NIAAA: State of the Science

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American Society of Clinical Psychopharmacology (ASCP)
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No Disclosures

Relative Scope of the Problem: Opioids versus Alcohol

Opioids	
Misuse*	**11,401,000**
% of population	**4.2**
OUD	**2,110,000**
% of population	**0.8**
ED visits	**408,079** Primary reason
	1,461,770 All opioid-related
Deaths	**47,600** Total overdoses
	17,029 Prescription opioids
	28,400 Fentanyl and similar
	15,482 Heroin

Opioid + alcohol overdose deaths
7,270 (15% of all opioid overdose deaths involved alcohol in 2017)

Alcohol	
Use	**178,736,000**
% of population	**65.7**
AUD	**14,500,000**
% of population	**5.3**
ED visits	**1,714,757** Primary reason
	4,936,690 All alcohol-related
Deaths	**~88,000** Total deaths
	49,544 Acute – overdose, injury
	38,880 Chronic – liver, cancer

***Any past year heroin use or prescription opioid use other than as prescribed

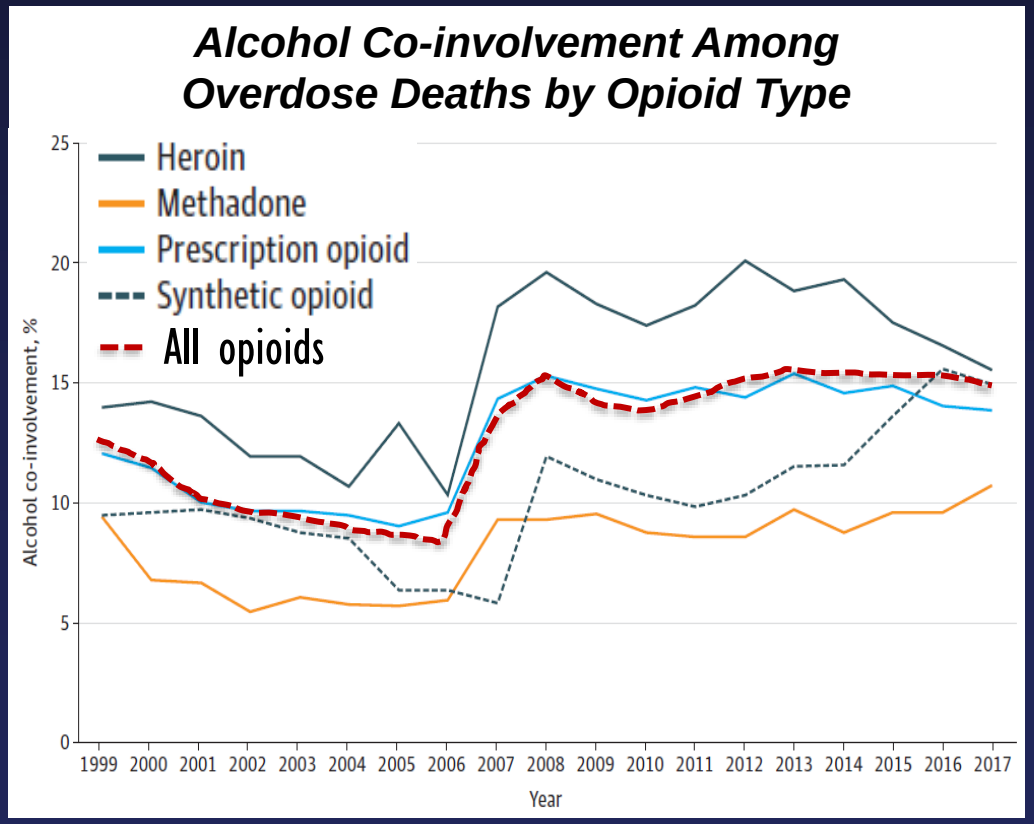
Sources: NSDUH, 2017 people aged 12+; Nationwide Emergency Department Sample, 2016; CDC Overdose Death Data, 2017; CDC Alcohol Related Death Inventory, 2006-2010; White et al, 2018

Courtesy of Dr. Aaron White, NIAAA

NIH National Institute on Alcohol Abuse and Alcoholism

Alcohol Involvement in Opioid Overdose Deaths

- Opioid deaths, 1999-2017: **399,230** (per CDC WONDER database)
  - Alcohol co-involvement for all opioid overdose deaths increased nonlinearly from 12.4% in 1999 to 14.7% in 2017
  - Alcohol co-involvement persisted near **15% for all opioid overdoses since 2008**
- State-level rates of binge drinking were significantly correlated with alcohol co-involvement in all opioid overdose deaths
- Alcohol use is a modifiable risk factor for opioid overdose

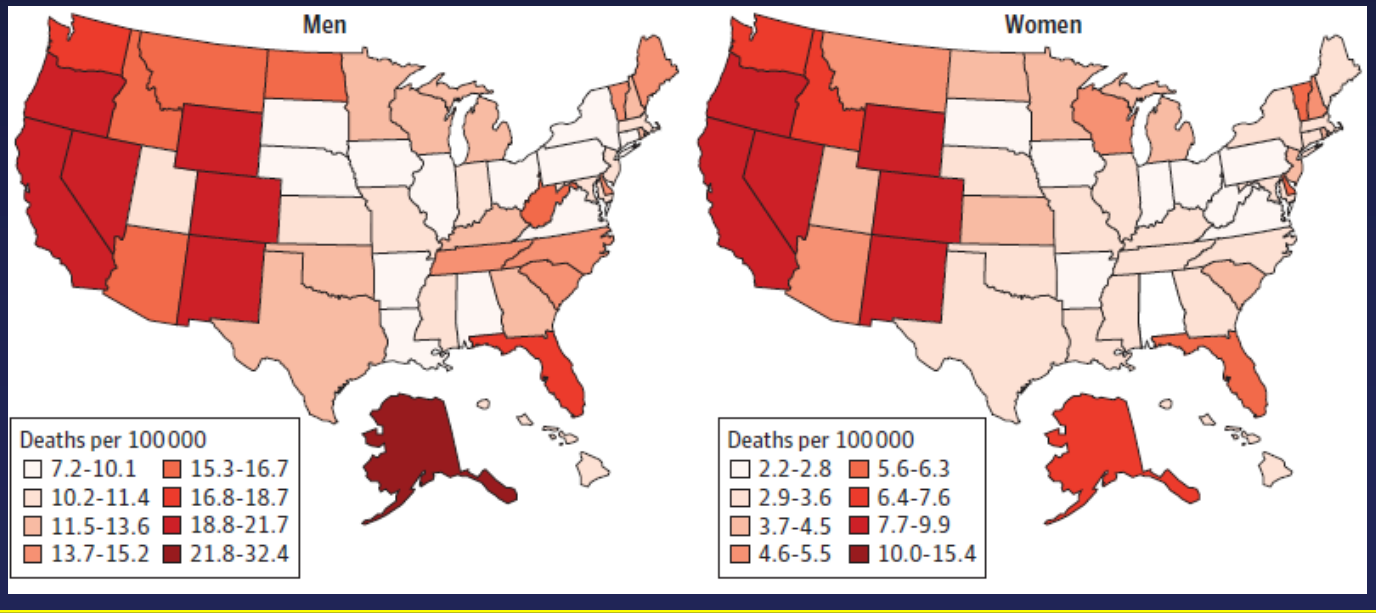


Citation: Tori ME, Larochelle MR, and Naimi TS. *JAMA Netw Open*. 2020 Apr 1;3(4):e202361.

Alcohol-Related Mortality: A Series of Reports

- **Alcohol-related deaths, 1999-2017: 944,880 (per CDC WONDER database)**
  - **Alcohol-related mortality doubled from 1999 to 2017**
  - **Death rates were highest among men and middle-aged and older adults (ages 45-74)**
  - **Increase in death rate over time was greater in women than men**

Age-standardized rates of alcohol-induced death among non-Latino white individuals 2000-2003



Citations: White AM, Castle IP, Hingson RW, and Powell PA. *Alcohol Clin Exp Res*. 2020 Jan;44(1):178-187.
Spillane S, Shiels MS, Best AF, Haozous EA, Withrow DR, Chen Y, Berrington de Gonzalez A, and Freedman ND. *JAMA Netw Open*. 2020 Feb 5;3(2):e1921451

