# NIAAA Update: Changing the Conversation Around Alcohol

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Collaborative Research on Addiction at the National Institutes of Health
Joint National Advisory Council
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## Staff Transitions: Abe Bautista, PhD

Dr. Abraham Bautista retired from his position as the Director of the Office of Extramural Activities (OEA) after 20 years of Federal Service.

Abe was responsible for extramural grant and contract review, the management of chartered initial review groups and special emphasis panels, and all grants management activities.

Abe served as the Executive Secretary of NIAAA's Advisory Council and was responsible for overseeing and coordinating committee management activities, including federal advisory committees.

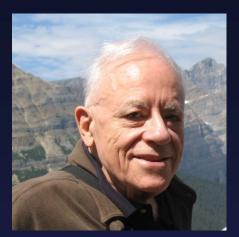
In his retirement Abe looks forward to expanding his travels and finding other exciting ways to fill his days. He will be missed!

Dr. Philippe Marmillot is the Acting OEA Director.

Dr. RV Srinivas is serving as Executive Secretary for the NIAAA Advisory Council.



### In Memoriam: Enoch Gordis, MD



Dr. Enoch Gordis served as the NIAAA director from 1986 to 2001. Dr. Gordis emphasized science as a way of understanding alcohol use disorder. Trained in internal medicine, he conducted research in the laboratory of Dr. Solomon Berson and Nobel Laureate Dr. Rosalyn Yalow during his residency at Mount Sinai Hospital in New York. Subsequently he worked in Dr. Vincent P. Dole's research laboratory at New York's Rockefeller University, where he began his career in the study

of addiction. He later worked with psychiatric researcher Dr. Ruth Fox, who helped introduce disulfiram in the United States as a medication to treat alcohol problems. In 1971, Dr. Gordis founded and directed a new alcohol treatment program at Elmhurst Hospital in Queens, NY. He remained there until his appointment to NIAAA.

At NIAAA, Dr. Gordis is remembered as a visionary leader. During his tenure as director, he oversaw the launch of several innovative research initiatives, including the Collaborative Study on the Genetics of Alcoholism, the National Longitudinal Alcohol Epidemiologic Survey, the Integrative Neuroscience Initiative on Alcoholism, and the Combining Pharmacotherapies and Behavioral Interventions clinical study.

Dr. Gordis' leadership embodied his love of science, his compassion as a clinician, and his demeanor as a gentleman. He inspired many and left a lasting impact on NIAAA, NIH, and the alcohol research field.

## Alcohol by the Numbers: Scope of the Problem

Alcohol			
Past-year use	174,339,000		
% of population	62.3%		
DSM-5 AUD	29,544,000		
% of population	10.6%		
ED visits	<b>1,714,757</b> Primary reason		
	<b>4,936,690</b> All alcohol-related		
Deaths	140,557  Annual deaths		
	58,277		
	Acute (e.g., injury)		
	<b>82,279</b> Chronic (e.g., liver disease)		

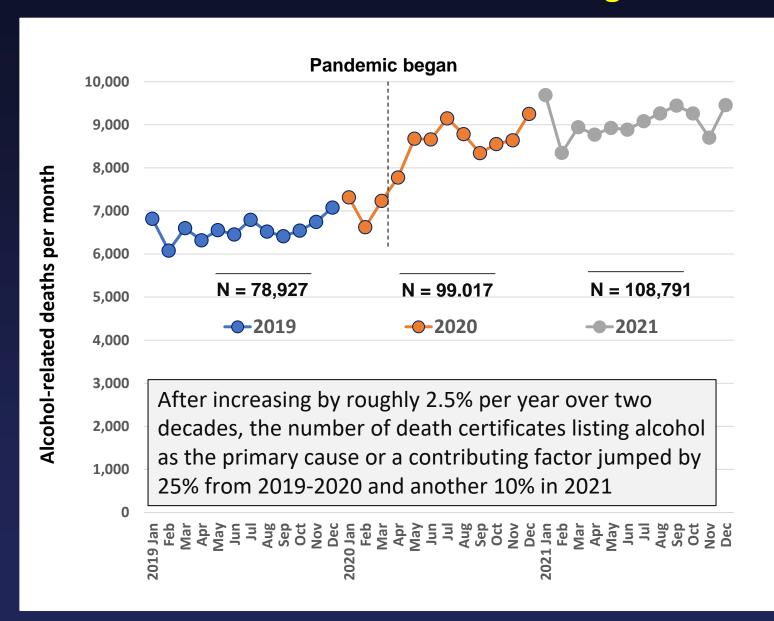
## Deaths Involving Alcohol Are Increasing

