

## Closing the Treatment Gap: Challenges and Opportunities

George F. Koob, Ph.D.

Director

National Institute on Alcohol Abuse and Alcoholism



National Institute  
on Alcohol Abuse  
and Alcoholism

Keynote Address  
10<sup>th</sup> Annual  
Penn State  
Addiction Conference  
November 11, 2024



1

## What is the Treatment Gap?

- The **treatment gap** refers to the difference between the number of people who need alcohol treatment and the number who receive it.  
(Too few people who need help, get help)
- There are evidence-based behavioral treatments and three FDA-approved medications for alcohol use disorder (AUD), but
- less than 10% of individuals receive *any* treatment
- and, less than 2% receive medication

2

## NIAAA Efforts to Close the Treatment Gap

- Raising awareness about the scope of the problem by tracking drinking trends and consequences
- Embracing the changing culture around alcohol in society
- Advancing Alcohol Screening, Brief intervention, and Referral to treatment (SBIRT) as part of routine healthcare and the concept of early detection or “pre-addiction”
- Advancing diversity, equity, inclusion and accessibility in the alcohol field
- Combating stigma
- Addressing challenges and solutions for treatment of alcohol use disorder (AUD)
- Assessing and implementing the Addictions Neuroclinical Assessment framework: Window on individualized etiology, prevention and treatment
- Facilitating Medications Development
- Enhancing recovery research
- Supporting research to integrate alcohol use disorder (AUD) treatment with treatment for co-occurring conditions – hepatologists leading the way
- Advancing knowledge by disseminating NIAAA resources

3

## Raising Awareness about the Scope of the Problem by Tracking Drinking Trends and Consequences



National Institute  
on Alcohol Abuse  
and Alcoholism



4

## Quote

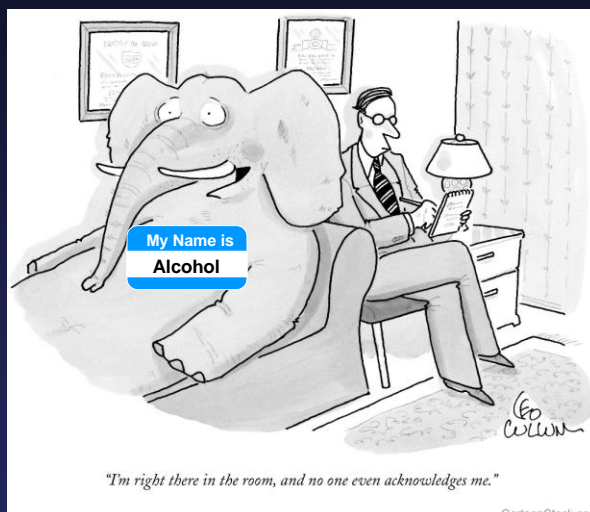
**“Most middle- and high-income countries globally have become largely inured to the endemic premature mortalities related to more commonly used substances such as alcohol and tobacco. While these account for a much larger number of deaths and economic and social harms than opioids each year, the devastation wreaked by these substances, their casualties, and the associated blood and tears are all relatively willingly absorbed into the social fabric.”**

***John F. Kelly and Sarah E. Wakeman, 2019***

From *Current Clinical Psychiatry*, Editors John F. Kelly, Sarah E. Wakeman, 2019, *Treating Opioid Addiction*, Current Clinical Psychiatry, Human Press, Switzerland. ISSN 2626-241X ISSN 2626-2398 (electronic); ISBN 978-3-030-16256-6; ISBN 978-3-030-16257-3 (eBook) <https://doi.org/10.1007/978-3-030-16257-3>

5

## Changing the Conversation to Include Alcohol



**“I’m right there in the room, and no one even acknowledges me.”**

6

## Alcohol by the Numbers: Scope of the Problem

Alcohol	
Past-year use	177,278,000
% of population	62.5%
DSM-5 AUD	28,859,000
% of population	10.2%
Emergency department visits	4,274,523 <small>Annual average 2016-2021</small>
Hospitalizations	1,987,498 <small>Annual average 2016-2021</small>
<b>Deaths</b>	<b>178,307</b> <small>Annual average 2020-2021</small>
	<b>61,063</b> <small>Acute causes (e.g., injuries)</small>
	<b>117,245</b> <small>Chronic causes (e.g., liver disease)</small>

### Deaths Involving Alcohol Are Increasing

Death certificates listing alcohol increased 25.5% in 2020 and another 10% in 2021 before declining slightly by 3% in 2022

There were 13,524 alcohol-related traffic fatalities in 2022 – 31% higher than a decade earlier.

Intoxicating levels of alcohol (BACs  $\geq 0.1\%$ ) are found in 21% of deaths from suicide, 37% from falls, 31% of drownings.

Alcohol misuse accounts for nearly half of liver disease deaths each year.

NSDUH 2023 Tables 2.26A&B, 2021 Nationwide Emergency Department Sample, CDC Alcohol-Related Disease Impact, National Highway Traffic Safety Commission, Alpert et al 2022, National Center for Vital Statistics, (Chen et al., 2022)

Note that emergency department visit and hospitalization numbers reflect all visits in which alcohol was listed as a factor.

7

## Acknowledging Health Risk at All Levels

**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.

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

**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

**Neurologic**

Ischemic stroke  
Hemorrhagic stroke

**Oral Cavity**

Esophageal cancer  
Oral cavity cancer

**Cardiac**

Cardiac Arrhythmias  
Cardiomyopathy  
Ischemic heart disease  
Hypertension

**Muscle**

Myopathy  
Wasting

**Pancreas**

Acute pancreatitis  
Chronic pancreatitis

**Immune dysregulation**

**Cancers**

Oral cavity, breast, liver, colon, rectum

**Metabolic**

Diabetes

**Injuries, Falls, Overdoses, Deaths**

8

Handouts are intended for use by participants of this conference. Unauthorized distribution or use is prohibited.

