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U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES • National Institutes of Health • National Institute on Alcohol Abuse and Alcoholism

FEATURE

ALCOHOL AND HIV/AIDS: A CONFOUNDING COMBINATION

People have used and abused alcohol for thousands of years. By contrast, the human immunodeficiency virus (HIV) has been around for about 30 years. The cause of acquired immunodeficiency syndrome (AIDS), HIV has claimed more than 25 million lives, making it one of the world's leading infectious killers.

The interaction of alcohol with HIV tells a bleak story. Alcohol use is common among HIV-infected individuals, and large studies show that alcohol misuse is closely intertwined with the HIV/AIDS epidemic. Addressing alcohol problems among those already infected with HIV and those who are at risk for HIV infection is an important strategy for preventing new cases of AIDS and new cycles of HIV infection.

"On many different levels, alcohol problems confound efforts to prevent new HIV infections and effectively treat existing infections," says Kendall J. Bryant, Ph.D., coordinator, Alcohol and AIDS research at the National Institute on Alcohol Abuse and Alcoholism (NIAAA).

Many non-AIDS-related conditions are more common among HIV-infected individuals than among demographically similar uninfected individuals. The fact that half of all HIV-infected individuals in the United States will be over 50 years old by the year 2015 further complicates the issue of comorbid health problems among these individuals.

Dr. Bryant adds: "This multi-morbidity has resulted in an age-associated increase in the number and variety of medications prescribed to HIV-infected individuals. Any continued alcohol abuse by these increasingly frail individuals, who are taking increasing numbers and varieties of medications, may portend a greater risk of immune dysfunction, toxicity, and organ system failure."

In addition, research shows that alcohol use may increase the likelihood that individuals will engage in behaviors that increase their risk for HIV infection and undermine the effectiveness of many HIV prevention efforts. For example, alcohol impairs judgment and cognition. It makes people less inhibited and more likely

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A CLOSER LOOK

A CLOSER LOOK: DRINKING BY THE BUCKET AND HIV RISK IN AFRICA

In a beer hall in Zimbabwe, a group of men will share this 2-liter bucket of a popular, inexpensive African beer called "chibuku." Beer halls often serve as community centers, mainly for men, in lower-income areas. Throughout the day and into the night, men pass these buckets of beer around, often sipping vast quantities. Add the ready availability of sex workers nearby, and you have a recipe for the spread of HIV. That's why prevention researchers in Africa are aiming HIV interventions at patrons of beer halls and other informal drinking places called "shebeens."

Alcohol has helped fuel the HIV/AIDS epidemic ravaging southern Africa, where 20 percent to 40 percent of sexually active adults are HIV positive (Fisher et al., 2007). Many studies in Africa link alcohol use with a greater risk of HIV infection in both men and women. Compared with nondrinkers, the heaviest drinkers are twice as likely to have HIV (Fisher et al., 2007). Research also confirms that beer hall patrons, along with men and women who meet sex partners in shebeens, are more likely to engage in risky sex practices that can spread HIV (Lewis et al., 2005, Kalichman et al., 2008a).

In recent years, NIAAA-funded researchers introduced alcohol-related HIV interventions in Africa, with mixed success. A randomized controlled trial in South Africa offered shebeen patrons a single, 1-hour counseling session to build HIV risk-reduction skills (Kalichman et al., 2008b). Results showed a significant, but short-term, drop in alcohol use before sex, unprotected sex, and other risk measures, especially in lighter drinkers. Further work will be needed to see if interventions can achieve longer-term results and reduce risks in heavier drinkers. Another randomized controlled trial in 24 beer halls in Zimbabwe trained heterosexual male "peer educators" to help their friends avoid high-risk sex connected with drinking (Fritz et al., 2011). This intervention, conducted during a period of economic and social upheaval, did not reduce risky behaviors. The researchers emphasize, however, that "it remains an imperative to productively engage men in HIV prevention," especially in drinking venues where alcohol, risky sex, and HIV connect.

