovative use of graphics and videos, and interactive communications strategies.

To improve public understanding about the effects of alcohol on health and alcohol interventions, and to reduce the stigma associated with alcohol-related conditions, NIAAA will:
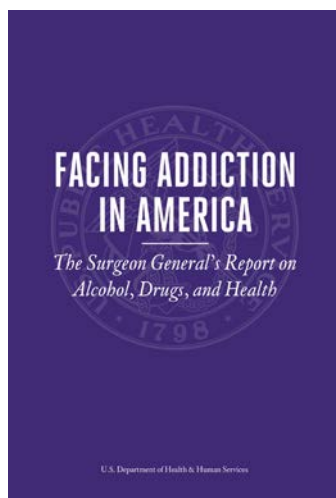
- **Continue to develop and promote culturally appropriate, evidence-based materials for diverse audiences regarding the health effects of alcohol, AUD as a chronic disease, and options for preventing and treating alcohol-related conditions.**

- **Develop an AUD treatment navigator to help individuals with the complex process of evaluating, selecting, and pursuing appropriate treatment for AUD.**

- **Expand the use of state-of-the-art methods for sharing the latest research and health information with a wide range of audiences.**

- **Strengthen the capacity to work strategically with news media and other broadcast platforms to disseminate evidence-based information to a large and more diverse audience.**

- **Continue to assess NIAAA's communications resources and strategies to determine if they are meeting their goals, and revise them accordingly.**

Objective 5b: Develop and promote tools and resources to assist health care providers, researchers, and policymakers in addressing alcohol misuse, alcohol use disorder, and other alcohol-related health consequences

In addition to developing resources for individuals in need, NIAAA develops resources for professionals. Health care providers are on the front lines of alcohol prevention and treatment, yet many are unfamiliar with the full range of evidence-based alcohol interventions, and others may be uncomfortable using them. Following studies showing that alcohol screening and brief intervention (SBI) can reduce risky drinking among adults, NIAAA developed *Helping Patients Who Drink Too Much: A Clinician's Guide* and *Alcohol Screening and Brief Intervention for Youth: A Practitioner's Guide* to help health care providers implement SBI in their practices. Hundreds of thousands of copies of these guides have been distributed to doctors, nurses, and mental health practitioners. NIAAA also developed online training courses, based on the guides, with Medscape, an organization that provides research and health information for physicians and other health professionals. More than 20,000 providers have obtained continuing medical education credit for completing the *Clinician's Guide* training, and more than 37,000 have received credit for completing the *Youth Guide* training. NIAAA's College Alcohol Intervention Matrix (CollegeAIM), a research-based, interactive, user-friendly decision tool and guide designed to help colleges and universities address alcohol misuse on their campuses, is another example of a product developed for a specific professional group—higher education officials, particularly alcohol and other drug program and student life staff responsible for addressing student drinking on campuses.

Researchers and policymakers are also an important audience for NIAAA's information. NIAAA's Alcohol Policy Information System (APIS) is designed primarily as a tool to facilitate research on the effects and effectiveness of alcohol-related policies, and it contains a wealth of information relevant to others interested or involved with alcohol policy issues. NIAAA is also collecting, reviewing, and evaluating the evidence-based, peer-reviewed literature on interventions to prevent and treat alcohol and other substance misuse among Native Americans and Alaska Natives. The findings will be made available to the public, and they are expected to facilitate additional research and guide tribal authorities in selecting interventions appropriate for their communities.

To assist service providers, researchers, and policymakers to address alcohol-related problems, NIAAA will:

- **Continue to promote and disseminate evidence-based tools to assist professionals in addressing alcohol misuse across the lifespan and in diverse populations and settings.**

- **Develop, evaluate, disseminate, and validate evidence-based resources to facilitate the implementation of effective alcohol prevention and treatment interventions for special populations.**

- **Establish a publicly available database of measures employed in alcohol research that are available in languages other than English to facilitate alcohol research with diverse populations.**

Objective 5c: Strengthen partnerships to extend the reach of the alcohol-related health information developed and distributed by NIAAA, and facilitate the implementation of evidence-based preventive and treatment interventions

Strategic partnerships play an increasingly important role in NIAAA's communications efforts. NIAAA collaborates with other Federal agencies, scientific societies, professional and advocacy organizations, educators, and patient, family, and community groups, among others, on a wide range of initiatives. These partnerships extend the reach of the alcohol-related health information developed and distributed by the Institute, and they facilitate the implementation of evidence-based prevention and treatment interventions.