Death certificates listing alcohol increased 25.5% from 78,927 in 2019 to 99,017 in 2020, the first year of the pandemic. And 10% more to 108,891 in 2021.

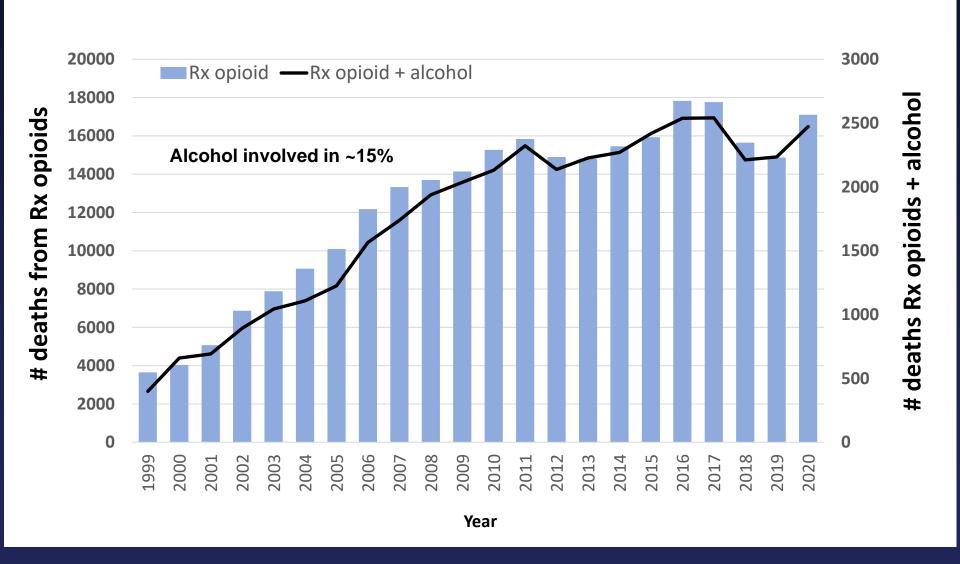
Alcohol was listed in 1 in 6 (16%) drug overdose deaths in 2020 and 2021.

Alcohol-related traffic fatalities increased by 14% to 11,654 in 2020 – highest since 2008.

### **Alcohol-Related Deaths Increased During the Pandemic**



## Alcohol Involvement in Deaths Due to Prescription Opioid Overdoses



### **Alcohol, Pain, and Opioids**

The Rx and Illicit Drug Summit in April included a session with Drs. Larry Tabak, Nora Volkow, and George Koob. Key alcohol-related messages were:

- The opioid crisis overlaps with other public health challenges, such as undertreated chronic pain, mental illness, and alcohol use disorder.
- Alcohol misuse contributes to pain (both emotional and physical), and pain contributes to alcohol misuse through drinking to cope.
- There are overlapping brain mechanisms in chronic pain, alcohol use disorder, and opioid use disorder. A detailed understanding of this relationship provides an opportunity for preventing and treating these problems.
- Addressing alcohol misuse in individuals with chronic pain and opioid use disorder may help improve patient outcomes.