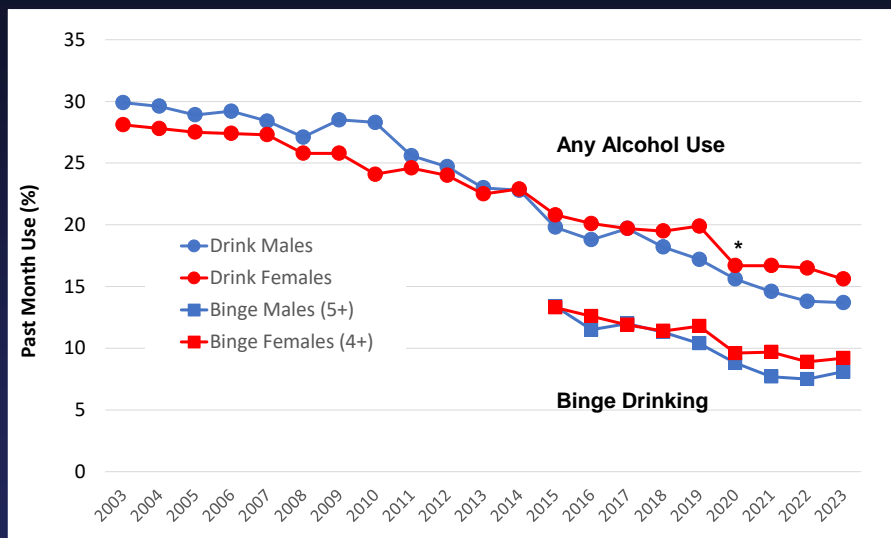
Any names or ages used on the upcoming slides are fictitious and not referring to an actual patient. 4

## Scope of the Problem –Trends in Alcohol Misuse and Consequences

- Changing patterns of alcohol use among adolescents and young adults
- Women and alcohol
- Older adults and alcohol
- Effect of the COVID-19 pandemic on alcohol use and its consequences

