

**NIAAA DIRECTOR'S REPORT  
ON INSTITUTE ACTIVITIES TO THE 166TH MEETING  
OF THE NATIONAL ADVISORY COUNCIL ON  
ALCOHOL ABUSE AND ALCOHOLISM**

**MAY 7, 2024  
HYBRID MEETING**

**George F. Koob, Ph.D.  
Director**

**National Institute on Alcohol Abuse and Alcoholism  
National Institutes of Health**

**<https://www.niaaa.nih.gov/about-niaaa/advisory-council>**

# **INSTITUTE & NIH UPDATES**

# **In Memoriam: Dale Hereld, MD, PhD**

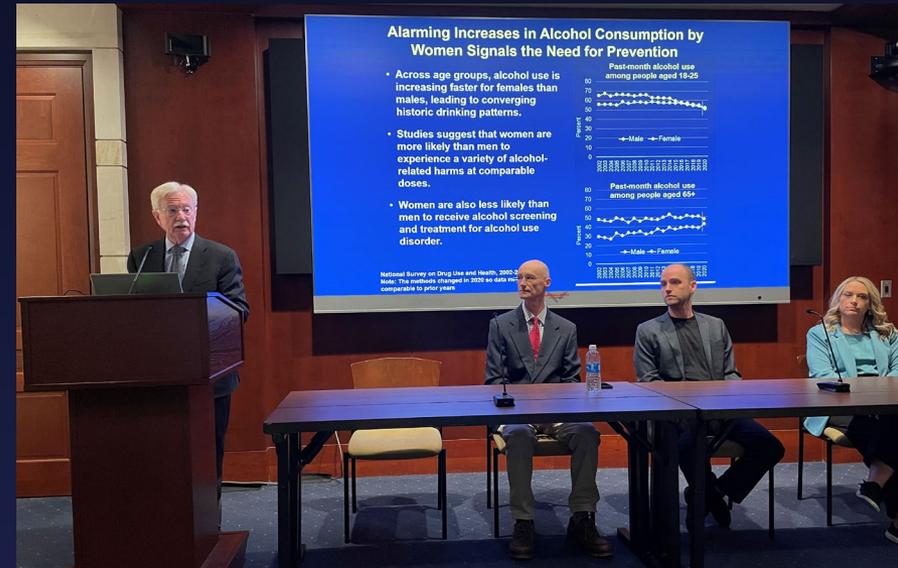


**Dr. Dale Hereld served as a Health Scientist Administrator in the NIAAA Division of Metabolism and Health Effects (DMHE) from 2008 until his retirement in 2019. In this role, he managed the fetal alcohol spectrum disorders (FASD) research portfolio and was the NIAAA Project Scientist for the Prenatal Alcohol, SIDS, and Stillbirth Research (PASS) Network, the Collaborative Initiative on FASD (CIFASD) research consortium, and the Collaboration on FASD Prevalence (CoFASP) research consortium. Dr. Hereld also represented NIAAA on many NIH-wide committees and projects.**

**Dr. Hereld was a beloved member of the NIAAA family. You counted yourself lucky to have known him, witnessed his charm and kindness, or experienced a touch of his quick-witted humor. He will be deeply missed by his family, friends, and NIAAA colleagues.**

# Friends of NIAAA Congressional Briefing

- On March 21<sup>st</sup>, NIAAA participated in a Congressional Briefing sponsored by the Friends of NIAAA, the American Psychological Association, and the Congressional Addiction, Treatment, and Recovery Caucus.
- The briefing, titled **“Preventing Alcohol Misuse: Research to Improve and Save Lives”** featured:
  - Opening remarks by Rep. Paul Tonko, Co-chair of the Addiction, Treatment, and Recovery Caucus and Dr. William Wiczorek, Chair of the Friends of NIAAA
  - An overview of the needs and opportunities in prevention research
  - Drs. Paschall, Livingston, and Lewis discussed their research on individual and environmental approaches for alcohol misuse prevention



