# NIAAA Director's Report on Institute Activities to the 159<sup>th</sup> Meeting of the National Advisory Council on Alcohol Abuse and Alcoholism

February 10, 2022 Virtual 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





### In Memoriam: Richard Saitz, MD, MPH

Dr. Richard Saitz passed away in January 2022. Dr. Saitz made enormous contributions to alcohol research in the domains of prevention and treatment. He was a driving force in developing screening and brief interventions for alcohol and other substance misuse, integrating addiction medicine in routine health care, and improving the quality of care in general health settings. Dr. Saitz was an outstanding, highly innovative researcher, dedicated physician, beloved mentor, and highly respected colleague.



### In Memoriam: John Spitzer, MD

Dr. John Spitzer passed away in January 2022. Dr. Spitzer led the Department of Physiology at the Louisiana State University Health Sciences Center (LSUHSC) in New Orleans, LA from 1973-2001. He was a strong proponent of collaborative and interdisciplinary research and training and helped to establish the LSUHSC Comprehensive Alcohol Research Center and the LSUHSC Alcohol and Drug Abuse Center of Excellence that continue today. He will be remembered for his resilience, dedication to mentorship, and commitment to advancing interdisciplinary research.



### **NIAAA Staff Transitions**

### **New Staff**

NIAAA Office of the Director

Candice England

**Drennan Lindsay** 

Division of Intramural Clinical and Biological Research

Dr. Muhammad Arif

Dr. Szabolcs Dvoracsko

Post-Baccalaureate Intramural Research
Training Award (IRTA) Fellows: Madeline
Behee, Zev Jarret, Rodrigo Sandon Veliz,
Victoria Offenberg, Nina Westcott, Eli Winkler,
Jinpyo Seo, Carlos Melendez, Logan Johnson,
Josephine Nimely, Ana Oliverio

### **Departing Staff**

Jamie Greuber Deborah Adams (retired)

James Loewke (retired)

More details are available in the Director's Report.

### FY 2022 Budget

We are currently operating under a continuing resolution as the budget for 2022 has not been finalized.

### **NIAAA Funding Opportunities**

(See Director's Report for Complete Listing)

Collaborative Partnership between Research Centers in Minority Institutions (RCMI) and Alcohol Research Centers (U54, RFA-AA-21-015): This announcement invites U54 applications for the planning and implementation of collaborative partnerships between Research Centers in Minority Institutions (RCMI) and institutions with extensive alcohol research programs, including NIAAA-funded alcohol research centers and consortia. *Scientific Contacts: Dr. Hemin Chin and Dr. Elizabeth Powell* 

Investigational New Drug (IND)-enabling and Early-Stage Development of Medications to Treat Alcohol Use Disorder and Alcohol-Associated Organ Damage (U43/U44, PAR-22-102; UT1/UT2, PAR-22-103): This funding opportunity offers support to small businesses for the optimization, development, and translation of pharmaceutical research discoveries into new treatments for disorders that fall under the mission of NIAAA. Scientific contacts: Dr. Jenica Patterson and Dr. Svetlana Radaeva

#### Notices issued by NIAAA

- Notice of Special Interest (NOSI): Epidemiology and Prevention of Alcohol Misuse in Understudied Young Adult Populations; Military, Workforce, and Community College: NOT-AA-22-001
- Notice of Special Interest (NOSI): Administrative Supplements and Urgent Competitive Revisions on Coronavirus Disease 2019 (COVID-19) within the Mission of NIAAA: <u>NOT-AA-22-002</u>
- Request for Information (RFI): Unhealthy Alcohol Use in Active-Duty Military: NOT-AA-21-042

## Administrative Supplements to Recognize Excellence in Diversity, Equity, Inclusion, and Accessibility (DEIA) Mentorship

- This administrative supplement recognizes the crucial role great mentors play in the development of future leaders in the scientific research enterprise. Supplements will support existing awards of scientists who are engaged in outstanding mentorship with compelling commitments and contributions to enhancing diversity, equity, inclusion, and accessibility (DEIA) in the biomedical sciences.
- Awarded supplements will provide up to \$250,000.00 (direct costs; not to exceed the
  cost of the parent award), to grants supporting faculty members who have mentoring
  and/or mentorship as part of their existing awards and have demonstrated a
  commitment to outstanding mentorship and training, especially to individuals from
  groups identified as underrepresented in the biomedical sciences (e.g., see the Notice
  of NIH's of Interest in Diversity).