## NIAAA Efforts to Change the Conversation Around Alcohol

- Increasing knowledge about the harmful effects of alcohol
- Rethinking drinking in U.S. culture
- Promoting Screening, brief intervention, and referral to treatment ("SBIRT") as part of routine healthcare
- Supporting research to integrate treatment for alcohol use disorder with treatment for co-occurring conditions – Hepatologists leading the way
- Addiction Neuroclinical Assessment framework- window on individualized etiology, prevention and treatment
- Supporting recovery research
- Combating Stigma
- Disseminating NIAAA resources, including the Healthcare Professional's Core Resource on Alcohol

## **Changing the Conversation: Health Risk at All Levels**

Alcohol Misuse is Associated with More Than 200 **Diseases and Injury-Related Conditions** 

### The New York Times Even a Little Alcohol Can Harm Your Health

Recent research makes it clear that any amount of drinking can be detrimental. Here's why you may want to cut down on your consumption beyond Dry January.

### health

January 11, 2023

**Drinking Alcohol Increases** Cancer Risk—But Very Few Americans Are Aware of the Link

#### Lung

**Acute Respiratory Distress Syndrome Pneumonia** 

#### Bone

Impaired fracture repair Reduced bone density

#### Liver

Steatosis (fatty liver) **Steatohepatitis Fibrosis** Cirrhosis **Alcoholic hepatitis** Liver cancer

#### **Gastrointestinal**

**Gut leakiness** Microbial dysbiosis Colon and rectal cancer

#### **Mental Health**

**Alcohol Use Disorder** Co-occurring mental health conditions

### **Oral Cavity**

**Esophageal cancer Oral cavity cancer** 

**Neurologic** 

Ischemic stroke

Hemorrhagic stroke

#### Cardiac

Cardiac Arrhythmias Cardiomyopathy Ischemic heart disease **Hypertension** 

> Myopathy Wasting

#### **Immune**

Acute pancreatitis Chronic pancreatitis

#### Cancers

Oral cavity, breast, liver, colon, rectum

#### Metabolic **Diabetes**

Injuries, Falls, Overdoses, Deaths

dysregulation

Muscle

#### **Pancreas**

## Changing the Conversation Around Alcohol: Sober Curious Movement

The Washington Post

## The benefits of 'Dry January' last longer than a month, studies show

People who abstained from alcohol for a month started drinking less the rest of the year and showed striking improvements in their health.



By Anahad O'Connor

December 27, 2022 at 6:00 a.m. EST

### **Dry January has health benefits**

Taking a Break from Alcohol During Dry January



"Dry January helps us evaluate our relationship with alcohol... If you stop drinking in the month of January, and suddenly you feel better... then your body is trying to tell you something. You should listen to your body."



After celebrating the holidays, maybe it's time to try 'dry January'

January 3, 2023 · 7:17 AM ET Heard on Morning Edition

## Changing the Conversation Around Alcohol: Mocktails

The Washington Post

### Do mocktails really help you drink less alcohol?

Nonalcoholic drinks may help those staying sober for Dry January, but they could be a trigger for anyone with alcohol use disorder

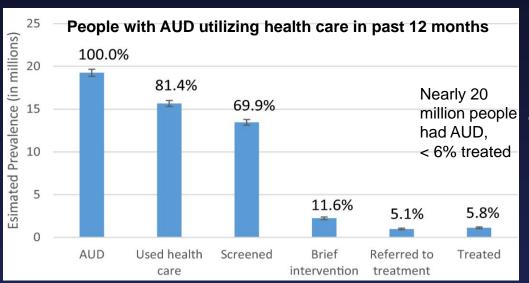




Not just 'Dry January': More Baltimore bars are offering alcohol-free drinks year-round

