ASAM VIRTUAL

REVIEW COURSE

in Addiction Medicine

2026



COURSE SYLLABUS:
FULL-SIZE SLIDES

https://elearning.asam.org/review-course

Welcome to the 2026 ASAM Review Course!

This course is widely recognized as the essential and foundational course for physicians who are preparing for the addiction medicine exam or for a career in addiction medicine. With a comprehensive curriculum, covering everything from neurobiology and pharmacology to individual substances and ethical concerns, the course offers a streamlined overview of addiction medicine delivered by an outstanding faculty lineup.

As part of registration, attendees will receive access to:

- 15 hours of live and on-demand lectures featuring national and international experts in addiction medicine.
- Weekly office hours with featured faculty and access to peers.
- Carefully crafted study guide offering suggestions on how to incorporate lectures and additional resources.

Letter from Committee Chair

Dear Colleague:

We are pleased to welcome you to the 2026 ASAM Virtual Review Course in Addiction Medicine! As of 2023, an estimated 54.2 million Americans aged 12 and older needed treatment for a substance use disorder in the past year – yet, only 23% of those received the help they needed (NSDUH). With this alarming statistic, we appreciate each of you for taking the time to learn more about addiction, the process of becoming certified, and for working with us to help bridge this gap.

On behalf of the Program Planning Committee, I encourage you to get the most out of your experience by taking advantage of everything The ASAM Virtual Review Course has to offer. We look forward to connecting with you!

Sincerely,



Jonathan D. Avery, MD, FASAM, *Chair*

Learning Objectives

Upon completion, participants should be able to:

- Demonstrate practical knowledge on the neurobiology of addiction and articulate its activity in terms useful in a clinical setting.
- Describe the effects of alcohol, nicotine/tobacco, and other drugs in both tolerant and non-tolerant individuals.
- Describe the process for diagnosing addiction and differentiating the symptoms of addiction from those of other medical or psychiatric disorders.
- Explain the various pharmacologic and psychosocial treatments for addictive disorders and describe the factors that should be considered in selecting a treatment modality to match the needs of a specific patient.
- Describe the precipitants of relapse and current evidence-based practices to prevent and manage relapse.

Course Planning Committee

Jonathan Avery, MD, FASAM, *Chair*
Faye Chao, MD
Mashal Khan, MD
Annie Levesque, MD, MSc, FASAM
Carolyn Warner-Greer, MD, FACOG, FASAM

Addiction Medicine Certification Exam Information

There are two organizations offering addiction medicine certification exams: the American Board of Preventive Medicine (ABPM) and American Osteopathic Association (AOA). The ASAM Review Course curriculum is carefully mapped to their exam blueprints.

ABPM Addiction Medicine Exam Blueprints

CORE CONTENT AREAS	
25%	Definitions
	Genetics
	Pharmacokinetic and Pharmacodynamic Principles
	Pharmacology
	Neurobiology of Addiction
20%	Epidemiological Concepts
	Epidemiological Trends of Substance Use Disorders
	Prevention
40%	Screening, Assessment, and Brief Intervention
	Overview of Addiction Treatment
	Management of Inpatient and Outpatient Intoxication, and Withdrawal
	Pharmacologic Interventions for Addictions
	Behavioral Interventions
	Co-Occurring and Medical Disorders among Patients with Alcohol and Other Drug Use and Addiction
	Co-Occurring Psychiatric Disorders among Patients with Alcohol and Other Drug Use and Addiction
	Pain and Addiction
15%	Ethical, Legal, and Liability Issues in Addiction Practice

SUBSTANCE AREAS	
15-20%	Alcohol
7-10%	Sedatives
7-10%	Stimulants
10-15%	Opioids
7-10%	Cannabinoids
15-20%	Nicotine
0.5-3%	Hallucinogens
0.5-3%	Dissociatives
0.5-3%	Inhalants
0.5-3%	Anabolic steroids
1-3%	Other substances
1-3%	Nonsubstance addiction
1-5%	General/All substances combined

AOA Addiction Medicine Exam Blueprint

CORE CONTENT AREAS	
24%	Pharmacology
18%	Epidemiology and Genetics
15%	Treatment
14%	Legal Aspects
12%	Diagnosis
11%	Special Populations
6%	Prevention

Learn More

Explore ABPM's Website:
https://www.theabpm.org/become-certified/subspecialties/addiction-medicine/

Explore AOA's Website:
https://certification.osteopathic.org/addiction-medicine/

Explore ASAM's Certification Guide:
https://www.asam.org/education/addiction-medicine-certification

Claiming Credit & Certificate

Claim credit anytime between July 27, 2026, and July 27, 2027.

Review Course Registrants:

1. Type https://eLearning.ASAM.org into your web browser.
2. Log in to the eLearning Center (eLC), using your ASAM.org username and password (what you used when registering for the course).
3. After logging in, select “My Dashboard” from the top menu (on mobile devices, you will find “My Dashboard” by clicking the three horizontal lines in the header).
4. Locate “Evaluation & Certificate - Live Attendees of the 2026 Review Course in Addiction Medicine,” which will be under "Courses and Sessions.”
5. Click “Content” and find the box that says “Complete Evaluation.” Click the button that says, “Fill out Survey.”
6. After you have completed the evaluation, select the box labeled “Claim Credit & Certificate” and click the button that says, “Claim Medical Credits.”
7. Select your provider type and the number of hours you attended, then click “Submit.”
8. Print out your certificate or save it on your device.

Watching Sessions On-Demand

Relive the course or catch sessions you missed! Registrants of the ASAM 2026 Virtual Review Course in Addiction Medicine receive complimentary access to their sessions on-demand in the ASAM eLearning Center. On-demand sessions will be available from July 27, 2026 – July 27, 2029.

Did You Know?

Sessions are also available as audio-only, so you can review on-the-go.

More Information

Learn more about ASAM by visiting: https://asam.org

If you have any questions or experience any issues, please contact ASAM Staff at education@asam.org

Review Course Schedule & Table of Contents

The full course schedule, including speaker information, live stream links, time changes, and more is available on the course website: https://reviewcourse.asam.org/.

Thursday, July 23, 2026

Time	Session	Page #
10:00 am – 10:05 am	**Welcome and Course Overview** *Jonathan D. Avery, MD, FASAM*	
10:05 am – 11:05 am	**Neurobiology of Addiction: Key Concepts and Models** *Petros Levounis, MD, MA, DFASAM*	7
11:05 am – 12:05 pm	**Alcohol Use Disorder: Neurobiology, Diagnosis and Treatment** *Ricardo Restrepo, MD, MPH, FASAM*	47
12:05 pm – 12:15 pm	**Break**	
12:15 pm – 1:00 pm	**Sedative Use Disorder: Research and Practice** *Ricardo Restrepo, MD, MPH, FASAM*	155
1:00 pm – 1:40 pm	**Opioid Use Disorder: Science, History, and Clinical Implications** *Soteri Polydorou, MD*	242
1:40 pm – 2:20 pm	**Pain and Addiction: Trends and Treatments** *Edwin A. Salsitz, MD, DFASAM*	297
2:20 pm – 2:40 pm	**Break**	
2:40 pm – 2:45 pm	**Interesting Case** *Edwin A. Salsitz, MD, DFASAM*	352
2:45 pm – 3:30 pm	**Nicotine Use Disorder: Public Health and Practice** *Jonathan D. Avery, MD, FASAM*	364
3:30 pm – 4:15 pm	**Cannabis Use Disorder: Science, Trends, and Clinical Implications** *Mashal K. Khan, MD*	439
4:15 pm – 4:25 pm	**Break**	
4:25 pm – 5:25 pm	**Stimulant Use Disorder: From Neurobiology to Public Health** *Siddarth Puri, MD*	513
5:25 pm – 6:00 pm	**Other Classes of Drugs: Pharmacology and Epidemiology** *Annie Levesque, MD, MSc, FASAM*	592
6:00 pm – 6:35 pm	**Behavioral Addiction: Criteria, Challenges and Considerations** *Faye Chao, MD*	652

Friday, July 24, 2026

Time	Session	Page #
10:00 am – 10:05 am	**Welcome Back & Day Two Overview** *Jonathan D. Avery, MD, FASAM*	
10:05 am – 10:25 am	**Evolution of Addiction and Treatment: History and Impact** *Timothy K. Brennan, MD, MPH*	704
10:25 am – 11:30 am	**Epidemiology: Core Concepts and Applications** *Jeffrey J. DeVido, MD, MTS, FAPA, FASAM*	733
11:30 am – 12:00 pm	**Prevention and Public Health: From Theory to Practice** *Amutha V. Rajagopal, MD, MPH, FASAM*	807
12:00 pm – 12:15 pm	**Break**	
12:15 pm – 12:35 pm	**Genetics and Gender: Impacts on Diagnosis and Care** *Leslie A. Hayes, MD*	845
12:35 pm – 1:35 pm	**Pharmacology and Toxicology: Principles, Applications, and Limitations** *Lewis S. Nelson, MD, MBA*	903
1:35 pm – 2:15 pm	**Medical Co-Morbidities: Diagnosis, Prevention and Complications** *Carolyn Warner-Greer, MD, FACOG, FASAM*	972
2:15 pm – 2:35 pm	**Break**	
2:35 pm – 2:45 pm	**Interesting Case** *Edwin A. Salsitz, MD, DFASAM*	1009
2:45 pm – 3:30 pm	**Psychiatric Co-Morbidities: Complexities of Diagnosis and Care** *Mason S. Turner, MD, DFASAM*	1024
3:30 pm – 4:00 pm	**Pregnancy and Newborns: Considerations from Science to Systems** *Leslie A. Hayes, MD*	1090
4:00 pm – 4:30 pm	**Treatment for Different Stages of Life: Adolescents, Young Adults, and the Elderly** *Michael I. Fingerhood, MD*	1161
4:30 pm – 4:45 pm	**Break**	
4:45 pm – 5:15 pm	**Psychosocial Interventions: Cognitive Behavioral Therapy and Motivational Interviewing** *Eve N. Lasswell, PsyD*	1208
5:15 pm – 5:45 pm	**Psychosocial Interventions: Mutual Help and Social Support** *Smita Das, MD, PhD, MPH*	1231
5:45 pm – 6:30 pm	**Ethics and the Law: Principles and Implications** *David Y. Kan, MD, DFASAM*	1252

ASAM REVIEW COURSE 2026

Neurobiology of Addiction: Key Concepts and Models

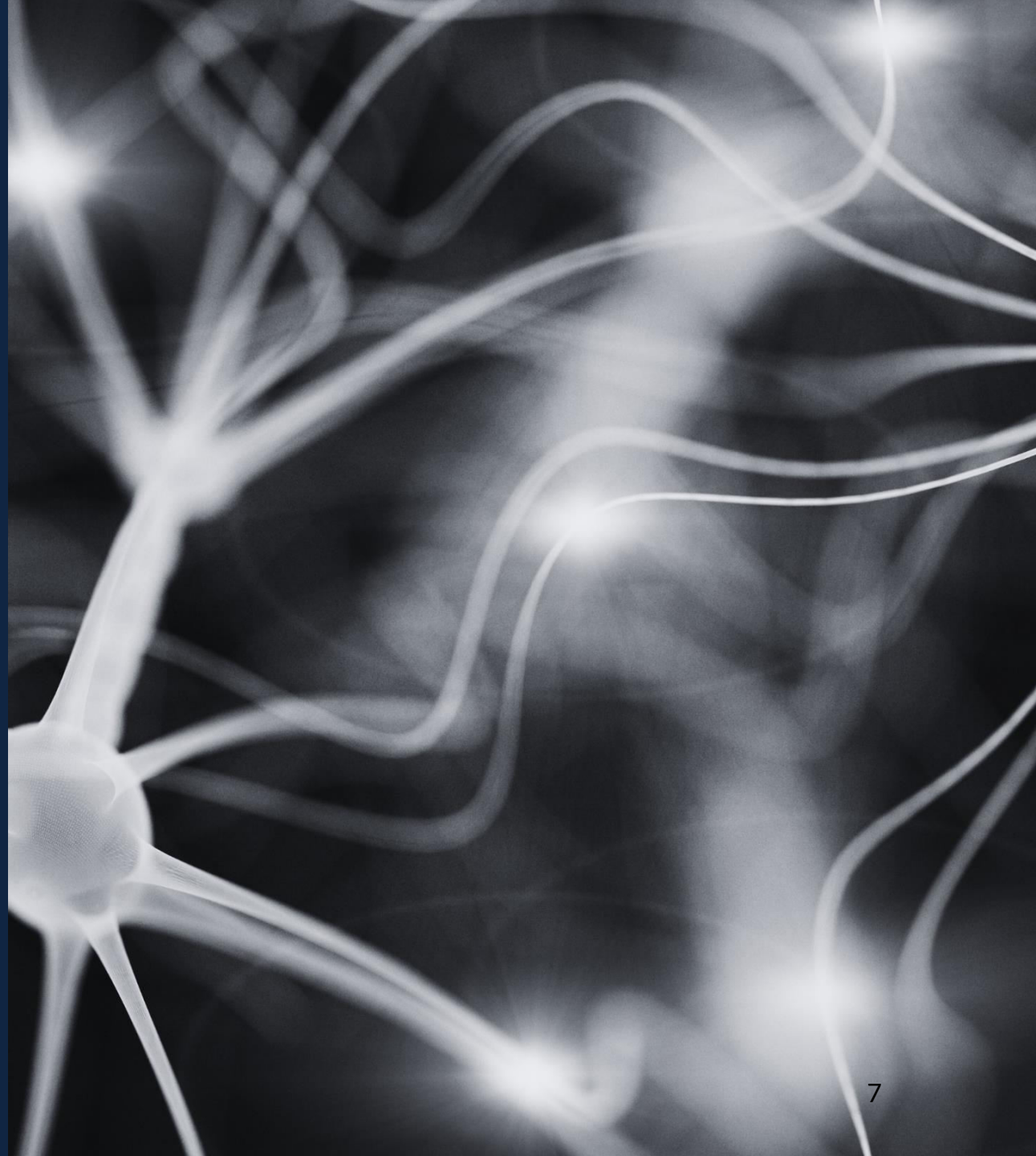
Petros Levounis, MD, MA

Professor and Chair, Department of Psychiatry, and Associate Dean, Rutgers New Jersey Medical School

Chief of Service, University Hospital, Newark, New Jersey

Director, Northern New Jersey Medications for Addiction Treatment Center of Excellence

Past President, American Psychiatric Association





Financial Disclosure

Petros Levounis, MD, MA

- No relevant disclosures

LEARNING OBJECTIVE

Identify key neurotransmitters, brain pathways, and brain structures implicated in addiction and addiction treatment.



Outline



1. Neurotransmitters
2. The Fundamental Model
3. The New and Improved Model
4. Treatments

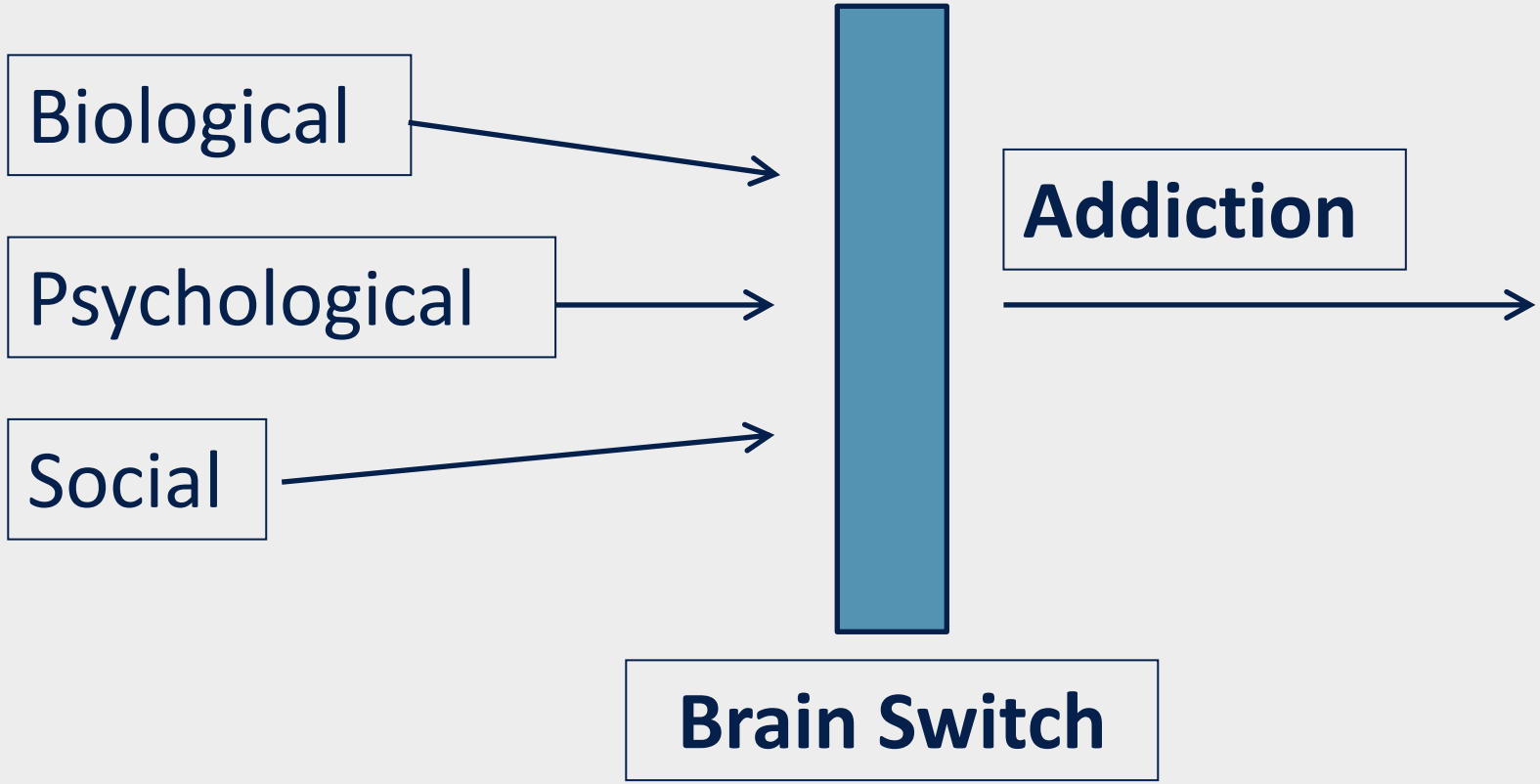
Neurotransmitters

Substance	Endogenous Neurotransmitter
Alcohol	GABA / Glutamate*
Amphetamines & Cocaine	Dopamine
Benzodiazepines & GHB	GABA
Cannabis	Anandamide
Hallucinogens & MDMA	Serotonin
Nicotine	Acetylcholine
Opioids	Endorphins
Phencyclidine & Ketamine	Glutamate*

*Drug acts as an antagonist at the NMDA subtype of the glutamate receptor.

The Fundamental Model

Addiction: A Biopsychosocial Illness



Olsen and Levounis, Sober Siblings, 2008

The Root Cause of the Disaster

ADDICTION RARE IN PATIENTS TREATED WITH NARCOTICS

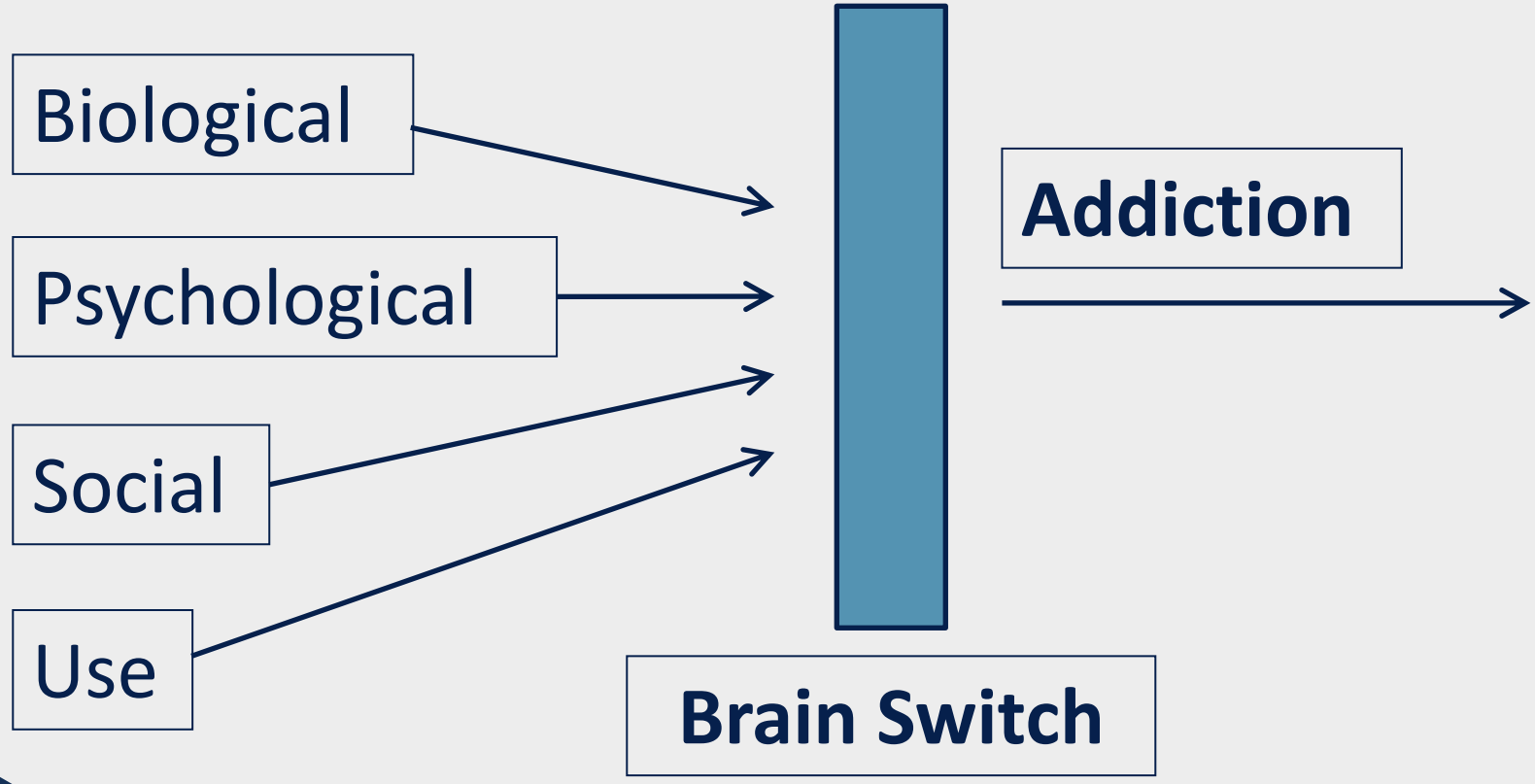
To the Editor: Recently, we examined our current files to determine the incidence of narcotic addiction in 39,946 hospitalized medical patients[1] who were monitored consecutively. Although there were 11,882 patients who received at least one narcotic preparation, there were only four cases of reasonably well documented addiction in patients who had no history of addiction. The addiction was considered major in only one instance. The drugs implicated were meperidine in two patients,[2] Percodan in one, and hydromorphone in one. We conclude that despite widespread use of narcotic drugs in hospitals, the development of addiction is rare in medical patients with no history of addiction.

JANE PORTER
HERSHEL JICK, M.D.
Boston Collaborative Drug Surveillance Program
Waltham, MA 02154 Boston University Medical Center

1. Jick H, Miettinen OS, Shapiro S, Lewis GP, Siskind Y, Slone D. Comprehensive drug surveillance. JAMA. 1970; 213:1455-60.
2. Miller RR, Jick H. Clinical effects of meperidine in hospitalized medical patients. J Clin Pharmacol. 1978; 18:180-8.

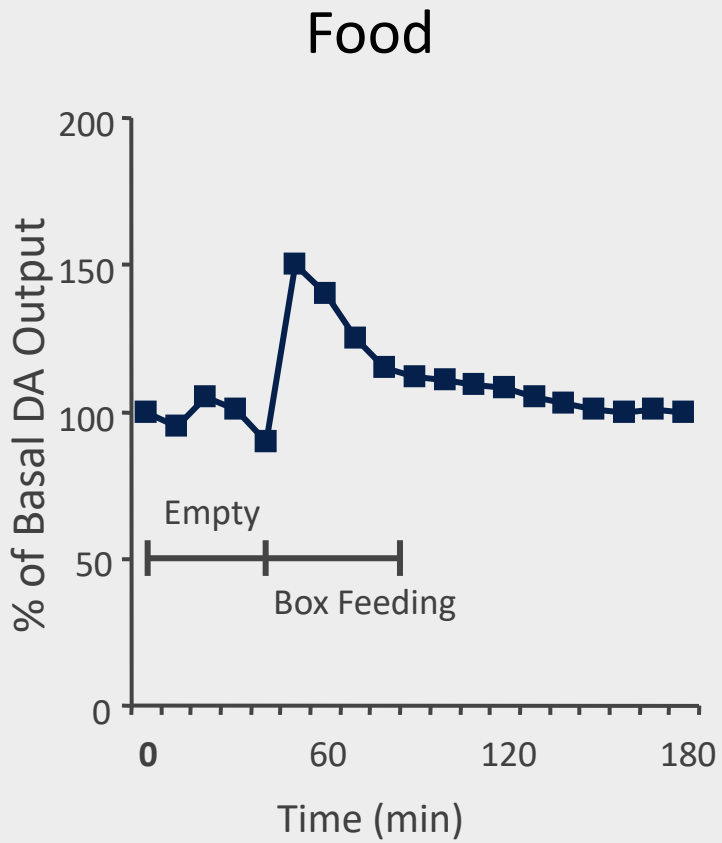
Porter and Jick, N Engl J Med, January 10, 1980

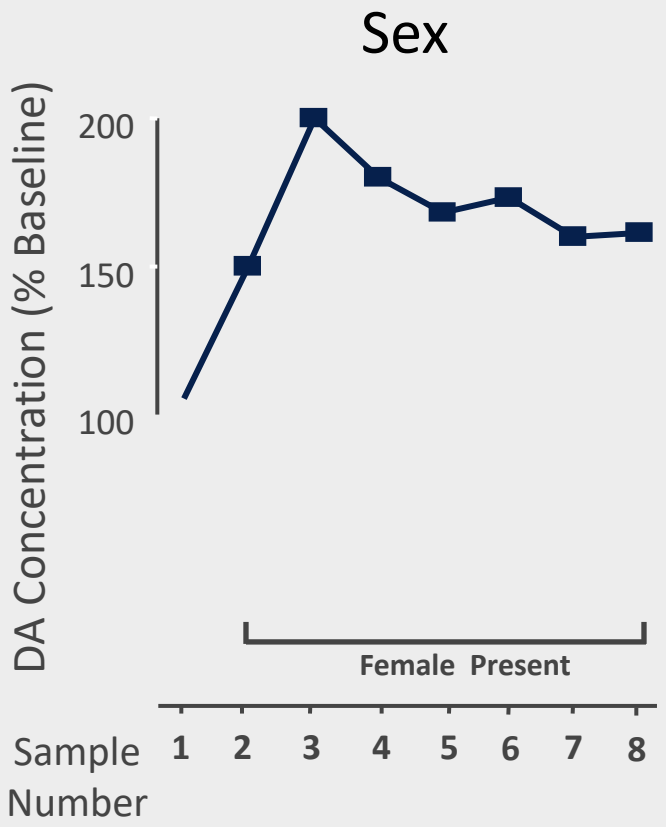
Addiction: A Biopsychosocial Illness



Olsen and Levounis, Sober Siblings, 2008

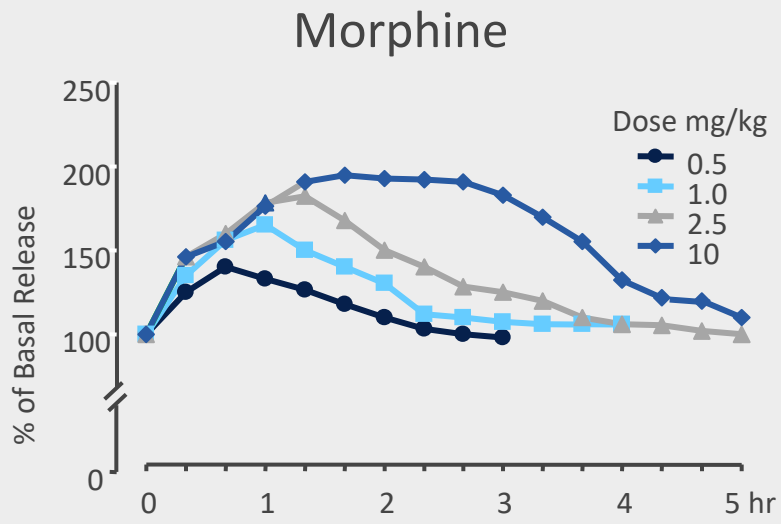
Basal Ganglia (Nucleus Accumbens) and Binge/Intoxication

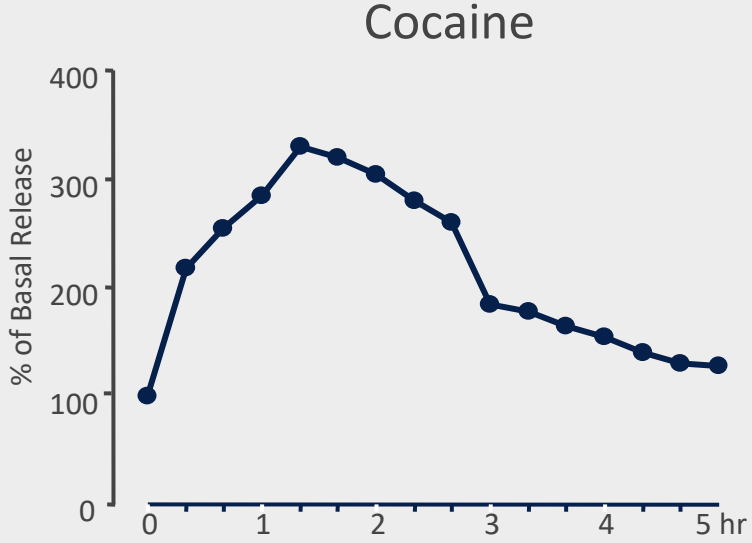


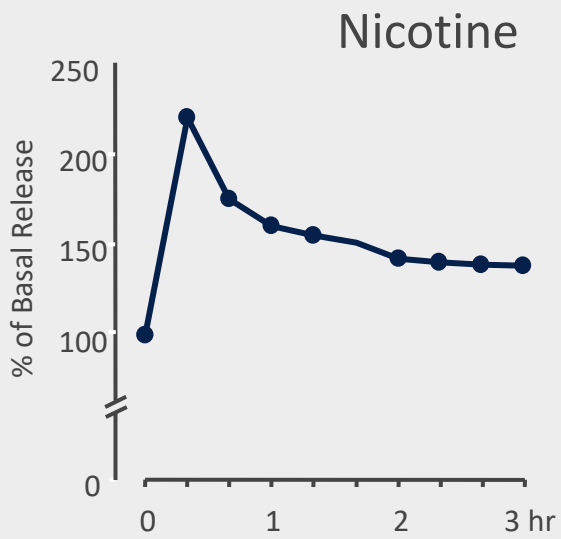


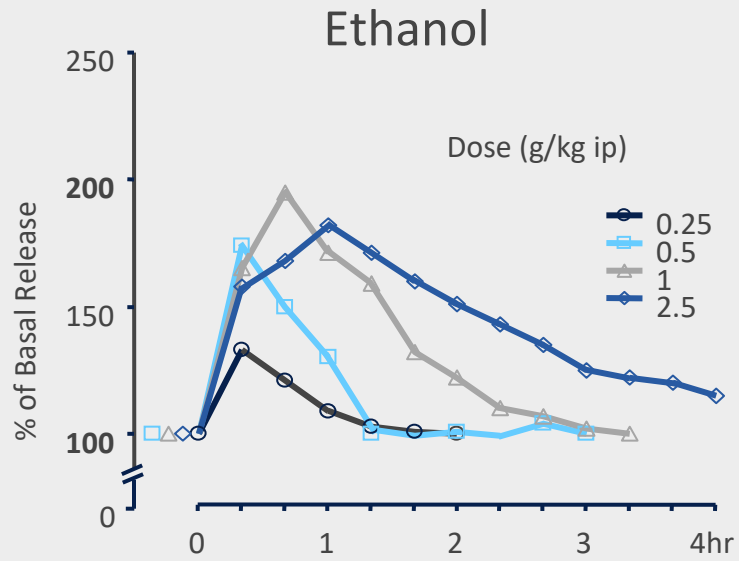
Adapted from: Di Chiara et al, Neuroscience, 1999; Adapted from: Fiorino and Phillips, J Neuroscience, 1997; courtesy of Nora D. Volkow, MD

Effects of Drugs on Dopamine Levels



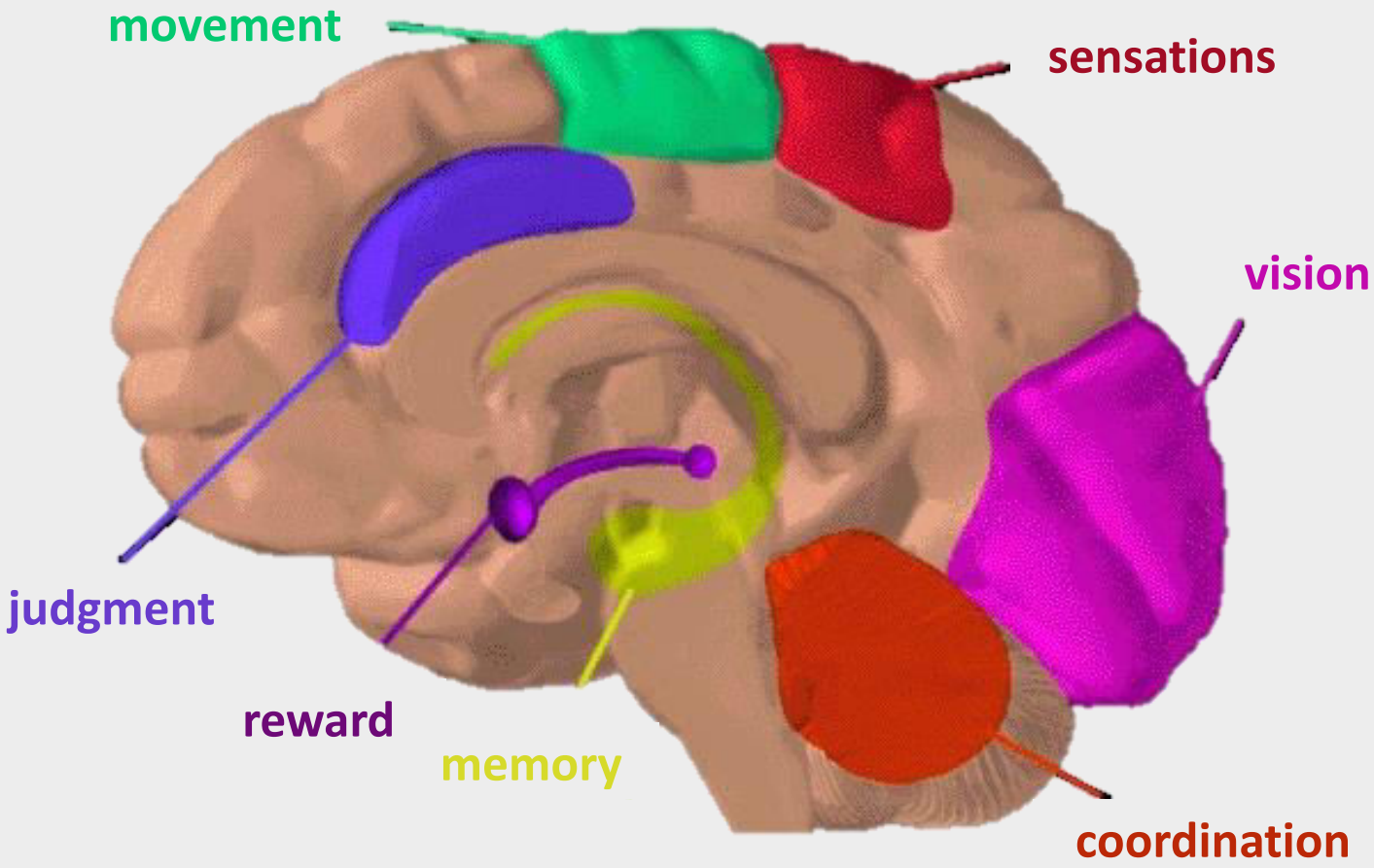






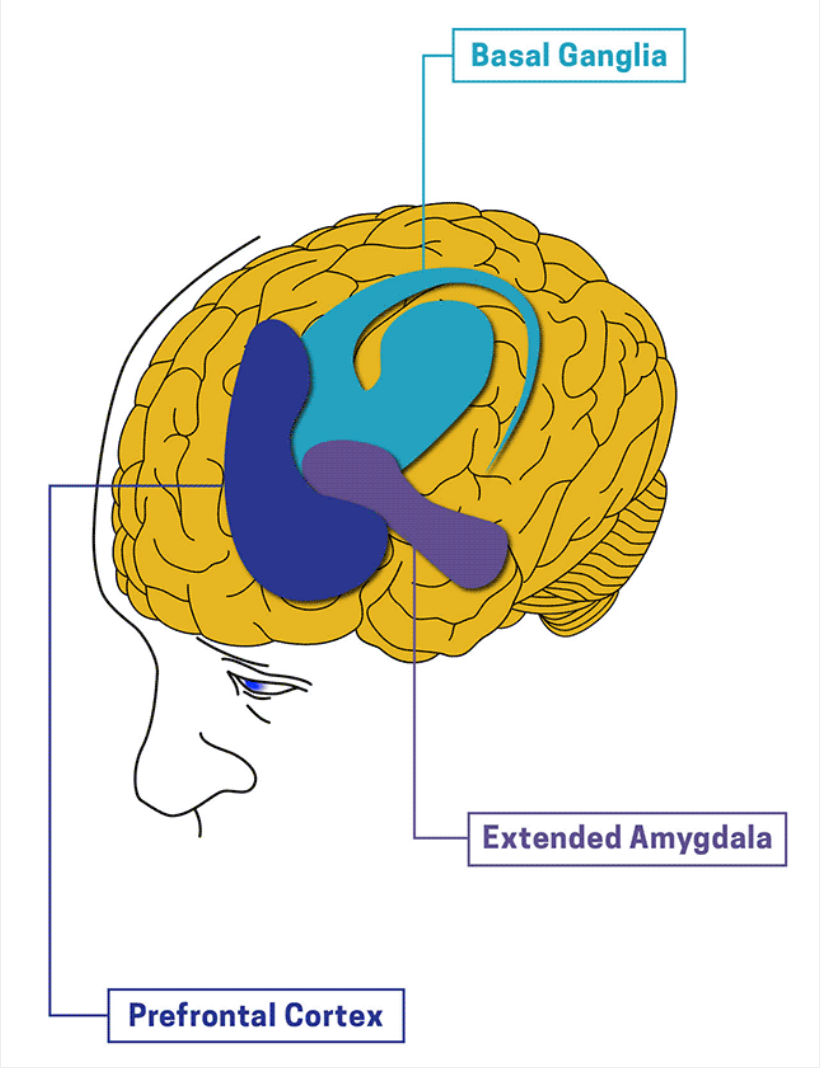
Adapted from: Di Chiara and Imperato, Proceedings of the National Academy of Sciences USA, 1988; courtesy of Nora D Volkow, MD

Hippocampus and Extended Amygdala



National Institute on Drug Abuse, NIDA.NIH.gov, 2000

Prefrontal Cortex and Executive Function



National Institute on Drug Abuse, NIDA.NIH.gov, accessed on May 1, 2026

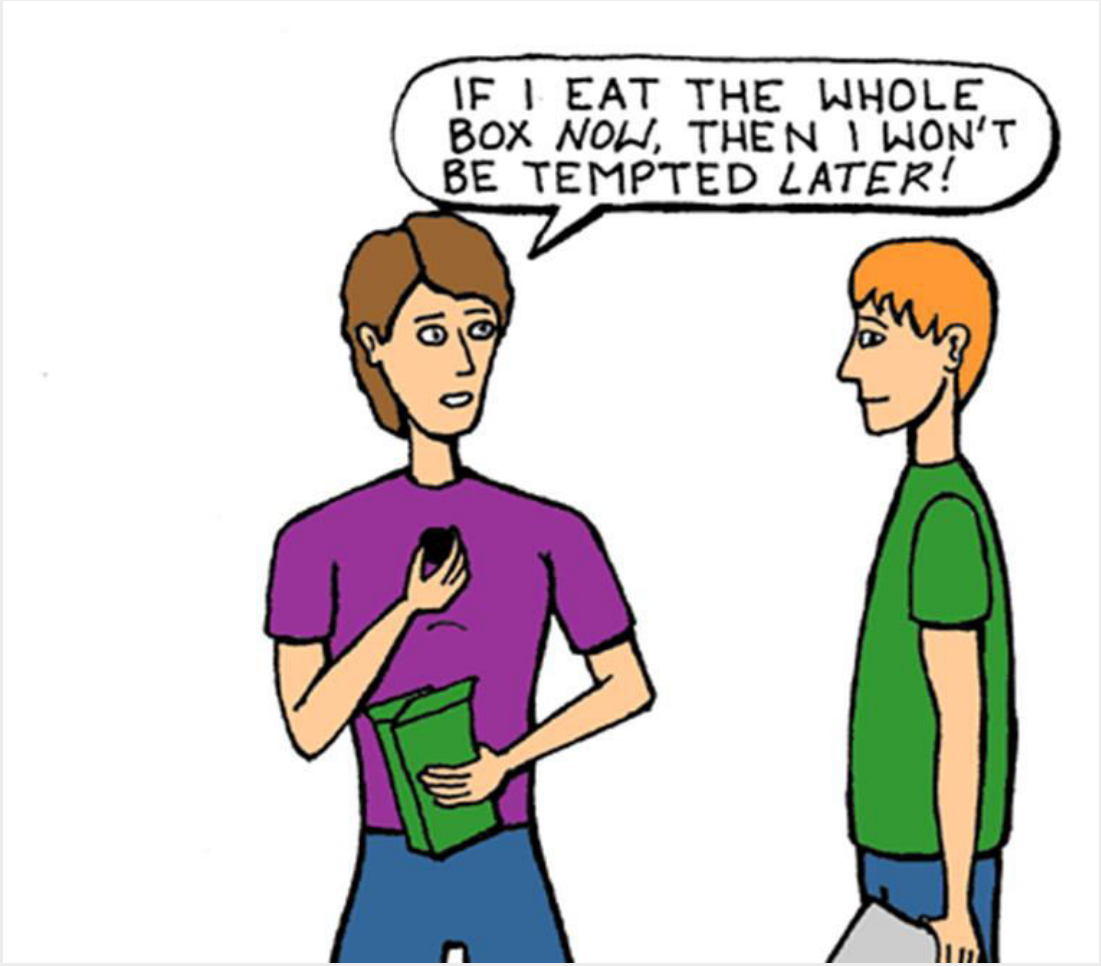
The New and Improved Model

Three Novel Areas

Motivational Circuitry (Medial OFC)	Antireward Pathways (Extended Amygdala)	Interoception (Insula)

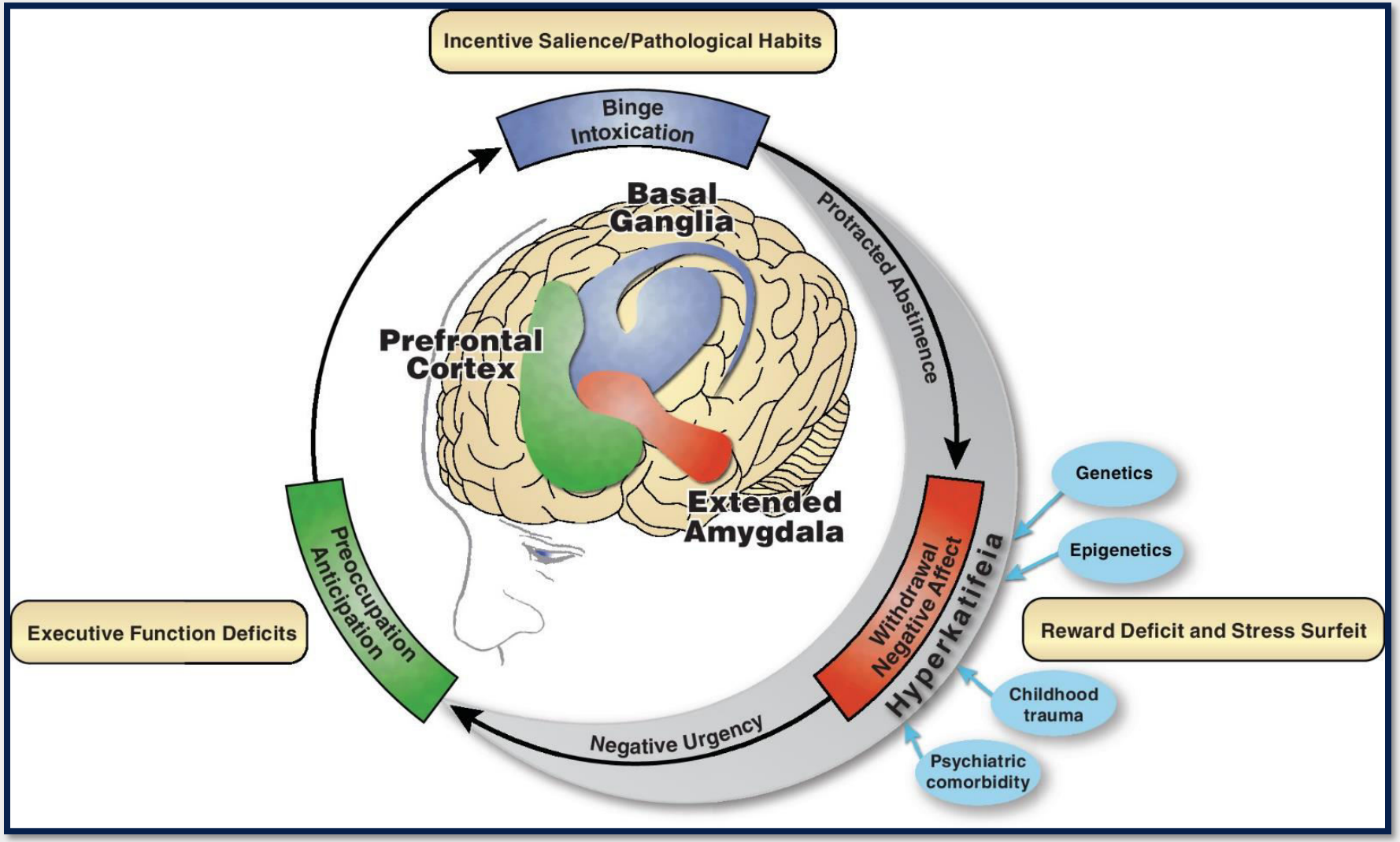
Levounis, Journal of Medical Toxicology, 2016

Medial Orbitofrontal Cortex (OFC) and Preoccupation/Anticipation



Levounis, Arnaout, and Marienfeld, Motivational Interviewing for Clinical Practice, 2017

Extended Amygdala and Withdrawal/Negative Affect



Koob, American Journal of Psychiatry, 2020

Reward Systems

Game #1

A. A sure gain of $250
B. 25% chance to gain $1,000, 75% chance to gain nothing.



Adapted from: Tversky and Kahneman, Science, 1981

Reward Systems

Game #1

A. A sure gain of $250 **84%**

B. 25% chance to gain $1,000, 75%
chance to gain nothing **16%**



Adapted from: Tversky and Kahneman, Science, 1981

Anti-Reward Systems

Game #2

A. A sure loss of $750
B. 25% chance to lose nothing, 75% chance to lose $1,000.



Adapted from: Tversky and Kahneman, Science, 1981

Anti-Reward Systems

Game #2

A. A sure loss of $750 **13%**

B. 25% chance to lose nothing, 75%
chance to lose $1,000. **87%**



Adapted from: Tversky and Kahneman, Science, 1981

Human Nature

People avoid risks to ensure gains.

People take risks to avoid definite losses.

Psychology trumps probability.

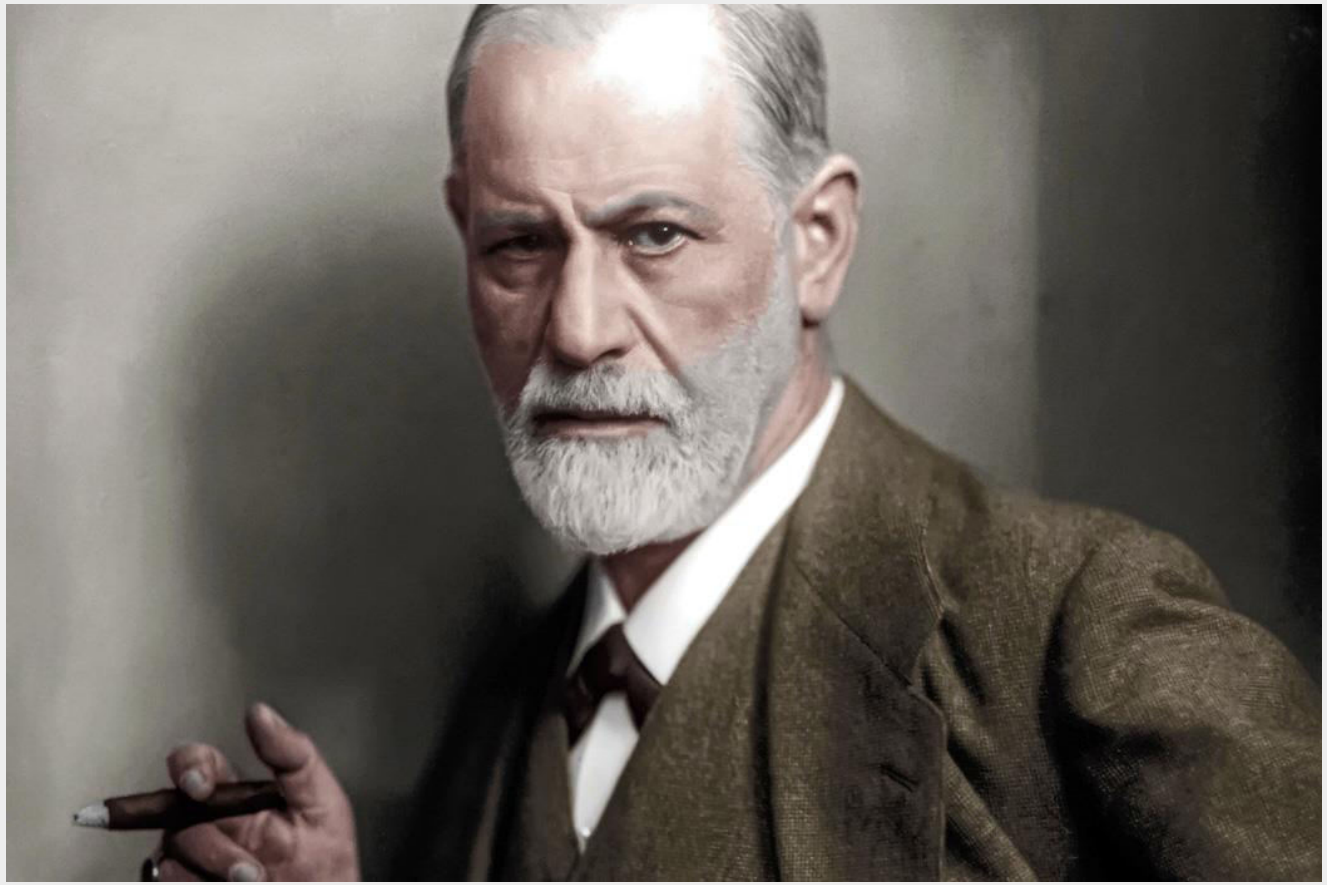
The Ultimate Gatekeeper: Insula



Zerbo, Schlechter, Desai, and Levounis, Becoming Mindful, 2017

Treatments

1st Wave: Psychoanalysis



2nd Wave: Boot Camps

The prototype, Synanon, was founded in California in 1958 to address heroin addiction. The goal was to:

- break down defenses,
- bust through denial, and
- reshape the individual's personality.

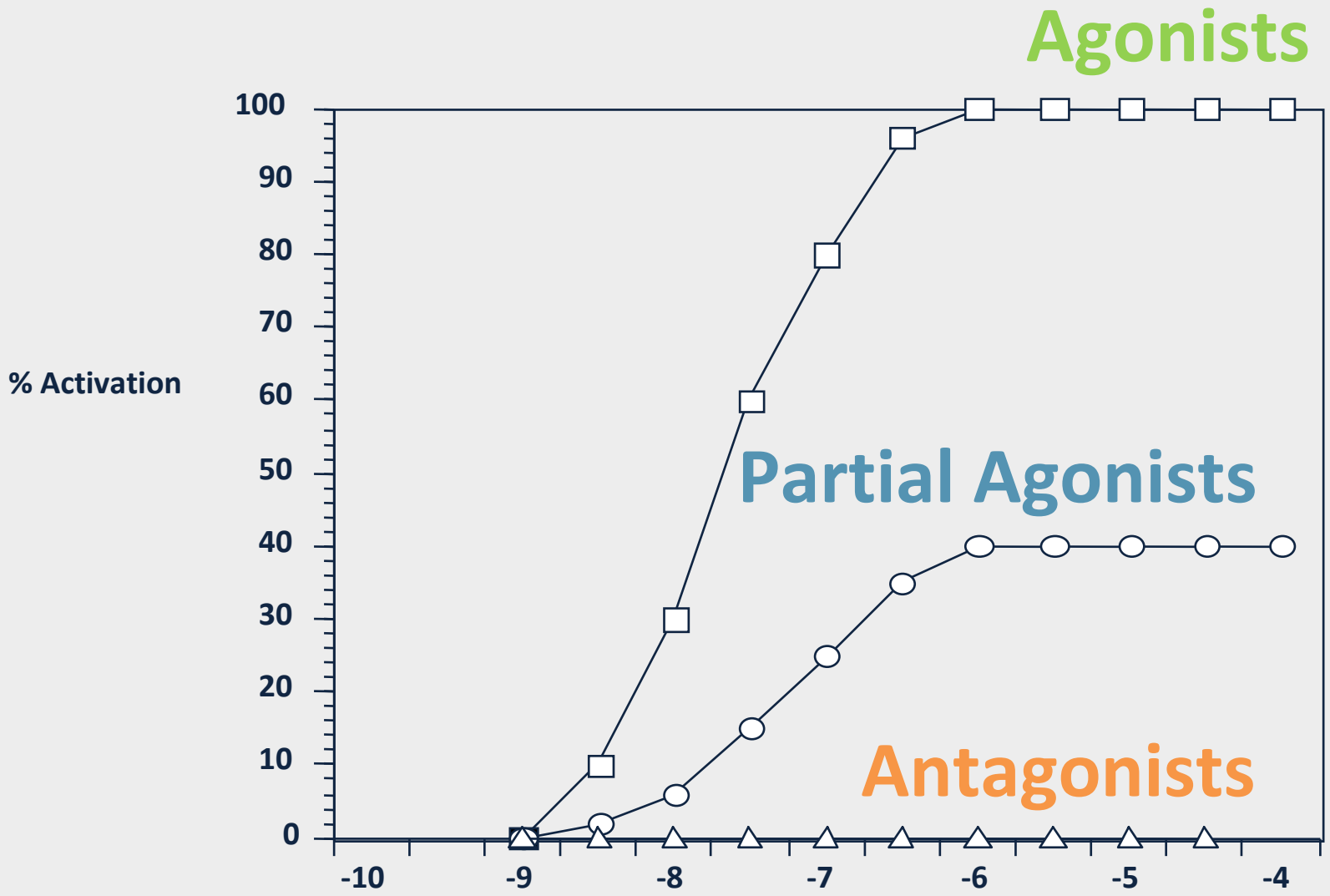
3rd Wave: Current Treatments

Medications

Mutual Help

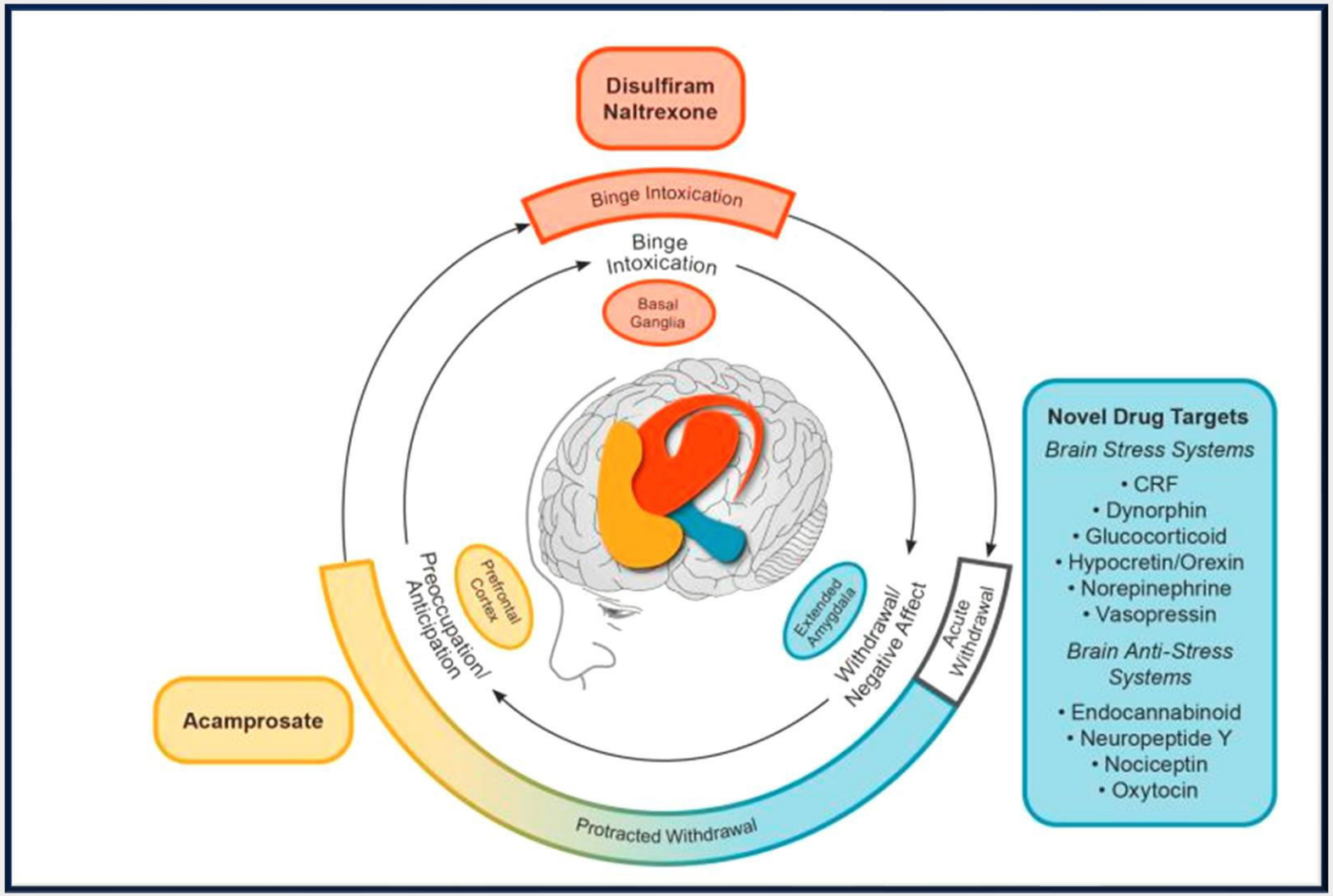
Psychotherapy and Counseling

Medications (opioids and tobacco)



Renner JA, Chen C, Suzuki J, and Levounis P, *Buprenorphine Treatment of Opioid Use Disorder, 3nd Edition*, American Psychiatric Association Publishing, 2026, in press

Medications (alcohol and possibly others)



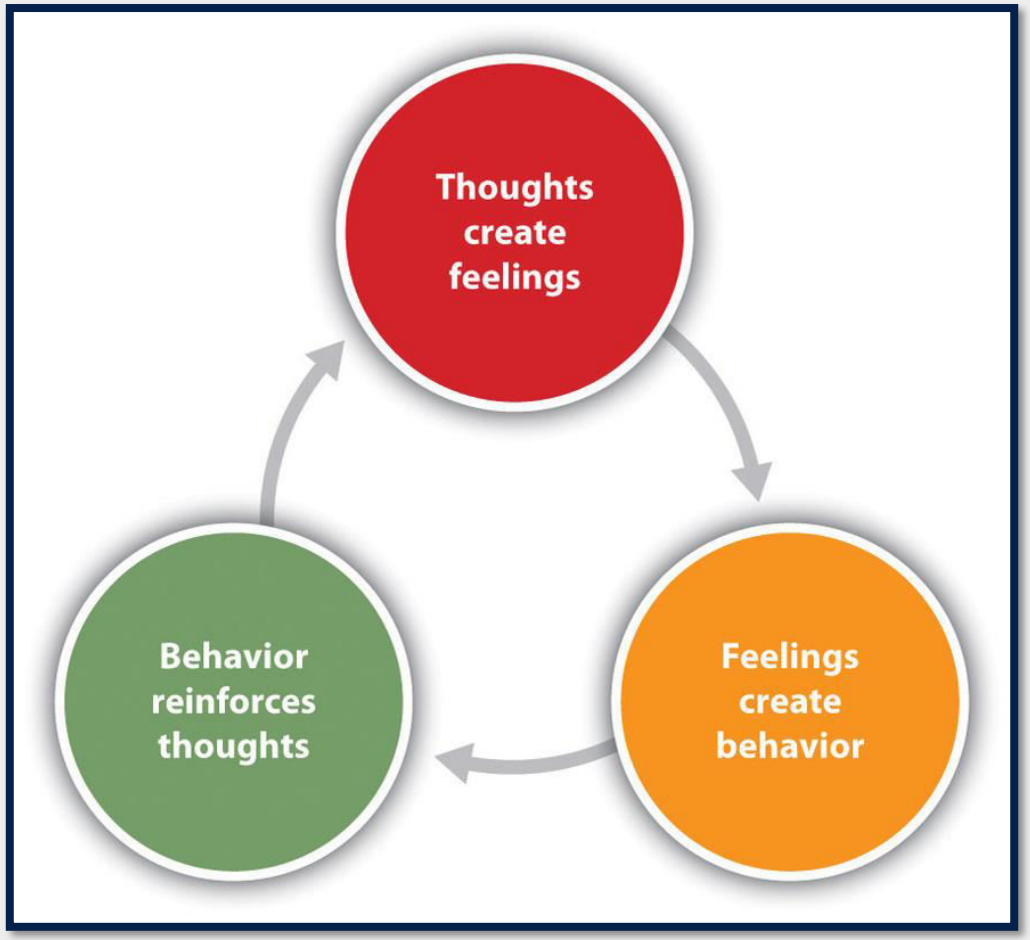
Mason BJ and Heyser CJ, Alcohol use disorder: the role of medication in recovery, Alcohol Research, 2021; DeVido J, Marienfeld C, Kranzler HR, and Levounis, P, Clinical Manual of Addiction Psychopharmacology, 3rd Edition, American Psychiatric Association Publishing, 2026

Mutual Help

MEDICAL STUDENTS	PATIENTS	WHAT MED STUDENTS THINK PATIENTS THINK
1. Housing	1. Inner Peace	1. Housing
2. Government	2. God	2. Outpatient Treatment
3. Medical Services	3. Medical Services	3. Medical Services
4. Outpatient Treatment	4. AA	4. Job
5. Job	5. Housing	5. Trusting People
6. Community	6. Spirituality	6. AA
7. Trusting People	7. Outpatient Treatment	7. Inner Peace
8. Inner Peace	8. Community	8. Community
9. God	9. Government	9. Government
10. Spirituality	10. Trusting People	10. Spirituality
11. AA	11. Job	11. God

Goldfarb LM, Medical student & patient attitudes toward religion and spirituality in the recovery process, American Journal of Drug & Alcohol Abuse, 1996; Fazzio L, Galanter M, Dermatis H, Levounis P, Evaluation of medical student attitudes toward Alcoholics Anonymous, Substance Abuse, 2003

Cognitive Behavioral Therapy & Motivational Interviewing



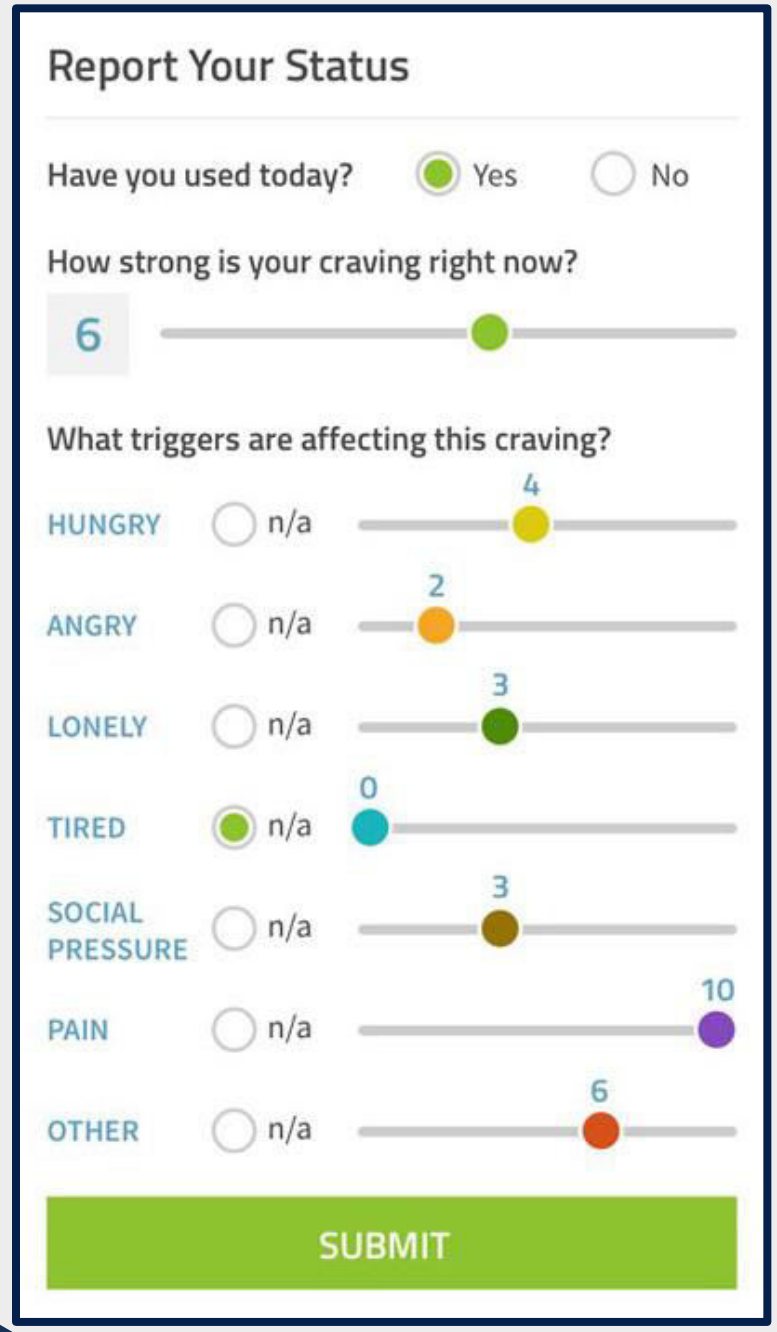
Levounis, Zerbo, and Aggarwal, Pocket Guide to Addiction Assessment and Treatment, 2016

4th Wave: Mindfulness

"Between stimulus and response there is a space. In that space is our power to choose our response. In our response lie our growth and our freedom."