See <u>NOT-OD-22-057</u> for more information. NIAAA point of contact: Dr. Abe Bautista

## **Summarizing the Early Research on Mental Health During the COVID-19 Pandemic**

### U.S. and worldwide declines in mental health

• A research team examining the impact of COVID on global mental health examined data from 204 countries and found significant increases in anxiety disorders and major depression during the pandemic, particularly for women and younger people (COVID-19 Mental Disorders Collaborators, 2021)



 Another study reported an increase in the percentage of U.S. adults (18+) with symptoms of anxiety or depression and in the percentage of people who received counseling or medication for mental health conditions after the pandemic began (Vahratian et al., 2021)

## Global Increase in Symptoms of Depression and Anxiety in Children and Adolescents During COVID-19 Pandemic

- Researchers analyzed data from 29 studies measuring symptoms of anxiety and depression in people 18 and under during the pandemic
- Prevalence of clinical symptoms was 25.2% for depression and 20.5% for anxiety

 Findings suggest 1 in 4 youth globally are experiencing clinically elevated depression symptoms, while 1 in 5 are experiencing elevated

anxiety symptoms during the pandemic

- These estimates are double the pre-pandemic estimates
- Estimates are higher in studies conducted later in the pandemic, suggesting that the problem continues to worsen



## Summarizing the Early Research on Drinking During the COVID-19 Pandemic

### **Increasing alcohol consumption among some groups**

- We are still learning how the COVID pandemic is impacting alcohol use, but research has shown that some people are drinking more while others are drinking less (Systematic reviews: Acuff et al., 2021; Schmidt et al., 2021; Roberts et al., 2021)
- Higher levels of stress related to distance learning, family related issues, financial issues, and being confined to the home were associated with drinking more often and more heavily (Grossman et al., 2021)
- In several studies, increases in drinking were more likely for women, particularly those reporting increases in stress (e.g., Rodriguez et al., 2020)
- Factors most consistently associated with increases in drinking include:
  - Income loss/financial stress
  - Greater depression or anxiety
  - Greater general psychological distress
  - Greater drinking to cope with stress



## Determinants of Health That May Influence Alcohol Misuse and Health Equity

Social determinants of health (SDOH) include broad aspects of social and physical environments that impact quality of life and health outcomes.

SDOH can influence the likelihood of developing and recovering from AUD, contribute to alcohol-related health disparities, and impose additional burdens on brain systems involved in stress and emotion regulation, also increasing vulnerability for AUD.



## Social Determinants and Alcohol Misuse: NIAAA Research Findings

- Recent NIAAA-supported research explored the link between discrimination, heavy drinking, and mental health in Latinx communities:
  - Participants who engaged in heavy drinking reported feelings of exclusion that led to symptoms of anxiety and depression that, in turn, led to drinking to cope.
- Another study examined the relationship between adverse childhood experiences (ACEs), racial microaggressions, and alcohol misuse in emerging adults (ages 21-25) who reported heavy drinking two or more times in the past month.
  - Experiencing more ACEs was associated with higher alcohol consumption and more negative consequences of alcohol misuse.
  - For Black young adults, racial microaggressions were also associated with more negative consequences of alcohol misuse.

