

# Joint Meeting of the National Advisory Council on Alcohol Abuse and Alcoholism, National Cancer Advisory Board, and National Advisory Council on Drug Abuse



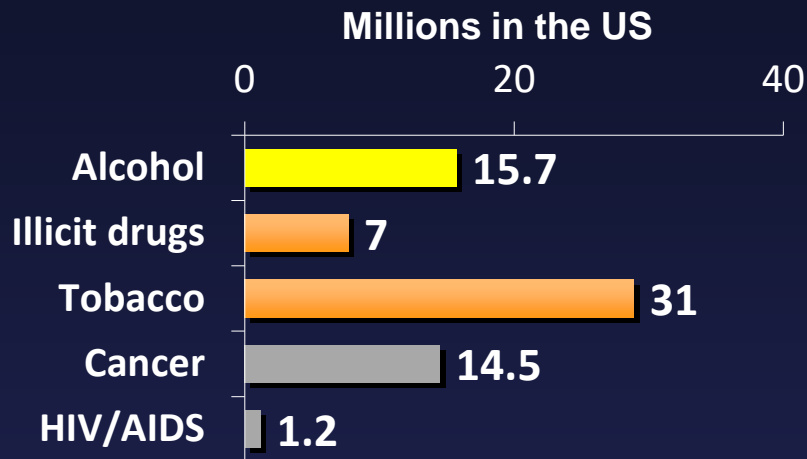
**George F. Koob, Ph.D.**  
**Director**

**National Institute on Alcohol Abuse and Alcoholism**  
**May 3, 2017**

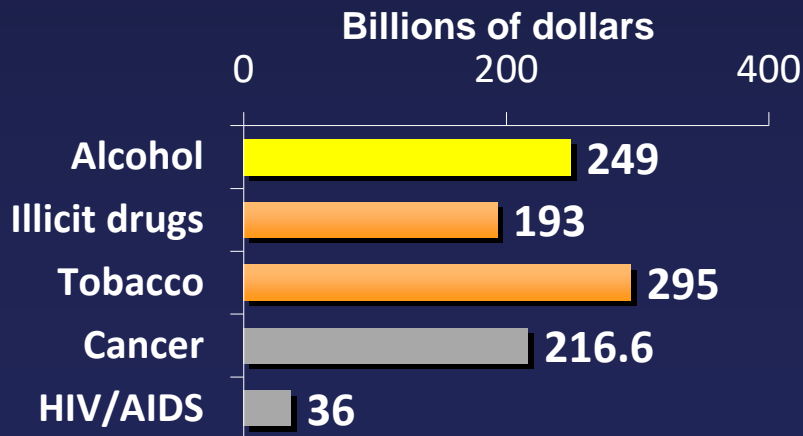


# Cost and Scope of Alcohol-Related Problems

## Prevalence of disorder/disease



## Cost to society



- 14% of people age 18+ met DSM-5 AUD criteria in past year
- ~ 88,000 people die annually from alcohol-related causes in the U.S.
- ~ 50% of all liver disease in the U.S. attributable to alcohol misuse
- Increase in the intensity of underage binge drinking and hospitalizations in last 10 years
- **<10% of people with AUD get any treatment**

Sources: Prevalence – NSDUH (2015), NCI (2014), CDC (2016); Cost – CDC (2015), National Drug Intelligence Center - National Drug Threat Assessment (2011), 2014 Surgeon General's Report, NHLBI (2012), Hutchinson et. al. 2006.