Photo courtesy of Katherine Fritz, director of global health, International Center for Research on Women

Sources:
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FEATURE

NIAAA SUPPORTS NEW CONSORTIUMS FOR ALCOHOL AND HIV/AIDS RESEARCH

Whether you are 5 or 55, cooperating with others can be a challenge. For a long time, alcohol and HIV researchers rarely collaborated. But drinking has a big impact on the health of people with HIV/AIDS. Helping patients manage their alcohol use can go a long way toward improving health outcomes—especially over the long term. That is why studies on the connections between these issues are critical.

Beginning in 2001, NIAAA made building bridges between alcohol researchers and HIV/AIDS researchers a priority by establishing a longitudinal study of veterans with both HIV/

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to engage in unprotected sex and other risky behaviors. Heavy drinking is associated with risky sexual behaviors and with using drugs that may increase HIV exposure risk.

Alcohol use also may make biomedical approaches to HIV prevention and treatment less effective. Recent research demonstrates that alcohol use prevents patients from reliably adhering to their medication regimens. Alcohol likely has the same effect on patients who need to adhere to even stricter prevention and treatment strategies for comorbid conditions such as tuberculosis.

Veterans Aging Cohort Study

We have learned about the interaction between HIV and alcohol primarily from observational studies conducted over long periods of time. One of the most important of these studies is the Veterans Aging Cohort Study (VACS). Initiated in 1999 and supported by NIAAA and other institutes of the National Institutes of Health, the VACS is a multisite, multiwave study conducted on an ongoing basis at eight Veterans Health Administration health care facilities throughout the United States. The VACS is the largest HIV- and alcohol-focused study of its kind. It focuses on HIV-positive patients and HIV-uninfected control patients being treated at infectious disease and general medicine clinics.

The primary aim of the VACS is to explore the long-term interaction of alcohol with HIV in the broader context of aging. VACS investigators demonstrated alcohol's association with nonadherence to treatment and increases in HIV viral load, symptoms, and comorbid disease. The VACS also has shown that alcohol-related biomarkers predict decreased survival and that even moderate alcohol use shortens survival.

In studies of patient and provider attitudes, the VACS found that HIV providers are often unaware of hazardous alcohol consumption and are less likely to counsel patients about alcohol use than are general medical providers.

The VACS has been instrumental in identifying risk factors for disease progression among people with HIV/AIDS and alcohol problems. VACS research findings will help both physicians and people living with HIV to understand how best to optimize their medical care. For example, the VACS Risk Index, a prognostic tool that reflects alcohol-, HIV-, and comorbid disease-related injury, provides a much-needed means for assessing the effects of all types of interventions in HIV-infected populations.

"The VACS study is helping to generate a new standard of care for HIV-infected individuals with substance abuse," says Dr. Bryant.

FEATURE: *NIAAA Supports New Consortiums . . . Continued from page 2*

AIDS and alcohol problems. That study, known as the Veterans Aging Cohort Study (VACS), included more than 6,000 alcohol-using veterans and a comparison cohort of more than 100,000 HIV-positive veterans. The VACS grew into a highly successful study that spawned more than 200 articles and presentations. It shed light on the significant effect alcohol has on HIV/AIDS outcomes, including morbidity and mortality. Researchers also developed the VACS Risk Index, which measures how frail an HIV/AIDS patient is based on a composite of medical indicators.

Now, NIAAA is building on the success of the VACS by bringing together a new group of researchers in both alcohol usage and HIV/AIDS. The Consortiums for HIV/AIDS and Alcohol Research Translation (CHAART) involves researchers at The Johns Hopkins University, Yale University, Brown University, Boston University, the University of Alabama, the University of Washington, and several Florida-based institutions. All of these institutions are already involved in both alcohol and AIDS research. All of them are studying large-scale cohorts, much like the VACS continues to do.