## **Improving Health Disparities** in Alcohol Health Services

Examples of new NIAAA health services research projects to address health disparities:

- One project is assessing the effectiveness of a culturally adapted, personalized feedback intervention among Latinx individuals with alcohol misuse and anxiety within community-based health clinics
- Another study is exploring the impact of various combinations of follow-up engagement after alcohol-related hospitalization and assessing alcohol-related outcomes across racial and ethnic groups, including analysis of social determinants of health
- A third study is examining barriers to AUD care by surveying Medicaid health plan policies related to delivery and management of AUD treatment and their relationship with access to and outcomes of care for racial/ethnic minorities, women, and rural Americans

## In Press Defining Recovery from Alcohol Use Disorder: Development of an NIAAA Research Definition

- The article presents the newly developed NIAAA definition of recovery from AUD based on qualitative feedback from key recovery stakeholders (e.g., researchers, clinicians, and recovery specialists). The operational definition can be used by diverse stakeholders to increase consistency in recovery measurement, stimulate research to better understand recovery, and facilitate the process of recovery.
- Recovery is viewed as both a process of behavioral change and an outcome that incorporates two key components:
  - Remission from DSM-5 AUD and
  - Cessation from heavy drinking (a non-abstinent recovery outcome)
- The NIAAA definition of recovery also emphasizes the importance of biopsychosocial functioning and quality of life in enhancing recovery outcomes.

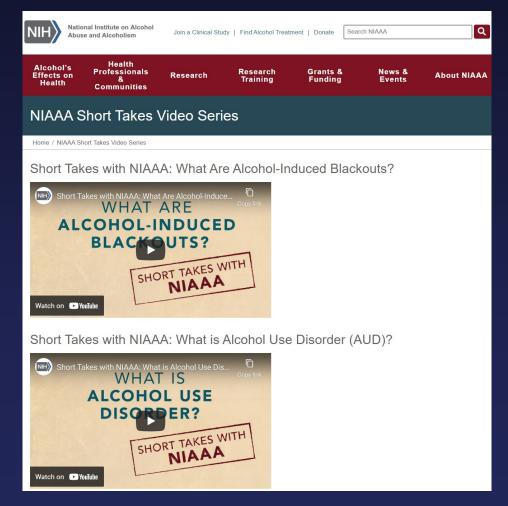
## New Resource: "Short Takes" Video Series to Enhance Understanding about Alcohol Terms

NIAAA recently released a video series called "Short Takes with NIAAA," a collection of brief 60-second videos that explain commonly used—but often misunderstood—alcohol terms.

The first installment includes videos on:

- Alcohol use disorder
- Blackouts
- Alcohol overdose (in Spanish and English)
- Binge drinking

Videos are expected to be helpful to both the general public and health care providers.



## Research Highlights

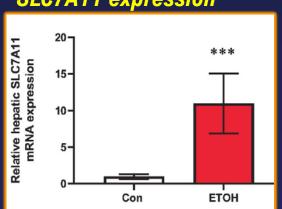
## Epigenome-Wide Association Study of Alcohol Consumption in N = 8161 Individuals and Relevance to Alcohol Use Disorder Pathophysiology: Identification of the Cystine/Glutamate Transporter SLC7A11 as a Top Target

Chronic heavy alcohol consumption is strongly associated with alterations in DNA methylation, a process that influences gene transcription. Identification of alcohol-associated methylome variation might provide novel insights into pathophysiology and innovative treatment targets for alcohol use disorder (AUD). Using the largest epigenome-wide association study of alcohol consumption to date (N=8161), investigators identified 2504 methylation sites and five leading gene targets—including SLC7A11, a cystine/glutamate transporter. Biological validation and follow-up studies confirmed a substantial role for SLC7A11 in AUD. Given the prominent function of glutamate signaling in brain and liver, the results identify SLC7A11 as a novel target for therapeutic intervention in AUD.

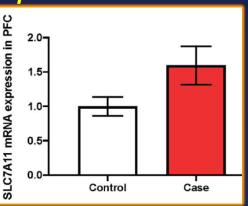
### Association of a SLC7A11 methylation site with clinical phenotypes, liver enzymes, and lipids