(Left to Right) Drs. George Koob, M.J. Paschall, Melvin Doug Livingston, Melissa Lewis

# Budget

- On March 23<sup>rd</sup>, President Biden signed the *Further Consolidated Appropriations Act of 2024*.
  - NIH received a total of \$47.2 billion, a 0.8% decrease below the fiscal year 2023 enacted level.
  - NIAAA received \$595.3 million for fiscal year 2024, the same amount appropriated in fiscal year 2023.
  - As part of this Act, NIH will increase annual pay 4% for predoctoral trainees and 8% for postdoctoral scholars supported by the Ruth L. Kirschstein National Research Service Awards. Eligible recipients will also receive \$500 increases in subsidies for childcare (from \$2,500 to \$3,000) and an additional \$200 for training-related expenses. (NOT-OD-24-104)

# Senior Staff Announcement



**Dr. Philippe Marmillot has been selected as NIAAA's new Director of the Office of Extramural Activities, where he served as the Acting Director prior to his new appointment. In this new role, Dr. Marmillot will provide oversight of NIAAA's grants management, peer review, and committee management activities, including serving as Executive Secretary of the NIAAA Advisory Council. He will also serve as the Referral Officer and Research Integrity Officer for the Institute. Dr. Marmillot joined NIAAA in 2007 as a Scientific Review Officer.**

# New NIH Common Fund Program to Support Clinical Research in Primary Care Settings

- The health of the U.S. population is declining, and the decline is steepest among underserved and underrepresented populations.
- Through a new Common Fund program, NIH seeks to improve health outcomes and research equity by:
  - Establishing a **primary care-focused** clinical research network that is disease-agnostic, facilitating clinical research in mission areas across all ICs
  - **Integrating innovative research with routine clinical care** in real-world settings
  - Creating a foundation for sustained **engagement with communities underrepresented in clinical research**

- **Timeline:**



- NIH anticipates providing \$5M in fiscal year 2024 and \$25M in fiscal year 2025 for this Common Fund program.
- Following initial funding, the budget is projected to increase to ~\$50-100M per year after assessing feasibility and budget requirements.

# Update on White House Initiative on Women's Health Research

- In November 2023, the White House announced a new initiative to galvanize the federal government to close research gaps and improve women's health.



- As part of this initiative, on March 18<sup>th</sup>, President Biden announced an Executive Order focused on the following key areas:
  - Prioritizing investments in women's health research
  - Stimulating new research on women's midlife health
  - Developing and strengthening research and data standards that enhance the study of women's health
  - Assessing unmet needs to support women's health research
  - Integrating women's health across the federal research portfolio

# NIH Notice of Special Interest (NOSI) on Women's Health Research

- In coordination with the White House Initiative on Women's Health Research, NIH issued a NOSI to highlight our interest in applications focused on diseases and health conditions that predominantly affect women, that present and progress differently in women, or that are female-specific ([NOT-OD-24-079](#)). All NIH Institutes and Centers are participating.
- NIAAA's specific areas of interest are:
  - Research focused on the mental health of women, including alcohol and other substance use disorders.
  - Research on health issues that affect young women including the etiology, prevention, and treatment of alcohol misuse.  
**(Note that alcohol misuse among certain subpopulations of young women has increased and now exceeds their male counterparts for the first time, and that alcohol misuse increases women's risk for alcohol-related pathology in all age groups compared to young men)**
  - Research to understand the mechanisms through which environmental factors influence resilience and disease among women across the lifespan.