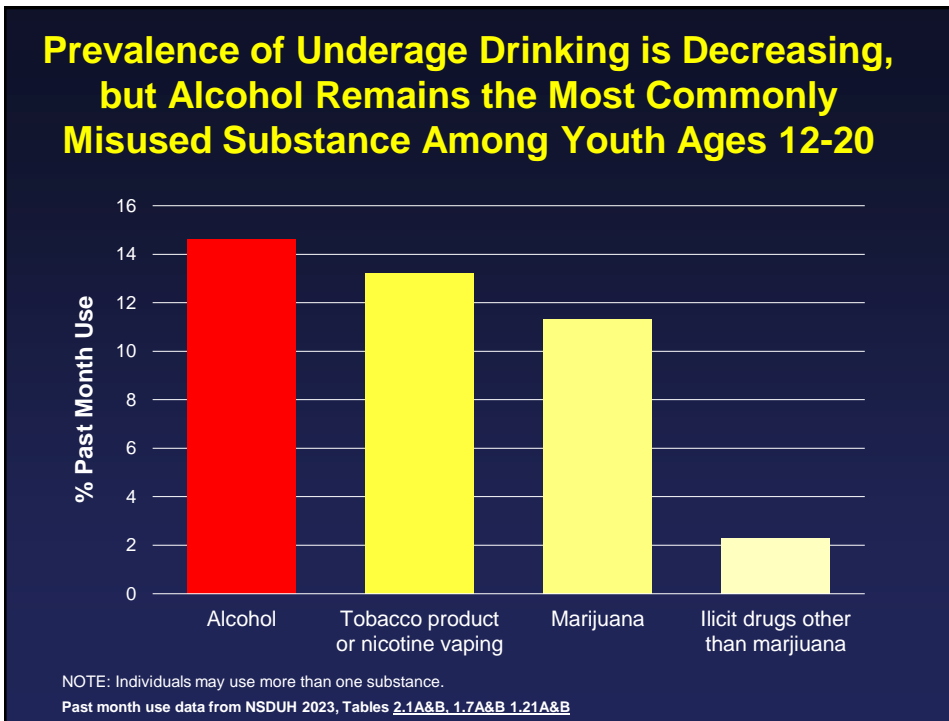
9

## Alcohol Use and Binge Drinking are Declining Among 12-20 Year Olds, More for Males than Females

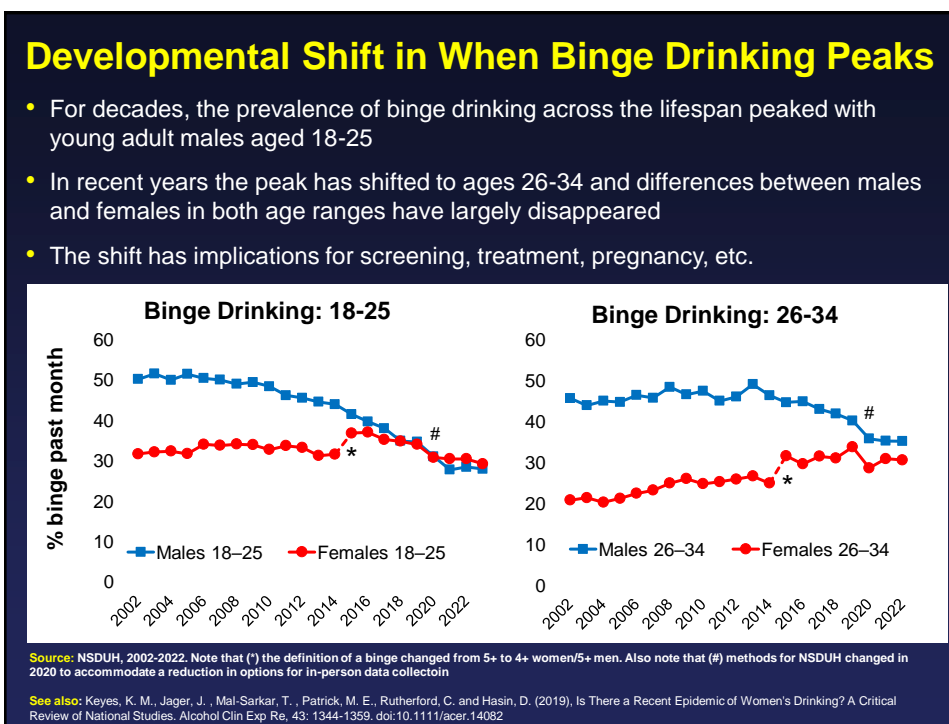


**Source:** Data from the National Survey on Drug Use and Health; Binge = 4+ drinks for females or 5+ drinks for males  
 \* = Methodological changes occurred in 2020 so caution should be used when comparing estimates between 2020 and prior years. See the 2020 National Survey on Drug Use and Health: Methodological Summary and Definitions for details.

10



11



12

## Male and Female Drinking Patterns Are Converging in Different Ways in Different Age Groups

- **Adolescents (12-17) and young adults (18-25)**
  - Prevalence of past month alcohol use is decreasing faster for males than females
  - Females in both age groups are now more likely to drink and binge drink than males
- **Adults (26-64)**
  - Prevalence of past month alcohol use increased slightly for females and decreased slightly for males
- **Older adults (65+)**
  - Prevalence of past month alcohol use increased for females but not for males

**Source:** National Survey on Drug Use and Health, 2002-2022

**See also:** Keyes, K. M., Jager, J., Mal-Sarkar, T., Patrick, M. E., Rutherford, C. and Hasin, D. (2019), Is There a Recent Epidemic of Women's Drinking? A Critical Review of National Studies. *Alcohol Clin Exp Re*, 43: 1344-1359. doi:10.1111/acer.14082

13

## Alcohol and Women's Health

Studies suggest that women are more likely than men to experience a variety of alcohol-related harms at comparable doses, including:

- Hangovers (Vatsalya et al. 2018)
- Blackouts (Hingson et al., 2016)
- Liver disease (Guy and Peters, 2013)
- Brain atrophy (Ceylanisik et al., 2010)
- Cognitive deficits (Flannery et al., 2007)
- Cardiomyopathy (Fernández-Solà and Nicolás-Arfelis, 2002)
- Faster progression of AUD (Diehl et al., 2007)
- Certain cancers (Liu et al, 2015)
- Larger increases in alcohol-related ED visits, hospitalizations and death for women than men over past 20 years (White et al. 2020)
- Women are less likely than men to receive treatment for AUD (Gilbert et al., 2019)

### **Risk-severity paradox:**

Women experience greater harms at lower doses of alcohol over shorter periods of time

More research is needed to better understand sex differences in alcohol use and consequences

- Only 26% of 230 structural neuroimaging studies on substance use over 23 years evaluated sex differences (Lind et al., 2017)

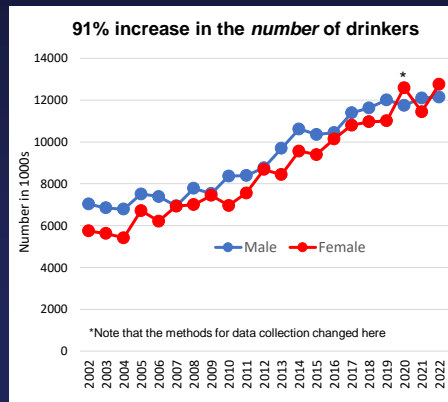
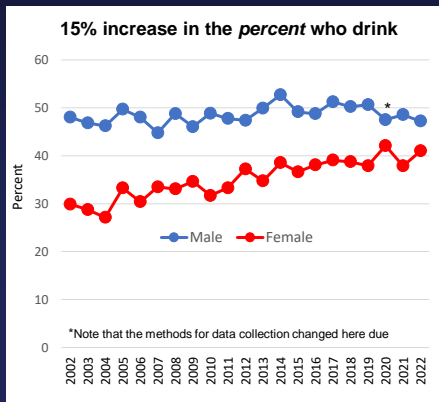
14

## Concerns About Alcohol Use Among Older Adults

The size of the population aged 65+ is growing rapidly and both the percent and number of older drinkers are increasing

The *percentage* of people 65+ who drank alcohol in the past month increased 15% overall between 2002-2022, but only for women (37%) and not men (-1.7%)

Due to the rapid increase in the size of the population 65+, the *number* of older drinkers increased 91% overall between 2002-2022



15

## Concerns About Alcohol Use By Adults Aged 65+

- Alcohol affects behavior and health differently as we age. Health consequences of alcohol tend to shift from acute causes (injuries) to chronic causes (e.g., cancer, heart disease) with age
- Older adults:
  - Are more sensitive to the sedative effects of alcohol, as well as to the effects of alcohol on reaction time, balance, attention, and driving
  - Have higher blood alcohol levels because of loss of lean muscle, increases in body fat, reductions in body weight, and less body water
  - Take more medications that may interact with alcohol
  - Have an increased risk of injury from falls that is compounded by alcohol
- Both alcohol and aging:
  - Involve widespread inflammation that can contribute to cardiovascular diseases and cancer
  - Disrupt sleep

Sources: [Novier et al., 2015](#); [Sklar et al., 2014](#); [Vogel-Sprott and Barrett, 1984](#); [Price et al., 2018](#)