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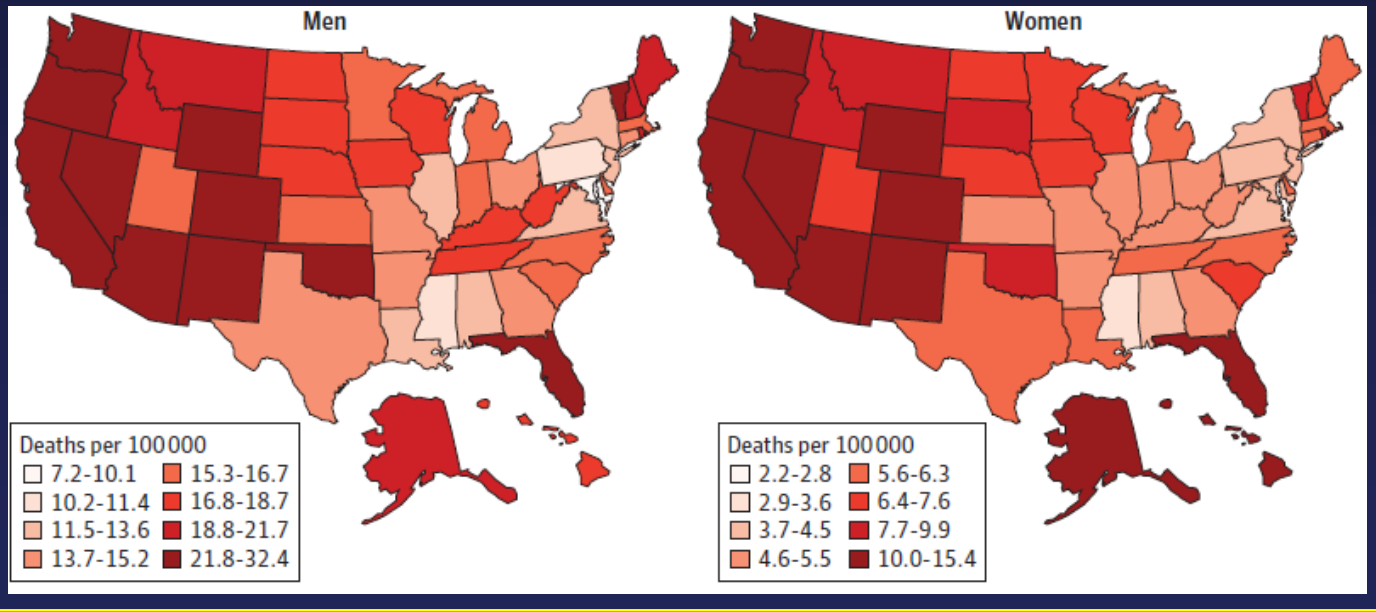

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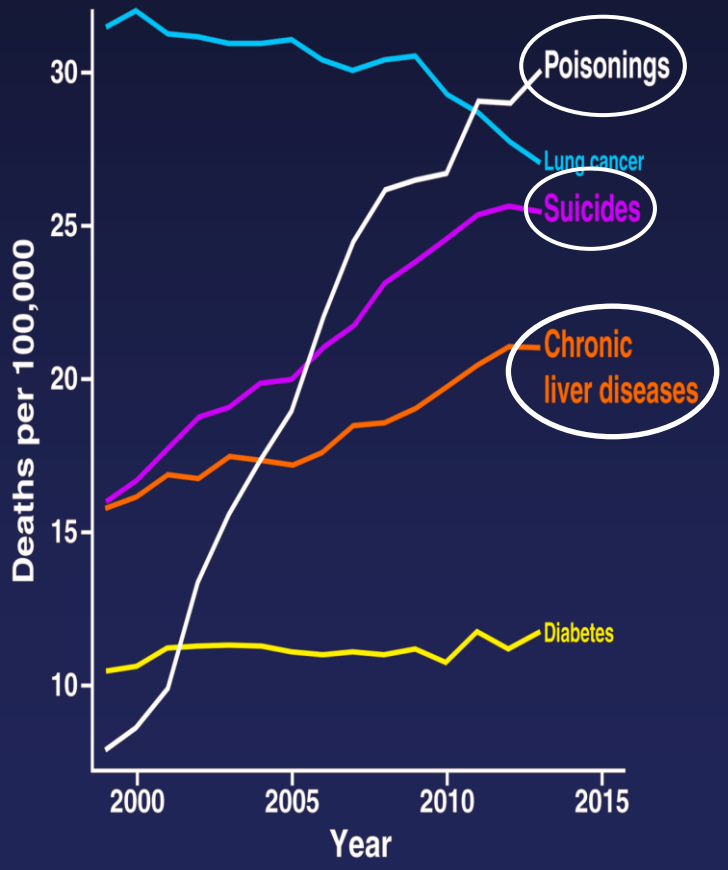
“Deaths of Despair”: Update

Mortality by cause among White non-Hispanics (age 45-54)



Case & Deaton. PNAS 2015;112:15078-15083

Deaths of despair contribute to the decreasing life expectancy in the U.S. observed since 2014 (Woolf et al., 2019)

Alcohol plays a prominent role in deaths of despair, contributing to:

~20% of all drug overdoses (Warner et al., 2016)

~26% of all suicides (Ertl et al., 2019)

~50% of liver disease deaths (Yoon and Chen, 2018)

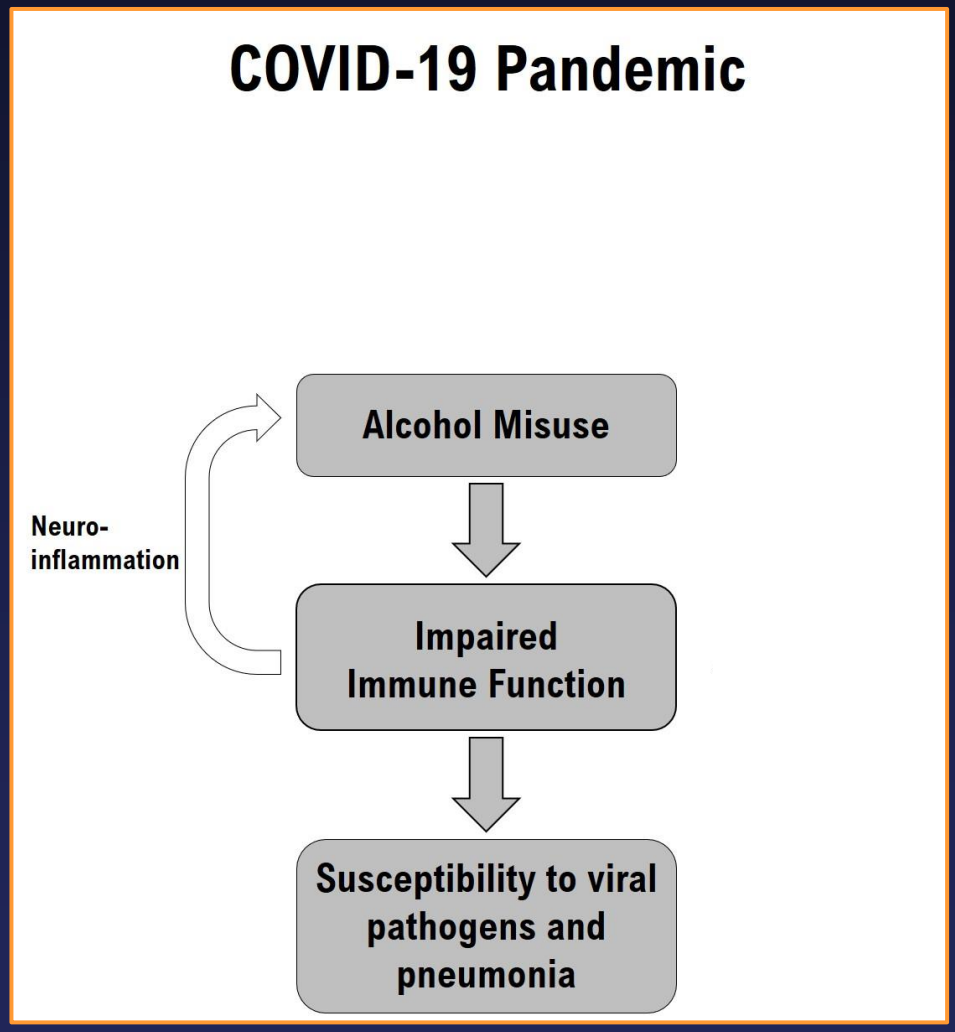
Since 2015, these patterns of increased mortality are now observed across many racial/ethnic groups and age groups (Woolf et al., 2018)

Role of Alcohol in the COVID-19 Pandemic

Impact of alcohol use on COVID pandemic

Biological effects: Alcohol effects on immune function

Chronic alcohol consumption increases the risk for Acute Respiratory Distress Syndrome (ARDS), with increased need for mechanical ventilation, prolonged intensive care unit stay, and higher incidence of mortality



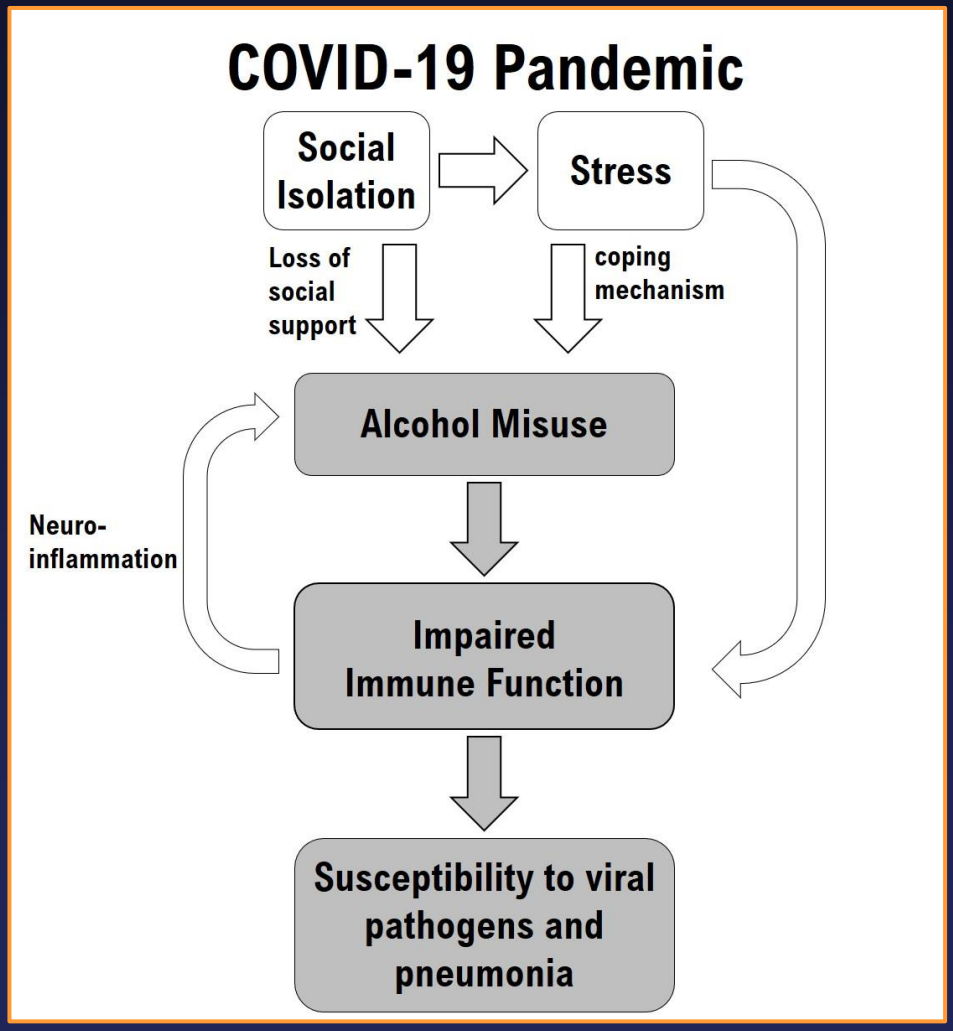
Role of Alcohol in the COVID-19 Pandemic