### Changing the Conversation: Moving Beyond Screening

Alcohol Screening <u>but little Brief Intervention and Referral to Treatment</u>

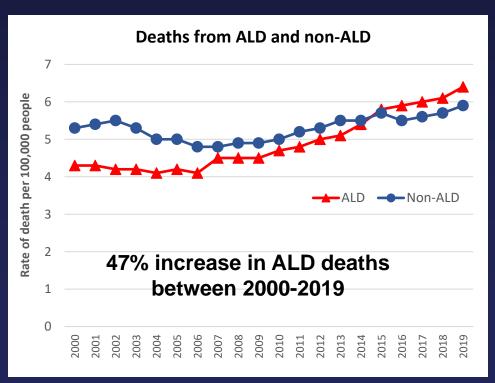


Using NSDUH data, Mintz et. al. 2021 showed screening, but little advice and referral for people with alcohol use disorder.

- In addition to its importance in preventing and intervening in alcohol use disorder, screening for alcohol misuse can also help clinicians spot other health-related issues.
- Other health issues may also help clinicians spot possible alcohol misuse.

### Hepatologists are Changing the Conversation Around Alcohol and Liver Disease

- Alcohol misuse accounts for nearly half of liver disease deaths each year
- Alcohol associated liver disease (ALD) is the most common alcohol-related cause of death and the leading cause of liver transplantation
- ALD-related deaths increased 47% between 2000-2019 (Chen and Yoon, 2022)
- Rates increasing faster for women and among young adults ages 25-34 (Tapper and Parikh, 2018; Chen and Yoon, 2022)



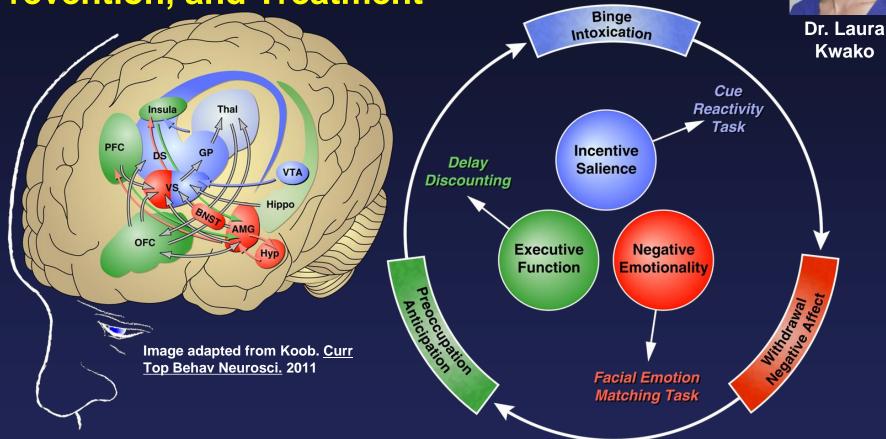
## Paradigm shift: Integrated treatment

- Integrated treatment of ALD and AUD can improve patient outcomes (<u>Leggio and</u> <u>Jung, 2022</u>)
- Treating AUD with medications reduces the likelihood of developing ALD and the progression of existing ALD (Vannier et al., 2022)
- Behavioral or pharmacotherapy for AUD after discharge from hospitalization for ALD reduces readmission and death (Peeraphatdit et al., 2019; Winters et al., 2021)

### **Early Liver Transplant for ALD**

- Currently, many U.S. transplant centers typically require a 6-month period of alcohol abstinence prior to liver transplantation:
  - To select patients who will be more likely to abstain from alcohol after transplant
  - To exclude patients from transplant who might improve and not require transplant
- Yet, it is not realistic in severe alcohol-associated hepatitis, where a majority (75-90%) of patient deaths occur within 2 months of diagnosis.
- Data suggests that patients who receive a liver transplant without the 6-month waiting period (called early liver transplant) have <u>similar</u> <u>survival outcomes and alcohol relapse rates</u> as patients who receive a transplant after the 6-month waiting period.
- To build on this research, NIAAA recently issued a Request for Applications to encourage studies on factors that influence the selection, management, and outcomes of patients who receive early liver transplantation.