These consortiums will build on an infrastructure already in place and promote collaboration between multiple universities. The consortium model will help develop practical solutions for AIDS and alcohol-related problems in aging populations. Consortium members will openly share data on critical variables and outcome information for their interventions. They will also share their intervention research outcomes with a centralized operations research center located in New York City.

The operations research center includes mathematical researchers who model and simulate AIDS and alcohol interactions and then validate them against real-world outcomes. They will help translate research into a database of practical models that the medical community can implement with the HIV/AIDS population.

"The ultimate goal of these consortiums and the operations research center is to improve public health by synthesizing the outcomes of multiple strands of research," explains Kendall J. Bryant, Ph.D.,

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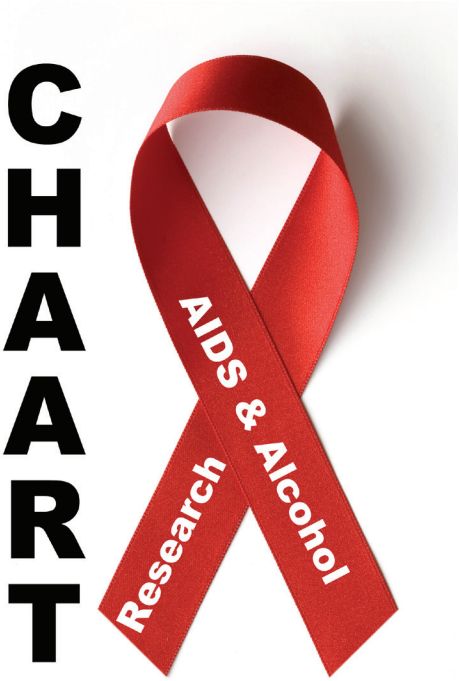
FEATURE: *NIAAA Supports New Consortiums . . . Continued from page 3*



coordinator, Alcohol and AIDS research at NIAAA and scientific collaborator on CHAART.

NIAAA's role is to provide scientific direction and funding to develop the structure for the collaboration. So far, the first phase of the project is complete. This phase included forming the consortiums, implementing alcohol and/or HIV interventions, and creating an administrative collaborative component to provide resources such as specimen banks, methodological data analysis, and executive steering committees.

Ultimately, the results of the research will become options that critical decision makers such as patients, providers, health care administrators, health policymakers, and the community in general can choose from to improve public health.

Collaborating institutions are investigating the effects of:

- Integrated stepped care and pharmacotherapy on HIV-infected patients with unhealthy alcohol use (Yale University);
- Naltrexone and topiramate on HIV-infected women with at-risk drinking (Florida institutions);
- A brief intervention on HIV-infected gay men (Brown University);
- A computerized brief intervention and pharmacotherapy on HIV-infected patients with at-risk drinking habits (The Johns Hopkins University); and
- High-dose buprenorphine on HIV-infected patients who are also opioid dependent and heavy drinkers (Boston University).

NEWS FROM THE FIELD

THE IMPACT OF PARENTAL PERCEPTIONS ON COLLEGE STUDENTS' DRINKING

Alcohol misuse is a problem on many college campuses across the country. Parents' attitudes toward drinking are known to influence the drinking behaviors of young adolescents, but less is known about how parental attitudes influence the drinking of older adolescents, including college students. Researchers recently published a study that looked at parents' perceptions of other parents' attitudes toward college student drinking, and how those perceptions affected their own attitudes.

In the study, college students took an online assessment of their attitudes toward drinking and also of their own drinking behaviors. For extra course credit, the students recruited their parents to complete an assessment of their attitudes toward student drinking and their perceptions of the attitude of other parents (peers) toward student drinking.

The researchers found that parents overestimated other parents' permissiveness toward their respective child's drinking. Such overestimation of other parents' permissiveness influenced their attitudes toward their own child's drinking. The researchers also found that parental attitudes toward drinking were associated with their child's attitudes toward drinking.

One method of combating these misperceptions, the researchers suggest, is to include parents in educational efforts that increase parent awareness and involvement. For example, schools can send flyers and other information home to parents and schedule educational events when large numbers of parents will be on campus.