Impact of COVID pandemic on alcohol use and treatment

Isolation: Physical distancing can lead to social isolation or loss of social support, which can lead to stress

Stress: Drinking to cope with the stress of the pandemic

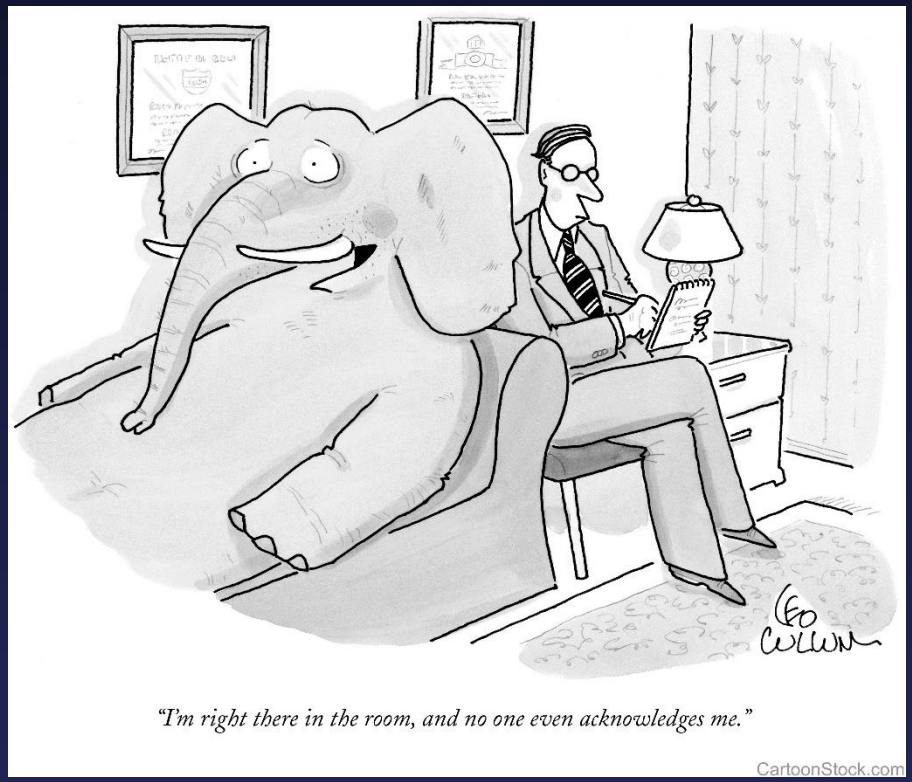
Treatment and Recovery: Physical distancing poses challenges for those with alcohol use disorder and emphasizes the need for telehealth and virtual meeting options for individuals seeking treatment or in recovery from AUD



Alcohol and Mental Health – The Elephant in the Room

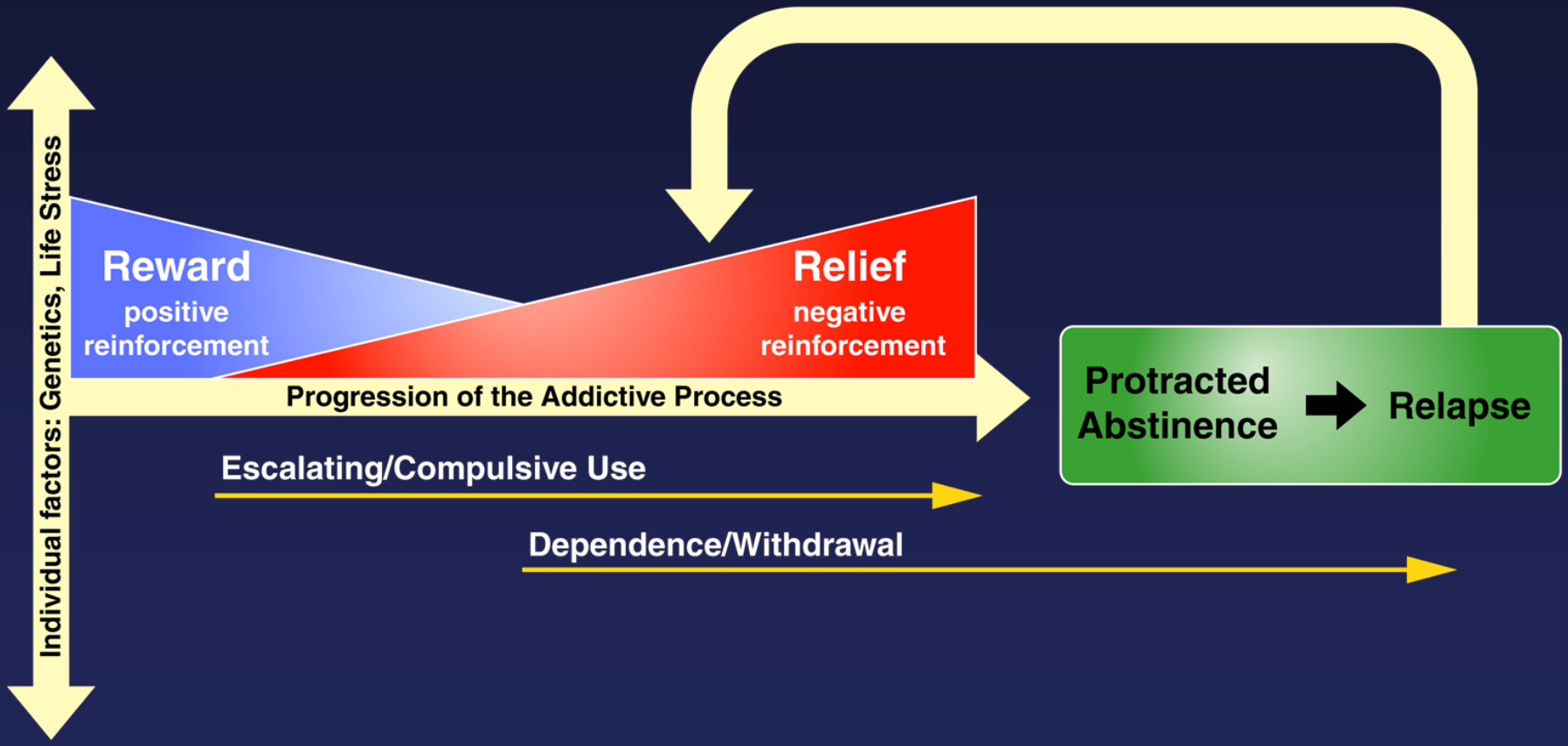
Alcohol misuse correlates with poor mental health

- Often precedes diagnoses of mental health conditions
- Commonly used in an effort to cope with symptoms
- In the end it makes the prognoses worse
- Similarly, mental health conditions complicate treatment for AUD

