

Alcohol Alert

Number 79

NIAAA: 40 Years of Research Leadership

Forty years ago, Federal legislation placed new emphasis on solving America's alcohol problems and created the National Institute on Alcohol Abuse and Alcoholism (NIAAA). Since then, NIAAA has led an increasingly effective effort to both define alcohol issues as medical in nature and to address them using evidence-based findings.¹



This *Alcohol Alert* reflects on 40 years of NIAAA's research and outreach accomplishments and provides insight into the future direction of this important work.

The Institute's Formation and Impact

Passage of the Comprehensive Alcohol Abuse and Alcoholism Prevention, Treatment, and Rehabilitation Act of 1970—also known as the Hughes Act—created NIAAA as a high-profile agency in charge of addressing problems related to alcohol consumption. Researchers and policymakers who wrote the law were bringing to light a shift in scientific thinking about alcohol problems that had begun in the 1930s with the formation of Alcoholics Anonymous. Instead of viewing alcoholism as resulting from personal weakness, researchers and health care providers were beginning to view it as a curable public health problem.

NIH first began conducting research on alcoholism in the 1960s within the National Institute of Mental Health, but Hughes Act supporters recognized that a more visible entity was needed to further legitimize the alcohol field by coordinating and funding research. Indeed, since its formation, NIAAA has vastly broadened the scope of alcohol research and brought essential health messages to the public.

The Institute has supported research that demonstrates the underlying heritable and physiological nature of alcohol abuse and dependence as well as their roles in related diseases. Medication studies funded by NIAAA have resulted in the approval of drugs to treat alcoholism and put new compounds into clinical trials. The Institute has researched public policies that have had measurable effects on alcohol-related problems in the United States. Through these and other research and public health initiatives, NIAAA has affected nearly all areas related to alcohol use, abuse, and dependence, with the goal of improving understanding and health in the United States and around the world.

The work supported by the Institute has transformed our understanding of alcohol abuse and dependence and their treatment.



National Institutes of Health

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National Institute on Alcohol Abuse and Alcoholism

NIAAA-Supported Research

During its 40 years, NIAAA frequently has studied populations and pursued research areas that traditionally have been under-served. For example, the Institute supported research on fetal alcohol spectrum disorders (FASD) at a time when many scientists doubted the negative effects of alcohol on prenatal development. NIAAA held the first international research conference on FASD in 1977 and issued the first government health advisory on FASD on June 1, 1977. Research supported by NIAAA has helped define the range and prevalence of FASD, as well as methods to help prevent these alcohol-related problems.² These efforts led to major legislation in 1988, requiring that alcoholic beverage containers be labeled to warn drinkers of the adverse consequences alcohol can have on the developing fetus.

Lifespan Perspective. NIAAA’s groundbreaking research and public policy work surrounding FASD demonstrate the value of examining alcohol’s effects on a single period of a person’s life. In 2006, NIAAA released its Five-Year Plan, the *NIAAA Strategic Plan for Research*, which employs a new framework for organizing research: a lifespan perspective. Such an approach shows promise for honing research questions and providing a focus for outreach efforts with respect to particular life stages.

For example, research now shows that the brains of adolescents continue developing into young adulthood. This finding has far-reaching implications for underage alcohol use. At the same time, adolescents tend to engage in risky behaviors and experience the effects of alcohol differently from adults. They are less sensitive to the negative effects of alcohol, such as sleepiness, but more likely to have trouble with complex tasks like driving. This profile highlights the need for further research into alcohol’s effects on development and for prevention and intervention strategies targeted at youth.³

Prevention Through Policy. Government policies can offer powerful tools for addressing alcohol-related consequences experienced by populations such as youth. Policy research supported by NIAAA evaluates the effects of laws and policies on measures such as deaths from motor vehicle crashes.

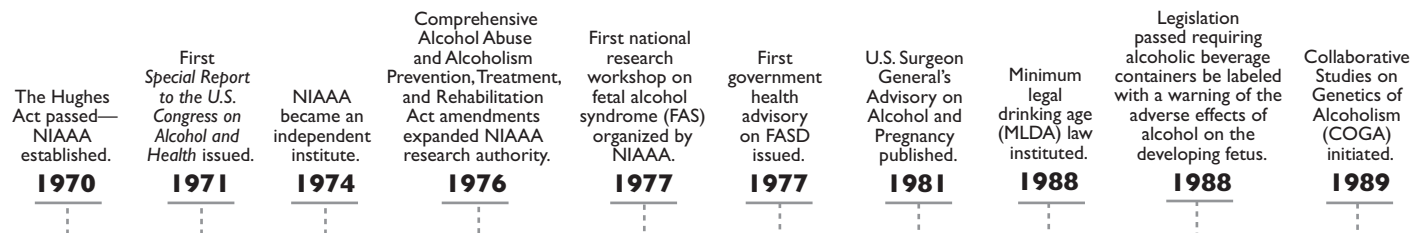
One of the most effective alcohol policies on the books today is the minimum legal drinking age (MLDA) law. Research indicates that laws like the two core MLDA statutes (prohibiting possession or purchase of alcohol by youth) can influence underage drinking-and-driving fatalities. Between 1988, when MLDA laws were instituted, and 1995, alcohol-related traffic fatalities for people aged 15–20 declined by nearly half, from 4,187 to 2,212.⁴