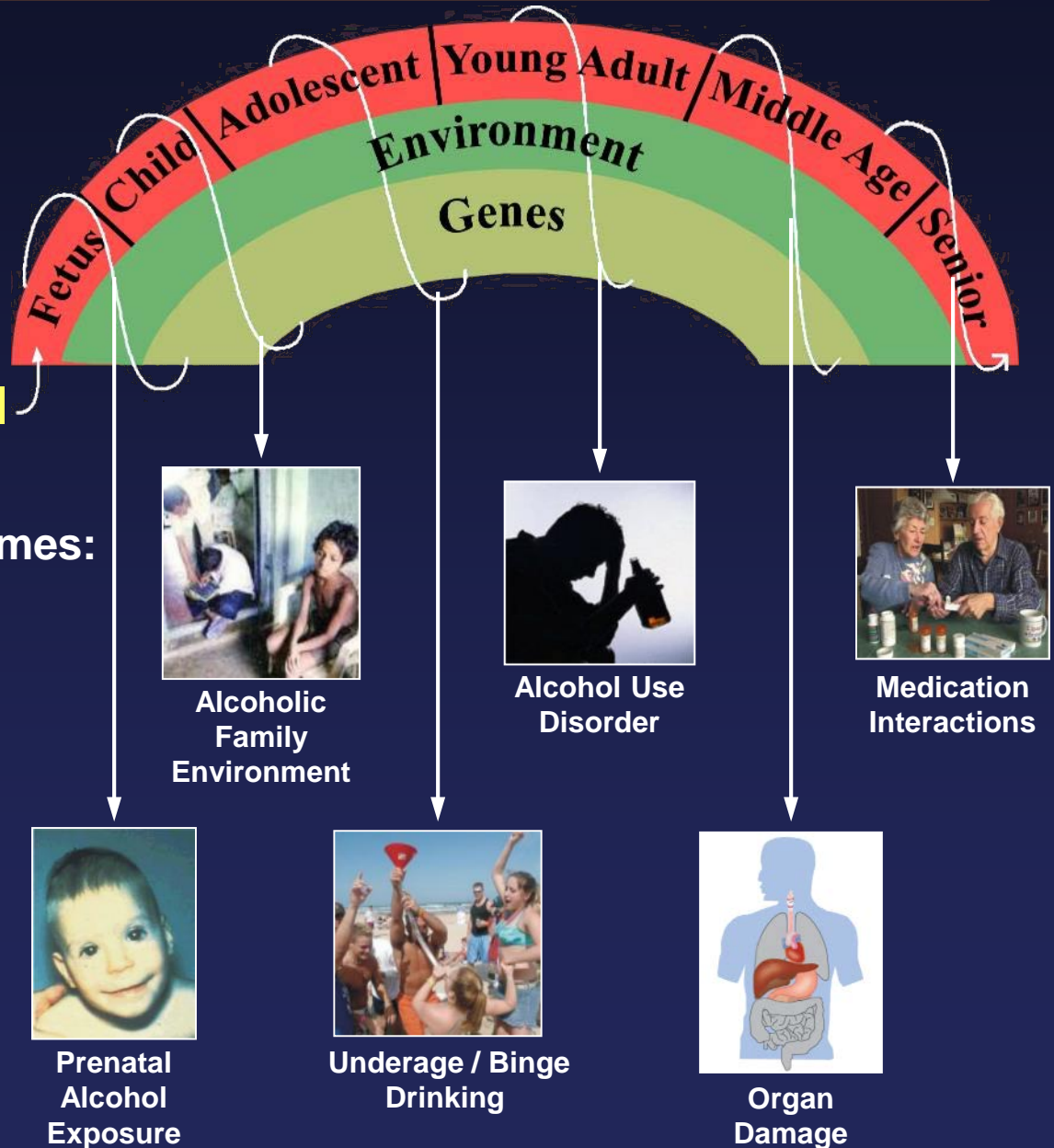
# Alcohol Effects Across the Lifespan

NIAAA supports research to study how alcohol can affect health and well-being at various stages of life

**Alcohol**

Lifespan Transcending Themes:

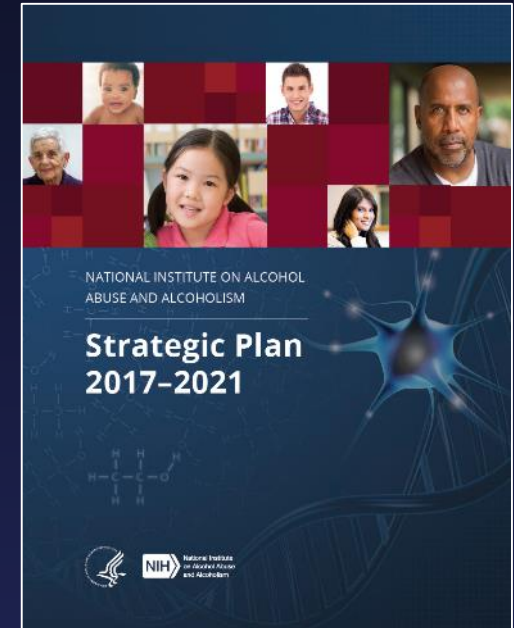
- Neurobiology
- Metabolism
- Genetics
- Epigenetics
- Epidemiology
- Health Services Research



# NIAAA Strategic Plan: 2017-2021

## Strategic Priorities

- Identify **Mechanisms** of Alcohol Action, Alcohol-Related Pathology, and Recovery
- Improve **Diagnosis** and Tracking of Alcohol Misuse, Alcohol Use Disorder, and Alcohol-Related Consequences
- Develop and Improve Strategies to **Prevent** Alcohol Misuse, Alcohol Use Disorder, and Alcohol-Related Consequences
- Develop and Improve **Treatments** for Alcohol Misuse, Alcohol Use Disorder, Co-occurring Conditions, and Alcohol-Related Consequences
- Enhance the **Public Health Impact** of NIAAA-Supported Research