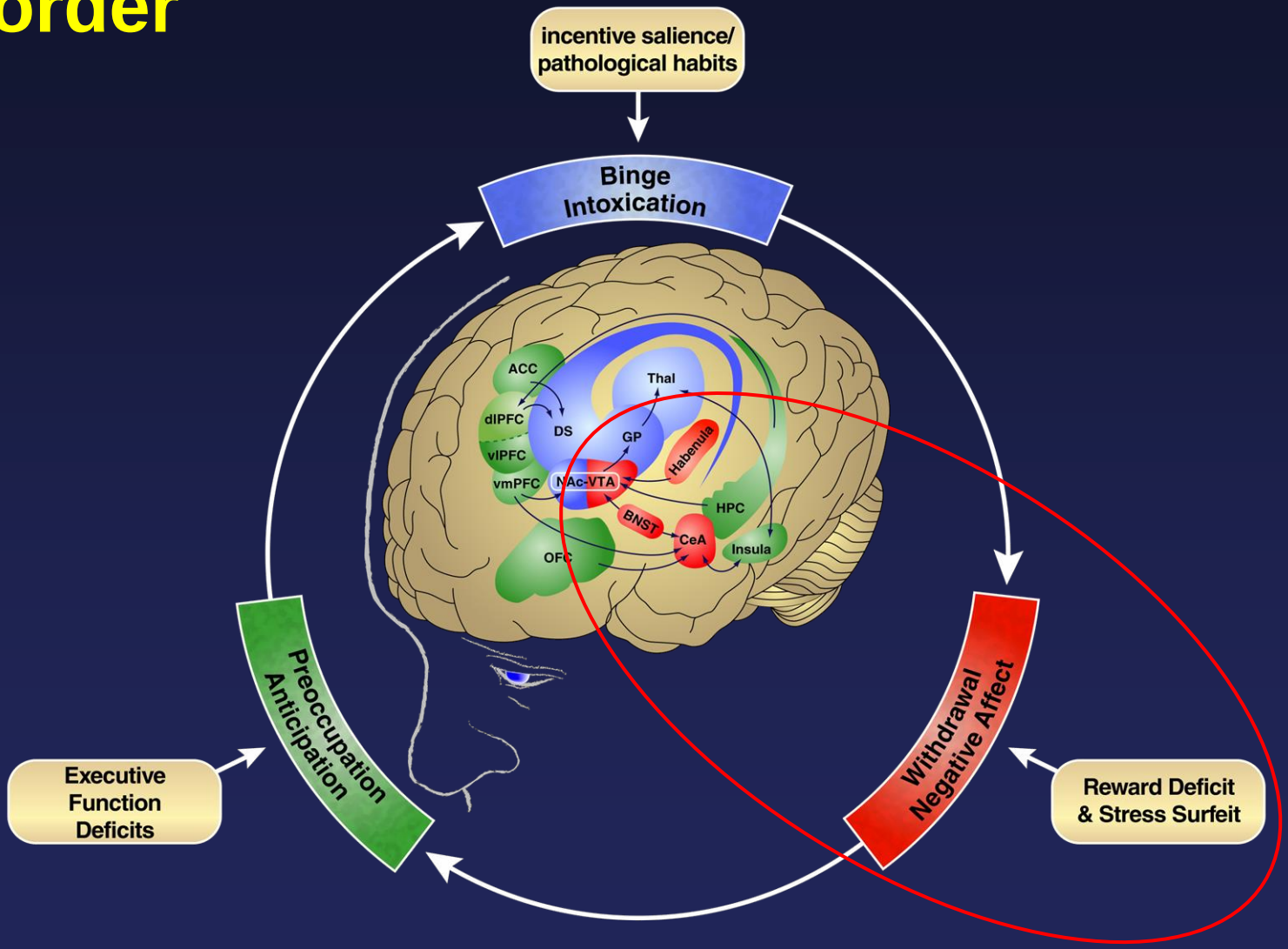


Sources: Centanni, S. W., Bedse, G. , Patel, S. and Winder, D. G. (2019), Driving the Downward Spiral: Alcohol-Induced Dysregulation of Extended Amygdala Circuits and Negative Affect. Alcohol Clin Exp Res; Mäkelä P, Raitasalo K, Wahlbeck K (2015) Mental health and alcohol use: a cross-sectional study of the Finnish general population, European Journal of Public Health, 25, 2, 225–231; Markou A, Kosten TR, Koob GF (1998) Neurobiological Similarities in Depression and Drug Dependence: A Self-Medication Hypothesis. Neuropsychopharmacology 18, 135–174.

Etiology of Addiction

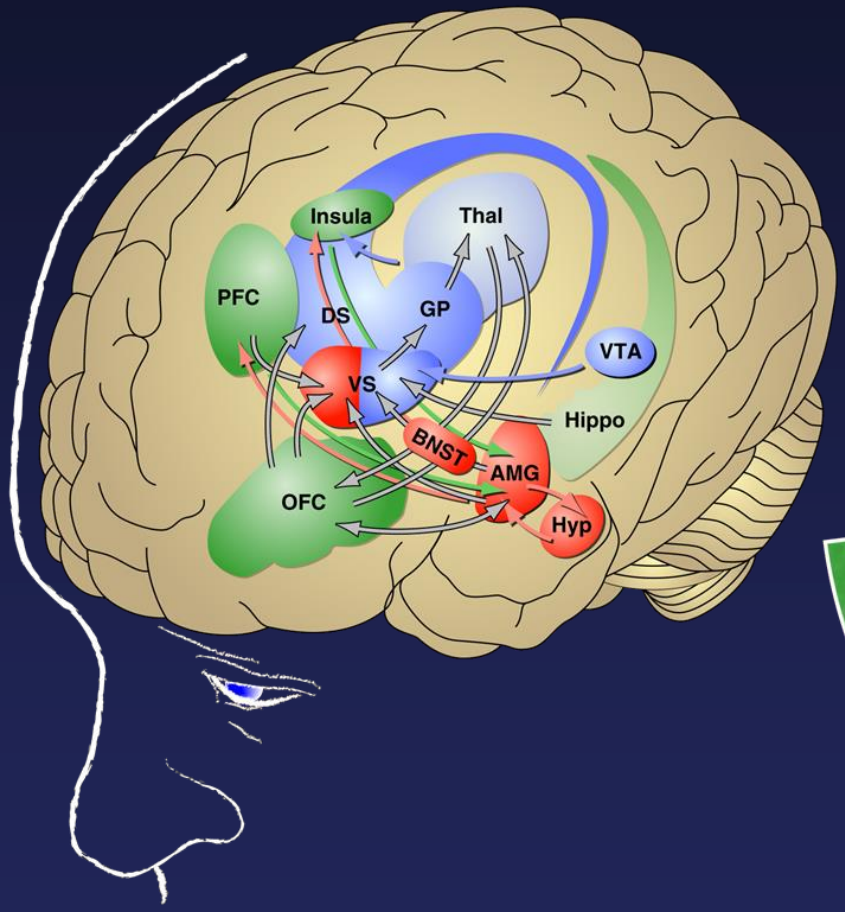


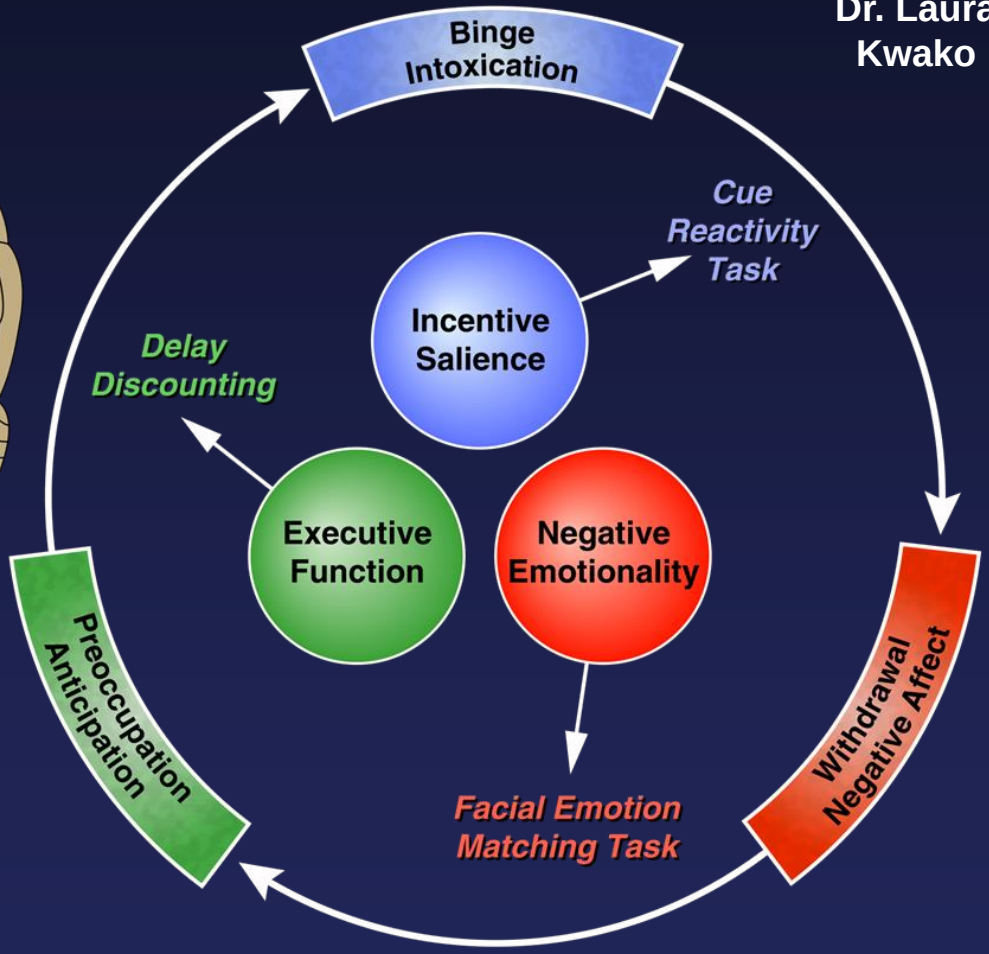
Conceptual Framework for Neurobiological Bases Driving Substance Alcohol Use Disorder



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

Dr. Laura Kwako





Adapted from Koob. Curr Top Behav Neurosci. 2011

Modified from: Kwako LE, Momenan R, Litten RZ, Koob GF, Goldman D. Addictions neuroclinical assessment: a neuroscience-based framework for addictive disorders. Biological Psychiatry, 2016, 80:179-189

Unidimensional Factor Structure, Construct Validity, and Measurement Invariance of the ANA Negative Emotionality Domain Among Individuals Seeking Treatment for AUD