16

## Alcohol and Mental Health are Intertwined

- AUD is highly co-morbid with mental health disorders.
  - The prevalence of AUD among people with anxiety and mood disorders ranges from about 20-40%.
  - Between 30-60% of people who seek AUD treatment have post-traumatic stress disorder.
- Alcohol misuse often precedes diagnoses of mental health conditions.
- Alcohol misuse is commonly used in an effort to cope with symptoms, but in the end, alcohol misuse makes the prognosis worse.
- Similarly, mental health conditions complicate treatment for AUD.
- The Covid-19 pandemic contributed to a global decline in mental health

Centanni SW, Bedse G, Patel S, and Winder DG. 2019. Driving the Downward Spiral: Alcohol-Induced Dysregulation of Extended Amygdala Circuits and Negative Affect. *Alcohol Clin Exp Res*

Mäkelä P, Raitasalo K, and Wahlbeck K. 2015. Mental health and alcohol use: a cross-sectional study of the Finnish general population. *European Journal of Public Health*, 25(2): 225-231

[NIAAA Healthcare Professional's Core Resource on Alcohol \("Mental Health Issues"\)](#)

17

## Alcohol, Pain, and Opioids are Intertwined

- The opioid crisis overlaps with other public health challenges, such as undertreated chronic pain, mental illness, and alcohol use disorder.
- Alcohol misuse contributes to both physical and emotional pain, 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, opioid use disorder, or both, may help improve patient outcomes.

Dr. Koob at the Rx and Illicit Drug Summit in 2023 during a session with Dr. Larry Tabak and Dr. Nora Volkow.



18

# Embracing the Changing Culture Around Alcohol in Society




National Institute on Alcohol Abuse and Alcoholism

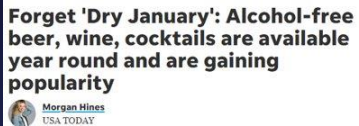


19

## The Sober Curious Movement and Increasing Alcohol-free Options Highlight a Cultural Shift




**You may need a Sober October more than you think. Experts explain how to do it right**




**Forget 'Dry January': Alcohol-free beer, wine, cocktails are available year round and are gaining popularity**

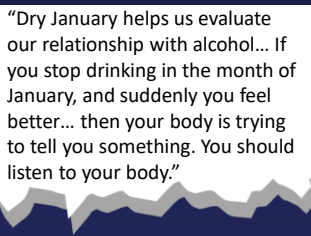
Morgan Hines  
USA TODAY




**Dry January has health benefits**  
Taking a Break from Alcohol During Dry January




**“The general consensus now is that there is no amount of alcohol that is good for your health,” says Dr. Sanjay Gupta, CNN Chief Medical Correspondent**



“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.”



**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



**yahoo/life**  
**Jennifer Garner says she is cutting back on alcohol: 'The older I get, the more I want to protect my brain'**

20

## Promoting Alcohol Screening, Brief intervention, and Referral to treatment (“SBIRT”) as part of routine healthcare/ Concept of early detection or “pre-addiction”



21

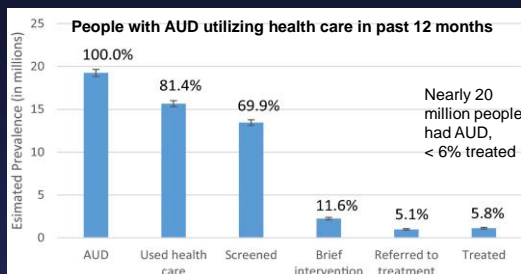
## Closing the Treatment Gap by Promoting Screening, Brief Intervention, and Referral to Treatment

- We have a large gap in the continuum of care for alcohol misuse.
- NIAAA is promoting the use of screening, brief intervention, and referral to treatment as part of routine healthcare
- Screening for alcohol misuse can also help clinicians spot other physical and mental health-related issues
- Kaiser Permanente Northern California introduced alcohol as a Vital Sign (AlcVS), in a systematic screening process for unhealthy drinking in 2013.
  - Their tagline “we screen everyone” normalizes what can be a sensitive subject.
  - They found that alcohol SBI in primary care significantly improved drinking outcomes independent of AUD treatment, and that alcohol SBI among patients with hypertension reduced both alcohol use and blood pressure. (Chi et. al. 2022, Chi et. al. 2023)

22

## Moving Beyond Screening to Address the Treatment Gap

- While alcohol screening is common, there is still **little brief intervention and referral to treatment**.



Using NSDUH data, Mintz et al (2021) showed screening often occurs, but there is little advice and referral for people with alcohol use disorder.

- In the U.S., women appear to have lower odds of receiving brief intervention for unhealthy alcohol use across all age groups, particularly during middle age.
- Black women and Latina/Hispanic women appear to be less likely to receive brief intervention than women in other race/ethnicity groups (Parthasarathy S, et al.2023).

23

## Alcohol as a Vital Sign

- Alcohol consumption is an under-appreciated contributor to many health conditions and is often overlooked by health professionals in primary care and other healthcare settings.
- Approaching alcohol use as a vital sign and integrating alcohol screening, brief intervention, and referral to treatment (alcohol SBIRT) into routine care can increase the chances that an alcohol-related problem is identified and addressed.
- This approach can also help clinicians identify other physical and mental health-related issues affected by alcohol misuse.
- Approaching alcohol as a vital sign would also reduce stigma and normalize what can be a sensitive subject.
- Widespread implementation of alcohol SBIRT holds much promise for improving overall health outcomes and reducing healthcare costs.



24

## The Concept of “Preaddiction” May Improve Early Intervention of Substance Misuse

- The long latency from substance use to disorder offers a significant window of opportunity for clinical interventions to stop progression.
- The idea of “preaddiction” has been proposed to:
  - raise public awareness about potentially harmful patterns of substance use,
  - spur greater utilization of screening and brief intervention,
  - prevent overdose, and
  - promote the development of new interventions.