	Total sample (N = 615)			AUD-only subset (N = 372)				
Variables	Beta	SE	STAT	p value	Beta	SE	STAT	p value
Total drinks	-1.31	0.80	-1.63	0.104	-1.17	0.55	-2.15	0.0325
Number of drinking days	-0.84	0.07	118.53 <sup>a</sup>	<0.0001	-0.86	0.08	117.29 <sup>a</sup>	<0.0001
Heavy drinking days	-1.15	0.08	195.09 <sup>a</sup>	< 0.0001	-1.09	0.08	172.10 <sup>a</sup>	<0.0001
GGT	-5.46	0.55	-9.95	1.03E-21	-5.63	0.69	-8.18	1.67E-15
ALT	-2.08	0.42	-4.89	1.29E-06	-2.06	0.51	-4.07	5.32E-05
AST	-2.50	0.44	-5.69	1.97E-08	-2.47	0.57	-4.37	1.46E-05
HDL-cholesterol	0.16	0.24	0.7	0.4851	0.21	0.28	0.74	0.4619
LDL-cholesterol	-25.22	24.19	-1.04	0.2975	-37.09	27.27	-1.36	0.1747
Total cholesterol	-0.37	0.14	-2.65	0.0082	-0.45	0.16	-2.82	0.0051
Triglycerides	-1.47	0.35	-4.2	3.07E-05	-1.68	0.41	-4.13	4.13E-05
<sup>a</sup> Wald $\chi^2$ statistic was estimated by a poisson regression model.								

Rat liver: Alcohol intake increases SLC7A11 expression



Postmortem human PFC: Increased SLC7A11 expression in AUD

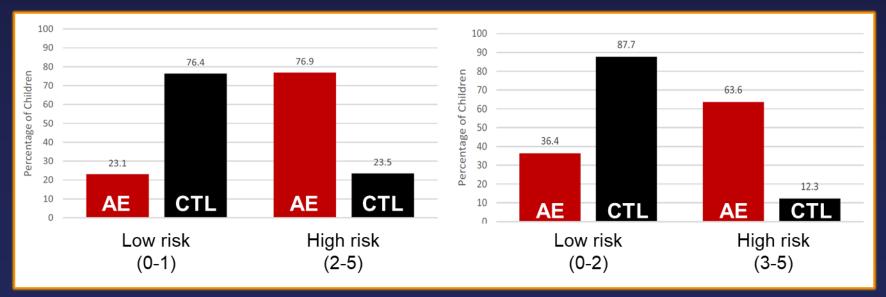


Citation: Lohoff FW, Clarke TK, Kaminsky ZA, Walker RM, Bermingham ML, Jung J, Morris SW, Rosoff D, Campbell A, Barbu M, Charlet K, Adams M, Lee J, Howard DM, O'Connell EM, Whalley H, Porteous DJ, McIntosh AM, Evans KL. Mol Psychiatry. 2021 Dec 2.

## Development and Validation of a Postnatal Risk Score that Identifies Children with Prenatal Alcohol Exposure

Investigators developed and validated an efficient and easily calculable risk score to identify an individual's risk of having been exposed to alcohol prenatally. Unlike previously published clinical tools for fetal alcohol spectrum disorder (FASD) assessment, the proposed risk score relies on measures that can be easily obtained, comprising physical measures (dysmorphology) as well as parent-reported measures of adaptive functioning and behavior for a total score of 0-5. With preliminary testing, the risk score shows promise in distinguishing alcohol-exposed children from control subjects, while correlating with cognitive outcomes. Importantly, the risk score could be easily deployed in a clinical setting as an early screening tool for FASD.

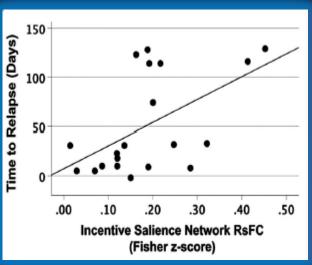
Percentage of alcoholexposed (AE) and control (CTL) subjects in each risk sub-group using 2 different risk cut-points.

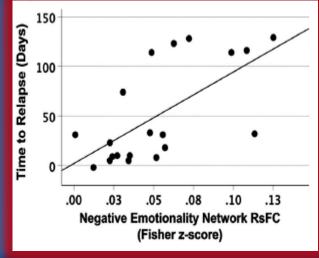


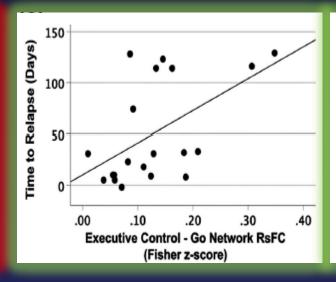
## Resting Hypoconnectivity of Theoretically Defined Addiction Networks during Early Abstinence Predicts Subsequent Relapse in Alcohol Use Disorder