Victor E. Frankl

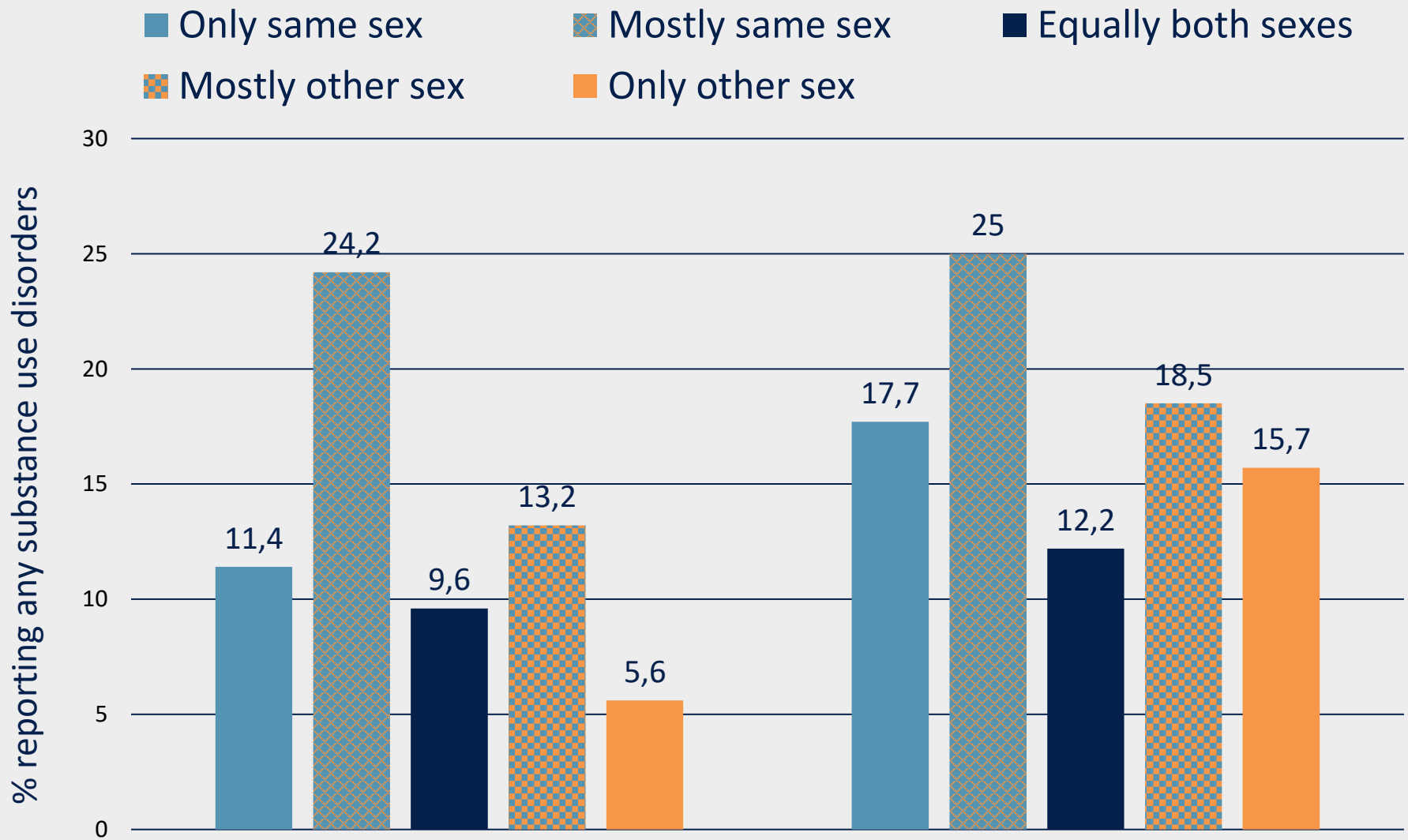
Frankl, Man's Search for Meaning, 1959;
Zerbo, Schlechter, Desai, and Levounis, Becoming Mindful, 2017



Digital Therapeutics (CBT Apps)

Mood Tools.org

And Back to Psychodynamics . . .



McCabe, Addiction, 2009; courtesy of Sean E. McCabe, PhD;

Levounis and Yarbrough, LGBTQ+ Mental Health, 2020

Neurotransmitters

Substance	Endogenous Neurotransmitter
Alcohol	GABA / Glutamate*
Amphetamines & Cocaine	Dopamine
Benzodiazepines & GHB	GABA
Cannabis	Anandamide
Hallucinogens & MDMA	Serotonin
Nicotine	Acetylcholine
Opioids	Endorphins
Phencyclidine & Ketamine	Glutamate*

*Drug acts as an antagonist at the NMDA subtype of the glutamate receptor.

In Summary

Addiction is the war between the hijacked pleasure and reward pathways of the basal ganglia and the executive function of the prefrontal cortex.

Motivational circuitry, the anti-reward pathways, and interoception complete the 2026 model of addiction.

Pharmacological Treatments:

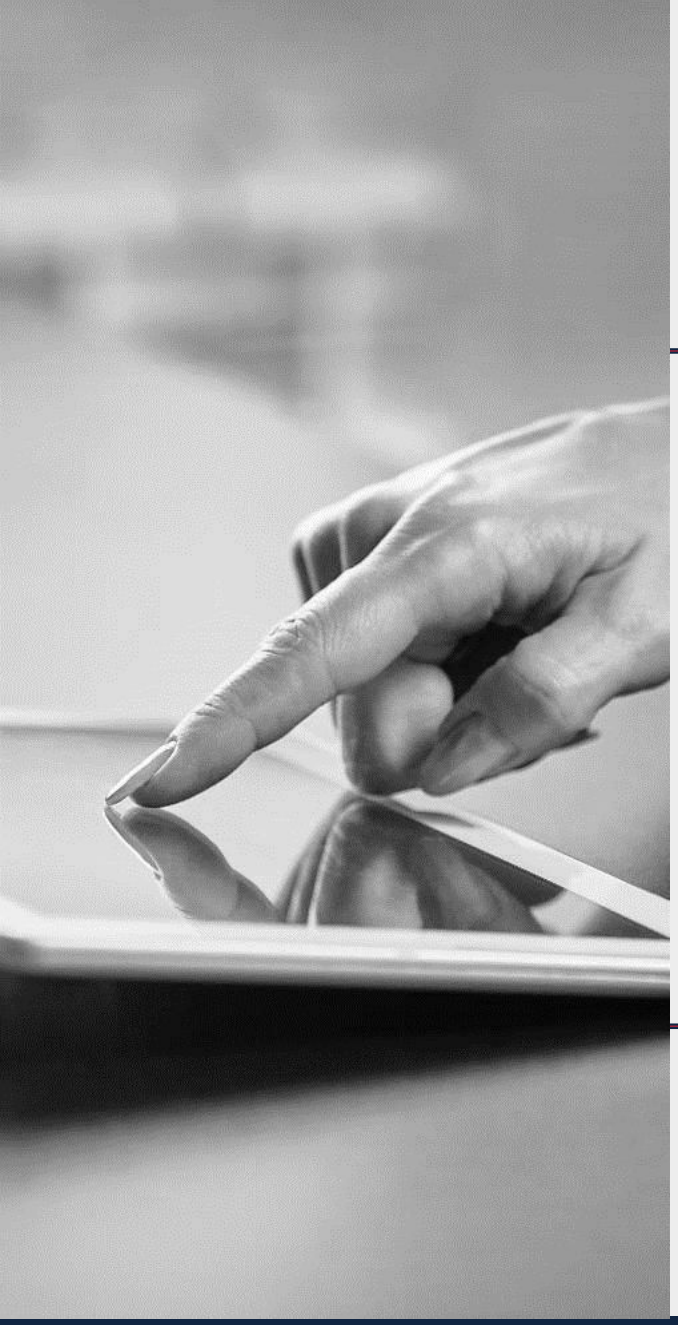
agonists, antagonists, and partial agonists.

Psychosocial Treatments:

mutual help, CBT, motivational interviewing, and mindfulness.

Know your neurotransmitters!

Thank You



Get in Touch

301.656.3920

education@asam.org

www.asam.org

ASAM REVIEW COURSE 2026

Alcohol Use Disorder: Neurobiology, Diagnosis and Treatment

Ricardo Restrepo, MD, MPH

Substance Abuse Treatment Program-SATP/Buprenorphine Clinic Medical Director

Health Science Clinical Professor at University of California, Riverside

Associate Clinical Professor at Charles Drew University, Los Angeles

Department of Psychiatry and Human Behavior





Financial Disclosure

Ricardo Restrepo, MD, MPH

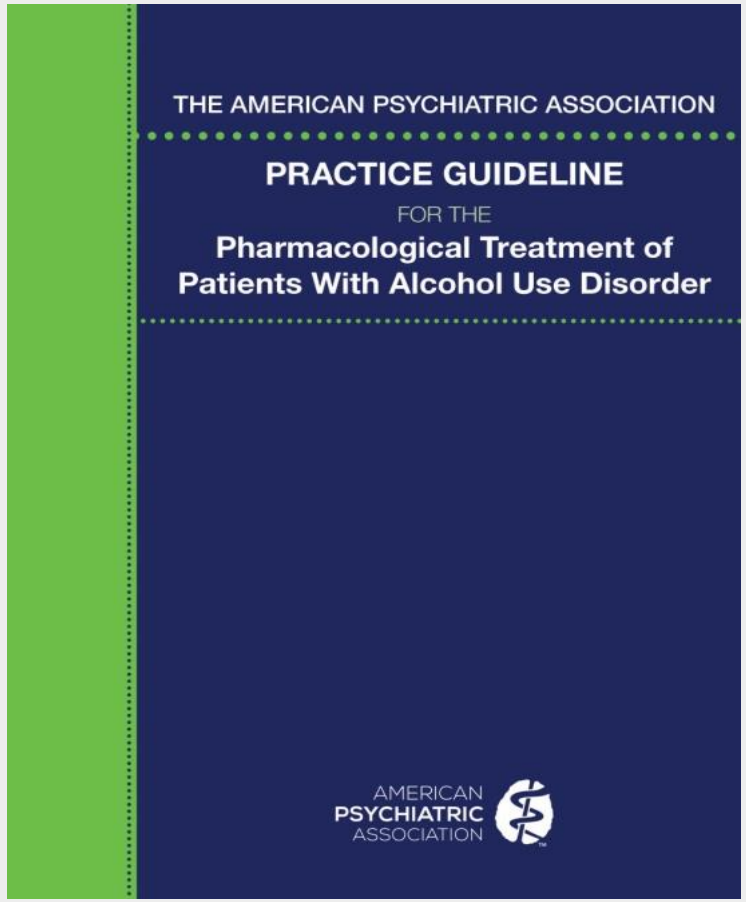
- No Disclosures

Outline

1. Historical View
2. Neurobiology
3. Epidemiology
4. SBIRT and Clinical Screening Test
5. Diagnosis
6. Biomarkers
7. Phases of Alcohol Treatment and Related Syndromes
8. CIWA-Ar and Management
9. Relapse Prevention Pharmacotherpy and Psychotherapy
10. New Directions
11. Conclusion

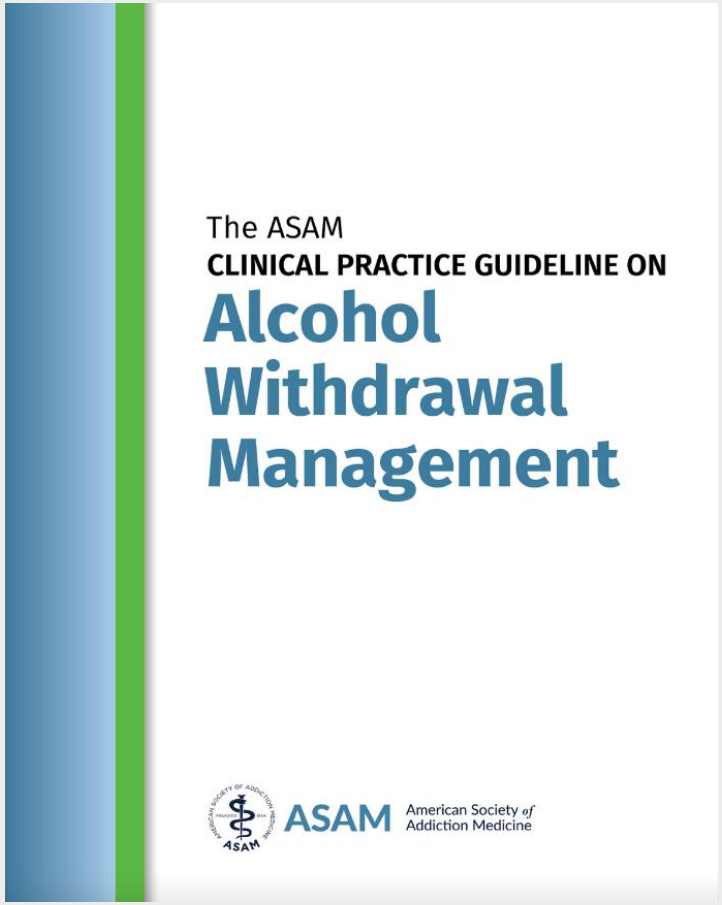
APA Practice Guideline for the Pharmacological Treatment of Patients With Alcohol Use Disorder

December 2017



ASAM Clinical Practice Guideline on Alcohol Withdrawal Management

January 2020



Historical View: Alcohol Use Disorder an Ancient Problem or a Disease?



After the flood, Noah plants a vineyard, makes wine and gets drunk. (Genesis 9:21)

"Who hath woe? Who hath sorrow? Who is always fighting? Who is always complaining? Who hath wounds without cause? Who has bloodshot eyes?

They who tarry long at the wine; when it sparkles in the cup.

Don't let the smooth taste deceive you. For in the end it bites like a poisonous serpent. And you will say, 'They hit me, but I didn't feel it.'

Your eyes will see strange visions and you will say strange thoughts. Yet when you awaken, you seek it yet again."

(Proverbs 23:29 (~1,000 BC)



Pliny the Elder: Gaius Plinius Secundus Naturalis Historia: "drunkeness brings pallor and sagging cheeks, sore eyes, and trembling hands that spill a full cup, of which the immediate punishment is a haunted sleep and unrestful nights…"

Case: RR

Mr. RR is a 58 –year-old, Latino, married, male owner of a music theater in Los Angeles. He is being referred for evaluation to assess his drinking and depression after his older brother, who in the past had problems with alcohol, recommended him.



Case: RR

He presents for his evaluation thinking alcohol helps him to manage:

- Depression
- Insomnia
- Irritability and anxiety

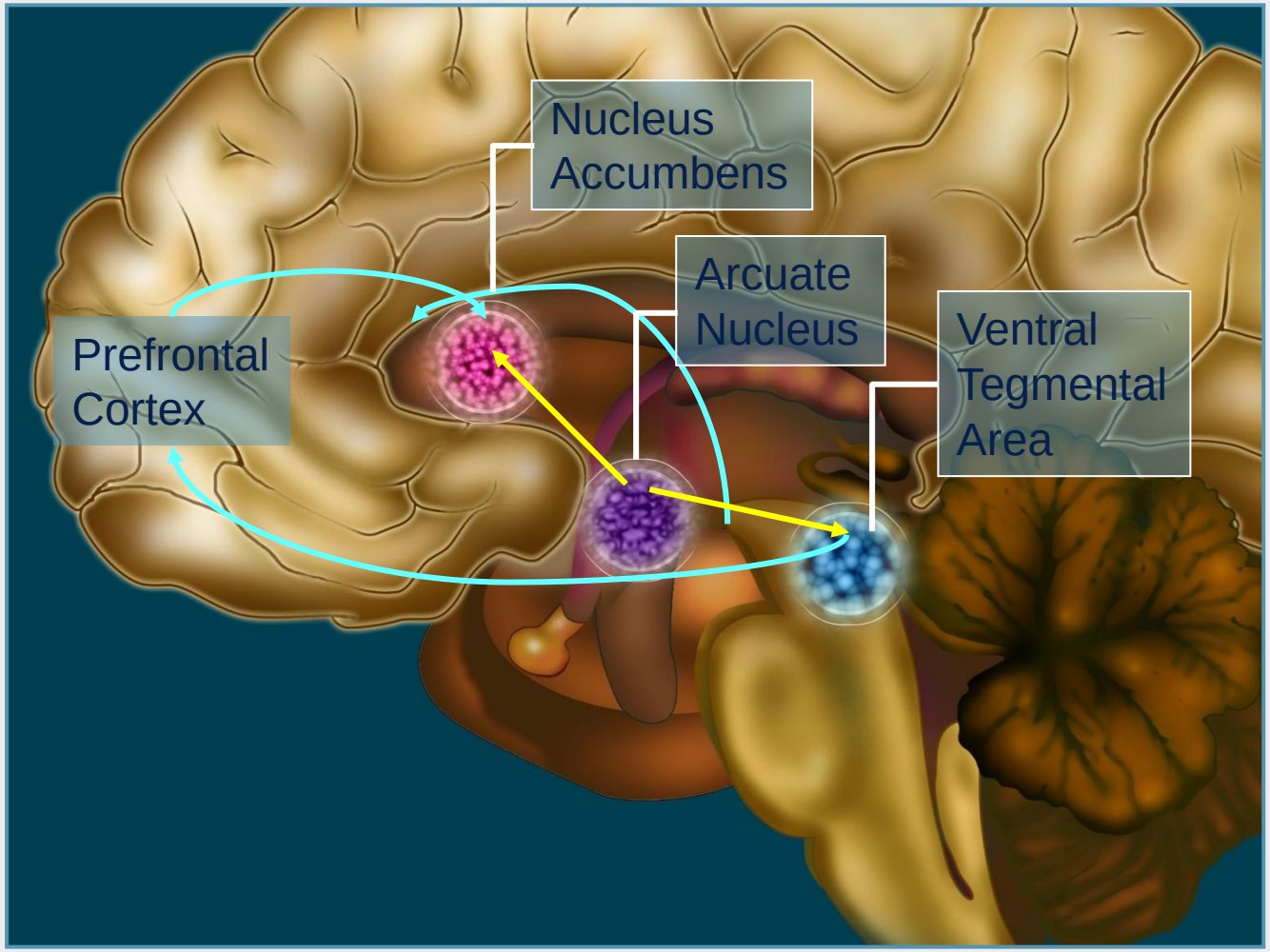


Case: RR

SA history: He reports that he grew up drinking. His first drink was at age four when he tasted the left-over alcohol from a party in his family home. He describes falling in love with the taste of wine and waited every weekend for his family to throw another party.



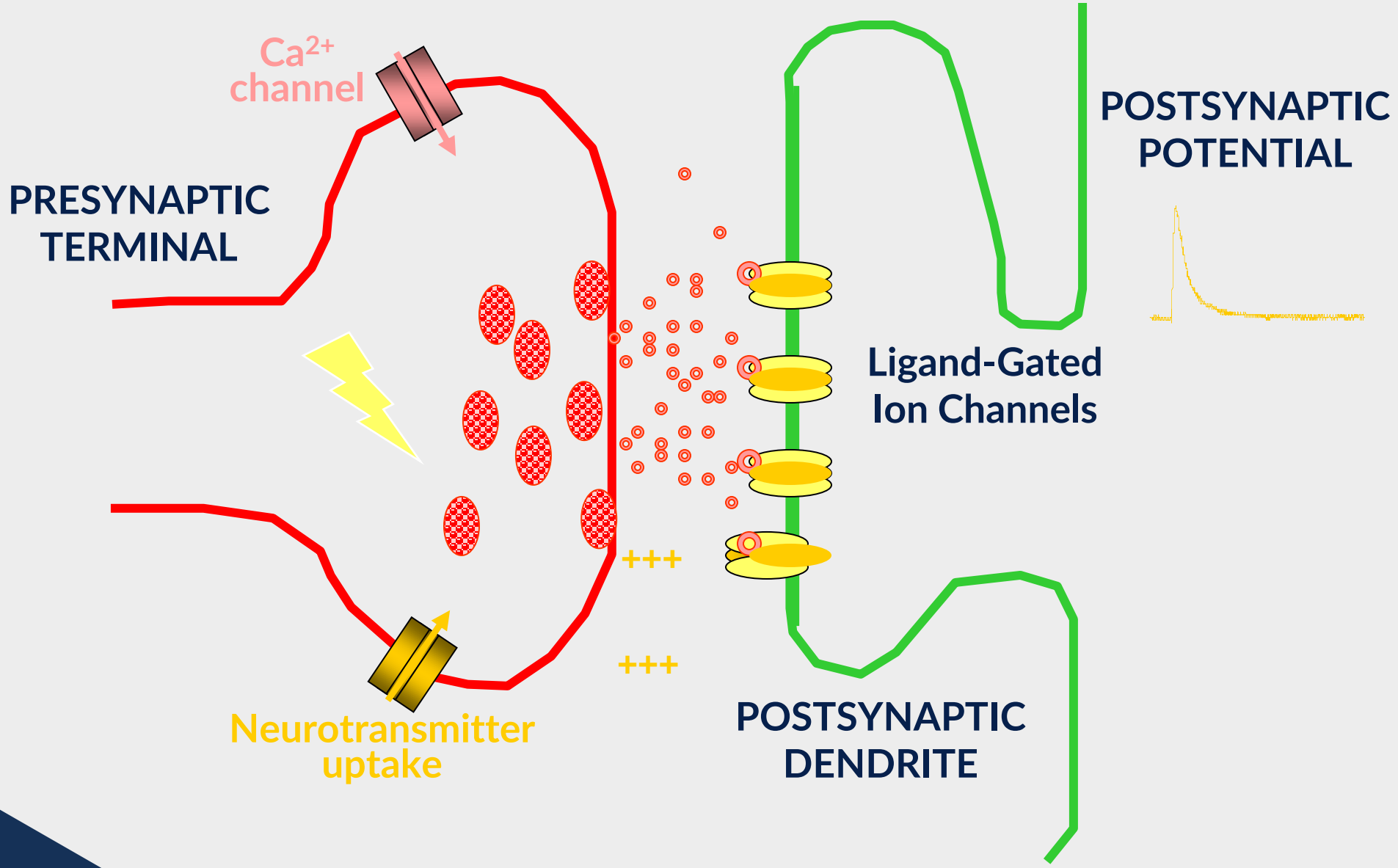
Alcohol Use Disorder a Disease?



Neurotransmitter Systems

GABA Inhibition	→	CNS
Glutamate	→	CNS Excitation
Opioid	→	Euphoria
Dopamine	→	Addiction
Serotonin	→	Impulsivity
Cannabinoid	→	Pleasant Feeling

Steps in Synaptic Transmission



Case: RR

Substance abuse h/x and symptoms

He then started to drink at age 12 years old on weekends and continued daily for the past 30 years. While he had difficulties quantifying the amount he consumes, he states that he rarely has "too much," although he admits occasionally missing work due to hangovers and driving while intoxicated (luckily, no accidents, no DUI).



Case: RR

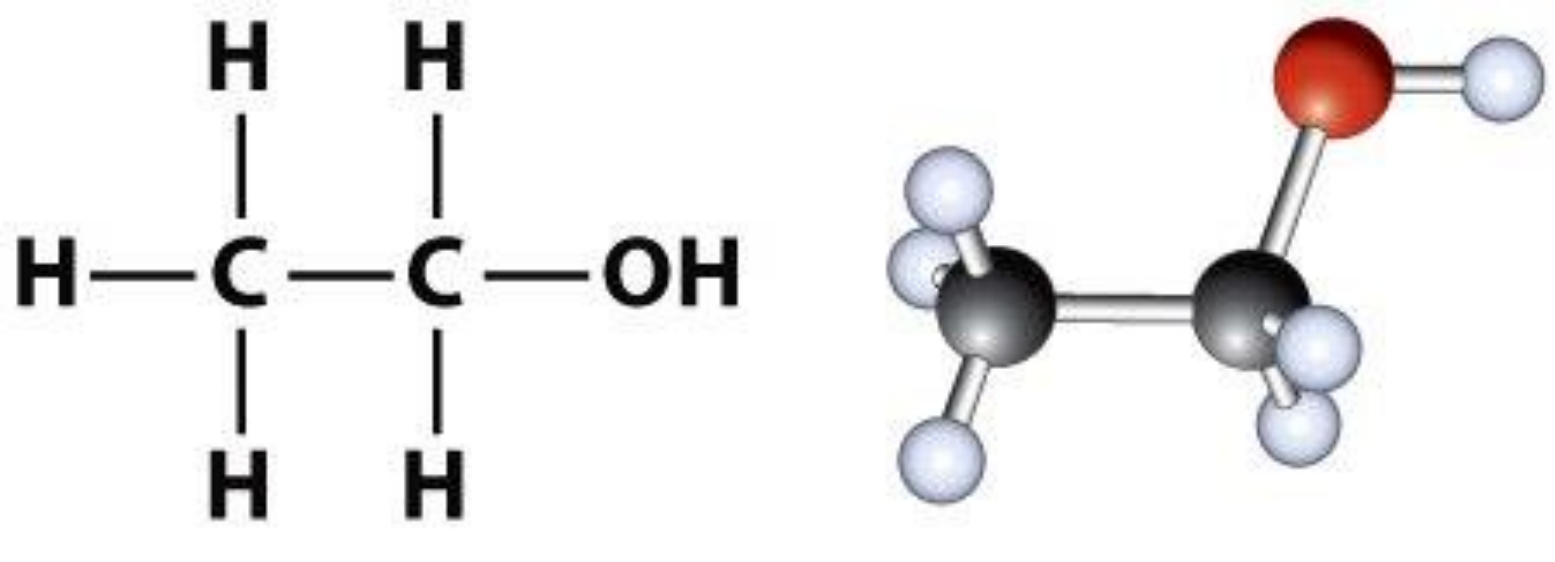
Substance abuse h/x and symptoms

His last drink was the previous night. He explained he often has diarrhea and shakes in the morning, which he attributes to “anxiety” because these symptoms are alleviated with 1 or 2 alprazolam that has been prescribed by his PCP for the past decade.

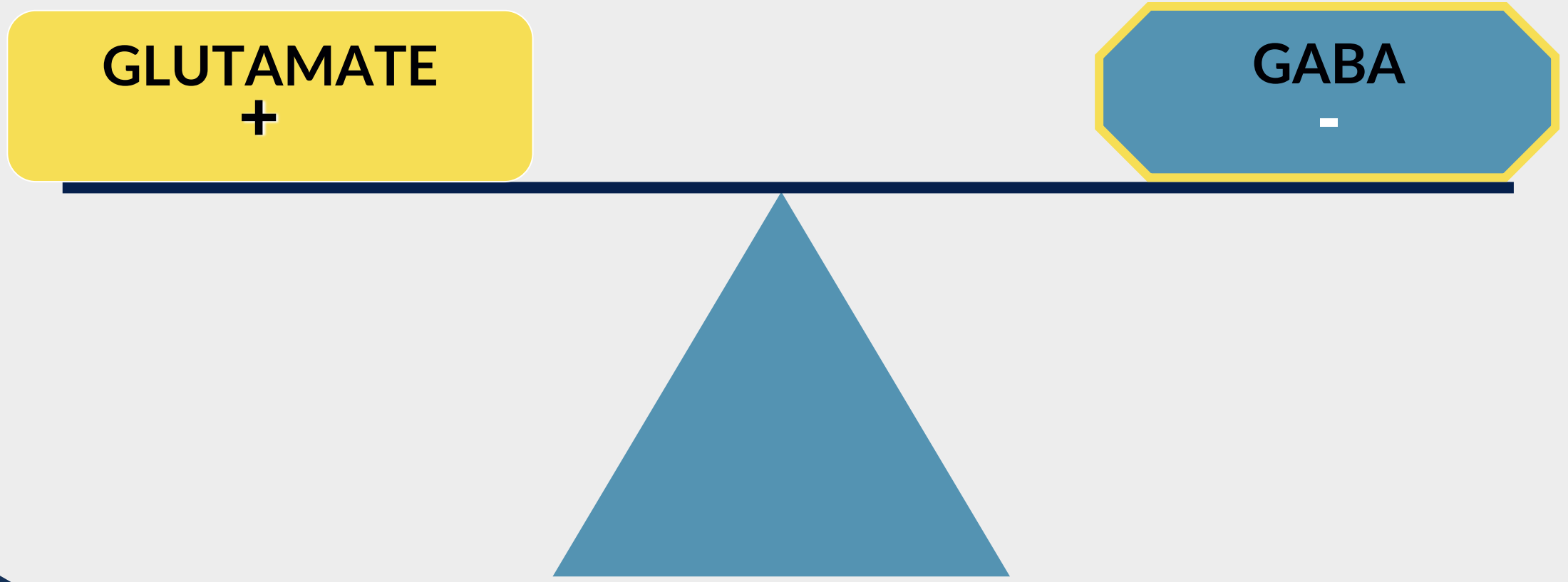
No other drugs or substance use history.



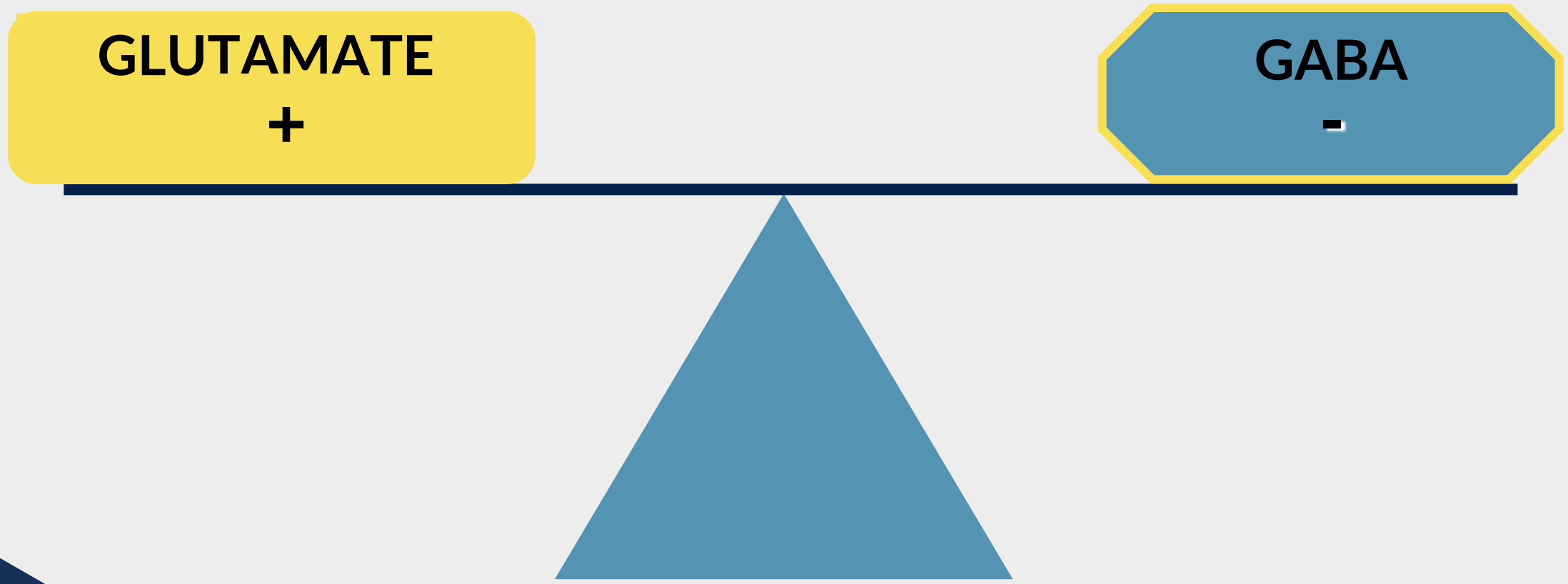
Alcohol (Ethanol C2 O1 H6)



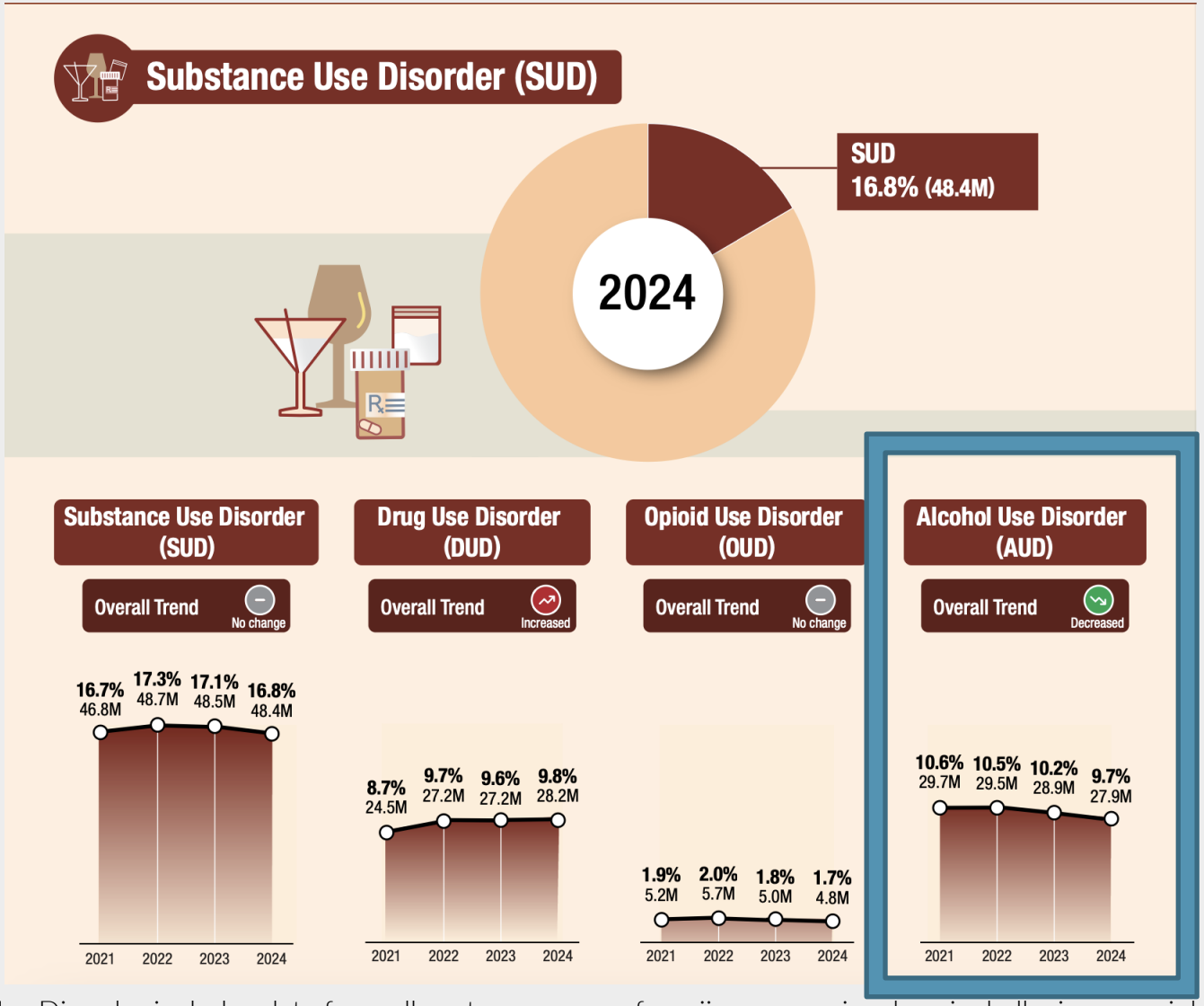
Acute Alcohol Intake



Chronic Alcohol Intake



Alcohol Use Disorder and Drug Use Disorder in the Past Year (SUD): Among People Aged 12 or Older with a Past Year; 2024



Note: Drug Use Disorder includes data from all past year users of marijuana, cocaine, heroin, hallucinogens, inhalants, methamphetamine, and prescription psychotherapeutic drugs (i.e., pain relievers, tranquilizers, stimulants, or sedatives)

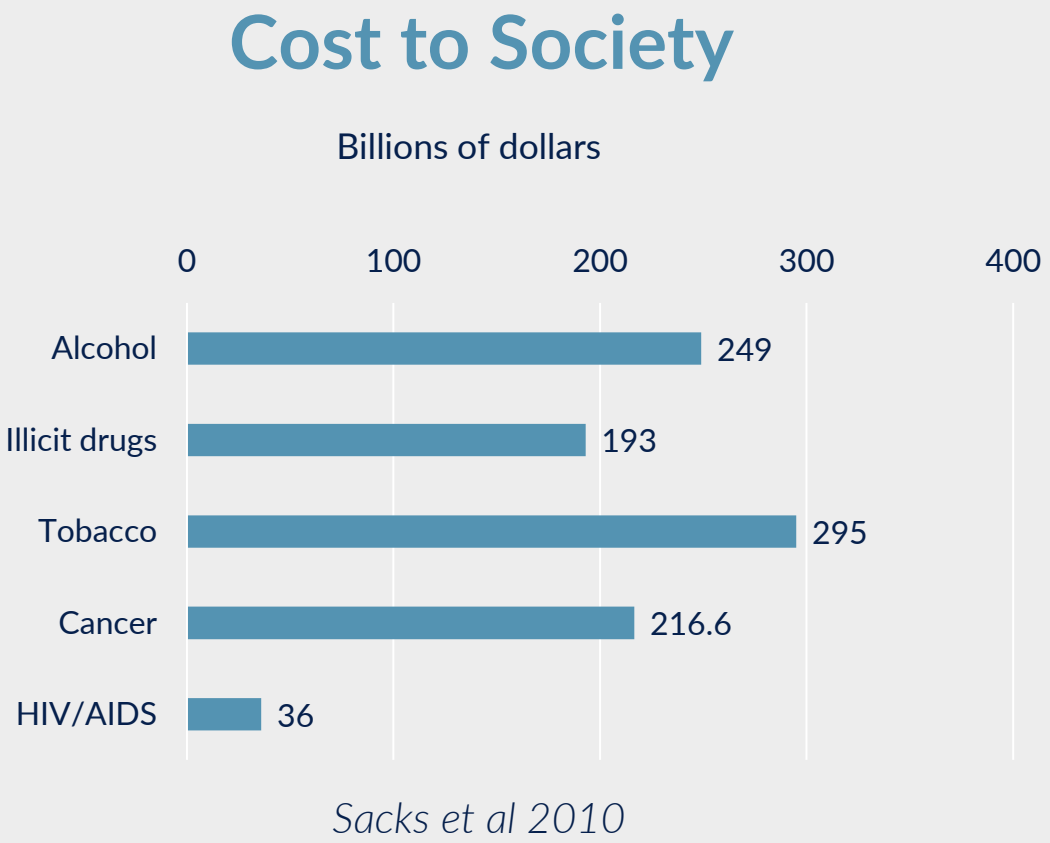
Epidemiology
Scope of Alcohol-Related Problems

- ~178,000 people die (488 each day) annually from alcohol-related causes in the U.S from 2024. (compared with a decade ago)
- Nearly 27.9 million people ages 12 and older had AUD in 2024
- 775,000 adolescents ages 12 to 17 with AUD in 2024:
  - **By Gender:** 520,000 girls (4.1% of girls this age) and 255,000 boys (1.9% of boys this age) had AUD.

4th leading preventable cause of death in U.S. is AUD

Sources: NSDUH , NIAAA, CDC 2024

Cost and Scope of Alcohol-Related Problems



Sacks et al 2010

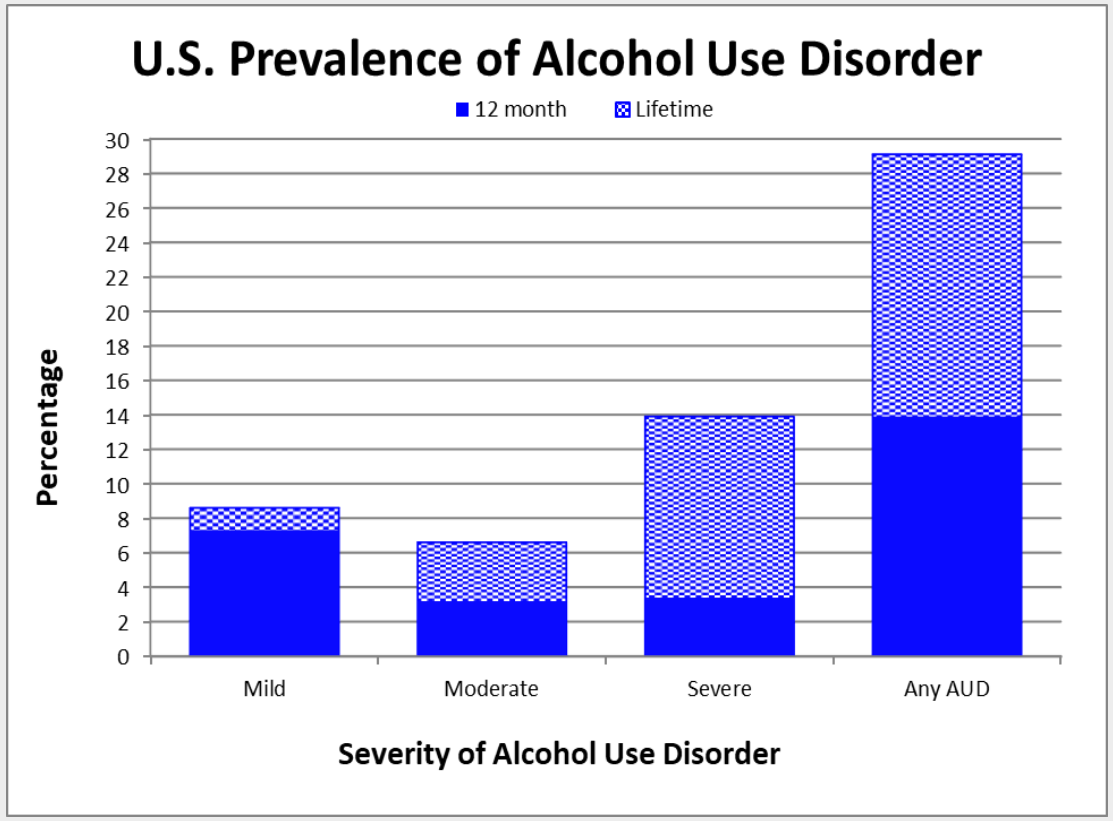
- ~ 50% of U.S. liver disease deaths attributable to alcohol misuse (2021)
- From 2003–2004 to 2021–2022, alcohol-related emergency department visits increased significantly among both genders, with a 101% rise among males and a 96% rise among females
- Among people who die by suicide, AUD is the second most common mental disorder and involved in roughly 1 in 4 deaths by suicide

Sources: Prevalence – NSDUH (2024), NIAAA 2024, CDC 2026 Krystkiewicz (Healthcare) 2025

Epidemiology/Prevalence

Prevalence:

- Worldwide (Slade et al., 2016)
  - Lifetime 20%
  - 12 month 8.5%
  - In 2012 about 3.3 millions deaths, or 5.9 % of a global deaths, were attributable to alcohol consumption
- U.S. (Grant et al. 2015, 2017)
  - Lifetime 29%, with severe alcohol use disorder (AUD) in about half
  - 12-month 13.9 %
  - 12-month rates of AUD increased by ~50% between 2001-2002 and 2012-2013



Based on data from Grant et al. Epidemiology of DSM-5 alcohol use disorder: results from the National Epidemiologic Survey on Alcohol and Related Conditions III. JAMA Psychiatry. 2015 Aug;72(8):757-66.
(Information shared by APA)

Epidemiology/Demographics

AUD affects individuals of all demographic groups

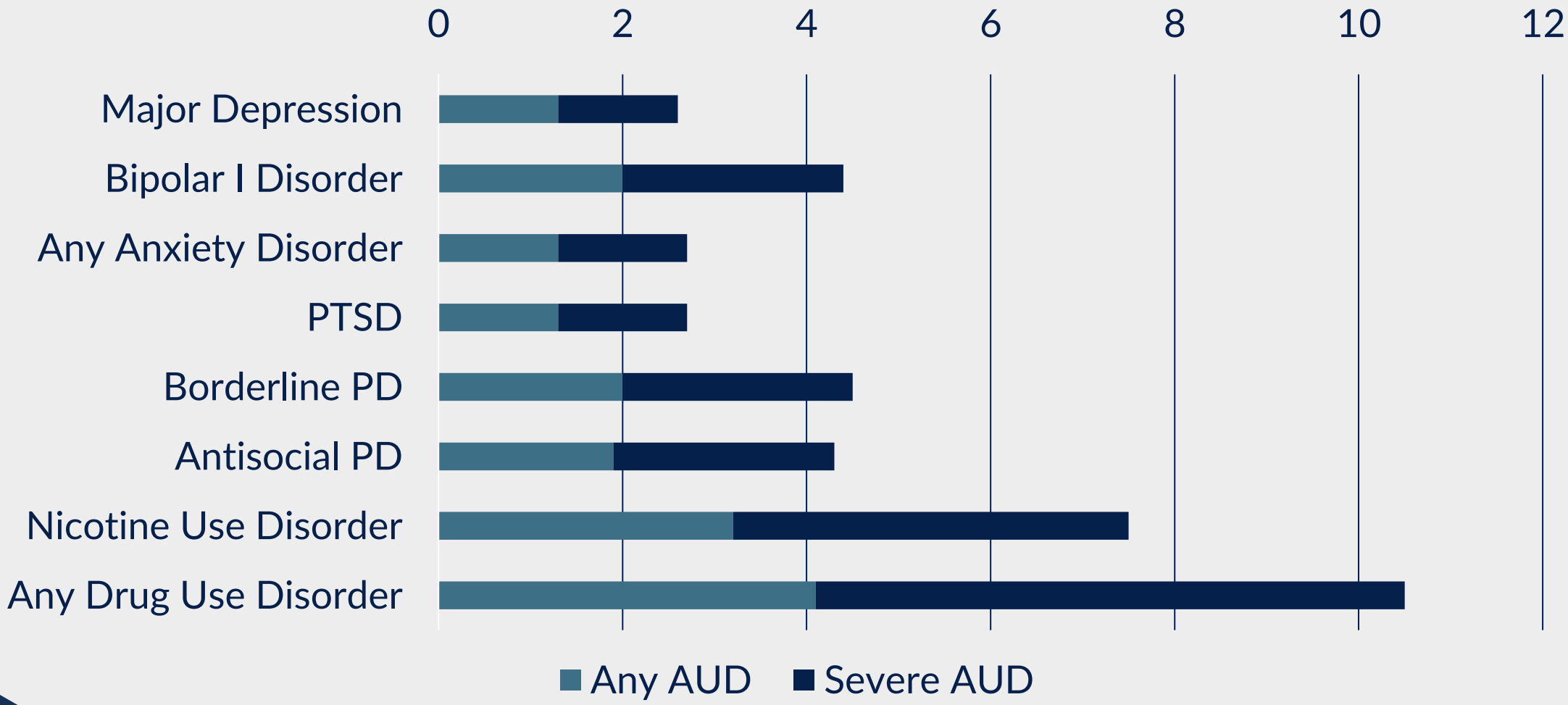
- Onset: 18-29 years

- Ethnicity (12-month prevalence):
  - American Indian/Alaska Native 19.2%
  - African American 14.4%
  - White 14%
  - Hispanic 13.6%
  - Asian-American/Pacific Islander 10.6%

- Gender (12-month prevalence):
  - Men 17.6%
  - Women 10.4%

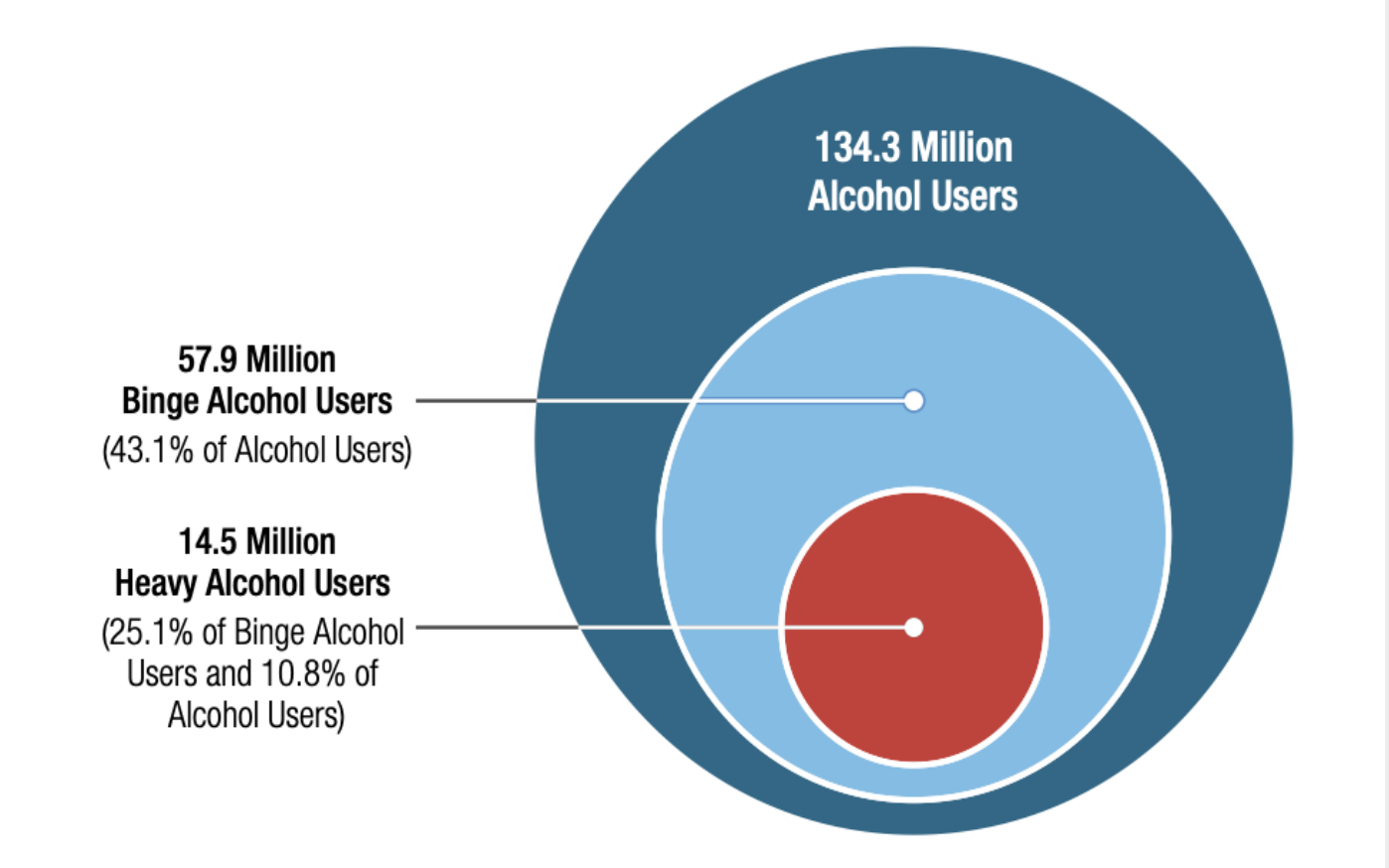
Grant et al. 2015

Adjusted Odds Ratios of Lifetime AUD and Other Conditions



Based on data from Grant et al. JAMA Psychiatry. Aug;72(8): 757-66, 2015 (information shared by APA)

Alcohol Use, Binge Alcohol Use, and Heavy Alcohol Use in the Past Month : Among People Aged 12 or Older; 2024



Note: Binge Alcohol Use is defined as drinking five or more drinks (for males) or four or more drinks (for females) on the same occasion on at least 1 day in the past 30 days. Heavy Alcohol Use is defined as binge drinking on the same occasion on 5 or more days in the past 30 days; all heavy alcohol users are also binge alcohol users.

National Survey on Drug Use and Health 2024

How Much is “too much”?

Heavy Drinking

- WOMEN:
  4 or more standard drinks in a sitting.
  (8 or more per week.)
- MEN:
  5 or more standard drinks in a sitting.
  (15 or more per week.)

Binge Drinking

- A pattern of drinking that brings blood alcohol concentration (BAC) levels to 0.08g/dl
- WOMEN:
  4 or more drinks on same occasion in about 2 hours
- MEN:
  5 or more drinks in same occasion in about 2 hours

Emerging Trend- High Intensity Drinking

Consuming ETOH at levels that are two or more times the gender-specific binge drinking thresholds

10 or more standard drinks (or alcoholic drink equivalents) for males and 8 or more for females

COVID and Alcohol Use Disorder

- Data from a national survey of U.S. adults on their drinking habits found that excessive drinking (such as binge drinking) increased by 21% during the COVID-19 pandemic.

- More than a dozen studies have found that 20% to 40% of individuals surveyed reported consuming more alcohol than usual during the pandemic, based on National Institute on Alcohol Abuse and Alcoholism (NIAAA) information

NIAAA National Institute on Alcohol Abuse and Alcoholism 2021

Alcohol use is increasing more in women than men in USA

Monthly Alcohol Use

Percentage of U.S men and women who reported drinking alcohol in the past month



Over the last century, gaps between males and females have narrowed for prevalence of drinking, total amount consumed, frequency, binge drinking, early onset drinking, having alcohol use disorder, drunk driving and self reported consequences

In a decade differences narrowed further. (Grant et al.,2017):

- AUD increased by 84% in women
- Compared with 35% in men

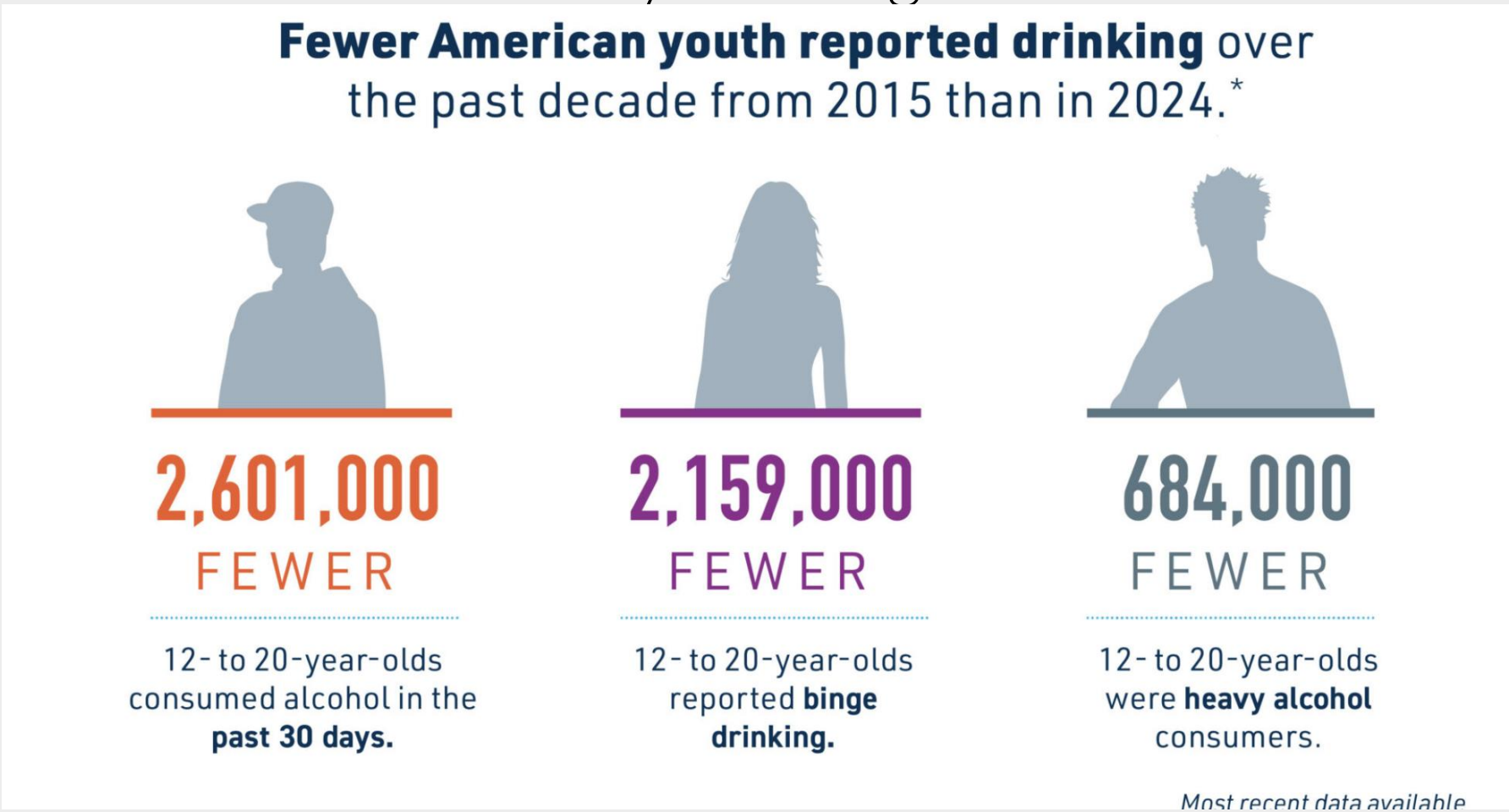
Higher health impact in women (Slade T et al. BMJ 2016)

- Blackouts
- Liver inflammation
- Brain atrophy
- Cognitive impairment
- Increased cancer risk

2024 National Survey on Drug Use and Health

Population-based epidemiological surveys show harmful drinking levels

Age is a known factor in heavy drinking.



Source: Responsibility.org, SAMHSA, NSDUH 2015-2024

DSM-5 : Criteria for Alcohol Use Disorders

1. Use In Larger Amounts / Longer Periods Than Intended
2. Unsuccessful Efforts To Cut Down
3. Excessive Time Spent Taking Drug
4. Failure To Fulfill Major Obligations
5. Continued Use Despite Knowledge Of Problems
6. Important Activities Given Up
7. Recurrent Use In Physically Hazardous Situations
8. Continued Use Despite Social Or Interpersonal Problems
9. Tolerance
10. Withdrawal
11. Craving



~~Legal problems~~

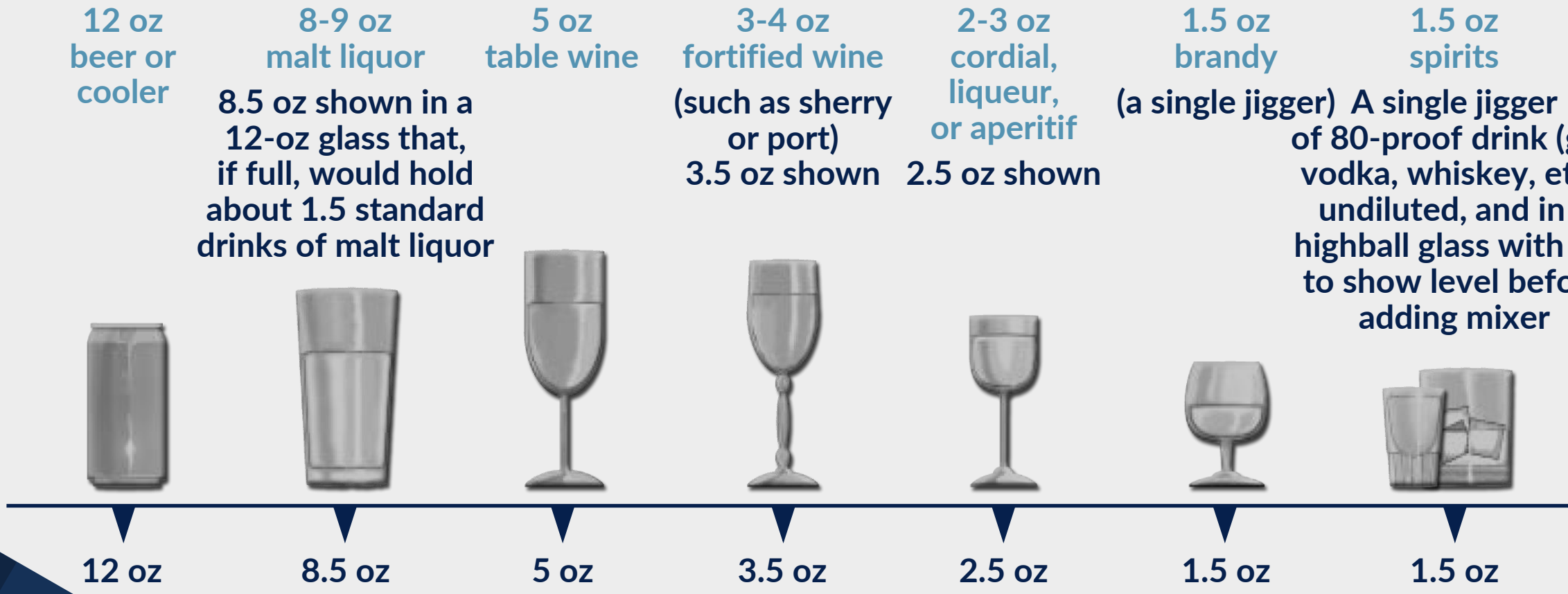
Severity:
0 To 1 Criteria: No Diagnosis
2 To 3 Criteria: Mild
4 To 5 Criteria: Moderate
6 Or More Criteria: Severe

Underdiagnoses and Unmet Treatment Needs

- Only 1 in 6 US adults report ever having asked by a clinician about their drinking behavior
- Despite high prevalence, societal cost, and available treatments, AUD remains undertreated
- Less than 10 % of those with a a 12-month AUD diagnosis receive any treatment:
  - Self-help groups
  - Psychotherapy
  - Pharmacological treatments (less than 2% receive pharmacotherapy)
- Treatment received by patients varies based on geography, insurance coverage, and formulary restrictions

What is a standard drink?

- 1 Standard Drink = 14 gr. (0.6 oz.) of pure alcohol.
- The average person metabolizes about 1 Standard Drink per hour.



Adapted from www.niaaa.nih.gov.

Intoxication Features

1 drink → BAC = ~15 mg% (0.015 g/dl)

BAC mg %	Clinical Manifestation
0-100 mg/dl	Well-Being
100-200 mg/dl	Incoordination
200-300 mg/dl	Ataxia
300-400 mg/dl	Stage 1 Anesthesia, amnesia, hypothermia
400-600 mg/dl	Coma
600-800 mg/dl	Death

The Rules of Twenties

Going Up

- MEN: Each drink adds 20 mg/dL to one's BAL.

- WOMEN: Each drink adds 40 mg/dL to one's BAL.

Coming Down

- We metabolize 20 mg/dL every 60-90 minutes (zero order kinetics).

Women and Pregnancy

- There are three general reasons that females show higher BACs (and greater intoxication) than males if they drink the same amount of alcohol.

- Body composition: In females a greater percentage of body mass is fat compared to males
  - Result – The concentration of alcohol is increased in the female bloodstream compared to the male body

- Stomach alcohol dehydrogenase (ADH): Females have very little of this enzyme compared to males
  - Result – Females do not metabolize alcohol before it gets out of the stomach. Therefore, the blood alcohol concentration (BAC) is higher for females versus males

- Liver ADH: Females have a less active form of this enzyme than males.
  - Result – Females do not metabolize alcohol as efficiently as males, thereby increasing the BA

Women and Pregnancy

Fetal Alcohol Spectrum disorders (FASD): Growth retardation, Facial malformations, Small head, Greatly reduce intelligence.

- FASD is the most common known preventable cause of mental impairment.
- The prevalence of FASD : 50 per 1,000 (May et al., 2009 and CDC 2016)
- 40,000 infants per year in US

Case: RR

Past Medical h/x: HTN for 10 years, GERD and H/x of pancreatitis.

Medications:

- Lisinopril 40 mg qam,
- Omeprazole 20 mg daily
- Zolpidem XR 6.25 mg qhs prn for insomnia
- Alprazolam 1-2 mg tid a day for anxiety.



Case: RR

Vital Signs: BP:150/95
Pulse: 90x'

CBC normal with the exception of Increased MCV equal 102 (80-96)
Electrolytes and renal function: normal
Hepatic function:

- GGT 141 (10-42),
- AST 60 (15-40)
- ALT 40 (10-40)
- AST/ALT ratio 1.5
- CDT score exceeded the cutoff and so you performed a diagnostic evaluation





Preventing and Treating AUD

There are evidence-based interventions for preventing and treating AUD:

- Screening, Brief Intervention, and Referral to Treatment (SBIRT)
- Professionally-led behavioral interventions
- FDA-approved medications
- Mutual support groups, such as Alcoholics Anonymous

SBIRT

- Screening quickly assesses the severity of substance use and identifies the appropriate level of treatment.
- Brief intervention focuses on increasing insight and awareness regarding substance use and motivation toward behavioral change.
- Referral to Treatment provides those identified as needing more extensive treatment with access to specialty care.

www.niaaa.nih.gov/guide
http://www.sbirtcolorado.org/healthcare_videosandwebcasts.php

Screening Tools

Alcohol Screening is an Effective Prevention Strategy

The CAGE Questionnaire

- Cut Down
- Annoyed
- Guilty
- Eye-Opener

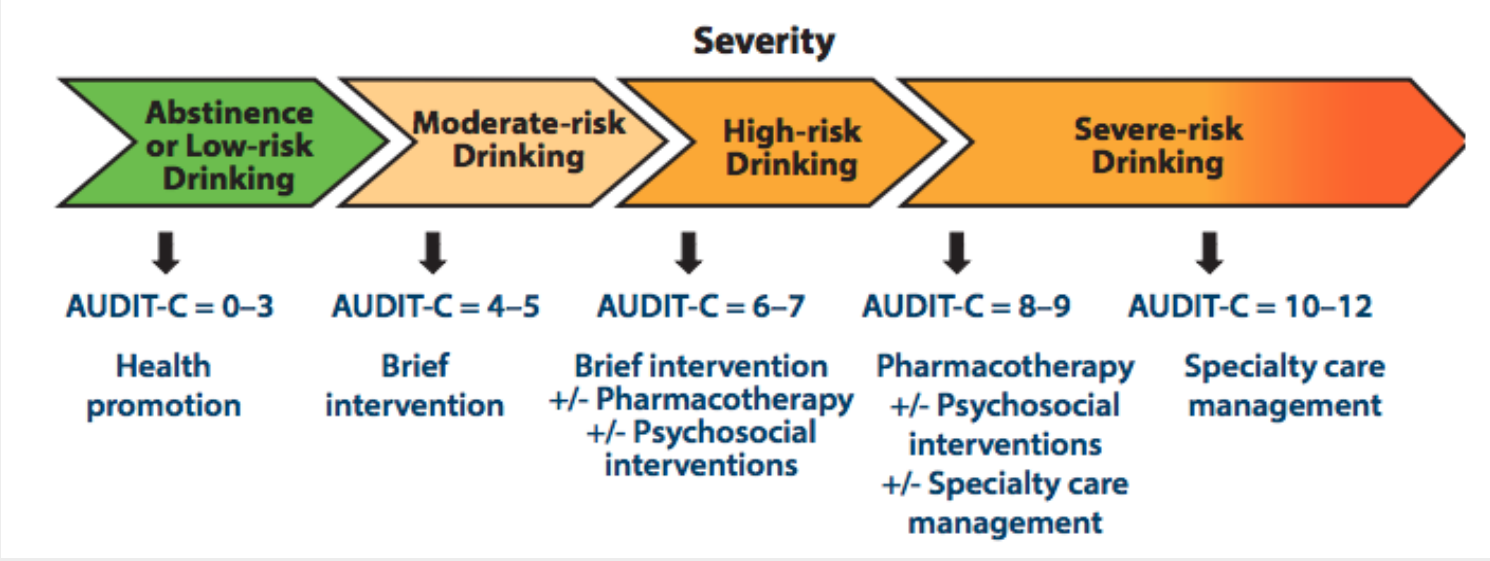
2 or more positive responses are strongly associated with alcohol dependence.

National Institute on Alcohol Abuse and Alcoholism (NIAAA): "Helping Patients Who Drink Too Much"

AUDIT-C Questionnaire

Alcohol Use Disorder Identification Test

Question	0 Points	1 Point	2 Points	3 Points	4 Points
How often did you have a drink containing alcohol in the past year?	Never	Monthly or less	2–4 times per month	2–3 times per week	4 or more times per week
On days in the past year when you drank alcohol how many drinks did you typically drink?	1–2	3–4	5–6	7–9	10 or more
How often do you have 6 or more drinks on an occasion in the past year?	Never	Less than monthly	Monthly	Weekly	Daily or almost daily



The Role of Biomarkers in The Treatment of ETOH

- Provide objective outcome measures in alcohol research or evaluating an alcohol treatment program.
- Screen for individuals unable/unwilling to accurately report drinking behavior (e.g., fear, embarrassment, or adverse consequences).
- Evidence of abstinence in individuals prohibited from drinking.
- Enhance patient motivation to stop/reduce drinking.
- Diagnosis tool by assessing contribution of alcohol to the disease.
- Identify relapse early.
- Fear of detection by biomarkers may dissuade drinking.