McLellan AT, Koob GF, Volkow ND. Preaddiction-A Missing Concept for Treating Substance Use Disorders. JAMA Psychiatry. 2022 Aug 1;79(8):749-751. PMID: 35793096

25

## Advancing Diversity, Equity, Inclusion, and Accessibility in Alcohol Research



National Institute  
on Alcohol Abuse  
and Alcoholism



26

## Interaction of Alcohol and Social Determinants of Health

- **Social determinants of health** apply to everyone but many disproportionately affect women and certain minorities
- A variety of **social determinants of health** can impact the likelihood of alcohol misuse and AUD, such as:
  - **Social environment** (e.g., growing up in a home with parental AUD, discrimination, racism, social isolation)
  - **Physical environment** (e.g., alcohol outlet density, exposure to violence)
  - **Health care services** (e.g., access to and quality of care)
  - **Economic stability** (e.g., job security, income)
  - **Education access and quality** (e.g., educational opportunities and support)
- Adverse **social determinants of health** serve as allostatic loads on the body's stress systems, increase vulnerability to mental and physical health conditions, and contribute to health disparities and inequities.
- Stressors can drive alcohol misuse to cope, which, in turn, exacerbates the initial problems, further fueling alcohol misuse.

27

## Closing the Treatment Gap by Addressing Minority Health and Health Disparities

- New and ongoing NIH-wide initiatives and NIAAA-supported programs are poised to advance our understanding of minority health and health disparities and promote health equity.
- Areas of opportunity include:
  - Identifying and addressing barriers to effective, evidence-based prevention, diagnosis, and treatment in healthcare and other settings
  - Developing culturally-informed prevention and treatment interventions to increase their uptake and effectiveness
  - Determining how social determinants of health interact with neurobiological and other mechanisms to contribute to alcohol misuse and alcohol-related health consequences

28

## **NIAAA's 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 is Underway**

- 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](#)

29

## **Combatting Stigma in the Alcohol Field**



National Institute  
on Alcohol Abuse  
and Alcoholism



30

## Words Matter

### NIAAA Terminology Recommendations

We can help alleviate the stigma associated with alcohol-related conditions by consistently using non-pejorative, non-stigmatizing language to describe these concerns and the people who are affected by them.

- Use **alcohol use disorder** instead of *alcohol abuse*, *alcohol dependence*, and *alcoholism*
- Use **alcohol misuse** instead of *alcohol abuse* when referring broadly to drinking in a manner that could cause harm
- Use **person-first language** to describe people with alcohol-related problems (e.g., **person with alcohol use disorder** instead of *alcoholic*, **person in recovery** instead of *recovering alcoholic*)
- Use **alcohol-associated liver disease** instead of *alcoholic liver disease*

Volkow ND, Gordon JA, Koob GF. Choosing appropriate language to reduce the stigma around mental illness and substance use disorders. *Neuropsychopharmacology*. 2021 Dec;46(13):2230-2232. PMID: 34276051.

31

## Addressing Challenges and Solutions for Treatment of Alcohol Use Disorder



National Institute  
on Alcohol Abuse  
and Alcoholism



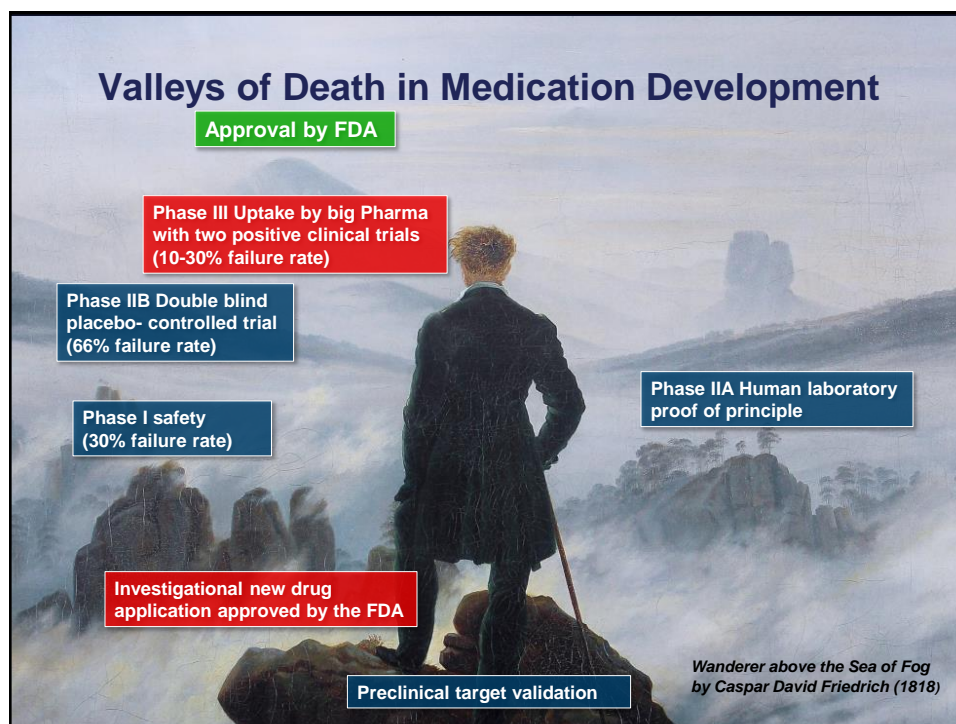
32

## Challenges for Medication Development Included Long Timelines, High Cost, and Low Success

- A major challenge is the long process between identifying preclinical treatment targets for AUD and the approval of a medication by the FDA. The first preclinical study with naltrexone was in 1980 and naltrexone was approved by the FDA 15 years later (in 1995). The first preclinical study with acamprosate was in 1987 and acamprosate was approved by the FDA 17 years later (in 2004).
- Less than 10% of novel agents make it through the “valley of death” from preclinical research to a Phase III clinical trial
- There is a lack of novel agents for AUD in the clinical pipeline
- Stigmatizing beliefs about people with substance use disorders can prevent treatment seeking, hamper clinical trial enrollment, and deter investment by industry
- As a result, there is a lack of venture capital funding and too few companies active in developing medications for substance use disorders

Koob GF. Annu Rev Pharmacol Toxicol. 2024 Jan 23;64:255-275; Brown DG, et al. Nat Rev Drug Discov. 2022 Nov;21(11):793-794.