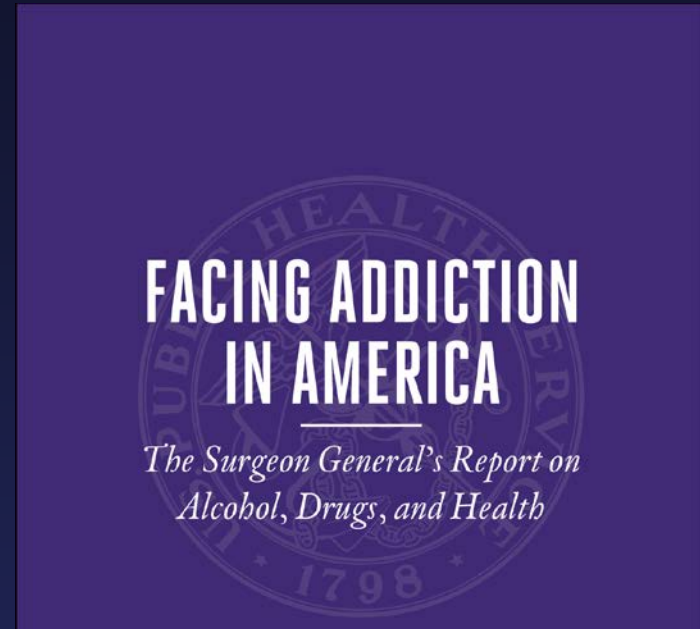
# **Key NIAAA Initiatives and Programs**

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- 1. Fetal Alcohol Spectrum Disorders – Prevention & Early Diagnosis**
- 2. Underage and Binge Drinking – NCANDA, ABCD, CollegeAIM**
- 3. Neurobiology of Alcohol Misuse and AUD**
- 4. Genetics of Alcohol Misuse and AUD**
- 5. Treatment and Recovery Research**
- 6. Medications Development**
- 7. Alcoholic Liver Disease**
- 8. Alcohol and HIV/AIDS**
- 9. Alcohol Biosensors**

# Surgeon General's Report on Alcohol, Drugs, and Health

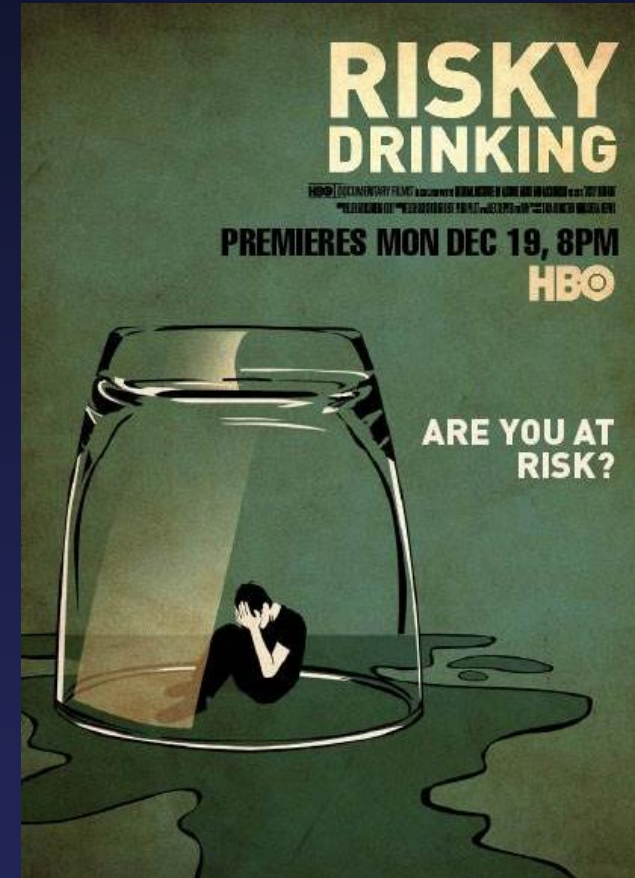
- First ever SGR addressing alcohol and other substance misuse, and SUDs
- NIAAA and NIDA played key roles in report development
- Presents state-of-the-science, with focus on:
  - Neurobiology
  - Prevention
  - Treatment
  - Recovery
  - Delivery of care
- Outlines future directions and recommendations for action



# HBO Documentary on Risky Drinking

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- Produced in conjunction with NIAAA and featuring NIAAA experts
- Described as a **no-holds-barred look at AUD** through the intimate stories of four people whose drinking dramatically affects their relationships
- Aims to provoke conversation about **how to identify risky drinking and to suggest alternatives to a one-size-fits-all approach for treating it**



Premiered December 19, 2016

# Wearable Alcohol Biosensor Challenge

- **Winning prototype submitted by BACtrack**, a company known for designing and selling portable breath alcohol testers for consumer use
- Their entry, the **BACtrack Skyn**:
  - Worn on the wrist
  - Detects alcohol in sweat
  - Offers continuous, non-invasive BAC monitoring
  - Stores data to a smartphone via Bluetooth
- **A Second Challenge is open (12/10/16 - 5/15/17)**
  - To design a wearable sensor using technologies that detect alcohol non-invasively in blood or interstitial fluid



ARE YOU UP TO THE CHALLENGE?