# NIAAA Funding Opportunities

*(See Director's Report for Complete Listing)*

- **Model Continuums of Care Initiative (MCCI) to Advance Health Equity and End Health Disparities Among Women and Girls in Racial/Ethnic Minority and Other Underserved Communities:** This funding opportunity will support the planning phase of MCCI.
  - The goal of MCCI is to reduce the prevalence and impact of multi-morbidity among racial/ethnic minority women and girls of reproductive age who are at risk of and living with mental health disorders, substance use disorders, and common co-occurring physical conditions.
  - Using implementation and dissemination science, the initiative proposes a continuum of care approach that integrates preventive health services, primary care, behavioral health, integrative care, and cardiopulmonary and endocrine specialties to fully address health care needs. [RFA-AA-24-006 \(U34\)](#),  
*Contact: Dr. Deidra Roach*

# Notices of Interest

- **Notice of Intent to Publish a Funding Opportunity for Specialized Alcohol Research Centers (P50), and Comprehensive Alcohol Research Centers (P60):** The overarching goal of these two forthcoming NIAAA-supported Notices of Funding Opportunity is to support a broad-based Alcohol Research Centers program to foster and conduct interdisciplinary, collaborative research on alcohol use disorder (AUD), alcohol misuse, alcohol-related problems, and other health-related consequences across the lifespan. NOT-AA-24-007 (P50) and NOT-AA-24-008 (P60), *Contact: Dr. Philippe Marmillot*
- **Request for Information (RFI): Innovative, Non-invasive Biosensing Technologies with High Accuracy and High-Resolution Detection of Blood Alcohol Levels:** NIAAA, in collaboration with the National Institute of Biomedical Imaging and Bioengineering, sought information on cutting-edge biosensing technologies to accelerate the development of a non-invasive inconspicuous wearable alcohol sensor that continuously detects blood alcohol concentrations with high accuracy in real-time. NOT-AA-24-005, *Contacts: Dr. Changhai Cui, Dr. Kathy Jung, Megan Ryan*

# Advancing Diversity, Equity, Inclusion, and Accessibility (DEIA) in Research

- **NIAAA is participating in multiple funding opportunities to increase research on health disparities:**
  - Transformative Research to Address Health Disparities and Advance Health Equity (U01 Clinical Trial Optional). ([RFA-NR-24-004](#))
  - NIH Blueprint and BRAIN Initiative Diversity Specialized Predoctoral to Postdoctoral Advancement in Neuroscience Award (F99/K00 Clinical Trial Not Allowed). ([RFA-NS-24-030](#))
- **Request for Information (RFI): Improving research frameworks to enable rigorous study of the effects of racism on brain and behavioral health across the lifespan.** NIAAA, NIMH, NIDA, and NIMHD are inviting input on identifying and addressing knowledge gaps in:
  - The impact of structural racism on brain, cognitive, and behavioral function across the lifespan, and
  - The role of structural and systemic racism on the conduct of brain and behavioral health research.

Responses are due by June 14<sup>th</sup> ([NOT-MH-24-190](#)).

# **New NIAAA Strategic Plan, Fiscal Years 2024-2028**

## **“Advancing Alcohol Research to Promote Whole Person Health and Well-Being”**

- The new NIAAA Strategic Plan is now live on the NIAAA website, <https://www.niaaa.nih.gov/strategic-plan>
- The plan charts a course for alcohol research over the next five years while maintaining flexibility to address emerging research opportunities and urgent public health needs.
- The plan is a living document, and we welcome your feedback.
- Thank you to all NIAAA staff who contributed to the strategic plan content, review, and website.
- Special thanks to the NIAAA Strategic Plan Team: Cara Anjos Breeden, Laura Manella, Laura Brockway-Lunardi, Bridget Williams-Simmons, and former NIAAA staff member Rachel Anderson.



# The Future is Now

- **The new strategic plan seeks to advance many long-held NIAAA research and research training priorities, and highlights key areas such as:**
  - **DEIA in the alcohol research enterprise**
  - **Women's health research**
  - **Whole person health and integrated health approaches**
  - **Data science (e.g., artificial intelligence) and data management**
  - **Translation and back translation of research findings**
  - **Social determinants of health in the context of risk and resilience**
  - **Social media impact on alcohol-related behaviors and outcomes, and social media as a tool for innovating interventions**

# What's Ahead

## Public Meeting of the Interagency Coordinating Committee on Fetal Alcohol Spectrum Disorders

May 9, 2024



ICCFASD fosters improved communication, cooperation, and collaboration among disciplines and federal agencies that address issues related to prenatal alcohol exposure.