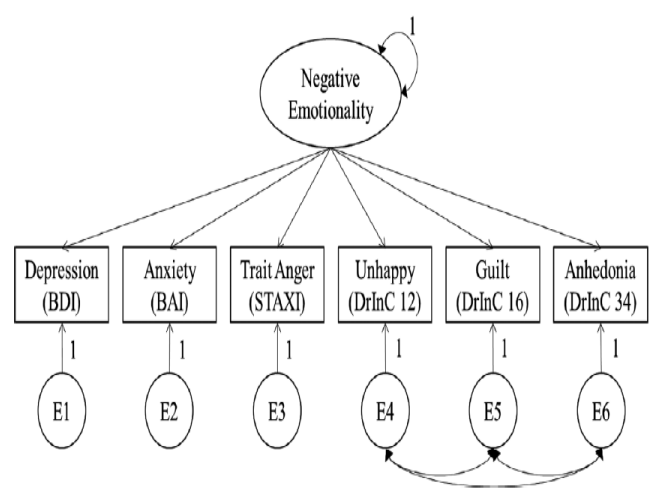


Table 1. Descriptive Statistics of All Measures Included in the Analysis at Baseline and 6- and 12-Month Follow-Ups

	Baseline		6-Month Follow-up		12-Month Follow-Up	
Measure	*n*	*M* (SD) or %	*n*	*M* (SD) or %	*n*	*M* (SD) or %
Depression (BDI)	551	14.8 (9.9)	455	11.1 (10.0)	477	11.3 (10.9)
Anxiety (BAI)	554	14.9 (11.5)	454	11.3 (11.6)	487	11.2 (11.5)
Trait Anger (STAXI)	538	22.3 (6.3)	458	20.1 (6.2)	487	19.7 (6.1)
DrInC Item 12: "I have been unhappy because of my drinking."	236	Never = 5.5% Once to twice a month = 30.5% Twice a week = 21.6% Daily/almost daily = 42.4%	169	Never = 26.0% Once or twice = 26.0% Once or twice a month = 10.1% Once a week = 7.1% Twice a week = 8.9% Almost every day = 21.9%	160	Never = 23.8% Once or twice = 27.5% Once or twice a month = 10.0% Once a week = 5.0% Twice a week = 11.3% Almost every day = 22.5%
DrInC Item 16: "I have felt guilty or ashamed because of my drinking."	230	Never = 6.0% Once to twice a month = 29.5% Twice a week = 21.4% Daily/almost daily = 43.2%	169	Never = 25.4% Once or twice = 22.5% Once or twice a month = 14.2% Once a week = 8.3% Twice a week = 9.5% Almost every day = 20.1%	160	Never = 24.4% Once or twice = 24.4% Once or twice a month = 11.3% Once a week = 5.0% Twice a week = 11.3% Almost every day = 23.8%
DrInC Item 34: "I have lost interest in activities or hobbies because of my drinking."	216	Never = 12.0% Once to twice a month = 26.9% Twice a week = 28.7% Daily/almost daily = 32.4%	167	Not at all = 40.1% A little = 25.1% Somewhat = 15.6% Very much = 19.2%	163	Not at all = 36.8% A little = 27.6% Somewhat = 13.5% Very much = 22.1%
Percent days abstinent	562	47.0 (30.0)	526	82.8 (27.6)	494	82.9 (29.1)
Drinks per drinking day	562	20.2 (13.0)	526	7.2 (10.0)	494	6.2 (9.5)

Table 4. Concurrent Associations between the Negative Emotionality Construct and Alcohol Use, Reasons for Drinking, and Gender

	Baseline *r* (95% CI)	6-month *r* (95% CI)	12-month *r* (95% CI)
Percent Days Abstinent	−0.066 (−0.192, 0.091)	−0.321 (−0.446, −0.178)	−0.331 (−0.456, −0.223)
Drinks per Drinking Day	0.297 (0.176, 0.410)	0.367 (0.211, 0.489)	0.393 (0.263, 0.513)
Drinks per Day	0.239 (0.100, 0.394)	0.466 (0.255, 0.617)	0.329 (0.234, 0.452)
Percent Heavy Drinking Days	0.133 (−0.029, 0.262)	0.349 (0.195, 0.474)	0.364 (0.261, 0.487)
RFD Drinking due to Negative Emotions	0.482 (0.384, 0.605)	0.538 (0.311, 0.708)	0.635 (0.425, 0.825)
RFD Drinking due to Social Pressure	0.188 (−0.327, −0.036)	−0.074 (−0.289, 0.161)	−0.129 (−0.342, 0.080)
RFD Drinking due to Urges/Withdrawal	0.336 (0.193, 0.466)	0.378 (0.169, 0.546)	0.346 (0.140, 0.524)
Gender (0 = women, 1 = men)	−0.244 (−0.381, −0.114)	−0.199 (−0.344, −0.048)	−0.127 (−0.273, 0.006)

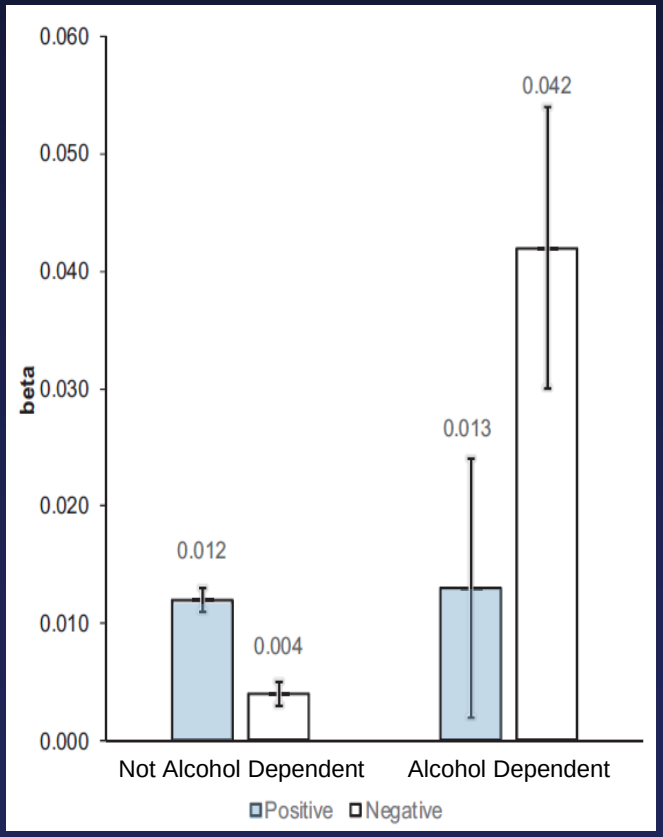
The negative emotionality domain demonstrated concurrent associations with more frequent and heavier drinking and drinking to regulate negative affect

Citation: Votaw VR, Pearson MT, Stein E, Witkiewitz K. *Alcohol Clin Exp Res*, 2020 Mar;44(3):679-688.

Positive and Negative Reinforcement are Differentially Associated with Alcohol Consumption as a Function of Alcohol Dependence

- Researchers used longitudinal data in young adults (ages 18-30) to test whether positive and negative reinforcement associated with alcohol consumption differed as a function of alcohol dependence (AD; DSM-III)
- 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

Within-person associations between positive and negative reinforcement and alcohol consumption as a function of AD diagnosis



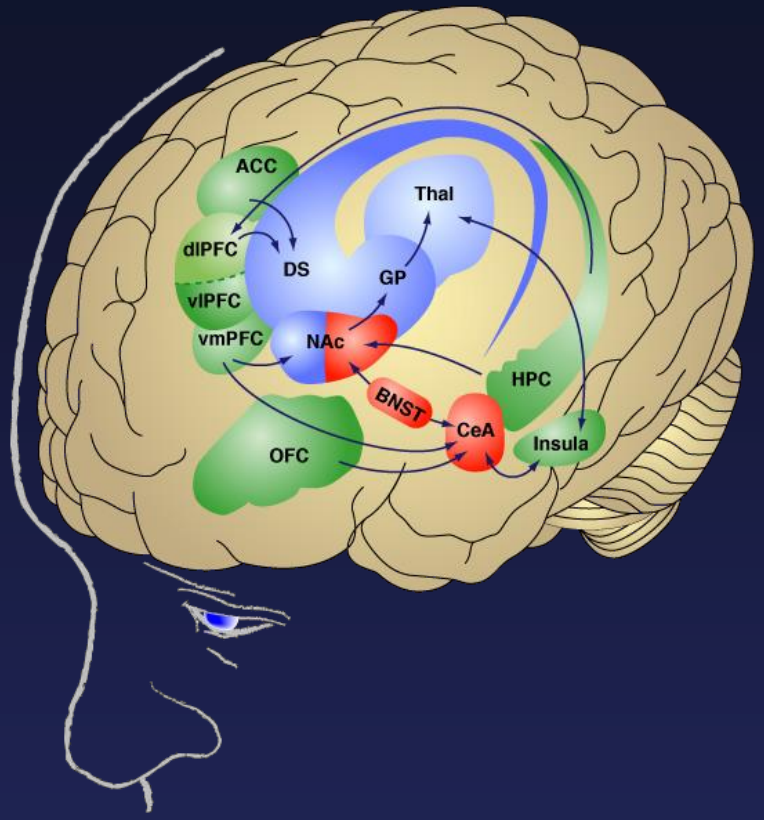
Citation: Cho SB, Su J, Kuo SI, Bucholz KK, Chan G, Edenberg HJ, McCutcheon VV, Schuckit MA, Kramer JR, and Dick DM. Psychol Addict Behav. 2019 Feb;33(1):58-68.