Create a **wearable alcohol biosensor** that can monitor blood alcohol levels in real time

First Prize: \$200,000  
Second Prize: \$100,000

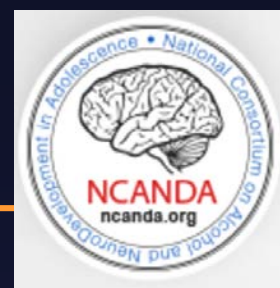
Submit Prototype by:  
Dec. 1, 2015

[LEARN MORE](#)





# Initial Findings from NCANDA

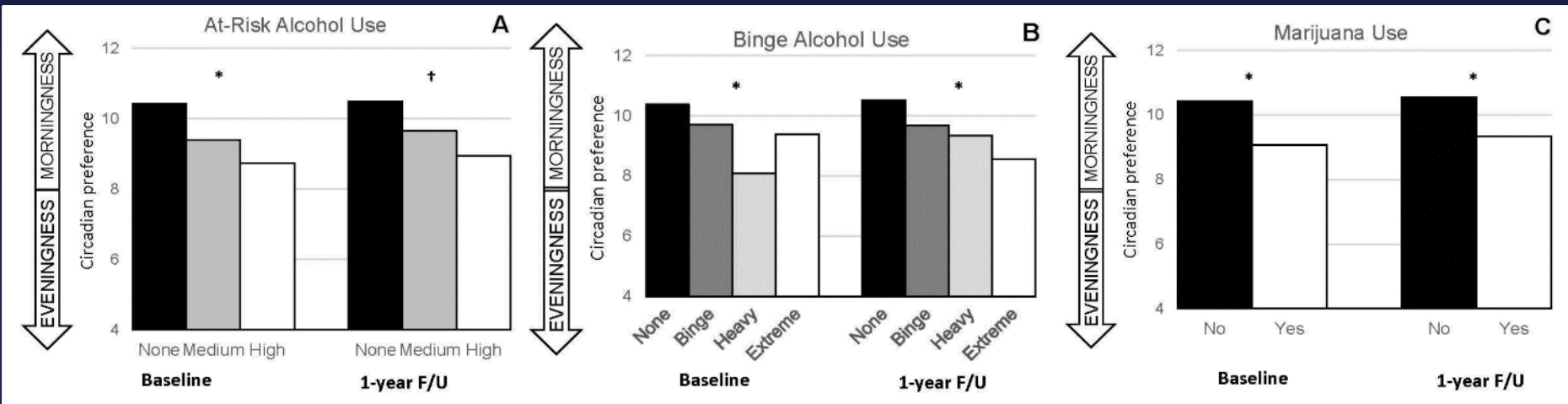


Eveningness and later sleep timing are associated with greater risk for alcohol and marijuana use in adolescence

## At-Risk Alcohol Use

## Binge Alcohol Use

## Marijuana Use



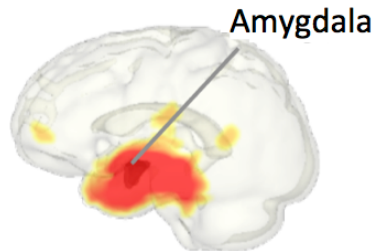
Hasler BP, Franzen PL, de Zambotti, Prouty D, Brown SA, Tapert SF, Pfefferbaum, Pohl KM, Sullivan EV, De Bellis MD. *ACER*. In Press

# Initial Findings from NCANDA

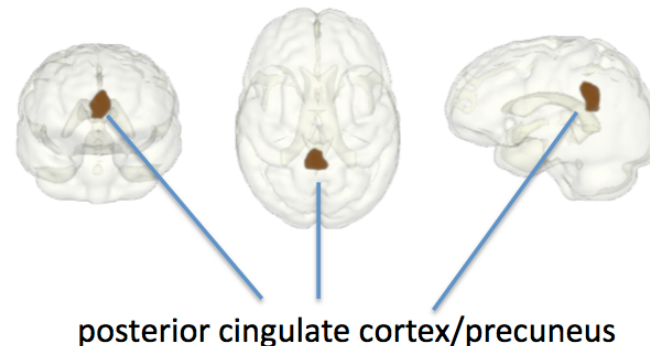


**Weaker functional amygdala-precuneus connectivity in youth who had exceeded NCANDA study entry criteria for drinking than youth who were no-to-low drinkers at entry**