Epidemiology. To help define the scope and context of alcohol problems nationwide, NIAAA supports epidemiologic studies. The Institute funded the National Epidemiologic Survey on Alcohol and Related Conditions (NESARC), the largest survey ever conducted on alcohol use and associated psychiatric and medical conditions (see sidebar). The survey was considered exceptional for its large size, high response rates, and breadth of content.

NESARC provided estimates indicating that 65 percent of the U.S. population drinks alcohol and that about 13 percent either abuse alcohol or are dependent on alcohol. The survey has been cited in more than 300 peer-reviewed journal articles, including more than 80 in the past year alone. Researchers also have used NESARC to begin to unravel how alcohol problems are related to other drug use disorders and mood disorders.

Genetics. Another important area of alcohol research focuses on determining who is at greatest risk of developing an alcohol use disorder. To this end, NIAAA has supported innovative studies of the genetic component of alcohol problems. In the 1970s, studies conducted with samples of twins and with people who were adopted first demonstrated that the tendency for alcoholism to “run in families” was not entirely attributable to the environment in which children grew up. In fact, genetic factors contribute between 50 percent and 60 percent of vulnerability to alcoholism.⁵

Which genes are responsible for this risk, however, still is a matter of intense research. Pinpointing gene variants can help identify people who might be more vulnerable to developing alcohol problems or who have more difficulty recovering from them. It is clear that the incidence and course of alcohol dependence relies on a variety of factors,



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1980

including co-occurring mental health disorders and social influences. To tease out genetic from environmental influences, the Institute created the Collaborative Studies on Genetics of Alcoholism (COGA) in 1989, a series of studies of the genes underlying vulnerability to alcoholism in a human population (see page 4). This ongoing research analyzes the genetic makeup of alcoholic and nonalcoholic family members and seeks to associate the genetic data with alcohol-related characteristics.^{6,7} To date, the list of genes associated with alcoholism in the COGA sample has grown to more than 20, highlighting a tremendous return from NIAAA's investment in this project.

Body Systems. Although genetic studies will have long-term value for early interventions with vulnerable populations, NIAAA also supports research that studies alcohol dependence and alcohol's effects on the body. For example, Institute-supported research first associated liver disease directly with alcohol use in 1975. Ongoing research is clarifying the mechanisms involved in liver and other tissue injury⁸ and in alcohol's varied effects—both beneficial and detrimental—on the heart.⁹

Alcohol abuse also severely suppresses the immune system, which helps protect the body from infections. As a result, alcoholic patients are more susceptible to infections such as tuberculosis, pneumonia, bacterial infections, or HIV/AIDS; show more rapid disease progression; and are more likely to die from these infections.¹⁰ This is particularly devastating in the context of HIV infection, where a certain subgroup of immune system cells already is depleted by the virus.

Treating alcohol dependence itself requires a look at how alcohol interacts with the central nervous system. One avenue of investigation identifies circuits and signaling chemicals in the brain to learn how they are affected by excess alcohol consumption and how they, in turn, affect the development of addiction. Signaling patterns are changed in the brains of alcohol- or drug-dependent people, and these changes contribute to the addiction cycle. Each of the affected brain circuits or systems involves signaling molecules—known as neurotransmitters—that provide potential targets for medicines to treat addiction. Compounds that block or partially block the activity of certain neuro-