The meeting will be held in person at 6700B Rockledge Drive and may be accessed online via NIH Videocast, <https://videocast.nih.gov>

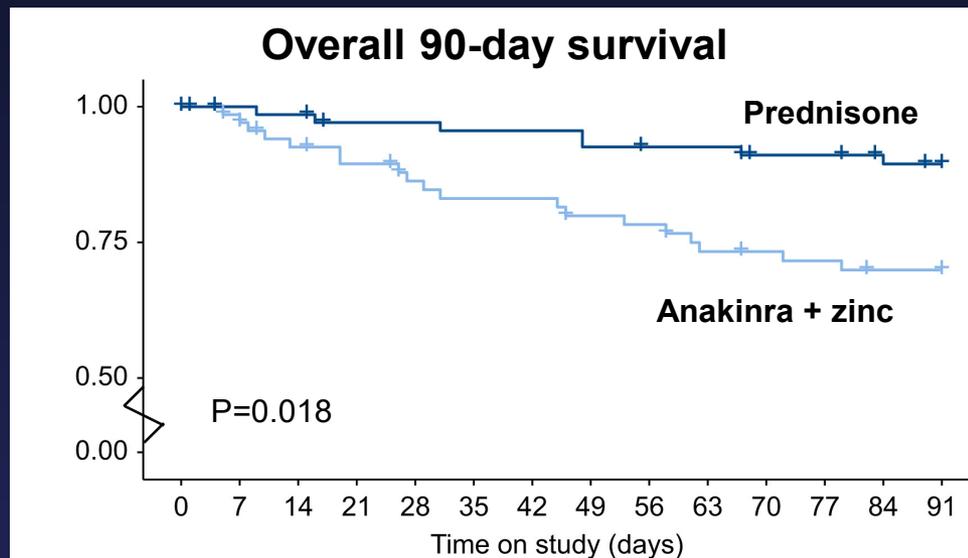
# RESEARCH HIGHLIGHTS

**Human Studies of Alcohol Misuse as  
a Whole-Body Disorder**

# Prednisone v. Anakinra + Zinc for Severe Alcohol-associated Hepatitis

Severe alcohol-associated hepatitis (SAH) is associated with high short-term mortality. A Phase IIb double blind randomized trial was conducted to compare the standard of care, prednisone, and anakinra + zinc. Glucocorticoids are the most common treatment, but they have not been shown to improve survival >30 days.

Elevated circulating cytokine levels, low zinc levels, and disrupted gut mucosal barrier are observed in patients with SAH and in animal models of alcohol-induced liver injury. In previous studies, anakinra, an IL-1 receptor antagonist with anti-inflammatory properties, was associated with a reduction in alcohol-induced hepatic steatosis in a preclinical model of AH, and in patients with SAH.