**Emotion Network (EMN) seed**



**Alcohol use history (matched groups)  
No/low > Exceeds Drinkers**



**117 youth in the exceeds drinking group had attenuated connectivity between the emotion network seed of the amygdala and default-mode network regions of the posterior cingulate cortex/precuneus relative to a subgroup of 117 no/low drinking youth matched to the drinkers in age, sex, education, ethnicity, and ratio of scanner manufacturer**

# College Binge Drinking and Blackout

- Past month binge drinking among college students:<sup>1</sup>

- **Overall: 37.9%**
- **Male: 39.4%**
- **Female: 36.5%**

- **Blackouts are common:**  
A 2012 survey of 26,000+ college students found that **32% experience a blackout each year** (34% male, 31% female)<sup>2</sup>

- **Blackout frequency predicts other alcohol-related consequences**

Table 3. Experienced Other Alcohol Problems According to Frequency of Blackouts in Past 6 Months: NEXT Generation Health Study, Wave 4 (N = 1,463, Drinkers)

Past 6 months	Frequency of blackouts in past 6 months <sup>a</sup>		
	None (N = 1,189)	1 to 2 (N = 218)	3 or More (N = 56)
Had a hangover	26%	78%	94%
Missed work/class	4	35	65
Got behind school/work	3	37	61
Did something they later regretted	11	58	76
Argued with friends	10	49	60
Damaged property	2	14	48
Trouble with police	1	11	28
Injured	4	16	55
Alcohol overdose	<1	6	8

<sup>a</sup>All relations  $p < 0.01$ .

Source: Hingson et al., 2016, ACER

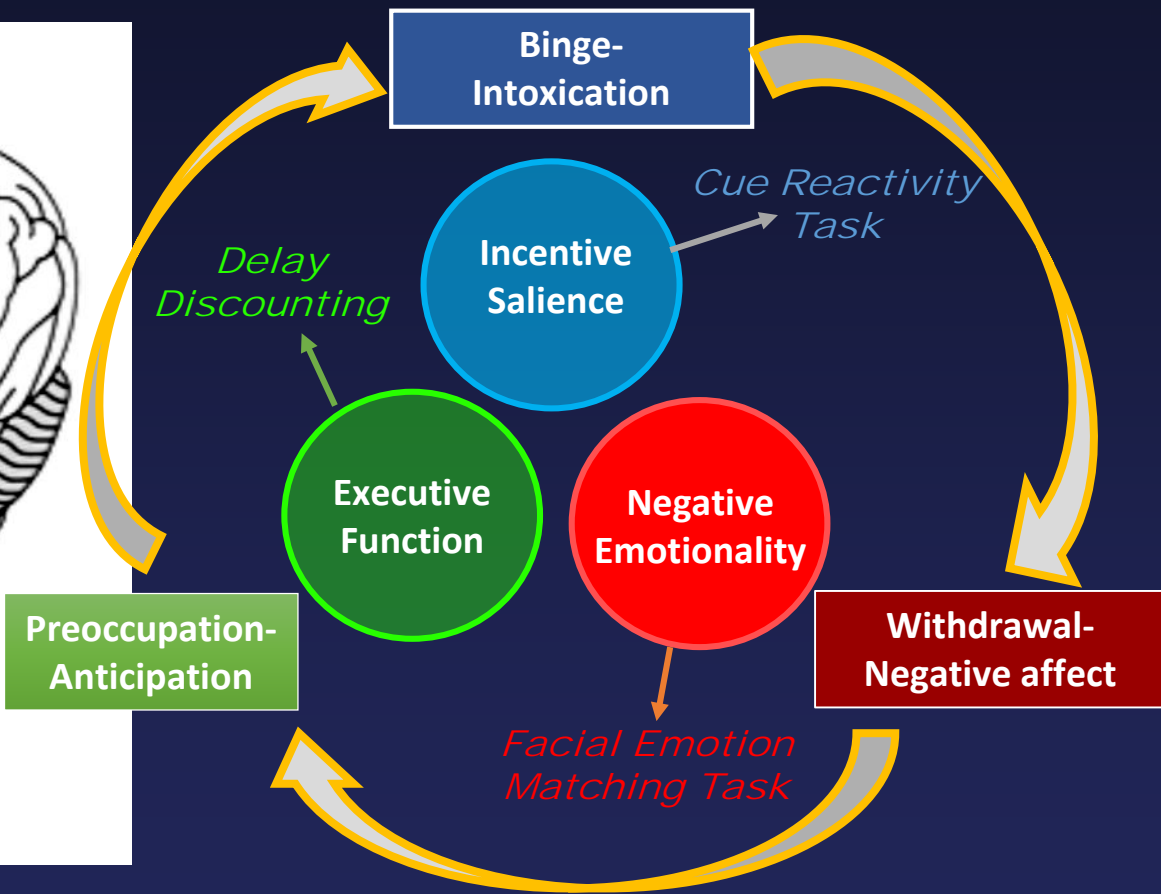
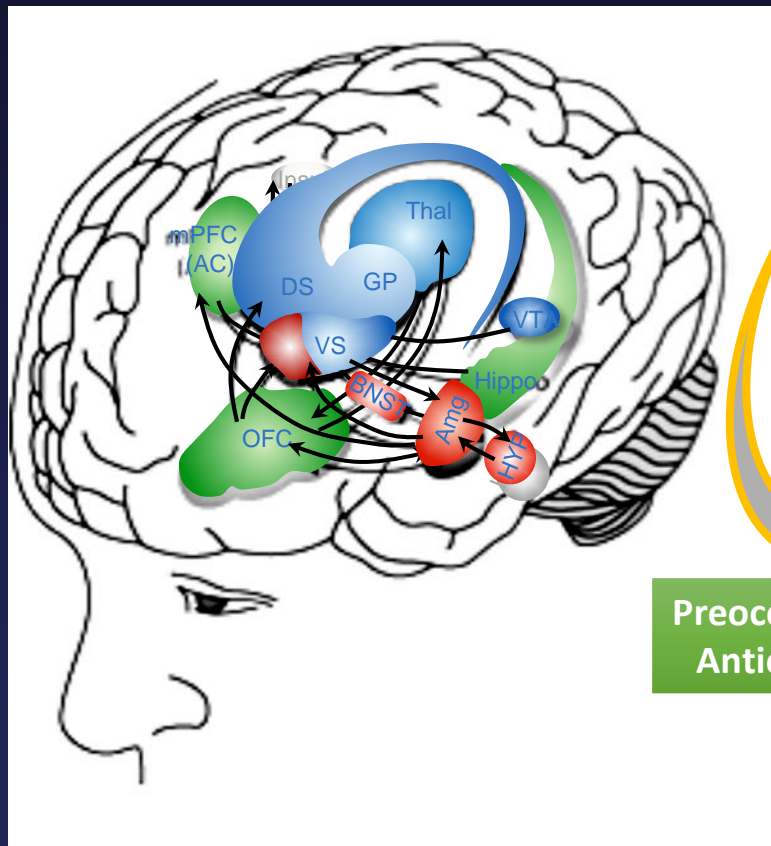
<sup>1</sup>National Survey of Drug Use and Health, SAMHSA, 2016; <sup>2</sup>American College Health Association, 2012