33



34

## Broadening End Points for the Approval of Medications for Alcohol Use Disorder May Spur More Progress

- **Current FDA clinical endpoints** for Phase III trials are:
  - Total abstinence (original)
  - No heavy drinking days (newer)
- These endpoints do not take into consideration the amount of alcohol consumed prior to treatment and may limit the development of medications that improve how a patient feels and functions.
- **A new endpoint** that is being considered is a reduction in World Health Organization drinking risk levels (very high, high, moderate, low), defined as mean alcohol consumption per day
  - This efforts stems from the American College of Neuropsychopharmacology collaboration with NIAAA, NIDA, FDA, EMA, academic researchers, and pharmaceutical companies to advance the methodology of AUD clinical trials

35

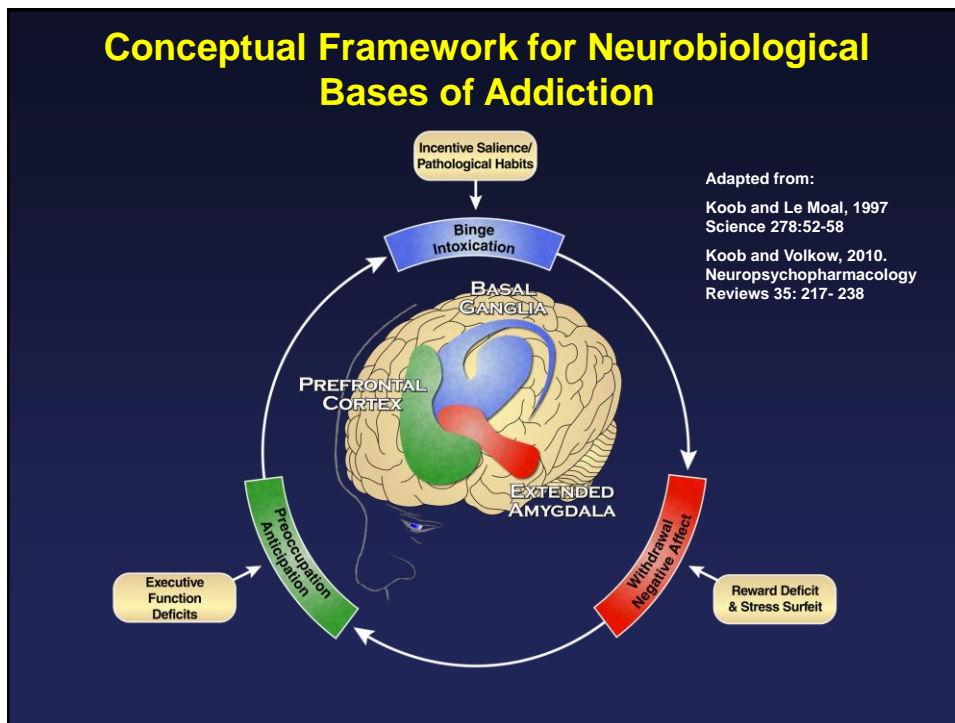
## Addictions Neuroclinical Assessment framework: Window on individualized etiology, prevention and treatment



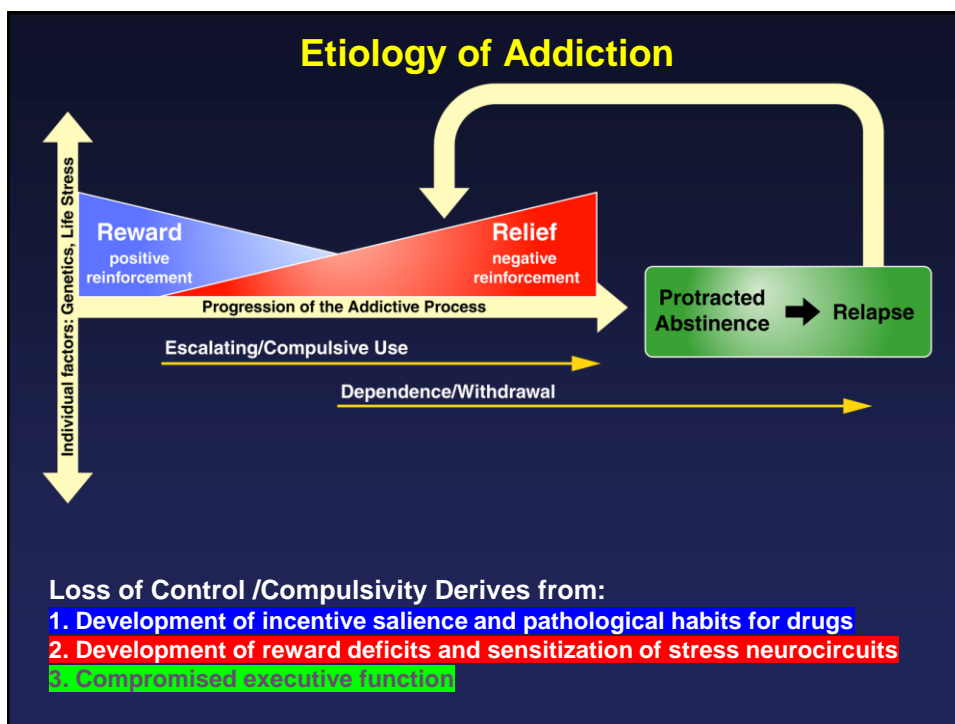
National Institute  
on Alcohol Abuse  
and Alcoholism