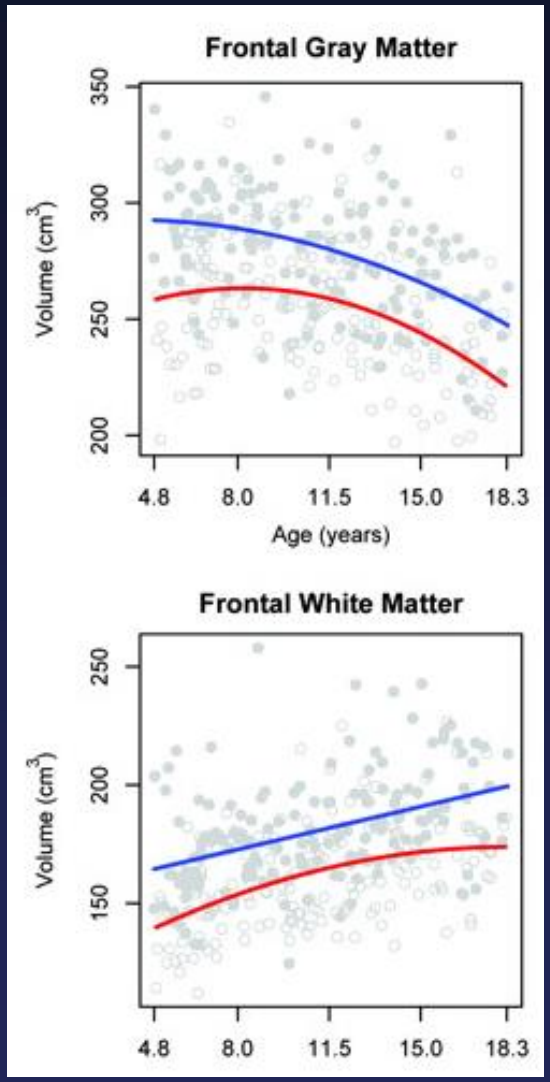
Update: Diagnosis and Treatment of Fetal Alcohol Spectrum Disorders

- FASD prevalence: as high as **1.1 – 5%** among four U.S. communities (May et al., 2018)

- Current research to improve screening, diagnosis, prevention, and treatment of FASD:
  - Refining **3D facial imaging** to improve diagnosis
  - Adapting a **neurobehavioral screening** tool (Decision Tree) for mobile use
  - Developing culturally-appropriate approaches for the **prevention** of alcohol-exposed pregnancies
  - Exploring **maternal immune profiles** as biomarkers of prenatal alcohol exposure and risk of neurodevelopmental delay
  - Testing **choline supplementation** to mitigate adverse effects of prenatal alcohol exposure
- NIAAA has established working groups of researchers to reach consensus and harmonize classification systems for research on FASD

Frontal Lobe Changes During Adolescence





- **Planning, decision-making, impulse control, memory, language, processing social cues**
- **Gray matter goes down, white matter goes up, overall size stays about the same**

From: Ball W et al with the Brain Development Cooperative Group (2012). Total and regional brain volumes in a population-based normative sample from 4 to 18 years: the NIH MRI Study of Normal Brain Development. *Cerebral Cortex*, 22(1):1-12.

Update: Longitudinal Brain Development Studies

National Consortium on Alcohol and Neurodevelopment in Adolescence (N-CANDA)

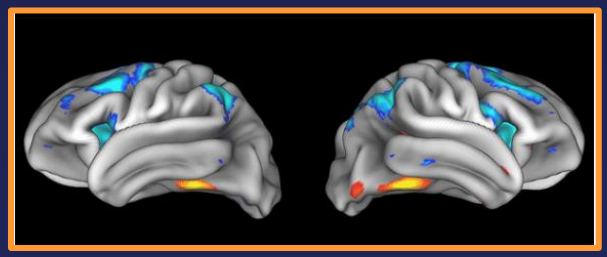
- Ongoing multisite longitudinal study of youth (ages 12-21) to elucidate the effects of alcohol exposure on the developing brain

- Recent results include evidence that youth who initiate heavy drinking have accelerated declines in gray matter volume and slower expansion of white matter at later time points

- N-CANDA laid the methodological foundation for the ABCD study

Adolescent Brain Cognitive Development (ABCD) Study

- Ongoing multisite study tracking the biological, cognitive, and behavioral development of youth (ages 9-10) over a 10 year period
- Enrollment is now complete! (N=11,875)
- Baseline curated data released in April 2019, available through the NIMH Data Archive
  - https://data-archive.nimh.nih.gov/abcd

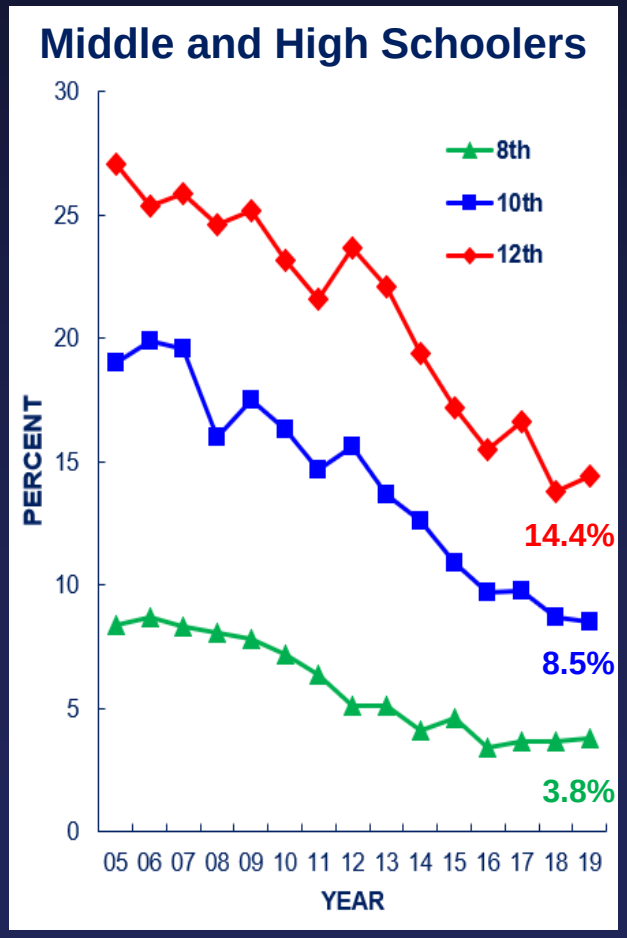


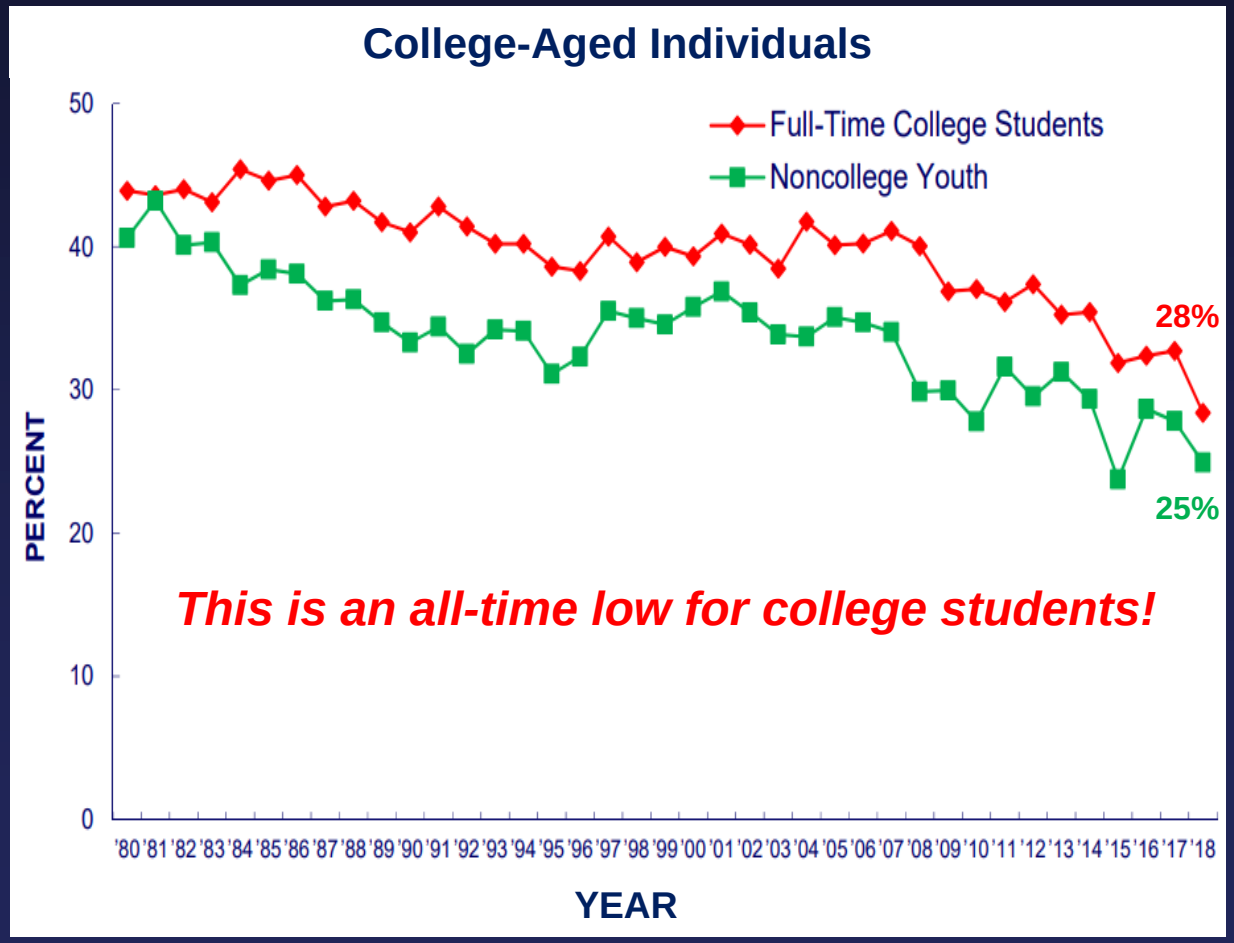
MRI of adolescent brains activated during a memory task in ABCD study.