NIAAA is proud to have partnered with the U.S. Surgeon General and other U.S. Department of Health and Human Services agencies on *Facing Addiction in America: The Surgeon General's Report on Alcohol, Drugs, and Health*. This comprehensive, first-of-its-kind report reviewed the state of the science of substance use and articulated an actionable set of recommendations for preventing and treating alcohol and other substance use disorders. NIAAA also collaborated with HBO on *Risky Drinking*, a powerful documentary that examines AUD through the intimate stories of four people whose drinking dramatically affected their lives. These initiatives, which were designed to provoke a national conversation about substance use, brought much-needed attention to the serious problem of alcohol misuse and showcased resources for addressing it.

NIAAA also partnered with the Substance Abuse and Mental Health Services Administration (SAMHSA) to raise awareness among health care providers about alcohol interventions. Together, the agencies convened a panel of experts in alcohol research, clinical care, medical education, and public policy to review the current evidence on the effectiveness of medications for the treatment of AUD. This initiative resulted in the development of *Medication for the Treatment of Alcohol Use Disorder: A Brief Guide*, which is designed to help clinicians incorporate pharmacotherapy into their alcohol treatment practices.

NIAAA, along with other NIH Institutes and Centers, SAMHSA, the Centers for Disease Control and Prevention, the Health Resources and Services Administration, and the White House Office of National Drug Control Policy, is engaged in a national initiative designed to grow the addiction medicine workforce and speed the integration of substance use prevention, early intervention, and treatment training into mainstream medicine. As part of this collaboration, NIAAA and its Federal partners are taking specific steps to improve physician training in substance use prevention and treatment, including supporting the accreditation of new addiction medicine fellowship training programs for residents and engaging medical education groups in designing and implementing national standards for training in addiction medicine.

SENATOR HAROLD HUGHES MEMORIAL AWARD

The Senator Harold Hughes Memorial Award recognizes the contributions of a nonresearcher whose work translates research into practice and builds bridges between the alcohol prevention, treatment, and policymaking communities. The award is named for former Governor of Iowa and U.S. Senator, Harold Hughes, who was a major force behind the Comprehensive Alcohol Abuse and Alcoholism Prevention, Treatment, and Rehabilitation Act of 1970 that established NIAAA.

Credit: U.S. Senate Historical Office

Previous Hughes Award recipients include:

Tom Donaldson, president and chief executive officer of the National Organization on Fetal Alcohol Syndrome (NOFAS), was recognized for his decades-long dedication to using current alcohol research to raise awareness about fetal alcohol spectrum disorders and the risks of drinking during pregnancy.

Jonathan Gibralter, Ph.D., president of Wells College, was recognized for his leadership in addressing the issue of high-risk drinking on the nation's campuses through a community-based, multifaceted approach that brings together college administrators and key constituents on and off campus.

Marianne "Mimi" Fleury, president and co-founder of the Community of Concern (CoC), was recognized for her work to establish coalitions across the country to address underage drinking, smoking, and substance use and to develop science-based resources for parents, school administrators, counselors, and students.

General Arthur T. Dean, chairman and chief executive officer of Community Anti-Drug Coalitions of America (CADCA), was recognized for his leadership in promoting healthy, drug-free communities by engaging, supporting, and empowering community leaders around the nation to implement evidence-based substance use prevention, treatment, and recovery strategies.

Higher education institutions are also important partners in alcohol prevention and treatment. Recognizing that harmful and underage drinking are significant problems on U.S. campuses, NIAAA formed a working group composed of college and university presidents to bring renewed national attention to this issue. The College Presidents Working Group to Address Harmful and Underage Drinking requested a tool that would allow them to assess evidence-based college drinking interventions based on their effectiveness, anticipated costs, and barriers to implementation. In response to that request, NIAAA developed CollegeAIM. The Institute will continue to collaborate with the Working Group to organize regional workshops to introduce college and university officials to CollegeAIM and demonstrate how schools can use it, as well as develop a guide for parents about alcohol and their college students.

NIAAA also partners with a wide range of community organizations. These groups have provided valuable opportunities for NIAAA to learn from community leaders about emerging issues and gaps in alcohol research, prevention, and treatment, which informs the Institute's research and communications efforts. Recognizing the value of community partners, NIAAA established the Senator Harold Hughes Memorial Award to recognize nonresearchers who translate research into practice. (See "Senator Harold Hughes Memorial Award," page 62.)