Addictions Neuroclinical Assessment: A Framework for Improved Diagnosis, Prevention, and Treatment



The goals of the Addictions Neuroclinical Assessment (ANA) are to identify how the three domains influence differences between people diagnosed with alcohol use disorder (AUD), which can then be used to guide treatment decisions, and to better understand the differences between individuals with and without AUD.

Kwako LE, Momenan R, Litten RZ, Koob GF, and Goldman D. Addictions neuroclinical assessment: a neuroscience-based framework for addictive disorders. Biol Psychiatry. 2016 Aug 1;80(3):179-89.

## Validation of Three Neurofunctional Domains in AUD by Deep Behavioral Phenotyping

**PREDICTORS** 

In a large, diverse clinical sample representing the spectrum of AUD, the three neurobiological domains hypothesized to be critical to the addiction cycle (incentive salience, negative emotionality, and executive function) could be identified through factor analysis.

Positive urgency AUD diagnosis Neuroticism Gender-**Negative** Extraversion Emotional abuse-Agreeableness **Emotionality** Sexual abuse-Trait anxiety Emotional neglect Aggression ADHD Attentional impulsivity **AUD** diagnosis Motor impulsivity Race **Executive** Non-planning impulsivity Emotional abuse Conscientiousness Sexual abuse **Function** Negative urgency Family history -Premeditation Age at first drink Perseverance Positive urgency MADRS depression **AUD** diagnosis Trait anxiety Incentive Race Distress when unable to drink **Salience** Emotional abuse Preoccupation with alcohol

LATENT

**FACTORS** 

**INDICATORS** 

Time thinking about alcohol

Strength of urge to drink

Measures of addiction, personality, cognition, behavior, and exposure to early-life stress were collected in 454 patients. The study confirmed the relevance of the three neurofunctional domains to AUD. Using a multiple indicators, multiple causes (MIMIC) approach, early life stress, and sociodemographic predictors were identified.

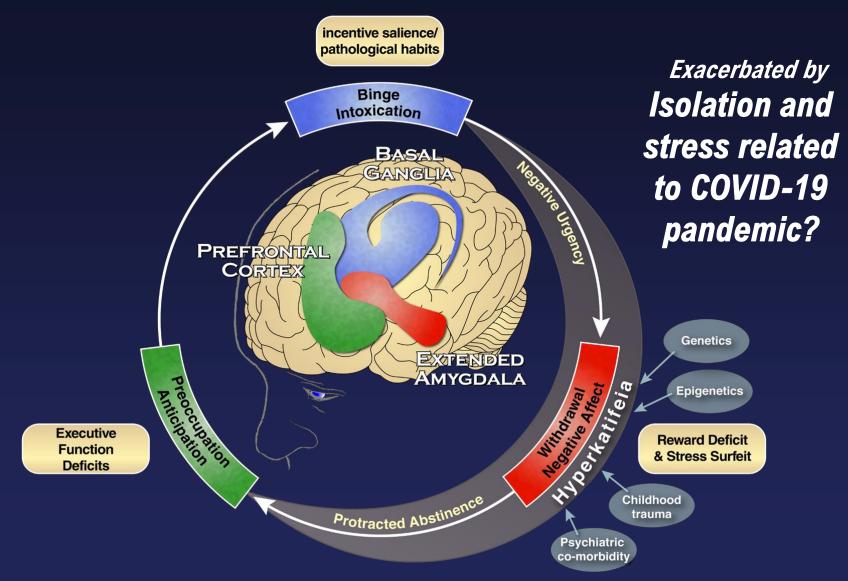
Kwako LE, Schwandt ML, Ramchandani VA, Diazgranados N, Koob GF, Volkow ND, Blanco C, and Goldman D. Neurofunctional domains derived from deep behavioral phenotyping in alcohol use disorder. Am J Psychiatry. 2019 Sep 1;176(9):744-753.