# COLLEGEAIM

- **College Alcohol Intervention Matrix:** evidence-based decision guide and interactive website to help schools address harmful and underage student drinking
- Rates **nearly 60 individual- and environmental-level interventions** based on factors such as cost, effectiveness, and ease of implementation
- NIAAA working with its College President's Working Group to hold regional workshops to introduce CollegeAIM to institutional officials and show them how to use it



# Stages of the Addiction Cycle: Associations with Neurocircuits & Addictions Neuroclinical Assessment



Adapted from: Koob GF. *Curr Top Behav Neurosci*, 2011 Jul 10.

Adapted from: Kwako LE et al. *Biological Psychiatry*, 80 (2016) 179- 189

# NIAAA Medications Development Program

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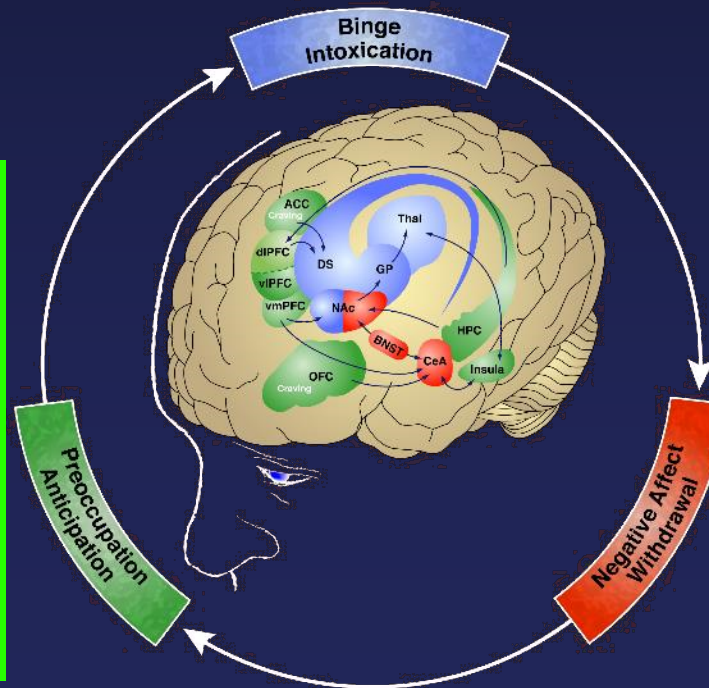
- **Division of Medications Development** established to coordinate efforts to identify, screen, and evaluate compounds for treating AUD
  - **Human laboratory screening studies** to bridge the gap between preclinical and clinical trials
  - **SBIR/STTR program** to bridge the “valley of death” between basic and clinical research by facilitating studies leading to the development of an **IND application to the FDA**
  - **NIAAA Clinical Investigations Group (NCIG)** to streamline AUD medications development by conducting “fast success/fast fail” phase II clinical trials with 18 month turn-around time
    - launched a clinical trial of gabapentin in June 2015
- **NIAAA’s intramural program** conducts clinical studies on novel compounds with AUD treatment potential
- **NIAAA disseminates information about treatment options including medications** to health professionals and the general public