Photo credit: Dr. Richard Watts and Dr. Hugh Garavan

Success in Reducing Binge Drinking in Underage and College-Aged Individuals

FIVE OR MORE DRINKS IN A ROW:
Trends in 2-Week Prevalence

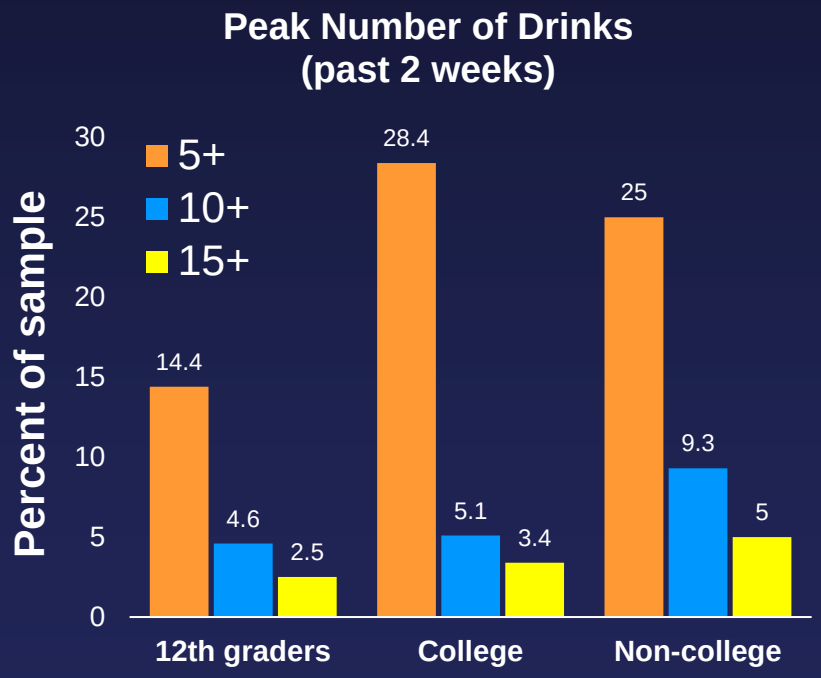




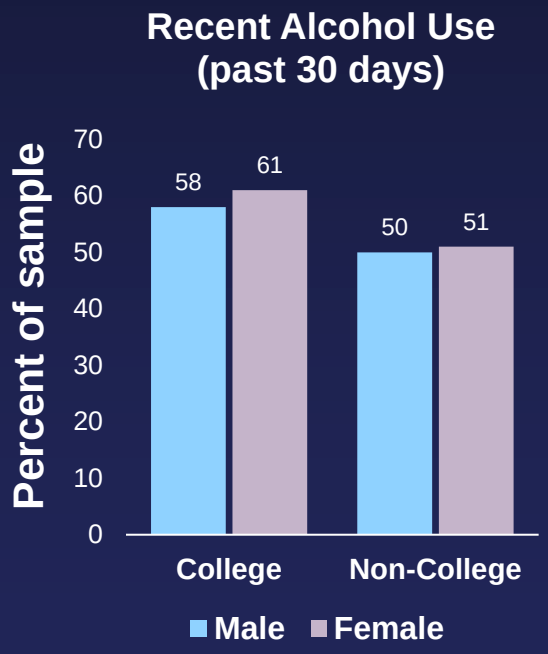
Source: Monitoring the Future 2018 and 2019

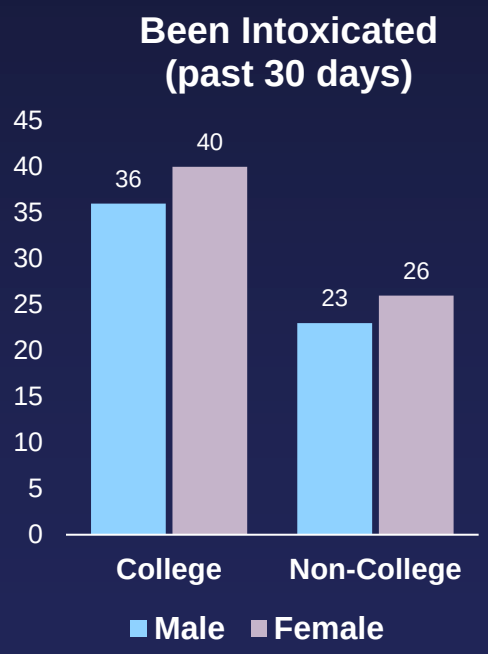
Emerging Issue:
But…It's Not All Good News For Young People

High Intensity Drinking



Disappearance of Gender Gaps and Reversal of Gender Patterns





Source: Monitoring the Future 2018 and 2019

Emerging Issue: Alcohol and Women's Health

- **Gaps between women and men are narrowing** for prevalence, early onset drinking, frequency and intensity of drinking, having AUD, drunk driving, and self-reported consequences (Grucza et al., 2018; Slade et al., 2016; White et al, 2015)

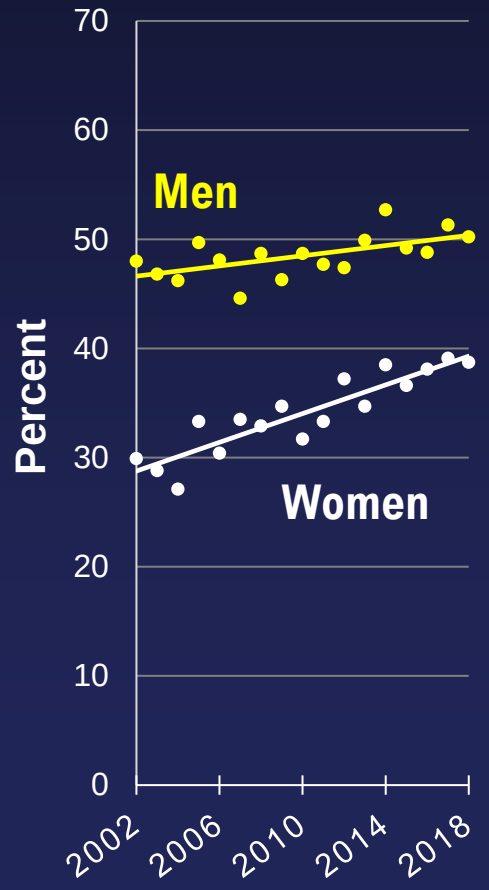
- Women **more likely to experience** blackouts, liver inflammation, brain atrophy, cognitive deficits, certain cancers, negative affect during withdrawal and stress, and anxiety-induced relapse (Becker and Koob, 2016)

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

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

Emerging Issue: Rising Alcohol Use Among Older Adults (Aged 65+)

From 2002-2018, past-month alcohol use increased for men and women aged 65 and older, with a greater increase observed in women.



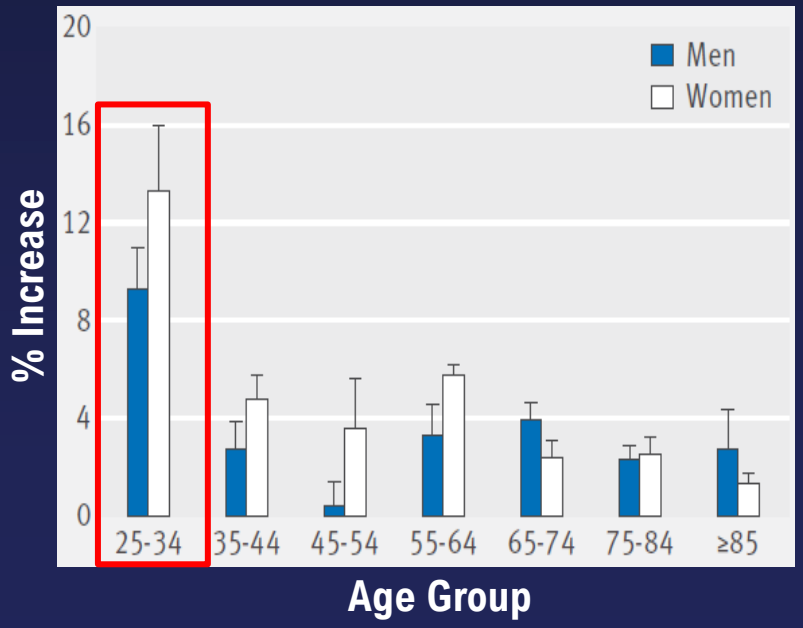
Source: NSDUH, 2018

- **1 in 10 older adults in the U.S. engage in binge drinking** (Han et al., 2019)
- Alcohol misuse among this population contributes to:
  - **Accelerated aging** in some brain regions, including the frontal cortex (Sullivan et al., 2018)
  - Pronounced **reductions in brain volume** in multiple cortical regions (Sullivan et al., 2018)
  - **Impaired cognitive function, learning, memory, and motor function** (Woods et al., 2016)
- In collaboration with the **National Institute on Aging**, NIAAA supports research investigating mechanisms by which alcohol affects brain aging processes to produce dementias and influences development of Alzheimer's disease

Priority: Integrating Treatment of Alcohol Use Disorder and Alcohol-Associated Liver Disease

- Nearly half of liver disease deaths are related to alcohol misuse
- ALD is the most common alcohol-related cause of death and the leading cause of liver transplantation
- ALD-related deaths have increased by 40.6% since 1999 (Woolf et al., 2019)
- **Greatest increase in deaths driven by alcoholic cirrhosis seen in young adults ages 25-34** (Tapper and Parikh, 2018)