NIAAA will establish strong partnerships with organizations that have the power to broaden and amplify its public health messages and effect real-world implementation of evidence-based interventions by pursuing the following objectives:

- **Work with Federal partners that have a role in health care delivery to translate alcohol prevention and treatment research into practice.**

- **Continue to partner with professional organizations to integrate substance use prevention, screening and brief intervention, and treatment into primary care and preventive medicine training, and to develop an addiction "core curriculum" for medical student training.**

- **Continue to partner with community groups to broadly disseminate evidence-based information on alcohol and the prevention and treatment of alcohol-related problems.**

- **Partner with legal and criminal justice organizations to raise awareness of evidence-based alcohol treatment options in criminal justice settings.**

- **Explore opportunities to collaborate with human resources and other employee services organizations to raise awareness in the workplace about preventing and treating alcohol misuse and helping individuals access appropriate care.**

References

1 Center for Behavioral Health Statistics and Quality. Table 2.43B. *2015 National Survey on Drug Use and Health: Detailed Tables.* Rockville, MD: Substance Abuse and Mental Health Services Administration; 2016.

2 National Institute on Alcohol Abuse and Alcoholism. Unpublished data from the 2012–2013 National Epidemiologic Survey on Alcohol and Related Conditions III (NESARC-III), a nationwide survey of 36,309 U.S. adults aged 18 and older.

3 Stahre M, Roeber J, Kanny D, Brewer RD, Zhang X. Contribution of excessive alcohol consumption to deaths and years of potential life lost in the United States. *Prev Chronic Dis*. 2014;11:130293.

4 World Health Organization. *Global Status Report on Alcohol and Health*. 2014. Geneva, Switzerland: World Health Organization; 2014.

5 Center for Behavioral Health Statistics and Quality. Table 5.4A. *2015 National Survey on Drug Use and Health: Detailed Tables.* Rockville, MD: Substance Abuse and Mental Health Services Administration; 2016.

6 Sacks JJ, Gonzales KR, Bouchery EE, Tomedi LE, Brewer RD. 2010 National and state costs of excessive alcohol consumption. *Am J Prev Med*. 2015 Nov;49(5):e73–79.

7 U.S. Department of Health and Human Services and U.S. Department of Agriculture. *2015–2020 Dietary Guidelines for Americans. 8th Edition*. http://health.gov/dietaryguidelines/2015/guidelines/. Accessed March 2017.

8 American Psychiatric Association. *Diagnostic and Statistical Manual of Mental Disorders, 5th Edition*. Washington, DC: Author; 2013.

9 Rehm J, Baliunas D, Borges GL, Graham K, Irving H, Kehoe T, Parry CD, Patra J, Popova S, Poznyak V, Roerecke M, Room R, Samokhvalov AV, Taylor B. The relation between different dimensions of alcohol consumption and burden of disease: An overview. *Addiction*. 2010 May;105(5):817–843.

10 NIAAA Facts and Statistics. https://www.niaaa.nih.gov/alcohol-health/overview-alcohol-consumption/alcohol-facts-and-statistics. Accessed April 2017.

11 Center for Behavioral Health Statistics and Quality. Table 2.84B. *2015 National Survey on Drug Use and Health: Detailed Tables*. Rockville, MD: Substance Abuse and Mental Health Services Administration; 2016.

12 Center for Behavioral Health Statistics and Quality. Table 5.4B. *2015 National Survey on Drug Use and Health: Detailed Tables*. Rockville, MD: Substance Abuse and Mental Health Services Administration; 2016.

13 Centers for Disease Control and Prevention (CDC). Alcohol-attributable deaths and years of potential life lost among American Indians and Alaska Natives—United States, 2001–2005. *MMWR Morb Mortal Wkly Rep*. 2008 Aug 29;57(34):938–941.

14 Center for Behavioral Health Statistics and Quality. Table 5.56B. *2015 National Survey on Drug Use and Health: Detailed Tables*. Rockville, MD: Substance Abuse and Mental Health Services Administration; 2016.

15 Drabble LA, Midanik LT, Trocki K. Reports of alcohol consumption and alcohol-related problems among homosexual, bisexual and heterosexual respondents: Results from the 2000 National Alcohol Survey. *J Stud Alcohol*. 2005;61(1):111–120.

16 Wray TB, et al. Systematic review of interventions to reduce problematic alcohol use in men who have sex with men. *Drug Alcohol Rev*. 2016 Mar;35(2):148–157.

17 Koob GF, Le Moal M. Drug abuse: Hedonic homeostatic dysregulation. *Science.* 1997 Oct 3;278(5335):52–58.

18 Koob GF, Volkow ND. Neurobiology of addiction: A neurocircuitry analysis. *Lancet Psychiatry.* 2016 Aug;3(8):760–773.

19 Goldman D, Oroszi G, Ducci F. The genetics of addictions: Uncovering the genes. *Nat Rev Genet*. 2005;6(7):521–532.

20 Bruha R, Dvorak K, Petrtyl J. Alcoholic liver disease. *World J Hepatol*. 2012;4(3):81–90.

21 Centers for Disease Control and Prevention. HIV in the United States: At A Glance. http://www.cdc.gov/hiv/statistics/overview/ataglance.html. Accessed April 2017.