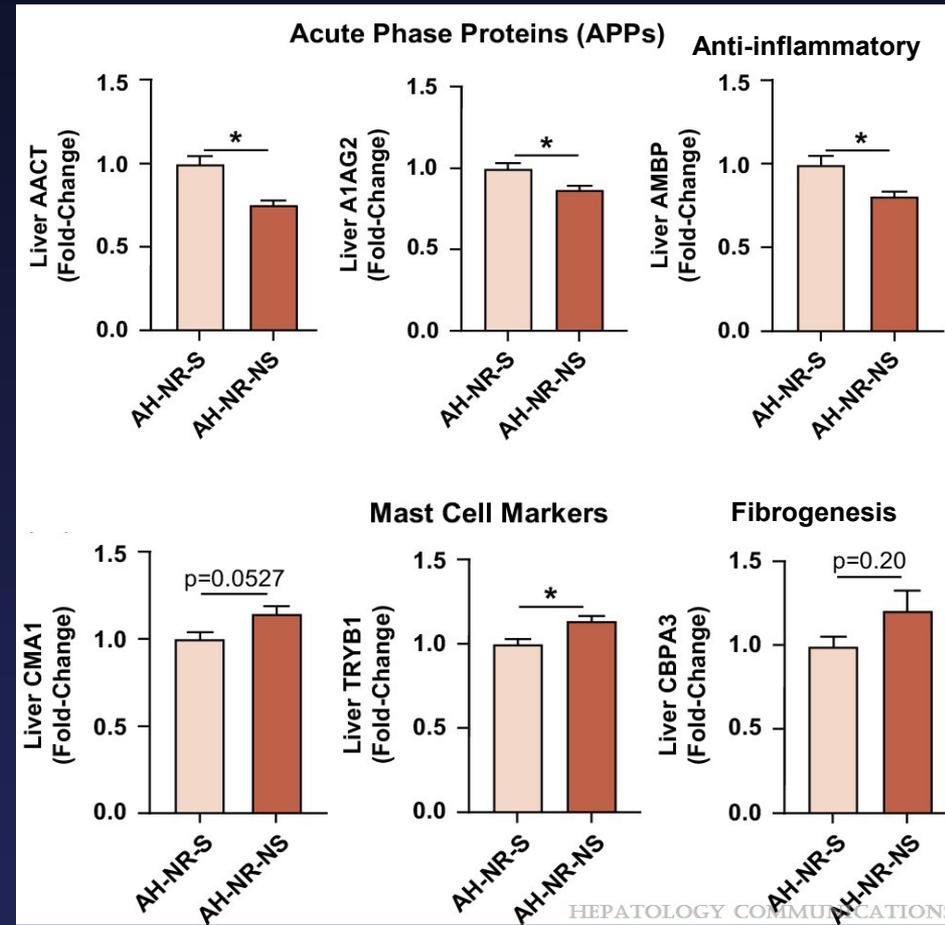
The randomized trial was stopped early after a prespecified interim analysis showed prednisone was associated with higher 90-day overall survival (90% vs. 70%) and transplant-free survival (88% vs. 64%) compared to anakinra + zinc. The findings suggest that tailoring the duration of glucocorticoid therapy using the Day-7 Lille score may be an effective strategy for promoting 90-day survival in individuals with SAH.

# Changes in Liver Proteins Associated with Glucocorticoid Responsiveness and Mortality in Alcohol-associated Hepatitis

Approximately 40% of patients with alcohol-associated hepatitis (AH) do not respond to glucocorticoids. In this study, researchers analyzed the proteome from samples obtained from patients with AH before treatment in 2 groups: AH subjects who responded to glucocorticoids (responders) and those that did not (non responders). Non responders were further divided into survivors for 24 weeks (n= 3) and non survivors (n= 4).

Several potential glucocorticoid mechanisms contributed to a lack of response to steroids. Analysis of differentially expressed proteins in treatment non-responders who survived 24 weeks relative to non survivors revealed several protein expression changes, including increased levels of acute phase proteins, elevated coagulation factors, and reduced mast cell markers.