transmitters could ameliorate the effects of these signaling changes.¹¹

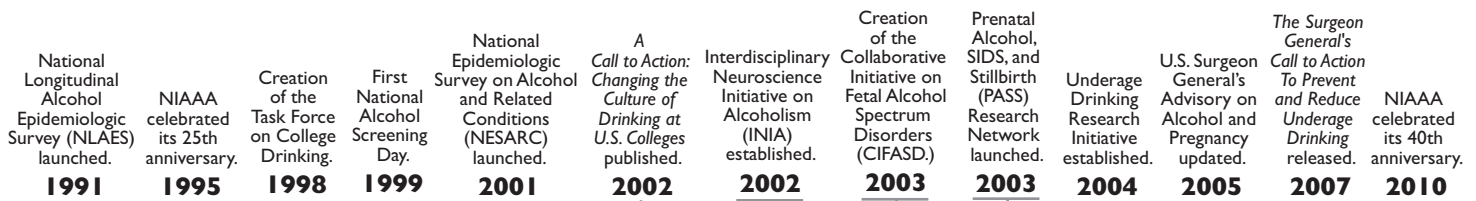
Medications. Concurrent with its efforts to understand the roots of alcohol dependence, the Institute dedicates significant resources to identifying promising medicines to treat alcoholism. In 1992, NIAAA supported human studies of naltrexone, which proved effective in reducing drinking among alcohol-dependent patients. The NIAAA-funded studies formed the basis for the Food and Drug Administration's (FDA's) approval of the drug for treatment of alcoholism. Further research trials led to FDA approval of a second medication, acamprosate, in 2004 and to new therapeutically useful formulations of naltrexone in 2006.¹ NIAAA now is funding exploration of new molecular targets, and testing of about 20 new compounds—including topiramate and ondansetron—is underway.¹¹ The Institute also studies special populations, such as those with other mental health disorders, adolescents, and minorities. And NIAAA is pursuing research to predict which patients are most likely to respond positively to certain medications (personalized medicine).

Outreach. As these pieces of research come together to provide a clearer picture of alcohol problems, NIAAA is vitally concerned with putting evidence-based findings into medical practice and informing the public. NIAAA has guided the alcohol field in public outreach, working with other Federal agencies and grassroots organizations. The Institute, for example, called attention to the problem of underage drinking in collaboration with the U.S. Surgeon General's office to produce *The Surgeon General's Call to Action To Prevent and Reduce Underage Drinking* in 2007.

The Institute works with communities to develop evidence-based tools that can be used to prevent alcohol use and related problems. Project Northland, an alcohol use prevention research approach for sixth, seventh, and eighth graders, and the Iowa Strengthening Families Program, focusing on families, have been among the more successful programs.¹²

To aid in diagnosing alcohol dependence, NIAAA produced a training guide, *Helping Patients Who Drink Too Much: A*

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Key Initiatives Sponsored by NIAAA

Collaborative Studies on Genetics of Alcoholism (COGA)—These studies to identify the genes underlying vulnerability to alcohol abuse and dependence have been ongoing since 1989.⁷ COGA investigators recruited families of alcoholics in which the alcohol-dependent patient has at least two close relatives who also are alcohol dependent; their data pool now extends to more than 15,000 people from 1,900 families. Researchers gathered extensive clinical, neuropsychological, electrophysiological, biochemical, and genetic data, and established a repository of specialized cell lines from study participants, to serve as a permanent source of DNA for genetic studies. NIAAA supports the distribution of these data and cell lines to qualified scientists in the broader research community.

Health Disparities Initiatives—Since 1989, NIAAA has increased fivefold its investment in health disparities research and community outreach. The goal is to reduce the differences in the incidence and burden of certain diseases and health conditions that exist among specific population groups in the United States and to encourage the creation of interdisciplinary, multiethnic research teams. With the support of the National Center on Minority Health and Health Disparities (NCMHD), NIAAA is collaborating with minority-serving institutions to ensure that the clinical knowledge and experience of minority-serving health care providers reach those conducting health disparities research.

Interagency Coordinating Committee on Fetal Alcohol Syndrome (ICCFAS)—NIAAA chairs ICCFAS, which coordinates Federal activities surrounding disorders related to prenatal alcohol exposure. The committee includes NIH (including the National Institute of Child Health and Human Development), the Department of Health and Human Services (including the Agency for Healthcare Research and Quality, the Centers for Disease Control and Prevention, the Maternal and Child Health Bureau of the Health Resources and Services Administration, the Indian Health Service, and the Substance Abuse and Mental Health Services Administration), the Department of Education, the Office of Special Education and Rehabilitative Services, and the Department of Justice Office of Juvenile Justice and Delinquency Prevention.

Medications Development Program—With this program, NIAAA is discovering new medications and finding more effective ways to move them into clinical practice. The drug-approval process involves preclinical testing, clinical trials, and dissemination of trial results to clinicians. To improve the chance of success for promising compounds, NIAAA formed the Medications Development Working Group, with experts in areas such as molecular genetics and cell biology, animal and human models and clinical trials, and health services and technology transfer. NIAAA funds about 70 grants on medications development and has its own program to conduct early Phase II clinical trials.

National Longitudinal Alcohol Epidemiologic Survey (NLAES)/National Epidemiologic Survey on Alcohol and Related Conditions (NESARC)—Over two decades, NIAAA conducted two large surveys of adults 18 years old and older with questions about alcohol consumption, alcohol use disorders (AUDs), family history of alcoholism, alcohol treatment, health conditions, major depressive disorder, and basic demographic information. NESARC (2001–2005 in two phases) and NLAES (1991–1992) were designed to assess the incidence of AUDs and co-occurring psychiatric illnesses. Both NLAES and NESARC used the same instruments for diagnosing AUDs, making it possible to track trends over time.