22 Pandrea I, Happel K, Amedee A, Bagby G, Nelson S. Alcohol's role in HIV transmission and disease progression. *Alcohol Res Health*. 2010;33(3):267–279.

23 Sorensen TI, et al. *Lancet*. 1984;324(8397):241–244; Teli MR, et al. *Lancet*. 1995;346(8981):987–990; Mathurin P, et al. *Aliment Pharmacol Ther*. 2007;25(9):1047–1054.

24 Morgan TR, Mandayam S, Jamal MM. Alcohol and hepatocellular carcinoma. *Gastroenterology*. 2004;127(5 Suppl 1):S87–596; Fattovich G, et al. *Gastroenterology*. 2004;127(5 Suppl 1):S35–50.

25 Lim SS, Vos T, Flaxman, AD, et al. A comparative risk assessment of burden of disease and injury attributable to 67 risk factors and risk factor clusters in 21 regions, 1990–2010: A systematic analysis for the Global Burden of Disease Study 2010. *Lancet*. 2012;380(9859):2224–2260.

26 Colby SL, Ortman JM. *Projections of the Size and Composition of the U.S. Population: 2014 to 2060*. *Current Population Reports*. P25–1143. Washington, DC: U.S. Census Bureau; 2015.

27 *Report on the Impact of Deployment of Members of the Armed Forces on Their Dependent Children.* Washington, DC: U.S. Department of Defense; October 2010.

[28] May PA, Gossage JP, Kalberg WO, Robinson LK, Buckley D, Manning M, Hoyme HE. Prevalence and epidemiologic characteristics of FASD from various research methods with an emphasis on recent in-school studies. *Dev Disabil Res Rev*. 2009;15(3):176–192.

[29] Grant BF, Goldstein RB, Saha TD, Chou SP, Jung J, Zhang H, Pickering RP, Ruan WJ, Smith SM, Huang B, Hasin DS. Epidemiology of DSM-5 alcohol use disorder: Results from the National Epidemiologic Survey on Alcohol and Related Conditions III. *JAMA Psychiatry*. 2015;72(8):757–766.

[30] NIH Fact Sheet. Alcohol-related traffic deaths. https://report.nih.gov/nihfactsheets/ ViewFactSheet.aspx?csid=24. Accessed February 2017.

[31] Johnston LD, O'Malley PM, Miech RA, Bachman JG, Schulenberg JE. *Monitoring the Future National Survey Results on Drug Use, 1975–2015*: *Overview, Key Findings on Adolescent Drug Use*. Ann Arbor, MI: Institute for Social Research, The University of Michigan; 2016.

[32] National Highway Traffic Safety Administration Fatality Analysis Reporting System. Available at http://www-fars.nhtsa.dot.gov. Accessed March 2017.

[33] U.S. Census Bureau Population and Housing Unit Estimates Datasets. Available at https://www. census.gov/programs-surveys/popest/data/data-sets.html. Accessed March 2017.

[34] U.S. Department of Health and Human Services. *The Surgeon General's Call to Action to Prevent and Reduce Underage Drinking*. Washington, DC: U.S. Department of Health and Human Services, Office of the Surgeon General; 2007.

[35] Hingson RW, Zha W, Weitzman ER. Magnitude of and trends in alcohol-related mortality and morbidity among U.S. college students ages 18–24, 1998–2005. *J Stud Alcohol Drugs Suppl*. 2009;(16):12–20.

[36] Center for Behavioral Health Statistics and Quality. Table 5.26B. *2015 National Survey on Drug Use and Health: Detailed Tables*. Rockville, MD: Substance Abuse and Mental Health Services Administration; 2016.

[37] Litten RZ, Falk DE, Ryan ML, Fertig JB. Discovery, development, and adoption of medications to treat alcohol use disorder: Goals for the phases of medications development. *Alcohol Clin Exp Res*. 2016;40:1368–1379.

[38] Kaitin KI, Milne CP. A dearth of new meds. *Sci Am*. 2011 Aug;305(2):16.

[39] Morgan S, Grootendorst P, Lexchin J, Cunningham C, Greyson D. The cost of drug development: A systematic review. *Health Policy*. 2011;100(1):4–17.

U.S. Department of Health and Human Services
National Institutes of Health
National Institute on Alcohol Abuse and Alcoholism

www.niaaa.nih.gov

April 2017