Types of ETOH Biomarkers

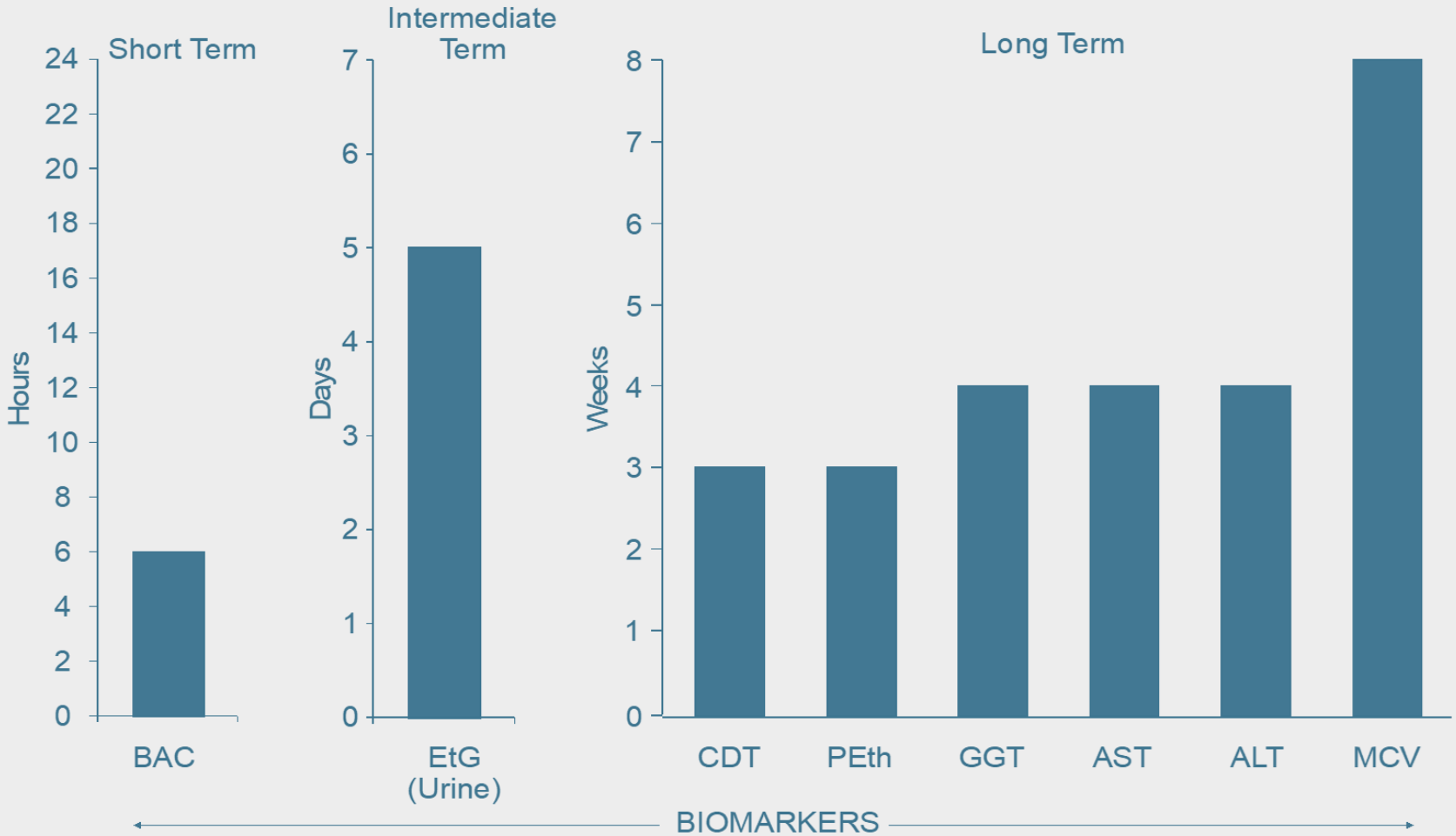
Indirect Tests

- Manifestations of organ damage often due to drinking
  - gamma glutamyltransferase (GGT)
  - aspartate amino transferase (AST, SGOT)
  - alanine amino transferase (ALT, SGPT)
  - macrocytic volume (MCV)
- Reflections of alcohol's effects on other metabolic processes -
  - carbohydrate-deficient transferrin (CDT) - Only FDA Approved alcohol biomarker

Direct Tests

- Reflections of alcohol use
  - ethyl glucuronide (EtG) and ethyl Sulfate (EtS)- 5 days
  - Phosphatidylethanol (PEth)– Form just in the presence of ETOH in RBCs-28 days Test > 20ng/ml
    -Sensitivity 90-99%
    -Specificity 100%

Window of Assessment for Various Alcohol Biomarkers



SAMHSA (Substance Abuse and Mental Health Services Administration) The Role of Biomarkers in the treatment of alcohol use disorders, 2012 Revision

Characteristics of Assessment for Various Alcohol Biomarkers

Marker	Time to Return to Normal with Abstinence	Level of Drinking	Comments	Blood test normal range
GGT	2-4 weeks of abstinence	~ 5 drinks (>60g/day) for several weeks	Many sources of false positives—liver disease, diabetes, smoking, obesity, age, anticonvulsants, etc.	W: 0-45 U/L M: 0-53 U/L
SGOT/AST	2-4 weeks of abstinence	Unknown but heavy	Many sources of false positives (see GGT) in addition to excessive coffee consumption	10 - 34 U/L
SGPT/ALT	2-4 weeks of abstinence	Unknown but heavy	Many sources of false positives (see GGT) Less sensitive than AST	8-37 U/L
MCV	Up to several months	Unknown but heavy	Slow return to normal limits even with abstinence renders it a poor independent indicator of relapse. More specific than GGT. Unlike other markers, no strong gender effect	80-100fL
CDT	2-4 weeks	~ 5 drinks(>60g/day) for 2 weeks	Few sources of false positives. Good marker of relapse	<60 mg/L

Diagnostic Sensitivity and Specificity of Biomarkers

	Sensitivity (%)	Specificity (%)
CDT	69	92
CDT/transferrin	65	93
GGT	73	75
AST	50	82
ALT	35	86
MCV	52	85

Bell, et al. Alcoholism: Clinical and Experimental Research 1994

Case: RR

His last drink was the previous night. He explained he often has insomnia, diarrhea, palpitations, and shakes in the morning, which he attributes to "anxiety" because these symptoms are alleviated with 1 or 2 alprazolam that has been prescribed by his PCP for the past decade.



Phases of Alcoholism Treatment

Detoxification

- Primary goal is to achieve an alcohol-free state
- Wide spectrum of severity
- Drug-specific syndromes: opiates, cocaine, alcohol, benzodiazepines

Relapse Prevention

- Primary goal is to maintain an alcohol-free state
- Chronic Treatment

Introduction Alcohol Withdrawal

Epidemiology

Neurobiology

- Neurotoxicity
- Kindling

Management of Alcohol Withdrawal

- Benzodiazepines
- Anticonvulsants

Real World Implications

- Outpatient vs. Inpatient
- Evaluation and Management

Epidemiology of Alcohol Withdrawal

- Not well studied
- Significant symptoms occur in 13% to 71% of individuals presenting for detoxification
- Up to 10% of individuals undergoing alcohol withdrawal require inpatient medical treatment
- Estimated mortality up to 2%

Saitz R, Mayo-Smith MF, Roberts MS, Redmond HA, Bernard, DR, Calkins DR. JAMA. 1994;272:519-523.

Alcohol Withdrawal and Kindling

- Repeated episodes of alcohol withdrawal likely to worsen
- Exacerbation of symptoms may be due to a kindling process
- Positive relationship of alcohol withdrawal seizures to repeated detoxification

Managing Alcohol Withdrawal

Principles of treatment

- Alleviate symptoms
- Prevent progression of symptoms
- Treat underlying comorbidities

Alcohol Withdrawal Treatment

- Substitute cross-dependent drug (benzodiazepine)
- Gradually withdraw substitute drug
- Supplement vitamins and minerals
  - Thiamine
  - Folic acid
  - Multivitamin
- An array of acid–base disorders and electrolyte disorders can occur in patients with chronic alcohol-use disorder, irrespective of their social circumstances.
- Supportive treatment
  - Decrease stimulation, increase fluid and caloric intake

Alcohol Withdrawal Treatment

Thiamine Deficiency

Thiamine

- Important cofactor for several enzymatic reactions
- Cerebral glucose utilization
- Glutamate elimination

Wernicke's Encephalopathy

- Partial to complete paralysis of extra ocular muscles
- Nystagmus
- Ataxia
- Mental disturbances
- Mortality: 10-20% if untreated
- Treatment: Thiamine replacement PRIOR dextrose administration

Korsakoff's Psychosis

- Antegrade amnesia
- Confabulations

States of AWS

1. Autonomic Hyperactivity
2. Hallucinations
3. Neuronal excitation
4. Delirium Tremens

There is not necessarily a linear progression.

States of AWS

Autonomic Hyperactivity

- Clear Sensorium
- Tremulous
- Diaphoresis
- Anxiety
- Nausea/Vomiting
- Increase cathecolamines in urine, serum and CSF
- Start 6 hrs after last drink Peak 24-48 hrs

Hallucinations

- Most common= VISUAL

Neuronal excitation

- Seizures (Generalized Tonic – Clonic)
- Up to 10%
- Most common in first 24 - 48 hours after last drink

States of AWS

Delirium Tremens (DTs)

- Most often occur within 72 hours after the last drink
- Delirium with Tremor
- Autonomic hyperactivity
- Hallucinations
- Electrolyte abnormalities
- Dehydration
- Hemodynamic instability
- Mortality up to 15%
- Cardiovascular/respiratory collapse

CIWA-Ar

Clinical Institute Withdrawal Assessment of Alcohol, Revised

- It requires under two minutes to administer
- It requires no medical knowledge
- It provides you with a quantitative score that predicts the severity of withdrawal from alcohol

Assessment of Alcohol Withdrawal CIWA-Ar

Symptoms	Range of Scores
Nausea and Vomiting	0 (no nausea, no vomiting) -7 (constant nausea and/or vomiting)
Tremor	0 (no tremor) - 7 (severe tremors, even with arms not extended)
Paroxysmal sweats	0 (no sweat visible) - 7 (drenching sweats)
Anxiety	0 (no anxiety, at ease) - 7 (acute panic states)
Agitation	0 (normal activity) - 7 (constantly trashes about and pacing)
Tactile disturbances	0 (none) - 7 (continuous hallucinations)
Auditory disturbances	0 (not present) - 7 (continuous hallucinations)
Visual disturbances	0 (not present) - 7 (continuous hallucinations)
Headache	0 (not present) - 7 (extremely severe)
Orientation/clouding of sensorium	0 (orientated, can do serial additions) - 4 (Disorientated for place and/or person)

CIWA-Ar Determining Need of Pharmacotherapy

- <8: Minimal – Mild AW, Drug therapy not necessarily indicated
- 8-15: Moderate AW, Drug therapy indicated.
- >15: Severe, Drug therapy absolutely indicated, consider inpatient treatment

http://www.chce.research.va.gov/apps/PAWS/quiz/q1.html

Mechanisms Underlying Alcohol Withdrawal

- Multiple neuroadaptive changes in CNS
  - Decreased GABA activity
  - Increased glutamate activity
  - Upregulated calcium channel activity
  - Increased noradrenergic activity

- Alcohol withdrawal is associated with increased CNS activity

CNS=central nervous system; GABA=gamma-aminobutyric acid.

Anton RF, Becker HC, eds. Pharmacotherapy and pathophysiology of alcohol withdrawal. (Handbook of Experimental Pharmacology.) 1995.

Case: RR

You apply your knowledge and training through Motivational Interviewing. Your open–ended questions and affirmations reviewed with patient's possibilities set the bases for a good rapport with Mr. RR. As part of the treatment dialogue, you showed Mr. RR. his BP elevation 150/90, CIWA:8, and his scores on the CDT, GGT and AST/ALT. You noted that the values were outside the reference ranges for the tests.



Case: RR

You then explained, in a direct, yet empathetic manner, the significance of the scores and noted that GGT and AST/ALT levels this high can reflect liver damage and that CDT levels this high usually reflect heavy drinking. Mr. RR then agrees to start an outpatient alcohol treatment program.



Treatment Plan

There are several evidence-based options for non-pharmacological treatment that have minimal harms:

- Motivational Enhancement Therapy (MET): manualized psychotherapy based on the principles of motivational interviewing; shown to have a small to medium effect size on achieving abstinence
- Cognitive Behavioral Therapy (CBT): focusing on the relationships between thoughts, feelings, and behaviors; help manage urges and triggers

Treatment Plan

There are several evidence-based options for non-pharmacological treatment that have minimal harms:

- Medical Management (MM): manualized treatment that provides education and strategies to support abstinence and promote medication adherence
- Community based peer support groups such as Alcoholics Anonymous (AA) and other 12-step programs: helpful in achieving long-term remission but not for replacing formal medical treatment

Alcohol Detoxification
Use of Benzodiazepines

- First line agent (gold standard)
- Loss of inhibition/sedation due to lack of ETOH
- Treatment: Replace the GABA activation (inhibition)
- Benzodiazepines:
  - If hepatic impairment: oxazepam or lorazepam
  - Provide dosing for 24 hour intervals – patient must be re-evaluated before more is provided
    - Vital Signs
    - CIWA-Ar

Benzodiazepines options

Chlordiazepoxide

- Only available in oral form (PO)
- Longer half life than most benzos (5-30 hrs)

Diazepam

- Lipophilic → rapid onset of action

Lorazapem

- Available in oral form (PO) and IV
- Half life (12-18 hrs)
- Simple metabolism of hepatic glucuronidation (no active metabolite)
- Ideal for patients with cirrhosis/liver damage and elderly population

Clinical Institute Withdrawal Assessment Scale for Alcohol, Revised (CIWA-Ar)

Nausea and Vomiting
0 – No nausea or vomiting
1
2
3
4 – Intermittent nausea with dry heaves
5
6
7 – Constant nausea, frequent dry heaves and vomiting

Paroxysmal Sweats
0 – No sweat visible
1 – Barely perceptible sweating, palms moist
2
3
4 – Beads of sweat obvious on forehead
5
6
7 – Drenching sweats

Agitation
0 – Normal activity
1 – Somewhat more than normal activity
2
3
4 – Moderate fidgety and restless
5
6
7 – Paces back and forth during most of the interview or constantly thrashes about

Visual Disturbances
0 – Not present
1 – Very mild photosensitivity
2 – Mild photosensitivity
3 – Moderate photosensitivity
4 – Moderately severe visual hallucinations
5 – Severe visual hallucinations
6 – Extreme severe visual hallucinations
7 – Continuous visual hallucinations

Tremor
0 – No tremor
1 – Not visible, but can be felt at finger tips
2
3
4 – Moderate when patient's hands extended
5
6
7 – Severe, even with arms not extended

Tactile Disturbances
0 - None
1 – Very mild paraesthesias
2 – Mild paraesthesias
3 – Moderate paraesthesias
4 – Moderately severe hallucinations
5 – Severe hallucinations
6 – Extremely severe hallucinations
7 – Continuous hallucinations

Headache
0 – Not present
1 – Very mild
2 - Mild
3 - Moderate
4 – Moderately severe
5 - Severe
6 – Very severe
7 – Extremely severe

Auditory Disturbances
0 – Not present
1 – Very mild harshness or ability to frighten
2 – Mild harshness or ability to frighten
3 – Moderate harshness or ability to frighten
4 – Moderately severe hallucinations
5 – Severe hallucinations
6 – Extremely severe hallucinations
7 – Continuous hallucinations

Orientation and Clouding of the Sensorium
0 – Oriented and can do serial additions
1 – Cannot do serial additions
2 – Disoriented for date but not more than 2 calendar days
3 - Disoriented for date by more than 2 calendar days
4 – Disoriented for place/person

Cumulative scoring

Cumulative score	Approach
0 – 8	No medication needed
9 – 14	Medication is optional
15 – 20	Definitely needs medication
>20	Increased risk of complications

Indications for Outpatient withdrawal treatment

- CIWA <8 or some with CIWA 8 –15
- No hx. of AW seizures/delirium
- No serious medical/surgical problems
- No serious psychiatric/drug hx
- Social support
- Supervision/housing available

Indications for inpatient withdrawal treatment

- History of DTs or withdrawal seizures
- Alcohol withdrawal severity (CIWA>10) + other criteria (e.g Abnormal lab results, Utox + for other substances)
- Pregnancy
- Major medical/surgical problems
- Inability to tolerate oral medication
- Imminent risk to harm himself and/or others
- Active psychosis or cognitive impairment
- Recurrent unsuccessful attempts at ambulatory detoxification

Muncie HL Jr, Yasinian Y, Oge' L. Am Fam Physician. 2013 Nov 1;88(9):589-95.
Lindsay et al. Journal of Addiction Medicine September 2020

Treatment of Mild-Moderate Alcohol Withdrawal CIWA-Ar- 8 to 14

Long-acting Benzodiazepines:

- Chlordiazepoxide (Librium) 50-100 Mg Po Q 6-8 Hrs.
- Diazepam (Valium) 10-20 Mg Po Q 6-8 Hrs.

Short-acting Benzodiazepines:

- Lorazepam (Ativan) 2-4 Mg Po Q 1-4 Hrs.

Treatment of Severe Alcohol Withdrawal CIWA-Ar > 15

Diazepam 10 mg IV

- Repeat 5 mg IV q 5 Min Until Calm

Lorazepam 4 mg po q 1 hr, PRN

- Moderate To Severe Liver Disease
- Elderly Or Confused Patients
- Very Ill Or Debilitated Patients
- Can Be Given PO, IV Or M

Alcohol Detoxification

Use of Anticonvulsants

Anticonvulsants Reduce Gaba Activity

- CBZ: Reduced rebound withdrawal & post-detox drinking (Malcolm, 2002)
- Gabapentin normalizes alcohol-induced effects on GABA and glutamate; has no hepatic metabolism
- Gabapentin more effective than lorazepam in reducing post-detox drinking (Myrick, 2009)
- Gabapentin, divalproex & vigabatrin may prove useful
- Caution: CBZ & divalproex have limited use in patients with severe hepatic or hematologic disease

Alcohol Detoxification

Anticonvulsants Effectiveness and Limitations

Advantages	Disadvantages
• No abuse liability • Cognition • Neuroprotective • Protracted Withdrawal	• Limited clinical experience • Hematological side effects • Liver toxicity

When to Consider Pharmacotherapy

- Anti-craving Medication as the new standard of care
  - Consider immediately post-detoxification for ALL patients with alcohol use disorder
  - Efficacy requires counseling and/or frequent physician monitoring
- Most FDA approved medications for SUDs can be used in outpatient settings
- Exception: Methadone maintenance therapy: can only be used for treatment of opioid addiction in licensed opioid treatment programs

Pharmacogenetics in AUD treatment

Medication	Genetic Variant	Outcome Moderated	Notable Studies
Topiramate	*GRIK1* (rs2832407)	Heavy drinking days (%); side effects	Kranzler et al., 2014 (2); Ray et al., 2009 (4)
Naltrexone	*OPRM1* (Asn40Asp), (rs1799971), DRD4 VNTR	Heavy drinking days (%); abstinence rates; relapse to heavy drinking	Anton et al., 2008 (12); Kim et al., 2009 (13); Oslin et al., 2003 (14); Tidey et al., 2008 (15)
Ondansetron	LL/LS/SS (5-HTTLPR) (rs1042173), *SLC6A4* (5-HTTLPR)	Drinks per drinking day; days abstinent (%)	Johnson et al., 2011 (9)
Sertraline	5-HTTLPR triallelic *SLC6A4*	Heavy drinking days (%); drinking days (%)	Kranzler et al., 2011 (8)
Acamprosate	*GATA4* (rs1327367)	Relapse	Kiefer et al., 2011 (10)
Disulfiram	*DBH* (rs161115)	Adverse events	Mutschler et al., 2012 (11)

Note: OPRM 1 predictive value for NTX response has not been supported
(Schacht, J., Randall, P., Latham, P. *et al 2017)*

Batki & Pennington (2014) Am J Psychiatry
Hartwell and Kranzler (2019)Expert Opinion on Drug Metabolism & Toxicology

Alcohol Use Disorder (Relapse Prevention) FDA Approved

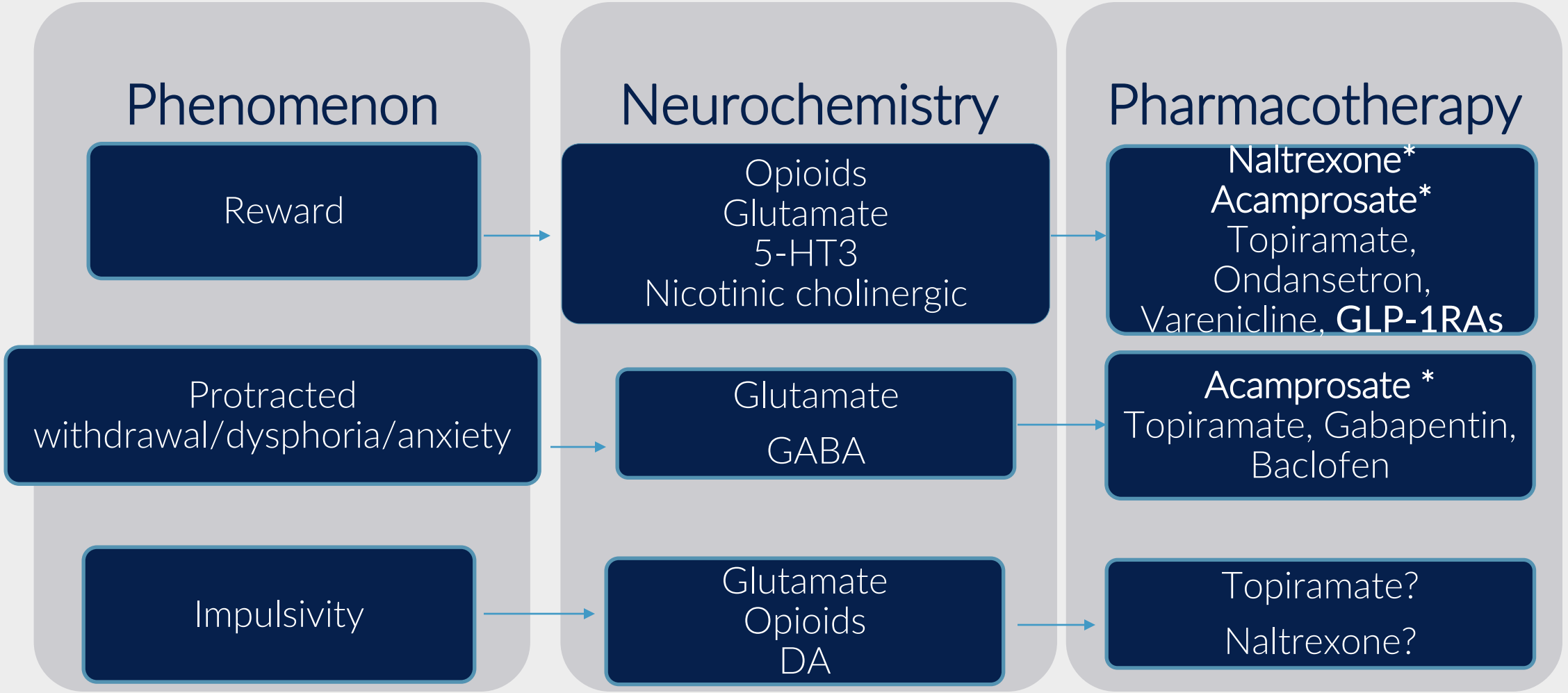
- Naltrexone (Revia): 1994
- Long Acting Naltrexone IM (Vivitrol): 2006

↓ Binge drinking

- Acamprosate (Campral): 2004 → Maintain abstinence
- Disulfiram (Antabuse): 1949 → With supervision improve treatment adherence
- Nalmefene (2016)
  European Medicines Agency (EMA)

↓ Heavy drinking days

Neurochemical Targets for AUD



Pharmacotherapy of Alcohol Use Disorder:

Naltrexone-oral/Mechanism of Action

- Reduces positive reinforcement (reward craving)
  - Potent inhibitor at mu opioid receptors
- Modulates the mesolimbic dopamine system in the VTA & projections to the nucleus accumbens
- There is mixed evidence around markers that predict a favorable response to naltrexone treatment, such as:
  - Male sex
  - A positive family history of alcoholism
  - High levels of craving,
  - Polymorphism (asp variant) of the opioid receptor gene OPRM1?

Pharmacotherapy of Alcohol Use Disorder:

Naltrexone-oral/Mechanism of Action

- The patient does not experience the full euphorogenic/reinforcing effect of alcohol.
  - suppresses/reduces endogenous opioids (beta-endorphin) involved in the reinforcing (pleasurable) and subsequent reduces DA in NAc effects of alcohol and possibly craving

- Prevents a slip from becoming a full-blown relapse

Pharmacotherapy of Alcohol Use Disorder:

Naltrexone-oral / Effectiveness

- Effective in reducing relapse to heavy drinking.
- A meta-analysis of (N:16 studies and 2347 patients) found a:
  - risk decrease (RD) for a return to any drinking
  - (risk decrease = −0.05; 95% CI, −0.10 to −0.002; number needed to treat = 20)
- (19 studies N: 2875) found also a:
  - risk decrease (RD) of binge drinking
  - (risk decrease = −0.09; 95% CI, −0.13 to −0.04; number needed to treat = 12)
- Medication compliance may be a limiting factor in oral treatment.

Kranzler Hr et al JAMA 2018 ; Srisurapanont M, Jarusuraisin N. Cochrane Database Syst Rev 2005;(1):CD001867.

Pharmacotherapy of Alcohol Use Disorder:

Naltrexone-oral / Dosing and Safety

Oral Naltrexone Hydrochloride

- FDA approved dose: 50 mg per day
- Antagonist of mu , delta and kappa opioid receptors.
- Antagonizes opioid-containing agents, but no other significant drug-drug interactions.

- Some have used 100 mg daily with rationale that naltrexone has been effective for heroin addiction at doses of 100mg-100mg-150 mg q Monday, Wednesday, and Friday; an effective plasma concentration can be obtained even if some doses are missed

Pharmacotherapy of Alcohol Use Disorder:

Naltrexone-oral /Dosing and Safety

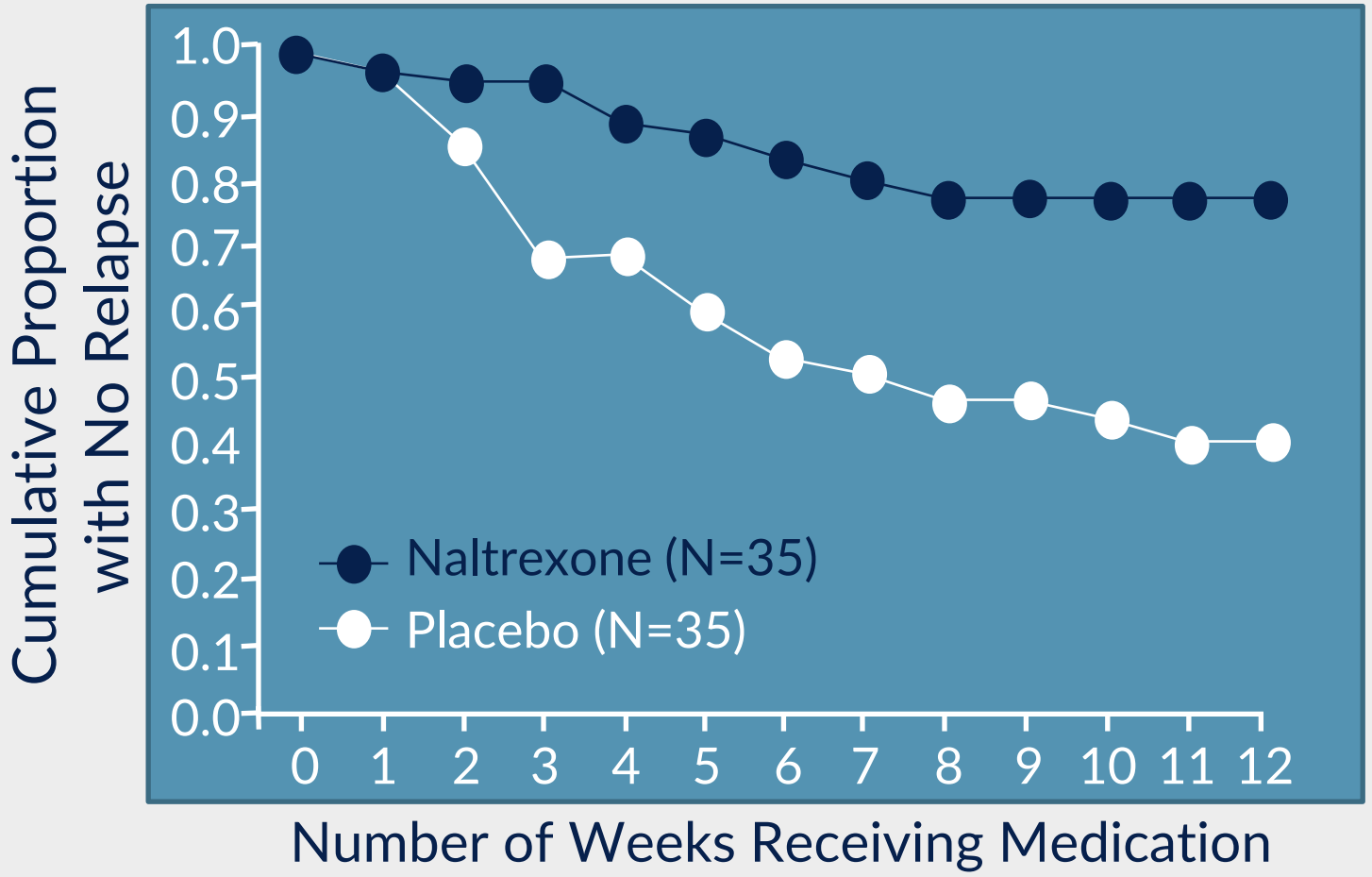
- Side effects
  - GI: abdominal pain, diarrhea, decreased appetite, nausea
  - Sedation: daytime sleepiness, fatigue, insomnia, headache

- Reversible hepatoxicity
  - LFT's should be monitored closely (check LFT's prio starting medication)

- Works best with complaint patients
  - Requires counseling (CBT) or frequent MD monitoring visits (Project Combine, 2006)
  - Efficacy questioned in women (O'Malley, 2007)

Physician's Desk Reference (www.PDR.net) and Epocrates. Accessed on September 1, 2011.

Naltrexone-Oral in the Treatment of Alcohol Use Disorder



Volpicelli et al., Arch Gen Psychiatry, 1992

Pharmacotherapy of Alcohol Use Disorder:

Long-Acting Naltrexone (IM)

Extended-Release - Injectable Naltrexone

- 1 injection per month/ 380 mg
- 100 μm diameter microspheres of naltrexone and polymeric matrix.

- Advantages: once a month injection can be done in clinician's office
- Better adherence with once monthly dosing
- More stable plasma concentrations compared to the oral formulation

Garbutt et al. JAMA. 2005;293:1617-1625. Physician's Desk Reference (www.PDR.net) and Epocrates. Accessed on September 1, 2012.

Pharmacotherapy of Alcohol Use Disorder:

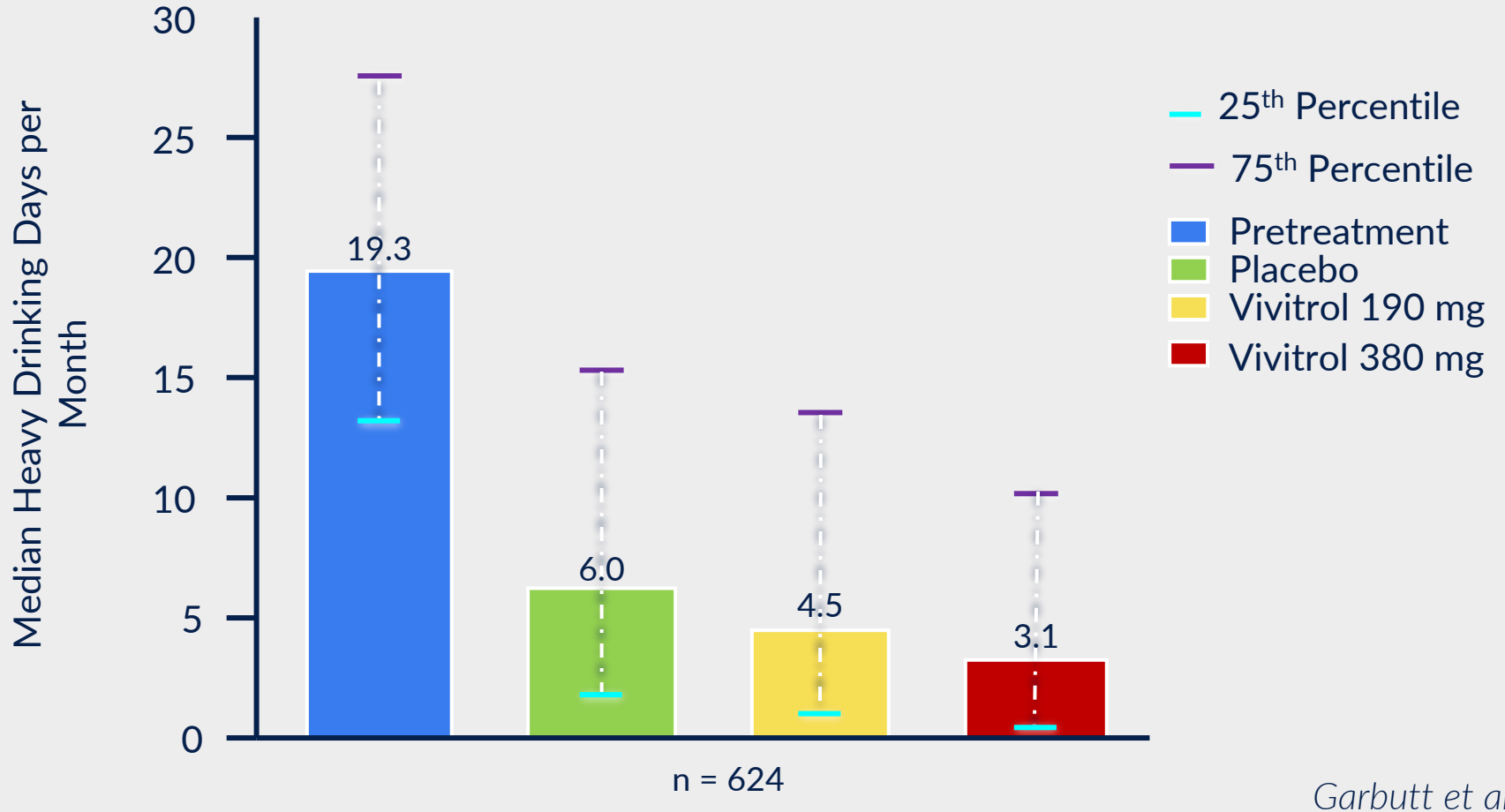
Long-Acting Naltrexone (IM) Dosing and Safety

Extended-Release Injectable Naltrexone

- Side effects: nausea & headaches; more sedation than with the oral formulation
- LFT's should be monitored closely
- Injection site reactions possible
- Best results in patients sober 1 week prior to starting the medication
- Efficacy shown in more severe alcoholics
- Reduction in heavy-drinking days (48.9% vs 30.9% on placebo)
- Pregnancy Category C , acceptable for use when breastfeeding

Pettinati HM, Alcohol Clin Exp Res, May 2011

Naltrexone-injectable in the Treatment of Alcohol Use Disorder Results: Heavy Drinking Days

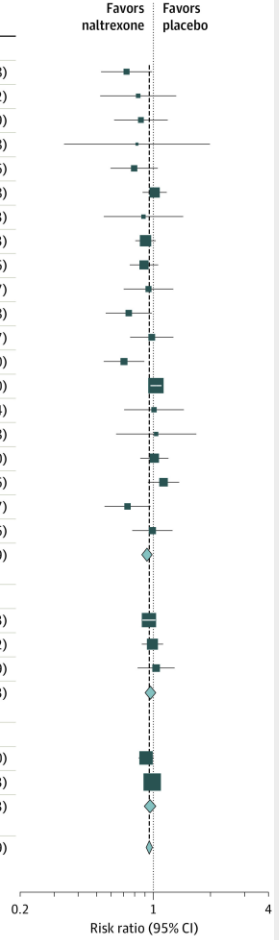


Garbutt et al., JAMA 2005; 293

Evidence of Naltrexone in both forms PO and IM

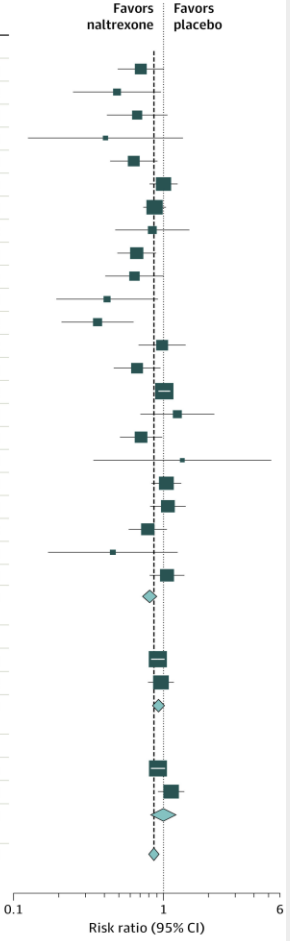
Return to Any Drinking, Naltrexone vs Placebo

Source	Duration, wk	No./total No. (%) Naltrexone	Placebo	Risk ratio (95% CI)
Naltrexone, 50 mg/d oral				
O'Malley et al,[50] 1992	12	27/52 (51.9)	38/52 (73.1)	0.72 (0.53-0.98)
Volpicelli et al,[63] 1995	12	21/54 (38.9)	21/45 (46.7)	0.83 (0.53-1.32)
Volpicelli et al,[64] 1997	12	27/48 (56.3)	32/49 (65.3)	0.86 (0.62-1.19)
Oslin et al,[54] 1997	12	6/21 (28.6)	8/23 (34.8)	0.82 (0.34-1.98)
Anton et al,[18] 1999	12	36/68 (52.9)	42/63 (66.7)	0.79 (0.60-1.06)
Chick et al,[27] 2000	12	70/85 (82.4)	64/79 (81.0)	1.02 (0.88-1.18)
Lee et al,[42] 2001	12	19/35 (54.3)	11/18 (61.1)	0.89 (0.55-1.43)
Krystal et al,[40] 2001	12	255/418 (61.0)	140/209 (67.0)	0.91 (0.81-1.03)
Morris et al,[49] 2001	12	43/55 (78.2)	49/56 (87.5)	0.89 (0.75-1.06)
Gastpar et al,[31] 2002	12	41/84 (48.8)	45/87 (51.7)	0.94 (0.70-1.27)
Ahmadi and Ahmadi,[15] 2002	36	32/58 (55.2)	43/58 (74.1)	0.74 (0.56-0.98)
Guardia et al,[34] 2002	12	53/101 (52.5)	54/101 (53.5)	0.98 (0.76-1.27)
Kiefer et al,[37] 2003	12	26/40 (65.0)	37/40 (92.5)	0.70 (0.55-0.90)
Balldin et al,[20] 2003	24	55/56 (98.2)	59/62 (95.2)	1.03 (0.97-1.10)
Killeen et al,[38] 2004	12	30/51 (58.8)	21/36 (58.3)	1.01 (0.70-1.44)
Petrakis et al,[58] 2005	12	21/59 (35.6)	22/64 (34.4)	1.04 (0.64-1.68)
Morley et al,[48] 2006	12	44/53 (83.0)	50/61 (82.0)	1.01 (0.86-1.20)
O'Malley et al,[52] 2007	12	49/57 (86.0)	38/50 (76.0)	1.13 (0.94-1.36)
O'Malley et al,[51] 2008	16	22/34 (64.7)	30/34 (88.2)	0.73 (0.56-0.97)
Baltieri et al,[22] 2008	12	35/49 (71.4)	39/54 (72.2)	0.99 (0.78-1.26)
Heterogeneity: $\tau^2=0.01$, $I^2=35.07\%$, $H^2=1.54$ Test of $\theta_i=\theta_j$: Q(19) = 29.26, $P=.06$				0.93 (0.87-0.99)
Naltrexone, 100 mg/d oral				
Anton et al,[19] 2006	16	241/309 (78.0)	254/309 (82.2)	0.95 (0.88-1.03)
Oslin et al,[53] 2008	24	95/120 (79.2)	96/120 (80.0)	0.99 (0.87-1.12)
Pettinati et al,[59] 2010	14	39/49 (79.6)	30/39 (76.9)	1.03 (0.83-1.29)
Heterogeneity: $\tau^2=0.00$, $I^2=0.00\%$, $H^2=1.00$ Test of $\theta_i=\theta_j$: Q(2) = 0.70, $P=.70$				0.97 (0.91-1.03)
Naltrexone, injection				
Kranzler et al,[39] 2004	12	130/158 (82.3)	141/157 (89.8)	0.92 (0.84-1.00)
Garbutt et al,[30] 2005	24	388/415 (93.5)	198/209 (94.7)	0.99 (0.95-1.03)
Heterogeneity: $\tau^2=0.00$, $I^2=54.45\%$, $H^2=2.20$ Test of $\theta_i=\theta_j$: Q(1) = 2.20, $P=.14$				0.96 (0.90-1.03)
Overall Heterogeneity: $\tau^2=0.00$, $I^2=25.82\%$, $H^2=1.35$ Test of group differences: $Q_b(2)=0.99$, $P=.61$				0.95 (0.92-0.99)



Return to Heavy Drinking, Naltrexone vs Placebo

Source	Duration, wk	No./total No. (%) Naltrexone	Placebo	Risk ratio (95% CI)
Naltrexone, 50 mg/d oral				
O'Malley et al,[50] 1992	12	24/52 (46.2)	34/52 (65.4)	0.71 (0.50-1.01)
Volpicelli et al,[63] 1995	12	10/54 (18.5)	17/45 (37.8)	0.49 (0.25-0.96)
Volpicelli et al,[64] 1997	12	17/48 (35.4)	26/49 (53.1)	0.67 (0.42-1.06)
Oslin et al,[54] 1997	12	3/21 (14.3)	8/23 (34.8)	0.41 (0.13-1.35)
Anton et al,[18] 1999	12	26/68 (38.2)	38/63 (60.3)	0.63 (0.44-0.91)
Chick et al,[27] 2000	24	57/85 (67.1)	53/79 (67.1)	1.00 (0.81-1.24)
Krystal et al,[40] 2001	12	183/418 (43.8)	105/209 (50.2)	0.87 (0.73-1.04)
Monti et al,[47] 2001	12	16/64 (25.0)	19/64 (29.7)	0.84 (0.48-1.49)
Morris et al,[49] 2001	12	28/55 (50.9)	43/56 (76.8)	0.66 (0.49-0.89)
Latt et al,[41] 2002	12	19/56 (33.9)	27/51 (52.9)	0.64 (0.41-1.00)
Guardia et al,[34] 2002	12	8/101 (7.9)	19/101 (18.8)	0.42 (0.19-0.92)
Ahmadi and Ahmadi,[15] 2002	12	12/58 (20.7)	33/58 (56.9)	0.36 (0.21-0.63)
Gastpar et al,[31] 2002	12	34/84 (40.5)	36/87 (41.4)	0.98 (0.68-1.40)
Kiefer et al,[37] 2003	12	20/40 (50.0)	30/40 (75.0)	0.67 (0.47-0.95)
Balldin et al,[20] 2003	24	53/56 (94.6)	58/62 (93.5)	1.01 (0.92-1.11)
Killeen et al,[38] 2004	12	21/51 (41.2)	12/36 (33.3)	1.24 (0.70-2.18)
Anton et al,[17] 2005	12	33/80 (41.3)	46/80 (57.5)	0.71 (0.51-0.98)
Huang et al,[36] 2005	14	4/20 (20.0)	3/20 (15.0)	1.33 (0.34-5.21)
Morley et al,[48] 2006	12	39/53 (73.6)	43/61 (70.5)	1.04 (0.83-1.31)
O'Malley et al,[52] 2007	12	39/57 (68.4)	32/50 (64.0)	1.07 (0.81-1.40)
O'Malley et al,[51] 2008	16	22/34 (64.7)	28/34 (82.4)	0.79 (0.59-1.05)
Brown et al,[25] 2009	12	4/20 (20.0)	10/23 (43.5)	0.46 (0.17-1.24)
Mann et al,[45] 2013	12	86/169 (50.9)	41/85 (48.2)	1.05 (0.81-1.38)
Heterogeneity: $\tau^2=0.03$, $I^2=58.72\%$, $H^2=2.42$ Test of $\theta_i=\theta_j$: Q(22) = 53.29, $P<.001$				0.81 (0.72-0.90)
Naltrexone, 100 mg/d oral				
Anton et al,[19] 2006	16	207/309 (67.0)	226/309 (73.1)	0.92 (0.83-1.02)
Oslin et al,[53] 2008	24	73/120 (60.8)	76/120 (63.3)	0.96 (0.79-1.17)
Heterogeneity: $\tau^2=0.00$, $I^2=0.00\%$, $H^2=1.00$ Test of $\theta_i=\theta_j$: Q(1) = 0.17, $P=.68$				0.93 (0.84-1.01)
Naltrexone, injection				
Kranzler et al,[39] 2004	12	122/158 (77.2)	132/157 (84.1)	0.92 (0.82-1.02)
ALK21−014,[16] 2011	12	90/152 (59.2)	78/148 (52.7)	1.12 (0.92-1.37)
Heterogeneity: $\tau^2=0.01$, $I^2=66.35\%$, $H^2=2.97$ Test of $\theta_i=\theta_j$: Q(1) = 2.97, $P=.08$				1.00 (0.82-1.21)
Overall Heterogeneity: $\tau^2=0.02$, $I^2=54.99\%$, $H^2=2.22$ Test of group differences: $Q_b(2)=5.00$, $P=.08$				0.86 (0.80-0.93)



McPheeters M et al., Pharmacotherapy for Alcohol Use Disorder: A Systematic Review and Meta-Analysis. JAMA. 2023 Nov 7;330(17):1653-1665. doi: 10.1001/jama.2023.19761. PMID: 37934220; PMCID: PMC10630900

Protracted Withdrawal Symptom

- Sleep dysregulation
- Irritability
- Mood instability
- Anxiety

Pharmacotherapy of Alcohol Use Disorder:

Acamprosate/ Mechanism of Action

- Stabilizes glutamatergic neurotransmission altered during withdrawal (Littleton 1995).
- Chronic ETOH exposure alters GABA & NMDA systems
  - Restores balance between inhibitory & excitatory neurotransmission
- Anticraving, reduced protracted withdrawal
- Reduce negative reinforcement (abstinence craving)
- No abuse liability, hypnotic, muscle relaxant, or anxiolytic properties

Pharmacotherapy of Alcohol Use Disorder:

Acamprosate/ Effectiveness

- Effective in improving abstinence.
- A meta-analysis (16 studies; N = 4847) concluded that acamprosate treatment was associated with a greater reduction than placebo in the risk of drinking among abstinent patients but no reduction in the likelihood of binge drinking.
  - (risk decrease = −0.09; 95% CI, −0.14 to −0.04; number needed to treat = 12)
- The US trial showed efficacy only in patients motivated for abstinence.

Jonas et al Jama 2014; Kranzler HR, Gage A. Am J Addict. 2008;17:70-76. Mason BJ et al. J Psychiatr Res. 2006;40:383-93.

Pharmacotherapy of Alcohol Use Disorder:

Acamprosate/Dosing and Safety

- 666 mg three times a day (2000 mg daily)

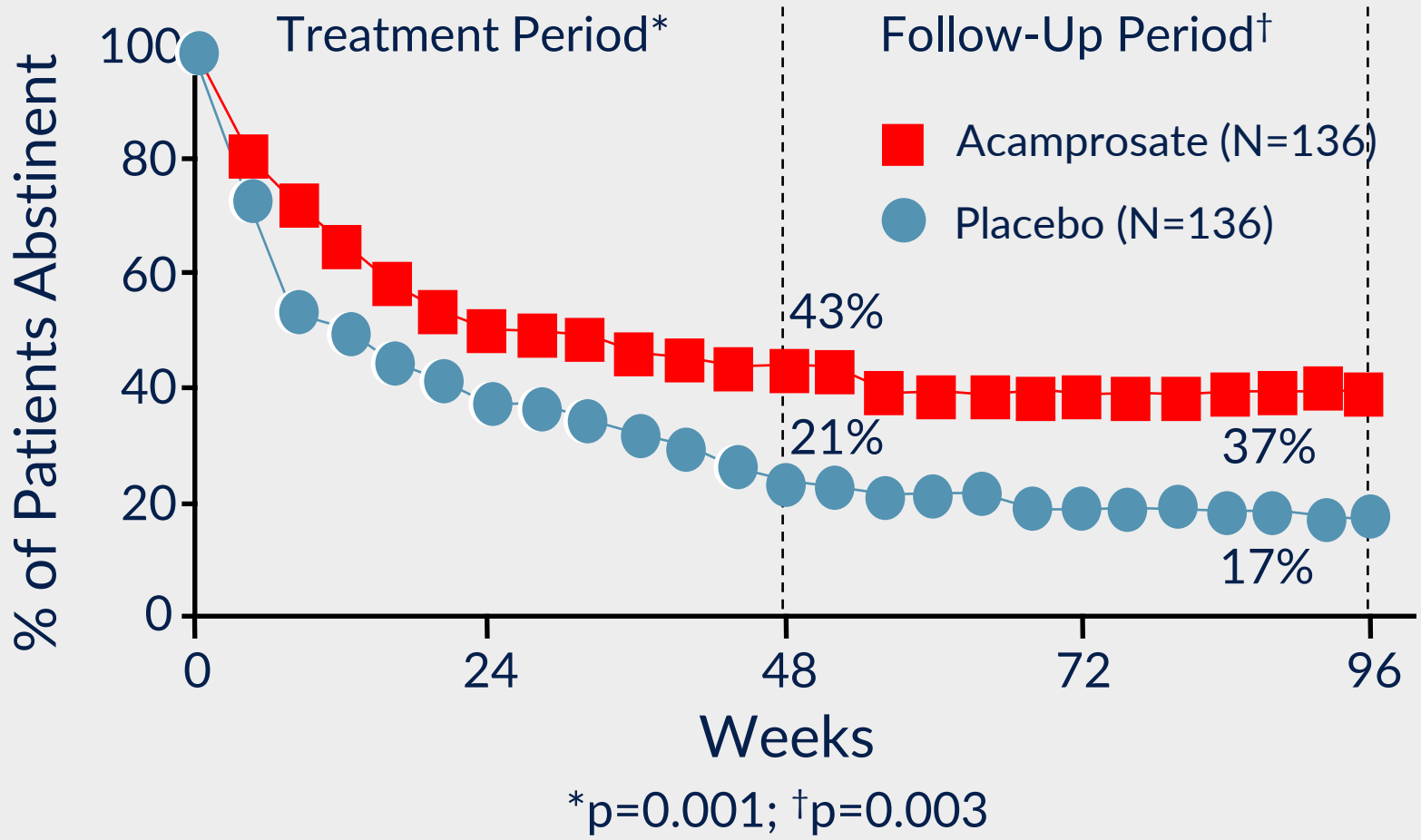
- Excreted by the kidneys; no liver metabolism
- Contraindicated: significant renal disease with creat cl <30ml/min or those who are pregnant

- Mild diarrhea (16% acamprosate vs. 10% placebo)

- Recommendation: patients with hepatic disease or those treated with opioids. Advantage when a patient is taking multiple medications

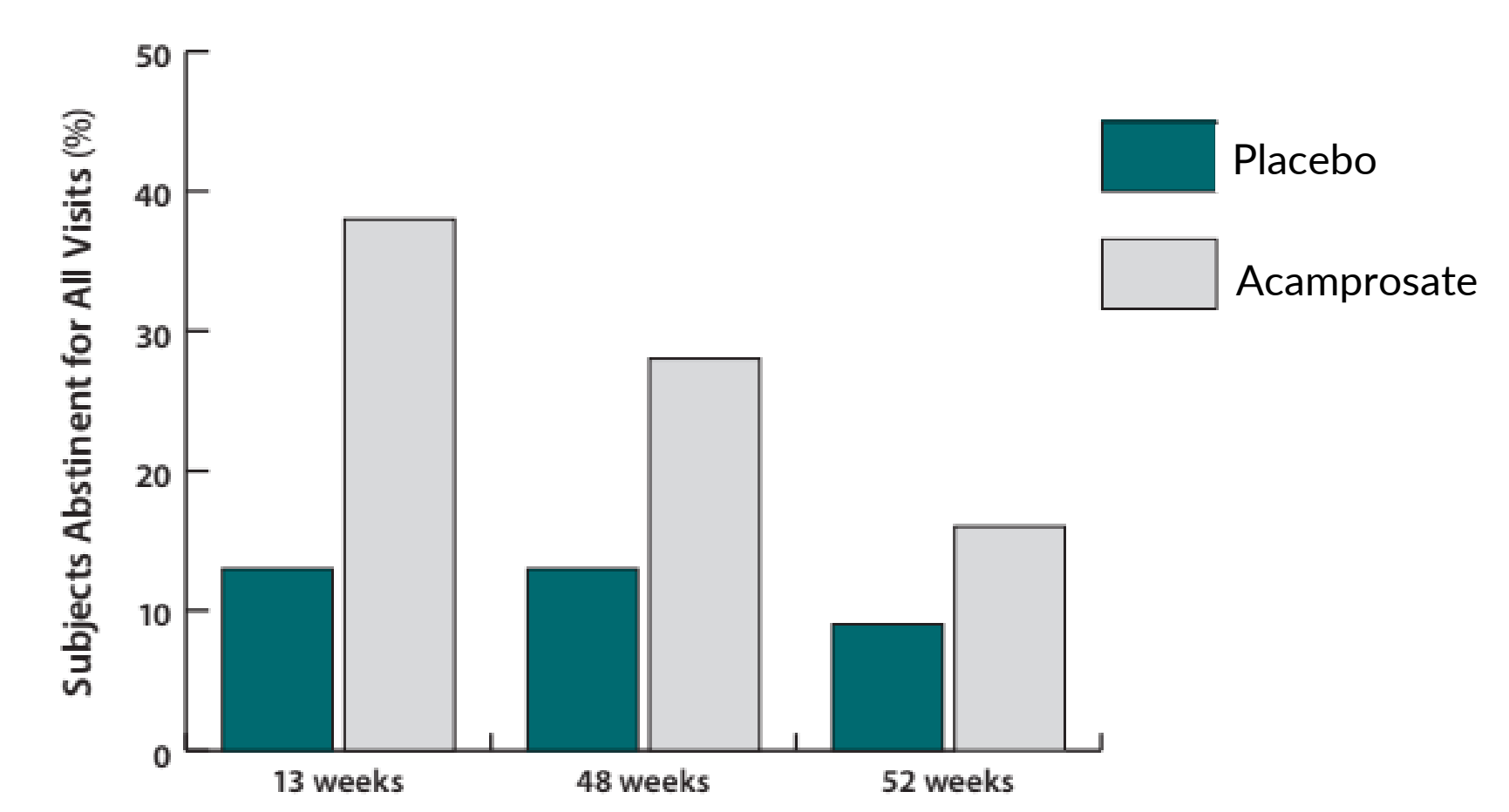
- No drug-drug interactions.
- Pregnancy category C

Acamprosate in the Treatment of Alcohol Use Disorder



Sass et al., Arch Gen Psychiatry, 1996

Acamprosate in the Treatment of Alcohol Use Disorder

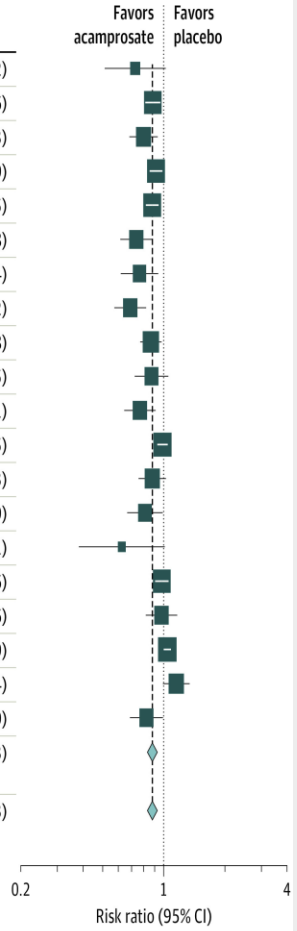


Kranzler HR, Gage A. Acamprosate efficacy in alcohol-dependent patients: summary of results from three pivotal trials. Am J Addict. 2008;17(1):70–6.

Evidence of Acamprosate

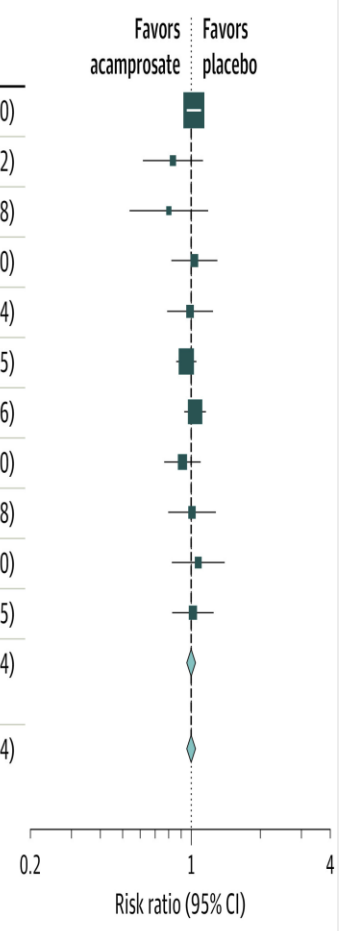
Return to Any Drinking, Acamprosate vs Placebo

Source	Duration, wk	No./total No. (%) Acamprosate	Placebo	Risk ratio (95% CI)
Lhuintre et al,[43] 1985	13	22/42 (52.4)	31/43 (72.1)	0.73 (0.52-1.02)
Lhuintre et al,[44] 1990	12	208/279 (74.6)	245/291 (84.2)	0.89 (0.81-0.96)
Pelc et al,[56] 1992	26	42/55 (76.4)	45/47 (95.7)	0.80 (0.68-0.93)
Paille et al,[55] 1995	51	294/361 (81.4)	157/177 (88.7)	0.92 (0.85-0.99)
Whitworth et al,[65] 1996	52	183/224 (81.7)	208/224 (92.9)	0.88 (0.82-0.95)
Sass et al,[61] 1996	48	75/136 (55.1)	102/136 (75.0)	0.74 (0.61-0.88)
Poldrugo,[60] 1997	26	63/122 (51.6)	84/124 (67.7)	0.76 (0.62-0.94)
Pelc et al,[57] 1997	13	74/126 (58.7)	53/62 (85.5)	0.69 (0.57-0.82)
Geerlings et al,[32] 1997	26	96/128 (75.0)	116/134 (86.6)	0.87 (0.77-0.98)
Besson et al,[24] 1998	51	41/55 (74.5)	47/55 (85.5)	0.87 (0.72-1.05)
Tempesta et al,[62] 2000	26	87/164 (53.0)	115/166 (69.3)	0.77 (0.64-0.91)
Chick et al,[26] 2000	24	254/289 (87.9)	260/292 (89.0)	0.99 (0.93-1.05)
Gual and Lehert,[33] 2001	26	92/141 (65.2)	109/147 (74.1)	0.88 (0.75-1.03)
Kiefer et al,[37] 2003	12	30/40 (75.0)	37/40 (92.5)	0.81 (0.66-0.99)
Baltieri and De Andrade,[21] 2004	12	15/40 (37.5)	21/35 (60.0)	0.63 (0.39-1.01)
Anton et al,[17] 2005	16	244/303 (80.5)	254/309 (82.2)	0.98 (0.91-1.06)
Morley et al,[48] 2006	12	44/55 (80.0)	50/61 (82.0)	0.98 (0.82-1.16)
Mason et al,[46] 2006	24	328/341 (96.2)	240/260 (92.3)	1.04 (1.00-1.09)
Berger et al,[23] 2013	12	48/51 (94.1)	40/49 (81.6)	1.15 (0.99-1.34)
Higuchi et al,[35] 2015	24	86/163 (52.8)	105/164 (64.0)	0.82 (0.68-0.99)
Heterogeneity: $\tau^2 = 0.01$, $I^2 = 77.64\%$, $H^2 = 4.47$ Test of $\theta_i = \theta_j$: $Q(19) = 84.97$, $P < .001$				0.88 (0.83-0.93)
Overall Heterogeneity: $\tau^2 = 0.01$, $I^2 = 77.64\%$, $H^2 = 4.47$ Test of group differences: $Q_b(0) = 0.00$				0.88 (0.83-0.93)



Return to Heavy Drinking, Acamprosate vs Placebo

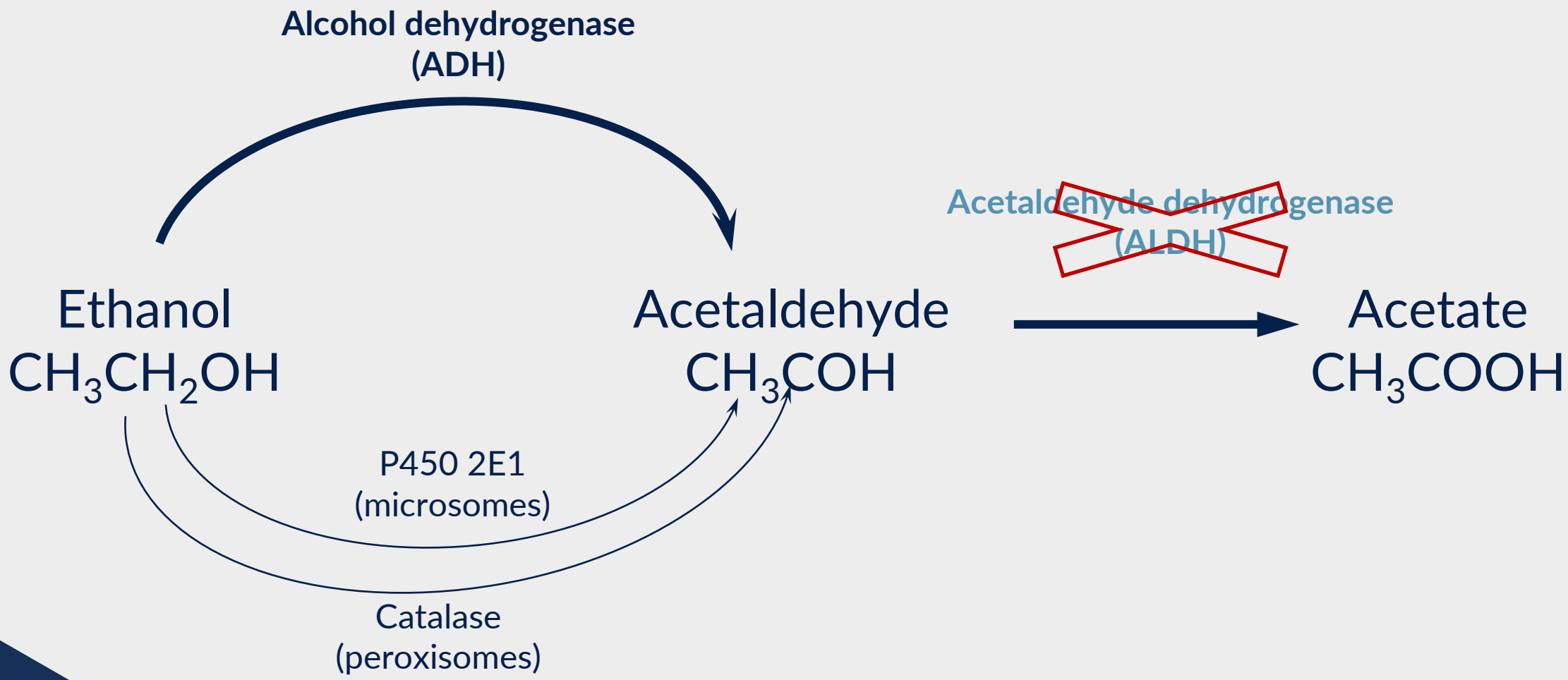
Source	Duration, wk	No./total No. (%) Acamprosate	Placebo	Risk ratio (95% CI)
Chick et al,[26] 2000	24	246/289 (85.1)	242/292 (82.9)	1.03 (0.96-1.10)
Kiefer et al,[37] 2003	12	25/40 (62.5)	30/40 (75.0)	0.83 (0.62-1.12)
Kiefer et al,[37] 2003	12	20/40 (50.0)	25/40 (62.5)	0.80 (0.54-1.18)
Morley et al,[48] 2006	12	40/55 (72.7)	43/61 (70.5)	1.03 (0.82-1.30)
Morley et al,[48] 2006	12	40/55 (72.7)	39/53 (73.6)	0.99 (0.79-1.24)
Anton et al,[19] 2006	16	211/303 (69.6)	226/309 (73.1)	0.95 (0.86-1.05)
Anton et al,[19] 2006	16	211/303 (69.6)	207/309 (67.0)	1.04 (0.93-1.16)
Mason et al,[46] 2006	24	143/341 (41.9)	119/260 (45.8)	0.92 (0.76-1.10)
Wölwer et al,[66] 2011	24	65/124 (52.4)	65/125 (52.0)	1.01 (0.79-1.28)
Mann et al,[45] 2013	12	89/172 (51.7)	41/85 (48.2)	1.07 (0.82-1.40)
Mann et al,[45] 2013	12	89/172 (51.7)	86/169 (50.9)	1.02 (0.83-1.25)
Heterogeneity: $\tau^2 = 0.00$, $I^2 = 0.00\%$, $H^2 = 1.00$ Test of $\theta_i = \theta_j$: $Q(10) = 5.90$, $P = .82$				1.00 (0.96-1.04)
Overall Heterogeneity: $\tau^2 = 0.00$, $I^2 = 0.00\%$, $H^2 = 1.00$ Test of group differences: $Q_b(0) = 0.00$				1.00 (0.96-1.04)



McPheeters M et al., Pharmacotherapy for Alcohol Use Disorder: A Systematic Review and Meta-Analysis. JAMA. 2023 Nov 7;330(17):1653-1665. doi: 10.1001/jama.2023.19761. PMID: 37934220; PMCID: PMC10630900

Pharmacotherapy of Alcohol Use Disorder:

Disulfiram Mechanism of Action



Pharmacotherapy of Alcohol Use Disorder:

Disulfiram/ Mechanism of Action

- Alcohol → Acetaldehyde  → Acetate

- Disulfiram irreversibly binds to acetaldehyde dehydrogenase inhibiting the metabolism of acetaldehyde to acetate.

- Acetaldehyde accumulates resulting in a very unpleasant reaction Disulfiram –Ethanol Reaction (tachycardia, headache, nausea/vomiting, hypotension, sweating, warmness and flushing of the skin, dizziness, blurred vision and confusion).

Pharmacotherapy of Alcohol Use Disorder:

Disulfiram Effectiveness

- Second Line Treatment
- In a meta-analysis of 22 studies was associated with:
  - Sustained abstinent compared to control conditions only in open-label studies

- Double-blind, placebo-control study design is not helpful as both the medication and the placebo pills may (or may not) result in fear of drinking.

- Most studies are negative, but disulfiram may be helpful for a better response than control conditions when medication adherence was supervised

Diehl et al. Alcohol Alcohol. 2010;45:271-277. Fuller RK et al. JAMA. 1986;256:1449-55.

Kranzler HR, Soyka M. Diagnosis and Pharmacotherapy of Alcohol Use Disorder: A Review. JAMA. 2018;320(8):815–824

Pharmacotherapy of Alcohol Use Disorder:

Disulfiram Dosing and Safety

- 250-500 mg daily.
  - First dose 12 hours after the last drink;
  - 500mg PO each morning for 1-2 weeks, then 250mg PO each morning

- Some liver toxicity; monitor LFTs at the beginning, 2 weeks, 3 months and then every 6 months. Caution with CAD. Contraindicated: psychosis, significant liver disease, esophageal varices, pregnancy, impulsivity, severe pulmonary disease, seizures, CRF (Barth et al., 2010)

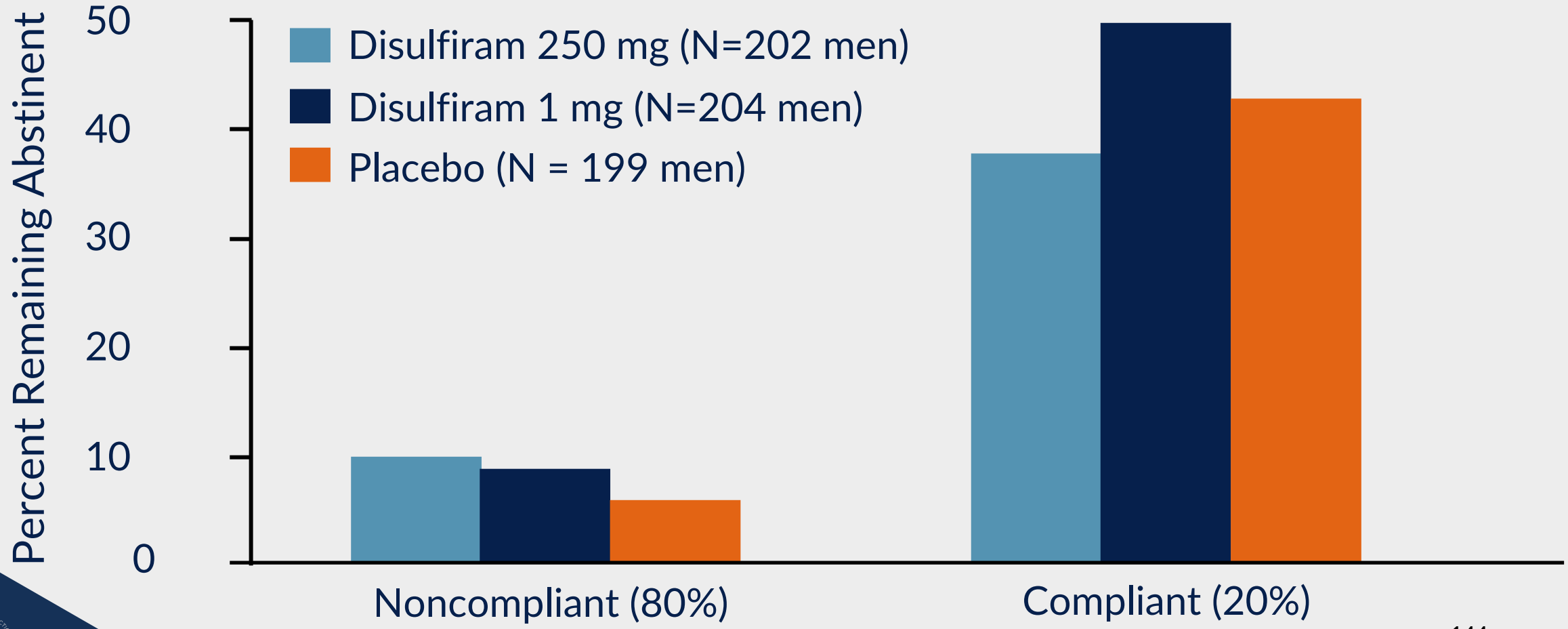
- Inhibits hepatic microsomal enzymes and increases drug levels (phenytoin, warfarin, isoniazid, metronidazole, TCA and benzodiazepines among others)
- Pregnancy category C

- SIDE EFFECTS: skin/acneiform eruptions, drowsiness, headache, metallic taste, decreased libido/potency

Physician's Desk Reference (www.PDR.net) and Epocrates. Accessed on March 1, 2018.