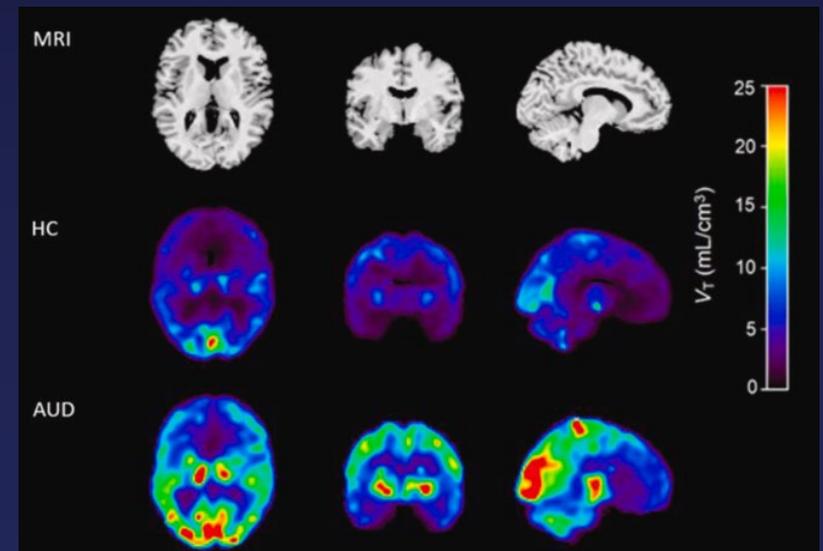
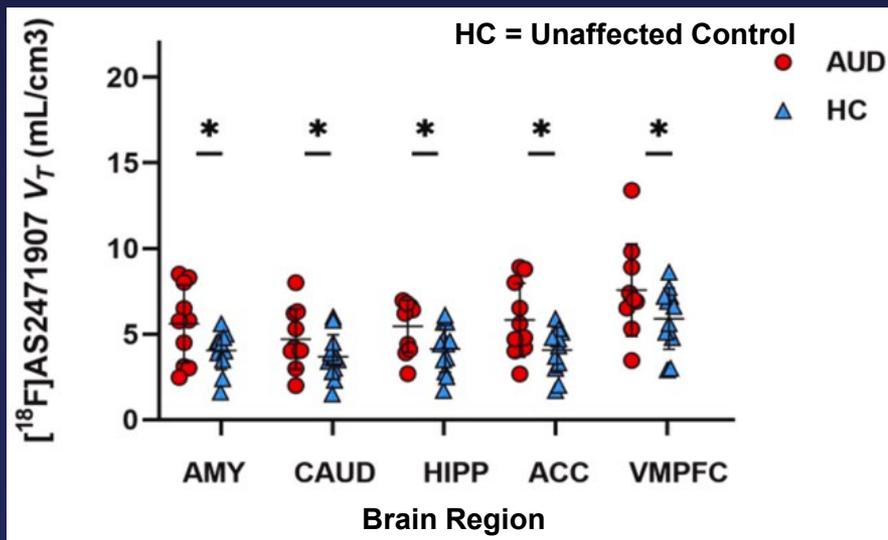
This study identified potential mechanisms contributing to a lack of steroid response in AH and a protein landscape that may influence AH non response mortality.