**Emotional neglect** 

## Additional Validation of the Three Neurofunctional Domains in Addiction

- Among heavy drinkers,
  - three factors: executive function, incentive salience, and emotionality, were all associated with current AUD, history of AUD, positive family history of AUD, earlier age of first drink, and history of childhood emotional abuse and physical neglect as predictors (DeMartini et al., 2021)
- Among problem drinkers,
  - four core constructs were identified: incentive salience, negative emotionality, executive function, and negative alcohol-related consequences (Nieto et al., 2021)
- In nontreatment- seekers,
  - deep phenotyping combined with factor analytic techniques implicated three intercorrelated neurofunctional domains that mapped on to the proposed ANA domains with methamphetamine use (Nieto and Ray, 2022)
  - In participants undergoing functional MRI after exposure to alcohol cues and negative cues, functional changes in the nucleus accumbens and amygdala were associated with incentive salience and negative emotionality domains (Al-Khalil et al., 2020)
- Among treatment seekers with AUD,
  - the incentive salience domain showed construct validity and demonstrated greater predictive validity for drinking outcomes compared to preexisting scales (Stein et al., 2021)
  - the negative emotionality domain showed construct validity and demonstrated concurrent associations with more frequent and heavier drinking and drinking to regulate negative affect (Votaw et al., 2021)

## Addiction as a Coping Response: Hyperkatifeia, Deaths of Despair, and COVID-19



From: Koob, GF, Powell, P., and White, A. Addiction as a Coping Response: Hyperkatifeia, Deaths of Despair, and COVID-19. Am J Psychiatry. 2020 Nov 1;177(11):1031-1037.

### **Changing the Conversation Around Recovery**

- Most people who need treatment receive no treatment of any kind, and little is known about what sustains longer-term recovery.
- To enhance health, NIAAA is expanding focus on longer-term recovery.
- NIAAA has defined recovery from alcohol use disorder (AUD) based on qualitative feedback from key recovery stakeholders (e.g., researchers, clinicians, and recovery specialists).
- Recovery is viewed as both a process of behavioral change and an outcome that incorporates time periods for two key components:
  - Remission from DSM-5 AUD
  - 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.

## **Greater Relief/Negative Emotionality at Baseline Predict Greater Drinking Intensity and More Frequent Heavy Drinking**

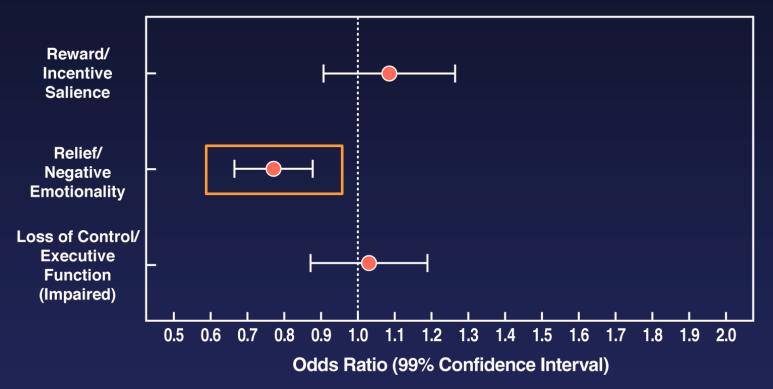
	% Heavy Drinking Days (PHDD)	
Predictor	β	B (SE), p value
Reward / incentive salience	.01	0.35 (0.87), p = 0.690
Relief / negative emotionality	.09	2.69 (0.53) <i>p</i> < 0.001
Loss of control / executive functioning		0.02 (1.17), <i>p</i> = 0.988

This study validated the 3 domains of the 3-stage addiction cycle (incentive salience, negative emotional states, and executive function) using measures from Project MATCH and COMBINE, two of the largest multisite alcohol clinical trials ever conducted. At 1 year follow up, relief/ negative emotion scores were associated with drinks per day and percent heavy drinking days. The results also support the utility of domains in predicting AUD treatment outcomes and recovery. The authors noted that the addiction cycle domains were more strongly associated with outcomes than AUD symptoms.

