

**What Can the National Epidemiological
Survey on Alcohol and Related
Conditions (NESARC)
Tell Us About Directions for Future
Research and Practice?**

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Department of Health and Human Services**

**Smart Practice, Practical Science: Blending
Treatment and Research**

**Miami Beach, Florida
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NIAAA Vision and Mission 2003 and Beyond

To support and promote the best science on alcohol and health for the benefit of all by:

- increasing the understanding of **normal** and **abnormal** biological functions and behavior relating to alcohol use
- improving the **diagnosis, prevention, and treatment** of alcohol use disorders
- enhancing **quality health care**



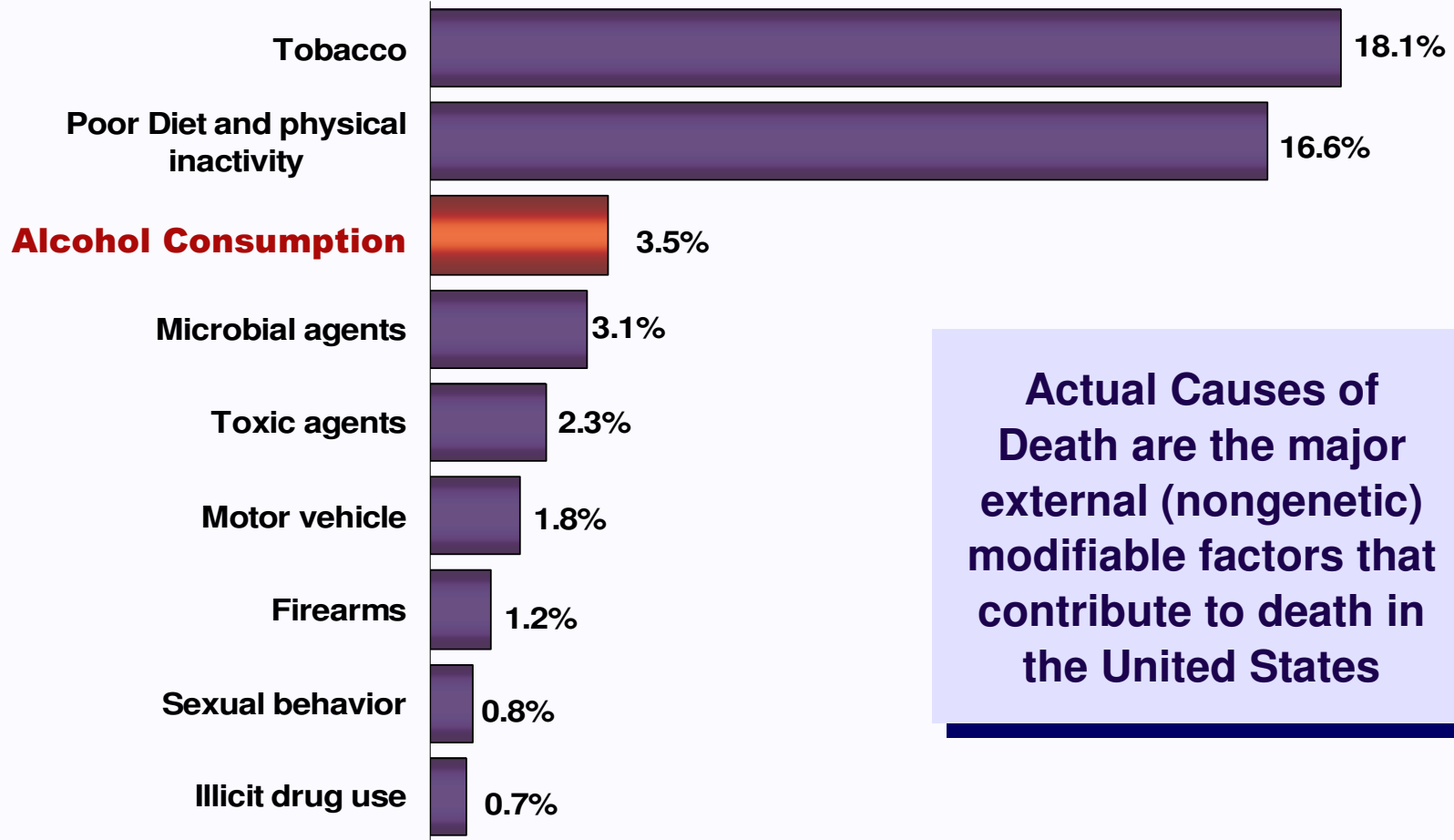
Extent of the AUD Problem in the United States

- **18 million** Americans (**8.5%** of the population age 18 and older) suffer from alcohol abuse or dependence
- Alcohol was the **third** leading actual cause¹ of death in 2000 (an estimated **85,000** deaths annually)
- Alcohol problems cost U.S. society an estimated **\$185 billion** annually

¹Actual Causes of Death are the major external (nongenetic) modifiable factors that contribute to death in the United States



Actual Causes of Death, United States - 2000

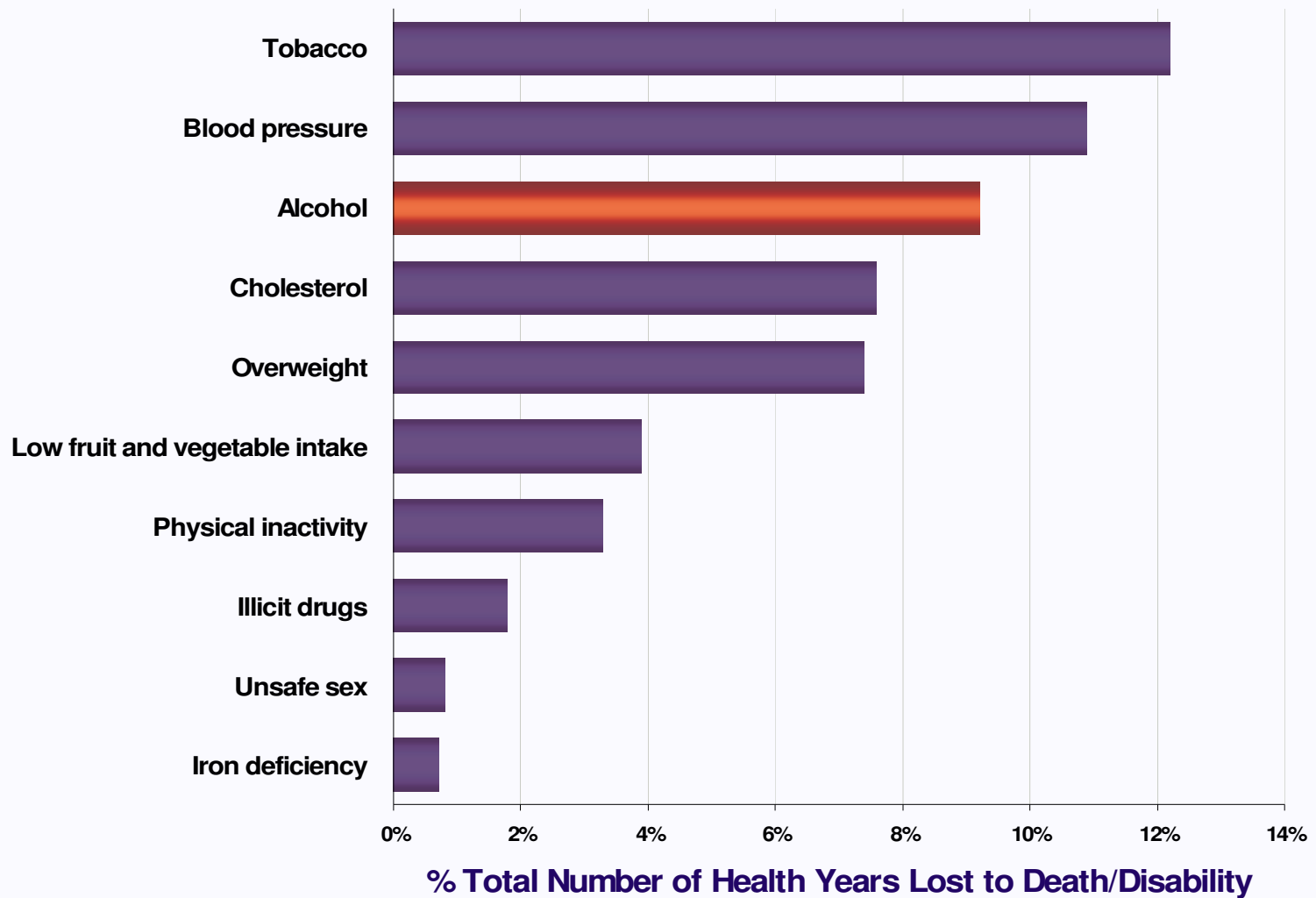


Actual Causes of Death are the major external (nongenetic) modifiable factors that contribute to death in the United States

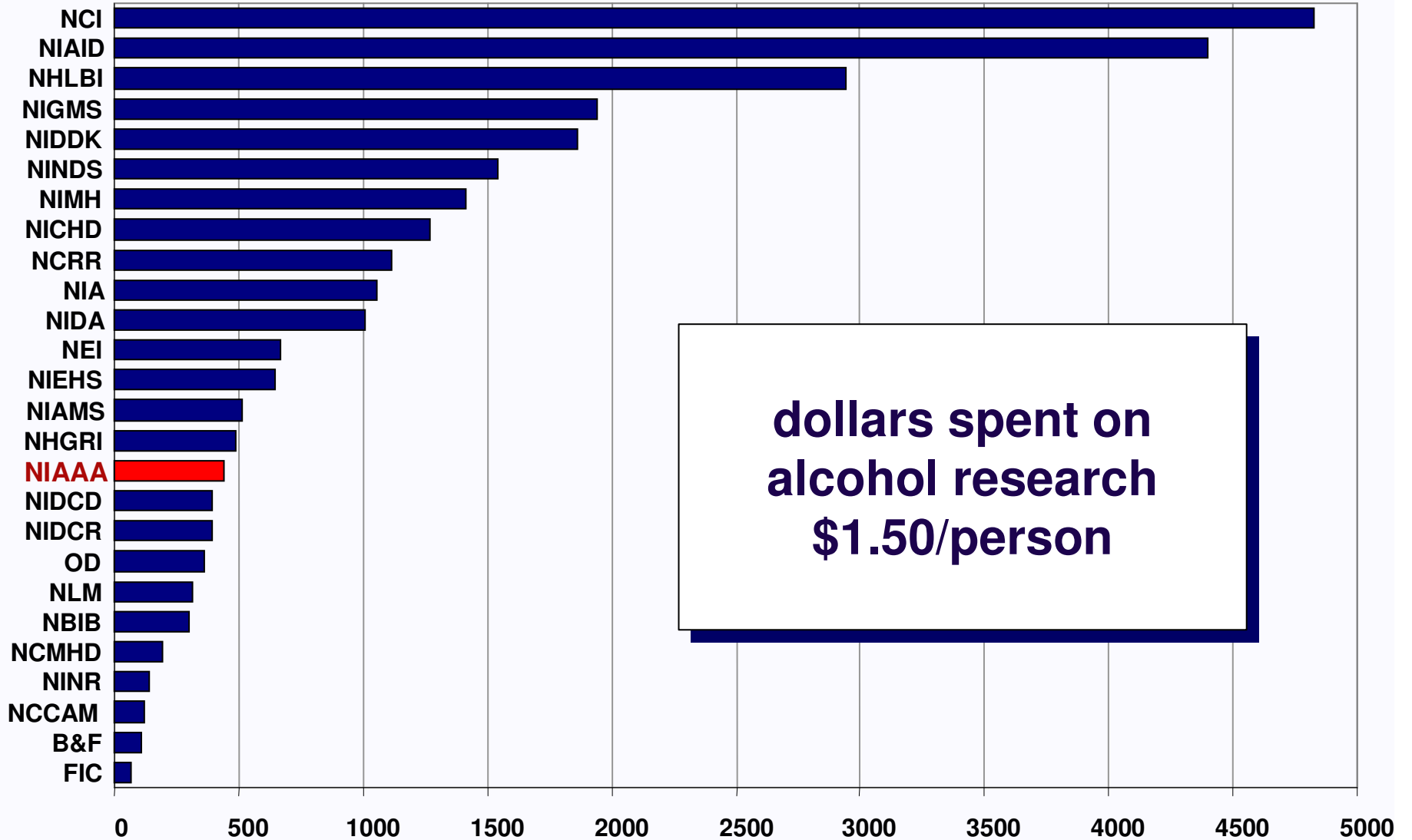
Mokdad AH, Marks JS, Stroup DF, Gerberding JL. JAMA (2004). 29:1238-45.