AH-NR-S = non-responder survivors  
AH-NR-NS = non-responder non-survivors

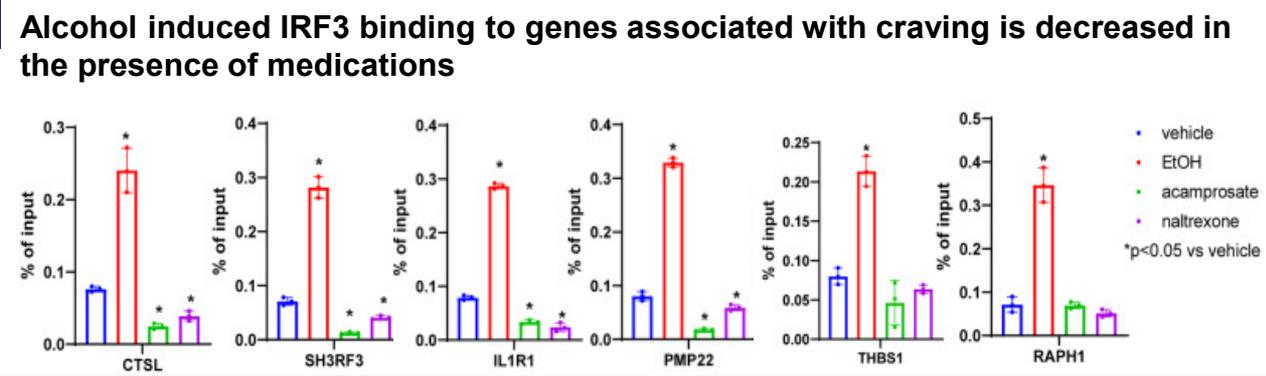
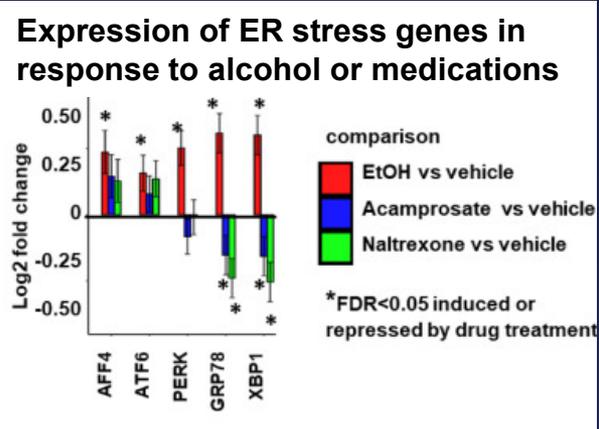
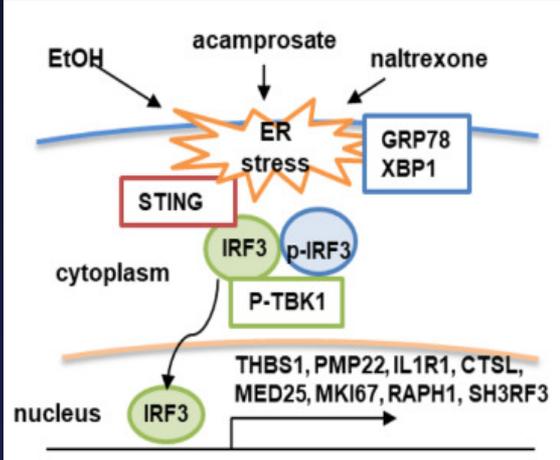
# Cortisol Marker Higher in Stress-Related Brain Regions in Individuals with Alcohol Use Disorder (AUD)

Chronic alcohol use is associated with a dysregulated hypothalamic pituitary adrenal response to stress. Researchers used a radiotracer and PET brain imaging to measure levels of 11 $\beta$ -hydroxysteroid dehydrogenase type 1 (11 $\beta$ -HSD1), a cortisol regenerating enzyme, in people with AUD and people without AUD. Findings indicated those with AUD had higher brain availability of this enzyme in prefrontal and limbic regions that are involved in stress pathophysiology, compared to unaffected individuals. In addition, higher enzyme availability in the ventromedial prefrontal cortex (vmPFC) was associated with drinks/week, quantity of drinks per episode, and AUD severity. The results suggest that central nervous system glucocorticoid activity is increased in individuals with AUD in addition to peripheral glucocorticoid dysregulation and provide an additional insight into the neural mechanisms of stress regulation dysfunction associated with AUD.



# AUD Medications Attenuate IRF3 Activation Associated with Alcohol-induced Endoplasmic Reticulum (ER) Stress and Alcohol Craving

In this study, researchers investigated possible molecular mechanisms associated with alcohol craving and the anti-craving AUD medications acamprosate and naltrexone using an AUD patient-derived iPSC astrocyte cell model with RNA-sequencing. Activation of the transcription factor IRF3 was associated with alcohol-induced ER stress, which could be attenuated by anti-craving medications. IRF3 regulation of genes associated with alcohol craving were in immune-related pathways, suggesting possible relationships between craving and inflammation. This study suggests that ER stress attenuation might be a target for anti-craving medications.