Witkiewitz K, Stein ER, Votaw VR, Hallgren KA, Gibson BC, Boness CL, Pearson MR, Maisto SA. Constructs derived from the addiction cycle predict alcohol use disorder treatment outcomes and recovery 3 years following treatment. Psychol Addict Behav. 2023 May:37(3):376-389.

## ...While Lower Relief/Negative Emotionality Predicted High Functioning Infrequent Drinking During Recovery

Lower Relief/Negative Emotionality Predicted Membership in the High Functioning Infrequent Drinking Profile as Compared to the Nonrecovery profile (Profile 4)

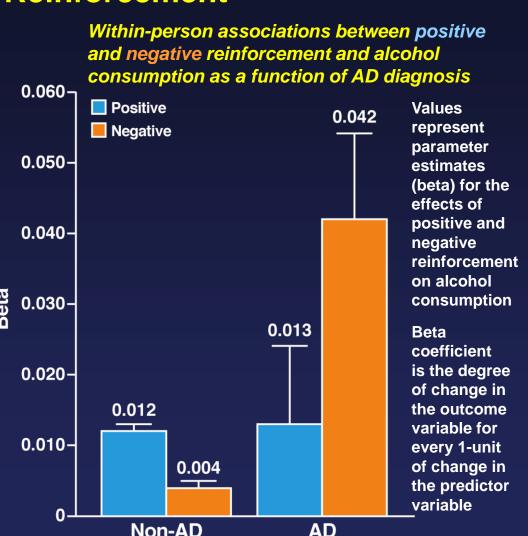


Four latent recovery profiles reflecting differing levels of drinking and functioning were derived based on indicators of alcohol use. Addiction cycle domains were used to predict membership in the high functioning infrequent drinking profile vs non-recovery profile.

Witkiewitz K, Stein ER, Votaw VR, Hallgren KA, Gibson BC, Boness CL, Pearson MR, Maisto SA. Constructs derived from the addiction cycle predict alcohol use disorder treatment outcomes and recovery 3 years following treatment. Psychol Addict Behav. 2023 May;37(3):376-389.

# Negative Reinforcement is More Strongly Associated with Alcohol Consumption in Alcohol Dependence than Positive Reinforcement

- Researchers used longitudinal data in young adults (2556 individuals, ages 18-30, 52% female) to test whether positive and negative reinforcement associated with alcohol consumption differed as a function of alcohol dependence (AD).
- The association between positive reinforcement and alcohol consumption did not significantly vary as a function of AD diagnosis.
- In contrast, the association between negative reinforcement and alcohol consumption increased in the presence of AD diagnosis.
   Similar effects were observed in males and females.



Cho SB, Su J, Kuo SI, Bucholz KK, Chan G, Edenberg HJ, McCutcheon VV, Schuckit MA, Kramer JR, Dick DM. Positive and negative reinforcement are differentially associated with alcohol consumption as a function of alcohol dependence. Psychol Addict Behav. 2019 Feb;33(1):58-68.

## Healthcare Professional's Core Resource on Alcohol: Informing the Conversation

- What every healthcare professional should know about alcohol
- Organized into 14 concise, practical, user-friendly articles
- For health care providers who are not addiction specialists, it can help overcome barriers to care for patients with alcohol problems including ways to counteract stigma in their practice



- Includes information about clinical impacts of alcohol, including cancer, pain, medication interactions, and co-occurrence with other substance use disorders and mental health disorders
- Free continuing education credit up to 10.75 credit hours

## **THANK YOU!**

### **Special thanks to:**

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