The researchers note that "the continued importance of parental attitudes and the influence they appear to have on college students and, therefore, emphasize the need to understand the problem of college alcohol use beyond the college environment to also include parents."

The article abstract can be found here:

Parents know best, but are they accurate? Parental normative misperceptions and their relationship to students' alcohol-related outcomes.

http://www.ncbi.nlm.nih.gov/pubmed/21683033

NEWS FROM THE FIELD

DRINKING AT MODERATE LEVELS MAY HELP HEART-ATTACK SURVIVORS

Drinking alcohol at moderate levels has previously been associated with a lower risk for coronary heart disease. Researchers now have completed a study suggesting that moderate drinking may also help reduce death rates among men who have had a myocardial infarction (MI).

In this study, researchers examined data from the Health Professionals Follow-Up Study, using data from 1,818 men who had a nonfatal MI. They studied the drinking habits of these men before and after their MI. Most men in the study did not change their drinking habits after their MI.

The researchers determined that long-term moderate alcohol drinking (up to two drinks per day) was associated with lower cardiovascular mortality, as well as death from all causes. The greatest benefits appear to have been among the group consuming two drinks per day or fewer (10–29.9 grams). No significant benefits were observed among those drinking more than two drinks (30 grams of ethanol) per day. They noted that the association was strongest among men with less severe cardiovascular damage from the MI (i.e., men with nonanterior infarcts or with mildly diminished ventricular function).

The researchers state that their results "clearly support the hypothesis that long-term moderate alcohol consumption among individuals prior to MI may be beneficial for all-cause and cardiovascular mortality."

This article abstract can be found here:

Long-term alcohol consumption in relation to all-cause and cardiovascular mortality among survivors of myocardial infarction: the Health Professionals Follow-up Study.

http://www.ncbi.nlm.nih.gov/pubmed/22453658

NEWS FROM THE FIELD

SEXUAL DEPRIVATION INCREASES FRUIT FLIES' ALCOHOL USE

Researchers are helping to explain the roots of addiction by using fruit flies to show that sexual rejection and deprivation directly influence the brain's reward systems. A study by investigators from the University of California, San Francisco, published in the March 16 issue of *Science*, showed that sexual deprivation increased the amount of alcohol the fruit flies ingested. The study also revealed a link between sexual deprivation and a neurotransmitter associated with alcohol consumption.

In the study, investigators exposed some male flies to female flies that had already mated and would reject the male flies' mating attempts. Another group of male flies was exposed to female flies that had not mated and would be receptive to the males' mating behavior. The males in both groups were then allowed to choose between food with 15 percent ethanol (alcohol) supplementation and food that had not been supplemented with alcohol. The males in the rejection group showed a higher preference for the ethanol-supplemented food. Another group of male flies experienced sexual deprivation without the social experience of rejection by being exposed to decapitated female flies. These males also showed a preference for the alcohol-supplemented food, thus demonstrating that it was deprivation alone that increased the males' preference for alcohol. A group of the males that had experienced sexual deprivation was later allowed to mate with receptive females; this group showed lower ethanol preference than a group that had been deprived and not allowed to mate.

In addition to connecting deprivation and alcohol preference, the researchers monitored neuropeptide F (NPF) in the different groups of flies. After comparing NPF levels among all of the groups of flies, the researchers found that males that had been rejected had the lowest NPF levels and those that

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NEWS FROM THE FIELD: *Sexual Deprivation . . . Continued from page 5*

had mated showed the highest levels. The researchers then manipulated NPF artificially and found that alcohol preference was lower among flies with artificially enhanced NPF levels and higher among those with artificially lowered NPF levels.

The mammalian version of NPF, neuropeptide Y (NPY), is known to regulate alcohol consumption. Having shown the link between fruit flies' NPF levels and alcohol-related behaviors, the researchers suggest that fruit flies may be a useful model for the impact of social experience and alcohol use.