# Novel AUD Targets by Stage of the Addiction Cycle

Dopamine receptors (DRD2)  
GABA<sub>A</sub> receptors (GABRA2)  
Opioid receptors (OPMR1)  
Acetylcholine receptors (CNRNA5)  
Glycine receptors (GLRA1)  
Serotonin receptors (HTR3A)  
Serine/Threonine Kinases (MTOR)  
Cannabinoid receptors (CNR1)  
GIRK channels (KCNJ6)

Norepinephrine receptor (ADRB2)  
Hypocretin (Orexin) receptor (HCRTR1)  
Neuropeptide Y receptor (NPY1R)  
CRF receptor (CRHR1)  
Kappa opioid receptor (OPRK1)  
Substance P receptor (TACR1)  
Nociceptin receptor (OPRL1)  
Oxytocin receptor (OXTR)  
**Vasopressin receptor (AVPR1B)**  
Glucocorticoid receptor (NR3C1)  
Neuroimmune factors (NFKB1)

Phosphodiesterases (PDE10A)  
Protein kinases (PRKCE)  
Transcription factors (CREB1, FOSB)  
NMDA & AMPA receptors (GRIN2B, GRIA1)  
Metabotropic glutamate receptors (GRM8)  
Actin cytoskeleton (ACTB)  
Matrix Metalloproteinase (MMP9)



# Vasopressin Receptor Antagonist as Possible Treatment for AUD

- Multisite clinical trial of ABT- 436, a novel V1b receptor antagonist
- ABT-436 significantly increased percentage of days abstinent
- Participants who reported high levels of stress responded better: decreased frequency of drinking and number of heavy drinking days

Neuropsychopharmacology (2016), 1–12  
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www.neuropsychopharmacology.org

A Phase 2, Double-Blind, Placebo-Controlled Randomized Trial  
Assessing the Efficacy of ABT-436, a Novel V1b Receptor  
Antagonist, for Alcohol Dependence

Megan L Ryan<sup>\*,1</sup>, Daniel E Falk<sup>1</sup>, Joanne B Fertig<sup>1</sup>, Beatrice Rendenbach-Mueller<sup>2</sup>, David A Katz<sup>2</sup>,  
Katherine A Tracy<sup>2</sup>, Eric C Strain<sup>3</sup>, Kelly E Dunn<sup>3</sup>, Kyle Kampman<sup>4</sup>, Elizabeth Mahoney<sup>4</sup>, Domenic A Ciraulo<sup>5</sup>,  
Laurie Sickles-Colaneri<sup>5</sup>, Nassima Ait-Daoud<sup>6</sup>, Bankole A Johnson<sup>6</sup>, Janet Ransom<sup>7</sup>, Charles Scott<sup>7</sup>,  
George F Koob<sup>1</sup> and Raye Z Litten<sup>1</sup> for the National Institute on Alcohol Abuse and Alcoholism Clinical  
Investigations Group (NCIG) Study Group