Burden of Disease Attributable to Alcohol Among the 10 Leading Risk Factors for Disease In Developed Countries



NIH FY 2005 Appropriation (Enacted)



dollars spent on
alcohol research
\$1.50/person

Dollars in millions



Alcohol Use Disorders

Alcohol Abuse

recurring personal, interpersonal, and societal problems

too much, too fast

Alcoholism (Alcohol Dependence)

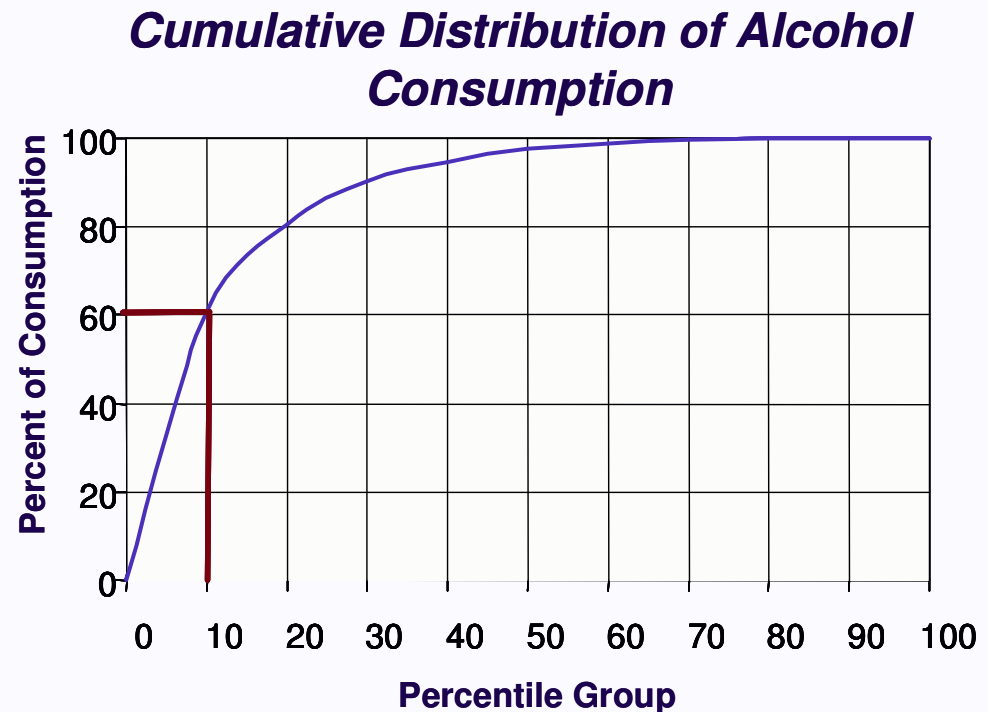
loss of control, preoccupation with drinking, compulsive drinking, and dependence

too much, too often



Cumulative Distribution of Alcohol Consumption in the United States

- **67%** of the population are drinkers*
- **Males** reported drinking **76%** and females **24%** of all alcohol consumed
- **60%** of the alcohol is consumed by **10%** of the population



* Individuals who reported drinking at least one drink in past 12-months

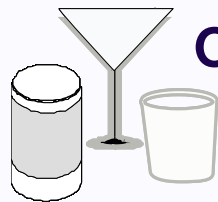
Greenfield and Rogers (1999). *J. Stud. Alc.* 60:79-89.



Drinking Patterns: Rates and Risks

Moderate Drinking

Most people abstain or drink moderately placing them at low risk for alcohol use disorders. In general, **Moderate Drinking** is up to **2 drinks/day** for **men**; up to **1 drink/day** for **women**
(USDA/HHS dietary guidelines)



One drink: one 12-ounce can or bottle of beer or wine cooler, one 5-ounce glass of wine, or 1.5 ounces of 80-proof distilled spirits.

Drinking Patterns: Rates and Risks

Risky Drinking

Nearly 3 in 10 U.S. adults engage in risky drinking patterns (NIAAA NESARC, 2003). These are:

- **Men:** More than **14** drinks in a typical **week**/more than **4** drinks on any **day**
- **Women:** More than **7** drinks in a typical **week**/more than **3** drinks on any **day**



Drinking Patterns: Rates and Risks

Binge Drinking

The National Advisory Council on Alcohol Abuse and Alcoholism has recommended the following definition of “Binge Drinking”:

A “binge” is a pattern of drinking alcohol that brings blood alcohol concentration (BAC) to 0.08 gm% or above. For the typical adult, this pattern corresponds to consuming **5 or more** drinks (male) or **4 or more** drinks (female) in about 2 hours. Binge drinking is clearly dangerous for the drinker and for society



The National Epidemiologic Survey on Alcohol and Related Conditions (NESARC)

- **43,000 nationally representative sample; 81% response rate.**
- **NESARC identifies:**
 - **current and lifetime prevalence rates for alcohol and co-occurring mental and substance use disorders**
 - **factors that impact on initiation, remission, chronicity, and stability of disorders**
 - **factors involved in the natural history of alcohol use and associated disorders**
- **The NESARC and future NESARC-related surveys will allow analysis of trends in the general population in a variety of areas including treatment and recovery**



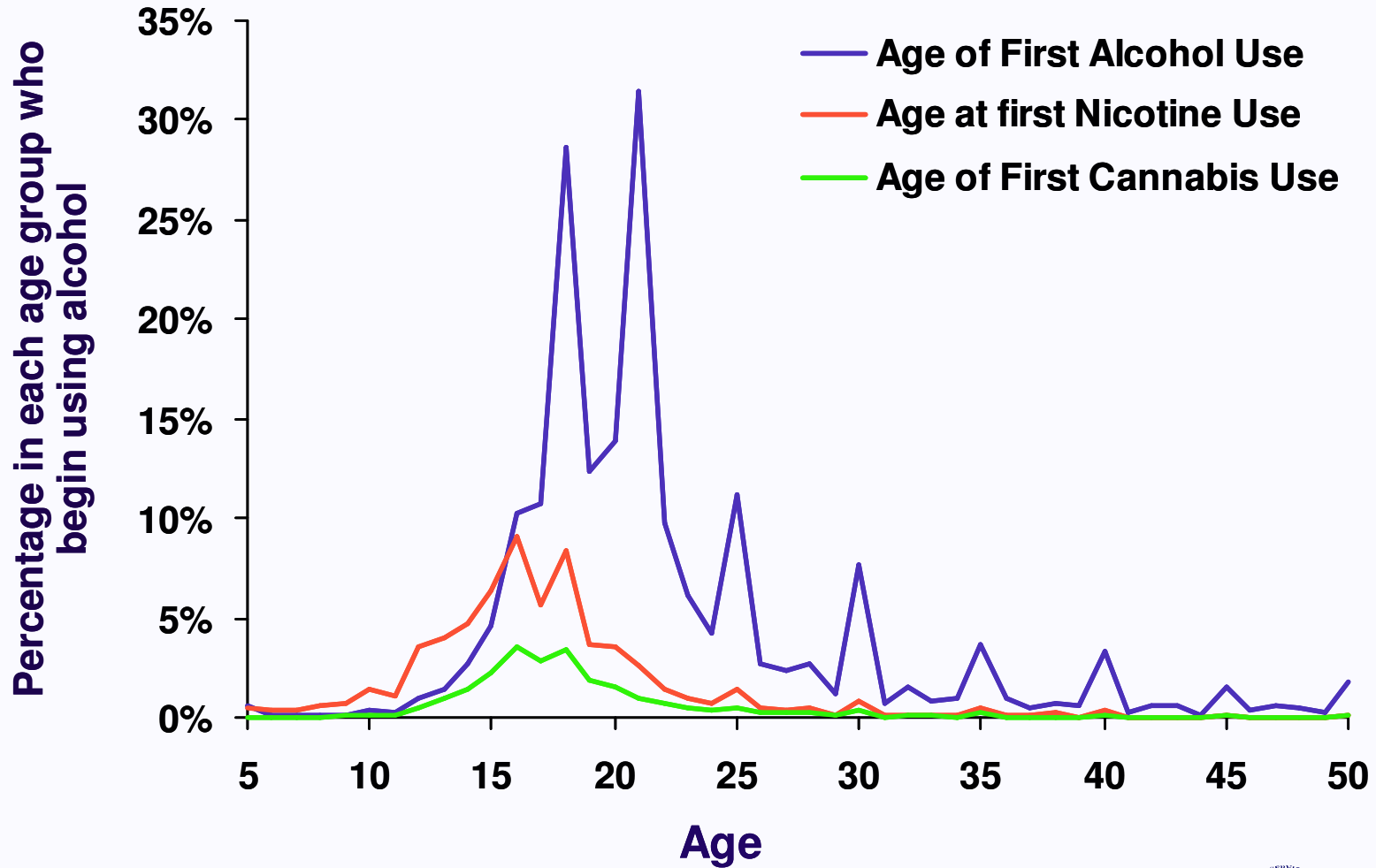
U.S. Adult Drinking Patterns and Risks 2001-2002

WHAT IS YOUR DRINKING PATTERN	HOW COMMON IS THIS PATTERN	YOUR CHANCES OF HAVING AN ALCOHOL DISORDER ARE...	
<p>Based on alcohol screening limits – number of drinks: <i>In a typical WEEK—14 (men), 7 (women)</i> <i>On any DAY—4 (men), 7 (women)</i></p>	Percent of U.S. adults aged 18+	Abuse without dependence	Dependence with or without abuse
Never exceeds the weekly <i>or</i> daily screening limits	72%	less than 1 in 100	less than 1 in 100
Exceeds only the weekly limit	2%	1 in 17	2 in 100
Exceeds only the daily limit less than once a week	14%	1 in 8 (12%)	1 in 20 (5%)
Exceeds only the daily limit once a week or more	2%	1 in 5 (19%)	1 in 8 (12%)
Exceeds both weekly and daily limits	10%	1 in 5 (19%)	more than 1 in 4 (27%)