The article abstract can be found here:

Sexual deprivation increases ethanol intake in Drosophila.

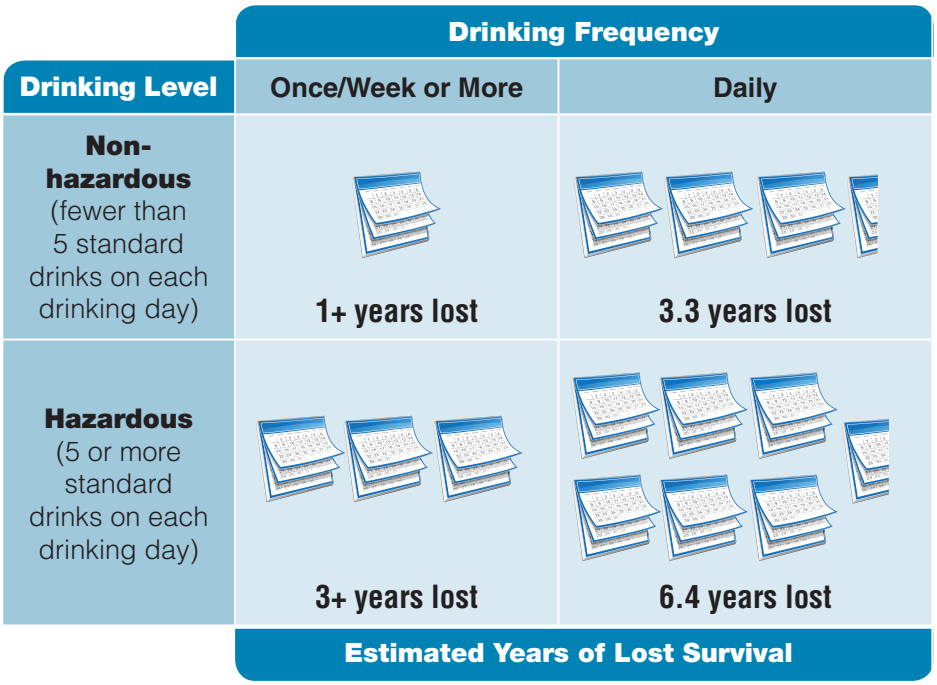
http://www.ncbi.nlm.nih.gov/pubmed/22422983

BY THE NUMBERS

DRINKING SHORTENS SURVIVAL FOR MANY HIV-POSITIVE INDIVIDUALS

HIV-positive individuals need to take their medications daily as prescribed, because skipping as little as 1 in 20 treatment days can reduce their life expectancy. Drinking alcohol is the most common risk factor for skipped medications, known as "nonadherence" to the regimen. Although missed doses are not always intentional, some patients plan medicine vacation days so they can drink and avoid the toxicity caused by combining the medications with alcohol. This choice compromises their treatment effectiveness in direct proportion to how much and how often they drink.

Using a computer simulation based on a sample of 3,545 HIV-positive patients, researchers estimated the years of lost survival attributed to different drinking patterns and related rates of medication nonadherence. They concluded that weekly "nonhazardous" drinking—which they defined as fewer than five drinks on each drinking day—cut at least 1 year from an estimated 22-year survival. Daily drinking at nonhazardous levels cut 3.3 years of survival. Weekly "hazardous" drinking—five or more drinks on each drinking day—cut at least 3 years from an estimated 16-year survival. Daily hazardous drinking cut 6.4 years, a 40 percent reduction in life expectancy. Patterns that mix lighter and heavier drinking days each week also reduce survival, the researchers say, at rates between the nonhazardous and the hazardous estimates. Only patients who drink lightly and less often than weekly, and who maintain a 95 percent rate of medication adherence, appear to avoid experiencing a substantial alcohol-related impact on their survival.