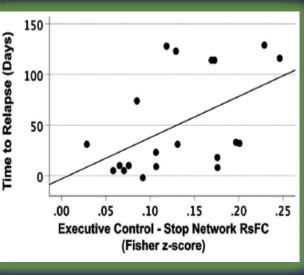
The present study investigated resting-state functional connectivity in brain networks related to three addiction domains (incentive salience, negative emotionality, and executive functioning) during early abstinence in predicting relapse in alcohol use disorder.

Compared to individuals who remained abstinent, those who relapsed had lower functional connectivity during early abstinence in all three brain networks, which predicted subsequent relapse.







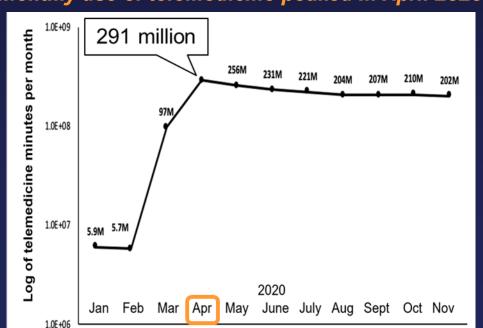


The brain networks also predicted time to relapse, whereas clinical self-reports were not reliable predictors. The findings highlight the value of functional brain connectivity as a biomarker of vulnerability for relapse and the potential of modulating functional connectivity in addiction networks as a treatment for AUD.

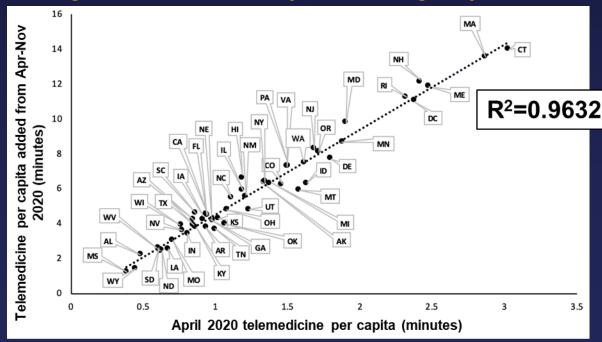
### **Quantifying COVID-19's Impact on Telemedicine Utilization**

COVID-19 pandemic era restrictions regarding in-person care led to widespread adoption of telemedicine-based healthcare. To investigate trends in telemedicine utilization over the course of the pandemic, researchers analyzed data from doxy.me (the largest free telemedicine platform) and the NIH Clinical Center. Analysis revealed that, nationally, use of telemedicine peaked in April 2020 at 291 million minutes, stabilizing at 200-220 million monthly minutes from May to November 2020. State-level data also revealed a correlation between states with early expansion of telemedicine capacity (i.e., New England and Mid-Atlantic states) and greater overall telemedicine expansion during the pandemic. Results paint a picture of how telemedicine has evolved throughout the pandemic.

#### Monthly use of telemedicine peaked in April 2020



States with early expansion of telemedicine capacity also had greater telemedicine expansion during the pandemic



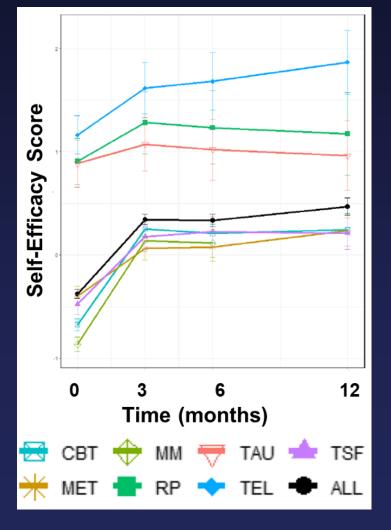
## Integrative Data Analysis of Self-Efficacy in 4 Clinical Trials for Alcohol Use Disorder

Self-efficacy is an individual's belief in their ability to organize and execute behaviors to achieve a desired outcome. In the context of AUD, an individual with high self-efficacy is confident in their ability to abstain or reduce heavy drinking in potential alcohol use situations.