Disulfiram in the Treatment of Alcohol Dependence

Disulfiram and Abstinence Rates (VA Cooperative Study)



Fuller RK et al. JAMA. 1986; 256:1449-1455

MAT + FDA Approved

Medication (typical dose)	Mechanism of action	Adverse effects	Cautions	Lab monitoring	Other
*Naltrexone (50-100mg PO daily or 380mg IM monthly)	Blocks opioid receptors May reduce rewarding effects of alcohol	Nausea Headache, dizziness, insomnia Anxiety *Injection site reaction	Need 7-10 days "opioid free" if patient previously receiving chronic opioids Do not use if: Current opioid use LFTs ≥ 5x upper limit of normal	LFTs prior and during treatment	Number needed to treat to reduce heavy drinking days is 12
*Acamprosate (666mg PO three times daily)	Levels out GABA + glutamate activity	Diarrhea	CrCl 30-50 mL/min: 333mg PO three times daily Do not use if: CrCl ≤ 30 mL/min	Renal function (basic metabolic panel) prior and during treatment	Prolongs periods of abstinence
*Disulfiram (250-500mg PO daily)	Blocks acetaldehyde dehydrogenase Blocks enzyme involved in dopamine metabolism	Disulfiram-alcohol reaction if combined Rare but notable: acute liver failure	Need ≥ 12h alcohol abstinence Many medication interactions Do not use if: Severe cardiac disease or coronary occlusion Primary psychotic disorder	LFTs prior and during treatment	Daily observed disulfiram Targeted disulfiram (e.g. weddings, reunions, holidays)

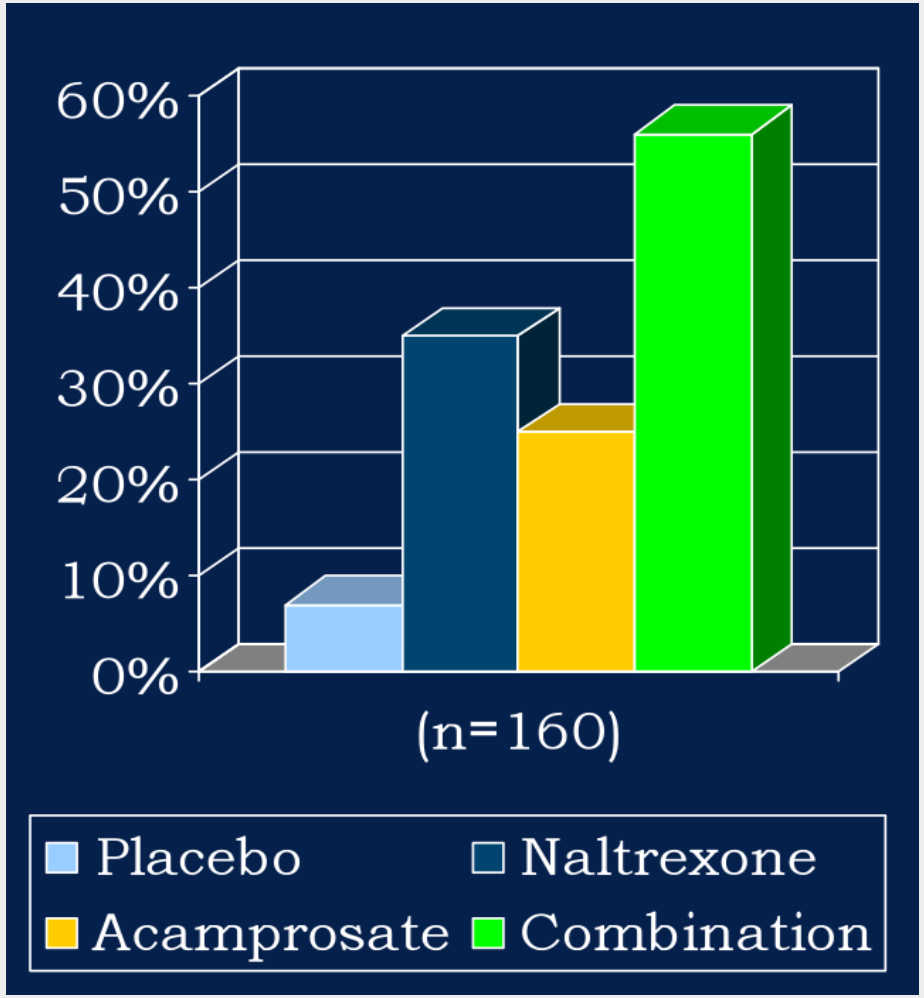
Combinations

- Naltrexone and acamprosate have different mechanisms of action and may work synergistically on cravings:
  - Naltrexone on positive reinforcement
  - Acamprosate on negative reinforcement

- Medications and psychotherapy.

Rosner S et al. J Psychopharmacol. 2008;22:11-23.

Naltrexone/Acamprosate



- Abstinence rates during a 12-week trial with:
  - Naltrexone 50 mg QD,
  - Acamprosate 666 mg TID.

- The combination of the two medications helped alcoholics stay abstinent (P=0.002) better than each drug alone.

Adapted from Kiefer F et al. Arch Gen Psychiatry. 2003;60:96.

Project MATCH

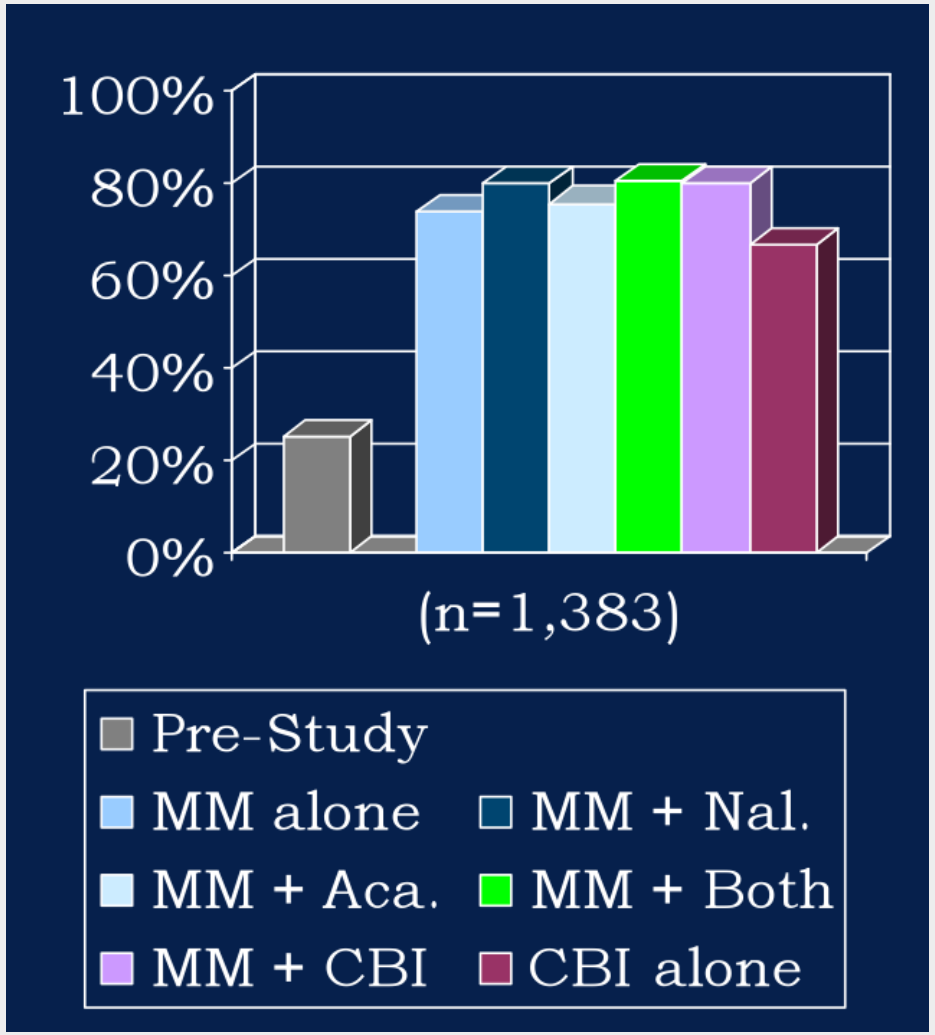
- Compared outcome efficacy for patients matched to treatments based on a prior hypotheses about 11 client attributes
- Treatment was for 12 weeks; follow-ups continued for years
- 12-Step programs, CBT and MET were compared
- Each of the three methods helped in the treatment of alcoholism
  - However outpatients who received TSF were more likely to remain abstinent after 1 year following treatment
- There were a few matching effects, and they were weak

The COMBINE Study

- 1383 patients with alcohol dependence randomized to varying combinations of oral Naltrexone, Acamprosate, combined behavioral intervention (CBI) and medical management (MM)
- Patients received naltrexone, acamprosate, both, or neither
- Half of patients received psychotherapy in addition to medical management
- One patient cohort received psychotherapy alone, no pills

JAMA. 2006;295:2003-2017

The COMBINE Study



- Percentage of abstinent days per month during a 16-week treatment trial with:
  - Naltrexone 100 mg QD,
  - Acamprosate 1 g TID.

- All treatment groups had an increase in % days abstinent. Overall effect was from 25% to 73%.

Adapted from Anton et al. JAMA. 2006;295:2003-2017.

The NIAAA COMBINE Study Results

- For patients receiving MM, naltrexone, or CBI therapy, improved outcomes over placebo plus MM
  - Naltrexone + MM had the best outcome
- Acamprosate did not add benefit to naltrexone or CBI, and was no more effective than placebo plus MM
- Taking tablets and seeing a health care professional was more effective than receiving CBI alone (possible placebo effect)
- One-year outcome: no significant differences among the groups

N=1383 (16 weeks trial)	Good Clinical outcome
MM and Placebo	58 %
MM and Placebo and CBI	71%
MM and Naltrexone	74%

CBI: Combined Behavioral Intervention
Good Clinical Outcome: Abstinence or drinking moderate amounts without problems P<0.025 (interaction p-value 0.02)

Adapted from Anton et al. JAMA. 2006;295:2003-2017

Other Pharmacological Agents

Anticonvulsants

- Topiramate
- Gabapentin
- Carbamazepine
- Valproic Acid

GABA agonist

- Baclofen

Alpha1 adrenergic blocker

- Doxazosin
- Prazosin

Alpha 2 agonists

- Clonidine

Serotonin (5-HT3) antagonists

- Ondansetron
- Mirtazapine

Selective Serotonin Reuptake Inhibitors

Partial agonist for the α4β2 nicotinic acetylcholine receptor subtype (nACH)

- Varenicline

Mu and delta opioid antagonist and partial kappa agonist

- Nalmefene

Glucagon-like peptide 1 (GLP-1) receptor agonist

- **Semaglutide**

Conclusions

- Identify the need of your patients to get treatment
- Substance use disorders are chronic, be ready for relapses
- Prevention is based on screening and early Intervention
- CIWA-Ar is your best ally for AWS
- AWS=BZD most effective, safest and cheapest treatment
- Medications for Alcohol Use Disorder are relatively safe but modestly effective
- Naltrexone is best for “cutting down.”
- Acamprosate is best for preventing “the first drink.”
- Pharmacotherapy and psychotherapy modalities can be offered by you
- Pharmacotherapy and psychotherapy modalities are effective and scientifically based approaches



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ASAM REVIEW COURSE 2026

Sedative Use Disorder: Research and Practice

Ricardo Restrepo, MD, MPH

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Health Science Clinical Professor at University of California, Riverside

Associate Clinical Professor at Charles Drew University, Los Angeles

Department of Psychiatry and Human Behavior





Financial Disclosure

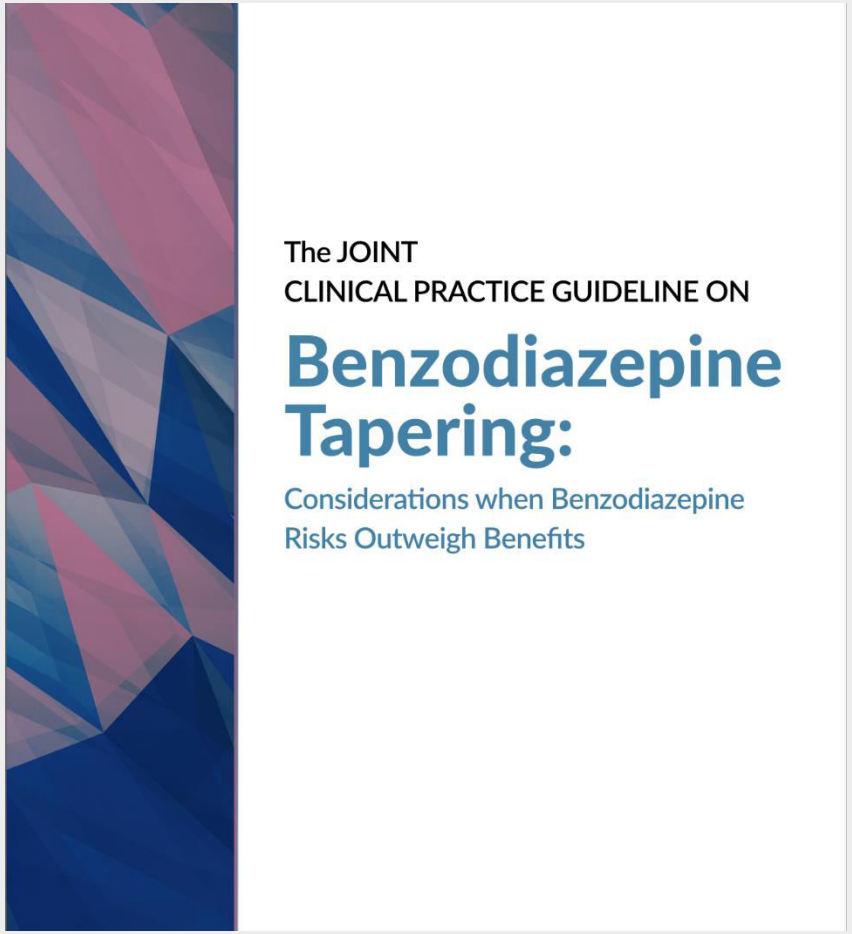
Ricardo Restrepo, MD, MPH

- No relevant disclosures

Outline

1. Historical View
2. Neurobiology
3. Epidemiology
4. Risk and Benefits of Benzodiazepines
5. Phases of Sedative-Hypnotic Treatment and related Syndromes
6. Selective nonbenzodiazepine hypnotic agents
7. Barbiturates
8. GHB
9. Conclusions

Benzodiazepine Tapering



ASAM Clinical Practice Guideline on Alcohol Withdrawal Management 2025

March 2025

Historical View

- First half of 20th century Barbiturates (starting with Barbital)
- 1950 Meprobomate
- 1950s Benzodiazepine were introduced as substitute for barbiturates (starting with Chlordiazepoxide)
- 1960s Benzodiazepines widely available and prescribed
- 1970s Benzodiazepines became the most commonly prescribed of all medications around the world

Historical View

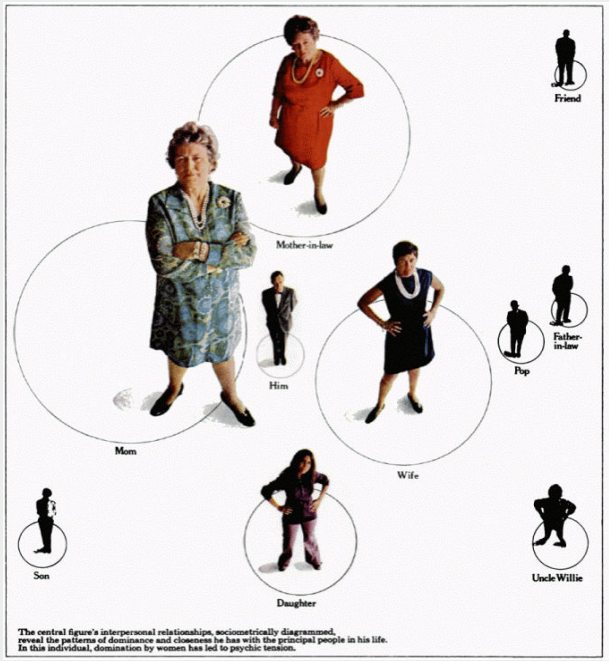
- 1980s Identification of medication losing efficacy over time and became associated with adverse effects
- 1990s Short acting benzodiazepines
- 2000s (drug tolerance and withdrawal) Not sufficient for dependence and nonbenzodiazepine hypnotic agents; elderly population risks
- 2014-present DSM 5 (sedative use disorder); guidelines adopted regarding use

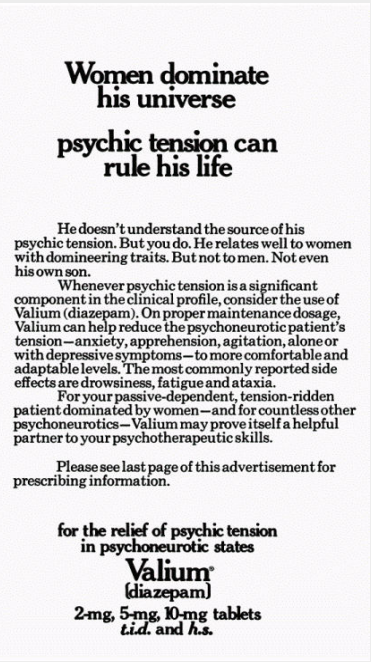
Types of Sedatives

- BZ- receptor agonist (BZRA)
  - Benzodiazepines
  - Selective non-benzodiazepine hypnotics (Z-drugs)
- Barbiturates
- Others: GHB and Paraldehyde, chloral hydrate, meprobomate


Her world orbits around doctors. Psychic tension rules her universe.
Her mother's obvious preferenc for her older sister has always rankled this patient. The deaths of her father an husband accentuated her alienation an hostility. Hypochondriasis is the way she disowns her conflicts.
While you gradually turn her away from somatic concerns and guide her through old, hidden problem areas you can ease her undue psychic tension with Valium® (diazepam).
Valium 10-mg tablets q.i.d. can help most psychoneurotic patients undergoing severe psychic tension and apprehension with or without associate depressive symptoms. The fourth table taken at bedtime, can combat anxiety-induced sleeplessness. For less severe tension states, Valium 5-mg tablets t.i.d. or q.i.d. may be adequate. Drowsi ness, fatigue and ataxia are the most commonly reported side effects. Tailo the dosage to the individual—a proce dure facilitated by the three convenien tablet strengths.
For hypochondriacs—and many other types of psychoneurotic patients walled in by situational stress—Valium by relieving psychic tension, may prov itself a useful adjunct to your healing skills.
Please see last page of this advertisement for prescribing information.
Valium® (diazepam)
2-mg, 5-mg, 10-mg tablets
Husband (deceased)
Father (deceased)
Neurologist
Allergist
General Practitioner
Gynecologist
Gastroenterologist
Mother
Older Sister
This childless widow's interpersonal relationships, sociometrically diagrammed, reveal the patterns of dominance, closeness, absence, and loss created by the principal people in her life.


Syndromes of the 1960s
The battered parent syndrome
She's the paradox of our age. Compared to her mother, she has more education, more usable income and more labor-saving devices. Yet she is physically and emotionally overworked, overwrought and—by the time you see her—probably overwhelmed.
What went wrong? Is parenthood something other than the rosy fulfillment pictured by the women's magazines? Is anxiety and tension fast becoming the occupational disease of the homemaker?
Some say it's unrealistic to educate a woman and then expect her to be content with the Cub Scouts as an intellectual outlet.
Or to grant that she is socially, politically and culturally equal, while continuing to demand domestic and biological subservience.
Or to expect her to shoulder the guilt burden of this child-centered age without unraveling around the emotional edges.
Or to compete with her husband's job for his time and involvement.
But whatever the cause, the consequences—anxiety, tension, insomnia, functional disorders—fill waiting rooms.
Sometimes it helps to add 'Miltown' to her treatment—to help her relax both emotional and muscular tension. It's no substitute for a week in Bermuda, or for emotional readjustment. But it will often make the latter easier for her, as well as for the physician.
And 'Miltown' has been doing just that—for a dozen years now—with substantial success.
Indications: Effective in relief of anxiety and tension states; adjunctively when anxiety may be a causative or disturbing factor. Fosters normal sleep through anti-anxiety and muscle-relaxant properties.
Contraindications: Previous allergic or idiosyncratic reactions to meprobamate. (Brief summary of prescribing information is continued on next page.)
Wallace Pharmaceuticals/ Cranbury, N.J.
when reassurance is not enough MILTOWN® (MEPROBAMATE)


Friend
Mother-in-law
Him
Father-in-law
Pop
Mom
Wife
Son
Daughter
Uncle Willie
The central figure's interpersonal relationships, sociometrically diagrammed, reveal the patterns of dominance and closeness he has with the principal people in his life. In this individual, domination by women has led to psychic tension.


Women dominate his universe
psychic tension can rule his life
He doesn't understand the source of his psychic tension. But you do. He relates well to women with domineering traits. But not to men. Not even his own son.
Whenever psychic tension is a significant component in the clinical profile, consider the use of Valium (diazepam). On proper maintenance dosage, Valium can help reduce the psychoneurotic patient's tension—anxiety, apprehension, agitation, alone or with depressive symptoms—to more comfortable and adaptable levels. The most commonly reported side effects are drowsiness, fatigue and ataxia.
For your passive-dependent, tension-ridden patient dominated by women—and for countless other psychoneurotics—Valium may prove itself a helpful partner to your psychotherapeutic skills.
Please see last page of this advertisement for prescribing information.
for the relief of psychic tension in psychoneurotic states
Valium® (diazepam)
2-mg, 5-mg, 10-mg tablets
t.i.d. and h.s.

Case: RR

A year later, Mr. RR, now 59-year-old Latino male with a past history of ETOH use disorder, anxiety, insomnia, and past medical history of HTN, GERD, and pancreatitis, arrives in the emergency department with a friend for confusion and diaphoresis.



Neurobiology (GABAA Receptor)

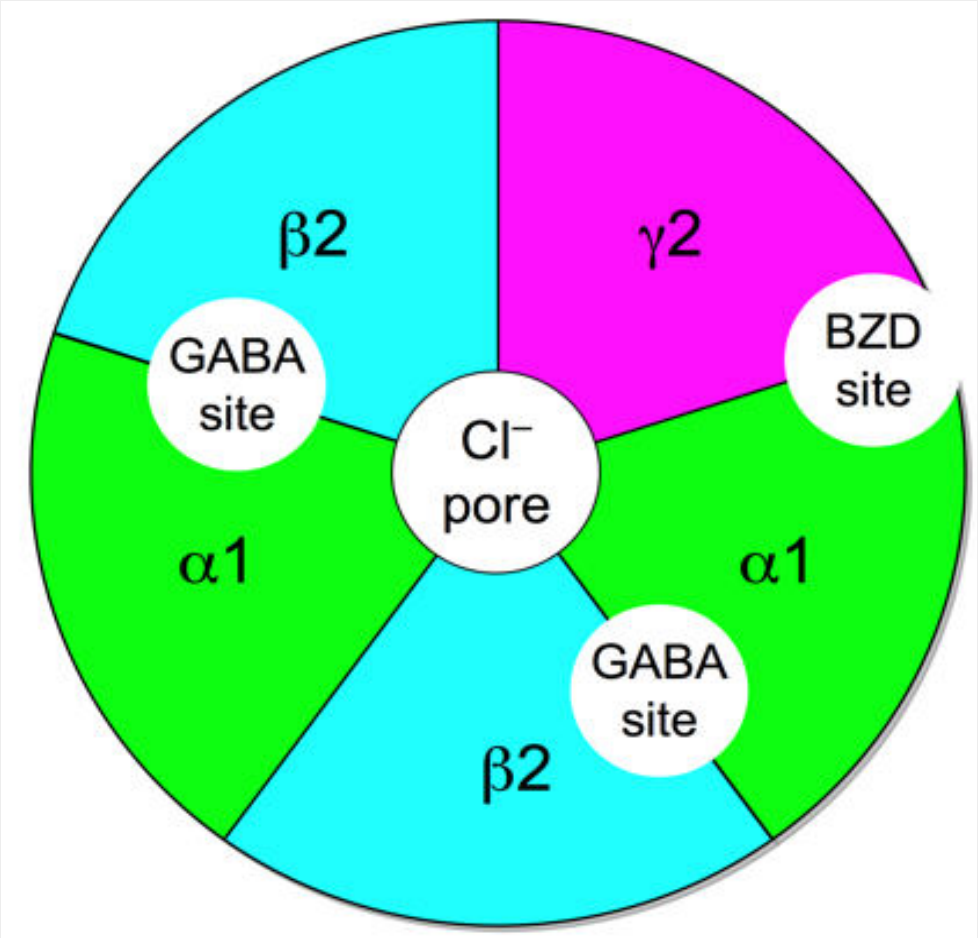
- GABA - the primary inhibitory neurotransmitter system in the CNS

- Transmembrane pentamer composed of:

2α , 2β

1γ

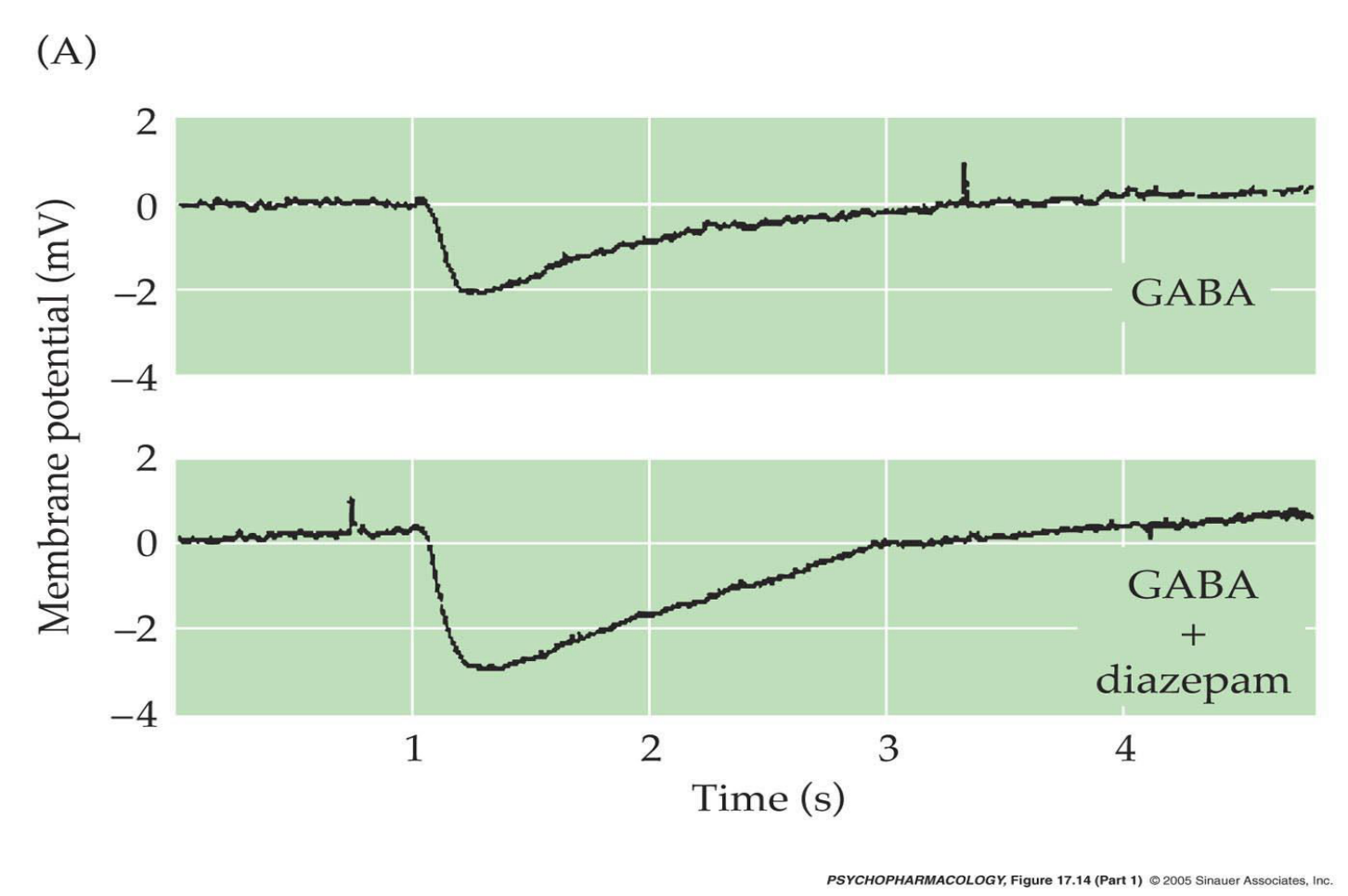
Neurobiology (GABAA Receptor)



Neurobiology (GABAA Receptor)

- GABA is estimated to be present in 40% of all synapses in the human brain
- It is an inhibitory neurotransmitter, opposed to excitatory neurotransmitters such as glutamate.
- It reduces the excitability of the post synaptic side of the synapse
- 2 types : GABAA ionotropic (prominent target for drugs) and GABA B metabotropic
- BZDs increase the number of time the Cl- channel opens (frequency)
- BBTs increase the duration of the opening of the Cl-channel

Effects of GABA and diazepam (benzodiazepine) on membrane potentials and chloride flux



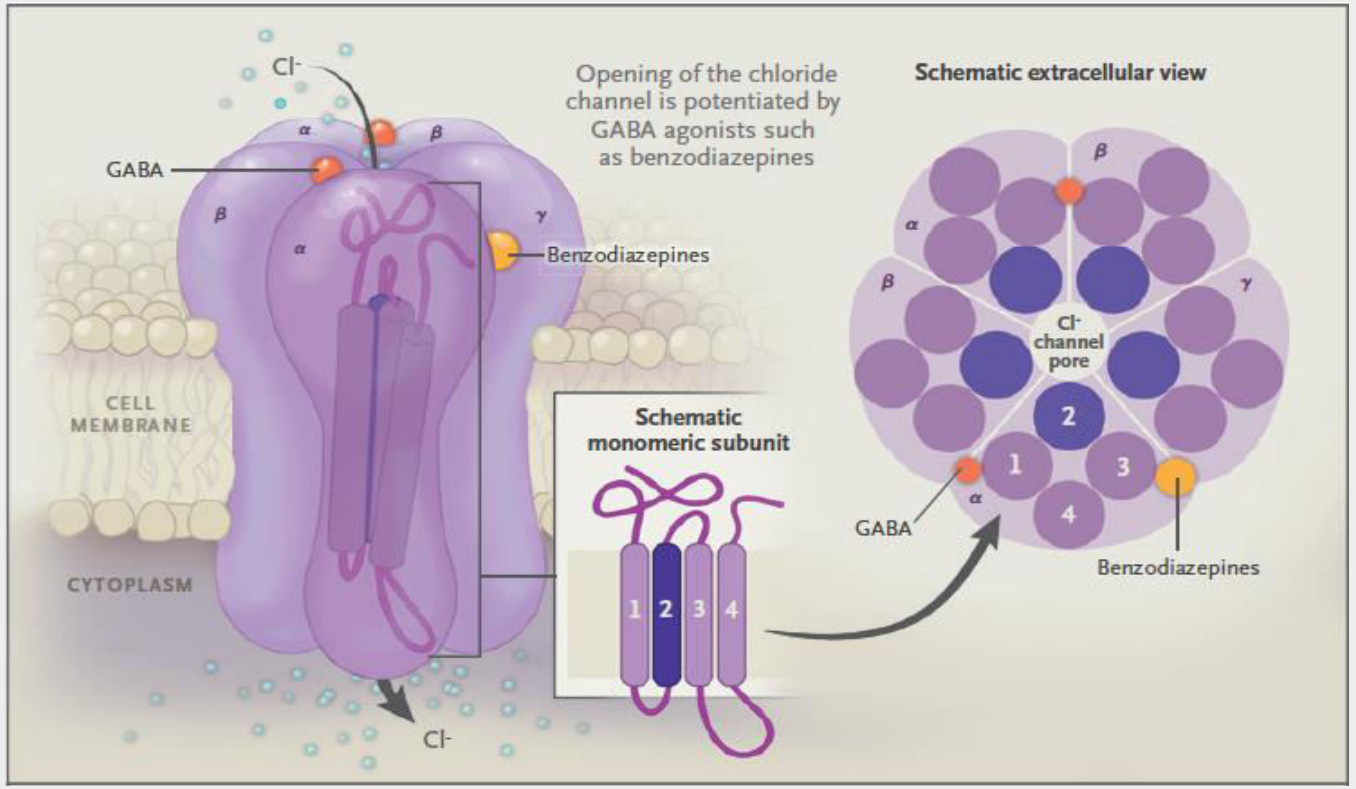
PSYCHOPHARMACOLOGY, Figure 17.14 (Part 1) © 2005 Sinauer Associates, Inc.

Neurobiology (GABAA Receptor)

Benzodiazepines require the presence of GABA

Barbiturates do not require the presence of GABA

Flumazenil blocks effects of benzodiazepine and zolpidem but not Barbiturates



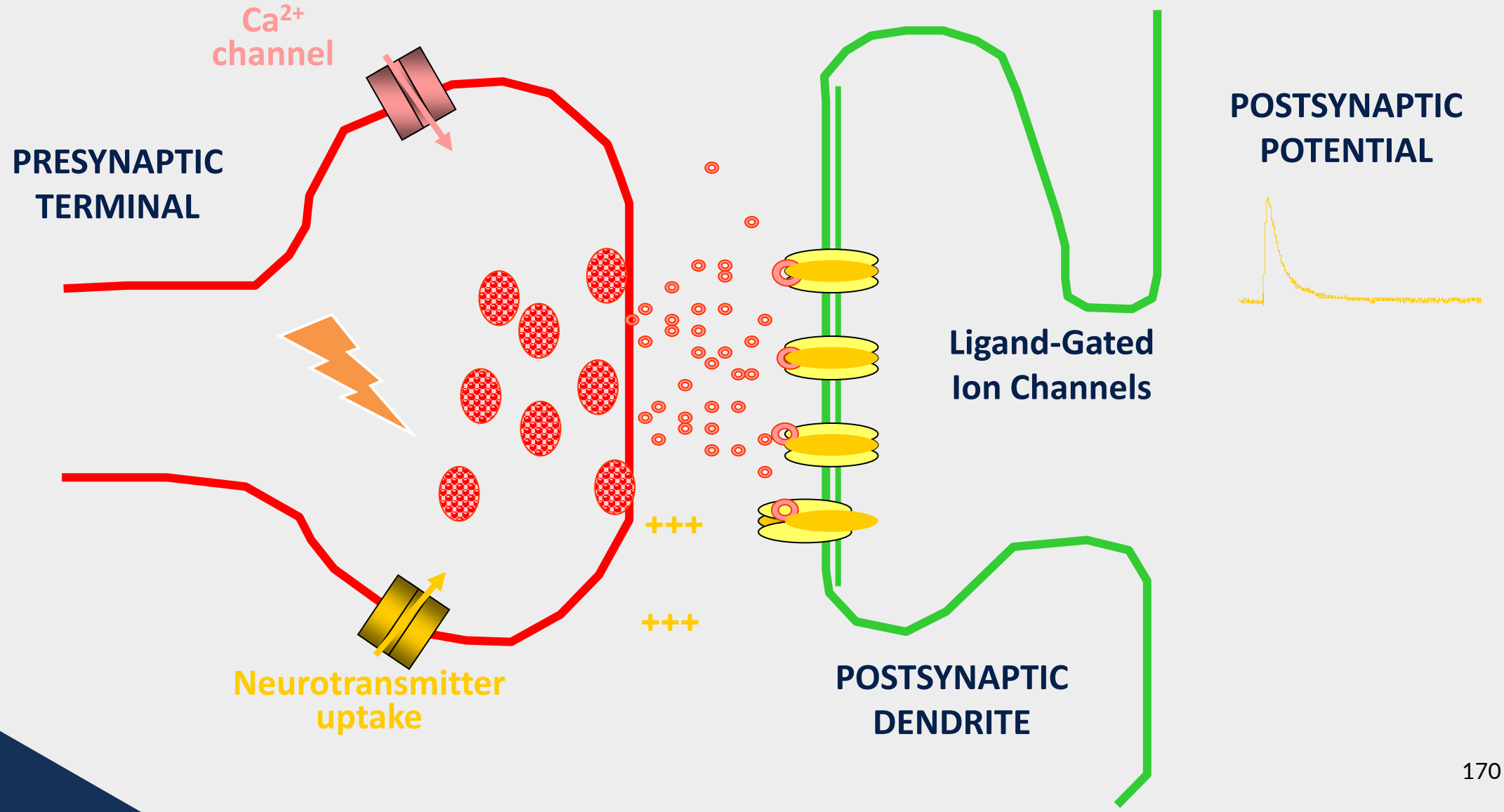
Soyka, N Engl J Med 2017; 376:1147-1157

Neurobiology (GABAA Receptor)

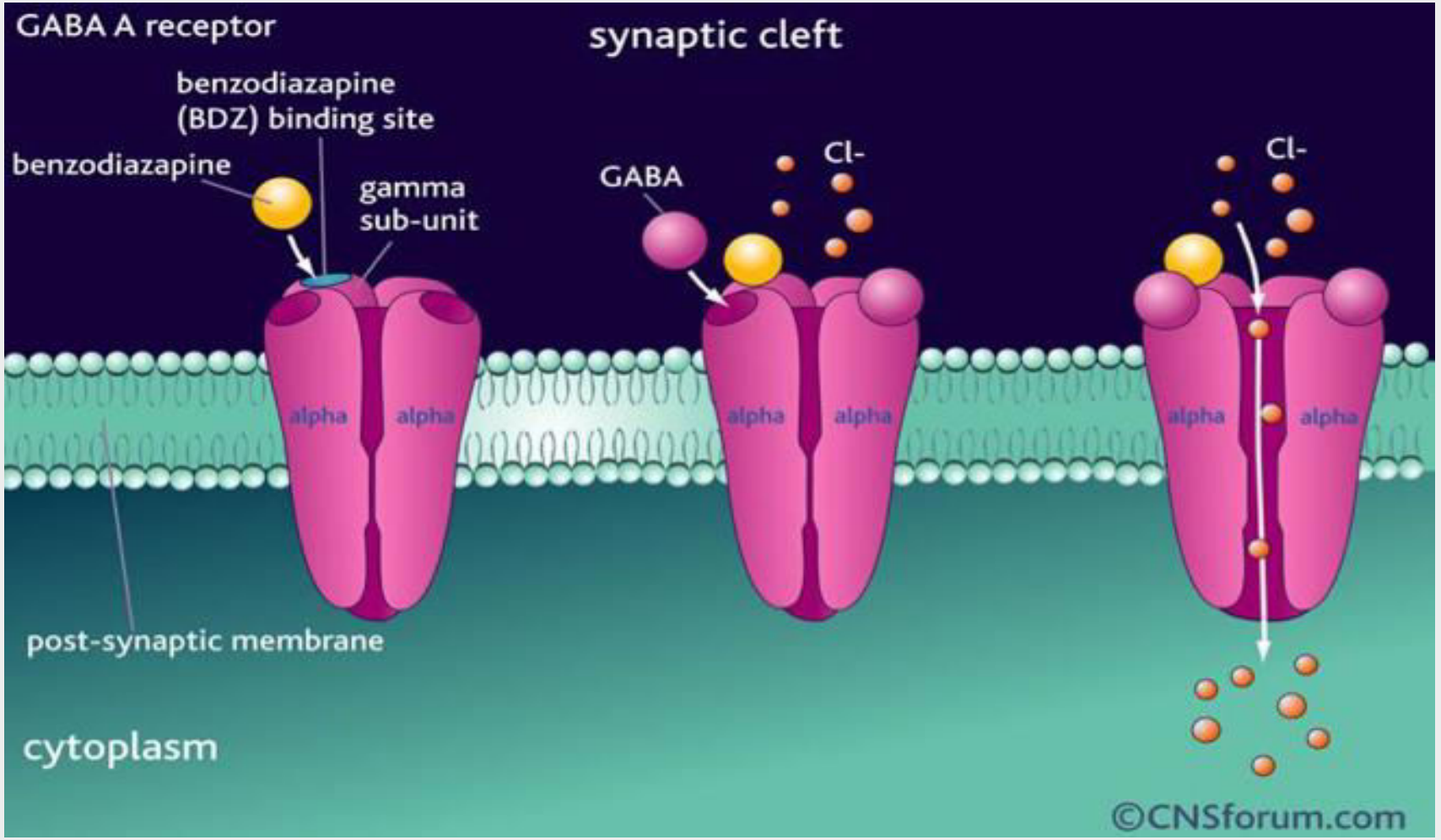
- Benzodiazepines
  - Bind a cleft of α and γ subunits
  - Increase the affinity of the receptor for GABA (frequency) : Chloride channel opening
  - BZD needs GABA

- Barbiturates (propofol):
  - Bind α subunit
  - Increase duration of channel opening
  - BBT does need GABA

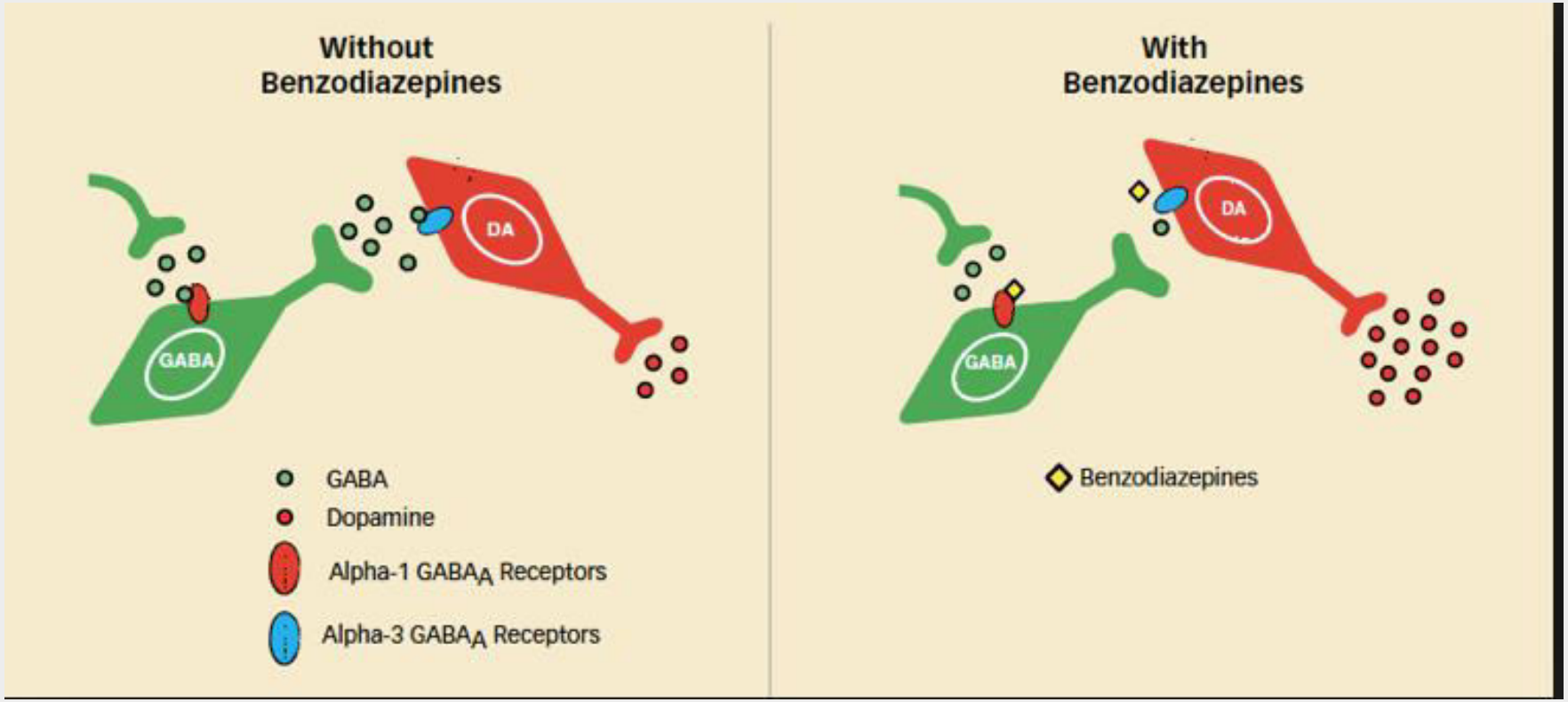
Steps in Synaptic Transmission



Neurobiology ($GABA_A$ Receptor)



Mechanism of Benzodiazepine Addiction (hypothesis)



NIDA NOTES APRIL 19, 2012

Epidemiology

- 80% of pts with benzo use disorder use other drugs
- 30-50% of pts with ETOH use disorders in detox and 44% of IV drug user also use BZD
- Average benzodiazepine use is about 2 :: 1

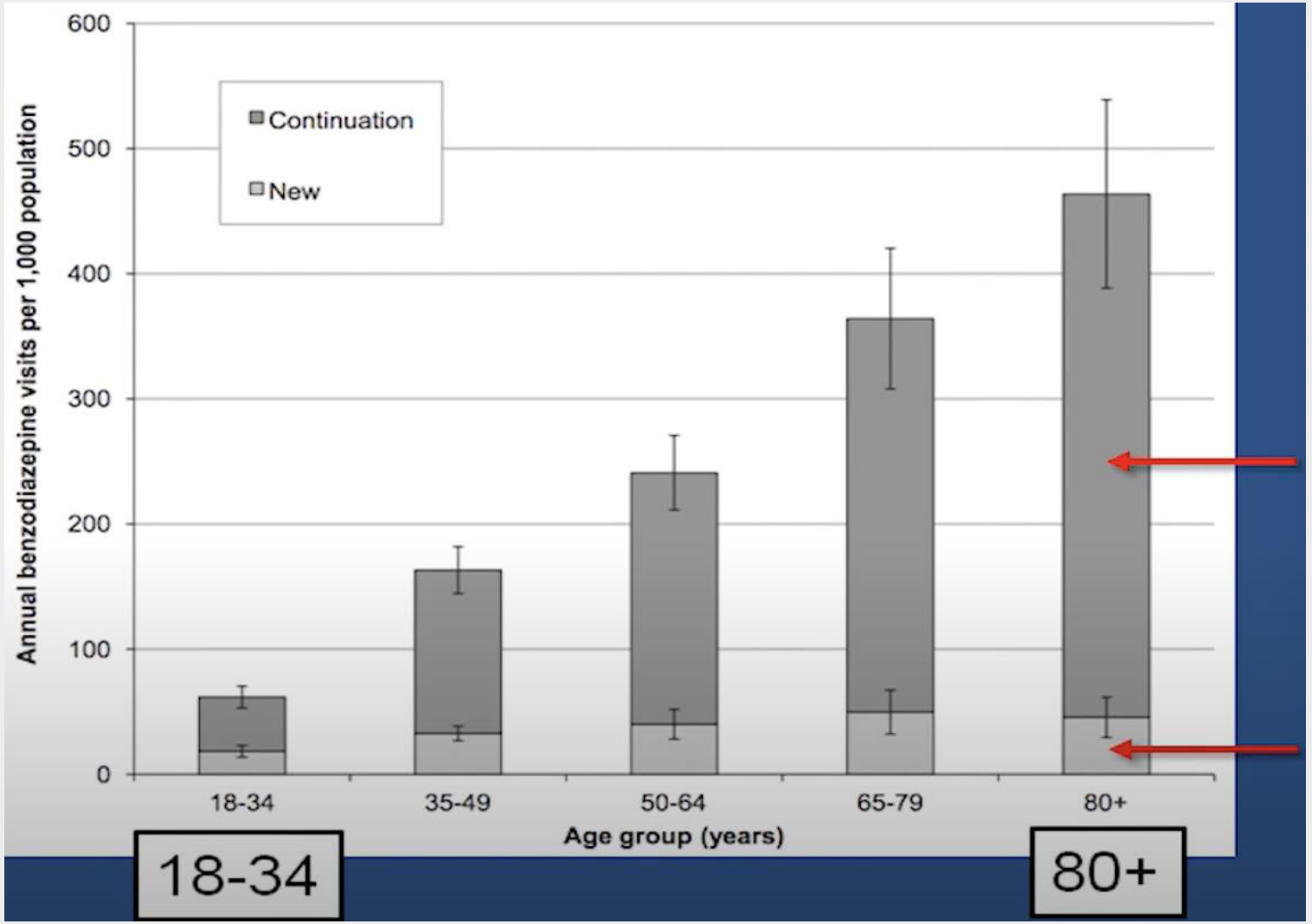


- Approximately 9.1 % of adults in U.S use benzos in the past year (NSDUH 2023)
- Use of benzodiazepines increases with age
- In the US, roughly 9 of 10 older adults who use benzodiazepines on a long-term basis are prescribed by PCP

Epidemiology

Use of Benzodiazepine accumulates with age

Annual BZD visits per 1,000 population



Continuation

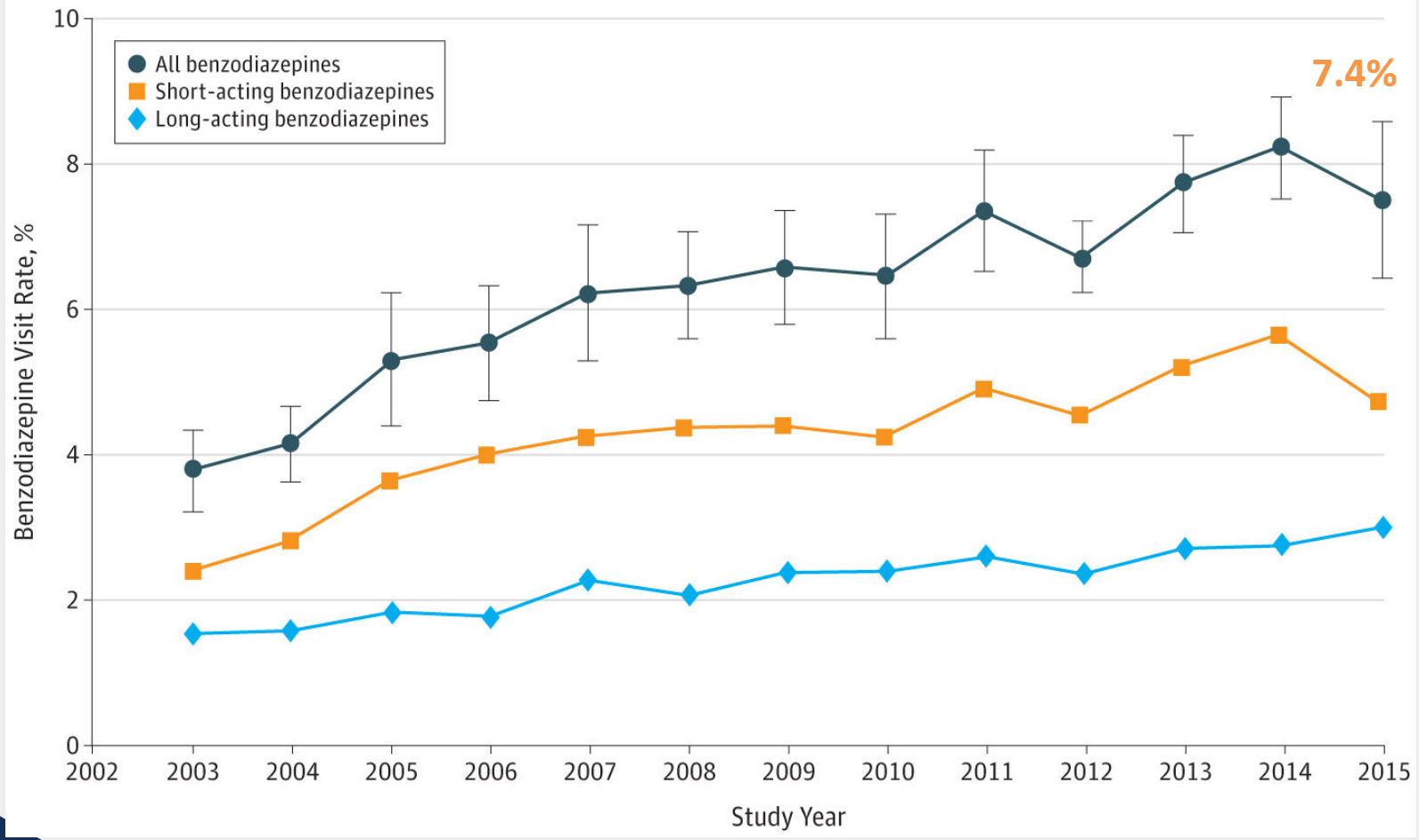
New

Age

Maus et al. JAGS 2016

Epidemiology

Benzodiazepine Visit Rate in United States



95% increase in BZD-related visits in 12 years

Benzo visit Rate %

Year

Agarwal SD, Landon BE. JAMA Netw Open. 2019 Jan 4;2(1)

Concurrent use of other Substances

- Rarely the initial or primary substance of abuse
- Rarely used alone to produced intoxication
- Usually abuse with other substances
- Healthy patients prefer placebo to benzodiazepines

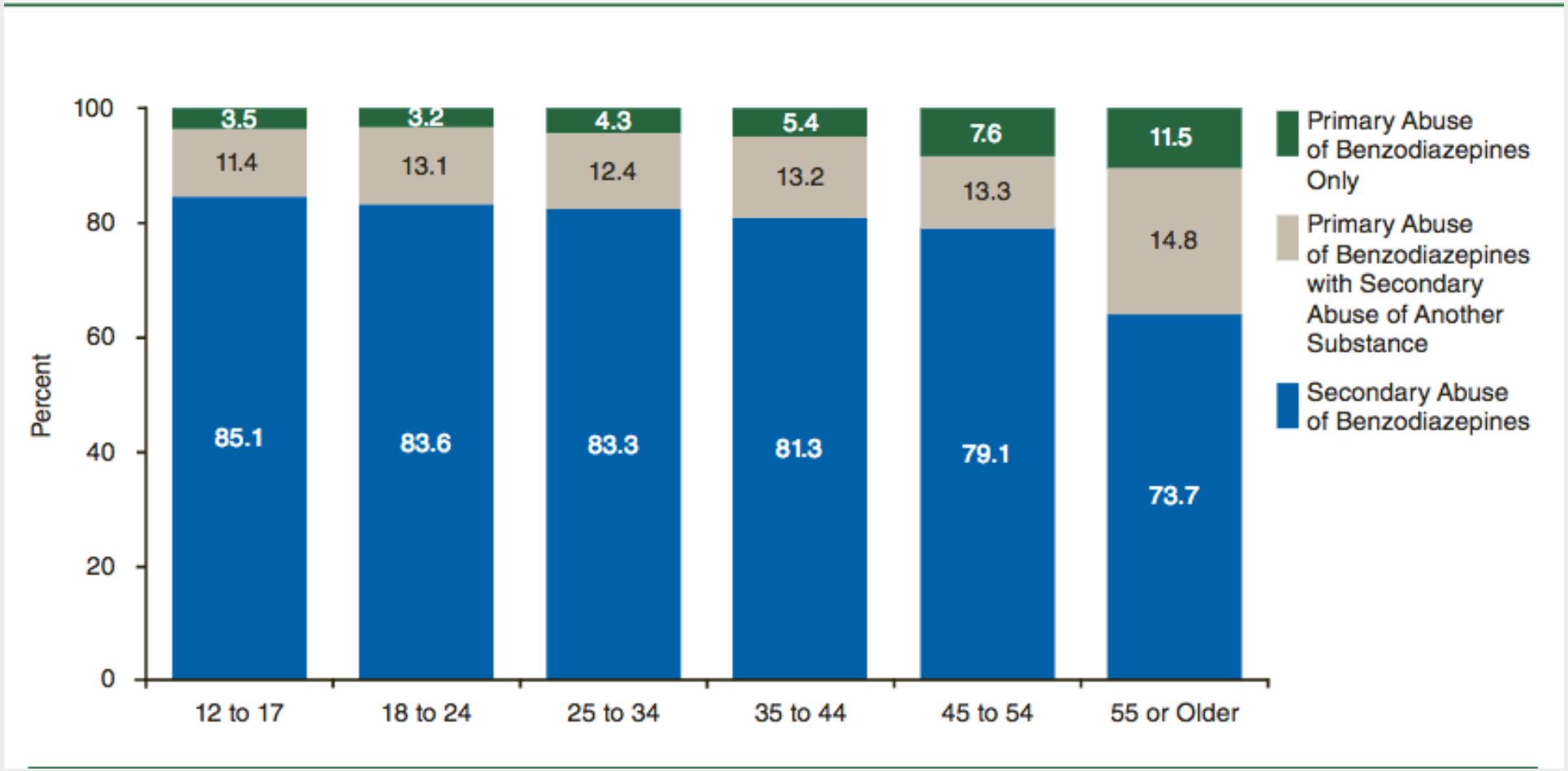
- *ETOH use disorder patients and their offspring are more likely to experience mood elevation with benzodiazepines*

Concurrent use of other Substances

- A high percentage of alcohol dependent patients use benzodiazepines regularly (29-76%)
- 70-96% of patients admitted to inpatient addiction treatment on high dose benzodiazepine use have concurrent dependence on other substances
- It is uncommon to see patients with substance use disorder just on benzodiazepines. Concurrent use with other drugs is common just with benzodiazepine use
- BNZD are prescribed in 1 out of 5 patients on opioids
- Lethality when sedatives-hypnotics are combined with:
  - ETOH + BNZ
  - methadone + BNZ
  - buprenorphine + BNZ
  - Other CNS depressants + BNZ

Epidemiology

Primary and Secondary Benzodiazepine Admissions, by Age in 2008



Note: Percentages may not sum to 100% due to rounding

Source: SAMHSA Treatment Episode Data Set (TEDS) 2008

Benzodiazepines + Opioids

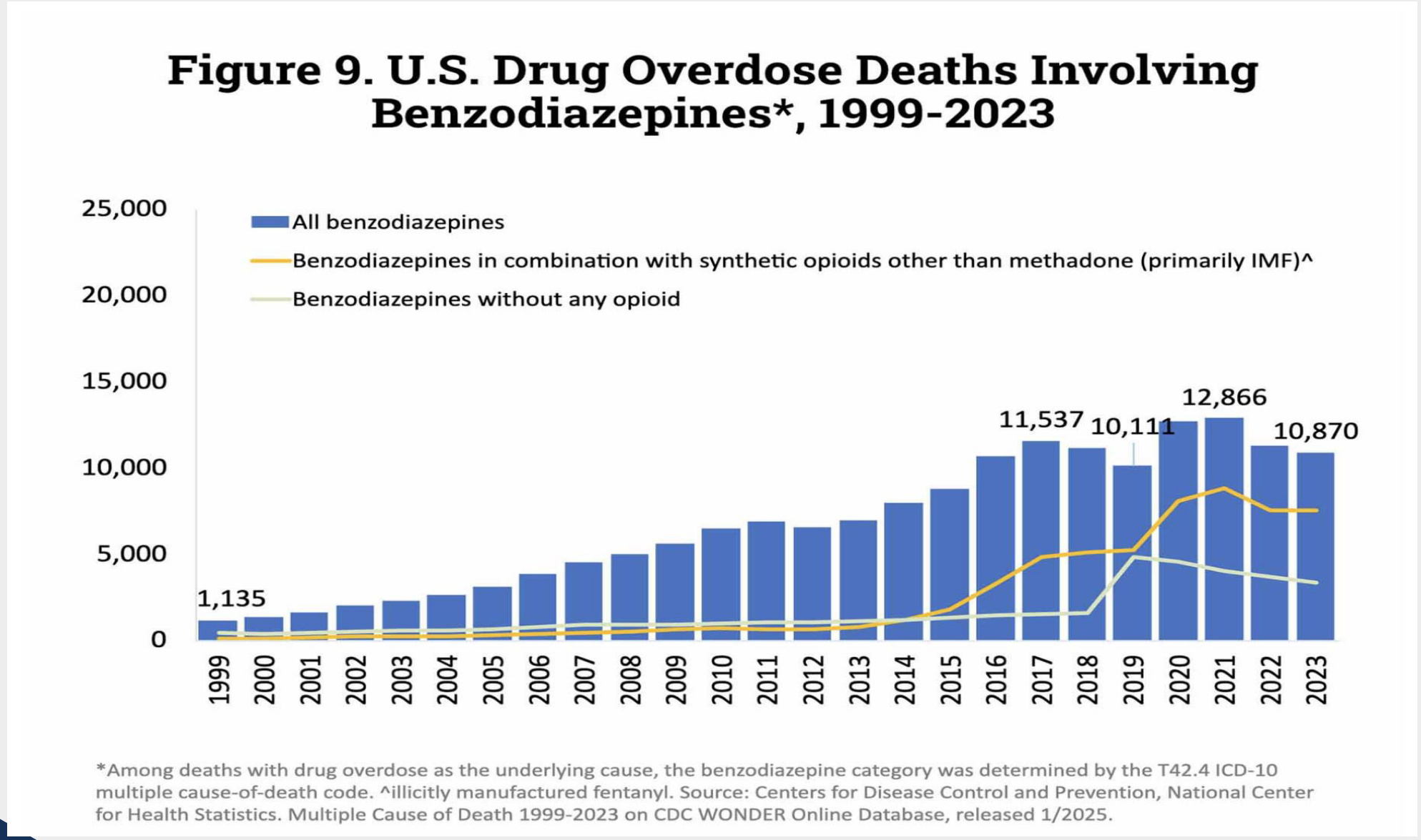
- Benzodiazepines (BZs) are the most frequently cited co-intoxicants involved in opioid-related morbidity and mortality.

- In 2010, the CDC reported 16,651 pharmaceutical opioid-related overdose deaths based on death certificate data- almost one of every three opioid-related deaths in 2010 also involved BZs

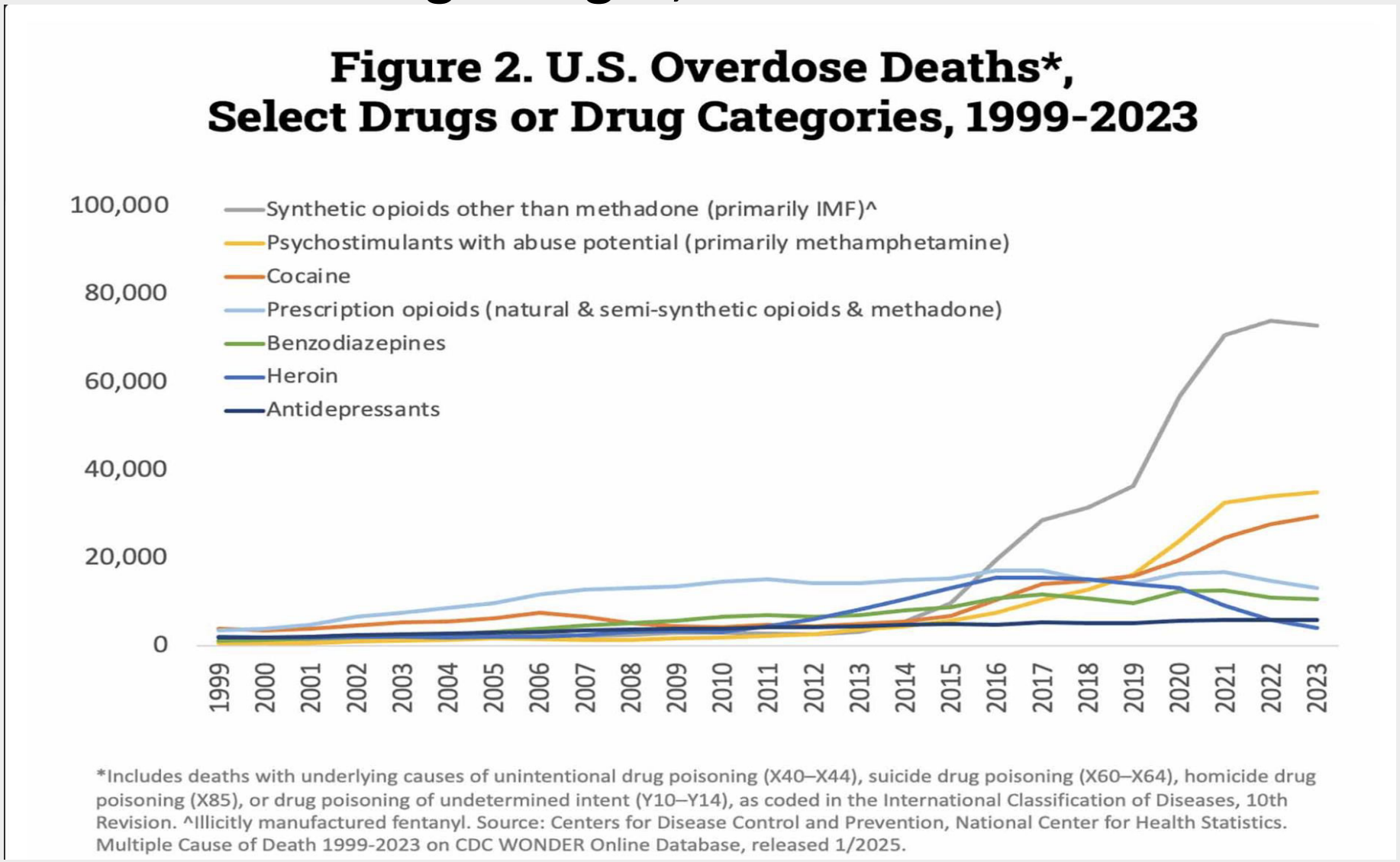
- On August 31, 2016, FDA issued a drug-safety communication about risks when opioid pain or cough meds are combined with BZs.

(Hwang et al., 2016; Jones, Mack & Paulozzi, 2013; DEA 2013)

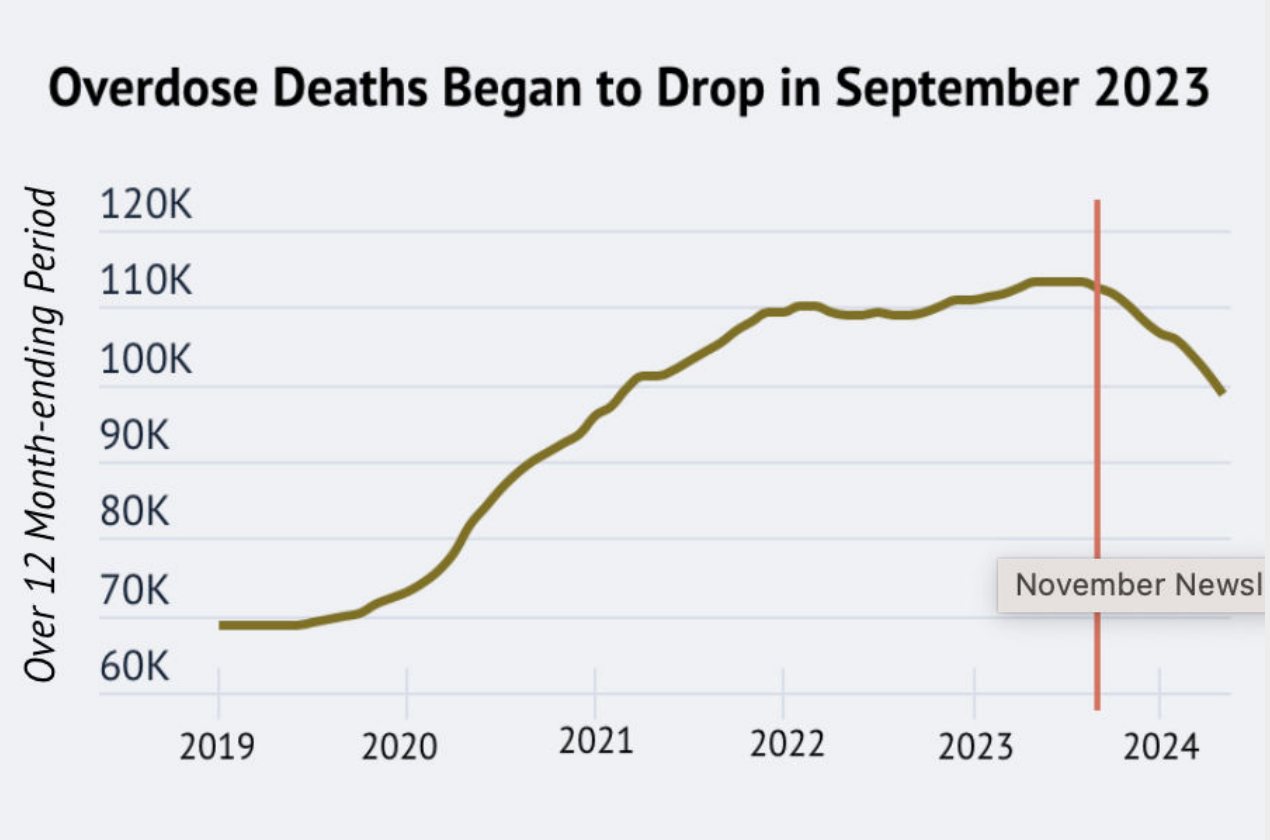
BZDs, by Opioid Involvement, Number among All Ages, 1999-2022



National Drug Overdose Involving Overdose Deaths, Number Among All ages, 1999-2023



Overdose Death Began to Drop



Potential Drivers of the Decrease Include:

- More naloxone availability
- Greater access to addiction treatment
- Crackdowns on illicitly manufactured fentanyl
- Less solitary use post-pandemic

Sources: Ahmad FB, Cisewski JA, Rossen LM, Sutton P. National Center for Health Statistics. Provisional drug overdose death counts. (October 2024).; Ovalle D. The Washington Post. Overdose deaths decline sharply after years of fentanyl-fueled surges. (October 2024).; NIHCM Foundation.

ED Visits: Risk of Serious Outcomes

	12-34 yo	35-44 yo	45-64 yo	65+
BZD alone	28%	30%	37%	39%
BZD + opioids	37%	43%	47%	59%
BZD + alcohol	35%	43%	51%	55%
BZD + opioids + alcohol	39%	47%	57%	70%

SAMHSA, DAWN Report, 12/18/2014

Epidemiology

- Most frequent abused pharmaceutical second only to opioids
- Alprazolam is the most frequently abused followed by Clonazepam, Lorazepam, and Diazepam
- BZDs are prescribed at about 65.9 million office-based doctor visits. That's a rate of 27 annual visits per 100 adults

National Health Statistics Report that examined data from the 2014-2016 National Ambulatory Medical Care Survey (NAMCS) 2020.