The Task Force on College Drinking—NIAAA sponsored a 3-year investigation by a group of educators, administrators, alcohol researchers, and students to address the problem of excessive drinking on U.S. college campuses. The group found that to address drinking on campuses, the colleges must reach individual students, the student body as a whole, and the surrounding community and base their alcohol programs on strong scientific evidence. The Task Force findings were published and are available at www.collegedrinkingprevention.gov.

Underage Drinking Prevention Campaign—Supporting the *Surgeon General's Call to Action To Prevent and Reduce Underage Drinking*, NIAAA and SAMHSA created the campaign and Web site to help parents have open and ongoing conversations with their preteen and teenage children about the risks of underage alcohol use. The Web site, www.underagedrinking.samhsa.gov, provides parents with tools and information they can use to talk with their children about alcohol use. Another Web site, NIAAA's The Cool Spot, www.thecoolspot.gov, is directed to children aged 11–13 and is based on a curriculum developed by the University of Michigan. The curriculum was created for the Alcohol Misuse Prevention Study, a large-scale project supported by NIAAA.

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Clinician's Guide, to help physicians identify alcohol problems and intervene with patients. The *Project COMBINE* and *Project MATCH* manuals also offer evidence-based guidelines for healthcare providers on treating alcohol use disorders.

NIAAA's education materials for the general public provide easy-to-read, scientifically based information about alcohol. *Rethinking Drinking*, for example, debunks myths about alcohol use and abuse and provides strategies for people who want to curtail their drinking.

Through collaborations with other organizations, NIAAA has been able to reach an even wider audience. With the National Institute on Drug Abuse and HBO, for example, NIAAA helped to produce HBO's *The Addiction Project*, a 14-part documentary that aired on the network and other media outlets. Further, the Institute has embraced "e-learning" with an online educational program for clinicians based on the *Clinician's Guide*.

Future Directions

NESARC and COGA. NESARC consumption data are being used to inform the development of low-risk drinking guidelines. Analyses of the survey also are helping NIAAA to identify populations at special risk for alcohol abuse and alcoholism. COGA scientists have launched a long-term study of high-risk youth ages 12–21 from families with a history of alcohol abuse. With followups every 2 years, the study should help elucidate the interaction of genes and the environment in the development of alcohol use disorders.

Complementing the ongoing search for genes, COGA scientists are studying the regulation of gene expression resulting from epigenetic changes (i.e. those that do not change the DNA coding sequence per se), which may also have an impact on alcoholism risk.

Medications. Medications development and the integration of pharmaceuticals into treatment involve a series of research challenges, but offer great promise.

Neuroscience research on brain-signaling systems involved in alcohol addiction has opened the possibility that existing medicines approved for other disease indications may be effective in alcoholism. These medicines already target the specific neurotransmitters implicated in addiction. NIAAA continues to support studies that test these compounds in animal models of alcoholism.

Alcohol researchers believe that, like diseases such as high blood pressure, diabetes, and cancer, alcoholism may respond to treatments that address multiple targets in the body. Future research will explore combinations of medications

as well as drugs with more than one site of action to find treatments that can produce optimal effects without increasing side effects among patients.

NIAAA also is interested in advancing personalized medicine for patients with alcohol problems. Research using technology that provides real-time images of the brain in combination with human characteristics translated into mathematical models should help scientists predict which treatments will be most effective for a given patient.

In addition to the challenge of getting drugs approved for clinical use, NIAAA continues to see barriers to medication use in real-world settings. Building on the success of the *Clinician's Guide*—where NIAAA gave practitioners tools for identifying and diagnosing people with alcohol problems—the Institute plans to develop strategies to include medicines in existing treatment approaches. Because medications development and integration into treatment is a complex task, NIAAA also hopes to create more collaborative networks and partnerships among government, academia, pharmaceutical companies, health care organizations, and other groups.

Conclusion

As NIAAA looks back on 40 successful years of bringing needed attention to rethinking, preventing, and solving alcohol-related problems, it is poised to take advantage of new research technologies to gain an ever-clearer picture of how and why some people develop these problems whereas others do not. Viewing alcohol use through a lifespan perspective, the Institute will improve public health by identifying vulnerable populations and supporting development and knowledge about interventions and medications to treat and prevent alcohol abuse and dependence.

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- ▶ ***Alcohol Research & Health*, 33(1&2) celebrates the 40th anniversary of the National Institute on Alcohol Abuse and Alcoholism (NIAAA) by reviewing the wide range of research supported by NIAAA since its creation. The articles cover the areas of genetics, neuroscience, epidemiology, health risks and benefits of alcohol consumption, prevention, treatment, and the role of NIAAA in the improvement of public health.**
- ▶ **For more information on the latest advances in alcohol research, visit NIAAA's Web site, www.niaaa.nih.gov**



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