Source: NIAAA National Epidemiologic Survey on Alcohol and Related Conditions



Age at Onset: DSM-IV Age of First Use of Alcohol, Nicotine, and Cannabis



Source: NIAAA National Epidemiologic Survey on Alcohol and Related Conditions

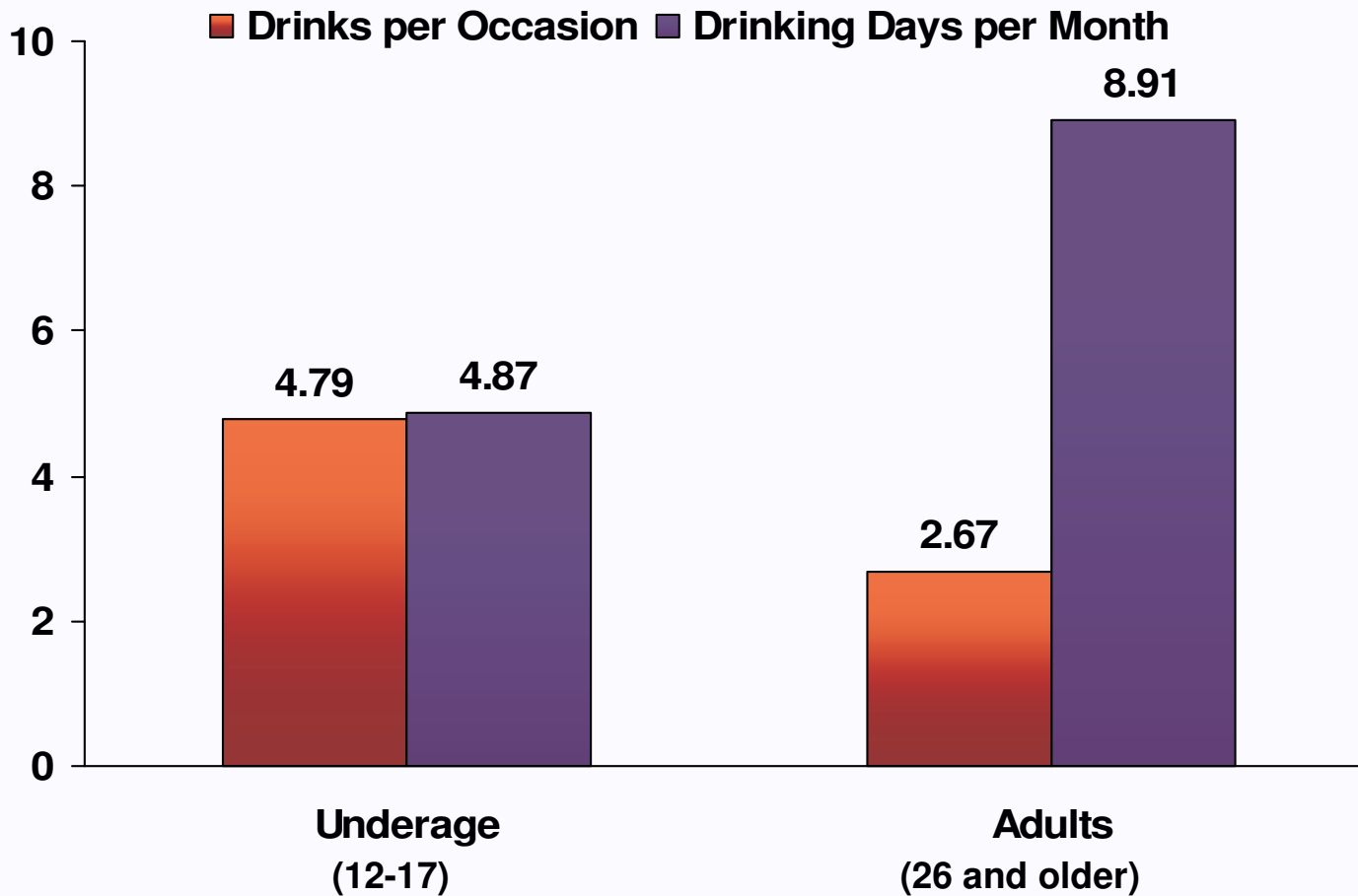


Underage Drinking

- **Alcohol** is the most **commonly used drug** by children and adolescents (SAMHSA National Survey on Drug Use & Health, 2003)
- Teenagers who begin drinking before **age 15** have **four times the risk** of developing alcohol dependence later in life
- Adolescents with histories of extensive alcohol use have noticeable **changes in brain function** that impair learning, memory (Brown et al., 2000), and problem solving; smaller hippocampal volume (De Bellis et al., 2000)
- Teens who use alcohol and drugs are more likely to be involved in **violent behaviors.**



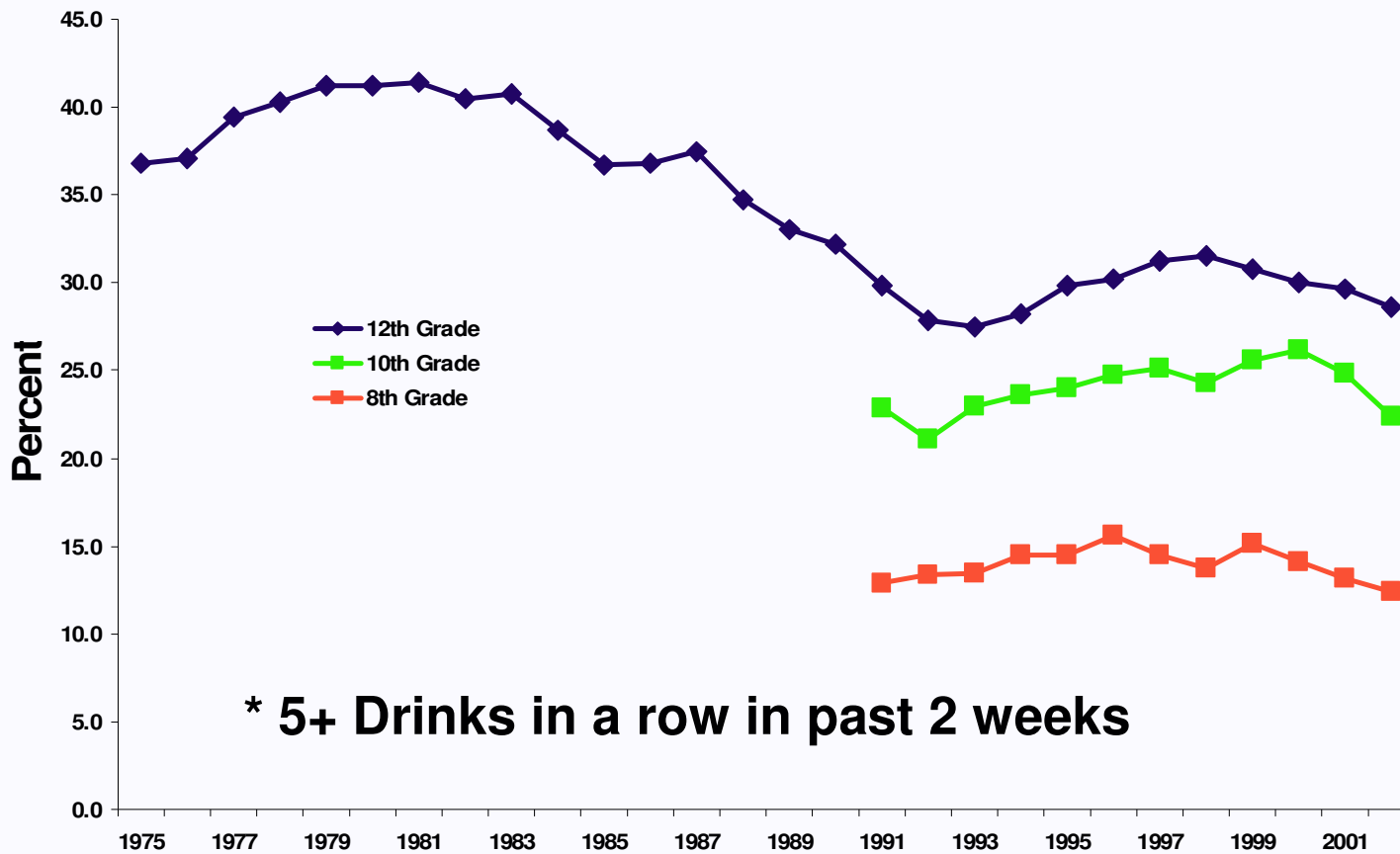
Youth Drink Less Frequently Than Adults, But Drink More Per Occasion



Source: SAMHSA National Survey on Drug Use and Health, 2002



Trends in the Percent of U.S. Students in 8th, 10th, and 12th Grades Who Reported Binge Drinking*, 1975-2002