According to the researchers, the years of lost survival are likely underestimates because the computer model was limited to alcohol's effects on medication nonadherence. Other studies show that alcohol may also shorten the survival of HIV-positive individuals by weakening the immune system, increasing medication toxicity, and speeding the progression of hepatitis C. In short, a wide range of research comes to the same conclusion: Individuals who are HIV positive and drink alcohol could improve or save years of life by cutting back on or, ideally, stopping drinking.

Source:
Braithwaite RS, Conigliaro J, Roberts MS, Shechter S, Schaefer A, McGinnis K, et al. Estimating the impact of alcohol consumption on survival for HIV+ individuals. *AIDS Care*. 2007 Apr;19(4):459-66.

NEWS FROM THE FIELD

MULTIPLE GENETIC FACTORS MAY BE CAUSE OF ALCOHOL DEPENDENCE

A recent study suggests that the criteria for alcohol dependence (AD) outlined in the *Diagnostic and Statistical Manual of Mental Disorders*, Fourth Edition (DSM-IV) reflect several genetic factors instead of a single dimension of genetic risk.

The study's authors analyzed data from more than 7,500 adult male and female twins in the Virginia Adult Twin Study of Psychiatric and Substance Use Disorders to determine the structure of genetic risk for AD. They found that the best-fit model for the DSM-IV criteria for AD reflected three underlying dimensions of genetic liability. The three factors reflect risk for (1) tolerance and heavy use, (2) loss of control with alcohol-associated social dysfunction, and (3) withdrawal and use despite problems.

Though these results are preliminary, the study's authors state that they could influence future efforts to study genetic risk factors for AD. The authors note that previous studies "have looked at the magnitude of aggregate genetic effects, developmental processes, or patterns of comorbidity assuming that AD reflected a single dimension of genetic liability." They recommend reconsidering these earlier conclusions in light of the results of this study. This new study indicates that several genetic factors—not just one—influence risk for AD. As a result, the study's authors argue that the assumption of a single genetic risk factor "is unwarranted and should not continue to be accepted before being subjected to empirical test."

The article abstract can be found here:

Evidence for multiple genetic factors underlying the DSM-IV criteria for alcohol dependence.

http://www.ncbi.nlm.nih.gov/pubmed/22105626

5 QUESTIONS WITH...

KENDALL J. BRYANT, PH.D.

Dr. Bryant is the coordinator of Alcohol and AIDS research at NIAAA.

1 Why is the connection between alcohol and HIV/AIDS so important?

Alcohol use is intertwined with HIV, including how the virus gets transmitted, how alcohol increases susceptibility to infection, and how alcohol accelerates disease progression and leads to premature death. Clearly, we need to address alcohol in all HIV prevention and treatment programs.

Alcohol impacts the spread of new infections by influencing the momentary decisions people make while drinking that lead to risky sexual behavior. This is significant because research shows that heavier drinking is directly related to higher numbers of concurrent sexual partners and doubles the risk for infection in the general population. Many in the highest-risk groups for infection in the United States, such as drug users, minority gay men, or sex workers, also have an alcohol use disorder.

Many HIV-infected people must now manage their chronic disease over a lifetime. Alcohol can increase the rate of disease progression and organ and tissue injury. Even limited alcohol use influences a patient's ability to stick to a treatment plan, while binge drinking often leads patients to abandon their treatment plans. Some patients deliberately don't take their medication so they can drink. Others just forget to take medication when they drink. To get the benefits of medication, patients must adhere to their regimens strictly. Skipping doses can lead to the loss of viral control, rapid disease progression, and premature death.

2 What has the research taught us so far?

That alcohol research is essential to HIV prevention and treatment. When I came to NIAAA 20 years ago, the connection between alcohol use and HIV seemed to be the last thing anyone wanted to think about. Up until 1993 there were only a few scholarly articles on alcohol and HIV, and most involved intravenous drug users. Now there are more than 6,000, with many focusing on the impact of alcohol. Not bad!

We also learned that we need to pay particular attention to drinking in HIV-infected individuals. There is no "safe" level of drinking for an HIV patient, but many continue to drink after diagnosis. We need to help patients reduce their drinking and lessen HIV-related consequences as much as possible.