Self-efficacy has been proposed as a key predictor of alcohol treatment outcomes and a potential mechanism of success in achieving abstinence or drinking reductions following alcohol treatment. The present study examined the effect of treatment on self-efficacy across four different treatment studies.

All active treatments, including cognitive-behavioral treatment, medication management, 12-step facilitation, motivation enhancement treatment, relapse prevention, and telephone continuing care, were associated with significant increases in self-efficacy from baseline to posttreatment that were maintained for up to a year. Treatment as usual in community settings, which consisted of weekly group therapy that included addiction counseling and 12-step recovery support, was not associated with significant increases in self-efficacy.

### Increases in self-efficacy over time following treatment



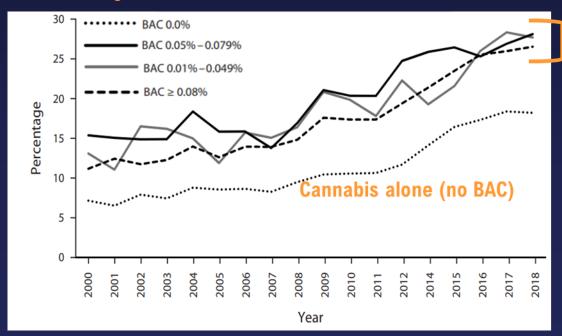
## Trends in Motor Vehicle Accidents with Alcohol and Cannabis Involvement From 2000 to 2018

From 2000 to 2018, alcohol was consistently involved in approximately 40% of motor vehicle crash fatalities. During this time, cannabis involvement and cannabis and alcohol coinvolvement in fatal motor vehicle crashes increased nationally.

Fatalities involving any cannabis more than doubled from 9% to 21.5%, and fatalities involving both cannabis and alcohol more than doubled from 4.8% to 10.3%.

More motor vehicle fatalities involved a combination of cannabis and alcohol (at any BAC level) than cannabis alone.

### Percentage of motor vehicle crash fatalities involving cannabis by blood alcohol concentration

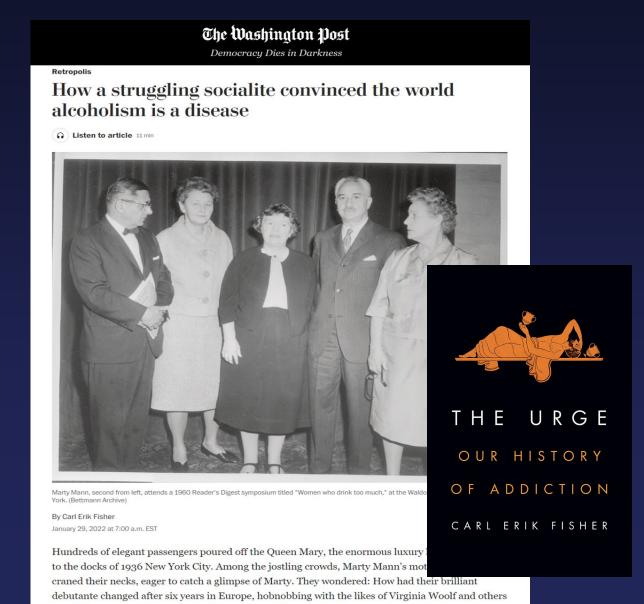


Cannabis in combination with varying BAC levels

## A History Lesson: The Story of Margaret Mann, "a brilliant strategist and a public-relations genius who played a crucial role in mid-century alcoholism advocacy"

"World War II was raging, and Mann was working in her new job, producing radio programs on American history. One featured Dorothea Dix, the 19th-century crusader who led a national campaign against the inhumane treatment of the mentally ill, and Mann was profoundly moved. What if there was a similar battle to be waged on behalf of alcoholics?

Soon afterward, she woke in the middle of the night with an epiphany, ran to her typewriter and typed out a detailed plan for a national campaign that would convince the public that alcoholism was not a moral but a medical condition."



### **THANK YOU!**

### Special thanks to:

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**Kat Tepas** 

**Aaron White** 

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