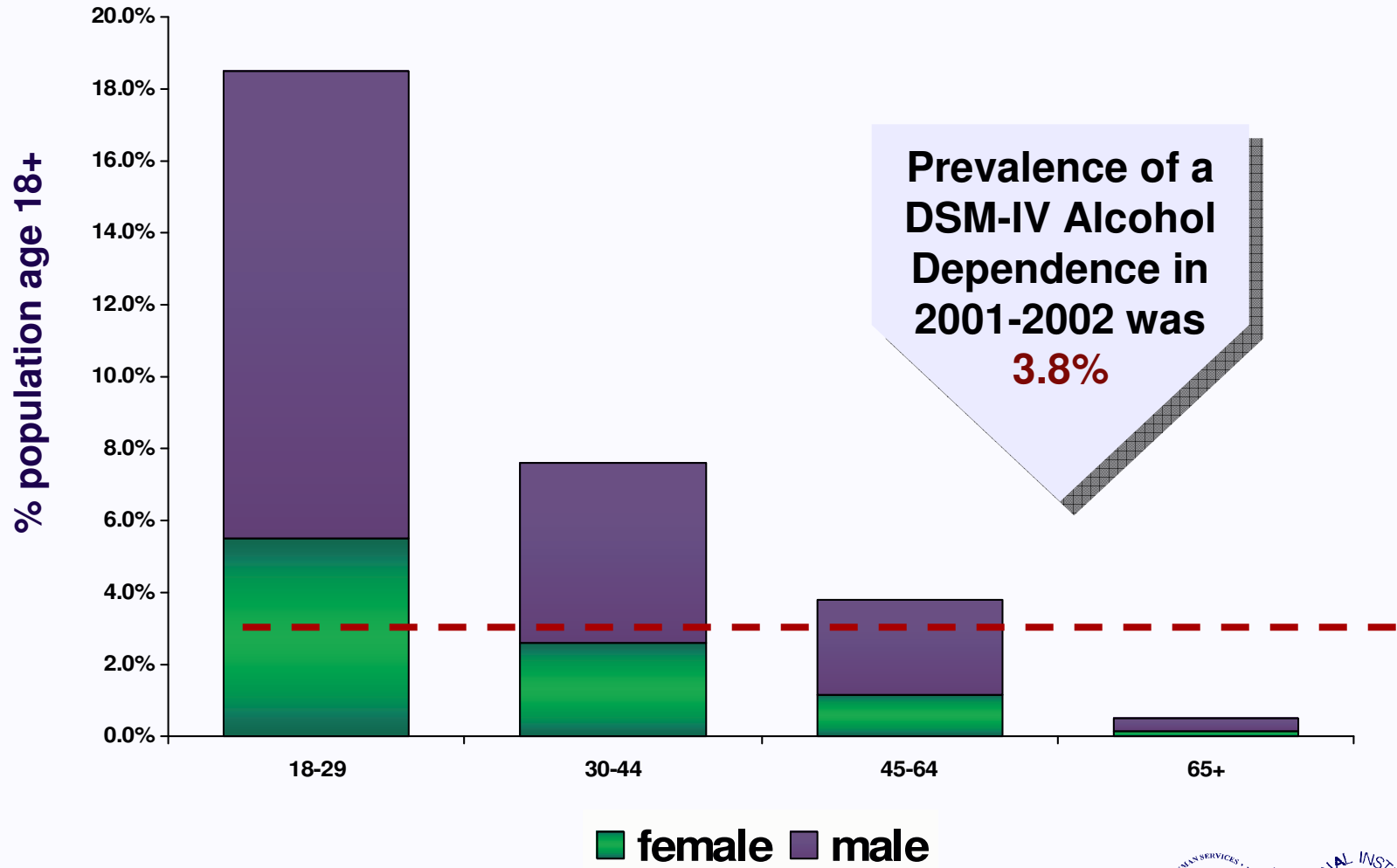


* 5+ Drinks in a row in past 2 weeks

Source: Monitoring the Future, 2002



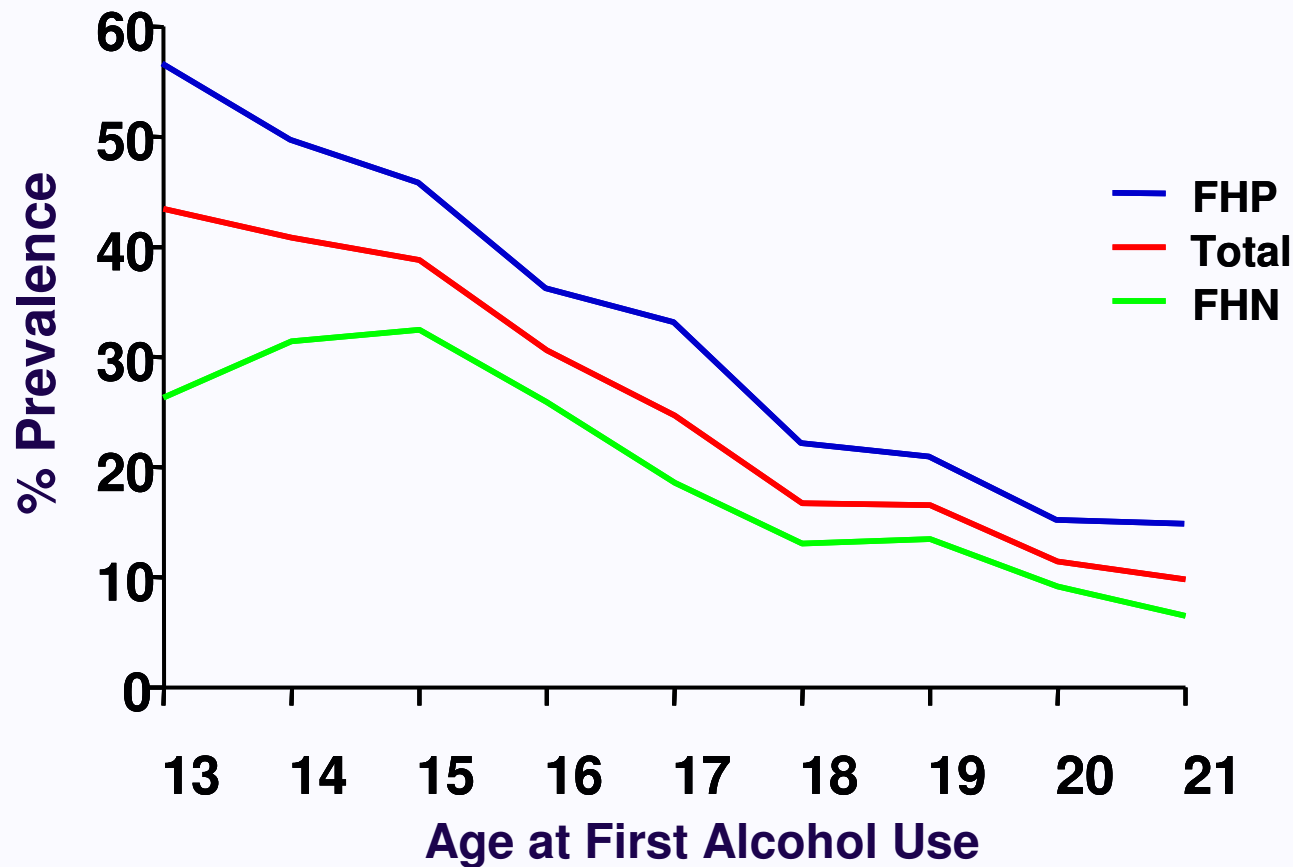
Prevalence of past-year DSM-IV alcohol dependence: United States, 2001-2002:



Grant, et al., (2004) *Drug and Alcohol Dependence*, 74:223-234



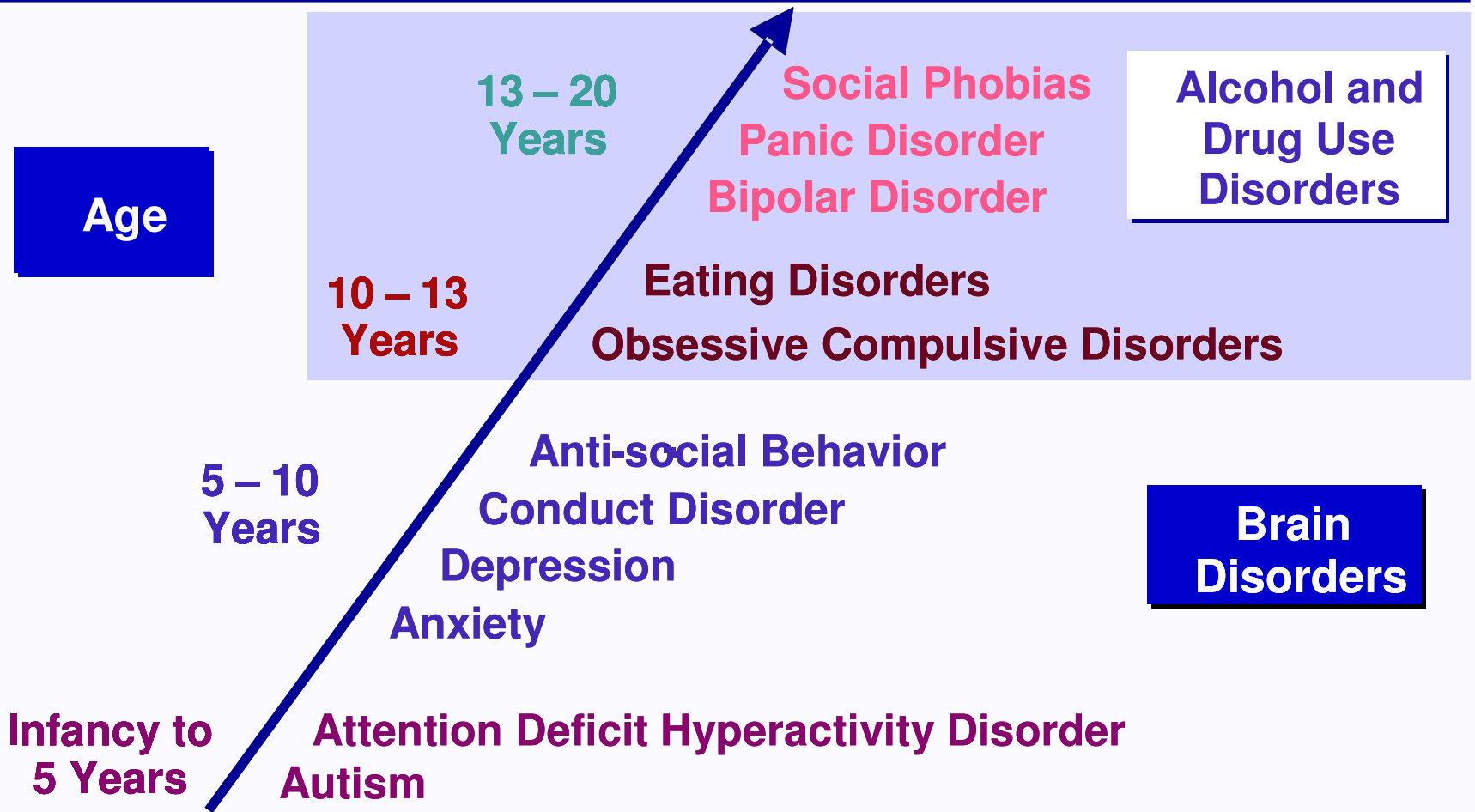
Prevalence of Lifetime Alcohol Dependence by Age of First Alcohol Use and Family History of Alcoholism



Grant and Dawson. *J Subst Abuse*. 1998;10(2):163-73.



Age of Onset of Brain Disorders



Developed from *Time Magazine*, January 20, 2003, p.82



Early Adolescent Problem Behavior and Adult Psychopathology

- Early adolescent problem behavior identifies a subset of youth who are at especially high risk for developing adult psychopathology, including AUD, suggesting general, rather than specific, mechanisms of risk. (Elkins et al (2004). *Am J Psychiatry* 161:670–676)
- Early abuse of alcohol is familial, and, at least in males, heritable. Early alcohol abuse is caused in part by genetic risk for disinhibitory psychopathology in males and to shared environmental factors in females. (McGue et al. (2001) *Alc. Clin Exp Res.* 25:1166-73.)



Odds of Co-occurrence of Current (12-month) DSM-IV Alcohol Dependence and Selected Psychiatric Conditions

Disorder	Odds
Anxiety Disorders	2.6x
Mood Disorders (especially Major Depression)	4.1x
Antisocial Personality Disorder	7.1x
Drug Dependence	36.9x
Nicotine Dependence	6.4x

NIAAA National Epidemiologic Survey on Alcohol and Related Conditions, 2004.



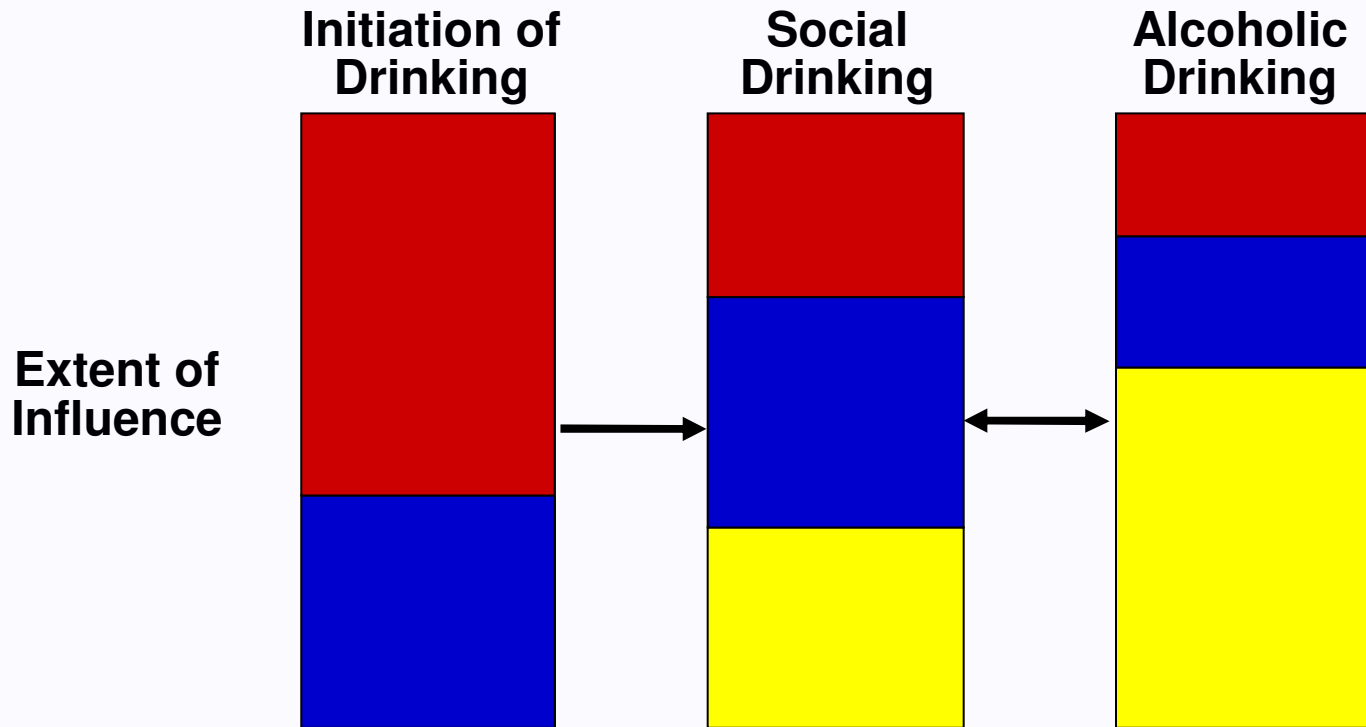
Alcoholism: Heterogeneity of Phenotypes (e.g., Type A-B, Type I-II)