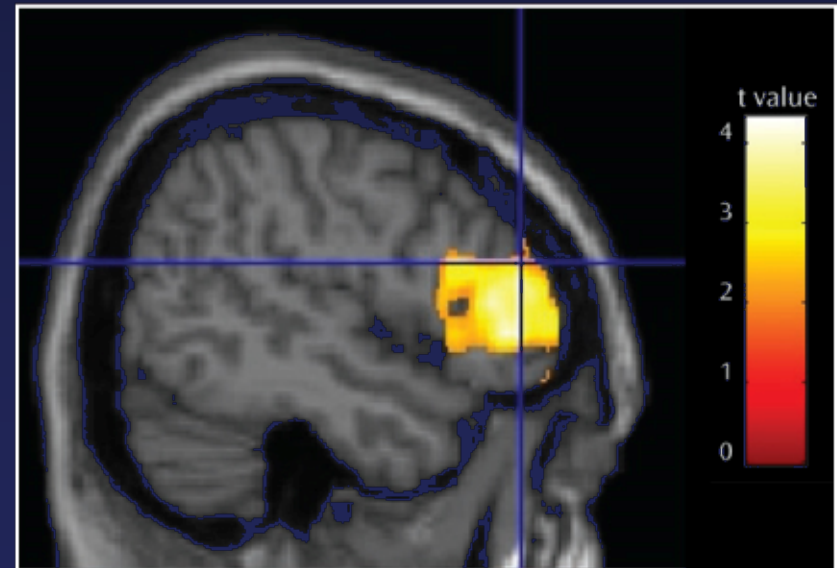
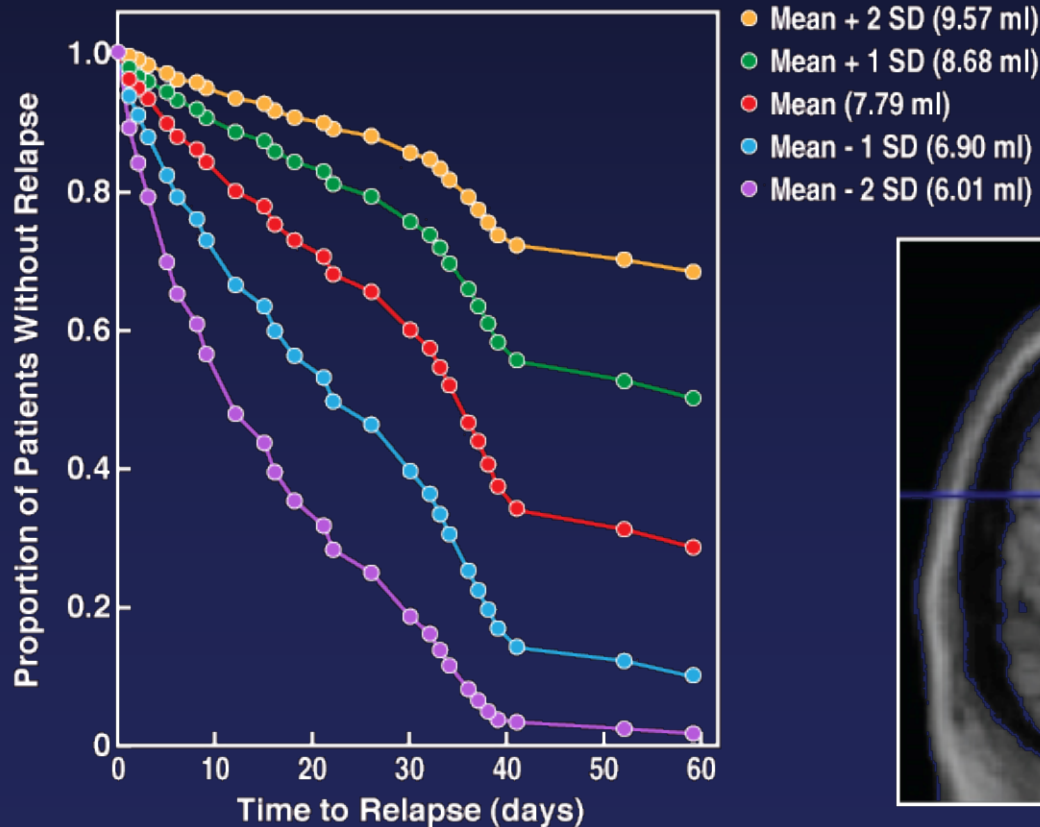
# Coming Soon: NIAAA Treatment Navigator

- To assist people in finding AUD treatment, NIAAA is developing the **NIAAA Alcohol Treatment Navigator<sup>SM</sup>**
- One-of-a kind resource will:
  - outline the features of evidence-based AUD treatment
  - describe the varied routes to recovery
  - provide tools for locating the most qualified treatment specialists



# Identifying Factors that Facilitate or Inhibit Recovery from Alcohol Use Disorder

## Gray Matter Volume Deficits Predict Time to Relapse in Alcohol-Dependent Patients



# Alcohol Policy Information System

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- **APIS database tracks and facilitates research on alcohol-related policies at the state and federal levels**
- **Recently expanded to include recreational marijuana policies:**
  - **Regulatory agency**
  - **Permitted products**
  - **Cultivation restrictions**
  - **Retail sales**
  - **Pricing controls**
  - **Taxation**
  - **Underage prohibitions**
  - **Impaired driving prohibitions**
  - **Local authority**
- **Additional policies under consideration for inclusion:**
  - **Structure of distribution system**
  - **Industry makeup**
  - **Tracking systems**
  - **Health and safety labeling**
  - **Packaging**
  - **Advertising**
  - **Public consumption**
  - **Home delivery**
  - **Open container**

# Thank You!

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