Average yearly increase in mortality due to liver disease, 2009-2016



From: Tapper and Parikh BMJ 2018;362:k2817

Paradigm shift:
"Whole person" treatment approach

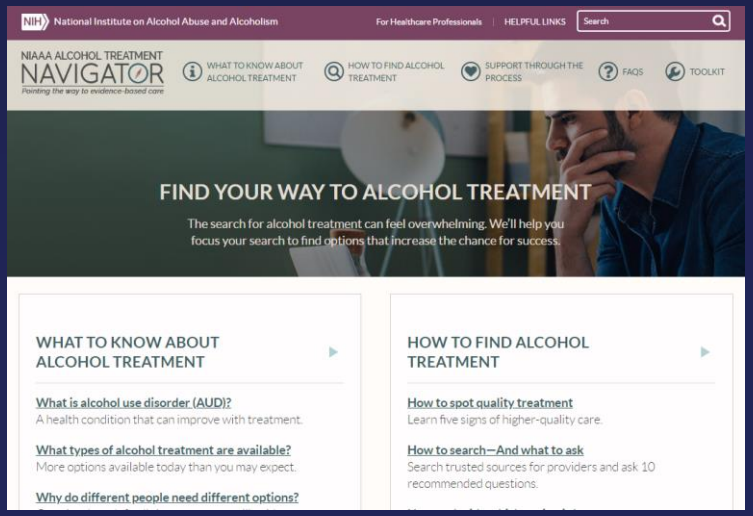
- **Integrated treatment** of ALD and AUD may improve patient outcomes
- A recent study of patients recovering from alcoholic hepatitis found that participation in alcohol rehabilitation shortly after hospital discharge was associated with improved outcomes, including reduced hospital readmission rates, alcohol relapse, and mortality (Peeraphatdit et al., 2019)

Priority: Resources for Clinicians

Updates to Alcohol Treatment Navigator

New portal to help healthcare professionals **build or expand their referral lists** to include providers offering science-backed AUD treatments, including **telehealth options**, that meet the varied needs of their patients

https://alcoholtreatment.niaaa.nih.gov/healthcare-professionals



In Development: Clinician's Core Resource

Modules include:

- Presentation in primary care
- Role in common co-occurring conditions
- Neuroscience
- Diagnostic criteria, recommended drinking limits
- Evidence-based therapies/medications
- Addressing stigma
- Interactions with commonly used medications

U.S. Dietary Guidelines for Alcohol Consumption

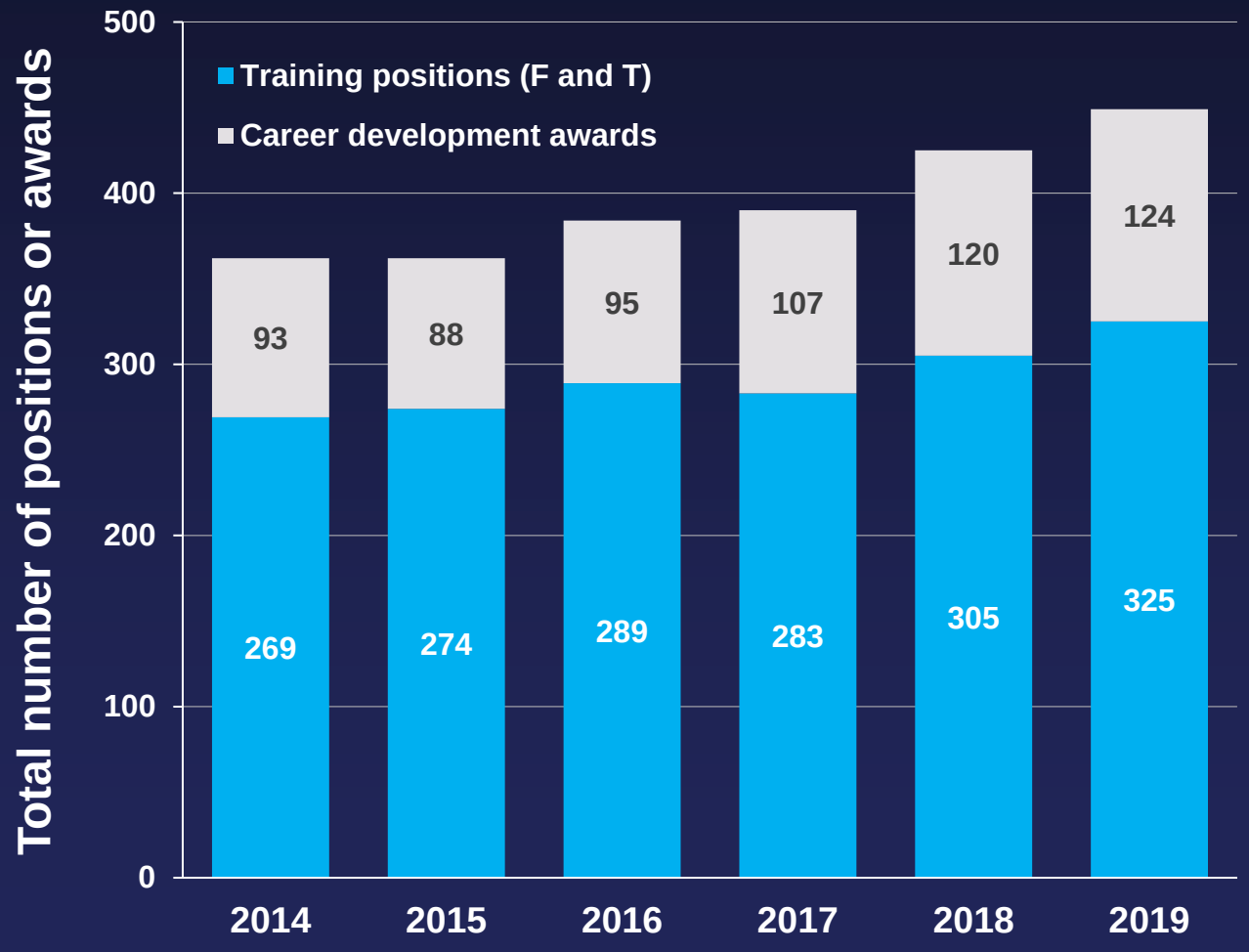
- **For adults 21 and older:**
  - No more than 2 drinks per day for men
  - No more than 1 drink per day for women
- **For individuals under age 21:**
  - No alcohol*
- **Others should avoid alcohol completely, including those who:**
  - Plan to drive or operate machinery, or participate in activities that require skill, coordination, and alertness
  - Have certain medical conditions or take certain medications
  - Are recovering from alcohol use disorder or are unable to control the amount that they drink
  - Are pregnant or trying to become pregnant

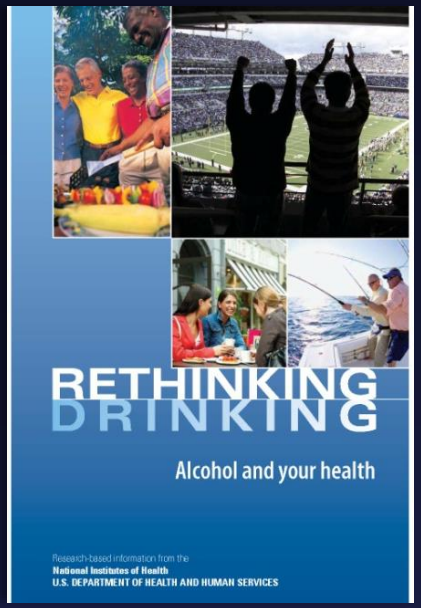
**The National Minimum Legal Drinking Age Act requires that States prohibit persons under 21 years of age from purchasing or publicly possessing alcoholic beverages as a condition of receiving State highway funds.*

Are we experiencing a cultural shift in attitudes about alcohol use?

- Observance of sober months (Dry January, Sober October, etc) is gaining popularity
- Sober Curious movement is also receiving a lot of attention: Practicing mindfulness versus going along with the dominant drinking culture
- These trends, largely driven by millennials, encourage a focus on wellness

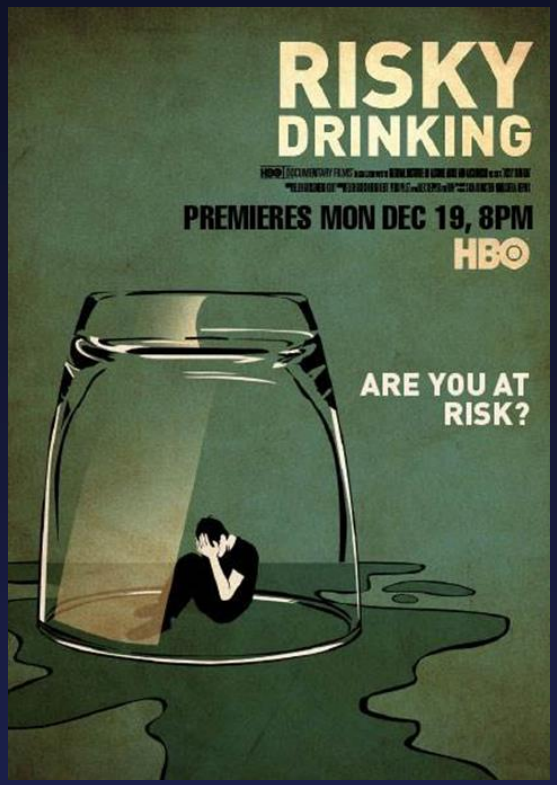
Supporting the Next Generation of Alcohol Researchers:
Increases in NIAAA Training and Career Development Awards





NIAAA

Your source for credible, evidence-based information about alcohol and health.



www.niaaa.nih.gov

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