Prevalence of Benzodiazepine Use

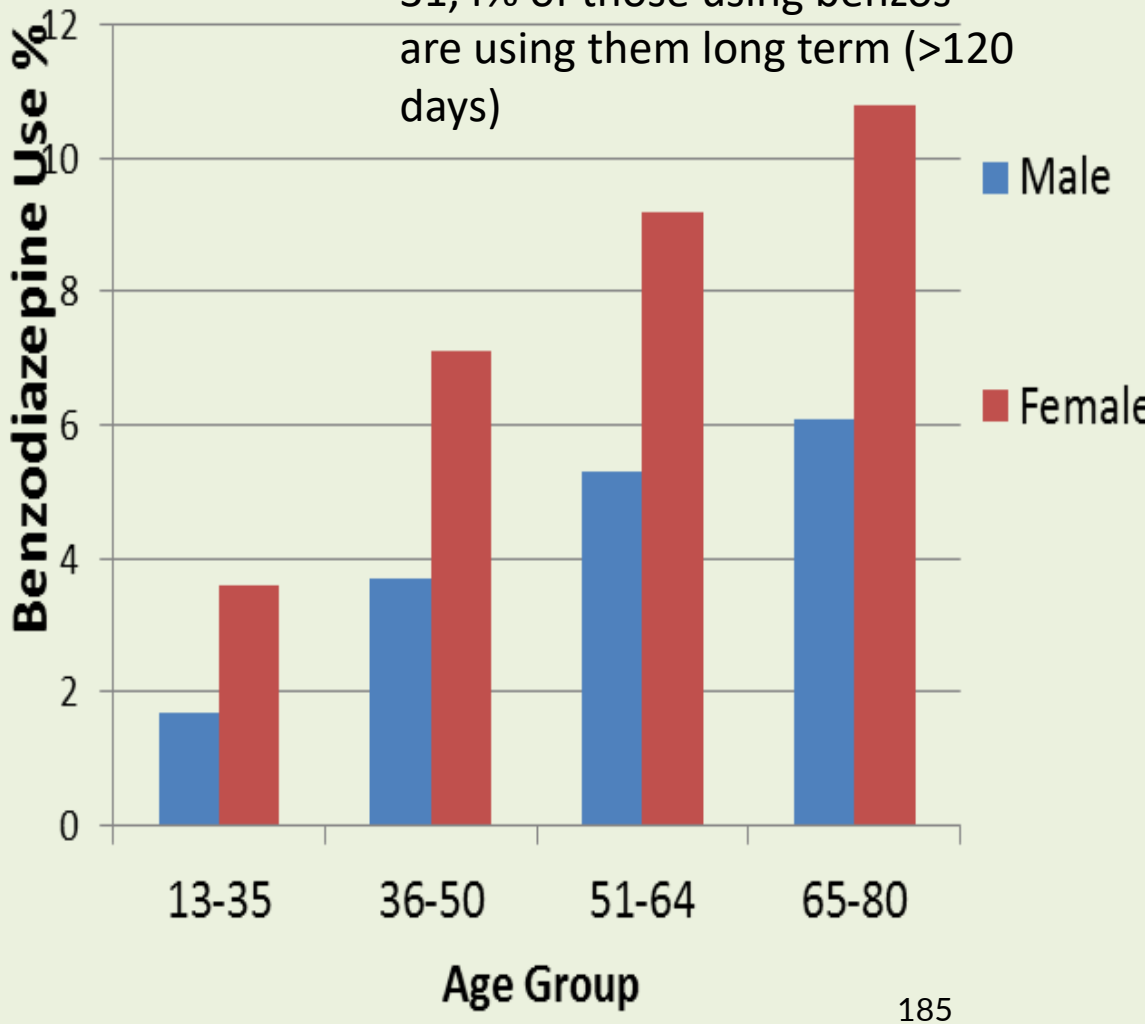
Benzodiazepines:

- Use is nearly twice as prevalent in women
- Increased utilization with increasing age
- Proportion of long-term use increases with age
- Prescribed at greater rates than antidepressants for the treatment of depression and anxiety

Bernardy NC, et al. J Gen Intern Med, 2013. 28(S2): p S542-8; Demyttenaere, K., et al.,. J Affect Disord, 2008. ***110****(1-2): p. 84-93.; Benitez, C.I., et al., Am J Geriatr Psychiatry, 2008.* ***16****(1): p. 5-13.; Maudsley Prescribing Guidelines in Psychiatry 12th Edition. 2015*

Figure 1. Prevalence of benzodiazepine use in the United States

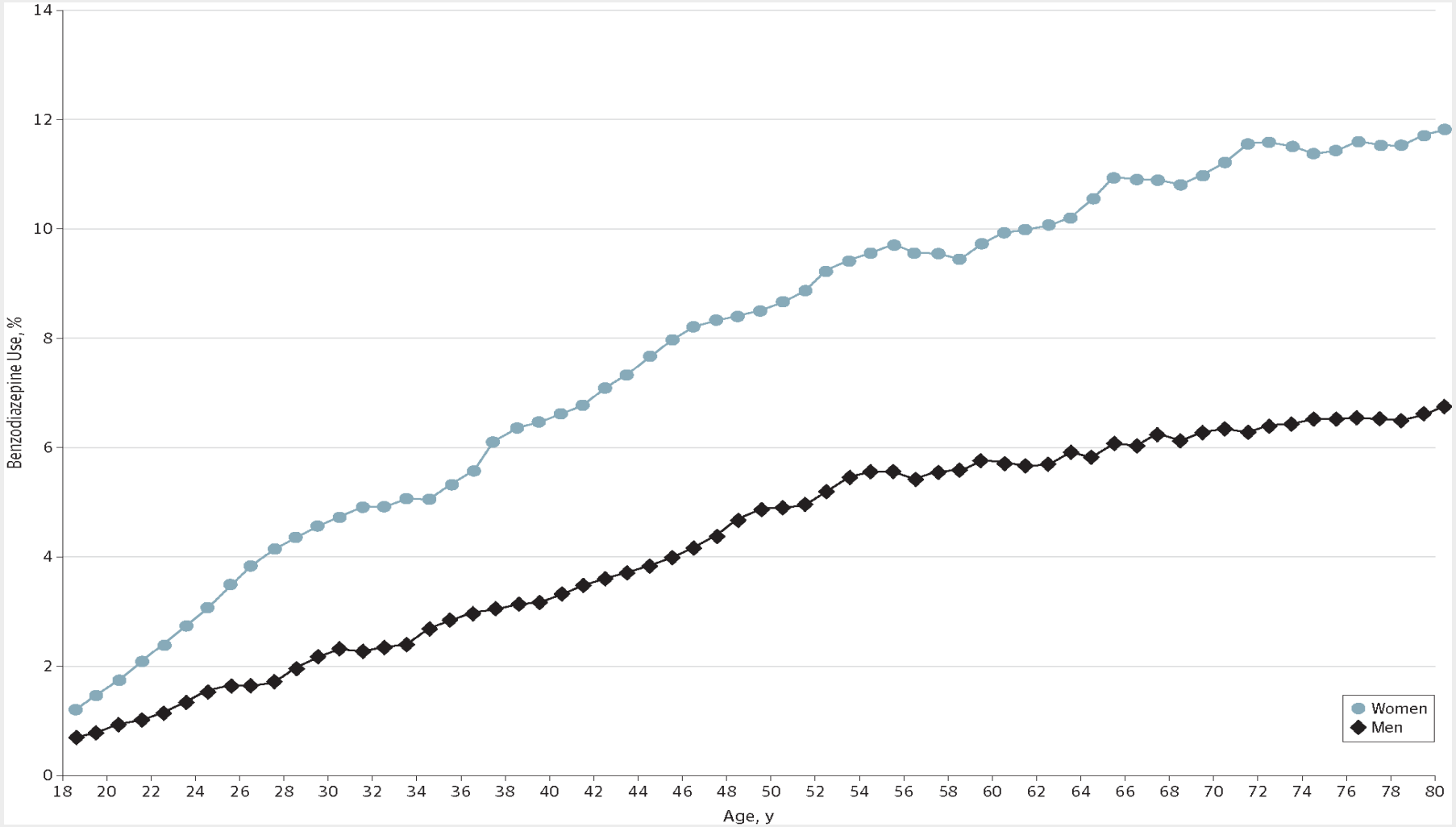
In the oldest group (65-80)- 31,4% of those using benzos are using them long term (>120 days)



Olfson M, et al. JAMA Psychiatry, 2015. ***72****(2): p. 136-42*

Epidemiology

BZD Use %



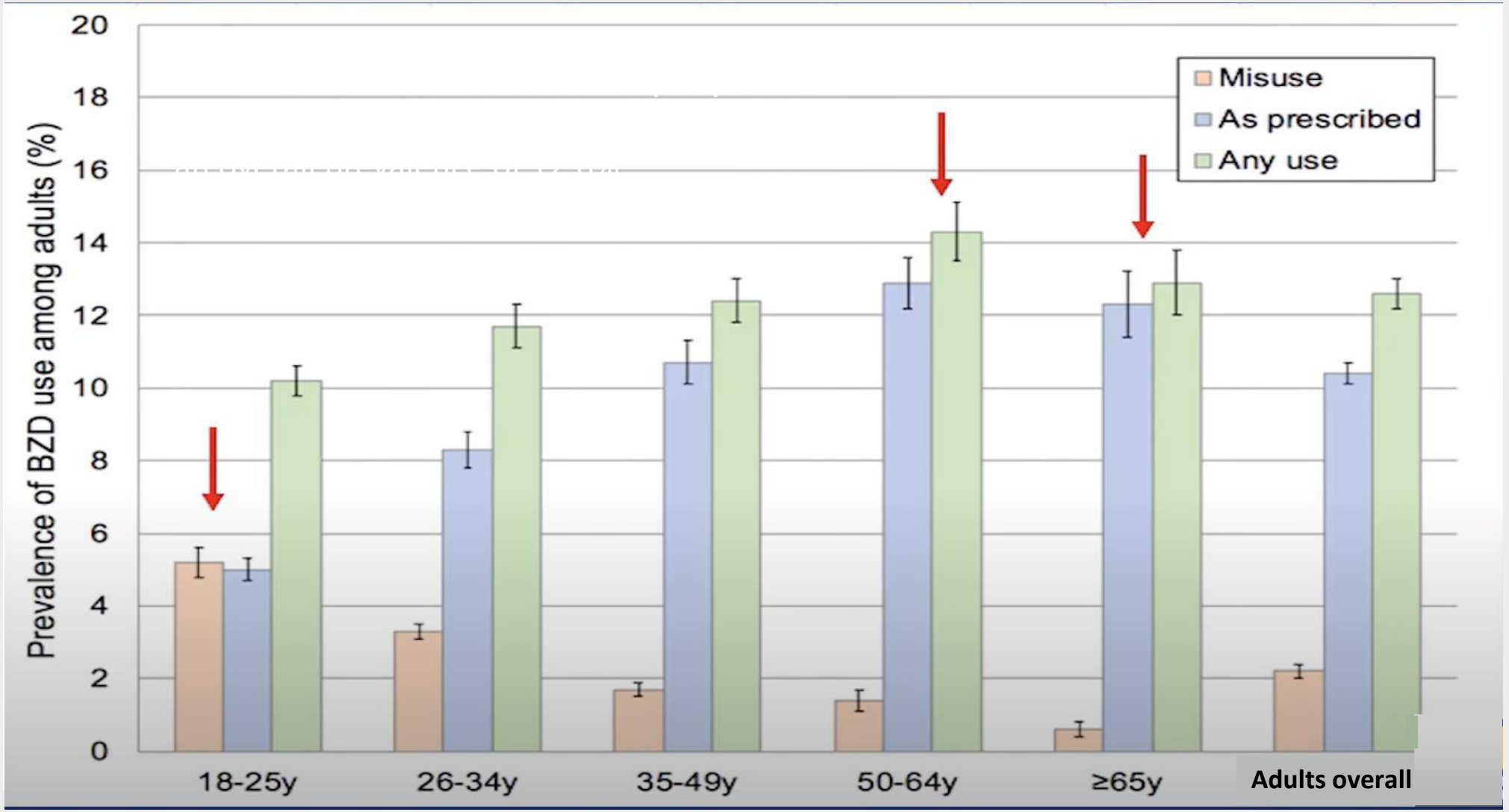
12% women

7% men

18 Age 80

Olfson M, et al. JAMA Psychiatry 2015;72(2):136-142.

BZD use accumulates with age



Prevalence of prescription benzodiazepine use and misuse among 2015 and 2016 NSDUH respondents ***(N=86,186),*** *by age group*

[a]NSDUH, National Survey on Drug Use and Health

Maust DT, Lin LA, Blow FC. Benzodiazepine Use and Misuse Among Adults in the United States. Psychiatr Serv. 2019;70(2):97-106. doi:10.1176/appi.ps.201800321

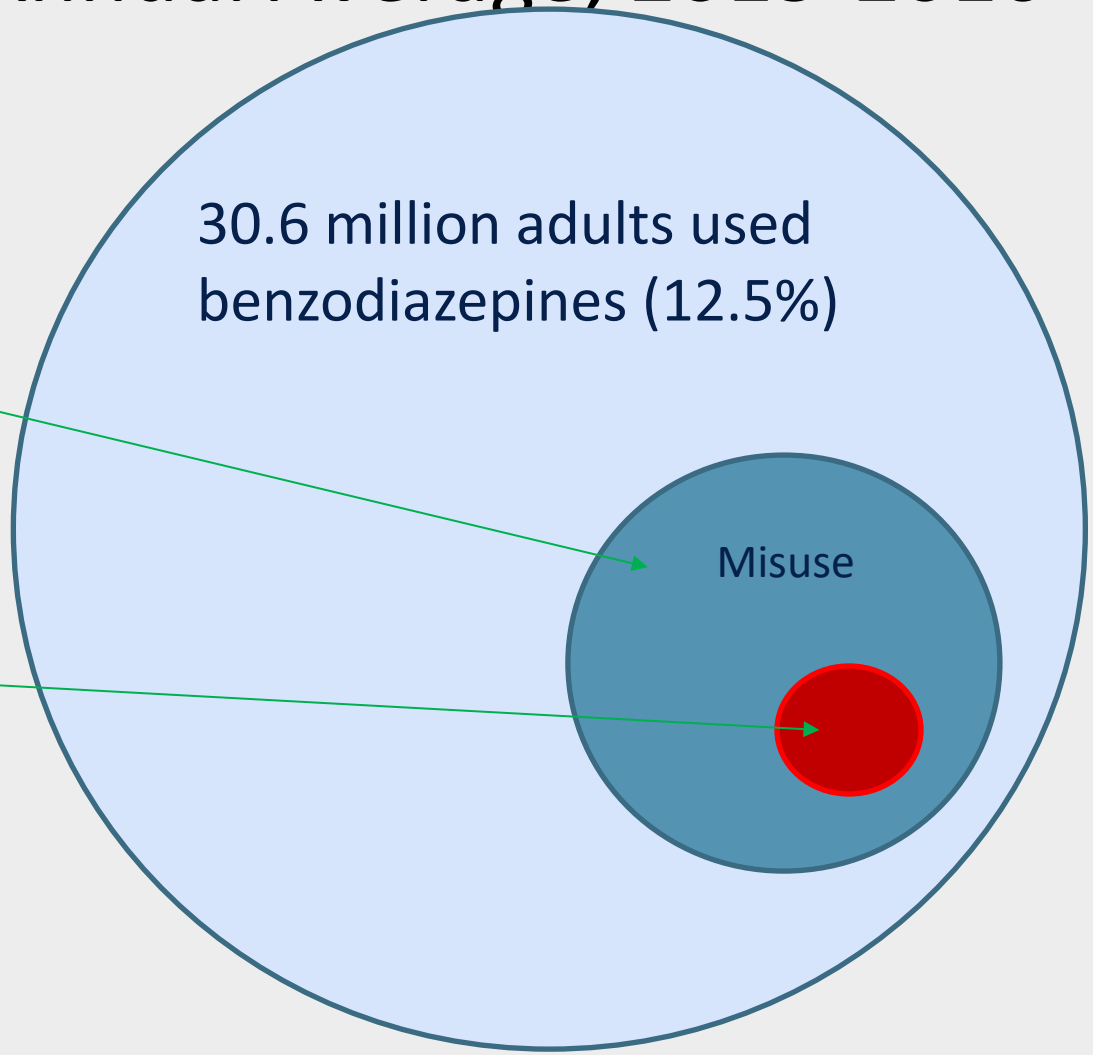
Benzodiazepine Use, Misuse, and Use Disorder Among Adults in the United States: Annual Average, 2015-2016

National Surveys on Drug Use and Health

5.3 million adults misused benzodiazepines (2.1%)

0.5 million adults had benzodiazepine use disorders (0.2%):

- 0.3 million had benzodiazepine dependence
- 0.2 million had benzodiazepine abuse



Maust DT et al, Benzodiazepine Use and Misuse Among Adults in the United States. Psychiatr Serv. 2019 Feb 1;70(2):97-106

Case: RR

- Mr. RR did not receive his alprazolam refill from his PCP because, after taper, patient returned to his original dose and ran out of the prescription sooner. Mr. RR is upset and decided to see a psychiatrist who had planned to prescribe medication if ROI to contact PCP is signed.



Case: RR

- Mr. RR reports that his heart has been racing and his insomnia has worsened; his friend states that, for the past four days, he has been having difficulty following conversations and focusing on daily tasks. He has been off alprazolam for seven days. Mr. RR denies any recent psychosocial stressors and does not endorse feelings of guilt, helplessness, or hopelessness. Furthermore, he denies any fever, nausea, vomiting, diarrhea, myalgia, abdominal cramps, or seizures. He denies any recent alcohol or illicit drug use.



Factors associated with prescribing benzos

- Anxiety
- Insomnia
- Pain
- Chronic Medical Condition
- Female
- White
- Retirement Low income
- Elderly
- Smoking
- Poor Health
- >1 Prescriber
- Computer prescribing

Agarwal SD, Landon BE. JAMA Netw Open. 2019 Jan 4;2(1)

Benzodiazepines and Addiction

Benzodiazepines are often not the primary substance abused and, when combined with other substances (e.g. alcohol, opioids), can have fatal consequences

- 5-10% - Patients newly started on benzodiazepines develop a substance use disorder
- 50% - Patients with substance use disorder history will develop a benzodiazepine use disorder
- 58-100% - Patients prescribed chronic benzodiazepines become physically dependent

Guina, J., et al., J Psychiatr Pract, 2015. 21(4): p. 281-303.; Substance Abuse: A Comprehensive Textbook (4th ed.). Baltimore. MD: Lippincott. Williams & Wilkins. 2004. pp. 302-312.; Substance Abuse and Mental Health Services Administration. The TEDS Report: Substance Abuse Treatment Admissions for Abuse of Benzodiazepines. . Rockville, MD., June 2, 2011.

Benzodiazepine Prescribing

- Patients associated with benzo long term-use:
  - Psychiatric co-morbidity
  - Less education
  - Loneliness/isolation
  - Avoidant coping behaviors
  - Older age (women, less education, low SES, chronic disease, functional limitations, cognitive impairment, anxiety, depression, insomnia)

Zandstra 2004; Sonnenberg 2022

Benefits and Risks

- Population
  - Therapeutic dose dependent
  - Prescribed high-dose dependent (sedative use disorder)
  - Recreational benzodiazepine use
- Risk factors for benzo use disorder:
  - Longer duration of BNZ use
  - Higher Benzodiazepine doses
  - Lower level of education
  - Greater insomnia severity
  - Current antidepressant use

Benefits and Risks

ACTION		CLINICAL USE
Anxiolytic	Relief of anxiety	Anxiety and panic disorders, phobias
		Agitated Psychosis
Hypnotic	Promotion of sleep	Insomnia
Myorelaxant	Muscle relaxation	Muscle spasms, spastic disorders
Anticonvulsant	Stop fits, convulsions	Fits to drug poisoning, some form of epilepsy, alcohol withdrawal
Amnesia	Impairment of short-term memory	Premedication for operations, sedation for minor surgical operations

Benefits and Risks
–prior prescribing benzodiazepines-

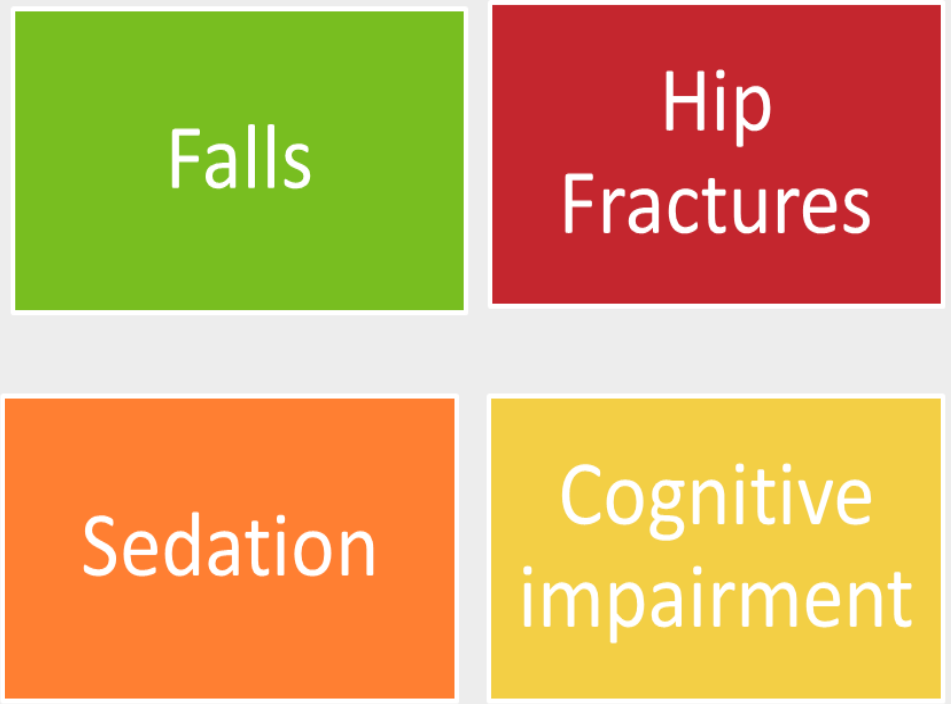
TOLERANCE and DOSE ESCALATION = WITHDRAWAL

- Examine the risk-benefit ratio
- Avoid nonbenzodiazepine hypnotic
- Short term use (4 weeks) is recommended

Royal College of Psychiatrists and The British Association for Psychopharmacology 2013

Benefits and Risks (concerns)

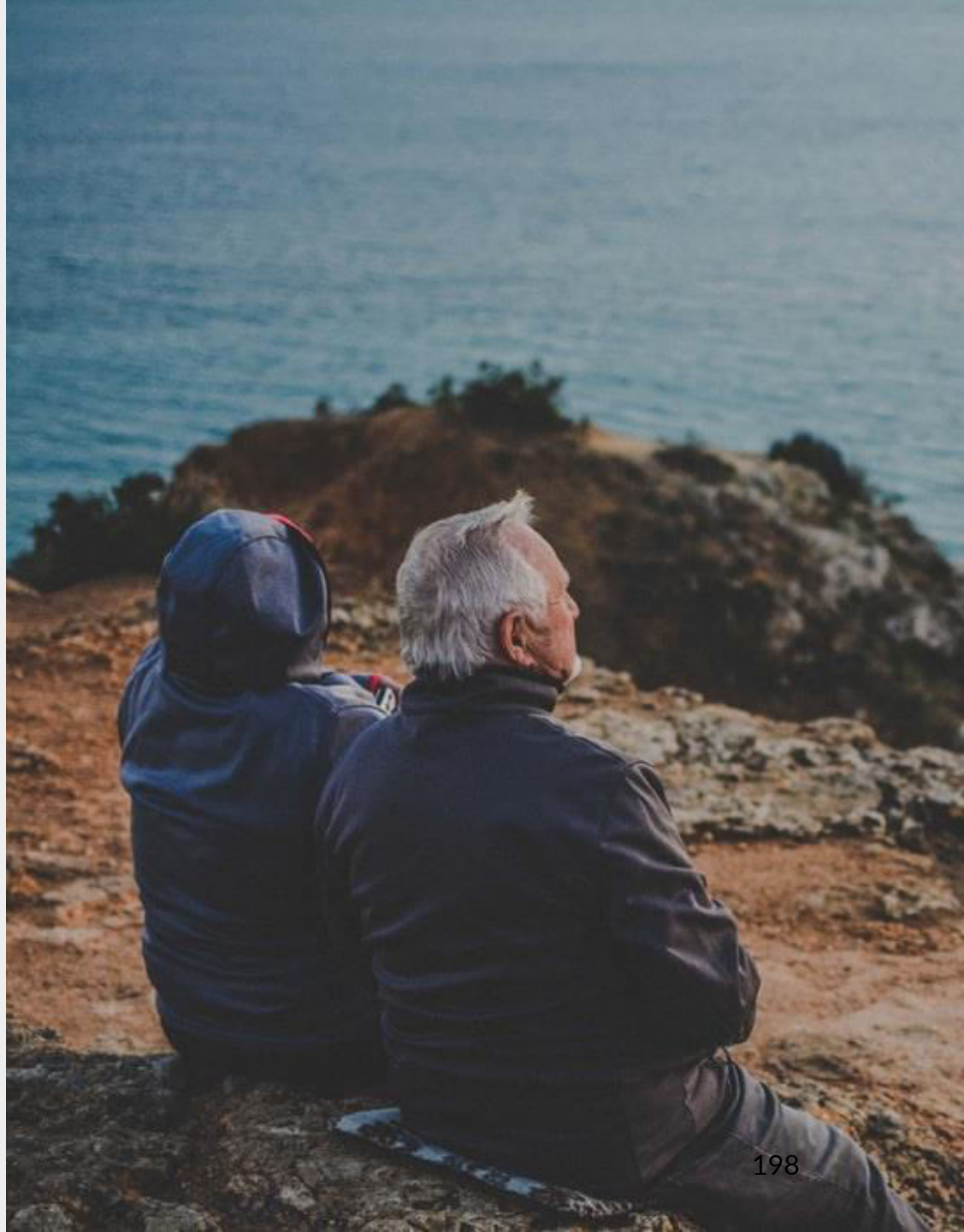
- Long term use have shown deficits in: learning, memory, attention and visual spatial ability
- Anterograde Amnesia
- Adverse effects:
  - May contribute to psychomotor impairment and increase the risk of falls and automobile accidents
  - Psychomotor impairment is characterized by:
  - - Slow reaction time
  - - Diminish speed and accuracy for motor tasks
- Increase risk of hip fractures (50% increase risk) and recurrent falls in the elderly population
- OD with Benzodiazepine alone are almost never lethal (high therapeutic index) but OD with BBT alone can be
- Withdrawal symptoms prolong sedative overuse



Cumming et al. Benzodiazepines and Risk of Hip Fractures in Older People. CNS Drugs17,2003

Benefits and Risks (concerns)

- The 2015 American Geriatrics Society Beers Criteria recommend avoiding benzodiazepines in this population. Despite these consensus recommendations and known risk factors:
  - Benzodiazepine use is three times more prevalent in older adults compared to younger adults
  - Roughly one-quarter of long-term benzodiazepine use is in patients ≥65 years of age



Considerations when prescribing BZs

- Examine the risk-benefit ratio
- Avoid nonbenzodiazepine hypnotic (Alternative)
- Inform patient of planned duration of therapy
- Prescribe for brief periods
- No refills without follow up
- Use random urine toxicology
- Attempt to taper dose
- Always check the Prescription Drug Monitoring Program (PDMP) before and during the treatment
- Formalize written treatment agreement

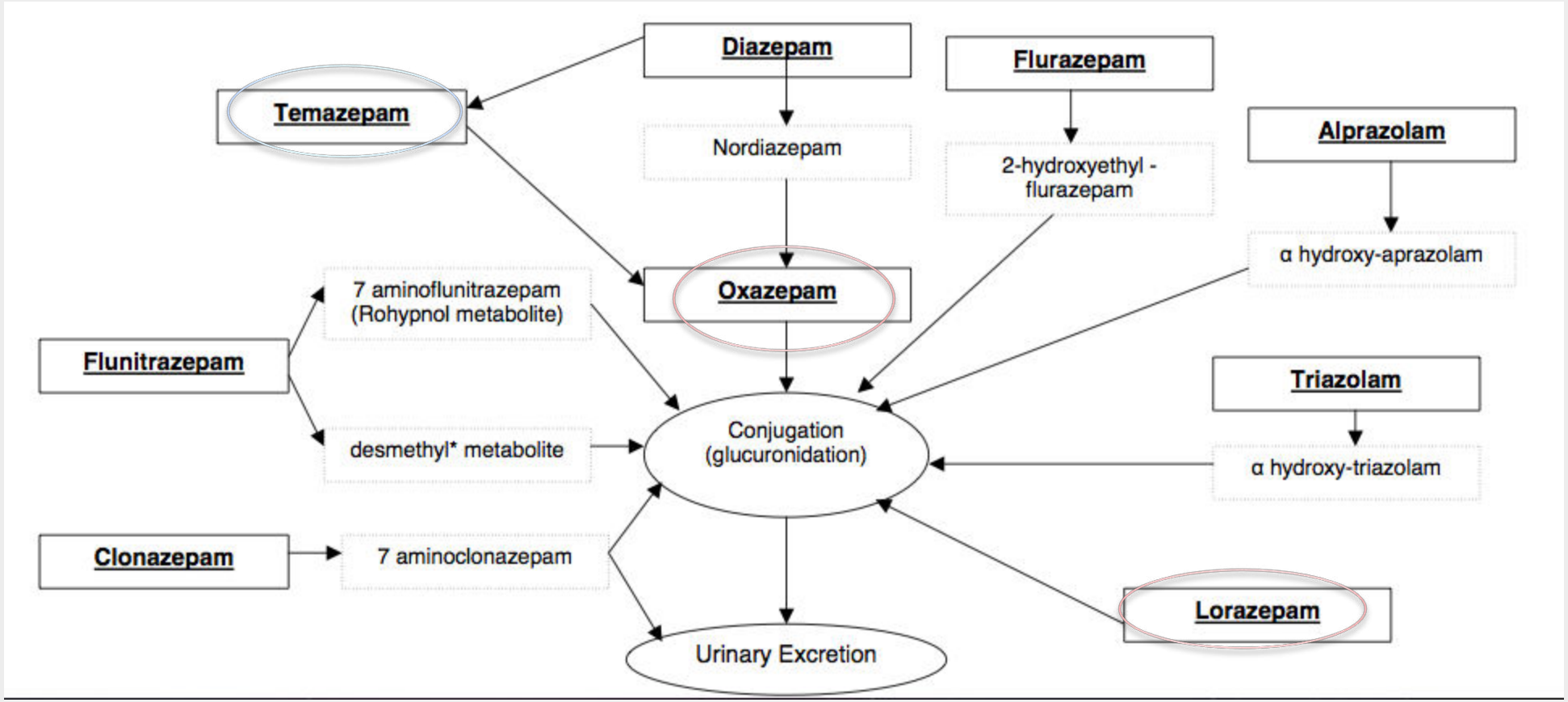
Phases of Sedative-Hypnotic Treatment and Related Syndromes



Equivalent Doses and Elimination half-lives of benzodiazepines

BENZODIAZEPINES	APPROXIMATELY EQUIVALENT DOSAGE (mg)	ELIMINATION HALF-LIFE (hrs)- (active metabolite)
Alprazolam *	0.5	6-12
Chlordiazepoxide	25	5-30 (36-200)
Clonazepam*	0.5	18-50
Diazepam	10	20-100 (36-200)
Flunitrazepam	1	18-26 (36-200)
Flurazepam	15-30	(40-250)
Lorazepam*	1	10-20
Oxazepam	20	4-15
Temazepam	20	8-22
Triazolam*	0.5	2

Benzodiazepine Metabolism



Types of Benzodiazepines

- 2-Keto benzodiazepines (Clonazepam, Diazepam, Chlordiazepoxide)
  - All have long half-lives (23-100 hours)
  - All have active metabolites (commonly desmethyldiazepam)
  - Some administered as Prodrug

- 3-Hydroxy Benzodiazepines (Oxazepam, Temazepam, Lorazepam)
  - Intermediate half-lives (most 10-15 hours)
  - No active metabolites (better in elderly/hepatic impaired)
  - Metabolized outside the liver (only need glucoronidation)

- Triazolo Benzodiazepines (Alprazolam, Triazolam)
  - Short to Intermediate half lives (anywhere from <12 hours)
  - Some have active metabolites

Pharmacokinetics

BZDs are differentiated by their pharmacokinetic profiles, based on lipophilicity and metabolism:

- Half-life (short, intermediate, long)
- Onset-of-action (rapid, intermediate, slow)
- Metabolic pathways (with or without active metabolites, with or without P450 involvement)
- Pharmacokinetics are affected by:
  - Routes of administration
  - Rates of absorption
  - Rates of elimination

Clinical Pharmacology 2017

Pharmacokinetics

LONG ACTING

- Chlordiazepoxide
- Diazepam
- Clonazepam

MEDIUM ACTING

- Lorazepam
- Oxazepam
- Temazepam

SHORT ACTING

- Alprazolam
- Triazolam
- Midazolam

Case: RR

PE: He was found to be tachycardic (pulse, 110 beats/min) and hypertensive (blood pressure, 170/90 mm Hg). His medical workup, including CBC count, electrolyte panel, liver function tests, blood glucose level, and urine toxicology screen were within normal limits.



Case: RR

MSE: Casually dressed male who appeared to be restless and irritable with twitches in his face and complains about tinnitus. He was oriented to time, place, and person. His speech was normal in rate and content. His mood was subjectively anxious and objectively dysphoric, and his affect was congruent with mood. His thought form was linear and goal directed. There was no evidence of paranoid ideations/delusions. He denied any auditory or visual hallucinations. He scored 30/30 on the Mini-Mental State Examination. He had good insight and judgment. He endorsed passive suicidal ideations, no plan. He denied any homicidal ideations



Management of Benzodiazepine Withdrawal

Variable presentation:

- There are no pathognomonic signs and symptoms of benzodiazepine withdrawal
- Assess for subjective and objective symptoms
- May have few concurrently observable hyper-adrenergic signs or vital sign fluctuations (unlike acute alcohol withdrawal)

Symptoms of anxiety state	Symptoms less common in anxiety states-relatively specific to benzodiazepine withdrawal
Anxiety, panic attacks, agoraphobia	Perceptual distortions, sense of movement
Insomnia, nightmares	Depersonalization, derealization
Depression, dysphoria	Hallucinations (visual, auditory)
Excitability, restlessness	Distortion of body image
Poor memory and concentration	Tingling, numbness, altered sensation
Dizziness, light headedness	Formication (skin “crawling”)
Weakness “jelly legs”	Sensory hypersensitivity (light, sound, taste, smell)
Tremor	Muscle twitches, jerks, fasciculation
Muscle pain, stiffness	Tinnitus
Sweating, night sweats	Psychotic Symptoms
Palpitations	Confusion, delirium
Blurred or double vision	Convulsions

Management of Benzodiazepine Taper

Challenging process for both patients and doctors if you do not have a treatment plan with your patient

Strategies:

- Gradual dosage tapering (avoid prn dosing)
- Psychological Support
- Reasons for prescribing
- Lifestyle
- Personality

Management of Benzodiazepine Taper

- Take into account dosage and type of benzodiazepine
- Environment stresses
- Amount of available support
- Prepare for months or a year for the taper
- Individualize treatment adjusted to patient's needs (personalized treatment)- Partnership with the patient

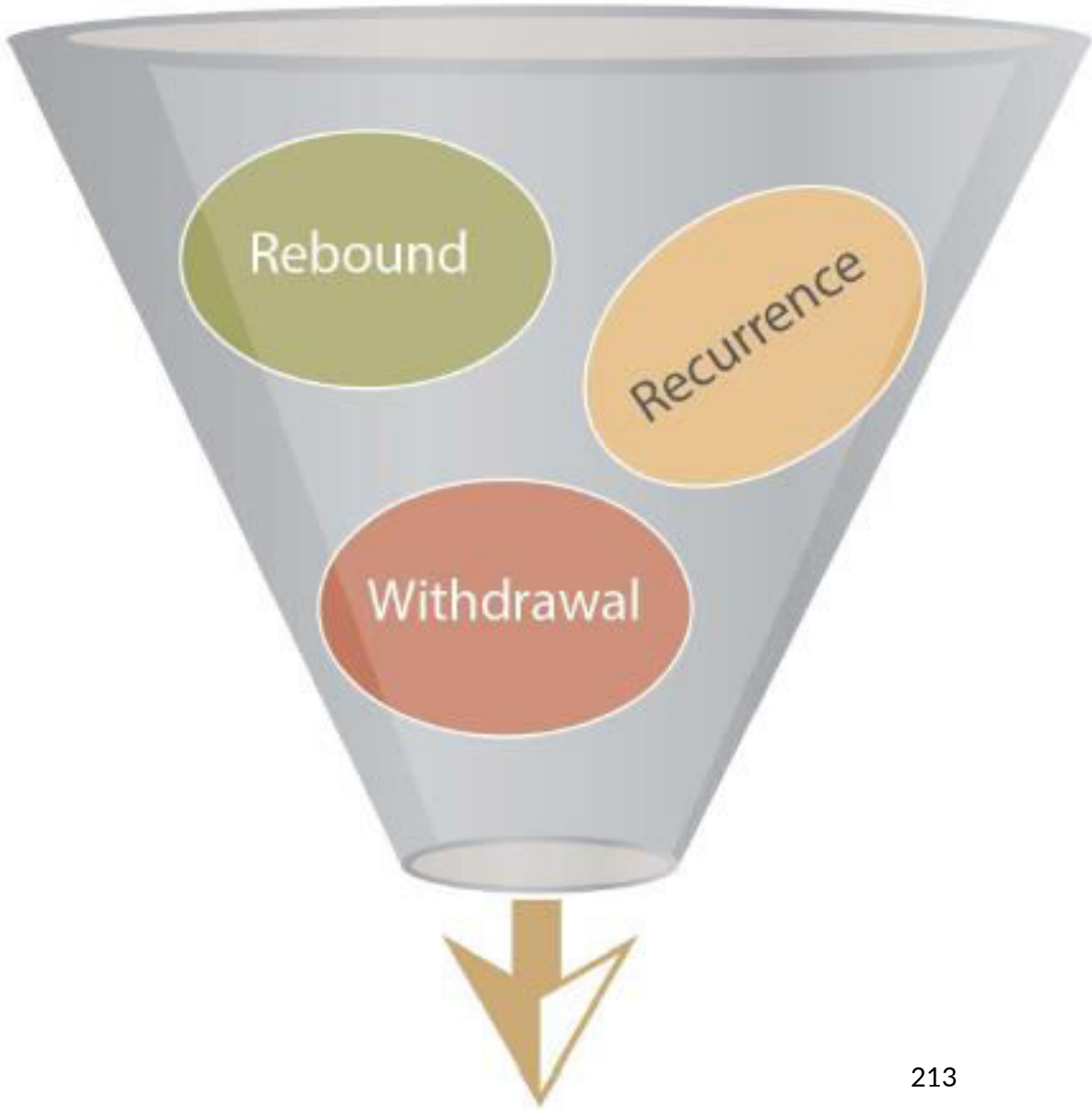
Management of Benzodiazepine Withdrawal /Taper

Time course and severity are influenced by:

- Duration of use: short vs. long term use
- Dose: low/therapeutic dose vs. high dose
- Pharmacokinetics: short vs. long acting
- Host factors: comorbid pathology or substance use disorder

What is the difference between withdrawal, rebound and recurrence?

- Recurrence: the person experiences the same symptoms and severity of symptoms that existed prior to treatment
- Rebound: occurs when a drug is withdrawn and the individual experiences anxiety symptoms that are more severe than those experience prior treatment
- Withdrawal: the time-limited development of unique symptoms as the result of discontinuing or decreasing the use of a psychoactive drug



Management of Benzodiazepine Withdrawal

Time and Severity can vary

- Short Acting BZs and those with active metabolites when stopped, can lead to WD sx within hours
- Long Acting BZs with active metabolites can take 48 hours – 7 days for WD sx to emerge
- Severe WD from BZs can be accompanied by delirium

Management of Benzodiazepine Withdrawal

Duration of use and therapeutic dose:

- >10 days use with therapeutic dose:
  some experience transient insomnia
- <2 weeks with therapeutic dose:
  Most experience rebound
- >2 months with therapeutic dose:
  Most experience mild withdrawal

Of patients who take a benzodiazepine for more than a month, 47% (n=1048) become dependent

De Las Cuevas et al 2003

Management of Benzodiazepine Withdrawal

Duration of use and therapeutic dose:

- >4 to 6 months with therapeutic dose;
- Most experience mild to moderate withdrawal

- >12 months with therapeutic dose:
- 20-80% experience moderate to severe withdrawal

Management of Benzodiazepine Withdrawal: When to Taper

- Over-sedation
- Cognitive impairment
- Concurrent Rxs or use of high-risk CNS depressants medications
  - Other BZs, non-BZ hypnotics, and OPIOIDS

- Alcohol use disorder and other SUDs
- Overuse, misuse, or BZ use disorder
- Patient request
- Older population at risk
- Other (PDMP/EMR findings)

National Center for PTSD 2013

MANAGEMENT/Systematic discontinuation

- Tapering
- Substitution and tapering

MANAGEMENT/Systematic discontinuation (deprescribing)

- Rate for dosage varies for different types of benzodiazepine pts:
- Withdrawal shows in 1- 7 days depending on half lives
- One-eight to one-tenth of the daily dose (5-25% bi weekly)
  - Begin dose reduction of **5-10%** over **2-4 weeks**
  - **Not to exceed 25% every 2 weeks**

Taper between 4 weeks to 6 months or more

Management of Benzodiazepine Withdrawal

Pharmacological /Strategies Treatment of Withdrawal

- Taper over months:
- Convert to longer acting agent like Clonazepam, Chlordiazepoxide, Diazepam)
- Taper gradually while starting alternative therapies if needed (months)
- Rebound psych meds for anxiety/sleep (Trazadone, Mirtazapine, Buspirone)
- Use of Anticonvulsant carbamazepine or valproate

Ashton H. The diagnosis and management of benzodiazepine dependence. Curr Opin Psychiatry. 2005; 18:249-255.

When do you see withdrawal symptoms?

- Short-acting BZD: oxazepam, triazolam, temazepam, alprazolam
- Short acting sedative-hypnotics: pentobarbital, secobarbital, meprobamate, metaqualone
  - Withdrawal onset in 12-24 hrs with
  - Peak of withdrawal intensity-day 1 to 5
  - Duration of acute withdrawal- 7 to 21 day

When do you see withdrawal symptoms?

- Long-acting BZD and sedative-hypnotics: diazepam, chlordiazepoxide, phenobarbital
  - Withdrawal Onset within 5 - 14 days of cessation
  - Peak of Withdrawal Intensity - Days 1 to 9
  - Duration of Acute Withdrawal - 10-28 days
    - Protracted withdrawal symptoms for months

Phenobarbital Substitution and Taper

- Substitution of benzodiazepine with equipotent dose of phenobarbital
- For inpatient, medically monitored setting only
- Effective Strategy for:
  - High dose dependent
  - Poly-Substance Dependence
  - Concurrent Alcohol/other Sedative Hypnotic
  - Unknown or erratic polypharmacy drug use

Phenobarbital Substitution and Taper

- Establish Stabilization Dose by Computing Phenobarbital equivalents
  - Alprazolam 1 mg=PB 30 mg
  - Clonazepam 2mg=PB 30 mg
  - Diazepam 10 mg=PB 30 mg
  - Lorazepam 2 mg=PB 30 mg
  - Carisoprodol 700 mg=PB 30 mg
- PB should be give TID or QID
- Maximum PB starting dose 500mg/day

Phenobarbital Substitution and Taper

- Monitor patient for signs of toxicity before administering each dose
- Signs of PB toxicity are easy to observe:
  - Sustained horizontal nystagmus
  - Ataxia
  - Slurred Speech

  - If intoxication observed:
    - If 1 sign of toxicity observed, skip one dose
    - If 2 signs of toxicity observed, skip 2 doses
    - Recalculate new daily dose

Phenobarbital Substitution and Taper

- Once stabilization dose is established: maintain patient on initial dose for two days
- If patient has neither signs of withdrawal or toxicity, then patient is moved to the withdrawal phase
- Decrease phenobarbital 30 mg/day unless signs of toxicity or withdrawal are seen
- If patient develops objective signs of withdrawal. Daily dose is adjusted upward by 50% and patient is stabilized before continuing withdrawal

Pregnancy

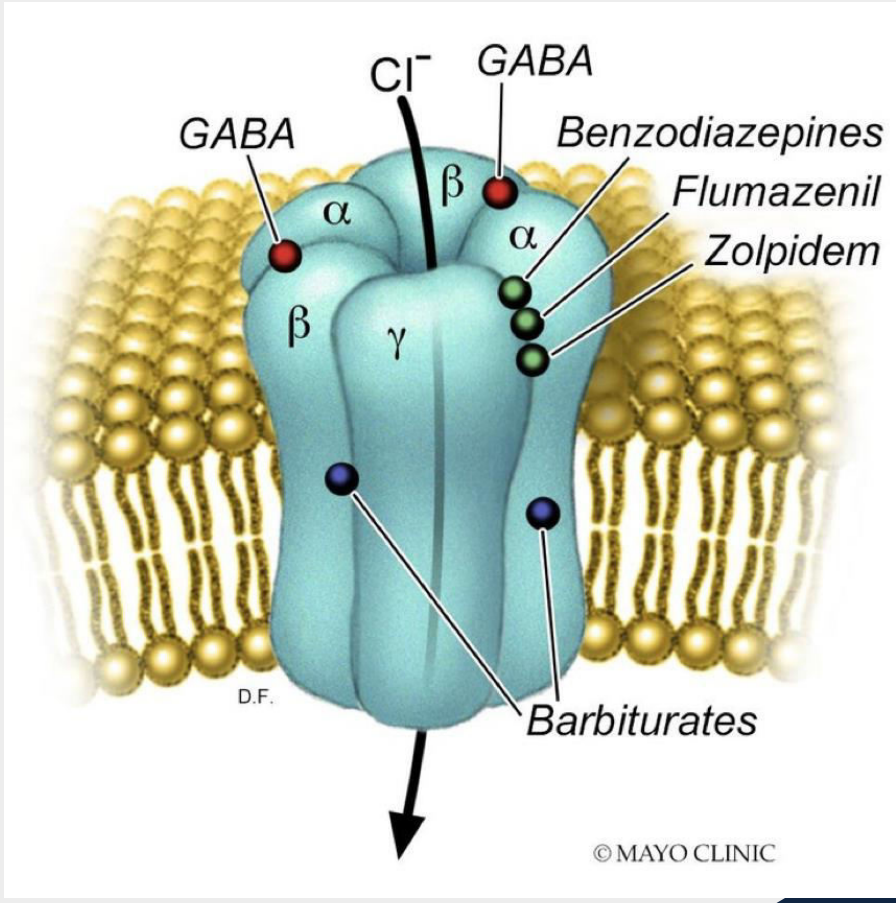
- Pregnant and lactating women are relatively contraindicated due to:
  - Ability of benzodiazepines to cross fetal placental barrier and to pass into breast milk
  - Teratogenic effects
  - Floppy baby syndrome
  - Neonatal withdrawal

Flumazenil

- Reverse the sedation produced by a benzodiazepine (Acute O.D with benzodiazepine)
- Nonspecific competitive antagonist of benzodiazepine receptor
- May up regulate BZ receptors
- IV use 1 mg monitor pt every 30-60 minutes
- Adverse effects: seizures, cardiac arrhythmias and acute precipitated withdrawal

Z-Drugs (Selective nonbenzodiazepine hypnotics)

- Zaleplon
- Zolpidem
- Eszoplicone
- Zoplicone*



- Lower the risk for residual daytime drowsiness due to shorter duration of action
- Short term use
- Bind to sub-types of GABA A receptors – α1 subunit that specifically modulate sleep and therefore are thought to have less unwanted side effects
- SE: risk of increased sleep- related behaviors
- Apply the general principles prescribing benzodiazepines to the Z-drugs

Barbiturates

- The oldest sedative hypnotics
- Classified in three different pharmacokinetics category
- In the past used for treatment of anxiety disorders
- BBT: low therapeutic index
- Replaced by benzodiazepines
- BBT induce the synthesis of hepatic cytochrome P450, thus alter their own metabolism and the metabolism of other meds

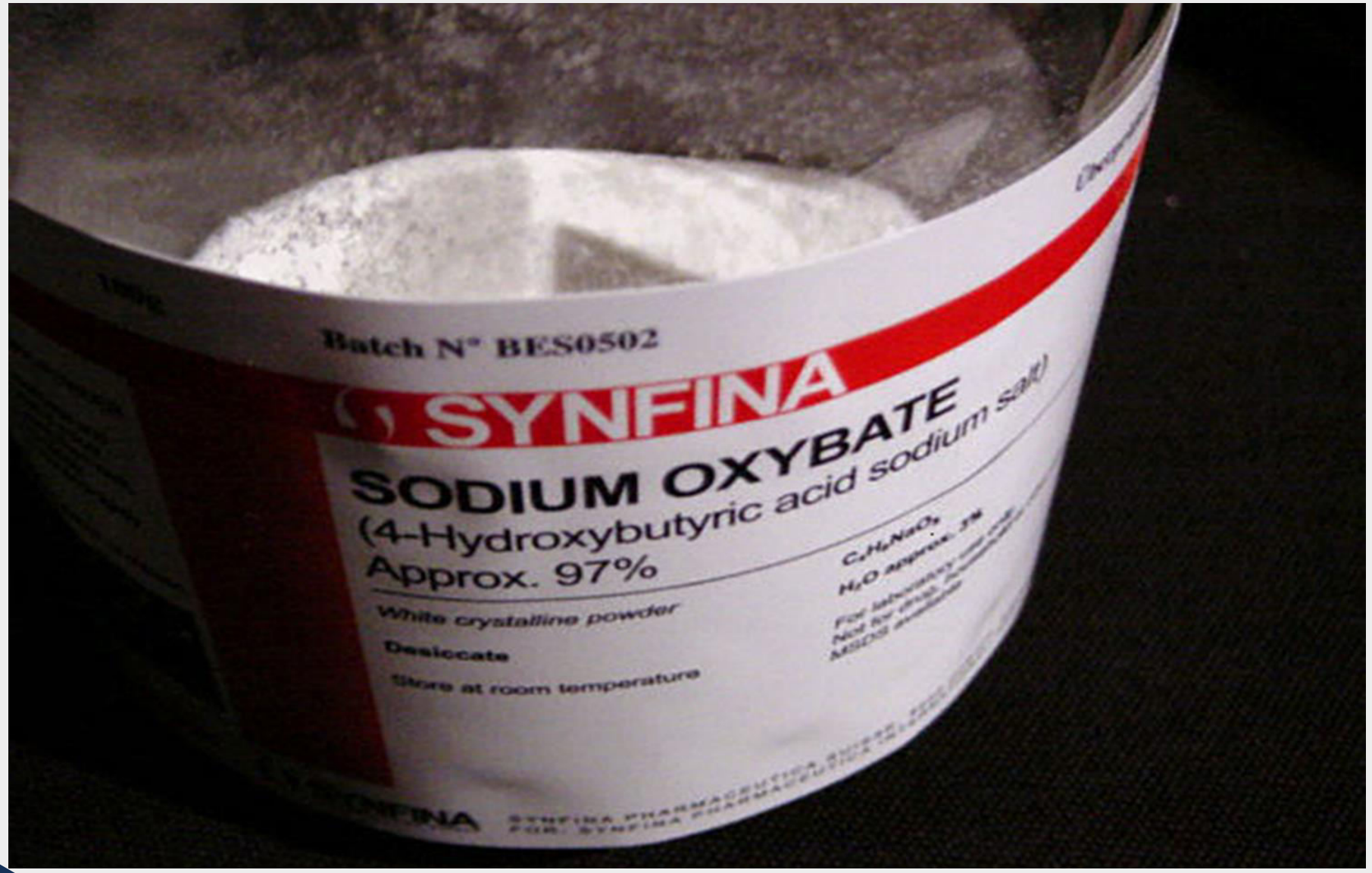
Barbiturates

Duration of Action	LS	Onset	Duration	Use
Ultrashort	H	10-20 s	20-30 min	IV anesthesia
Thiopental				
Methohexital				
Short/Intermediate	M	20-40 min	5-8 h	Surgical anesthesia and sleep induction
Amobarbital				
Secobarbital				
Pentobarbital				
Long	L	Over 1 h	10-12 h	Prolong sedation and seizure control
Phenorbarbital				
Meprobarbital				

GHB
Gamma-Hydroxy-Butyrate

“When I wake up,
I feel completely refreshed.
In comparison to the other drugs that
are supposed to be ‘clean,’
G really is clean.”

FDA approved: Narcolepsy with cataplexy



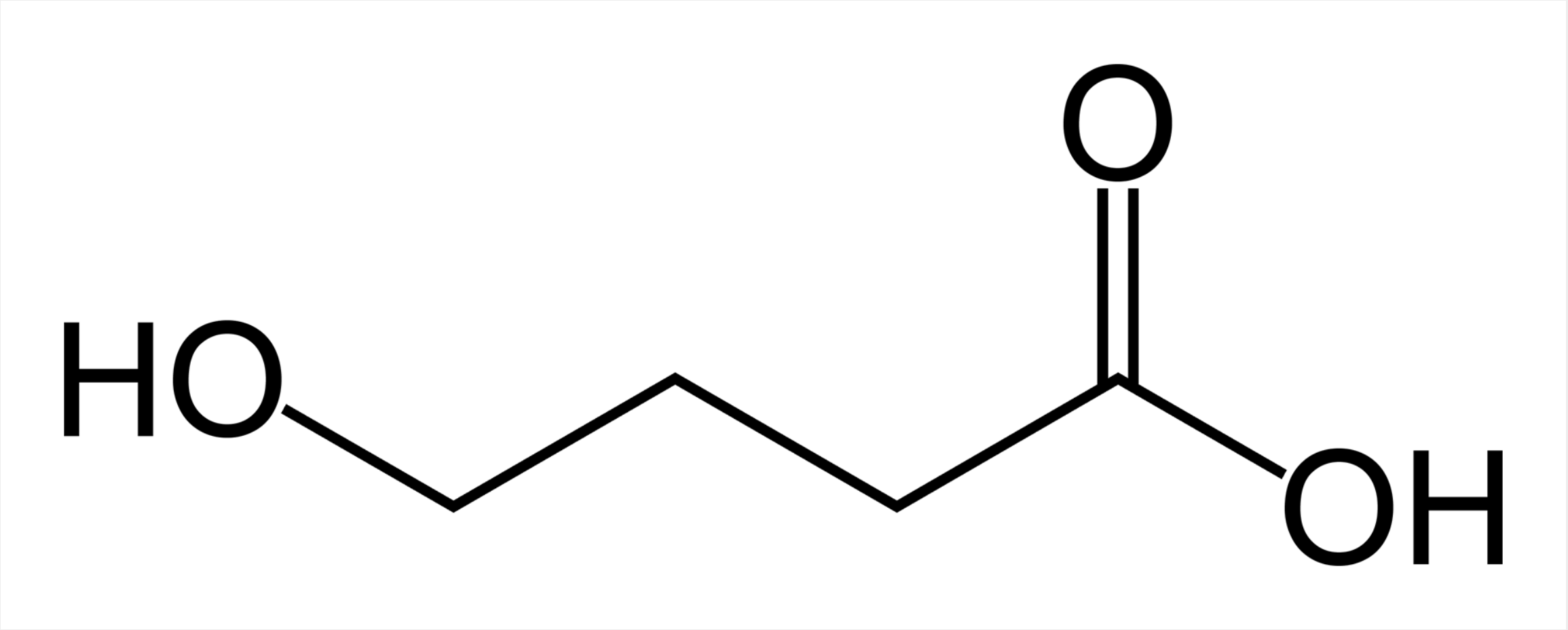
Effects

- Sensual drug, like MDMA, but also resulting in “the greatest sex ever.”
- Relaxation, tranquility, placidity, mild euphoria, disinhibition.
- Temporary amnesia (hence “the date rape drug”).
- Has been used as a muscle developer and fat burner

Neurobiology

- GHB is a neurotransmitter.
- Short half life (30 minutes)
- It is both a precursor and a metabolite of GABA.
- Activity on both the GABAB and the GHB binding sites, results in:
  - Temporary suppression of dopamine,
  - Subsequent marked release of dopamine, and
  - Increased release of endogenous opioids.
- Also it is a highly regulated Schedule III medication for narcolepsy (Xyrem).

The Molecular Structure



Intoxication

- Steep dose-response curve:
  - Ataxia, loss of coordination.
  - Respiratory depression, bradycardia, hypotension
  - Coma, persistent vegetative states, death
  - Overdose is a real danger (LD50 is only 5 times the recreational dose).
  - Synergistic effect with alcohol/other sedatives.

- Treat as a medical emergency:
  - ABCs, consider Intensive Care Unit admission.
  - Atropine for bradycardia.

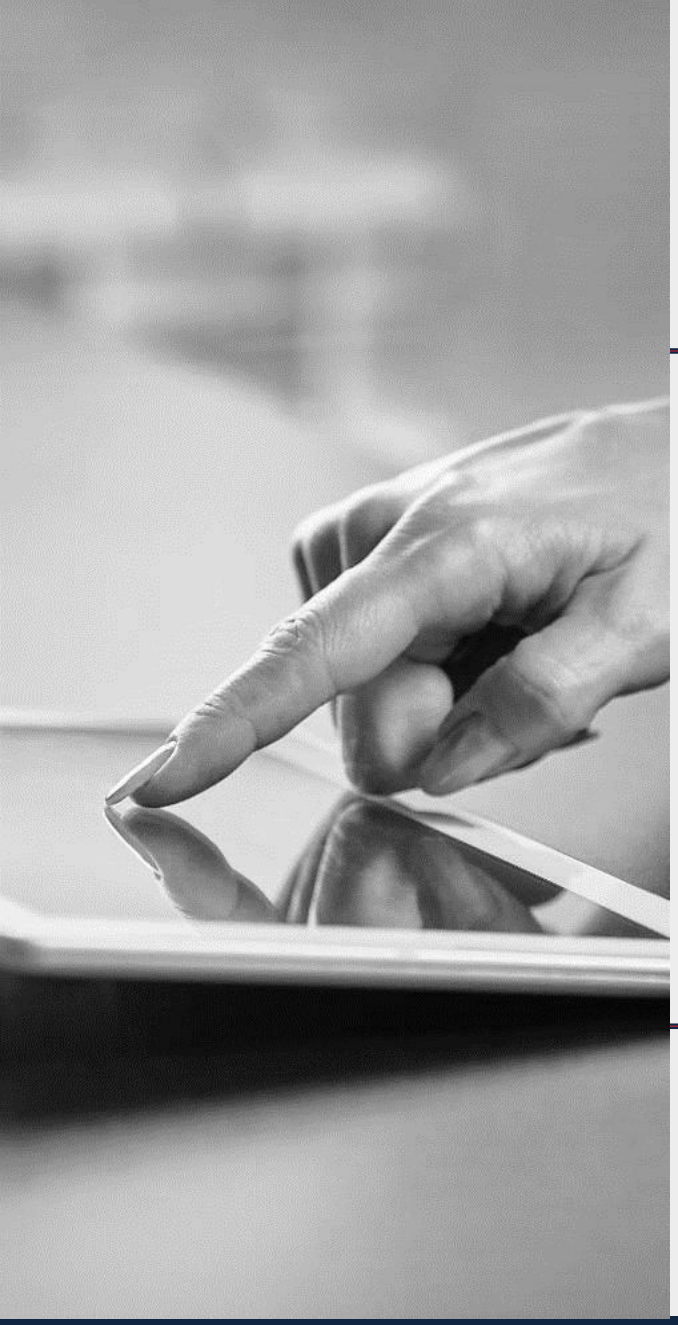
Withdrawal

- Withdrawal is rare but severe.
- Mild withdrawal may persist for several weeks after cessation of use:
  - Anxiety, tremor, insomnia.
  - “Feelings of doom.”
- Severe withdrawal resembles barbiturate withdrawal:
  - Treat with benzodiazepines.

Long Term Features

- Physiological dependence.
- Most patients who overdose on GHB recover completely.

- No FDA approved medications.
- MET and CBT are the major treatment modalities.