Influenced by:

- **Personality Traits (e.g., novelty seeking, anxiety)**
- **Internalizing/Externalizing Mental Disorders**
- **Co-occurring Genetic and Environmental Factors**
 - **alcohol specific/alcohol nonspecific**
- **Developmental Factors**
 - **early-onset/late onset**
 - **childhood trauma**

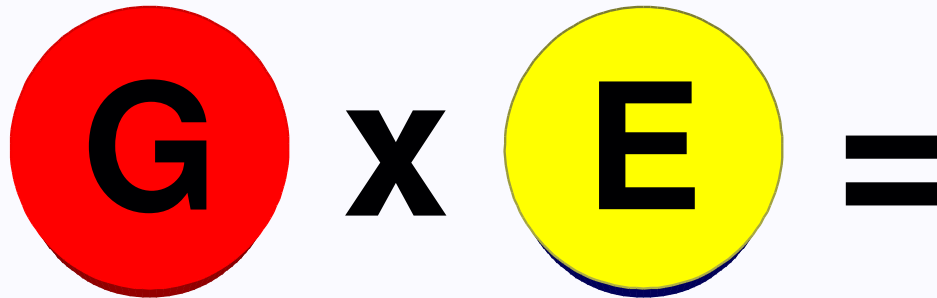


Initiation and Continuation of Drinking

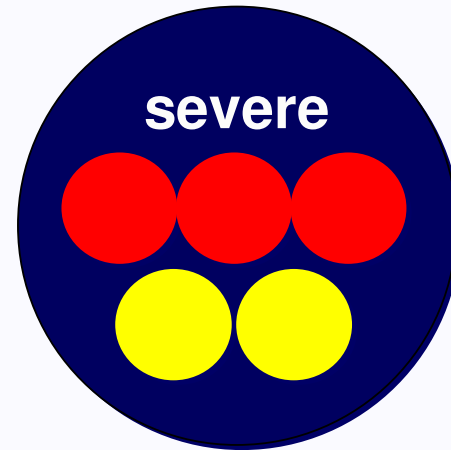
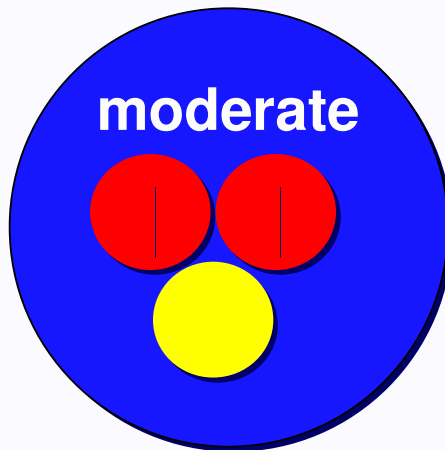
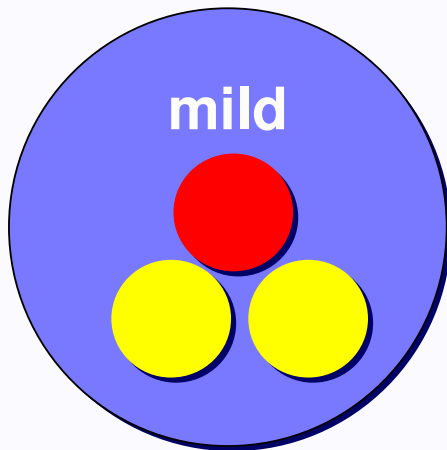


- Environmental (familial and non familial)
- Personality/Temperament
- Pharmacological effects of ethanol

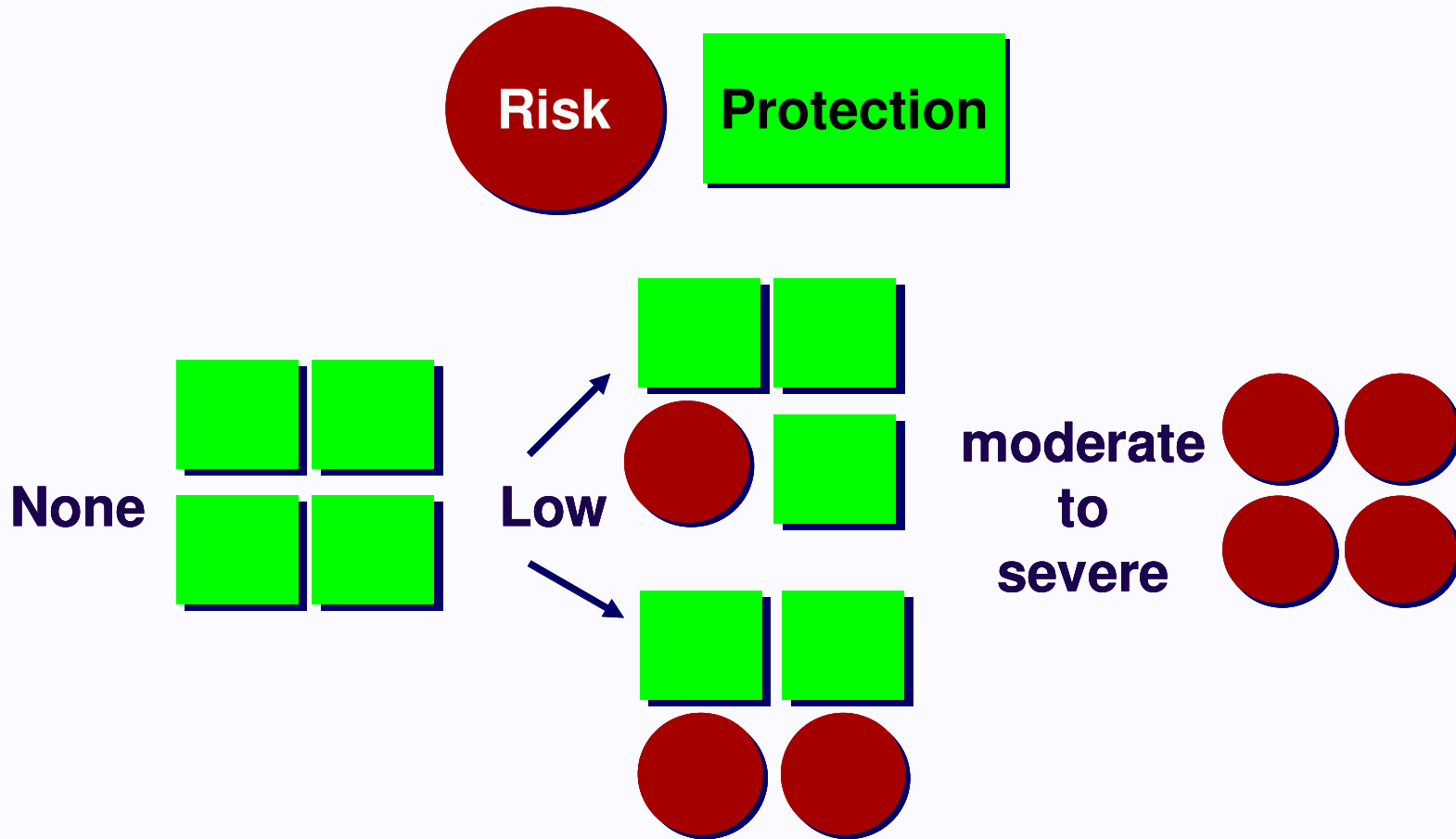
Alcohol Dependence: Gene-Environment Interactions



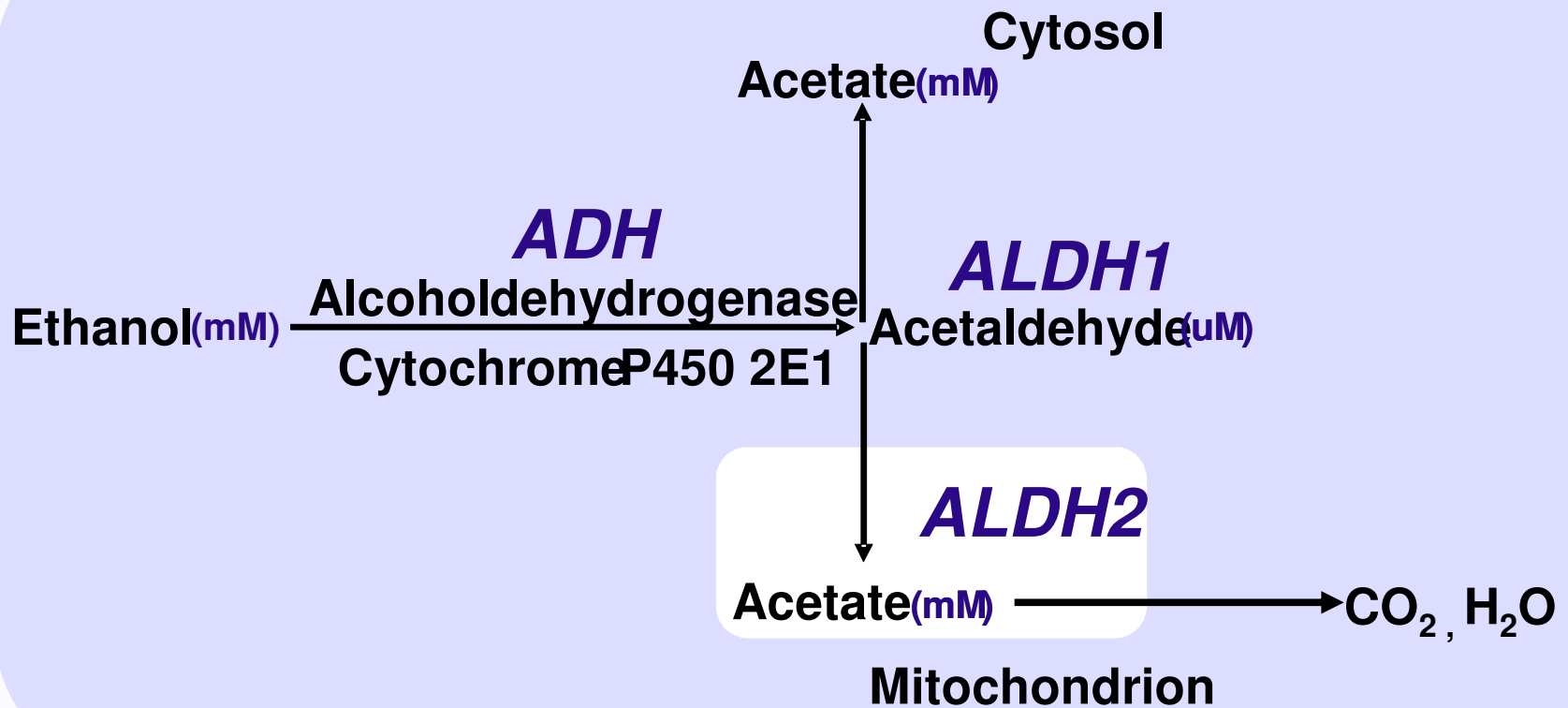
different types of
alcohol dependence
with different
characteristics and
levels of severity



Alcohol Dependence: Protection by Genes



Metabolism of Ethanol and Acetaldehyde in Liver Cells



Energy Yield: 7 cal/g



Protection Against Alcohol Dependence by Genetic Variants of Enzymes of Alcohol Metabolism

(Han Chinese Males in Taiwan)

	<i>ADH1B*2</i> (high activity)	<i>ALDH2*2</i> (low activity)
Nonalcoholic (n=50)	0.73	0.30
Alcoholic (n=50)	0.48†	0.06†

† $P < 0.001$

Thomasson et al (1991), *Am J Hum Genet.* 48:677-681



Gene-Environment Interaction: Aldehyde Dehydrogenase Genotypes in Japanese Alcoholics Over Time

<i>ALDH2</i> Genotypes	1979	1986	1992
<i>ALDH2</i> *2/*2	0.0	0.0	0.0
<i>ALDH2</i> *1/*2	2.5	8.0	13.0
<i>ALDH2</i> *1/*1	97.5	92.0	87.0

From: Higuchi et al. Lancet 343: 741-742, 1994.