36



37



38

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

Dr. Laura Kwako

Adapted from Koob. *Curr Top Behav Neurosci*. 2011

The goals of the ANA are to identify how the three domains influence differences between people diagnosed with 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. Biological Psychiatry, 2016*

39

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

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

PREDICTORS	LATENT FACTORS	INDICATORS
<ul style="list-style-type: none"> <li>AUD diagnosis</li> <li>Gender</li> <li>Emotional abuse</li> <li>Sexual abuse</li> <li>Emotional neglect</li> </ul>	Negative Emotionality	<ul style="list-style-type: none"> <li>Positive urgency</li> <li>Neuroticism</li> <li>Extraversion</li> <li>Agreeableness</li> <li>Trait anxiety</li> <li>Aggression</li> </ul>
<ul style="list-style-type: none"> <li>AUD diagnosis</li> <li>Race</li> <li>Emotional abuse</li> <li>Sexual abuse</li> <li>Family history</li> <li>Age at first drink</li> </ul>	Executive Function	<ul style="list-style-type: none"> <li>ADHD</li> <li>Attentional impulsivity</li> <li>Motor impulsivity</li> <li>Non-planning impulsivity</li> <li>Conscientiousness</li> <li>Negative urgency</li> <li>Premeditation</li> <li>Perseverance</li> <li>Positive urgency</li> </ul>
<ul style="list-style-type: none"> <li>AUD diagnosis</li> <li>Race</li> <li>Emotional abuse</li> <li>Emotional neglect</li> </ul>	Incentive Salience	<ul style="list-style-type: none"> <li>MADRS depression</li> <li>Trait anxiety</li> <li>Distress when unable to drink</li> <li>Preoccupation with alcohol</li> <li>Time thinking about alcohol</li> <li>Strength of urge to drink</li> </ul>

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 factors were identified as predictors.

*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, 176: 744-753.*

40

## Implications of the Three Neurofunctional Domains framework for alcohol Use Disorder (AUD)

- **Reduces stigma:** AUD is considered a brain disorder that can be treated.
- **Individualizes diagnosis and treatment:** Facilitates treatment based on individual differences in which domain one enters the addiction cycle.
- **Facilitates recovery:** Provides a framework to help clinicians focus on the different triggers for relapse
- **Facilitates prevention:** Provides a framework for identifying individuals with domain specific vulnerabilities both genetic and environmental

For example, high scores in the negative emotionality domain showed significant associations with more frequent and heavier drinking and drinking to regulate negative affect (Votaw et al., 2021).

41

## Facilitating Medications Development



National Institute  
on Alcohol Abuse  
and Alcoholism



42

## NIAAA Alcohol Pharmacotherapy Evaluation Program (APEP):

- **Small business Innovation Research (SBIR) and Small Business Technology Transfer (STTR) programs** facilitate studies leading to FDA IND applications
- **Human laboratory screening studies** bridge gap between preclinical and clinical trials
- **NIAAA Clinical Investigations Group (NCIG)** conducts “fast success/fast fail” phase II clinical trials with 18 month turn-around time
- **NIAAA Alcohol Interaction Program (ALC InX)** conducts alcohol-medication interaction studies
- **Intramural program** conducts clinical studies on novel compounds with AUD treatment potential

43

## Future Challenges: Targets for Medications Development to Reverse Hyperkatifeia in Withdrawal/Negative Affect Stage

Target	Functional Action
<i>Prostress modulators</i>	
CRF	CRF <sub>1</sub> receptor antagonists
Dynorphin	κ-Opioid receptor antagonists
Vasopressin	V <sub>1b</sub> receptor antagonists
Norepinephrine	α <sub>1</sub> -Adrenergic receptor antagonists α <sub>2</sub> -Adrenergic receptor agonists β-Adrenergic receptor antagonists
Hypocretin	Hcrt-1 receptor antagonists Hcrt-2 receptor antagonists
Neuroimmune system	Neuroimmune modulators Tumor necrosis factor Phosphodiesterase inhibitors
<i>Antistress modulators</i>	
NPY	Y <sub>1</sub> receptor agonists
Nociceptin	Y <sub>2</sub> receptor antagonists
Endocannabinoids	Nociceptin receptor agonists FAAH inhibitors MAGL inhibitors
Oxytocin	Oxytocin receptor agonists

From: Koob GF. Drug Addiction: Hyperkatifeia/Negative Reinforcement as a Framework for Medications Development *Pharmacol Rev*, 2021, 73:163-201.

44

## Enhancing Recovery Research



National Institute  
on Alcohol Abuse  
and Alcoholism



45

## 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.

Hagman BT, Falk D, Litten R, Koob GF. Defining Recovery from Alcohol Use Disorder: Development of a NIAAA Research Definition  
American Journal of Psychiatry

46

## Greater Relief/Negative Emotionality at Baseline Predicted Greater Drinking Intensity and More Frequent Heavy Drinking During Recovery

Beta coefficient is the degree of change in the outcome variable for every 1-unit of change in the predictor variable

Alcohol Consumption Outcomes at 1 Year Following Treatment	% Heavy Drinking Days (PHDD)	
Predictor	$\beta$	<i>B (SE), p value</i>
Reward / incentive salience	.01	0.35 (0.87), $p = 0.690$
Relief / negative emotionality	.09	2.69 (0.53) $p < 0.001$
Loss of control / executive functioning	.001	0.02 (1.17), $p = 0.988$

- This study validated the 3 domains of the 3-stage addiction cycle. Addiction cycle domains were more strongly associated with outcomes than AUD symptoms.
- Using measures from Project MATCH and COMBINE, the results of this study supported the utility of the domains of the 3-stage addiction cycle in predicting AUD treatment outcomes and recovery one year post treatment.
- At one year follow-up, relief/ negative emotion scores were associated with drinks per day and percent heavy drinking days. (

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; 37:376-389.