# Sober Curious and Temporary Alcohol Abstinence Participation Correlated with Greater Substance Use Treatment and with More Motivation to Quit Alcohol in Emerging Adults

Researchers examined familiarity with the Sober Curious movement and participation in temporary alcohol abstinence challenges in U.S. emerging adults (18-29). Those who participated in abstinence challenges or were aware of Sober Curious were more likely to report: heavy drinking in the past month, higher AUDIT-C scores, greater

prevalence of past-month cannabis use, and greater number of both past-year alcohol and cannabis consequences compared with those without awareness. However, those who were aware of Sober Curious or participate in challenges were also more likely to receive past-year substance use treatment and were more motivated to quit both alcohol and cannabis.

|                                       | Sober Curious Awareness |       | Challenge Participation |      |
|---------------------------------------|-------------------------|-------|-------------------------|------|
|                                       | No                      | Yes   | No                      | Yes  |
| Heavy drinking % (past month)         |                         |       |                         |      |
| No                                    | 92.4%                   | 7.6%  | 94.5%                   | 5.5% |
| Yes                                   | 88.5%                   | 11.5% | 91.2%                   | 8.8% |
| AUDIT score (M)                       | 4.6                     | 6.2   | 4.6                     | 6.4  |
| Alcohol Quit Ladder * (M)             | 7.5                     | 6.6   | 7.5                     | 6.6  |
| Alcohol consequences (past year) (M)  | 12.7                    | 15.6  | 12.9                    | 14.3 |
| Substance use treatment % (past year) |                         |       | 16.6                    | 19.2 |
| No                                    | 91.7%                   | 8.3%  | 93.6%                   | 6.4% |
| Yes                                   | 67.2%                   | 32.8% | 82%                     | 18%  |

% of ~1,650 participants. \*Lower score indicates greater readiness to quit.

# REMINDER OF NIAAAA RESOURCES

# NIAAA Web Resources For Youth

**NIAAA for Middle School:** Contains interactive activities to help parents, caregivers, and teachers introduce and reinforce key messages about peer pressure, resistance skills and other topics related to underage drinking.

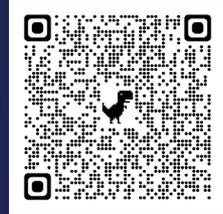
In this Section

- Too Soon = Too Dangerous
- Peer Pressure
- The Right to Resist
- Helpful Resources

NIAAA for Middle School



**NIAAA for Teens:** A research-based online resource for teens highlighting how alcohol affects your health, warning signs and symptoms, and where to get help for alcohol-related problems.



**Alcohol and Your Health**

**Facts About Teen Drinking** is a resource for teens, created by the National Institute on Alcohol Abuse and Alcoholism, with research-based information on underage drinking.

Research shows that underage drinking rates are declining. However, it is still important to know how alcohol affects your health, how to identify signs of a problem, and where to get help.

# Resources for the Public and Healthcare Professionals

## Rethinking Drinking

Website and print publication for a general audience to help individuals assess their drinking habits and find ways to make a change.



## CollegeAIM

Comprehensive information on prevention approaches found to be effective in college environments.



## Alcohol Treatment Navigator

Online resource that helps individuals understand and search for treatment options, including telehealth services. It also includes a portal to assist healthcare providers in making referrals for their patients.



## Healthcare Professional Core Resource

Online educational resource that covers the basics of what every healthcare professional needs to know about alcohol, including the many ways that alcohol can impact a patient's health, and provides strategies for alcohol screening and interventions.



[niaaa.nih.gov](http://niaaa.nih.gov)

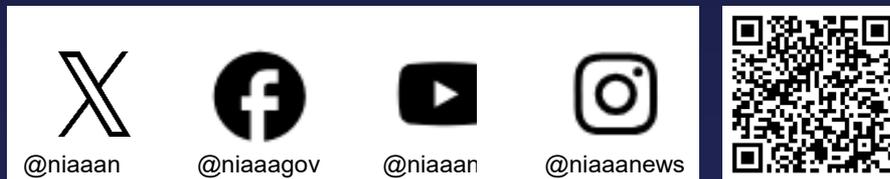
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*Special thanks to:*

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Van Van