Get in Touch

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ASAM REVIEW COURSE 2026

Opioid Use Disorder: Science, History, and Clinical Implications

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Financial Disclosure

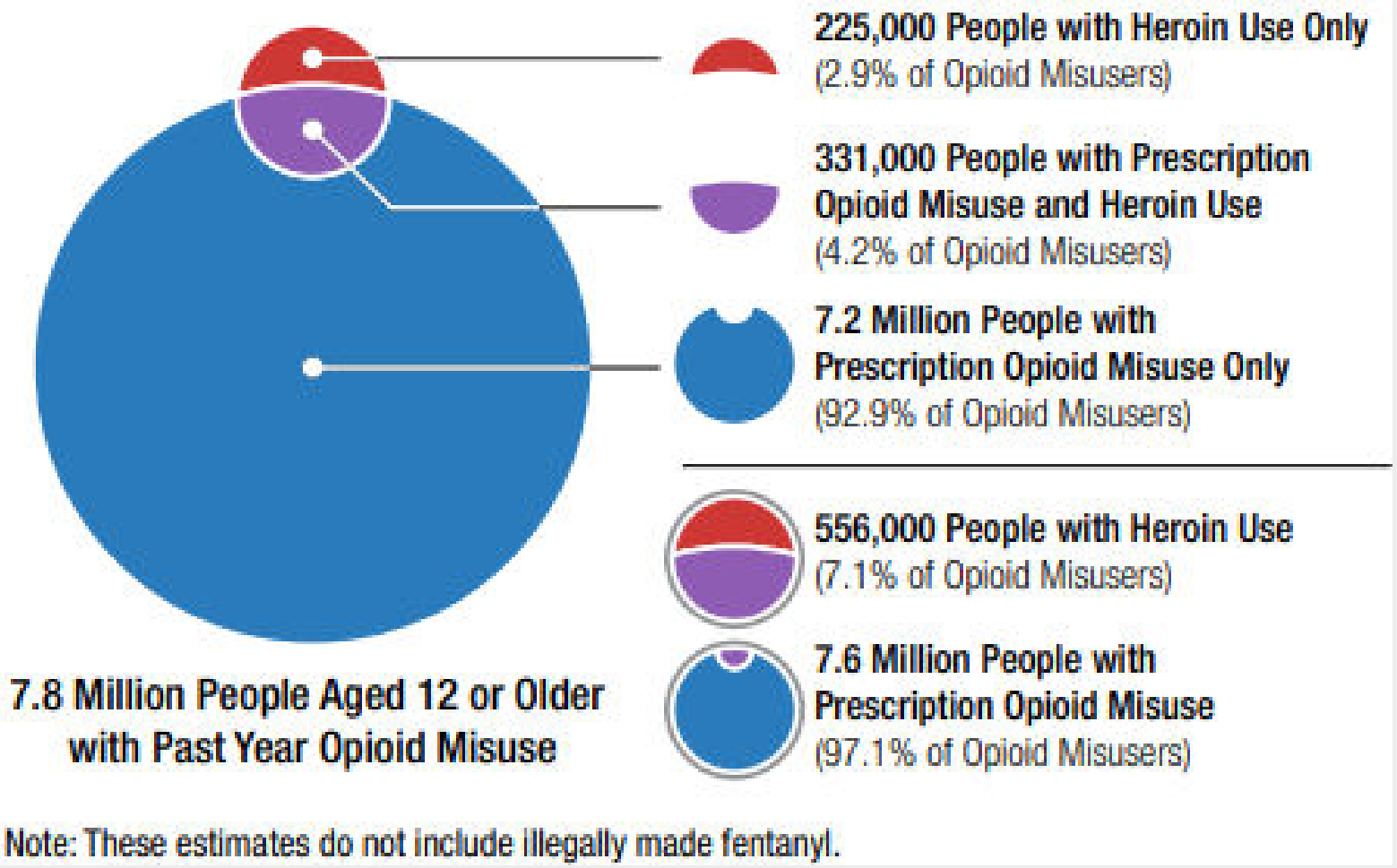
Soteri Polydorou, MD

- No relevant disclosures

Outline

1. Opioid Use Trends
2. History
3. Regulations
4. Neurobiology
5. Intoxication and Withdrawal
6. Medications for Opioid Use Disorder

The Need for Treatment



OUD estimates have ranged from 5 million to nearly 10 million in recent years

Lewer 2020; NSDUH 2022, 2023,2024, SAMHSA

The Need for Treatment

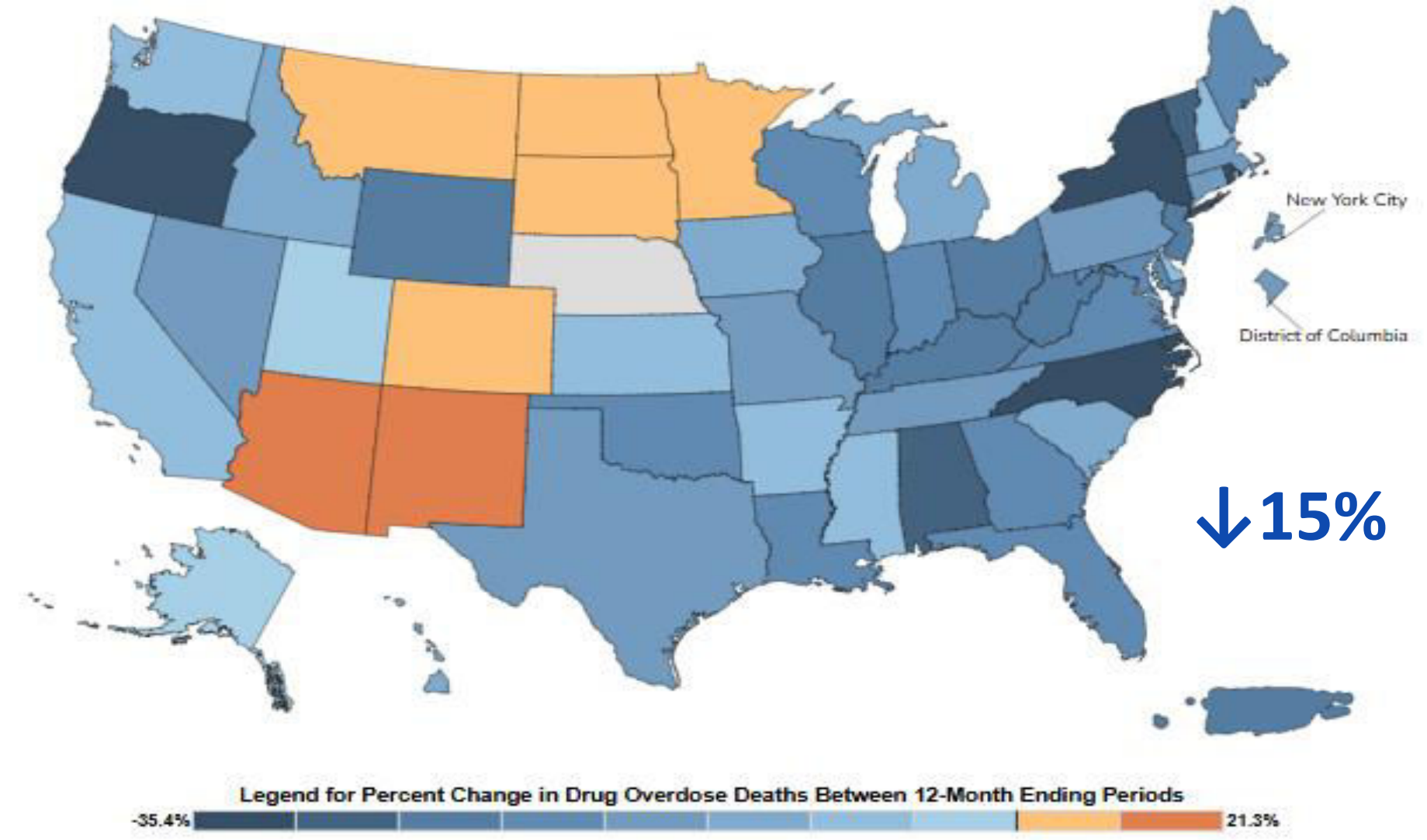
Nationally

- OUD associated with a 15-yr reduction in life expectancy
- Nearly 80,000 lethal ODs in 2024
- Almost 70% of all overdose deaths involve an opioid
- Nearly 90% of fatal opioid overdoses involve synthetic opioids, fentanyl
- 4 out of 5 new recent heroin users previously abused prescription opioids
- >140 OD deaths from opioids daily in US
- 2010 to 2016 heroin related deaths increased by 500%
- 2015 to 2019 fentanyl related deaths increased by over 400%

Leading Causes of Death in US 2024	Annual Deaths
Heart Disease	683,491
Cancer	619,876
Unintentional Injuries	197,449
Cerebrovascular Disease	166,852
Chronic Lower Respiratory Diseases	145,643
Alzheimer Disease	116,022
Diabetes Mellitus	94,445
Renal Disease	55,081
Chronic Liver Disease and Cirrhosis	52,274
Suicide	48,824

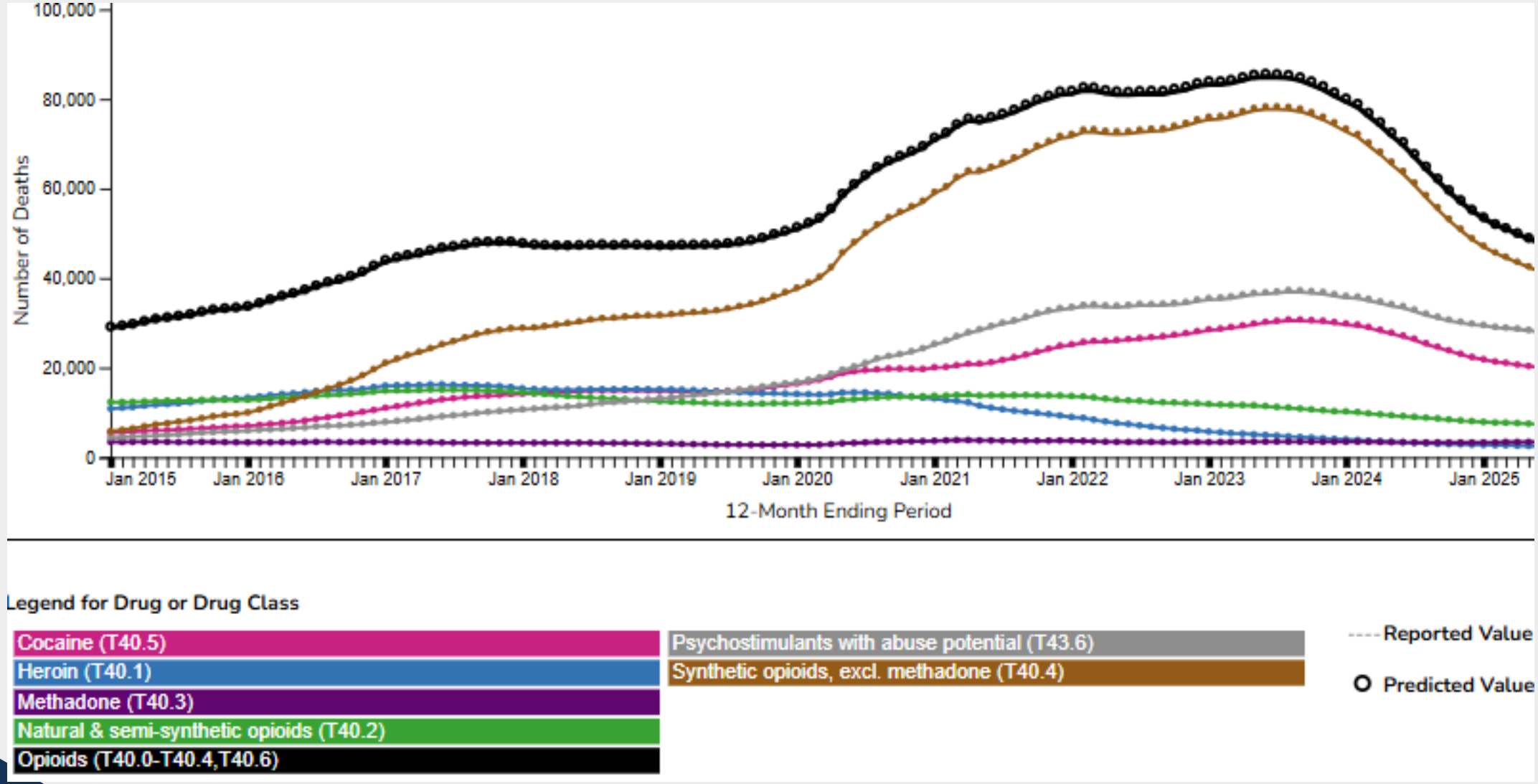
CDC, Health Alert Network, NSDUH, SAMHSA, CSAT, and DOHMH Bureau of Vital Statistics, National Center for health Statistics Data Brief 548 US Mortality 2024

Drug Overdose Deaths 12/2024 to 12/2025



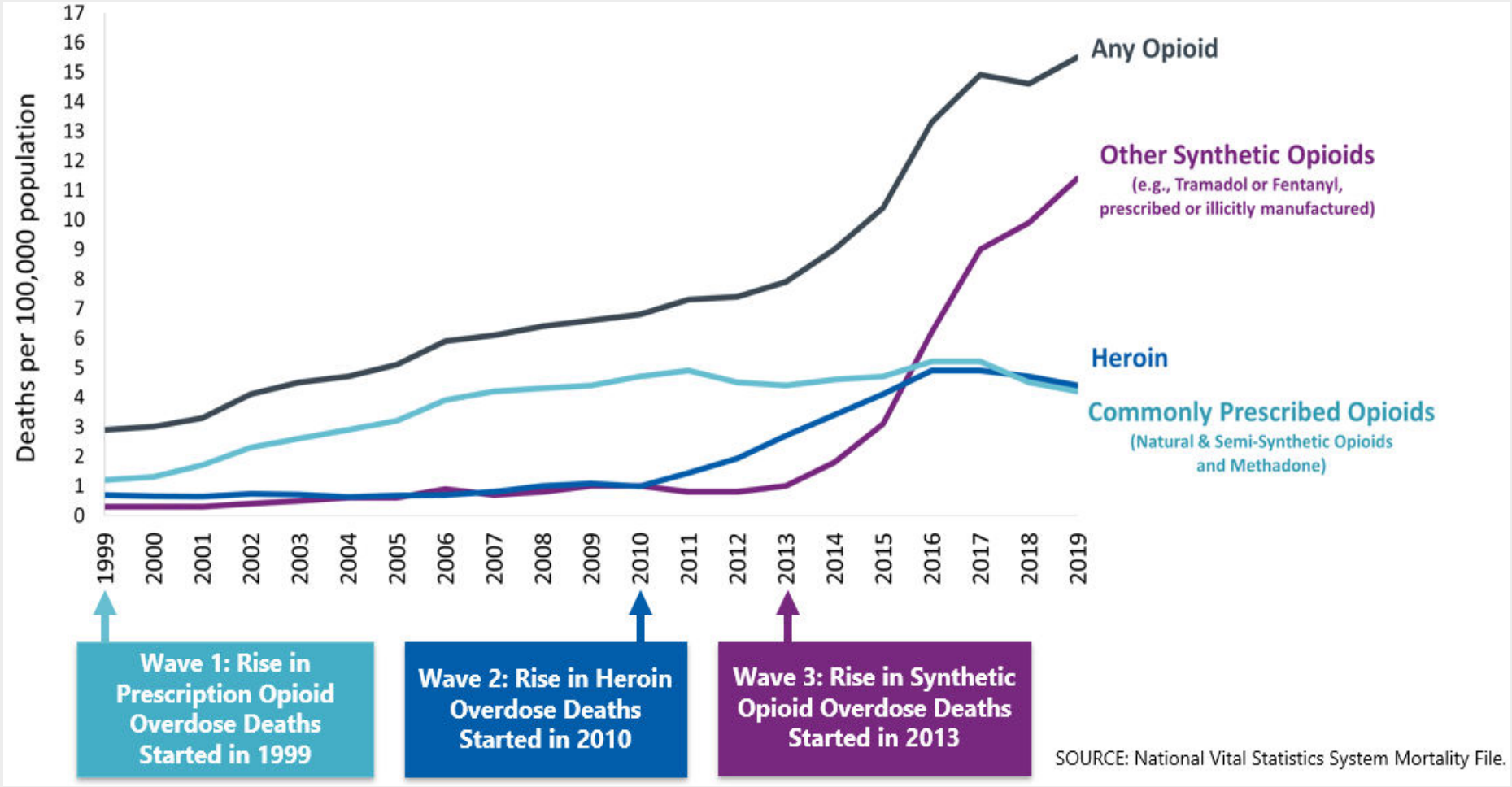
https://www.cdc.gov/nchs/nvss/vsrr/drug-overdose-data.htm

The Need for Treatment is Growing



Based on data available for analysis on 6/1/26, https://www.cdc.gov/nchs/nvss/vsrr/drug-overdose-data.htm#dashboard

Three Waves of Opioid Overdose Deaths



cdc.gov/drugoverdose

Unintentional Opioid Overdose

Experienced (non-fatal)

- Lifetime 24% - 94% (mean 45%, median 47%, SD 14%)
- Past Year 9% - 36% (mean 18%, median 17%. SD 10%)

Witnessed (non-fatal and fatal)

- Lifetime 48% - 96% (mean 73.3%, median 70%, SD 14%)

1 Year All Cause Mortality

- 5% of Non-Fatal Opioid Overdose Presentations to ED or Hospital Admission

Martins S et al 2015, Leece P, et al. 2020, Weiner S et al. 2020



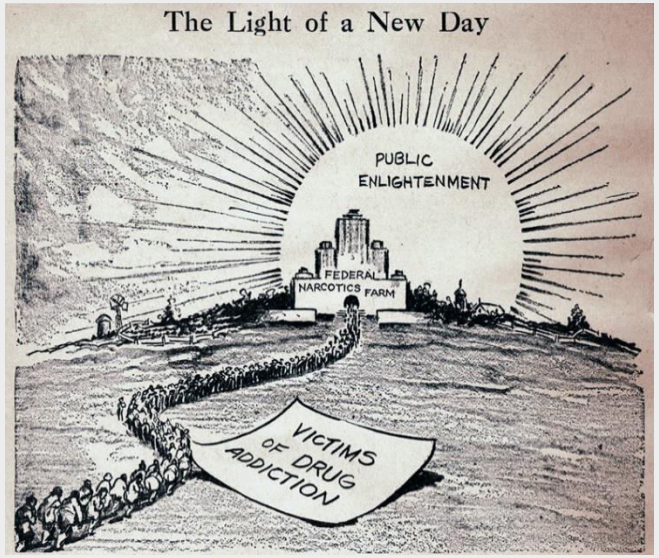
3400 BC



1898



1839



1935

U.S. Government Involvement

Congress passes multiple laws aimed at reducing the increase in heroin/morphine/opium addiction.

- 1905-Opium banned
- 1906-Pure Food and Drug Act- labeling of all medications by pharmaceutical companies
- 1914-Harrison Narcotics Act (HNA)
  - 1919- Supreme Court sides with Treasury interpretation that physician prescribing of opioids for treatment of opioid addiction was violation of HNA
  - Later Supreme Court rulings from 1921 and 1926 reverses interpretation of HNA saying the federal government had overstepped its authority to regulate the practice of medicine



© Cartoonbank.com



"We're from the F.B.I., going from house to house making sure that everyone is scared shitless."

U.S. Government Involvement

- 1970-Comprehensive Drug Abuse Prevention & Control Act (Controlled Substances Act)
- 1974 – Narcotic Addict Treatment Act of 1974
- 2000- Drug Addiction Treatment Act (DATA) of 2000– An Amendment to the Controlled Substances Act
  - Allows treatment of opioid dependence with narcotic schedule III, IV, V, or combinations of such drugs
  - Buprenorphine designated Schedule III and FDA approved for treatment of opioid dependence
  - Capacity to refer patients for counseling



U.S. Government Involvement

- 2016 Comprehensive Addiction and Recovery Act (CARA)
- 2018 Support for Patients and Communities Act
- 2020 HHS Public Health Emergency Declaration, DEA partners with SAMHSA (temporary)
- 2021 HHS Updates Practice Guidelines for the Administration of Buprenorphine for Treating OUD

By 2022, over 100,000 practitioners held waivers, 71,000 with 30-limit, 22,000 with 100-limit, <10,000 with 275-limit

2023 Consolidated Appropriations Act, Section 1262

Mainstreaming Addiction Treatment Act (MAT Act)

Buprenorphine DATA-Waiver is *ELIMINATED!*

Effective January 12, 2023

- A DATA-Waiver registration is no longer required to treat patients with buprenorphine for opioid use disorder
- Prescriptions for buprenorphine only require a standard DEA registration number
- No caps on the number of patients a prescriber may treat for opioid use disorder with buprenorphine
- The Act does not impact existing state laws or regulations that may be applicable

2024 HHS/SAMHSA 42CFR Part 8 Final Rule on Opioid Use Disorder Treatment

Opioid Treatment Programs ONLY

- Reduces barriers to receiving care
- Supports a patient-centered approach
- Promotes practitioner autonomy
- Removes stigmatizing and outdated language

https://www.federalregister.gov/documents/2024/02/02/2024-01693/medications-for-the-treatment-of-opioid-use-disorder



Highlights of the Final Rule

- Methadone: telehealth screening and full exam must be audio-visual, NOT audio only
  - 1st day methadone dose should not exceed 50mg, limited exceptions
- Buprenorphine: telehealth screening and full exam can be audio-visual or audio only
- Medication attendance schedule changes
- Allows medication units to be community pharmacies and allows them to offer take-home methadone
- Allows split dose as clinically indicated
- Allows Medical Directors to delegate responsibilities to other practitioners (NP/PA)
- Patient refusal of counseling does not preclude care at OTP

Methadone Take-Home Doses/Schedule

Take-home methadone schedules are significantly increased in regulation

- In treatment 0-14 days, up to 7 unsupervised take-home doses of methadone may be provided to the patient
- Treatment days 15-30, up to 14 unsupervised take-home doses of methadone may be provided to the patient
- From 31 days in treatment, up to 28 unsupervised take-home doses of methadone may be provided to the patient

Methadone Take-Home Doses/Schedule

In determining which patients may receive unsupervised doses, the medical director or program medical practitioner shall consider, among other pertinent factors that indicate whether the therapeutic benefits of unsupervised doses outweigh the risks, the following criteria:

1. Absence of active substance use disorders, other physical or behavioral health conditions that increase the risk of patient harm as it relates to the potential for overdose, or the ability to function safely;
2. Regularity of attendance for supervised medication administration;
3. Absence of serious behavioral problems that endanger the patient, the public or others;
4. Absence of known recent diversion activity; and
5. Whether take home medication can be safely transported and stored; and
6. Any other criteria that the medical director or medical practitioner considers relevant to the patient's safety and the public's health.

Overview

- Addictive drugs produce an enhancement in extracellular dopamine levels in the nucleus accumbens and other limbic structures as well as cortical areas.

- Endorphin-Opioid Receptor binding results in an increase in dopamine release in the mesolimbic and mesocortical pathways but unlike exogenous Opioid-OR binding the effect is less robust and does not result in habituation.

Terminology

Endorphins - describes the whole class of endogenous opioid ligands

- Beta-endorphin, enkephalin, dynorphin

Opioid - describes entire class of non-endogenous (natural or synthetic) and endogenous compounds that bind to one or more types of opioid receptors

- Methadone, fentanyl, oxycodone

Opiate - describes compounds naturally derived from the poppy plant

- Morphine, codeine

Opium Poppy: Papaver Somniferum



Alkaloid Content

- **Morphine,** 7-25%, opiate analgesic, named after Morpheus, the Greek God of dreams
- **Noscapine**, 4-15%, central acting antitussive, no morphine-like effect of dependence or tolerance
- **Codeine**, 1-6%, opiate analgesic
- **Thebaine**, 1-6%, important intermediate for the synthesis of semisynthetic opioids e.g., buprenorphine, oxycodone
- **Papaverine**, 1-5%. smooth muscle relaxant

***Poppy Seeds**: UDS → + Opiates, Morphine, Codeine (cut-off dependent)*

Endogenous Opioids & Opioid Receptors

Endorphin Class	**Opioid Receptor Type**
Beta-endorphin Endomorphin	Mu Opioid Peptide Receptor
Dynorphin	Kappa Opioid Peptide Receptor
Enkephalin	Delta Opioid Peptide Receptor
Orphanin/Nociceptin (opiate-like)	*Nociceptin/Orphanin FQ Peptide Receptor, Opioid Receptor Like-1*

Multiple opioid receptor polymorphisms identified

Opioid Receptors

All Opioid Receptors

Seven transmembrane domain

G protein-coupled

Primarily inhibitory pathways

Mu Opioid Receptor (OPRM) Activation (predominantly beta-endorphin)

Reduces cAMP

Inhibits transporter release of GABA, glycine, and glutamate

- Inhibition of GABA in ventral tegmental area (VTA)→increases dopamine release throughout mesolimbic (amygdala, ventral pallidum, hippocampus, NAcc)-mesocortical (prefontal cortex, orbitofrontal cortex, anterior cingulate) dopaminergic fields.

Opioid Receptors

Mu Opioid Receptor (OPRM) Activation (predominantly beta-endorphin)

- Widely dispersed across a wide variety of brain regions, including cortex, striatum, thalamus, hippocampus, locus coeruleus, ventral tegmental area, nucleus accumbens, amygdala

- Mu receptors also mediate rewarding properties of non-opioid drugs of abuse including cannabinoids, alcohol and nicotine, or even natural reinforcers such as social interactions

- Physiologic effects of **intoxication** and **withdrawal**

Opioid Receptors

Kappa Opioid Receptor (OPRK) Activation (predominately dynorphin A)

- Identified in various CNS regions such as the nucleus accumbens, caudate–putamen, olfactory tubercle, bed nucleus of the stria terminalis, medial preoptic area, paraventricular nucleus, supraoptic nucleus, dorsomedial, and ventromedial hypothalamus, amygdala, midline thalamic nuclei, periaqueductal gray, raphe nuclei, parabrachial nucleus, locus coeruleus, spinal trigeminal nucleus, and the nucleus of the solitary tract.

- Mediates **dysphoric** activities of both opioids and cannabinoids and therefore opposes mu receptors in regulating the hedonic tone and modulating stress-induced relapse.

Opioid Receptors

Delta Opioid Receptor (OPRD) Activation (predominately enkephalin)

- Identified in various CNS regions including thalamus, amygdala, NAcc, locus coeruleus, VTA, and others
- Lack of familiar opioid characteristics like respiratory depression, reinforcing effects as measured in self-administration studies, and opioid (mu or kappa) withdrawal symptoms.
- Delta receptors are less directly involved in hedonic control.
- Distinct from mu and kappa receptors, delta receptors may play a role in emotional responses and show **anxiolytic** activity along with benefits in analgesia resulting from inflammatory states.

Role of Endorphin Systems in Normal Physiologic Functions

- Endogenous response to pain
- Neuroendocrine functions
  - Stress-response systems including HPA axis
  - Reproductive function including HPG axis
- Immunologic function
- Gastrointestinal function
- Cardiovascular function
- Pulmonary function
- Mood, affect, cognition

Additional Opioid Effects

- CNS → Sedation, Analgesia, Euphoria
- GI → Constipation, Nausea
- Endo → ↓Testosterone, ↑Prolactin , ↓ FSH, LH
- Urinary → Retention
- Cardiovascular → Vasodilatation, ↑ QTc
- Miosis
- Tolerance Varies

Opioid Potency

Opioid	*Relative Potency*	*Lethal Dose*
Morphine	1x	1 Pea
Diacetylmorphine (heroin)	2x	1 Sunflower Seed
Fentanyl	100x	1 Sesame Seed
Sufentanil	500x	1 Grain of Sand
Carfentanil	10,000x	0.5 Grain of Salt

Role of Medications in the Treatment of Opioid Use Disorder

Overdose

- Acute intervention, possible reversal, and close monitoring

Withdrawal/Early Stabilization

- Reduction and stabilization of withdrawal symptoms
- Opportunity to initiate and engage in ongoing addiction treatment

Maintenance Therapy

- Prevents or eliminates withdrawal
- Diminishes or eliminates drug craving and use of illicit opioids
- Blocks or attenuates the effects of heroin and other abused opiates
- Risk/harm reduction, reduces overdose risk
- Increased treatment retention and engagement in comprehensive rehabilitation
- Decreased medical and psychiatric symptoms, improves health, reduced risk of HIV and Hep C infection
- Improved social determinants such as employment, family relations
- Decreased criminal behavior

Opioid Overdose

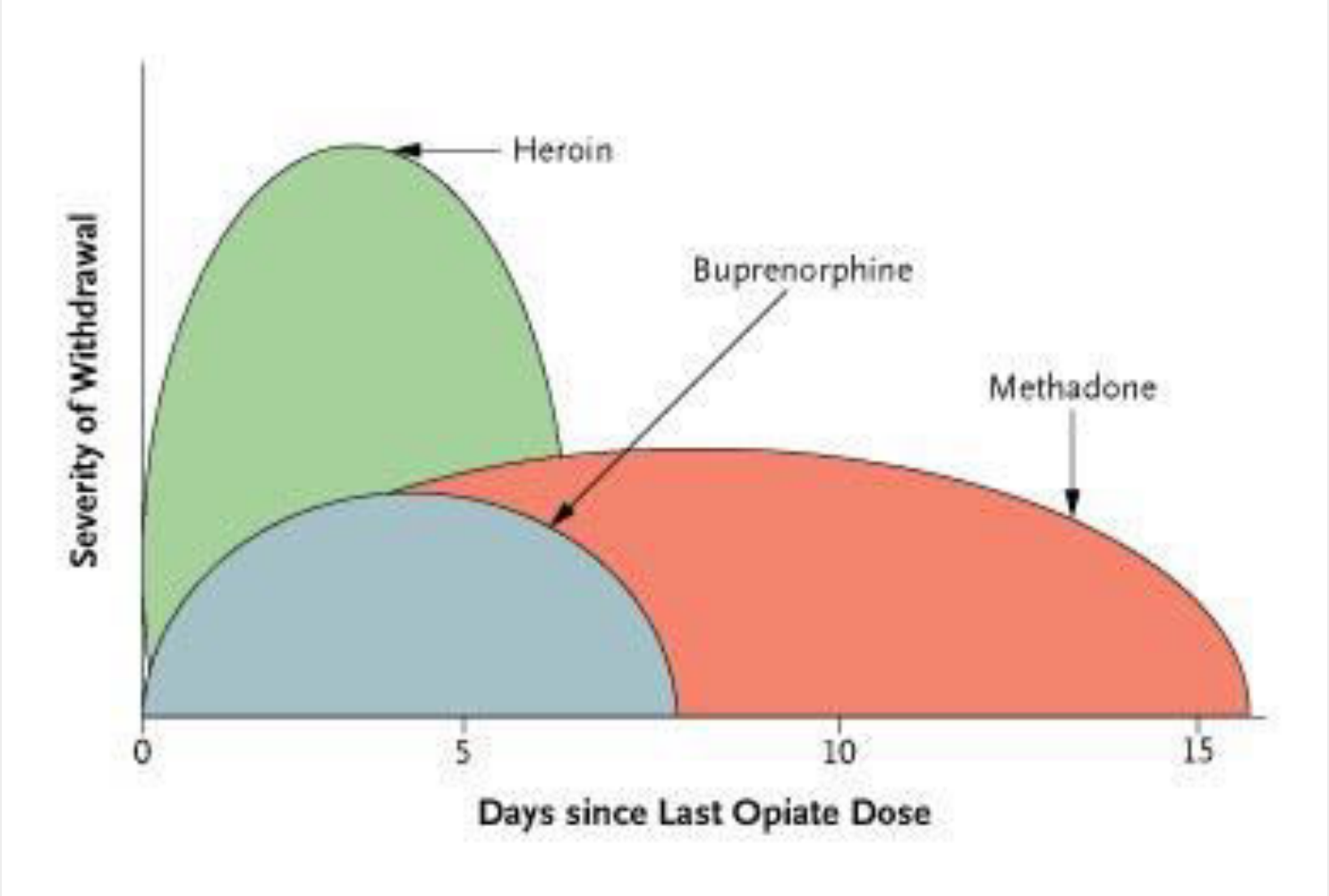
Classic Triad Seen In Overdose

- ***Miosis***
- ***Decreased level of Consciousness/Coma***
- ***Respiratory Depression (With Prolonged ↓ PO2)***
- Pulmonary Edema (Non-cardiogenic)
- Seizures
  - Meperidine, Tramadol

Management of Opioid Overdose

- Ventilatory support if needed
- Parenteral Naloxone
- If IV access, bolus 0.04mg-2mg with escalating doses q2-3min titrated to
  - RR>10/min
  - Improved level of consciousness
  - No withdrawal
  - If needed ongoing IV infusion 2/3 of initial bolus dose/hr.
- If no IV access, 0.4-2mg SQ or IM and observe
- Intranasal administration of 2 doses of Naloxone 4mg in OD Prevention Kits

Severity of Opioid-Withdrawal Symptoms after Abrupt Discontinuation of Equivalent Doses of Heroin, Buprenorphine, and Methadone



Kosten and O'Connor, 2003

Clinical Opiate Withdrawal Scale (COWS)

Clinical Opiate Withdrawal Scale

For each item, circle the number that best describes the patient's signs or symptom. Rate on just the apparent relationship to opiate withdrawal. For example, if heart rate is increased because the patient was jogging just prior to assessment, the increase pulse rate would not add to the score.

Patient's Name:_____ Date and Time _____/_____/_____:_____

Reason for this assessment:_____

Resting Pulse Rate: _____beats/minute *Measured after patient is sitting or lying for one minute* 0 pulse rate 80 or below 1 pulse rate 81-100 2 pulse rate 101-120 4 pulse rate greater than 120	**GI Upset**: *over last 1/2 hour* 0 no GI symptoms 1 stomach cramps 2 nausea or loose stool 3 vomiting or diarrhea 5 multiple episodes of diarrhea or vomiting
Sweating: *over past 1/2 hour not accounted for by room temperature or patient activity.* 0 no report of chills or flushing 1 subjective report of chills or flushing 2 flushed or observable moistness on face 3 beads of sweat on brow or face 4 sweat streaming off face	**Tremor** *observation of outstretched hands* 0 no tremor 1 tremor can be felt, but not observed 2 slight tremor observable 4 gross tremor or muscle twitching
Restlessness *Observation during assessment* 0 able to sit still 1 reports difficulty sitting still, but is able to do so 3 frequent shifting or extraneous movements of legs/arms 5 unable to sit still for more than a few seconds	**Yawning** *Observation during assessment* 0 no yawning 1 yawning once or twice during assessment 2 yawning three or more times during assessment 4 yawning several times/minute
Pupil size 0 pupils pinned or normal size for room light 1 pupils possibly larger than normal for room light 2 pupils moderately dilated 5 pupils so dilated that only the rim of the iris is visible	**Anxiety or Irritability** 0 none 1 patient reports increasing irritability or anxiousness 2 patient obviously irritable or anxious 4 patient so irritable or anxious that participation in the assessment is difficult
Bone or Joint aches *If patient was having pain previously, only the additional component attributed to opiates withdrawal is scored* 0 not present 1 mild diffuse discomfort 2 patient reports severe diffuse aching of joints/muscles 4 patient is rubbing joints or muscles and is unable to sit still because of discomfort	**Gooseflesh skin** 0 skin is smooth 3 piloerrection of skin can be felt or hairs standing up on arms 5 prominent piloerrection
Runny nose or tearing *Not accounted for by cold symptoms or allergies* 0 not present 1 nasal stuffiness or unusually moist eyes 2 nose running or tearing 4 nose constantly running or tears streaming down cheeks	Total Score _____ The total score is the sum of all 11 items Initials of person completing assessment: _____

Score: 5-12 = mild; 13-24 = moderate; 25-36 = moderately severe; more than 36 = severe withdrawal

This version may be copied and used clinically.

Journal of Psychoactive Drugs Volume 35 (2), April - June 2003

Source: Wesson, D. R., & Ling, W. (2003). The Clinical Opiate Withdrawal Scale (COWS). *J Psychoactive Drugs*, 35(2), 253–9.

Opioid Withdrawal

- Buprenorphine—DEA licensed prescribers, no longer limited to those with DATA waivers, MD/DO/PA/NP, OTP
- Methadone—Hospitalized, OTP, very limited other OP
- Symptomatic Meds, e.g., Clonidine, Lofexadine, NSAIDS, Imodium, B/Zs
- 72 Hour Rule: Methadone Dispense Only

Table 2. Medication Treatment for Opioid Withdrawal.*

Protocol	Examples	Effects and Comments
Medication		
Opioid agonists	Methadone (20 to 35 mg daily) or buprenorphine (4 to 16 mg daily), tapered over several days or weeks	Withdrawal symptoms are decreased in severity. Methadone and other opioid agonists are currently restricted to inpatient settings or licensed programs; buprenorphine is now approved by the FDA for this purpose.
Nonopioid drugs	Clonidine (0.2 mg 3 times daily) or lofexidine (0.2 mg twice daily), administered for approximately 10 days for heroin and 14 days for methadone	Withdrawal symptoms are decreased in severity. Lofexidine is less likely to produce hypotension but is not currently approved by the FDA for this purpose.
Rapid and ultra-rapid detoxification	Protocols include a variety of medications: opioid antagonists (noloxone or naltrexone), clonidine, sedatives, antiemetic agents, analgesics, anesthetics	Withdrawal is precipitated with an opioid antagonist, and symptoms are managed with a variety of adjuvant medications. Patients are awake or lightly sedated for rapid detoxification; they are under heavy sedation or general anesthesia for ultra-rapid detoxification. Both methods require special training, equipment, or both. Research on efficacy is limited.

* FDA denotes Food and Drug Administration.

Pitfalls Opioid Analgesic ODs

- Need for repeated naloxone treatment with longer acting opioids (methadone), and more potent opioids (fentanyl, carfentanil)
- Check for Fentanyl Patch under clothing
- Fentanyl chest wall/skeletal muscle rigidity
  - Rapid respiratory arrest
  - Most common with rapid IV administration, not dose related
  - Ventilation, naloxone, neuromuscular blocking agent
- Xylazine and Medetomidine (**non-opioid sedative**, alpha2 adrenergic agonist) identified with illicit fentanyl, sedating, naltrexone not effective, withdrawal not addressed by methadone/buprenorphine treatment, associated with complex/severe wounds
- Alert to possible acetaminophen or other OD

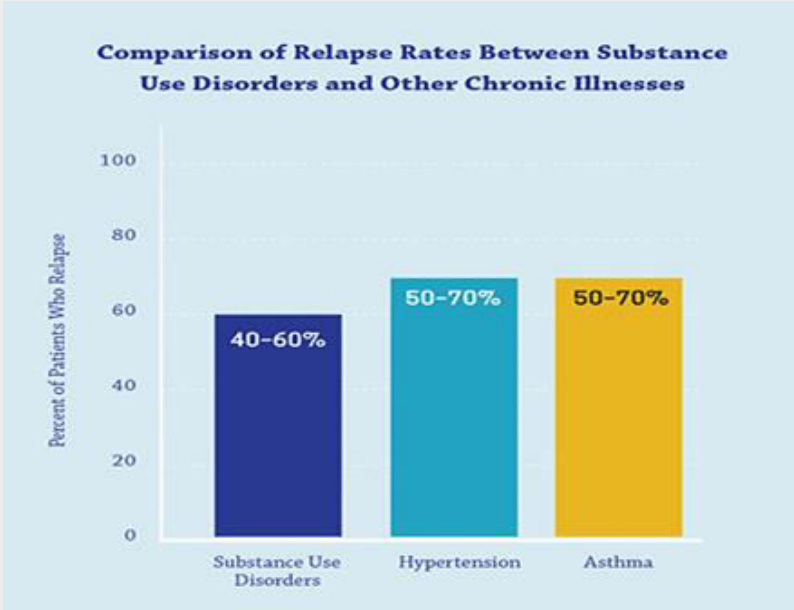
Atypical Opioids of Note

- ✓ **Nitazenes (isotonitazine, metonitazine, etc)** synthetic high potency opioids, developed originally in 1950s, never approved for use, identified in illicit drug supply since ~2020s, elevated OD risk potential
- ✓ **Mitragynine (Kratom)** low dose (1-5g) stimulant resembling caffeine/cocaine, high dose (5-15g) opioid effects, analgesic/sedation reversed by naloxone, possible assoc with hepatic cholestasis—dose dependent
- ✓ **Tianeptine** antidepressant similar to TCAs, mu and delta agonist, anticholinergic
- ✓ **Meperidine** → Normeperidine → Neuroexcitation, MAO interactions Serotonin Syndrome
- ✓ **Tramadol** weak mu, ↑ 5HT, ↑ NE, Seizures, (Sched. IV), serotonin syndrome
- ✓ **Tapentadol** mu agonist, ↑ NE (5HT), serotonin syndrome



Opioid Use Disorder Treatment Outcome*

Methadone Maintenance	**50 – 80%**
Buprenorphine-Naloxone Maintenance	**40 – 70%****
Naltrexone Maintenance (oral, depot)	**10 – 20%, 20-60%*****
“Drug Free” (no pharmacotherapy)	**5 – 20%**
Short-term Detoxification (any mode)	**5 – 20% (limited data)**



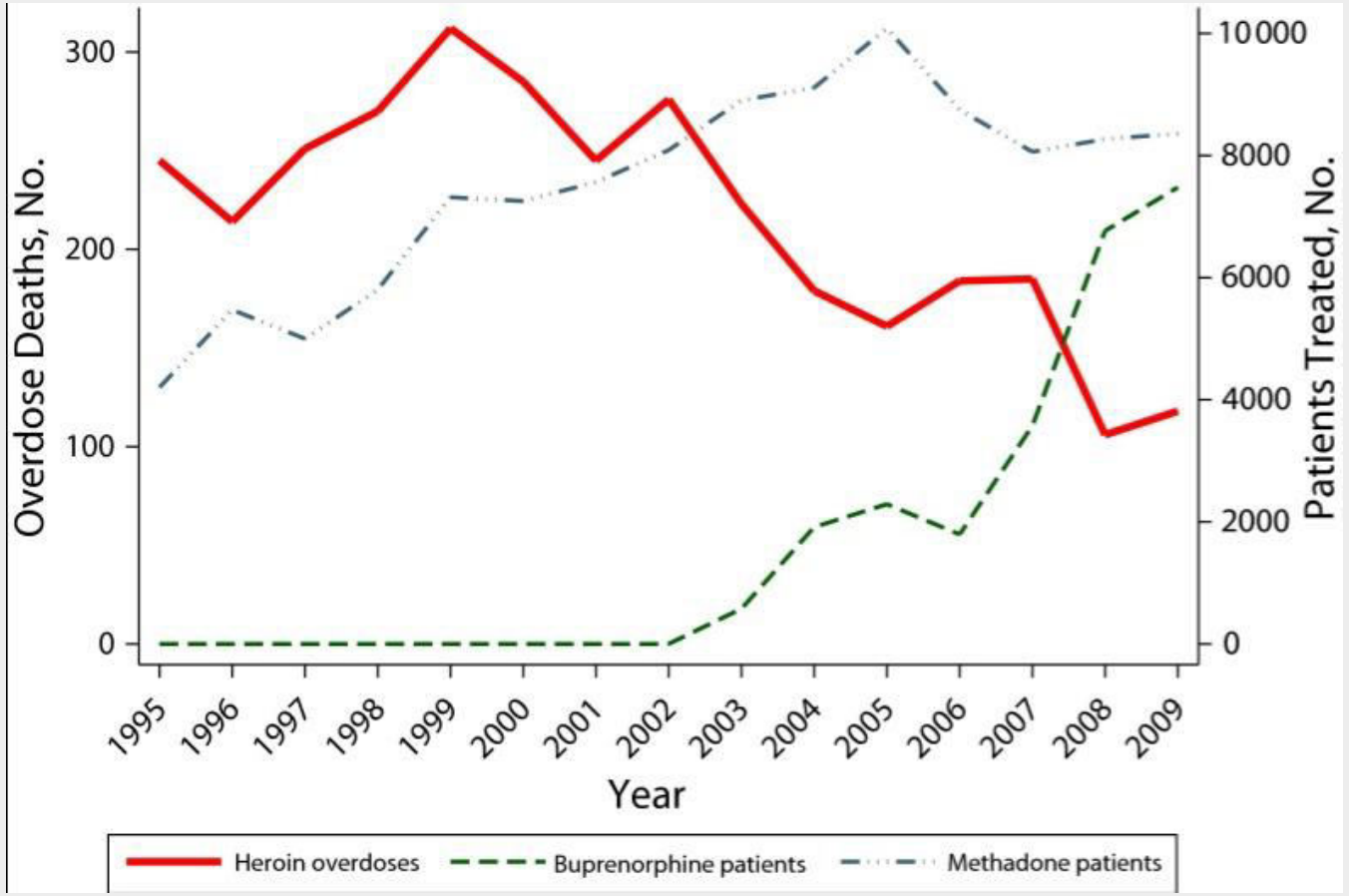
** One year retention in treatment and/or follow-up with significant reduction or elimination of illicit use of opiates*
*** Effective dose 16-24mgs equal to 60 to 80 mg/d or possibly greater of methadone.*
**** 6 month treatment with extended release naltrexone*

Methadone and Buprenorphine maintenance treatment reduces overdose risk by 37-86%

>350,000 in OTPs on methadone and est. >800,000 on buprenorphine

Kreek 1996, 2001, 2003, 2006, Krupitsky 2011, Fudala 2003, Weiss 2011, Woody 2008, Mattick 2009, Lee 2016+2017, CSAT

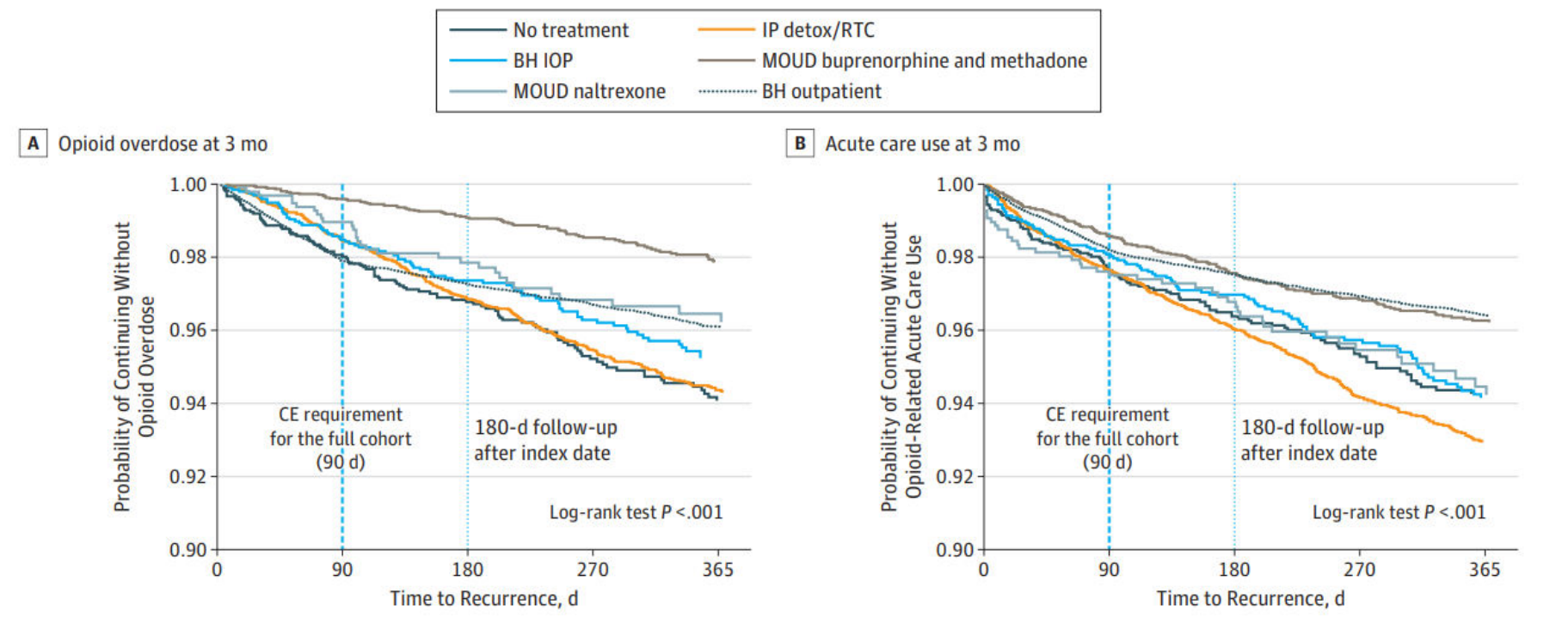
Access to Treatment



Buprenorphine treatment was associated with a 37% annual decline in heroin overdose deaths.

Schwartz RP. Am J Public Health 2013

Access to Treatment



Treatment with buprenorphine or methadone was associated with reduced risk of overdose and serious opioid-related acute care use at 3 month and 12 month follow up.

Wakeman et al. JAMA 2020

Buprenorphine

Onset of action 30-60min

Peak effect 90-100min, half-life 24-42 hr

Metabolism via CYP 3A4 isoenzyme

- Those on CYP 3A4 inhibitors (azole, antifungals, macrolide antibiotics, and HIV protease inhibitors) should be closely monitored, and dose adjustments may need to be made
- Those on CYP 3A4 inducers (phenobarbital, carbamazepine, phenytoin, and rifampin) should also be monitored, and dose adjustments may need to be made

Can alter liver enzymes

- Liver function should be monitored periodically depending upon any recent symptoms or history of hepatitis
- Consider dose reduction or transition to mono formulation if ≥3x upper limit of normal

Pregnancy

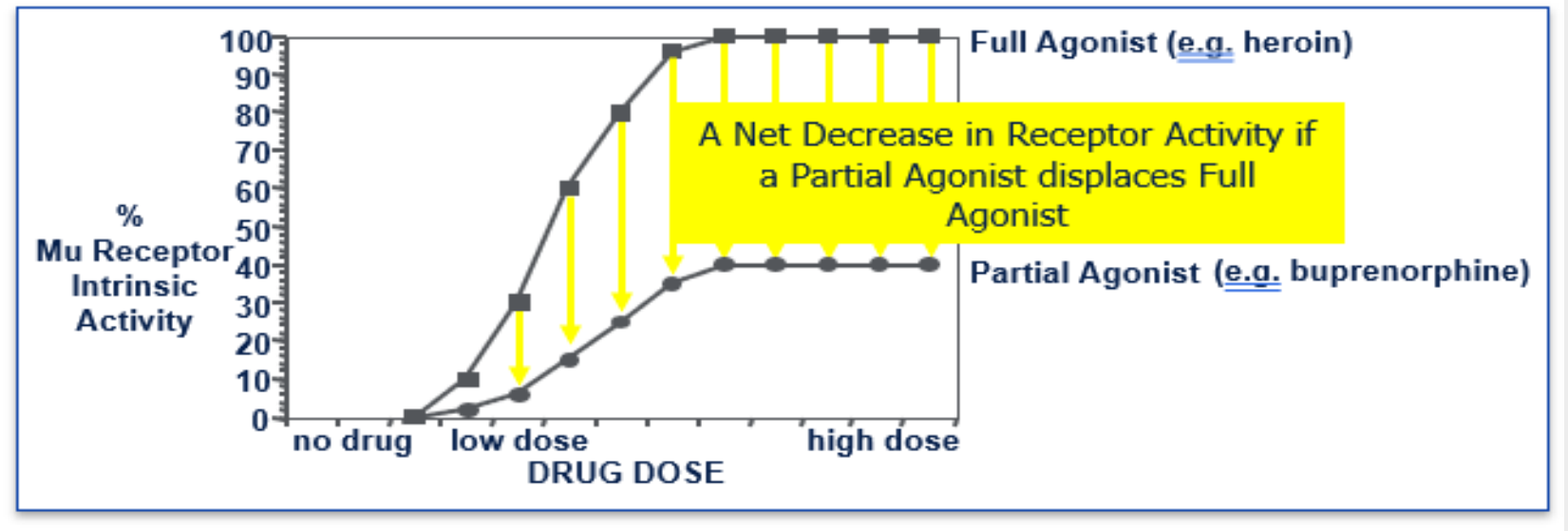
- MOTHER study, mono (without naloxone) formulation, reduced morphine/NAS/hospitalization

Buprenorphine

Partial agonist of the μ-opioid receptor and antagonist of the κ-opioid receptor.

- *High affinity* for μ-opioid receptor
  - Competes with other opioids and inhibits their effects
- *Slow dissociation* from μ-opiate receptor
  - Prolonged therapeutic effect

At low doses, acts as an agonist; in patients dependent on high doses of chronic opioids sudden initiation at high doses results in antagonist clinical effects.



Initiation

Opiate Withdrawal Symptoms

- 6-18 hrs after last use of short-acting opioids (heroin, oxycodone), or 24-48 hrs after longer-acting opioids (methadone)
- Clinical Opiate Withdrawal Scale (COWS) score of ≥8-10

Day 1: Start with buprenorphine (+/-naloxone) 2-4 mg SL

- Consider additional 2-4mg after 1-2 hrs if continued elevation of COWS and no precipitated withdrawal
- May consider additional 2-4 mg 6 hrs later if OWS persist
- FDA Approved Total Day 1 dose 8 mg, but may clinically increase dose further based on persistent OWS

Day 2: Provide total day 1 dose (routinely given as single dose)

- May increase by 4mg twice daily for ongoing symptoms (8 mg total)
- Total Day 2 dose 16 mg

Adjuvant medications:

- Clonazepam 0.5 to 1mg tid prn, Clonidine 0.1 to 0.2mg q4 prn, Trazadone 100mg qhs prn, NSAIDS, Antiemetics/GI (promethazine 25mg IM, loperamide 4mg PO, octreotide 50 mcg SQ), IVF

Low/Micro Dosing Inductions: Typically utilize 0.5mg initial dose while patient continues on full opioid agonist. Slow titration to maintenance doses over 3-7 days with d/c of full opioid agonists.

Initiated at-home with physician instructions, during hospitalizations, or ED assessments

SAMHSA Treatment Improvement Protocol 63; Salapenka et al. 2022; robbins et al. 2021; Penn Medicine https://penncamp.org/clinical/micro-dosing/

Low-Dose (Micro-Dose) Buprenorphine Initiation

Conventional Low-Dosing Initiation Protocol				
Day	Buprenorphine buccal*		Buprenorphine SL^	Full agonist
1	150 mCG – 1 film daily	OR	0.5 mG daily	Continue
2	150 mCG – 1 film BID	OR	0.5 mG BID	Continue
3	450 mCG – 1 film daily	OR	0.5 mG TID	Continue
4	STOP		2 mG daily	Continue
5	0		2 mG BID	Continue
6	0		4 mG BID	Continue
7	0		12 mG daily	STOP
8+	0		Titrate as needed	STOP
*Each buccal 150 mCG film is equivalent to buprenorphine 0.3 mG				
^Doses < 2 mG achieved by patient cutting prescribed 2 mG SL film i				
BID=twice daily; TID=three ti				

Rapid Low-Dosing Initiation Protocol				
Day	Buprenorphine buccal*		Buprenorphine SL	Full agonist
1	150 mCG every 4 hours	OR	0.5 mG every 4 hours	Continue
2	450 mCG every 4 hours	OR	1 mG every 4 hours	Continue
3	STOP		2 mG every 4 hours	Continue
4	0		Titrate as needed	STOP
*Each buccal 150 mCG film is equivalent to buprenorphine 0.3 mG				

Buprenorphine

Generic name	Brand Name	Route	Doses
Buprenorphine	Subutex	Sublingual tablets	2 mg; 8 mg
Buprenorphine/naloxone	Suboxone	Sublingual film	2 mg/0.5 mg; 4 mg/1 mg; 8 mg/2 mg; 12 mg/3 mg
Buprenorphine/naloxone	Suboxone	Sublingual tablets	2 mg/0.5 mg; 8 mg/2 mg
Buprenorphine/naloxone	Zubsolv	Sublingual rapid-dissolve tablets	0.7 mg/0.18 mg; 1.4 mg/0.36 mg; 2.9 mg/0.71 mg; 5.7 mg/1.4 mg; 8.6 mg/2.1 mg; 11.4 mg/2.9 mg
Buprenorphine extended-release injection for subcutaneous use	Brixadi	Subcutaneous	Weekly: 8 mg/0.16 mL; 16 mg/0.32 mL; 24 mg/0.48 mL; 32 mg/0.64 mL Monthly: 64 mg/0.18 mL; 96 mg/0.27 mL; 128 mg/0.36 mL
Buprenorphine extended-release injection	Sublocade	Subcutaneous	Monthly: Initiate 300 mg/1.5 mL after tolerance established of at least 4mg bup, 2nd injection as early as 1 week and up to 1 month after initial injection; then ongoing 100 mg/0.5 mL maintenance dose monthly (can increase to 300 mg)

Naltrexone

- Long-acting, competitive, non-selective opioid-antagonist with high affinity to mu-opioid receptors.
- Metabolism via CYP450
- Excretion predominately urine (53-79%), partial feces. 2% excreted unchanged
- Active metabolite 6-beta-naltrexol
- Half-life 4 hours for naltrexone and 13 hours for 6-beta-naltrexol
- High doses may be associated with hepatic toxicity, contraindicated if elev transaminases

Naltrexone

Antagonist of the μ-opioid receptor

- Withdrawal treatment for those with physical dependence
- POC toxicology
- Induction protocol

Oral formulation FDA approved 1984

- Once daily, 3xweek alternative
- Low adherence limits use to highly motivated populations *(Cornish 1997, Roth 1997)*

Long-acting formulation, Naltrexone-XR 380mg IM monthly, FDA approved for OUD in 2010, *Preferred Formulation*

- More effective than placebo *(Comer 2006, Krupitsky 2011, Tiihonen 2012)*
- More effective than treatment as usual in criminal justice population *(Lee 2016)*
- Lower medical/surgical related hospitalizations but not overall healthcare utilization found in those in criminal justice system as compared to TAU. *(Lee 2018)*
- Non-inferior to buprenorphine, when randomization occurred after opioid detoxification or those successfully inducted onto XR-NTX. *(Tanum 2017, Lee 2018)*
- Reported ODs in studies is low, however most did not report how overdose events were measured particularly those lost to follow-up. *(Jarvis 2018)*

➢ *Consider OD risk from interrupted antagonist treatment*

Methadone

- Approved by FDA 1972 for opioid dependence
- Mu opioid receptor agonist and NMDA antagonist (reduces development of tolerance)
- 2 enantiomers in equal amounts
  - *l (R)* active, *d (S)* inactive
  - Rapidly absorbed orally with detectable plasma levels at 30min but has a delayed onset of action with peak levels at 2-4 hours with sustained levels for 24 hours.
- Metabolized by CYP450 – several isoforms:
- CYP2D6 – may explain group who need very high doses
- Excreted in urine and feces
  - Avoids accumulation and reduces risk of toxicity for those with renal or liver dysfunction
- Half-life 24-36 hrs but may range from 4-91 hrs
  - **Avoid rapid titration!**

Methadone

- 2006 Black Box Warning – risk of QTc prolongation and possibly torsades de pointes/polymorphic VT, dose dependent
- Common side effects: ***constipation, diaphoresis, to a lesser extent sexual dysfunction***
- Safety profile well established including during pregnancy
- ***Beware Opioid Conversion Tables!***
- **Serum Level** – clinical presentation should direct dosing decisions but SML can serve as aid
  - Peak level drawn 2-4 hours after dosing
  - Trough level drawn prior to daily dosing ~24hrs
  - Peak SML less than twice trough

Methadone

1. Initial dose 10-20mg PO (50% dose IM), 20mg eliminates severe withdrawal, first 24hr dose 20-30mg TDD (not routinely recommended to exceed 40mg in first 24 hours, recent 42CFR Part 8 up to 50mg)
2. Craving reduced by increasing methadone dose by 5-10mg q three to seven days (80-120mg or greater)
3. “Blocking dose” (often 80-120mg or greater): tolerance that inhibits the euphoric high

After stabilization, methadone and buprenorphine do not produce euphoria or sedation.

ASAM 2017, 2015, SAMHSA TIP 63

The Basics for all OTPs

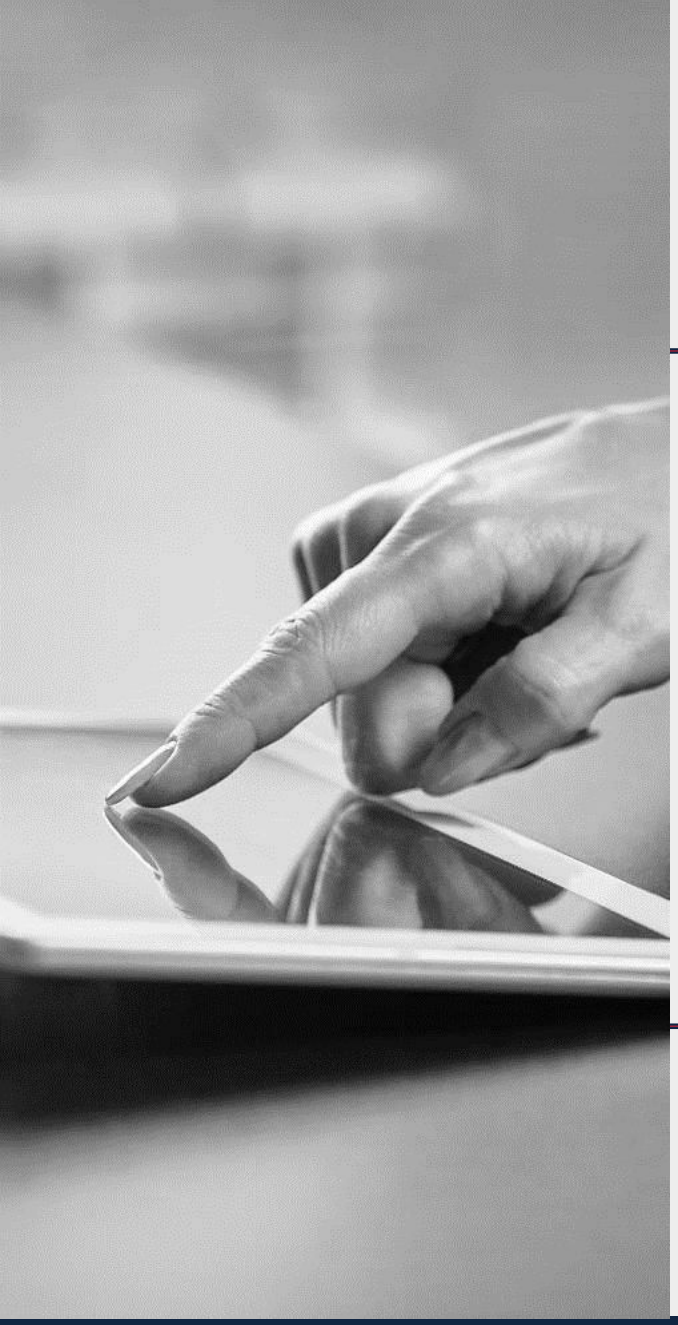
- Comprehensive Assessments
- Treatment Plans
- Toxicology Testing
- Diversion Control
- Multiple MAT options: methadone, buprenorphine, naltrexone
- New attendance schedule flexibility for medication dispensing
- Guest Medication
- Confidentiality, 42 CFR Part 2
- Regulatory Oversight

OUD - Fentanyl

	Buprenorphine	Naltrexone-XR	Methadone
Initiation after last opioid use	Traditional: 1-3 days LDB: same day HDB: 1-3 days	7-14 days for opioid detoxification	Same day
Induction withdrawal risk	Low-Moderate Precipitated withdrawal and post-acute withdrawal may last longer with subtherapeutic dosing	Moderate Precipitated withdrawal if given before completion of acute withdrawal treatment/detoxification Protracted withdrawal may persist 1-2 wks post-induction	Low Mild withdrawal may persist during early titration
Time to full therapeutic dose	1-3 days or longer	1-day post-administration	≥1 week, or longer
Craving Reduction	Moderate Ceiling partial agonist effect	Variable Mechanism of anti-craving effect poorly understood	High Dose-related full agonist effect

Medication and Treatment Setting – Selection Considerations

- Abstinence to Harm Reduction Continuum
- Chronic Pain or foreseeable need for opioid analgesia
- Pregnant or planning pregnancy
- Recent Overdose or high risk for overdose behavior
- Medical and Psychiatric Co-occurring Disorders
- Diversion Risk
- Additional substance use disorders
- Alternatives



Get in Touch

301.656.3920

education@asam.org

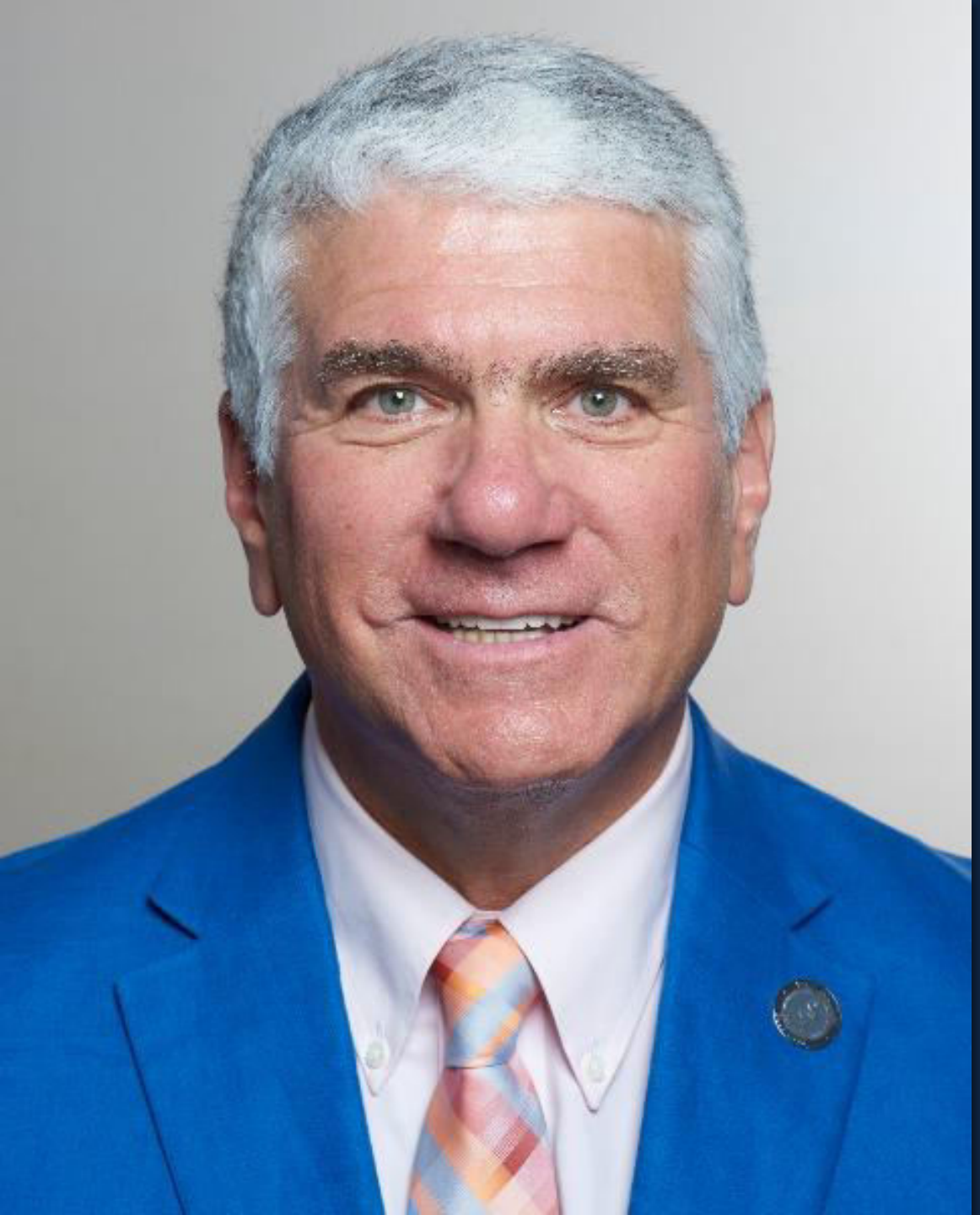
www.asam.org

ASAM REVIEW COURSE 2026

Pain and Addiction: Trends and Treatments

Edwin A. Salsitz, MD, DFASAM
Associate Clinical Professor of Psychiatry
Mount Sinai Beth Israel
New York, NY





Financial Disclosure

Edwin A. Salsitz, MD, DFASAM

- No relevant disclosures



JAMA. 2016;315(17):1826

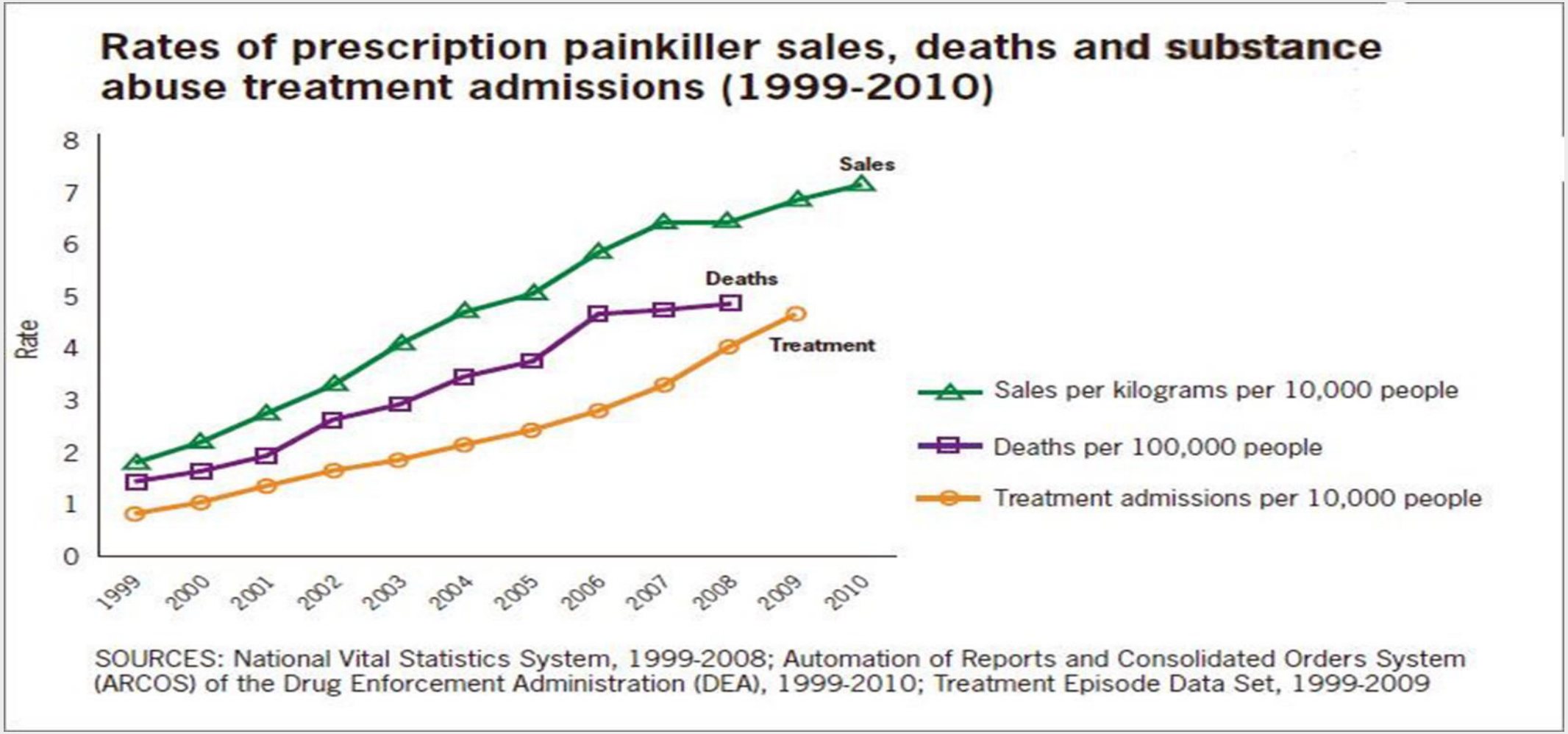
The Epidemic of Untreated Pain

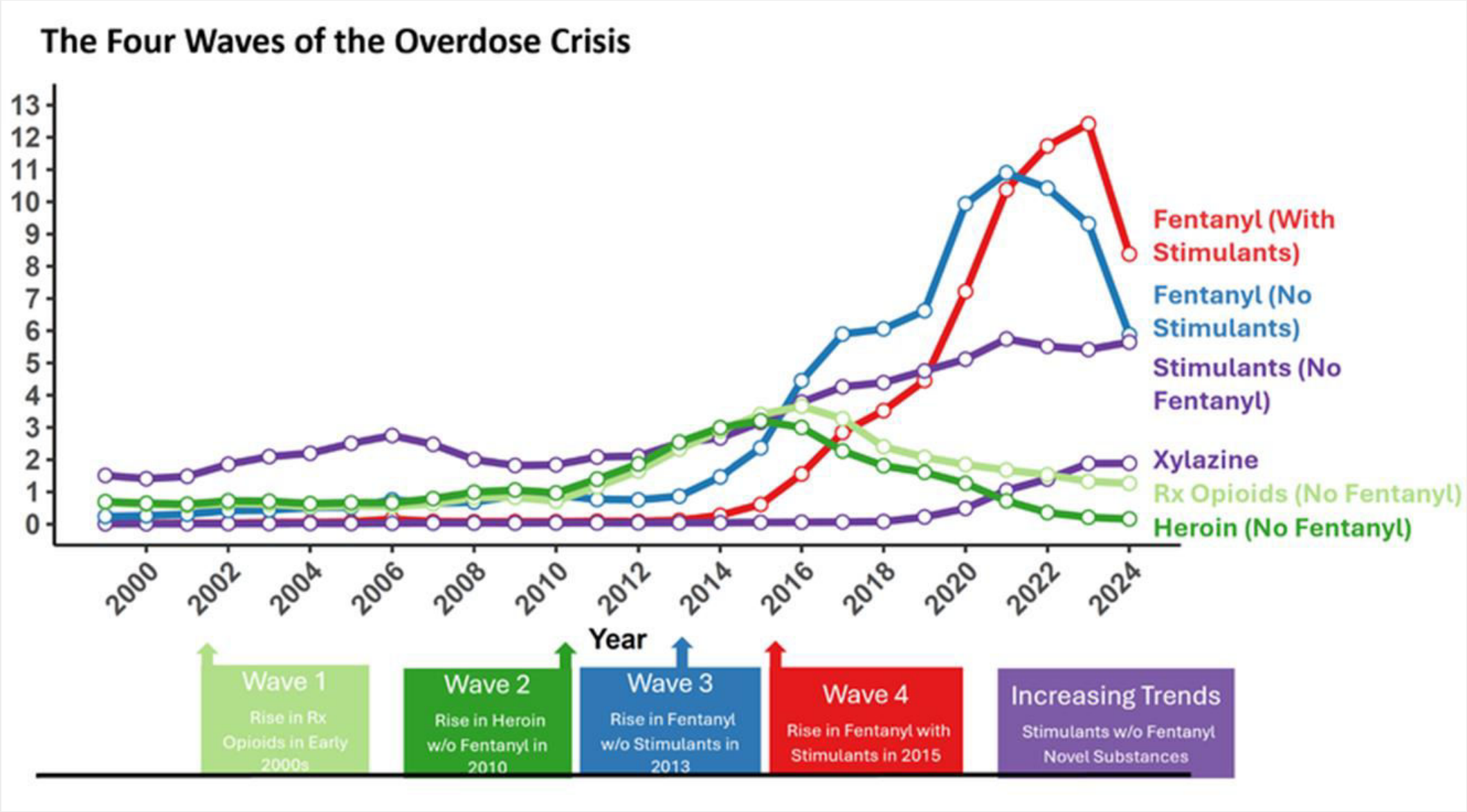
Alleviating Suffering 101
Pain Relief in the USA

- 2011 IOM Report: 116 Million Americans have pain which persists for weeks to years
- $560 - $635 Billion per year
- Some physicians overprescribe opioids, while others refuse to prescribe opioids
- Lack of education: Providers and Patients
- Headache, LBP, Neck Pain, Joint Pain, Fibromyalgia: CNCP

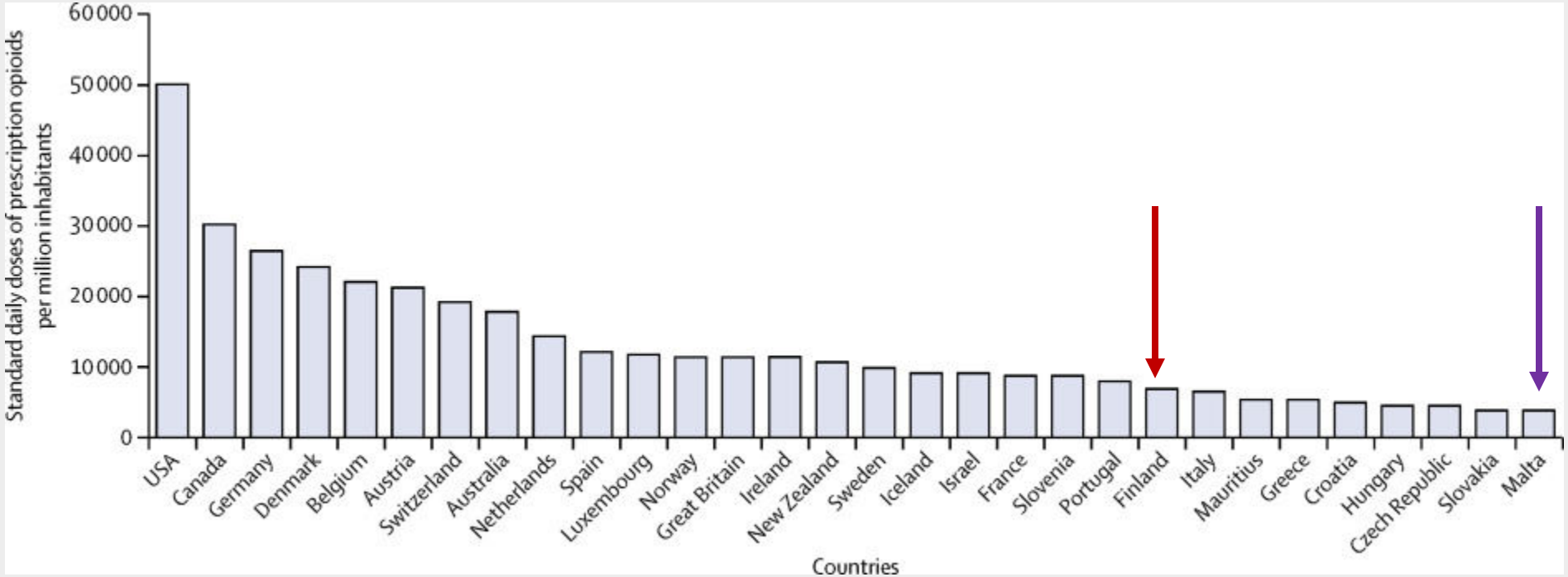
NEJM 366:3 Jan 19,2012

Rates of Opioid Overdose Deaths, Sales, and Treatment Admissions, United States, 1999–2010




The Four Waves of the Overdose Crisis
13
12
11
10
9
8
7
6
5
4
3
2
1
0
2000
2002
2004
2006
2008
2010
2012
2014
2016
2018
2020
2022
2024
Year
Fentanyl (With Stimulants)
Fentanyl (No Stimulants)
Stimulants (No Fentanyl)
Xylazine
Rx Opioids (No Fentanyl)
Heroin (No Fentanyl)
Wave 1
Rise in Rx Opioids in Early 2000s
Wave 2
Rise in Heroin w/o Fentanyl in 2010
Wave 3
Rise in Fentanyl w/o Stimulants in 2013
Wave 4
Rise in Fentanyl with Stimulants in 2015
Increasing Trends
Stimulants w/o Fentanyl
Novel Substances

Avoiding Globalization of the Prescription Opioid Epidemic



Top 30 Opioid-Consuming Nations 2012-2014

Lancet, Vol 390, 29 July–4 August 2017, Pages 437-439, Keith Humphreys

How Did We Get Here?