47

## Additional Ongoing Recovery Research Projects

Within NIAAA's portfolio of recovery research, projects include:

- Measuring neurobehavioral markers and predictors associated with long-term trajectories of recovery and relapse
- Understanding mechanisms of behavioral change associated with recovery outside of treatment
- Identifying factors associated with different phases of recovery, such as peer helping and social networks
- Assessing the benefits of secular mutual help organizations in sustaining recovery



48

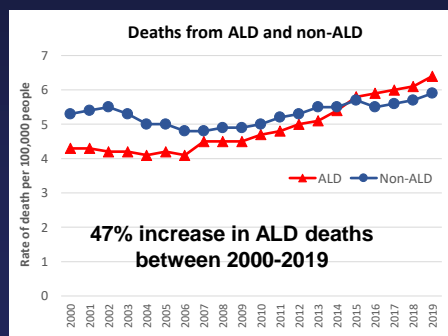
## Integration of Treatment of AUD with Treatment for Co-occurring conditions – Hepatologists are Leading the Way



49

## Integration of Treatment of AUD- Hepatologists are Leading the Way

- 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 ([Leggio and Jung, 2022](#))
- 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](#))

50

## Early Liver Transplants 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 similar survival outcomes and alcohol relapse rates as patients who receive a transplant after the 6-month waiting period.
- To build on this research, NIAAA issued a Request for Applications to encourage studies on factors that influence the selection, management, and outcomes of patients who receive early liver transplantation.

51

## Advancing Knowledge by Disseminating NIAAA Resources



National Institute  
on Alcohol Abuse  
and Alcoholism



52

## 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)


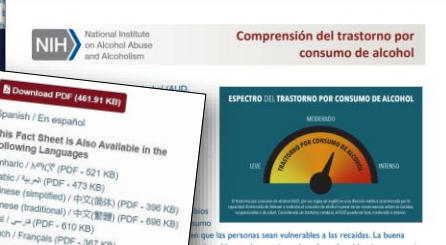






53

## Information for the Public

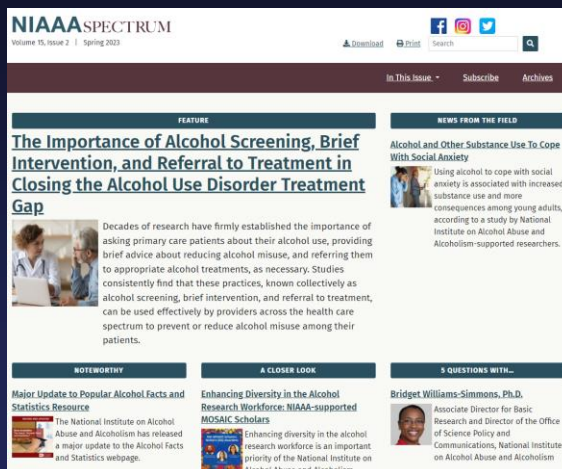
- NIAAA offers the public research-based information on drinking and its impact, in plain language.
- Materials are available in English and Spanish, and select content is also translated to more than a dozen languages.
- Visit [niaaa.nih.gov](http://niaaa.nih.gov) to find these free resources—and share them with your stakeholders and colleagues.

54

## NIAAA Spectrum

- *NIAAA Spectrum* is an online newsletter featuring articles and news updates on NIAAA and the alcohol field.
- Explore the newsletter and sign up for updates at [spectrum.niaaa.nih.gov/](https://spectrum.niaaa.nih.gov/)



55

## NIAAA's Open-Access Peer-Reviewed Journal

- 2024 marks the 50<sup>th</sup> anniversary
- Published online on a continuous, rolling basis
- Covers a wide variety of research topics and disciplines through invited reviews
- 2022 Impact Factor of 9.4

Visit the journal's website or LinkedIn page for more information on ARCR and its anniversary celebrations

[arcr.niaaa.nih.gov/](https://arcr.niaaa.nih.gov/)

[linkedin.com/company/alcohol-research-current-reviews](https://linkedin.com/company/alcohol-research-current-reviews)



56

## Summary: Strategies to Close The Treatment Gap

- Implement effective and efficient **screening, brief intervention, and referral to treatment** in a variety of clinical settings.
- Emphasize the identification and treatment of **mild AUD** before transition to moderate to severe AUD
- Combat alcohol-related **stigma** – words matter
- Broaden **clinical endpoints** for the approval of medications to treat alcohol use disorder to include reductions in drinking ‘risk levels,’ which are associated with clinical benefits.
- Facilitate research using the new NIAAA **definition of recovery**, which defines recovery as a process of behavioral change with measurable outcomes.
- Apply the **Addictions Neuroclinical Assessment** and the three **domains of addiction constructs** to improve treatment and recovery
- Educate **health professionals** and the **public** about how alcohol affects health, alcohol misuse and AUD, and treatment options.

Koob GF. Alcohol Use Disorder Treatment: Problems and Solutions. Annu Rev Pharmacol Toxicol. 2024 Jan 23;64:255-275. PMID: [38261428](#).

57

## THANK YOU!

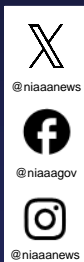
NIAAA is your source for credible, evidence-based resources on alcohol’s effects on health.

Visit our website  
[www.niaaa.nih.gov](http://www.niaaa.nih.gov)

Subscribe to  
our email updates



Follow us on  
social media



*Special thanks to:*  
**Laura Brockway-Lunardi**  
Fred Donodeo  
Kathy Jung  
Laura Kwako  
Laura Manella  
**Patricia Powell**  
Svetlana Radaeva  
Gregory Roa  
**Aaron White**  
**Bridget Williams-Simmons**



National Institute  
on Alcohol Abuse  
and Alcoholism



58