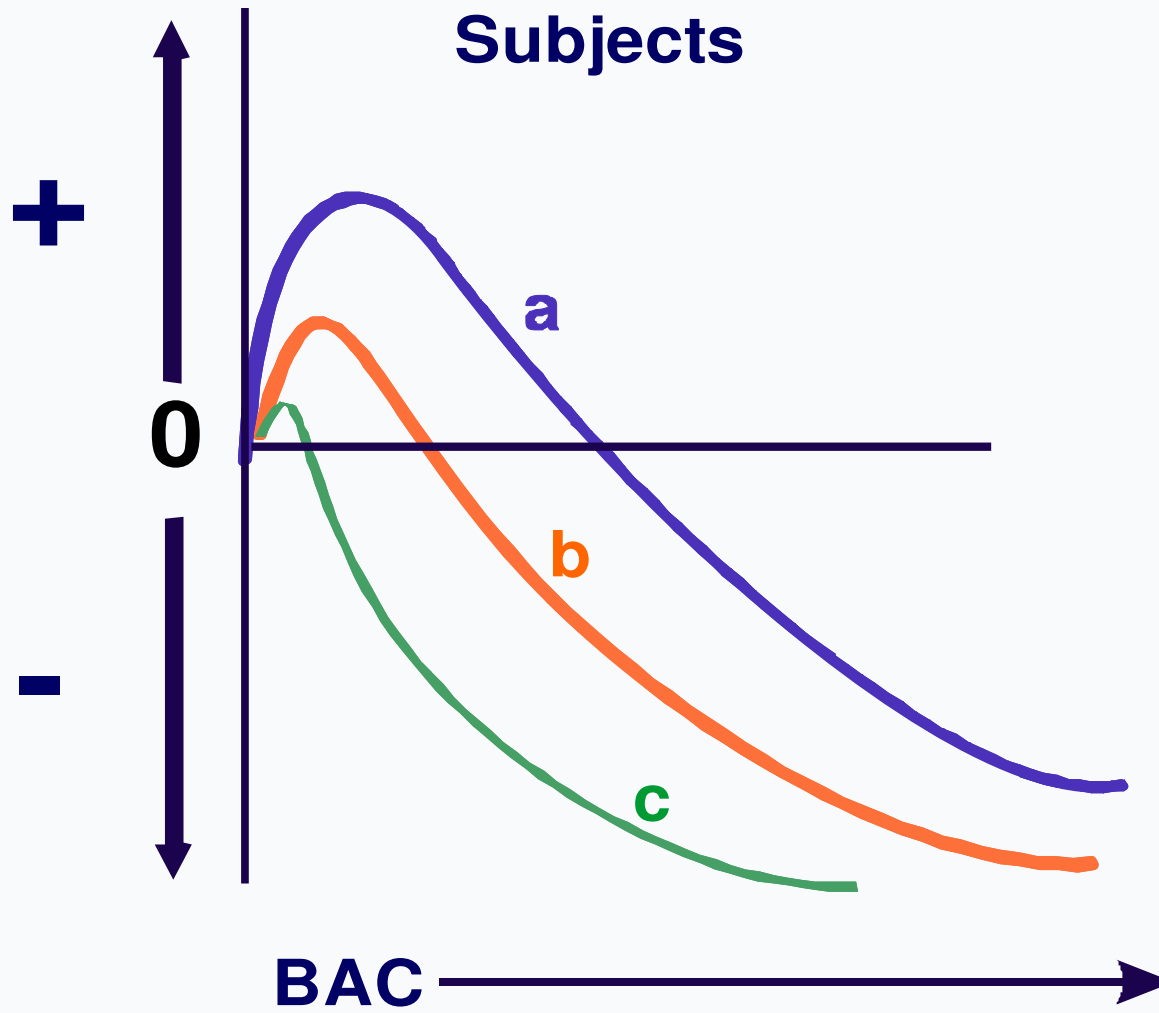
Between Individual Variations in Responses to Alcohol

- **Pharmacokinetics: absorption, distribution, and metabolism of alcohol**
3-4 fold
- **Pharmacodynamics: subjective and objective responses to alcohol**
2-3 fold

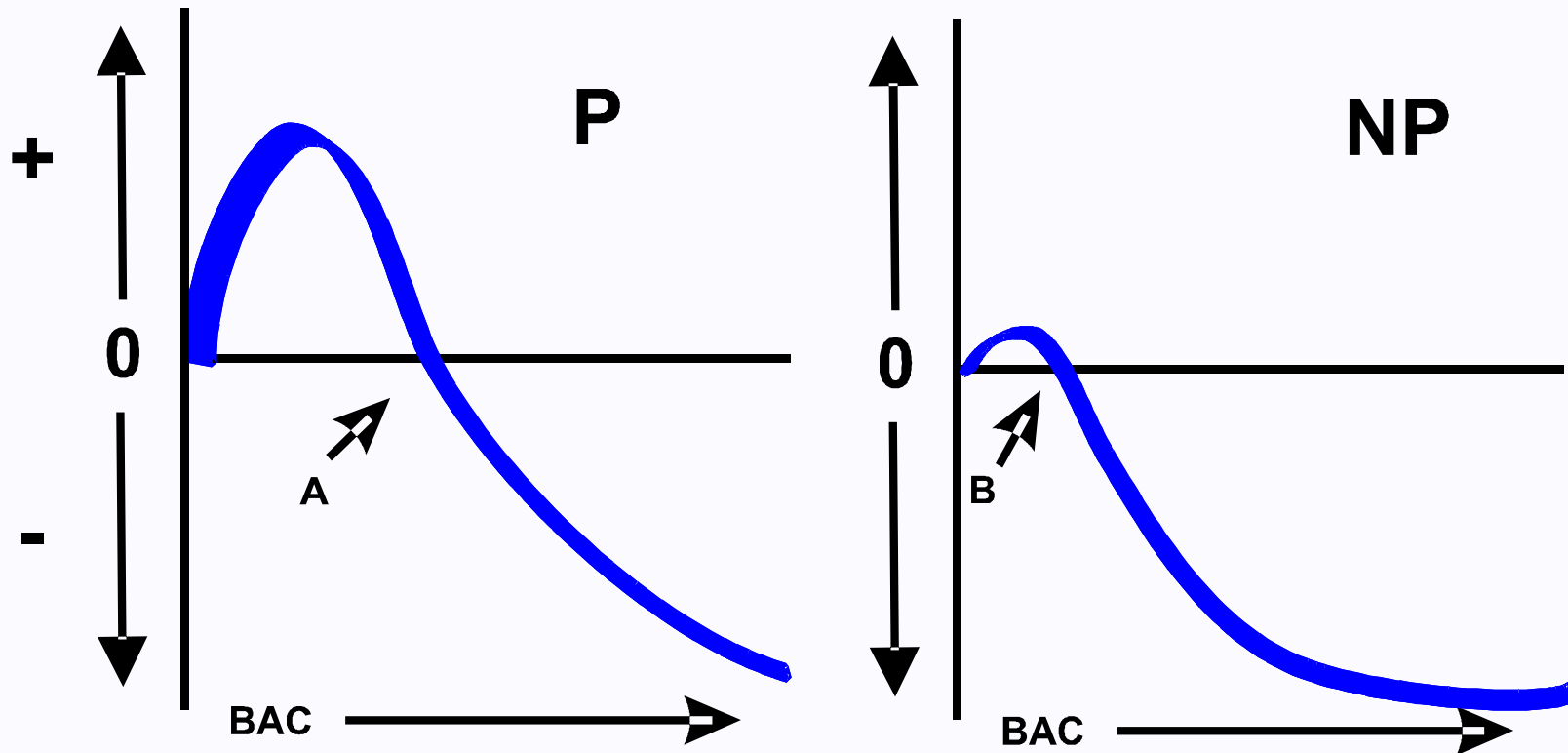
About one-half of these differences is genetic



Individual Variation in Response to Alcohol



Lessons Learned From Studies in Animal Models: Responses to Alcohol



Genes Confirmed for Alcoholism, a Common Complex Disorder

- Alcohol-specific

Aldehyde Dehydrogenase (ALDH2)

Alcohol Dehydrogenase (ADH)

- Non-specific to alcohol (e.g., shared with mental disorders, personality traits, and other endophenotypes)