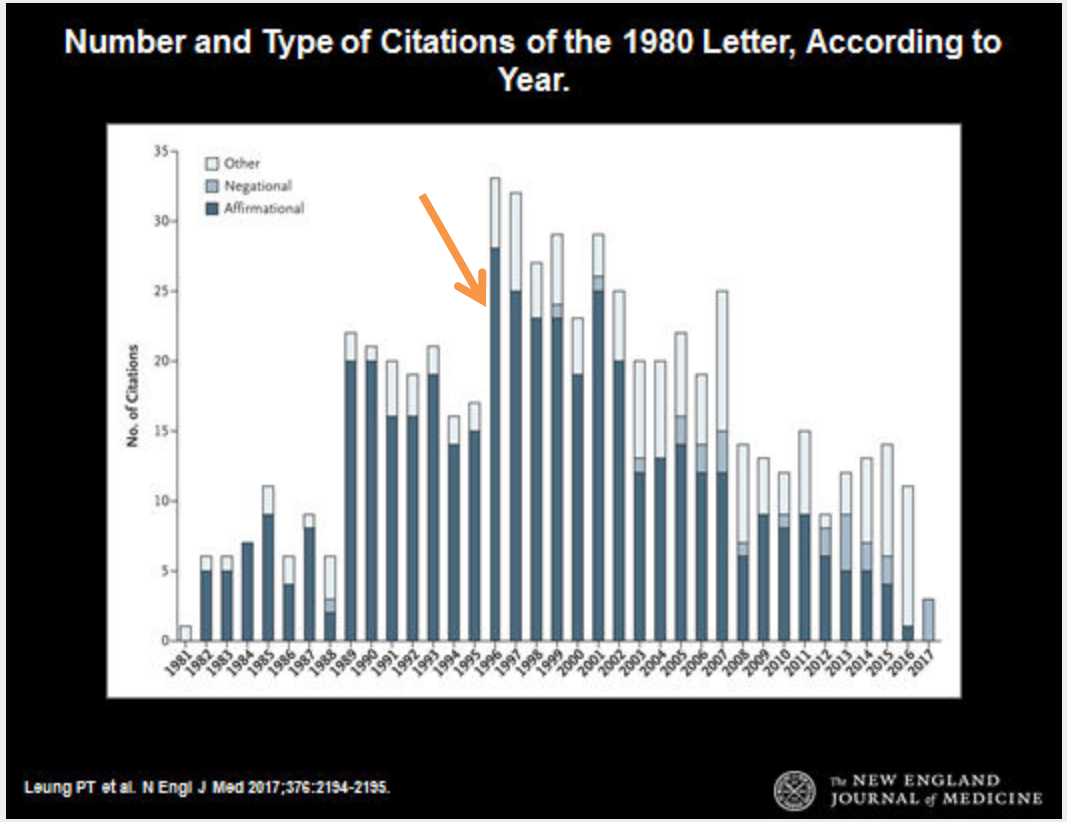
“Perfect Storm”

ADDICTION RARE IN PATIENTS TREATED WITH NARCOTICS

To the Editor: Recently, we examined our current files to determine the incidence of narcotic addiction in 39,946 hospitalized medical patients[1] who were monitored consecutively. Although there were 11,882 patients who received at least one narcotic preparation, there were only four cases of reasonably well documented addiction in patients who had no history of addiction. The addiction was considered major in only one instance. The drugs implicated were meperidine in two patients,[2] Percodan in one, and hydromorphone in one. We conclude that despite widespread use of narcotic drugs in hospitals, the development of addiction is rare in medical patients with no history of addiction.

JANE PORTER
HERSHEL JICK, M.D.
Boston Collaborative Drug Surveillance Program
Waltham, MA 02154 Boston University Medical Center

1. Jick H, Miettinen OS, Shapiro S, Lewis GP, Siskind Y, Slone D. Comprehensive drug surveillance. JAMA. 1970; 213:1455-60.
2. Miller RR, Jick H. Clinical effects of meperidine in hospitalized medical patients. J Clin Pharmacol. 1978; 18:180-8.



- **1980→ 2017: 608 citations** : ~75% used as evidence that addiction is rare with COT and made no mention that these were hospitalized patients with few doses of opioids.
- 11 other letters from 1980 were cited on average, 11 times.

N Engl J Med 1980; 302: 123.

N Engl J Med 376;22 June 2017

“Perfect Storm”

- 1995: Introduction of Oxycontin
- 1995: Pain is Fifth Vital Sign
- Publications indicating low risk of addiction
- Thought Leaders with Financial/Pharma Conflicts
- Patient Satisfaction Surveys: “…staff did everything they could to help you with your pain”
- Physicians successfully sued for not treating pain
- No Evidence for long term Effectiveness COT → CNCP
- Physical Dependence vs Addiction

Doctor liable for not giving enough pain medicine

June 14, 2001 Posted: 12:28 AM EDT (0428 GMT)



HAYWARD, California (CNN) -- In a civil case that could have broad ramifications for how patients in pain are treated, a California jury Wednesday found a doctor liable for recklessness and abuse for not prescribing enough pain medication to a patient, who later died of cancer.

The jury in Alameda County Superior Court called on the doctor to pay the patient's family $1.5 million dollars for pain and suffering of the patient. Under California law, however, the cap for such awards is $250,000, and the judge will likely reduce the jury's award.

A Doctor Who Prescribed 500,000 Doses of Opioids Is Sent to Prison for 40 Years

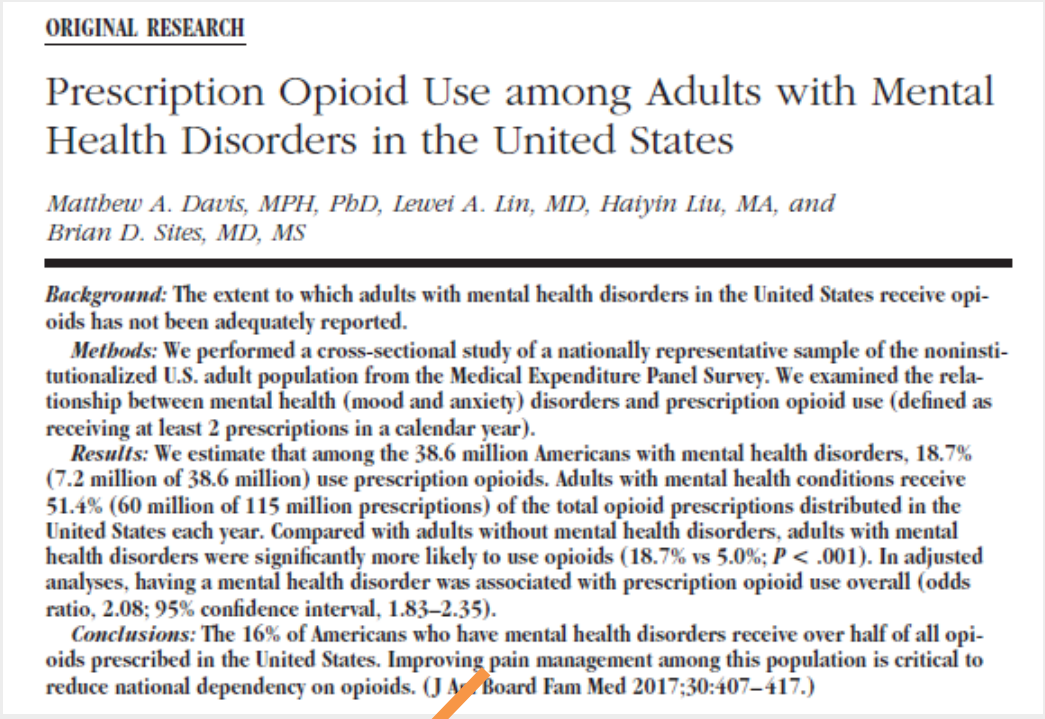
Dr. Joel Smithers was convicted of more than 800 counts of illegally prescribing opioids, and jurors found that the drugs he prescribed caused the death of a woman.



By Adeel Hassan

Oct. 2, 2019

A Virginia doctor who prescribed more than 500,000 doses of opioids in two years was sentenced to 40 years in prison on Wednesday for leading what prosecutors called an interstate drug distribution ring.



ORIGINAL RESEARCH

Prescription Opioid Use among Adults with Mental Health Disorders in the United States

Matthew A. Davis, MPH, PhD, Lewei A. Lin, MD, Haiyin Liu, MA, and Brian D. Sites, MD, MS

Background: The extent to which adults with mental health disorders in the United States receive opioids has not been adequately reported.

Methods: We performed a cross-sectional study of a nationally representative sample of the noninstitutionalized U.S. adult population from the Medical Expenditure Panel Survey. We examined the relationship between mental health (mood and anxiety) disorders and prescription opioid use (defined as receiving at least 2 prescriptions in a calendar year).

Results: We estimate that among the 38.6 million Americans with mental health disorders, 18.7% (7.2 million of 38.6 million) use prescription opioids. Adults with mental health conditions receive 51.4% (60 million of 115 million prescriptions) of the total opioid prescriptions distributed in the United States each year. Compared with adults without mental health disorders, adults with mental health disorders were significantly more likely to use opioids (18.7% vs 5.0%; $P < .001$). In adjusted analyses, having a mental health disorder was associated with prescription opioid use overall (odds ratio, 2.08; 95% confidence interval, 1.83–2.35).

Conclusions: The 16% of Americans who have mental health disorders receive over half of all opioids prescribed in the United States. Improving pain management among this population is critical to reduce national dependency on opioids. (J Am Board Fam Med 2017;30:407–417.)

Conclusions: **The 16% of Americans who have mental health disorders receive over half of all opioids prescribed in the United States.** Improving pain management among this population is critical to reduce national dependency on opioids.

Adverse Selection

J Am Board Fam Med 2017;30:407– 417

New Safety Measures Announced for Opioid Analgesics, Prescription Opioid Cough Products, and Benzodiazepines FDA: August 2016

Table 1. The Danger of Combining Opioids And Benzodiazepines

FDA Warning: Risks From Concomitant Use With Benzodiazepines or Other CNS Depressants

Concomitant use of opioids with benzodiazepines or other central nervous system (CNS) depressants, including alcohol, may result in profound sedation, respiratory depression, coma, and death.

- Reserve concomitant prescribing of (opioid) and benzodiazepines or other CNS depressants for use in patients for whom alternative treatment options are inadequate
- Limit dosages and durations to the minimum required
- Follow patients for signs and symptoms of respiratory depression and sedation

Source: US Food and Drug Administration website. Available at: http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm518697.

FDA Drug Safety Communication: FDA urges caution about withholding opioid addiction medications from patients taking benzodiazepines or CNS depressants: careful medication management can reduce risks

This provides updated information to the **FDA Drug Safety Communication: FDA warns about serious risks and death when combining opioid pain or cough medicines with benzodiazepines; requires its strongest warning (/Drugs/DrugSafety/ucm518473.htm)** issued on August 31, 2016.

Safety Announcement

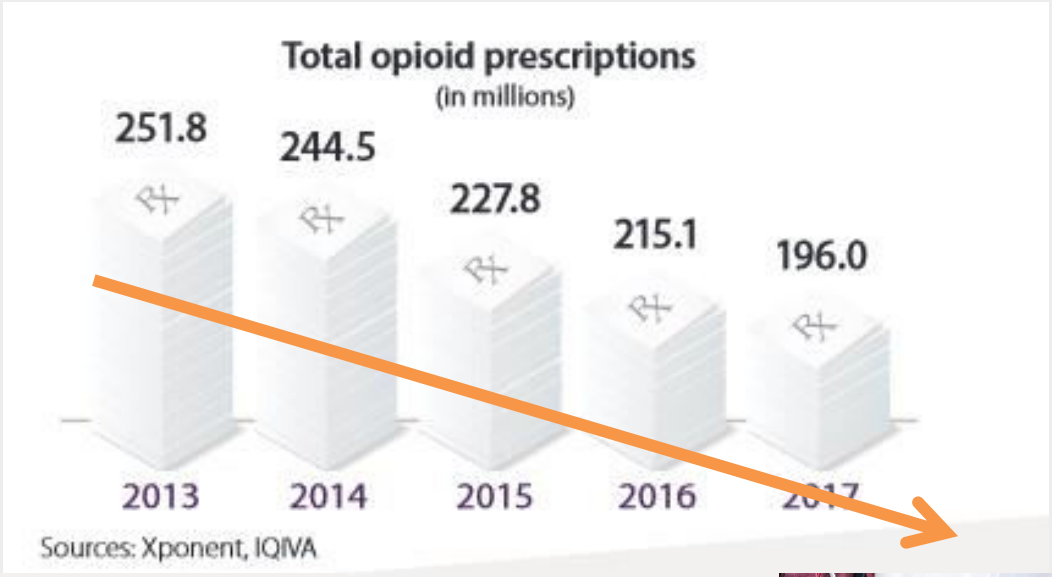
[9-20-2017] Based on our additional review, the U.S. Food and Drug Administration (FDA) is advising that the opioid addiction medications buprenorphine and methadone should not be withheld from patients taking benzodiazepines or other drugs that depress the central nervous system (CNS). The combined use of these drugs increases the risk of serious side effects; however, the harm caused by untreated opioid addiction can outweigh these risks. Careful medication management by health care professionals can reduce these risks. We are requiring this information to be added to the buprenorphine and methadone drug labels along with detailed recommendations for minimizing the use of medication-assisted treatment (MAT) drugs and benzodiazepines together.

Buprenorphine and methadone help people reduce or stop their abuse of opioids, including prescription pain medications and heroin. Methadone and buprenorphine have been shown to be effective in reducing the negative health effects and deaths associated with opioid addiction and dependency.[1] These medications are often used in combination with **counseling and behavioral therapies (https://www.samhsa.gov/medication-assisted-treatment/treatment#counseling-behavioral-therapies)**, and patients can be treated with them indefinitely. Buprenorphine and methadone work by acting on the same parts of the brain as the opioid that the patient is addicted to. The patient taking the medication as directed generally does not feel high, and withdrawal does not occur. Buprenorphine and methadone also help reduce cravings[2] (see Table 1. List of Buprenorphine and Methadone MAT Drugs).

Intended/Unintended Consequences in Reaction to the Prescription Opioid Epidemic

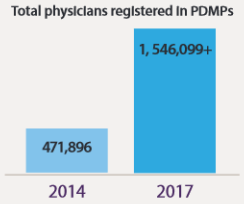
- Prescription Drug Monitoring Programs: PDMP
- Limits on the quantity and dosage prescribed
- UDTs become standard of care
- Education of prescribers: FDA REMS course on Safe and Effective Opioid Mgt.
- CDC Guidelines
- Tamper Resistant/Abuse Deterrent Formulations
- Patients Physically Dependent on Opioids Left in the Lurch
- HEROIN: Cheaper, Readily Accessible
- FENTANYL/Fentanyl Analogues

Physicians' Progress to Reverse the Nation's Opioid Epidemic
AMA Opioid Task Force 2018 Progress Report

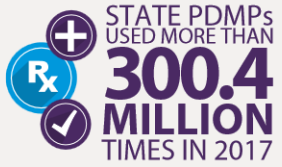


As PDMPs improve, America's physicians and health care professionals are using state PDMPs more than ever.

Prescription drug monitoring programs (PDMPs) are databases used to help inform physicians' clinical decisions. To optimize PDMP use, the AMA advocates for PDMPs to be integrated into physicians' clinical workflow to provide data at the point of care.



Today, more than **1.5 million** physicians and other health care professionals are registered in state-based PDMPs. Between 2016 and 2017, more than **241,000** individuals registered.[2]



Physicians and other health care professionals made more than **300.4 million PDMP queries** in 2017—a **121 percent increase** from 2016 and a **389 percent increase** from 2014.[3]



The AMA Opioid Task Force encourages all physicians to enhance their education.

In 2017, more than

549,700 PHYSICIANS

AND OTHER HEALTH CARE PROFESSIONALS

across the nation completed continuing medical education (CME) trainings and accessed other education resources offered by the AMA, state and specialty societies.

Physicians are helping to improve access to high-quality, evidence-based treatment for opioid use disorder.

There are now **more than 50,000** physicians certified to provide in-office buprenorphine for the treatment of opioid use disorder across all 50 states—a **42.2 percent increase** in the past 12 months.[7]

The AMA is encouraged that in the past year, nearly 15,000 physicians have become trained and certified to provide in-office buprenorphine.

To help ensure patients receive care, health insurance companies, Medicaid, and other payers must now remove administrative barriers, such as prior authorization for medication assisted treatment (MAT).

Journal of Pain Research

Dovepress
open access to scientific and medical research

Open Access Full Text Article

EDITORIAL

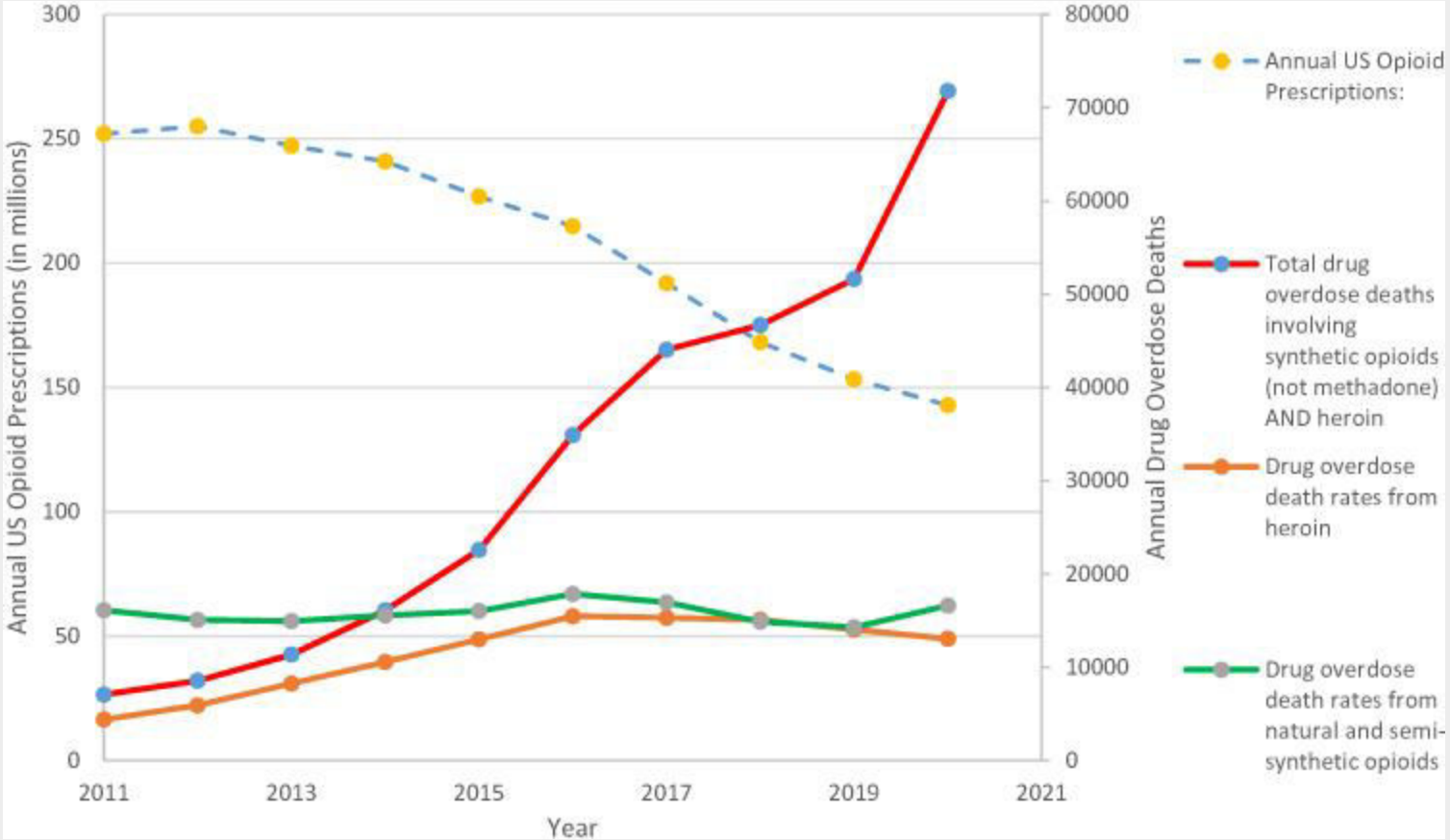
Misinterpretation of the "Overdose Crisis" Continues to Fuel Misunderstanding of the Role of Prescription Opioids

Jeffrey J Bettinger[1], William Amarquaye[2], Jeffrey Fudin[3–6], Michael E Schatman[7–9]

[1]Saratoga Hospital Medical Group, Saratoga Springs, NY, USA; [2]HCA Florida Brandon Hospital, Brandon, FL, USA; [3]President, Remitigate Therapeutics, Delmar, NY, USA; [4]Department of Pharmacy Practice, Albany College of Pharmacy & Health Sciences, Albany, NY, USA; [5]Department of Pharmacy Practice, Western New England University College of Pharmacy, Springfield, MA, USA; [6]Department of Pharmacy and Pain Management, Stratton VA Medical Center, Albany, NY, USA; [7]Department of Anesthesiology, Perioperative Care, and Pain Medicine, NYU Grossman School of Medicine, New York, NY, USA; [8]Department of Population Health – Division of Medical Ethics, NYU Grossman School of Medicine, New York, NY, USA; [9]School of Social Work, North Carolina State University, Raleigh, NC, USA

Correspondence: Michael E Schatman, Department of Anesthesiology, Perioperative Care, and Pain Medicine, NYU Grossman School of Medicine, 550 1st Ave., New York, NY, 10016, USA, Tel +425-647-4880, Email Michael.Schatman@NYULangone.org

Changes in Annual Opioid Prescriptions Compared to Overdose Death Rates from Different Types of Opioids



Journal of Pain Research 2022:15 949–958

CDC Guidelines:Opioids/Pain: 2016 vs 2022

- Similar Recommendations on Opioids as the last option for chronic pain and in many cases of acute pain. Always start with IR opioids for the shortest duration and lowest effective dose.
- Change in Tone: These are guidelines. Use Clinical Individualized Patient-Centered Judgments as to duration, dose, risk/benefit of COT, and need for tapering
- These Guidelines are not to be used by health systems, pharmacies, insurance companies, medical boards, or governments to determine standard of care

Start With Non-Pharmacologic Therapy

- Physical Therapy, Exercise
- Cold, Heat
- CBT, MI
- Meditation, Mindfulness
- Acupuncture
- Biofeedback
- Massage
- Aquatic Therapy
- Spinal Cord Stimulation (SCS)

Next Option: Non-Opioid Pharmacotherapy

- Acetaminophen (Efficacy), NSAIDS (Adverse Effects, Cardiac, Elderly)
- Anti-Depressants: TCAs, SSRIs, SNRIs
  - Neuropathic Pain, Nociplastic Pain (e.g., Fibromyalgia), Pain + Depression
- Anti-Convulsants: Gabapentanoids, Topiramate, Carbamazepine
  - Neuropathic Pain, Nociplastic Pain, Migraine Prophylaxis
- Topicals: Lidocaine Patch, NSAIDS, Capsaicin
- "Muscle Relaxants:" Baclofen, Cyclobenzadrine, Methocarbamol, Tizanidine
  - Avoid Benzodiazepines, Carisoprodol (Schedule IV)
- Ketamine: Acute Pain (e.g., ED)
- Interventional Procedures: Epidurals, Nerve Blocks, Neuro-Modulation

Novel Non-Opioid Analgesic

Pain Ther
https://doi.org/10.1007/s40122-024-00697-0

ORIGINAL RESEARCH

Pharmacology and Mechanism of Action of Suzetrigine, a Potent and Selective $Na_V1.8$ Pain Signal Inhibitor for the Treatment of Moderate to Severe Pain

Jeremiah D. Osteen · Swapna Immani · Tim L. Tapley · Tim Indersmitten · Nicole W. Hurst · Tiffany Healey · Kathleen Aertgeerts · Paul A. Negulescu · Sandra M. Lechner

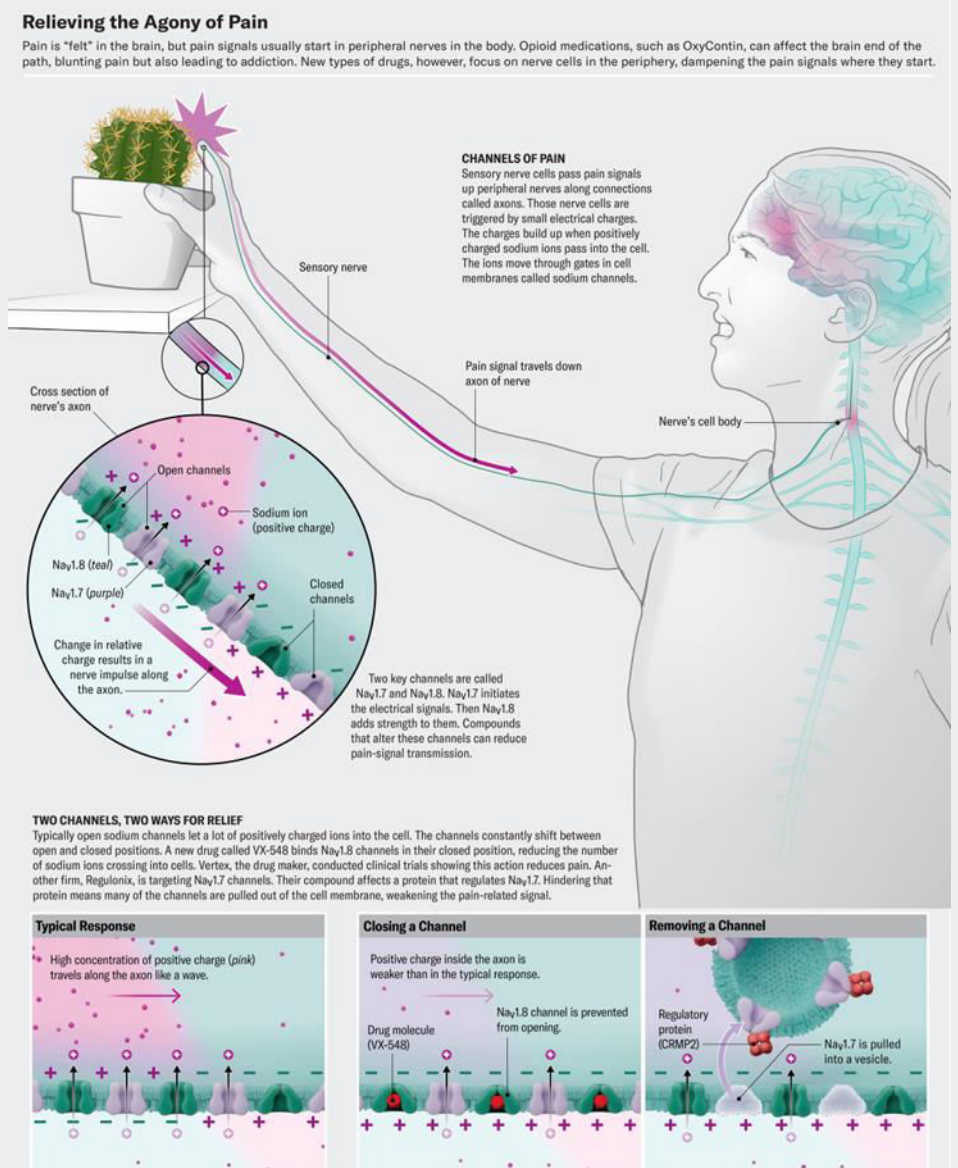
PNAS
RESEARCH ARTICLE | PHARMACOLOGY
BIOPHYSICS AND COMPUTATIONAL BIOLOGY

Nav1.8, an analgesic target for nonpsychotomimetic phytocannabinoids

CBD, **CBG**, CBN

Mohammad-Reza Ghovanloo[a,b,c,1], Sidharth Tyagi[a,b,c,d], Peng Zhao[a,b,c], and Stephen G. Waxman[a,b,c,1]

Edited by Donald Pfaff, Rockefeller University, New York, NY; received August 19, 2024; accepted December 5, 2024



Gabapentanoids: Conclusions

- Significant Misuse Among Patients with SUDs, Primarily OUD Receiving Methadone or Buprenorphine Maintenance.
- Significant Adverse Effects With Therapeutic Doses, and Increased Adverse Effects With Supra-Therapeutic Doses
- Must Adjust for **Renal Function**
- Full Recovery From Adverse Effects Is The Rule
- Death Is Uncommon, But Increased In Combination With Opioids
- Gabapentin Bioavailability ↓ With Increasing Dose (Zero Order PK)
- Weak Evidence For Off Label Pain Treatment
- Should Gabapentin Be Listed On PDMPs (e.g., Ohio, NJ)
- Pregabalin Schedule 5 listed
- Add Gabapentanoids To UDT Screens?

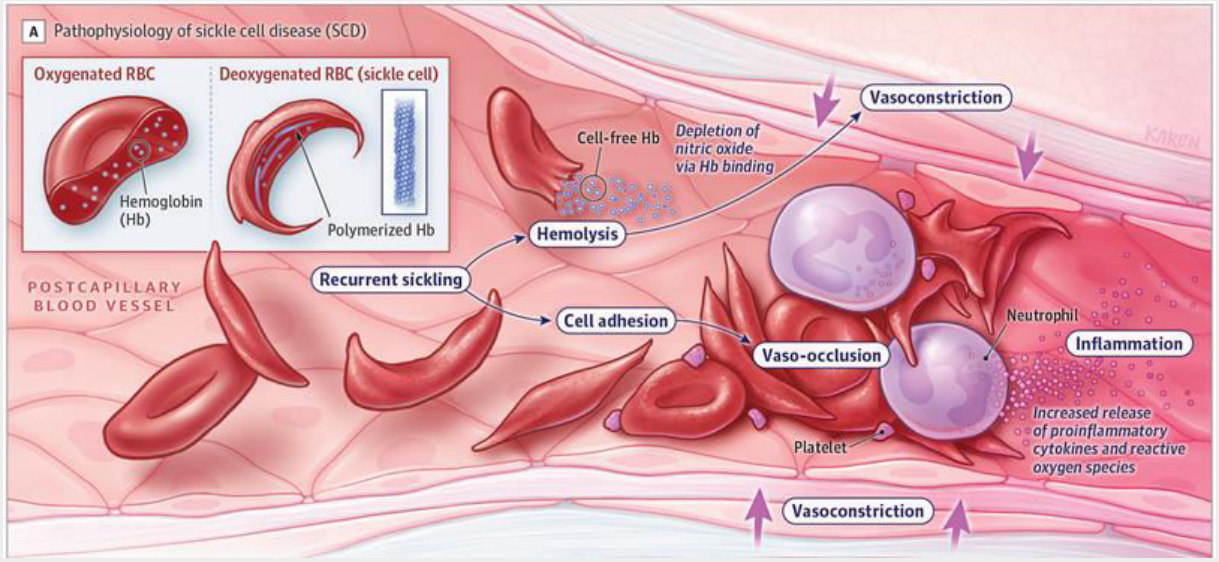
Opioid Pharmacotherapy

- Acute Pain: e.g., Post-Operative, Burn, Severe Trauma
- Limit Duration: NYS-7days
- Cancer Pain
- Palliative Care, Hospice
- End of Life Care
- **Sickle Cell Disease 2022 Guidelines**

- Chronic Opioid Therapy (COT) for
  - Chronic Non-Cancer Pain (CNCP)
    - Effectiveness, Safety, Adverse Effects,
    - IR vs. ER

Special Mention: Sickle Cell Disease

- Severe Acute and Chronic Pain
- Reduced Life Expectancy
- Prejudice and Stigma
- Racial Disparities in Opioid Rx



- Placed in the Cancer, Palliative Care and End of Life Category in the 2022 Revised CDC Guidelines
- Increasing Evidence for Buprenorphine Efficacy as COT



REVIEW

Annals of Internal Medicine

The Effectiveness and Risks of Long-Term Opioid Therapy for Chronic Pain: A Systematic Review for a National Institutes of Health Pathways to Prevention Workshop

Roger Chou, MD; Judith A. Turner, PhD; Emily B. Devine, PharmD, PhD, MBA; Ryan N. Hansen, PharmD, PhD; Sean D. Sullivan, PhD; Ian Blazina, MPH; Tracy Dana, MLS; Christina Bougatsos, MPH; and Richard A. Deyo, MD, MPH

Background: Increases in prescriptions of opioid medications for chronic pain have been accompanied by increases in opioid overdoses, abuse, and other harms and uncertainty about long-term effectiveness.

Purpose: To evaluate evidence on the effectiveness and harms of long-term (>3 months) opioid therapy for chronic pain in adults.

Data Sources: MEDLINE, the Cochrane Central Register of Controlled Trials, the Cochrane Database of Systematic Reviews, PsycINFO, and CINAHL (January 2008 through August 2014); relevant studies from a prior review; reference lists; and ClinicalTrials.gov.

Study Selection: Randomized trials and observational studies that involved adults with chronic pain who were prescribed long-term opioid therapy and that evaluated opioid therapy versus placebo, no opioid, or nonopioid therapy; different opioid dosing strategies; or risk mitigation strategies.

Data Extraction: Dual extraction and quality assessment.

Data Synthesis: No study of opioid therapy versus no opioid therapy evaluated long-term (>1 year) outcomes related to pain, function, quality of life, opioid abuse, or addiction. Good- and fair-quality observational studies suggest that opioid therapy for chronic pain is associated with increased risk for overdose, opioid abuse, fractures, myocardial infarction, and markers of sexual dysfunction, although there are few studies for each of these outcomes; for some harms, higher doses are associated with increased risk. Evidence on the effectiveness and harms of different opioid dosing and risk mitigation strategies is limited.

Limitations: Non–English-language articles were excluded, meta-analysis could not be done, and publication bias could not be assessed. No placebo-controlled trials met inclusion criteria, evidence was lacking for many comparisons and outcomes, and observational studies were limited in their ability to address potential confounding.

Conclusion: Evidence is insufficient to determine the effectiveness of long-term opioid therapy for improving chronic pain and function. Evidence supports a dose-dependent risk for serious harms.

Primary Funding Source: Agency for Healthcare Research and Quality.

Ann Intern Med. 2015;162:276-286. doi:10.7326/M14-2559 **www.annals.org**
For author affiliations, see end of text.
This article was published online first at www.annals.org on 13 January 2015.

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Initiating Opioid Treatment: CNCP

- Prescribers should regard initial treatment as a therapeutic trial
  - May last from several weeks to several months; start with IR Opioid
  - Decision to proceed w/ long-term treatment should be intentional and based on careful consideration of outcomes during the trial
    - Progress toward meeting therapeutic goals
    - Functional Improvement
    - Presence of opioid-related adverse effects
    - Changes in underlying pain condition
    - Changes in psychiatric or medical comorbidities
    - Identification of problematic drug-related behavior, addiction, or diversion

Chou R, et al. J Pain. 2009;10:113-30.

Can You Land the Opioid Plane?



Opioid Tapering/Deprescribing Strategies

- Patient Requests/Agrees vs Patient Resists
- Alternative Treatment if Pain Still Present
- Clonidine/Lofexidine Tablets and Patches
  - alpha 2 centrally acting adrenergic agonists→ ↓LC→ ↓NE
- Switch to Methadone
- Switch to Buprenorphine
- Symptomatic Meds: NSAIDS, Loperamide, Benzos(short course), non-benzo sleep meds
- Patients report favorable outcomes after tapering
- Opioid Induced Hyperalgesia

JAMA Internal Medicine May 2018 Volume 178, Number 5

The Journal of Pain, Vol 18, No 11 (November), 2017

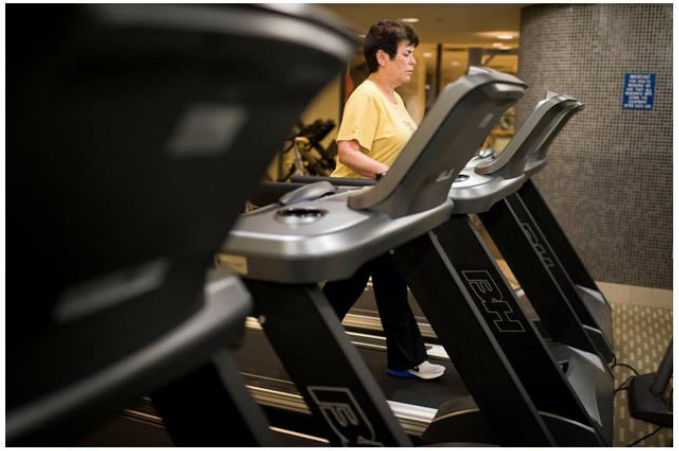


Dr. Alexis LaPietra used a non-opioid trigger point injection to treat Fausto Arce's muscle spasm, which was so painful he couldn't turn his head.
Mark Makela for The New York Times

New Opioid Limits Challenge the Most Pain-Prone



Paula Span
THE NEW OLD AGE JUNE 6, 2016



Irene Cohen, 69, may represent the future of older pain patients: less of a reliance on opioid painkillers and more of an emphasis on exercise and other nonmedicinal therapy.

Patients in Pain, and a Doctor Who Must Limit Drugs

By JAN HOFFMAN MARCH 16, 2016



FDA identifies harm reported from sudden discontinuation of opioid pain medicines and requires label changes to guide prescribers on gradual, individualized tapering

FDA Drug Safety Communication

Safety Announcement

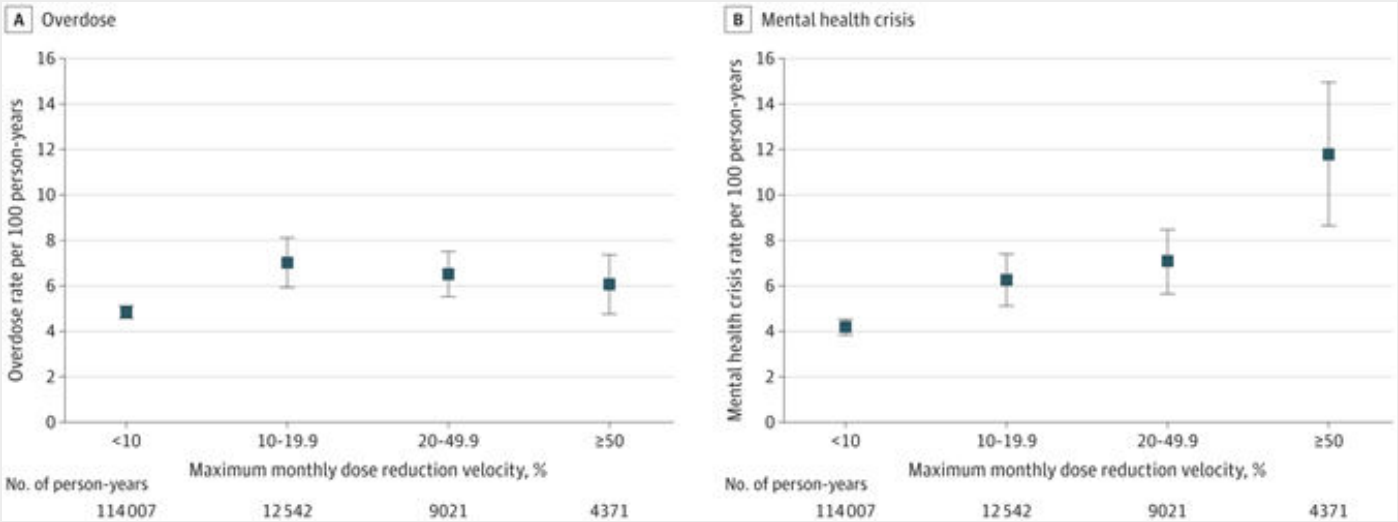
[4-9-2019] The U.S. Food and Drug Administration (FDA) has received reports of serious harm in patients who are physically dependent on opioid pain medicines suddenly having these medicines discontinued or the dose rapidly decreased. These include serious withdrawal symptoms, uncontrolled pain, psychological distress, and suicide.

The U.S. Food and Drug Administration (FDA) has received reports of serious harm in patients who are physically dependent on opioid pain medicines suddenly having these medicines discontinued or the dose rapidly decreased. **These include serious withdrawal symptoms, uncontrolled pain, psychological distress, and suicide.**

JAMA | Original Investigation

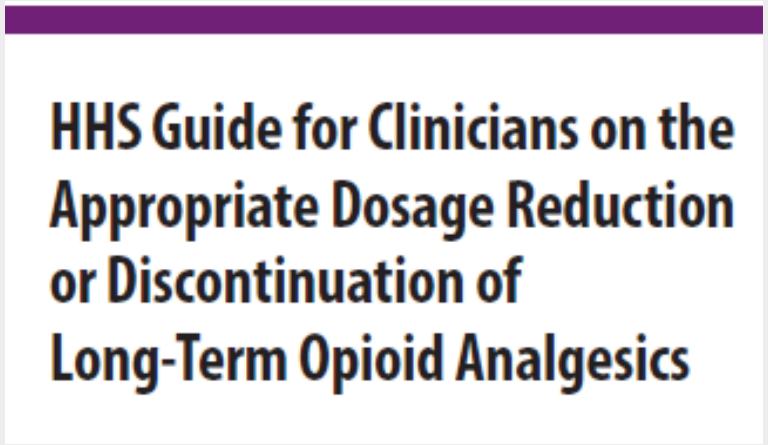
Association of Dose Tapering With Overdose or Mental Health Crisis Among Patients Prescribed Long-term Opioids

Alicia Agnoli, MD, MPH, MHS; Guibo Xing, PhD; Daniel J. Tancredi, PhD; Elizabeth Magnan, MD, PhD; Anthony Jerant, MD; Joshua J. Fenton, MD, MPH



CONCLUSIONS: Among patients prescribed stable, long-term, higher-dose opioid therapy, tapering events were significantly associated with increased risk of overdose and mental health crisis

JAMA. 2021;326(5):411-419



Oct. 2019

- The CDC Guideline for Prescribing Opioids for Chronic Pain **does not recommend opioid discontinuation when benefits of opioids outweigh risks.**
- Avoid misinterpreting cautionary dosage thresholds. Guideline recommends avoiding or carefully justifying increasing dosages **above 90 MME/day, it does not recommend abruptly reducing opioids from higher dosages.**
- **Avoid dismissing patients from care.**
- **Reinforced in the 2022 Guidelines**

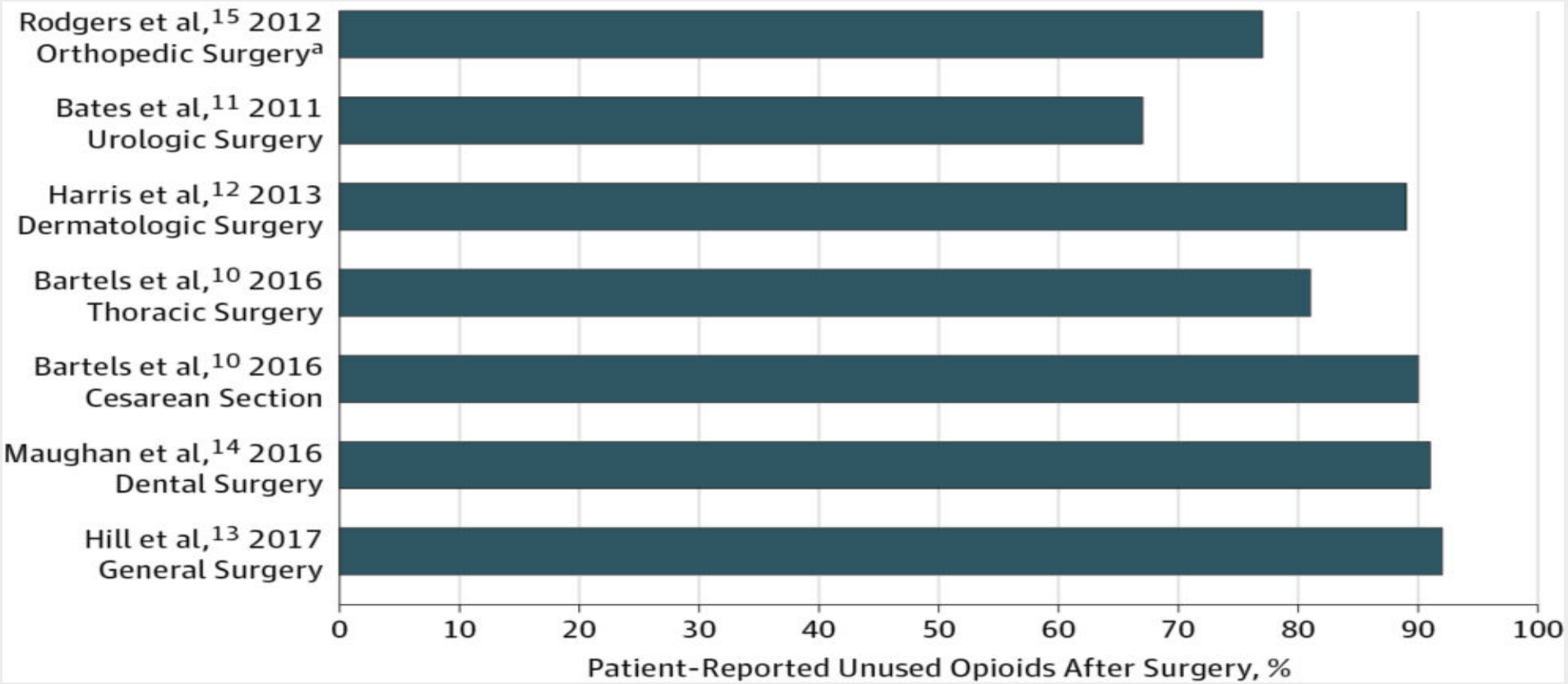
Cannabis and Cannabinoids

- **Chronic Noncancer Pain:** The International Association for the Study of Pain, the American College of Physicians (ACP), and the Canadian Rheumatology Association (CRA) **recommend against use of cannabis or cannabinoids as first-line treatment for chronic noncancer pain due to limited evidence of benefit and well-documented risks.** The **ACP and CRA recommend against use of inhaled cannabis to treat chronic noncancer pain** because the risk of adverse effects such as chronic bronchitis and exposure to contaminants likely outweigh the benefits.
- **Cancer Pain**: The 2024 ASCO guidelines state that there is **currently insufficient evidence to recommend for or against use of cannabis or cannabinoids to treat cancer pain.**
- **Nabiximols:** Standardized botanical extract with a THC:CBD 1:1 Ratio. Not FDA Approved in USA. Sativex buccal spray for MS spasticity. Some studies show reduction in neuropathic pain.
- **Psychiatric Indications:** The American Psychiatric Association and American Society of Addiction Medicine **recommend against use of cannabis or cannabinoids to treat any psychiatric disorder and emphasize that cannabis may exacerbate or precipitate mental illness, particularly psychosis and suicidality in individuals with depression**
- **Opioid Use Disorder:** Four studies (132 participants) examined the efficacy of cannabinoids among people with an opioid use disorder Random effects meta-analysis **revealed no significant effect on withdrawal symptoms or opioid craving**

JAMA 2026;335;(4):345-359
Lancet Psychiatry, Volume 13, Issue 4, Pages 304-315

From: **Prescription Opioid Analgesics Commonly Unused After Surgery: A Systematic Review**

JAMA Surg. Published online August 02, 2017.



Opioid Rx Disposal

- DEA Take Back Programs
- Some Pharmacies, Some Police Stations
- Mix with cat litter/coffee grounds, then seal in plastic bag and throw out in trash
- Flush down toilet: environmental issues
  - Fentanyl Patch: Flush only
- DO NOT throw out in trash in Rx bottle

Co-Prescribe Naloxone Formulations











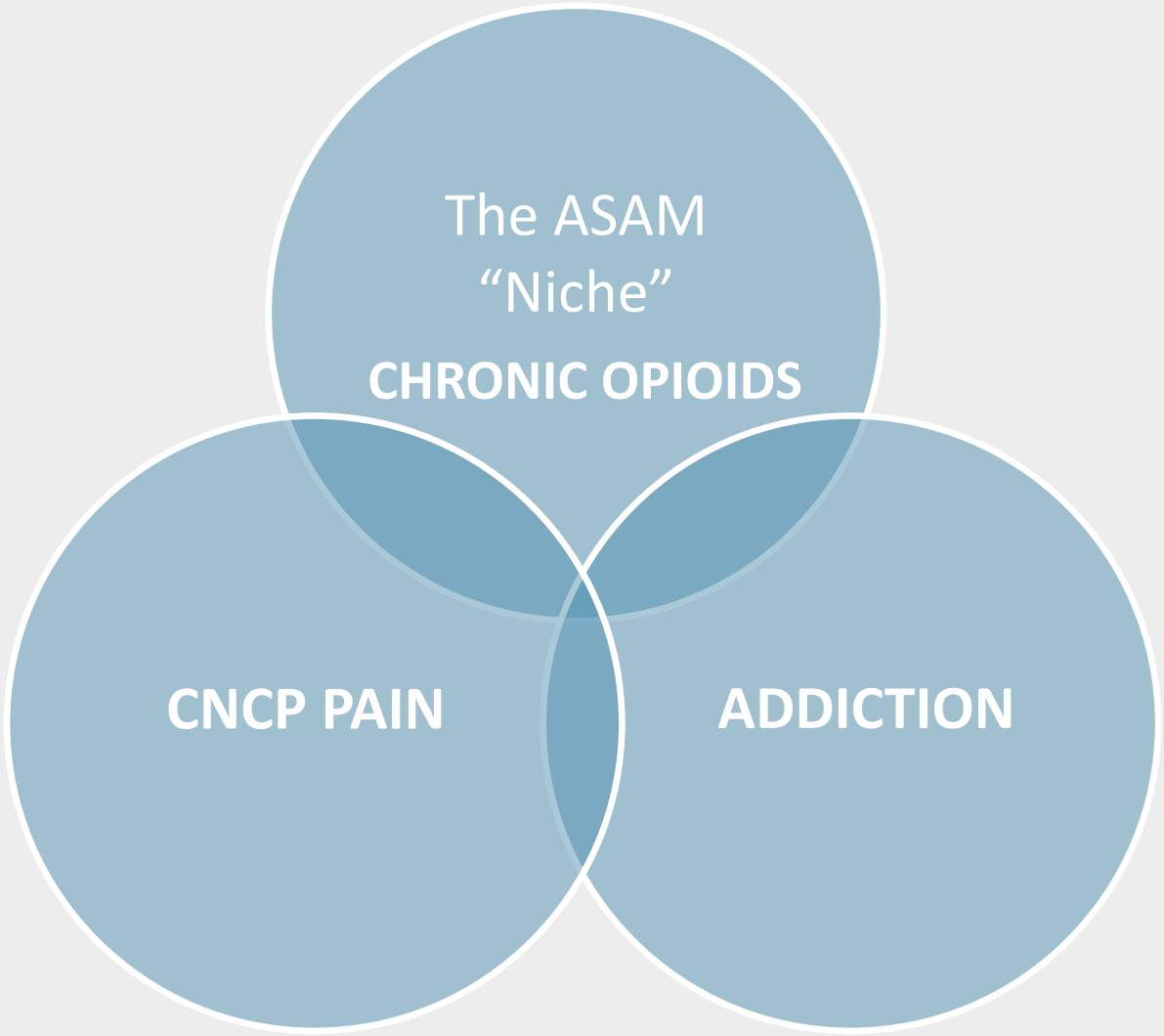
Naloxone 5mg



Nalmefene



Complex Intersection

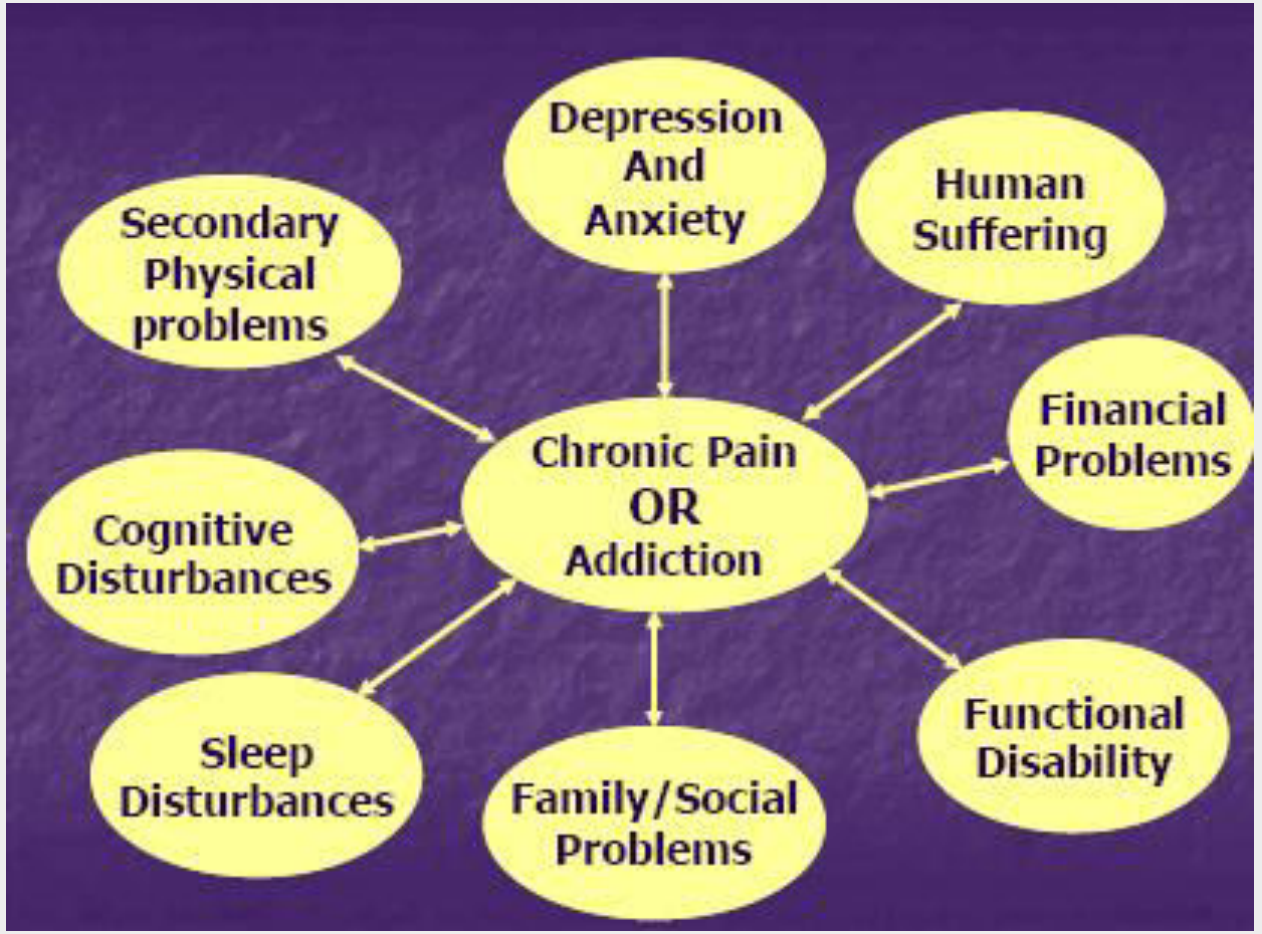


Pain and Addiction: Definitions

- "Pain is viewed as a biopsychosocial phenomenon that includes **sensory, emotional, cognitive, developmental, behavioral, spiritual and cultural components."** (IASP website)

- Addiction is a treatable, chronic medical disease involving **complex interactions among brain circuits, genetics, the environment, and an individual's life experiences.** People with addiction use substances or engage in behaviors that become compulsive and often continue despite harmful consequences.

Pain and Addiction



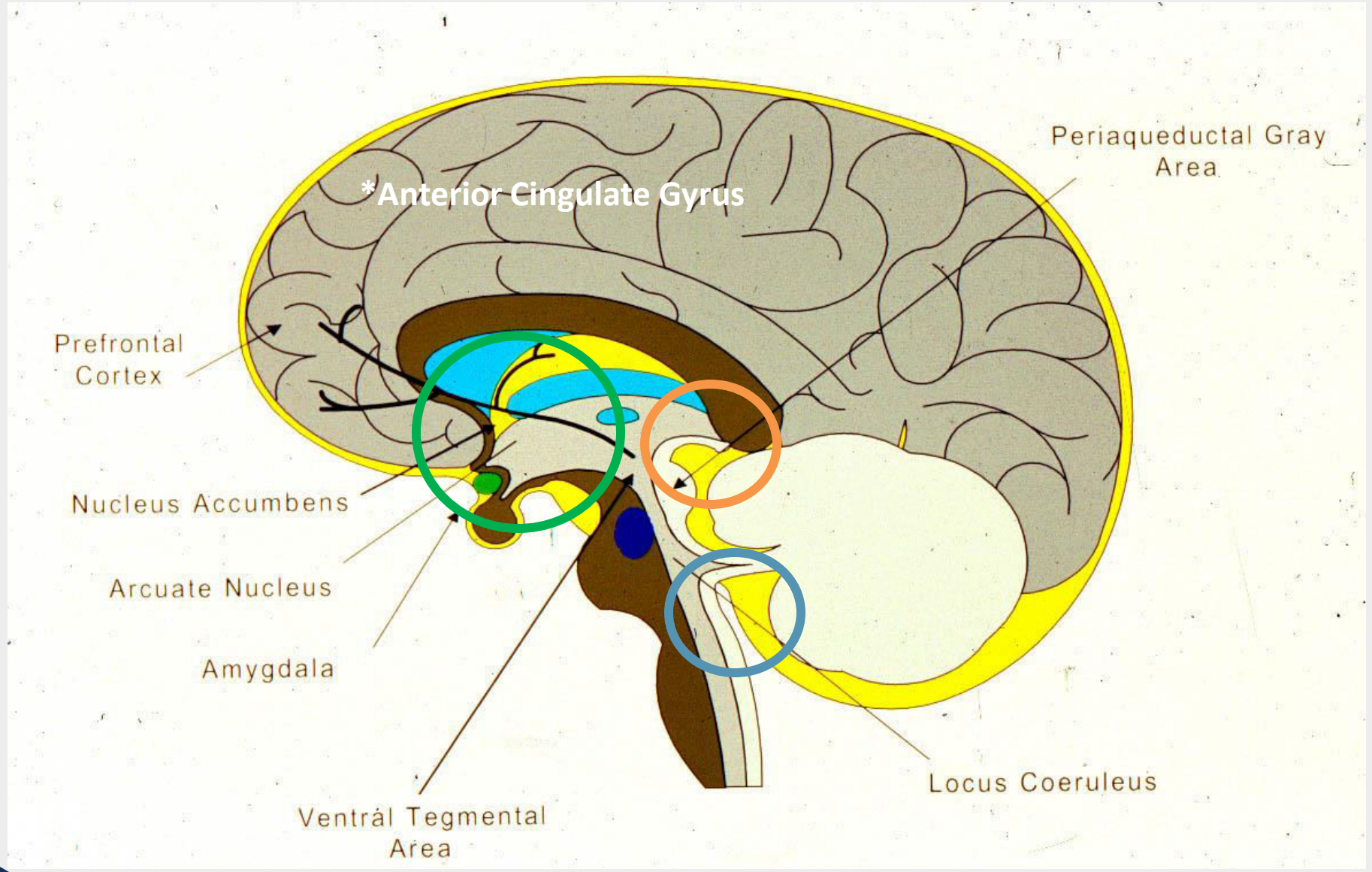
Ann Quinlan-Colwell, PhD, PCSS-O Webinar. 2011.

Pain and Addiction
Limited (e.g., UDT) Objective Measurements





Opioid Sites of Action in the Brain



“Exaggerated Response”
What Did It Feel Like The First Few Times?

- “All my problems disappeared.”
- “Felt like I was under a warm blanket.”
- “Thought this is how normal people feel.”
- “Forgot about all the abuse.”
- “Felt like the world was at peace.”
- “Totally relaxed.” “Not shy.”
- “Looking at a beautiful sunset.”
- “I was energized!”
- *Liking opioids: this is a vulnerability.*

Treating Pain in the Addicted Patient

- "Pain patients with a coexisting SUD are among the most challenging patients in medicine."
- Universal Precautions
- "Real Pain" may make opioids less rewarding/euphorogenic
- Addicted Patients Have Pain: Trauma, Lower Thresholds, Medical
- Screening Tests: ORT, SOAPP, others
- Untreated Pain is a trigger for relapse:
- Address both pain and addiction: **Consider the Bupe Formulations approved for OUD**

- Significant other to secure and dispense opioid medications
- Psychiatric Co-morbidity
- Active Addiction recovery program
- UTOX, pill counts, agreements, etc.
- Multidisciplinary Pain Program

Bailey, et al. Pain Medicine 2010; 11: 1803-1818

Treating Acute Pain in Patients On Methadone or Buprenorphine Maintenance

- The Maintenance Opioid Medication Will NOT Provide Adequate Analgesia
- Maintain the PO or SL Maintenance Dose of Methadone or Buprenorphine and Divide the Total Dose to TID/QID to Obtain Maximum Analgesic Effect
- Utilize IR Opioids (PCA, IV and PO) Consider Hydromorphone as Most Potent Oral IR Opioid
- Taper IR Opioid as Tolerated and Maintain Maintenance Medication
- There is No Need to Taper SL Buprenorphine Prior to Surgery (May Require Discussion with Surgery and Anesthesia)
- Patient on Buprenorphine-XR Formulations:
  - Currently only case reports: Multimodal Analgesia—opioids, non-opioid analgesics, regional anesthesia
  - If Surgery Elective Schedule at Trough Level of Bupe-XR Formulation: Monthly vs. Weekly
  - Product Insert: Treatment of Emergent Acute Pain: Treat pain with a non-opioid analgesic whenever possible. If opioid therapy is required, monitor patients closely because higher doses may be required for analgesic effect. (Same wording for both formulations)

Buprenorphine Formulations: FDA Approved for Pain not OUD

- Buprenex® Parenteral (IV, IM)
- Butrans® Transdermal (7 Day, 5, 7.5, 10,15, 20 mcg/hr)
- Belbuca® Buccal Film (75—900mcg q12h)

- Approved for pain but **NOT** OUDs
- Can **NOT** be used OFF LABEL for OUDs: Violates DATA 2000

JAMA Network Open. 2021;4(9)

Original Investigation | Substance Use and Addiction

Evaluation of Buprenorphine Rotation in Patients Receiving Long-term Opioids for Chronic Pain

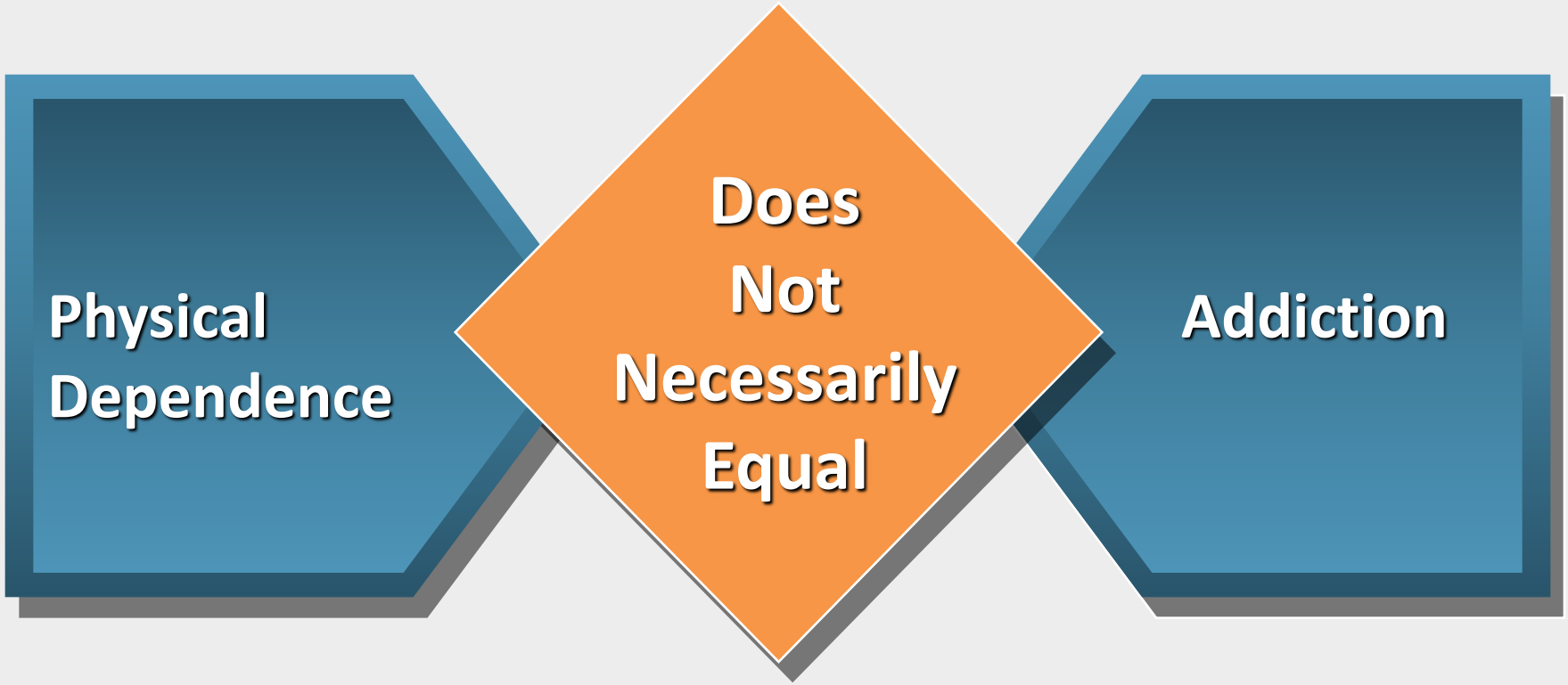
A Systematic Review

Victoria D. Powell, MD; Jack M. Rosenberg, MD; Avani Yaganti, BS; Claire Garpestad, MD; Pooja Lagisetty, MD, MSc; Carol Shannon, MPH; Maria J. Silveira, MD, MA, M

CONCLUSIONS AND RELEVANCE: In this systematic review, buprenorphine was associated with reduced chronic pain intensity without precipitating opioid withdrawal in individuals with chronic pain who were receiving LTOT. Future studies are necessary to ascertain the ideal starting dose, formulation, and administration frequency of buprenorphine as well as the best approach to buprenorphine rotation.

MEANING: These findings suggest that buprenorphine rotation may be a viable option for mitigating the harms of long-term opioid therapy in individuals with chronic pain who were receiving unsafe opioid analgesic regimens; further studies are needed to examine the best way to accomplish buprenorphine rotation.