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Also, people with HIV are less likely to seek traditional alcohol treatment services, making primary care settings important for interacting with these populations. Therefore, much of our research focuses on how alcohol affects interactions between infected and uninfected individuals in different settings and impacts the prevention of new infections. Interventions for alcohol need to be targeted to HIV treatment settings, emergency rooms, bars, truck stops, and other high-risk locations.

Research results need to better inform prevention and treatment in different settings. We must understand the factors that drive the HIV epidemic here in the U.S. and in other countries. How and where is the disease spread? What messages do we need to deliver about drinking and risk taking to prevent new HIV infections? Where should these be delivered and by whom? Which packages of interventions work best? Who selects and implements them? We can answer these questions if we focus more on how to apply research to different target audiences in real-world settings.

3 Are there any exciting developments on the horizon?

In the past, people with HIV/AIDS died fairly quickly. Today, new treatments mean that people can live with HIV/AIDS for many years. We need to develop new research methods that measure a patient's overall health in response to the disease. For example, in the Veterans Aging Cohort Study (VACS), we evaluate a patient's condition beyond the traditional HIV-related measures. Diagnostic tests capture the effects of other health conditions and behaviors, such as alcohol use, on disease progression and treatment response. This is an important advance because we can now monitor the success of our interventions in a holistic way. When the VACS score improves, the patient is doing better and is less likely to die. We will continue to find advances like this by viewing HIV/AIDS as a long-term disease.

4 There are several major plans that guide AIDS research at the National Institutes of Health (NIH). How have they influenced the work at NIAAA?

The NIH Office of AIDS Research creates a plan that identifies priority funding areas. This office helps guide HIV/AIDS research, particularly the integration of behavioral and biological studies.

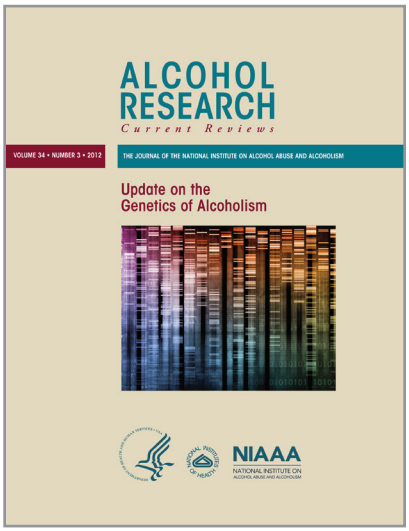
NIAAA reviews this plan carefully to identify opportunities for alcohol research. Currently, we play an important role in the research on aging populations, which creates excellent opportunities. We will need new types of research collaborations in this area. These plans will help guide this paradigm shift.

Alcohol use, along with other substance abuse, needs to be integrated into any plan to control HIV/AIDS.

5 You have held many interesting positions in your career. Tell us about one.

In 1984, I joined the Naval Submarine Medical Research Laboratory to develop psychological screening procedures. These tests were pretty exotic then, but they remain in use today!

I got to ride submarines, interview demolition divers, develop models of hyperbaric decompression sickness, and test shipboard computer-based medical diagnostic systems. I was dragged into interesting projects that to this day remain highly sensitive. One that made the news lately was the deployment of women aboard submarines—but that's another story.



Coming Soon: "Update on the Genetics of Alcoholism," the latest issue of NIAAA's *Alcohol Research & Health*, at *http://www.niaaa.nih.gov/Publications*.

ABOUT US

NIAAA Spectrum is NIAAA's first-ever webzine. With engaging feature articles, short news updates, and colorful graphics, *NIAAA Spectrum* offers accessible and relevant information on NIAAA and the alcohol research field for a wide range of audiences. Each issue includes feature-length stories, new research findings from the field, image and data analyses, and an interview with an NIAAA staff member or alcohol researcher. *NIAAA Spectrum* is published three times a year.

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