GABRA2

AD/eeg-beta

GABRA6

AD/response sensitivity

GABRB3

AD/severity

5-HTT

AD Type II/phobia

COMT

Anxiety/cognition/stress response

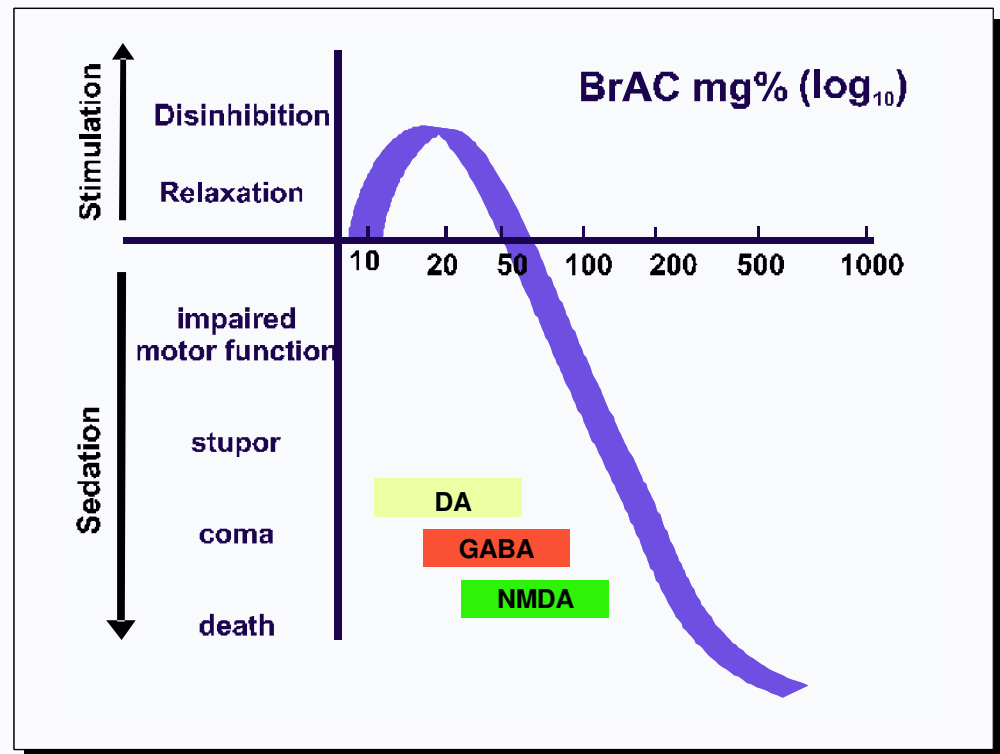
CHRM2

AD/Bipolar

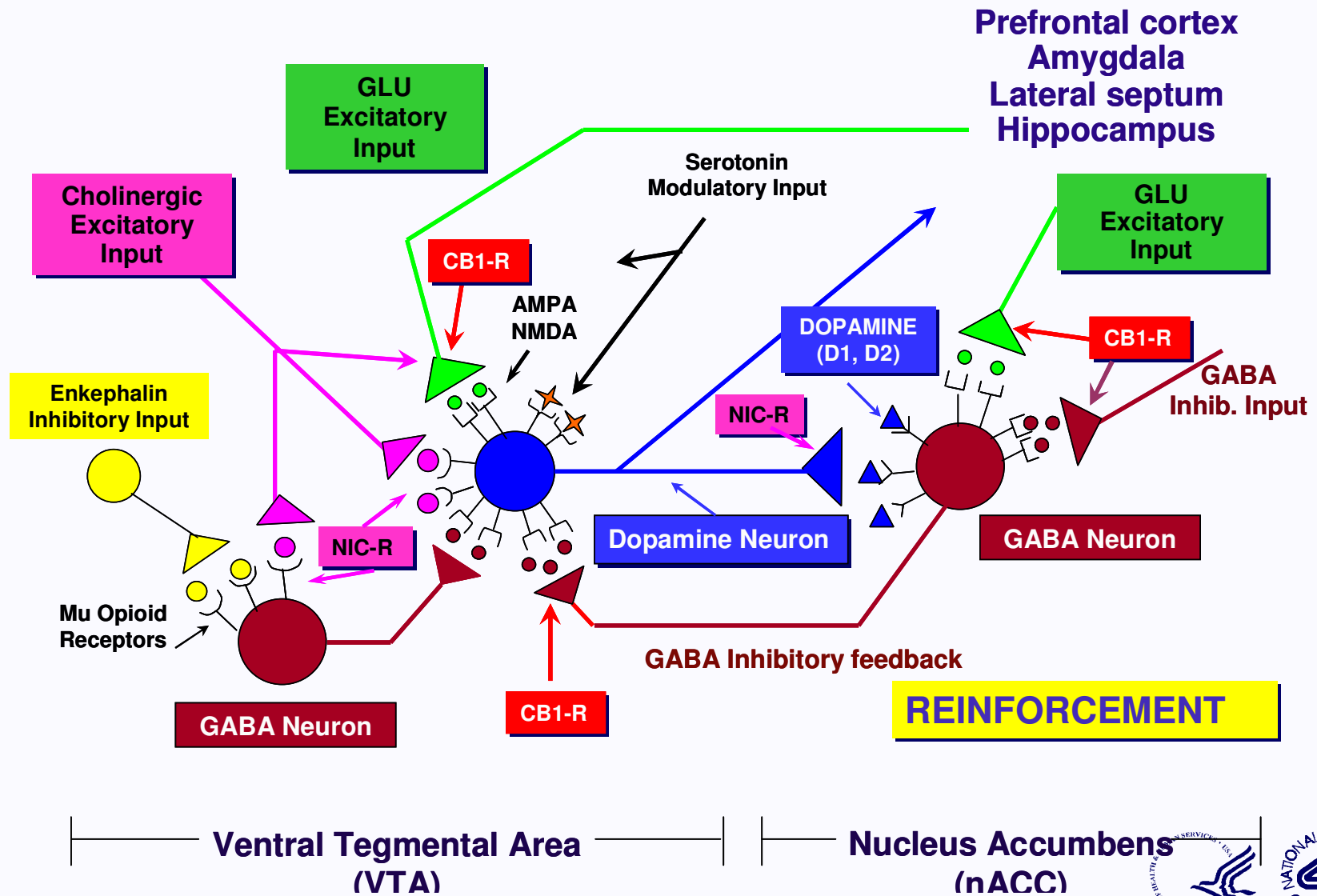


Alcohol Neuropharmacology

- All three compounds (ethanol, mM; acetaldehyde, μM ; acetate, mM) are psychoactive
- Behavioral response to alcohol is **biphasic**
- Between-individual variations are 3-4 fold, about one-half being genetic
- Multiple molecular targets in the brain (e.g., receptors and transporters of DA, GABA, and NMDA). Others include NAch, 5HT, CB, CRF, Adenosine, and Opioid)



Neurotransmitter/Modulator Relationships in Reinforcement



Medications for Treating Alcohol Dependence

	Medication	Target
FDA Approved	Disulfiram	Aldehyde Dehydrogenase
	Naltrexone	Mu Opioid Receptor
	Acamprosate	Glutamate-Related
<hr/>		
Under Investigation	Topiramate	GABA/Glutamate
	Valproate	GABA/Glutamate
	Ondansetron	5-HT₃ Receptor
	Nalmefene	Mu Opioid Receptor
	Baclofen	GABA_B Receptor
	Antalarmin	CRF1 Receptor
	Rimonabant	CB1 Receptor



Behavioral Therapies

Treatment Intervention	Primary Target Population(s)		
	High-risk drinkers	Alcohol abusers	Alcohol-dependent
Brief intervention	✓	✓	✓
Motivational enhancement therapy		✓	✓
Cognitive behavioral therapy			✓
Couples (marital) and family therapies			✓
Community reinforcement			✓

Selected References: Moyer et al., *Addiction* (2002) 97: 279-292; Miller et al., *Addiction* (2002) 97: 265-277; O'Farrell et al., *J. Sub. Abuse. Treat.* (2000) 18: 51-54



Brief Intervention

- Broad category of interventions varying in length and focus
- Addresses **high-risk drinking**
- Time-limited strategy focused on changing behaviors
- Common elements of brief intervention include:
 - raising awareness
 - advising change
 - monitoring through follow-up visits and supportive telephone consultations

See Moyer et al., *Addiction* (2002) 97:279-92



AUDIT-C¹

- Uses the first three **AUDIT** questions:

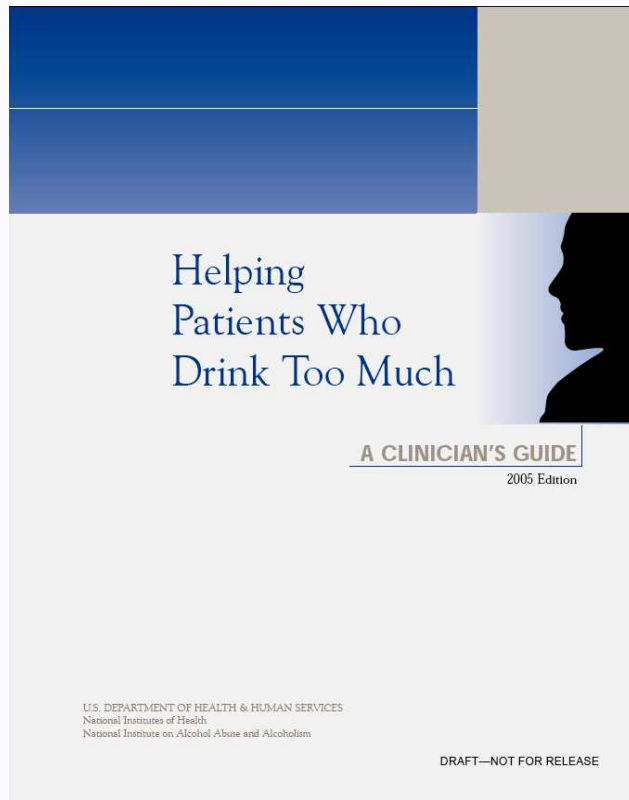
1. How often do you have a drink containing alcohol?
2. How many drinks containing alcohol do you have on a typical day when you are drinking?
3. How often do you have 6 or more drinks on an occasion?

- The **third question alone** is:

- **sensitive** for heavy drinking (79%) and alcohol abuse/ dependence (81%)
- **specific** (83%) for heavy drinking, abuse and dependence

¹Bush et al, Arch Intern Med. 1998;158:1789-1795

New Clinician's Guide Helping Patients Who Drink Too Much



Update takes advantage of new research information on screening and brief intervention. Its important new features include:

- ◆ **Simpler screen method** – a single question based on Question 3 of the AUDIT-C
- ◆ **New assessment strategy** that differentiates at-risk drinking from alcohol use disorders
- ◆ **Pocket guide** with new algorithm and prescribing information

Available from NIAAA in 2005

<http://www.niaaa.nih.gov>



Characteristics of Recovery From Alcoholism: New Findings from the NESARC

**Dawson et al., (2005). *Addiction*. 2005 Mar;100(3):296-8
NIAAA National Epidemiological Survey on Alcohol and
Related Conditions, 2001-2002**

The NESARC has allowed us to begin to define the recovery population, i.e., who recovers when and how, including:

- **Estimates of the hazard rates and cumulative conditional probabilities of recovery from DSM-IV alcohol dependence**
- **The impact of transitional life events on the recovery process (maturing out)**
- **Contrasts of the predictors of abstinent and nonabstinent recovery**
- **N= 4,422**

Selected Characteristics of Prior to the Past Year (PPY) Alcohol-Dependent Population (Age 18+)

- **The majority of adults with prior to the past year dependence are male, white, college-educated, with a FHP for alcohol dependence in first degree relatives**
- **More than one-third reported using tobacco and illicit drugs and having had a psychiatric disorder (mood, personality, and anxiety)**



Duration of Drinking to Onset of AD

For people who had **PPY alcohol dependence and were 14 or younger at first drink:**

- Smoking and FHP (1st degree relatives) are associated with earlier age at first drink and slightly later age at onset of dependence
- The mean duration to onset of dependence is 9.1 years

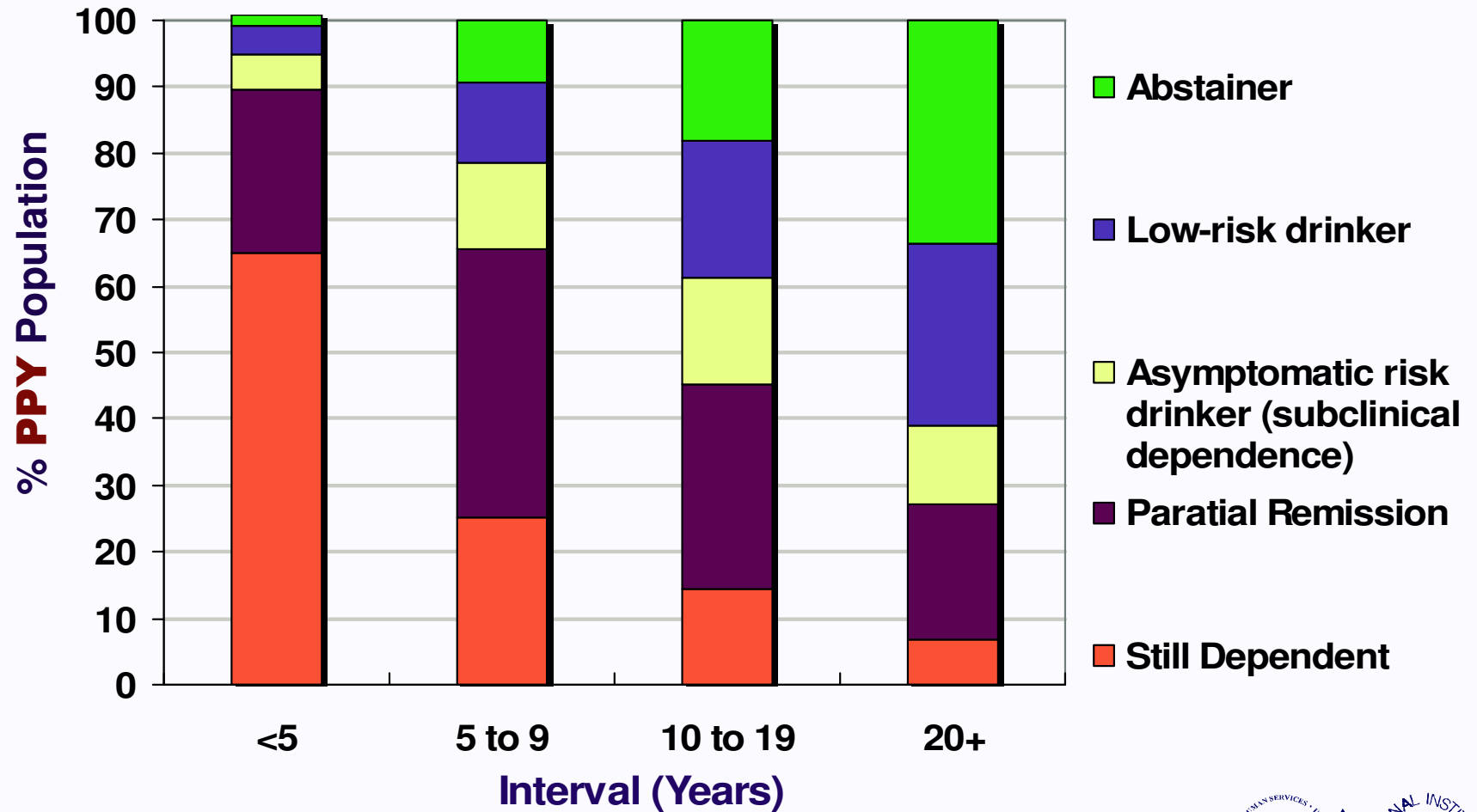


Recovery Status - U.S. Adults with alcohol dependence that began more than one year ago (i.e., prior to the past year or **PPY**)

Abstainers	18%
Low-risk drinkers	18%
Asymptomatic risk drinkers*	12%
Partial remission	27%
Still Dependent	25%

* (Men: 15+ drinks per week or 5+ drinks on any day;
Women: 8+ drinks per week or 4+ drinks on any day)

Past-year Status by Interval Since Onset of Dependence



Recovery Characteristics

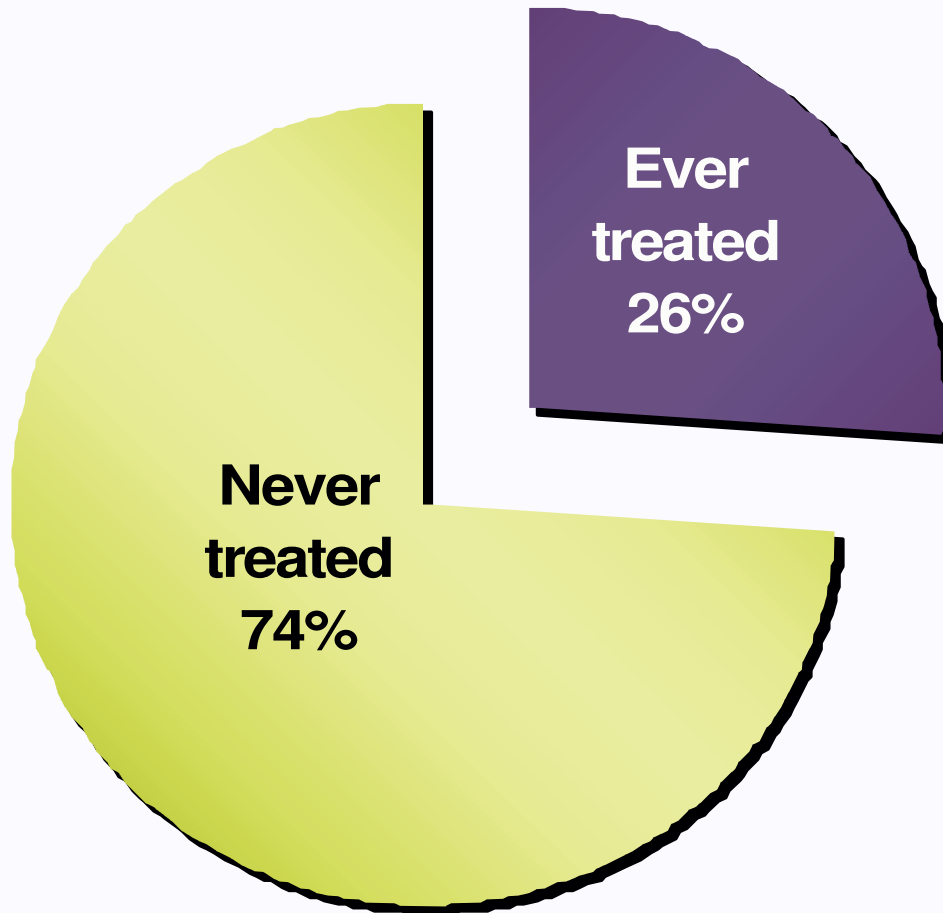
- Likelihood of **abstinent recovery** increased over time and among:
 - women, married or cohabiting individuals
 - early onset (18-24)
 - severe AD
- Likelihood of **low-risk drinking** increased over time and among:
 - married or cohabiting individuals
 - individuals who had a positive family history for alcohol dependence (FHP)
 - fewer AD symptoms



Recovery Characteristics

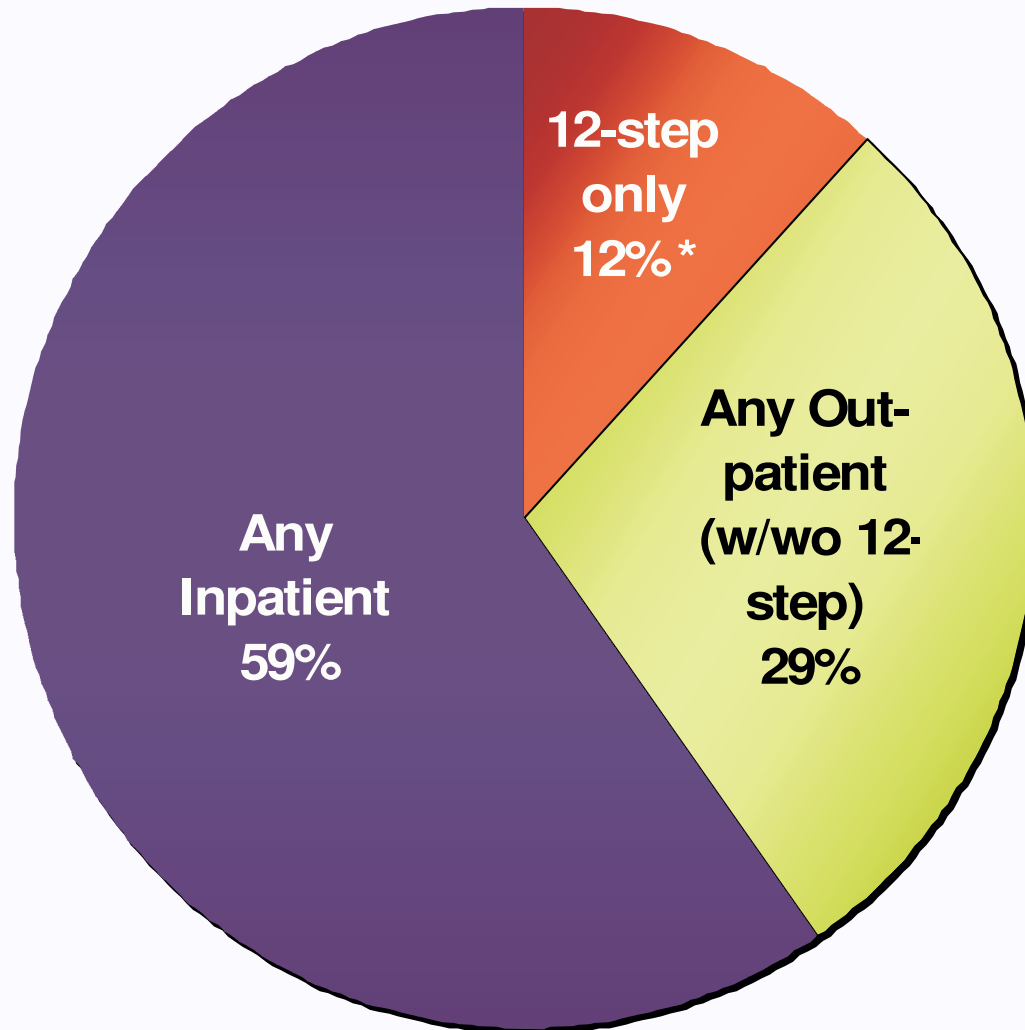
- The greater the peak quantity of alcohol consumed, the lower the likelihood of either type of recovery
- Personality disorder lowered likelihood of abstinent recovery
- Treatment for alcohol problems modified some of these effects

History of Prior Interventions in **PPY** Alcohol Dependence Subjects



The majority (74%) had never been treated

Type of Intervention Received



* Primarily AA



Likelihood Ratios for Treatment Effect on Selected Outcomes, by Type of Intervention

	Any Treatment	Any 12-Step	Any Outpatient	Any Inpatient
NA Recovery	NS*	NS*	1.6	NS*
AB Recovery	3.1	4.6	3.1	3.0

*No significant treatment effects



Treatment/Recovery Conclusions

- **Treatment significantly increases the likelihood of remission, recovery, and abstinence, may prolong the period of recovery, and appears to be most effective among those with the most severe disorders**
- **12-step programs are more strongly associated with abstinent recovery than any other form of treatment**



Limitations

- **Estimates based on respondent recall**
 - **years between age of onset and remission**
 - **symptoms of severity**
- **Cross-sectional study**
 - **data do not necessarily reflect the course of recovery across time for any individual**
- **Novel method of analysis**

Conclusions

- **Alcohol abuse and dependence** are common complex disorders arising from the interplay of alcohol-specific and non-specific genetic and environmental factors
- High rates of **comorbidity** with drug abuse, smoking, and mood and personality disorders persist from adolescence to adulthood
- Genetic animal models and understanding the neurotransmitters affected by alcohol provide opportunities for **pharmacotherapy** development
- Screening Behavioral **interventions** are **successful** in reducing hazardous alcohol consumption



Conclusions

- Treatment significantly increases the likelihood of recovery and remission
- Continued progress in understanding the mechanisms involved in the development of AUDs, will link *biology* and *psychology* and provide evidence-based approaches for *effective prevention and intervention*
- Developing models of dimensional severity in alcohol use disorders (as has been done in other disorders such as diabetes, and hypertension) is an important next step in preventing and treating AUDs



Acknowledgements

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- ▶ **Brenda G. Hewitt**