Pain and Addiction

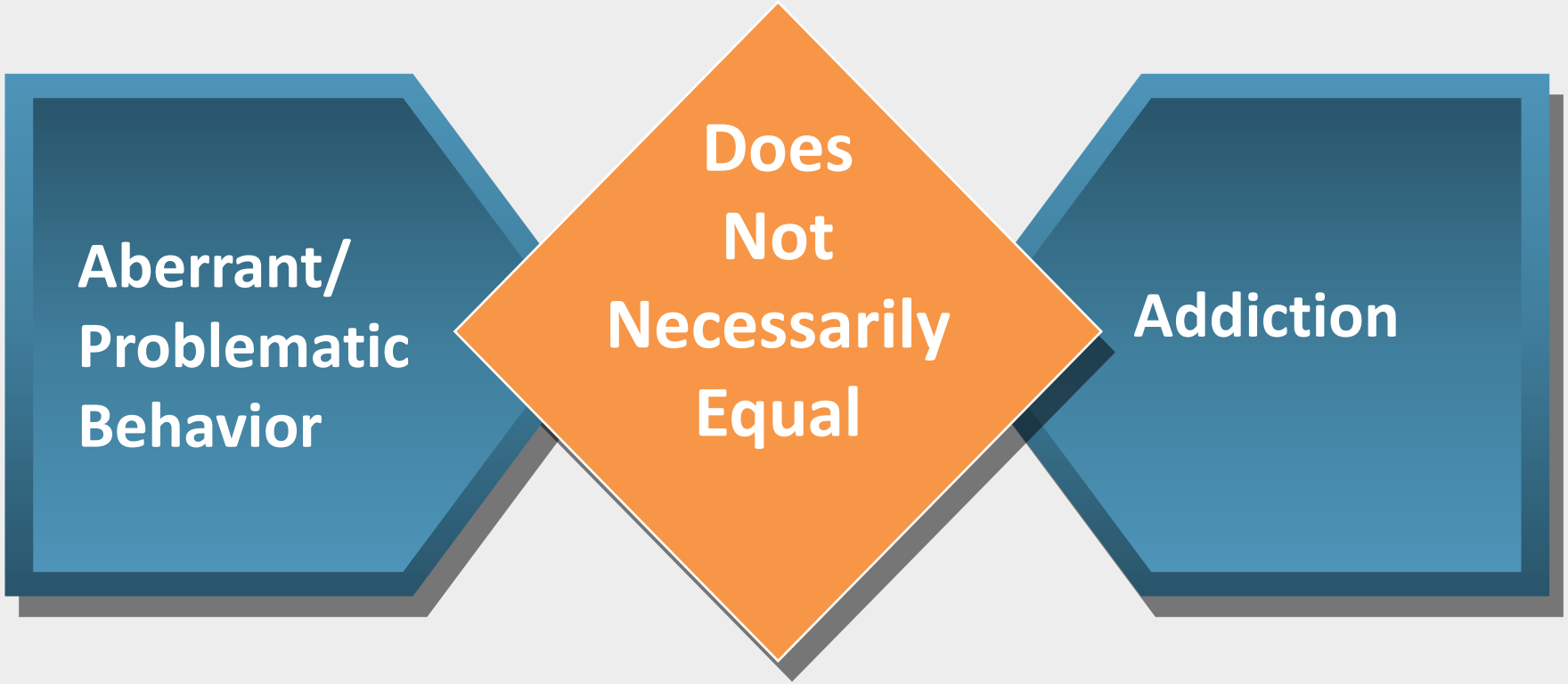


Definitions:
Complex Physical Dependence

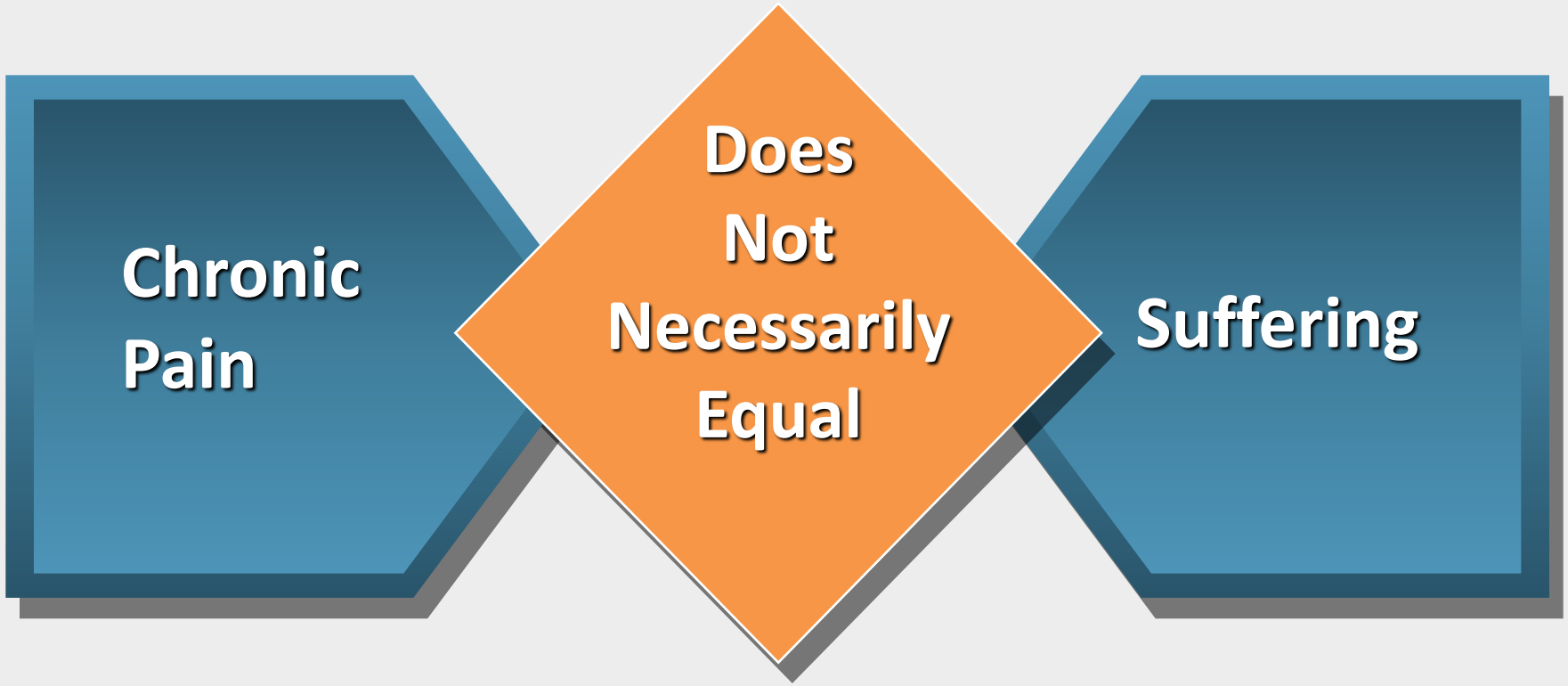
"Dependence on opioid pain treatment is not, as we once believed, easily reversible; it is a complex physical and psychological state that may require therapy similar to addiction treatment, consisting of structure, monitoring, and counseling, and possibly continued prescription of opioid agonists. Whether or not it is called addiction, **complex persistent prescription opioid dependence** is a serious consequence of long-term pain treatment that requires consideration when deciding whether to embark on long term opioid pain therapy as well as during the course of such therapy."

Opioid Dependence vs Addiction: A Distinction Without a Difference?
Ballantyne J, Sullivan M, Kolodny A, Arch Intern Med, 2012

Pain and Addiction

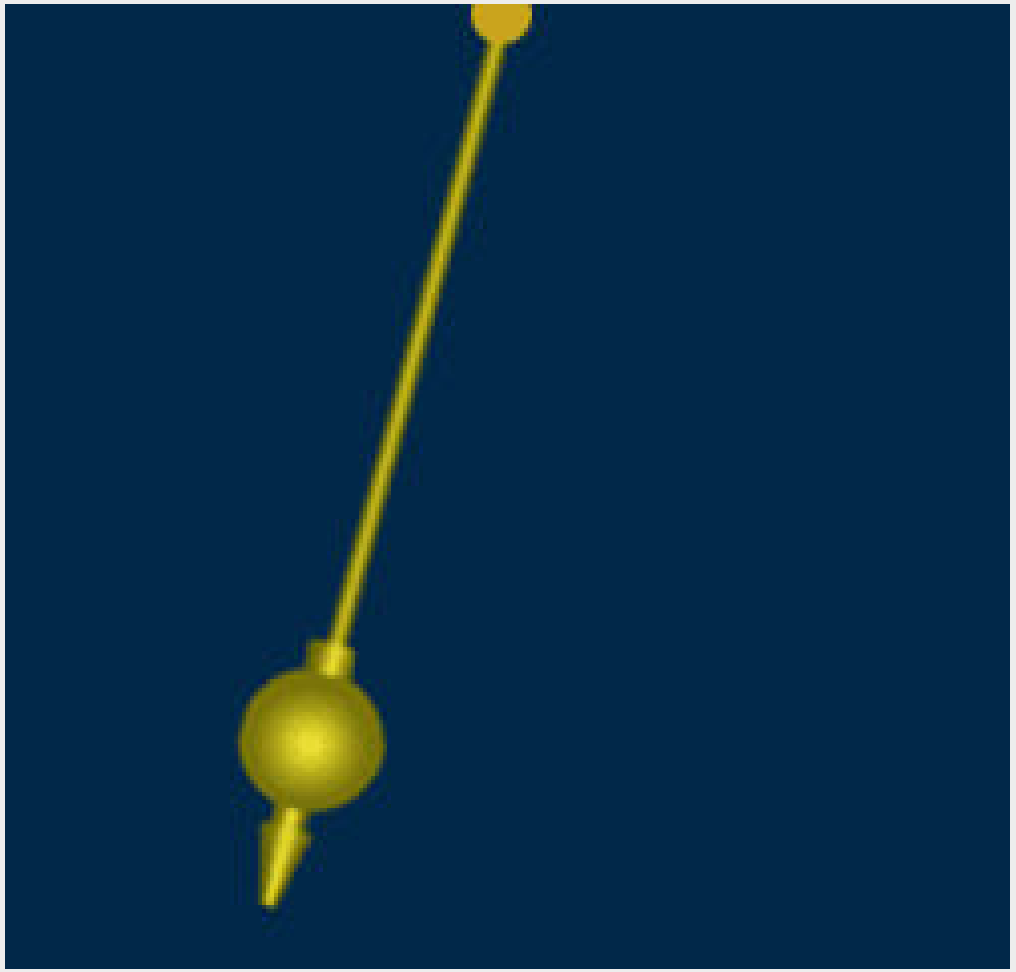


Pain and Addiction



Evolution Of Opioid Prescribing

Opioid Phobia



Opioid Philia

Opioid Cautious

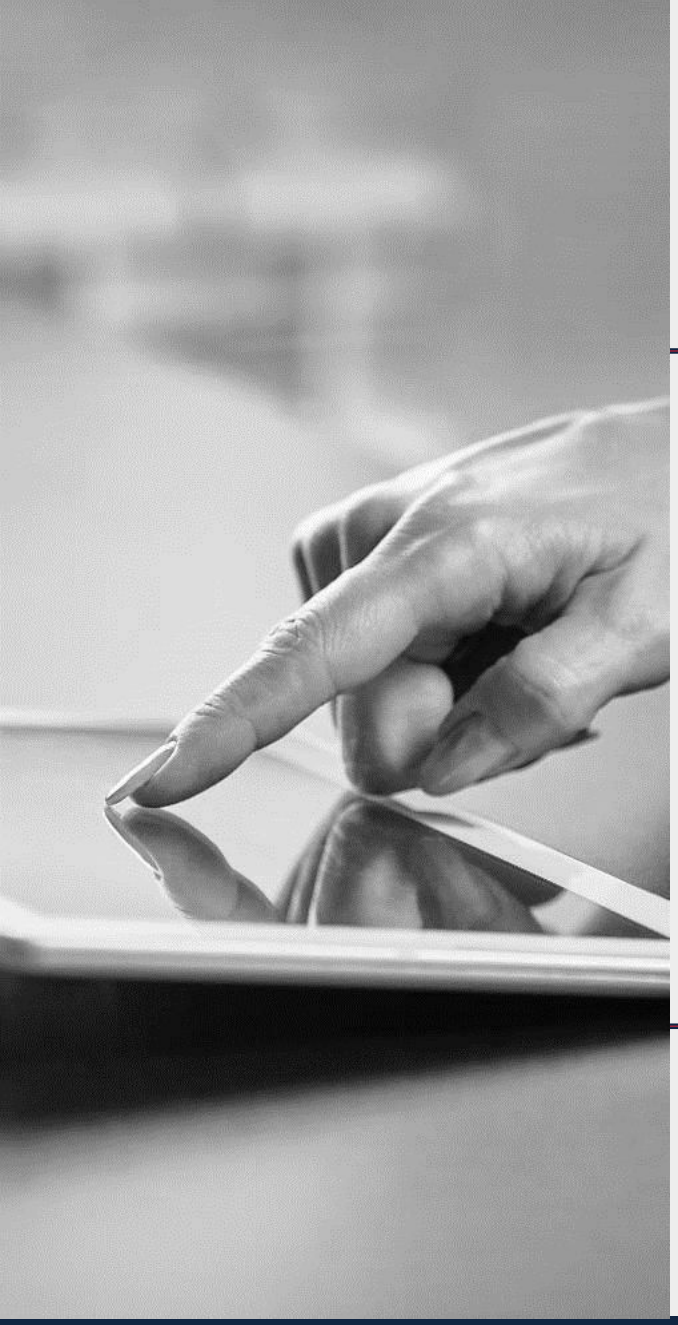
Multidimensional Pain Treatment

Pain Quotes

- "To have great pain is to have certainty. To hear that another person has pain is to have doubt." "Seeing Pain," Nicola Twilley (2018)
- "Physical Pain does not simply resist language, but actively destroys it." - "The Body in Pain" by Elaine Scarry (1985)
- "Morphine is God's own medicine" Sir William Osler
- We can't live without opioids; we have to learn to live with them.

Good luck on the exam and in your careers!





Get in Touch

301.656.3920

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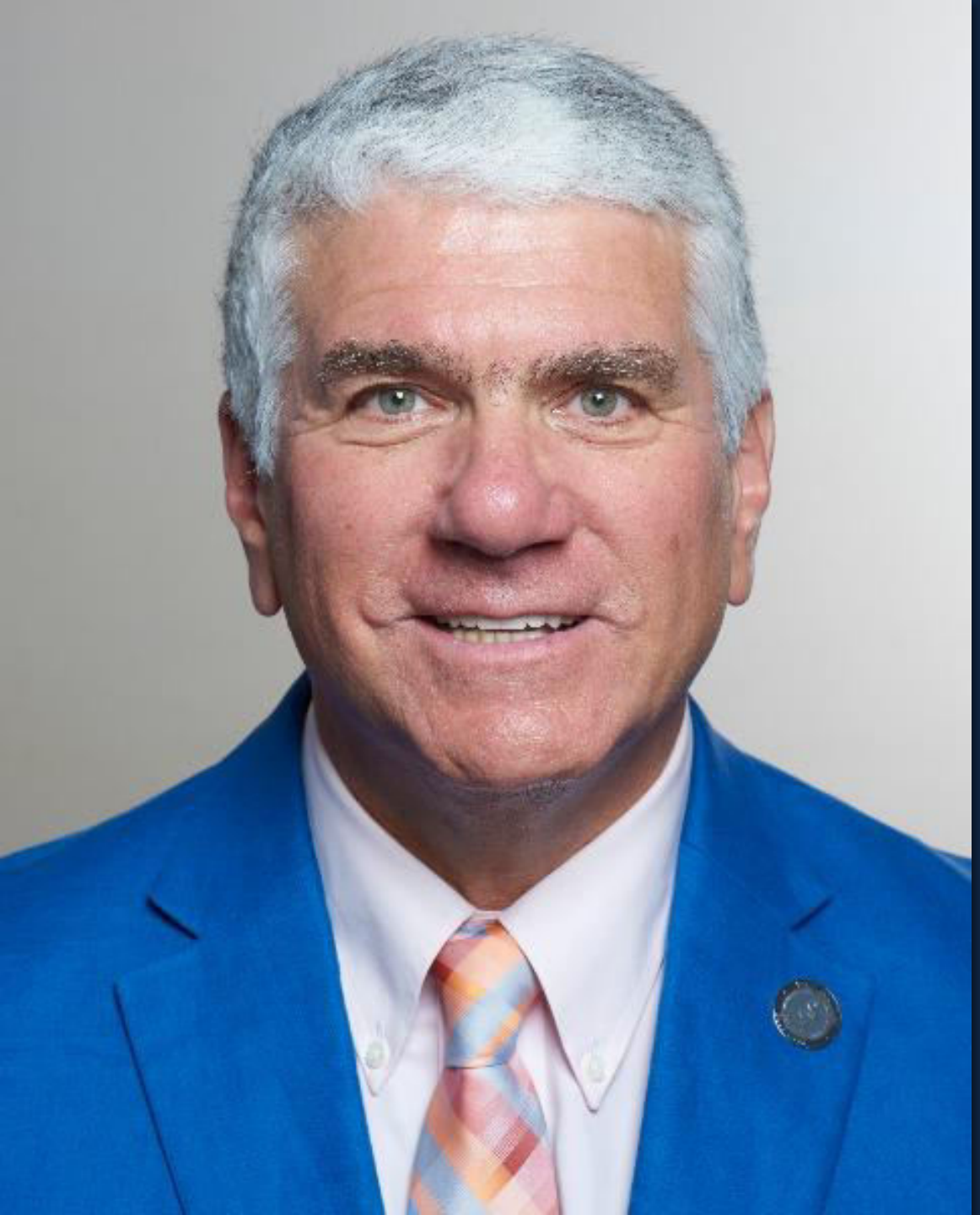
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ASAM REVIEW COURSE 2026

Interesting Cases: Applying Concepts to Unexpected Real-Life Scenarios

Edwin A. Salsitz, MD, DFASAM
Associate Clinical Professor
Mount Sinai Beth Israel
New York, NY





Financial Disclosure

Edwin A. Salsitz, MD, DFASAM

- No relevant disclosures

“Rapid Sudden Death” After IV Drug Use

Sudden Death IVDU

- 26 yo male
- 8 year hx of OUD
- Prescription Opioids→ IN Heroin→ IV Heroin last 12 months
- 3 non-fatal ODs last 8 months
- Non compliant with Bupe Rx and Psychosocial Tx
- Argued with his Mother: Went up to his Room: Mother heard a loud thud, found him on floor, unresponsive, with syringe and needle in his arm 5 minutes later.
- Naloxone Nasal Spray 4mg administered X2—No Response
- Patient could not be resuscitated by EMS

What Happened?

Sudden Death IVDU

- ? Typical Opioid Induced Respiratory Depression Fatal Overdose
  - Time Frame: ≥ 1 hour: Naloxone Reversal Effectiveness Evidence

- Post Mortem Toxicology: +Fentanyl, –Norfentanyl, +Heroin, –6-MAM, +Morphine

- **Fentanyl Induced Chest Wall Rigidity (“Wooden Chest”)**
  - **Fentanyl Induced Respiratory Muscle Rigidity & Laryngospasm**

Fentanyl Chest Wall Rigidity

- First Reported in 1953 in anesthesia literature
- Skeletal Muscle Rigidity: Chest Wall Most Common
- Most common with fentanyl and its congeners (lipid solubility)
- Most common with rapid IV administration
- ? Activation of the coerulospinal noradrenergic pathway, following mu receptor activation in LC
- Not dose related
- Reversed with naloxone (IV route in literature)
- Ventilatory Support
- Low or Absent Norfentanyl (appears in 2 minutes: CYP3A4(Inhb)

Burns, G et al Clinical Toxicology, Vol 54, No 5, 420-23, 2016

100 Accidental OD deaths 2017:
99% + FENTANYL
Only 3 cases + HEROIN

2 min: 3A4

Boonshoft School of Medicine
WRIGHT STATE UNIVERSITY

RESEARCH UPDATE ON FENTANYL OUTBREAKS IN THE DAYTON, OH AREA:

Acryl Fentanyl and Furanyl Fentanyl Commonly Found in Overdose Death Cases

UPDATE 04/28/2017

DAYTON, OHIO. The Dayton area (Montgomery County, Ohio) has recently experienced dramatic increases in heroin and other opioid-related problems. Unintentional drug overdose deaths increased significantly from 127 in 2010 to 264 in 2014. In 2016, there were 349 overdose deaths in Montgomery County, and 251 of them screened positive for fentanyl. Preliminary data from 2017 indicate continuing increases in overdose deaths.

Synthetic opioids/fentanyl analogues/metabolites	A. All cases (N=100)	B. Acryl Fentanyl Positives (N=56)	C. Furanyl Fentanyl Positives (N=39)
Fentanyl	99 (99%)	56 (100%)	39 (100%)
Norfentanyl	64 (64%)	39 (70%)	26 (67%)
Acryl fentanyl	56 (56%)		25 (64%)
Despropionylfentanyl	46 (46%)	26 (46%)	32 (82%)
Furanyl Fentanyl	39 (39%)	25 (45%)	
Carfentanil	3 (3%)	2 (4%)	1 (2.6%)
Acetyl Fentanyl	2 (2%)	1 (2%)	1 (2.6%)
Butyryl/isobutyrylfentanyl	1 (1%)	0 (0%)	0 (0%)
Furanyl Norfentanyl	1 (1%)	1 (2%)	1 (2.6%)
U47700	1 (1%)	1 (2%)	1 (2.6%)

Fentanyl-Induced Chest Wall Rigidity

Başak Çoruh, MD; Mark R. Tonelli, MD; and David R. Park, MD

Fentanyl and other opiates used in procedural sedation and analgesia are associated with several well-known complications. We report the case of a man who developed the uncommon complication of chest wall rigidity and ineffective spontaneous ventilation following the administration of fentanyl during an elective bronchoscopy. His ventilation was assisted and the condition was reversed with naloxone. Although this complication is better described in pediatric patients and with anesthetic doses, chest wall rigidity can occur with analgesic doses of fentanyl and related compounds. Management includes ventilatory support and reversal with either naloxone or a short-acting neuromuscular blocking agent. This reaction does not appear to be a contraindication to future use of fentanyl or related compounds. Chest wall rigidity causing respiratory compromise should be readily recognized and treated by bronchoscopists.

CHEST 2013; 143(4):1145–1146

CLINICAL TOXICOLOGY, 2016
VOL. 54, NO. 5, 420–423
http://dx.doi.org/10.3109/15563650.2016.1157722

Taylor & Francis
Taylor & Francis Group

CLINICAL RESEARCH

Could chest wall rigidity be a factor in rapid death from illicit fentanyl abuse?

Glenn Burns[a], Rebecca T. DeRienz[b], Daniel D. Baker[b], Marcel Casavant[c] and Henry A. Spiller[c]

[a]Central Ohio Poison Center, Ohio State University Medical Toxicology, Columbus, OH, USA; [b]Office of the Franklin County Coroner, Division of Forensic Toxicology, Columbus, OH, USA; [c]Department of Pediatrics, Central Ohio Poison Center, College of Medicine, Ohio State University, Columbus, OH, USA

ABSTRACT

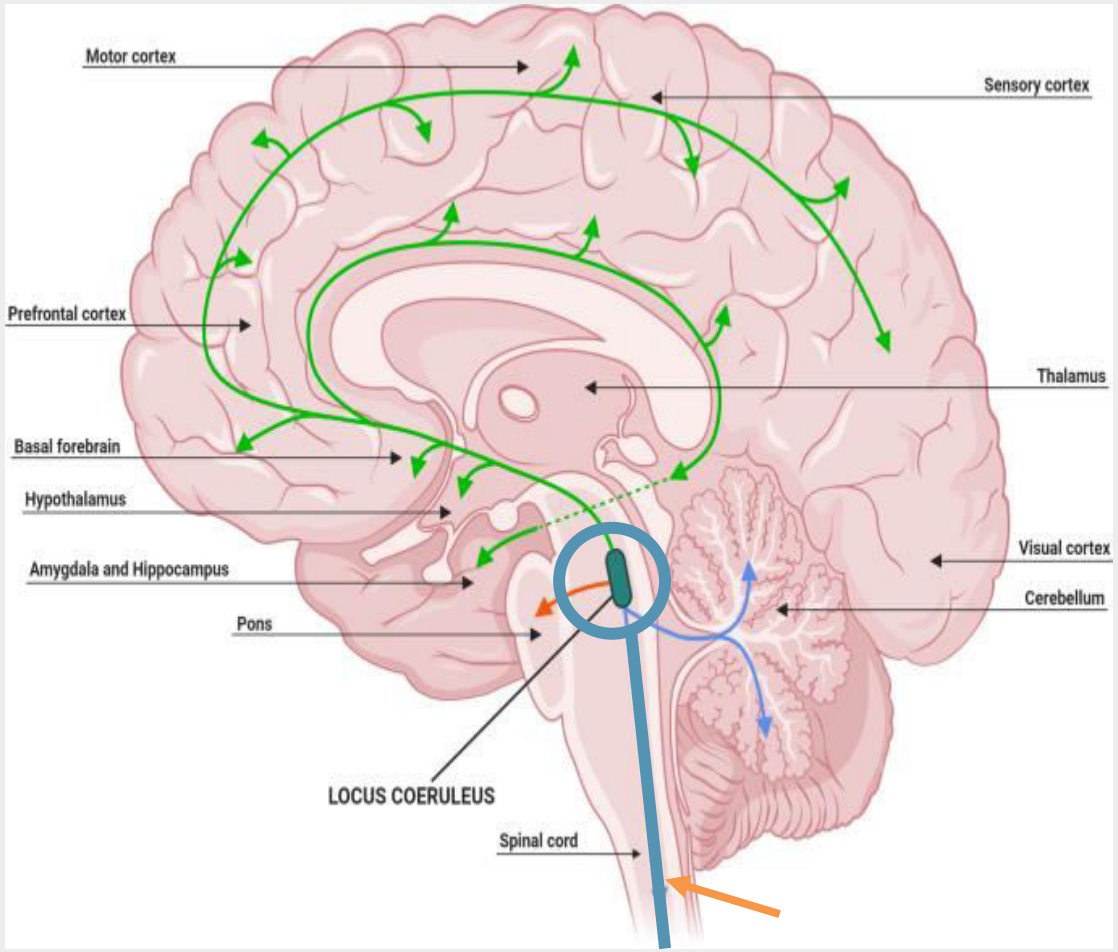
Background: There has been a significant spike in fentanyl-related deaths from illicit fentanyl supplied via the heroin trade. Past fentanyl access was primarily oral or dermal via prescription fentanyl patch diversion. One factor potentially driving this increase in fatalities is the change in route of administra-

High levels of fentanyl but not norfentanyl = rapid death onset, and is associated with acute chest rigidity

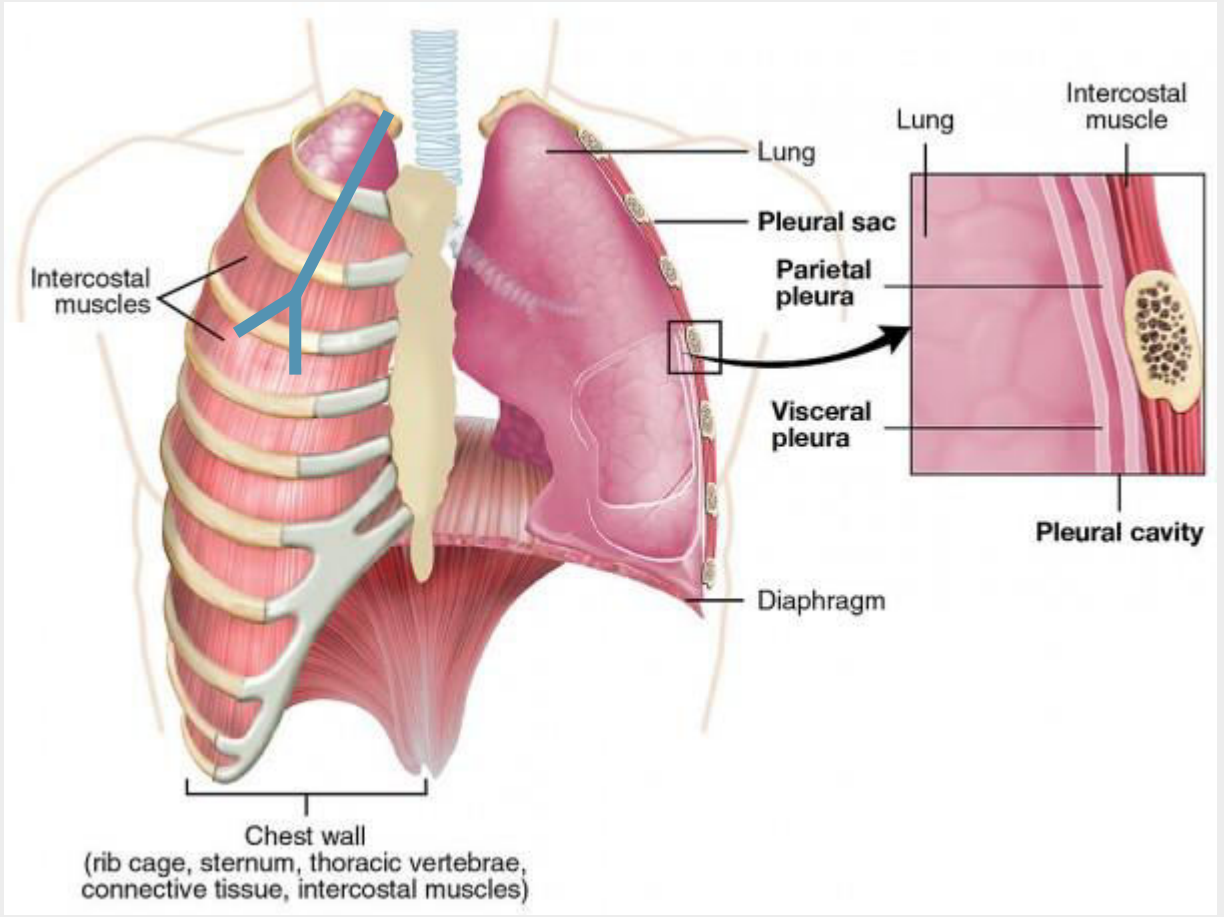
correlate with rises in norfentanyl levels. In several cases fentanyl concentrations were strikingly high (22 ng/ml and 20 ng/ml) with no norfentanyl detected. **Discussion:** The lack of any measurable norfentanyl in half of our cases suggests a very rapid death, consistent with acute chest rigidity. An alternate explanation could be a dose-related rapid onset of respiratory arrest. Deaths occurred with low levels of fentanyl in the therapeutic range (1–2 ng/ml) in apparent non-naïve opiate abusers. Acute chest wall rigidity is a well-recognized complication in the medical community but unknown within the drug abuse community. The average abuser of illicit opioids may be unaware of the increasing fentanyl content of their illicit opioid purchase. **Conclusion:** In summary we believe sudden onset chest wall rigidity may be a significant and previously unreported factor leading to an increased mortality, from illicit IV fentanyl use. Fentanyl and norfentanyl ratios and concentrations suggest a more rapid onset of death given the finding of fentanyl without norfentanyl in many of the fatalities. Chest wall rigidity may help explain the cause of death in these instances, in contrast to the typical opioid-related overdose deaths. Intravenous heroin users should be educated regarding this potentially fatal complication given the increasingly common substitution and combination with heroin of fentanyl.

ARTICLE HISTORY
Received 2 December 2015
Revised 12 February 2016
Accepted 17 February 2016
Published online 17 March 2016

KEYWORDS
Chest wall rigidity; fentanyl; heroin; norfentanyl; opioids; overdose

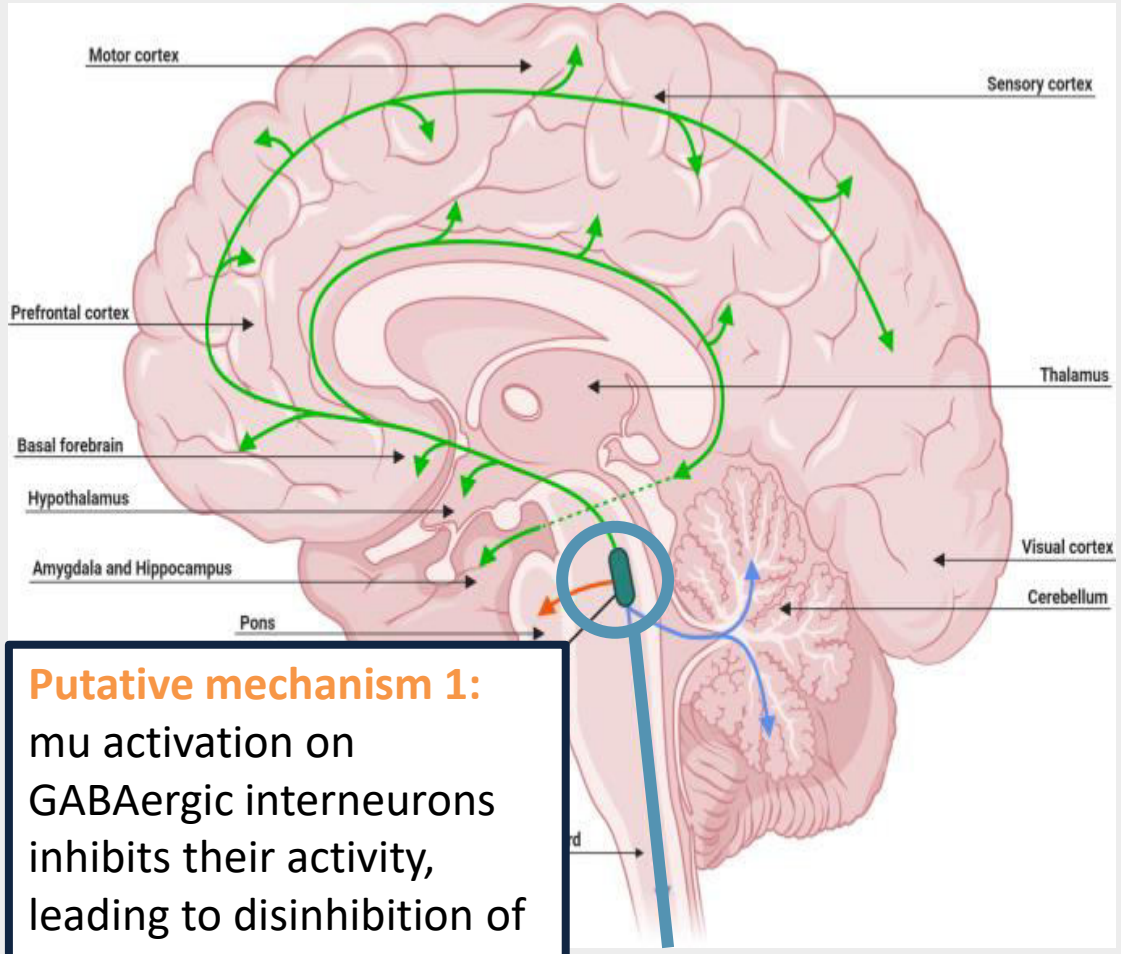


Spinal Motor Neuron

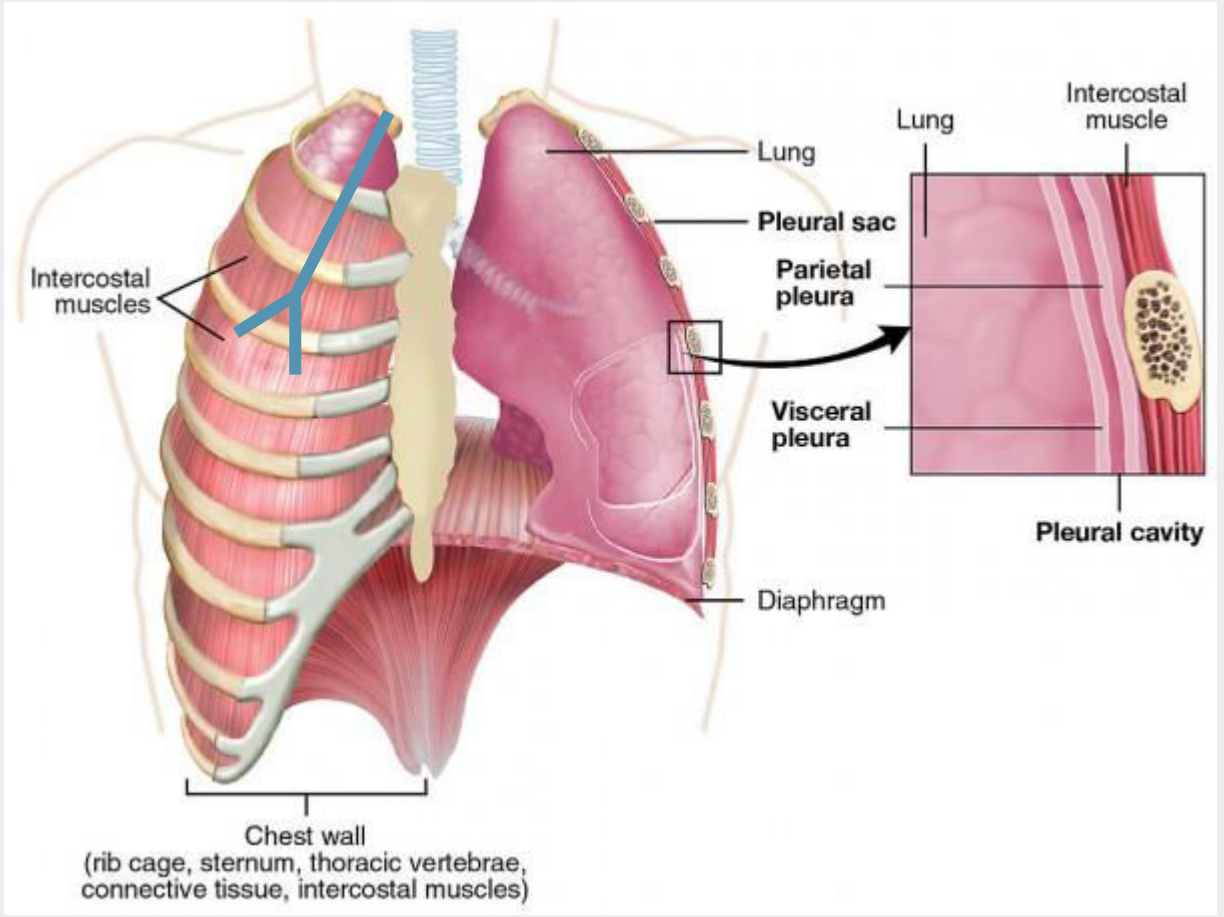


Activation of NE via GABA inhibition increases muscle tone

Courtesy Dr. Ferland



Putative mechanism 1:
mu activation on GABAergic interneurons inhibits their activity, leading to disinhibition of the LC



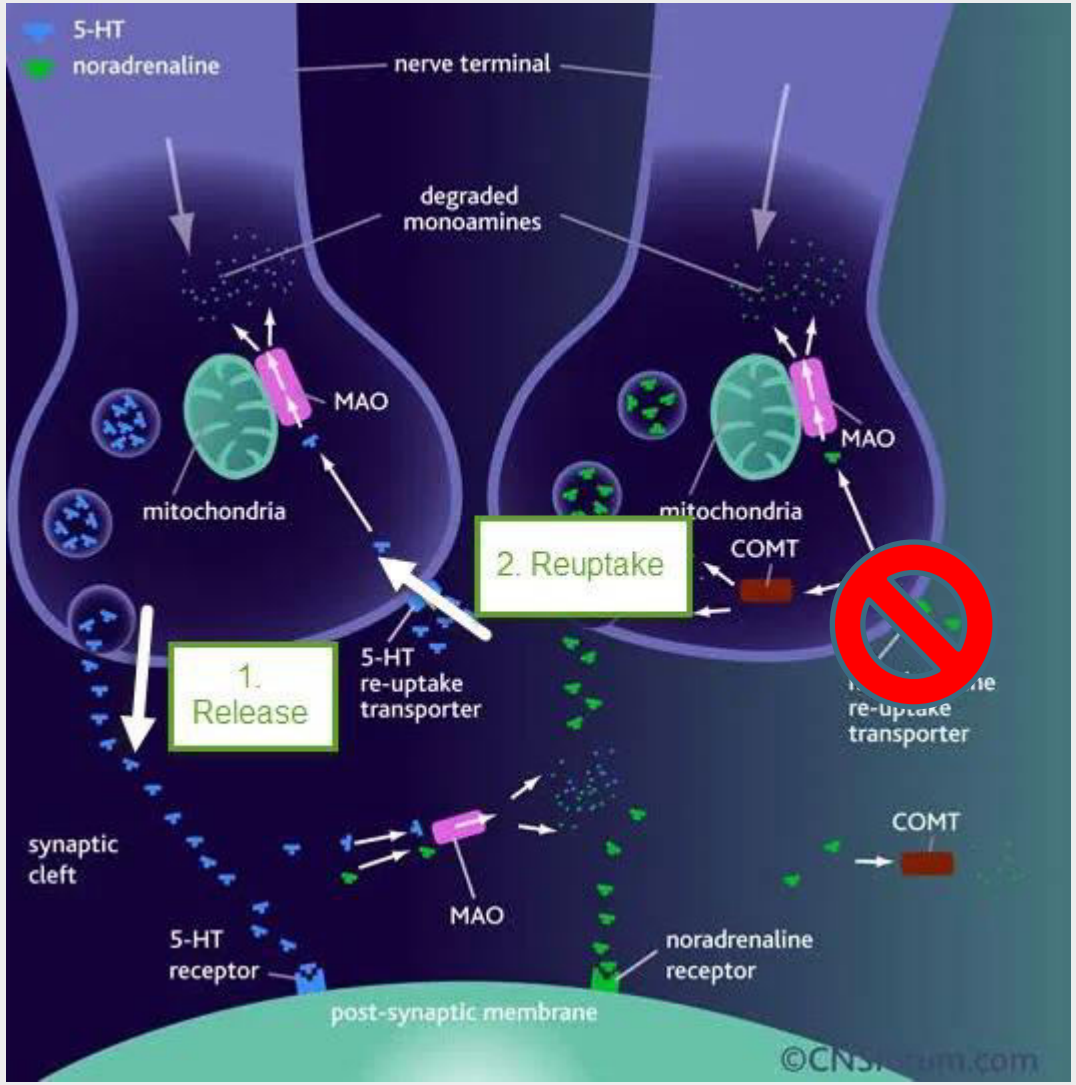
Continuous activation of LC leads hyper contraction of the cell wall

Courtesy Dr. Ferland

Putative mechanism 2:

fentanyl has been shown to block reuptake of NE

Importantly, naloxone does not affect this mechanism



Courtesy Dr. Ferland

ASAM REVIEW COURSE 2026

Tobacco Use Disorder: Public Health and Practice

Jonathan Avery, MD, FASAM
Professor of Clinical Psychiatry
Vice Chair, Addiction Psychiatry
Weill Cornell Medical College





Financial Disclosure

Jonathan Avery, MD, FASAM

- No relevant disclosures

History

- Native American tribes cultivated and used tobacco for many different purposes for thousands of years before the arrival of the Europeans. [1-2]
- Tobacco became an important economic influence in the British American colonies and the early United States. [1-2]
- The World Health Organization estimates that 1/3 adults smoke, and because tobacco use is on the rise in developing countries, it is one of the few causes of death that is increasing. (CDC, 2005) [3]
- Nicotine and the reinforcing sensory stimulation associated with tobacco use are responsive for the compulsive use of tobacco in the form of cigarettes, bidis, cigars, pipes, snuff, chewing tobacco, etc.

Epidemiology of Tobacco

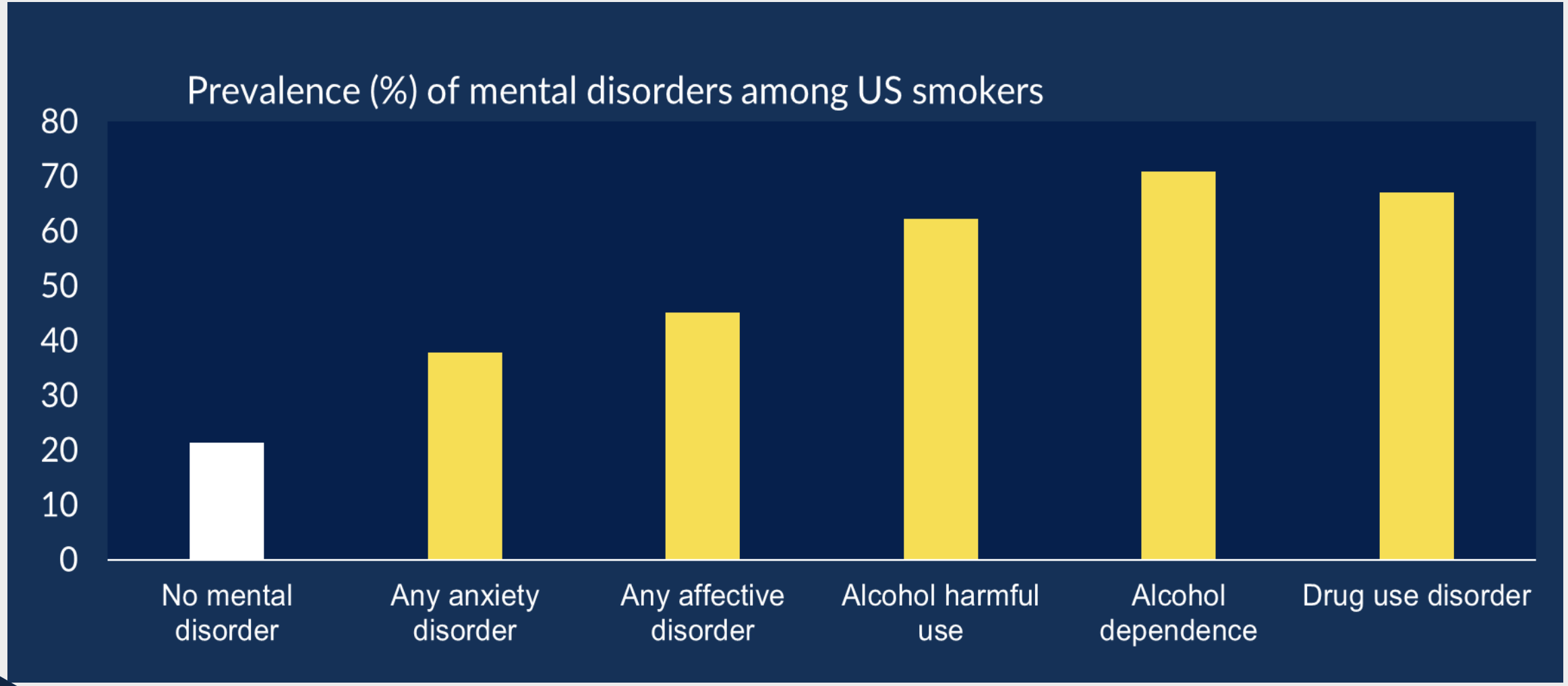
- **Prevalence has declined** in the US from 42% in 1965 to 14% in 2017 [4,5]
- Men are more likely to be smokers than women (15.8% vs. 12.2%) [6]
- >16 million Americans have smoking-related disease
- Accounts for **20%** of coronary-artery disease [7]

Morbidity and Mortality

- Leading cause of preventable death in the United States, accounting for about **440,000 premature deaths annually** [8]
  - **150K from CV disease**
  - **150K from cancer**
  - **150K from non-malignant pulmonary disease**

- Lost years of life: [9]
  - adult men: 13.2 yrs
  - adult women: 14.5 yrs

Epidemiology



[10] - Lawrence et al., 2009

Compounds in Tobacco Smoke

An estimated 4,800 compounds in tobacco smoke, including 11 proven human carcinogens [11]

Gases [12]

- Carbon monoxide
- Hydrogen cyanide
- Ammonia
- Benzene
- Formaldehyde

Particles [12]

- Nicotine
- Nitrosamines
- Lead
- Cadmium
- Polonium-120

Nicotine is the addictive component of tobacco products, but it does NOT cause the ill health effects of tobacco use.

Health Consequences

- Smokers die 10 years earlier than non-smokers on average
- Cancer: oral cavity, pharynx, larynx, bladder, esophagus, cervix, kidney, lung, pancreas, stomach, liver, bowel, acute myeloid leukemia [13]
- Cardiovascular disease, DM type [14]
- COPD, Asthma [15]
- Osteoporosis, cataracts and macular degeneration, early menopause, erectile dysfunction, gastric and duodenal ulcer disease, skin aging, periodontal disease [16]

Tobacco Associated Problems

- Barrier to Recovery
- Financial Hardships
- More Employment Difficulties
- More Housing Difficulties
- Poorer Mental Health
- More Relapse to Drugs and Alcohol
- Social Stigma
- Poorer Appearance
- More Fires in Home

Public Health Interventions [17]

- Anti-smoking advertisements
- Increasing taxes
- Age-restrictions
- Tobacco-free laws and policies
- Support for cessation

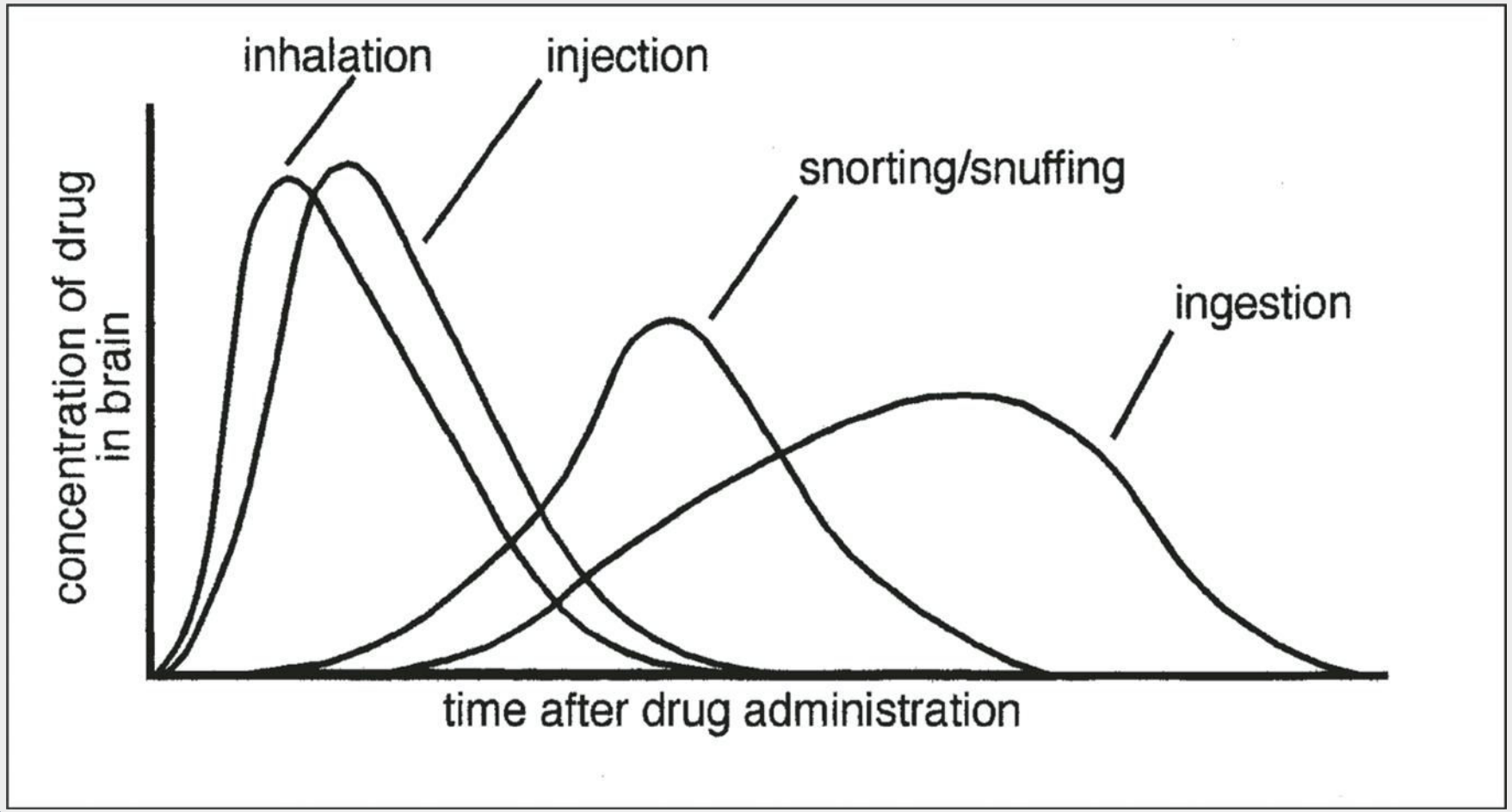
Pharmacology of Nicotine

- Naturally occurring alkaloid [3]
- Triggers the release of a variety of neuroactive hormones
- Acts as a nicotinic acetylcholine receptor (nAChR) agonist [3]
- Stimulant-like effect in the CNS: enhances concentration, alertness, arousal [3]
- Increase of dopamine in brain's reward circuitry [18]
- Enters the CNS in rapidly after inhalation [19]
- Rapid effect on CNS contributes to reinforcement and dependence

Routes of Use

- Nicotine and reinforcing sensory stimulation associated are responsible for the compulsive use of tobacco [20-23]
- Method of administration modifies the addictive potential associated with use [24]
- Compulsive use increases with rapid administration: smoking/vaping >> dermal patch, chewing

Smoking is the Fastest Route of Drug Administration



25 - https://science.education.nih.gov/supplements/nih2/addiction/guide/lesson3-1.html

Nicotine

- Reaches the brain 20 seconds after inhalation + gradually increases occupancy of the nAChRs over minutes [19]
- Smoking 1 cigarette leads to significant occupancy of alpha4beta2 containing nAChRs for >3 hrs [19]
- The initial relatively rapid rate of rise of nicotine occurs within minutes, though levels of nicotine-bound receptors continue to rise slowly/are maintained for hours [19]
- Rapid onset = allows smokers to control nicotine intake (by # of puffs, intensity of puffs, depth of inhalation)

Pharmacology of Nicotine

- Half-life is 2 hours [25, 26]
- Accumulation in various tissues throughout the body during the day [27]
- Continue to be release from tissues for 6-8 hours after smoking ceases during sleep [25, 26]
- Metabolized in the liver via cytochrome P450 enzymes [26]
- Major metabolite is cotinine [26]
- Crosses placenta and is found is breast milk [27]

Pharmacology

- Undergoes 1st pass metabolism [26]
- Oral bioavailability is 45% [26]
- Poorly absorbed from stomach 2/2 acidity of gastric fluid, but well absorbed in small intestine 2/2 alkaline environment [26]
- Renal clearance accounts for 2% to 35% (about 10%) of total nicotine clearance [28]
- Nicotine obtained via tobacco reaches high initial concentrations in arterial blood and lungs
    - Nicotine is then distributed to brain, storage adipose, muscle tissue from arterial blood
    - Avg steady-state concentration in body tissue is 2.6x that of the blood [26]

Pharmacology

- Once absorbed in bloodstream, nicotine has a volume of distribution of about 180 liters, with less than 5% of it binding to plasma proteins [26]
- Crosses placenta freely
- Found in the amniotic fluid and in the umbilical cord blood of neonates
- Found in breast milk at concentrations approximately 2x those found in blood

Sex and Race on Metabolism

- Women metabolize nicotine faster than men, 2/2 estrogen effect on CYP2A6 [29]
  - Even faster during pregnancy
- Related to CYP2A6 gene variants, African Americans obtain on average 30% more nicotine per cigarette, and they clear nicotine and cotinine more slowly than Caucasians. [30]
- Chinese American have a lower nicotine intake per cigarette, and slower metabolism (vs. Caucasians or Hispanics) 2/2 having a higher prevalence of CYP2A6 alleles (associated with slow metabolism) [31, 32]
  - Suggest why Chinese American smokers have lower rates of lung cancer than either African Americans or Caucasians [31, 32]

Biochemical Assessment

- Blood, salivary, and plasma cotinine can be used [33, 34]
  - others include expired breath CO, blood carboxyhemoglobin, + plasma/salivary thiocyanate concentrations
- 16-hr ½ life of cotinine makes it useful as a plasma and salivary marker of nicotine intake [35]
- The gold standard for estimating daily nicotine intake from tobacco use is the sum of nicotine and its metabolites in urine. [36]
- Measurement of the minor tobacco alkaloids anabasine and anatabine in urine can be used as a biomarker of tobacco use in individuals who are using nicotine medications. [37]

Drug Interactions from Tobacco Smoke

- Affects the pharmacokinetics or pharmacodynamic mechanisms
- absorption, distribution, metabolism, or elimination
- potentially causing altered response or toxicity
- Accelerates metabolism of many drugs, esp. those metabolize by CYP1A2 [38]
- Might increase CYP2E1 and inhibit CYP2A6 enzymatic activity [38]
- When smokes discontinue abruptly (i.e., when hospitalized) doses of such meds may need to be lowered to avoid toxicity [38]

Drug Interactions from Tobacco Smoke

Drugs that may have a decreased effect due to induction of CYP1A2 by tobacco smoke: [39]

- Caffeine
- **Clozapine**
- **Olanzapine**
- **Haloperidol**
- **Chlorpromazine**
- Fluvoxamine
- Theophyline

Quitting Smoking Effects on CYP1A2

- Risk for medication toxicity
- May ↑ levels acutely
- Consider dose adjustment
- Clozapine toxicity
- Seizures
- Reduce caffeine intake

- **Nicotine** (or NRT) **Does Not** Change Medication Levels

- Nicotine metabolized by **CYP2A6**

Pharmacodynamic Interactions: OCPs

- Alter the expected response or action of a drug
- Combined OCPs (estrogen + progestin) w/ smoking is very important
  - Increased risk of serious cardiovascular effects (stroke, MI, thromboembolism) [40]
- Recommended that OCPs are **contraindicated** in women > 35 yrs old AND are a heavy smoker (>15cigs/day) [40]

Pharmacodynamic Interactions

- Appear to enhance the procoagulant effect of **estrogens** [41]
- Results in less sedation from benzodiazepines and less analgesia from some opioids [42]
- Impairs the therapeutic effects of histamine H2 -receptor antagonists used in treating **peptic ulcers** [42]
- Cutaneous vasoconstriction by nicotine can slow the rate of absorption of subcutaneously administered **insulin** [43]

Pharmacologic Actions: CNS [44, 45]

- Acts on sympathetic system: increase BP, HR, cardiac output, and cutaneous vasoconstriction
- Causes muscle relaxation via simulation of Renshaw cells, via inhibition of motor neurons
- Higher doses: produces ganglionic stimulation -> releases adrenal catecholamines
- Very high doses cause hypotension, slowing of HR

Psychoactive Effects

- Causes arousal, relaxation, enhancement of mood/attention/rxn time [46-48]
- Results in relief of withdrawal sx of dependent smokers, rather than direct-enhancing effects [46-48]
  - Smokers may need regular doses of nicotine to feel normal rather than to enhance their capabilities/cognitive effects
- Psychoactive effects dependent on route, speed of administration, environmental factors
  - Subjective effects depend on pre-drug state, level of activity, g
    history, expectancy [49,50]

Genetic Predisposition

- GWAS: single nucleotide polymorphisms on... [51]
  - **CHRNA5-CHRNA3- CHRNB4 nAChR** subunit cluster on chromosome 15q25
    - associated w/ # of cigs/day, serum cotinine levels, lung cancer, peripheral artery disease, chronic lung dz
  - **CYP2A6,** primary enzyme responsible for the oxidation of nicotine and cotinine. [52-53]
    - Reduced function variants of the gene are associated with smoking fewer cigarettes per day and a lower risk of lung cancer
  - **Cell adhesion and ECM molecules** [54]
    - neural plasticity and learning are key determinants of individual differences in vulnerability to drug addictions
- Twin studies: [55-56]
  - monozygotic twins are more similar than dizygotic twins w/ smoking behavior
  - ½ of the total variance (28% to 84%) in smoking behavior are due to genetic effects
  - There is genetic influence on nicotine withdrawal symptoms as well

Psychiatric Comorbidities

- **37%** of those w/ a mental illness are smokers vs. **20%** of smokers who do not carry a mental illness. [57]
- Those with Sz, depression, ADHD have **higher prevalence** of cig smoking compared with general population

Sz: 70-88% are smokers [58]

- Diminished sensory gating to repeated stimuli, smoking can relieve negative sx (blunted affect, emotional withdrawal, lack of spontaneity)
- Smokers experience fewer side effects from antipsychotics (2/2 stimulating effects of nicotine), which might contribute to greater prevalence of smoking in ppl w/ Sz

ADHD: 40% are smokers [59]

- Associated with early initiation of regular cigarette smoking, even after controlling for confounding variables such as socioeconomic status, IQ, and psychiatric comorbidity
- transdermal patches improve the attentional symptoms of ADHD

Best Measure of Nicotine Dependence Severity

Heaviness of Smoking Index

- AM (upon awakening) Time to First Cigarette (TTFC) [46]
  - < 30 minutes = moderate
  - < 5 minutes = severe
- **Implications for Treatment Outcome**
- **Need for Medications**
- **Implications for Dose**

Tobacco Tolerance

- Causes effects of individual cigarettes tend to lessen throughout the day.
- Overnight abstinence allows considerable, but not complete, re-sensitization of nicotinic receptors to non-desensitized states
- Populations of nAChR subtypes that begin to change as other molecular mechanisms involving neuroadaptations come into play after days and weeks of tobacco use [47,48]

Tobacco Cravings

- Powerfully conditioned cues = cravings become associated with everyday events, become linked with mood
- High rates of relapse: [49]
  - Population surveys find that up to 75% of adults who smoke want to stop, but only 1/3 try to stop, and only 3% of those do without aids
  - 50% of individuals w/ past hx of MI, COPD, and other sequelae of smoking, revert to cig smoking days or weeks after leaving the hospital

Which of the following is a symptom of tobacco withdrawal?

A. Irritability

B. Hypersomnia

C. Elated Mood

D. Decreased Appetite

Tobacco Withdrawal

- Nicotine use is continued to avoid the negative sx associated with withdrawal (known as negative reinforcement)
- Majority of withdrawal sx are distressing, but not life-threatening
- Acute withdrawal sxs reach max. Intensity 24 - 48 hrs after cessation and then gradually diminish over weeks [50-51]
- Extrahypothalamic corticotropin-releasing factor (CRF-1) contributes to negative affect during withdrawal [52]
- CRF released in central amygdala following nicotine withdrawal -> produces anxiety behavior
- Pharmacological blockade of CRF1 receptors inhibits the anxiogenic effects in withdrawal

Tobacco Withdrawal Symptoms [53]

Emerge hours after last cigarette

Can last up to (4) weeks

- Depressed mood
- Insomnia
- Irritability, frustration or anger
- Anxiety
- Difficulty concentrating
- Restlessness
- Increased appetite or weight gain

MAO and Nicotine Dependence

- Cig smoking is associated w/ inhibition of monoamine oxidase A + B [54-56]
  - Not caused by nicotine itself, but the condensation products of acetaldehyde with biogenic amines, such as benzoquinones, 2-naphthylamine, harman, + others
- MAOs = metabolize catecholamines, including dopamine
- Rat studies: [57]
  - Pre-tx with MAO-I makes nicotine more rewarding and increases the likelihood and rate of acquisition of nicotine self-administration
  - Important consideration: anti-depressants also inhibit MAOs, therefore smoking-induced inhibition of MAO might contribute to the perceived benefit of smoking by some depressed patients

Systemic Toxicities

- **Tobacco smoke =** carries volatile and particulate phases that contain substances that are primarily responsible for the human morbidity and mortality [58]
  - Volatile = 500 compounds (nitrogen, CO, carbon dioxide, ammonia, hydrogen cyanide, and benzene)
  - Particulates = >3,500 (alkaloids nornicotine, anabasine, anatabine, myosmine, nicotyrine, and nicotine)

- **Tar:** contains many carcinogens, including polynuclear aromatic hydrocarbons, N-nitrosamines, and aromatic amines [58]

Toxicities: Pulmonary

- Causes imbalance between proteolytic and antiproteolytic forces in the lung [59]
- Heightens airway responsiveness

- High rates of COPD in tobacco smokers linked to: [59]
  - Exposure to tar, nitrogen oxides, hydrogen cyanide, and volatile aldehydes
  - These exposures results in oxidative stress and generation of superoxide radicals and hydrogen peroxide and lung damage

- Smokers with DNA damage from polynuclear aromatic hydrocarbons in the WBCs are 3x more likely to be dz with lung cancer than smokers with lower concentrations [60]

Toxicities: Cardiovascular

- **Increased risk** of CV toxicity 61
  - Related to exposure to oxidant chemicals and CO, + hydrogen cyanide, carbon disulfide, cadmium, and zinc
  - CO reduces oxygen delivery to the heart
  - Oxidant chemicals are primarily responsible for endothelial dysfunction, platelet activation, thrombosis, and coronary vasoconstriction

Other Effects and Toxicities

- **For women:** [62]
  - lower levels of estrogen
  - earlier menopause
  - increased risk of osteoporosis
  - alkaloids in tobacco smoke decrease estrogen formation by inhibiting an aromatase enzyme in granulosa cells or placental tissue

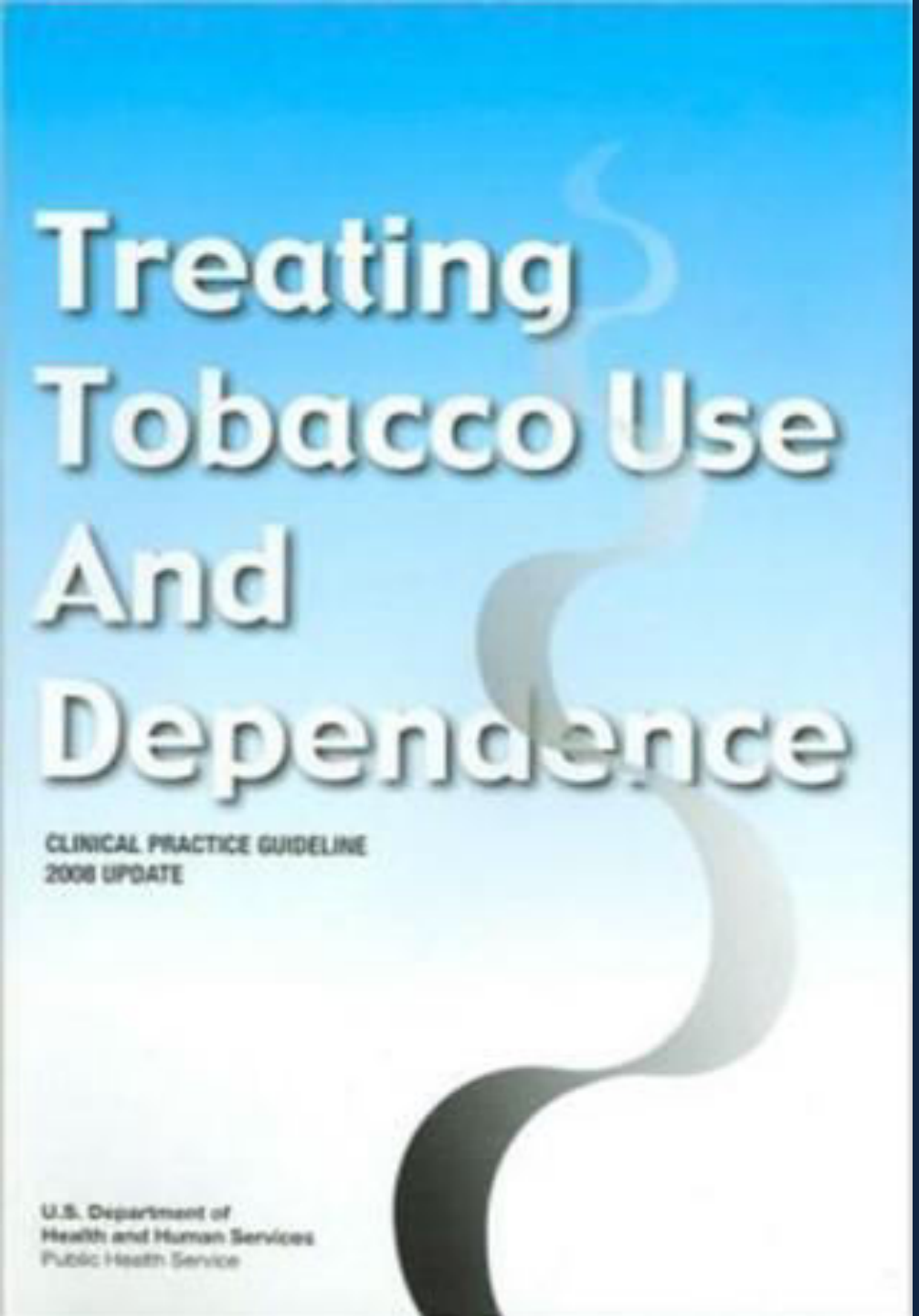
- **Skin changes:** [63]
  - yellow staining of fingers
  - precancerous and squamous cell carcinomas on the lips and oral mucosa
  - vasospasm and obliteration of small skin vessels
  - enhanced facial skin wrinkling

Predictors of Abstinence [64-66]

- Lower level of dependence
- Higher socioeconomic status: education, insured
- Older age
- Male gender
- No behavioral health comorbidity
- Fewer smokers in social networks
- Quit in first 7 days / # days quit
- Use of cessation treatment

Why is it so hard to quit?

- Smoking a drug is highly addicting
- **Treatment options are limited**
  - Few medication types
  - Limited (brief) counseling support
  - No levels of care
- **Utilization of treatment is poor**
  - Most don’t use counseling
  - Medications-too low dose, not enough time



Brief Intervention

2As and R (Ask, Advise, and Refer)

- Do you use Tobacco?
  - How much? What kinds?
  - Document tobacco use at visits
- How do you feel about quitting?
  - Can I give your name to someone to get more information?

Why Not Quit For One Day?

Or Six Hours?

- Save money
- Try free NRT
- Feel better
- Master a new skill
- Try other coping
- Not go outside in bad weathe





Quitline

1-800-QUIT-NOW

- Telephone counseling
- Toll-free / state funded
- Assessment
- 4 follow-up calls
- Good for transportation issues
- Scheduled calls from tobacco specialist
- Success rate in smoking cessation
- Many languages, free NRT

Pharmacologic Treatments

- First line (FDA-approved): [67]
  - Nicotine replacement therapy (NRT)
  - Bupropion
  - Varenicline

Counseling + Medications= Best Treatment Plan

- Second line (not FDA-approved): [67]
  - Nortriptyline

Which of the following is TRUE of nicotine replacement therapies (NRT)?

A. Most people who use NRT become long term users of it

B. These medications produce serum nicotine levels, which are higher than that of a smoked cigarette

C. Most people use NRT incorrectly or at too low a dose

D. Medicaid insurance never pays for coverage over the counter products like nicotine patch or gum

Nicotine Medications [68]

- Use high enough dose
- Scheduled better than PRN
- Use long enough time period
- Can be combined with bupropion
- Can be combined with each other
- Have almost no contraindications
- Have no drug-drug interactions
- Safe enough to be OTC

Oral Nicotine Spray [69,70]

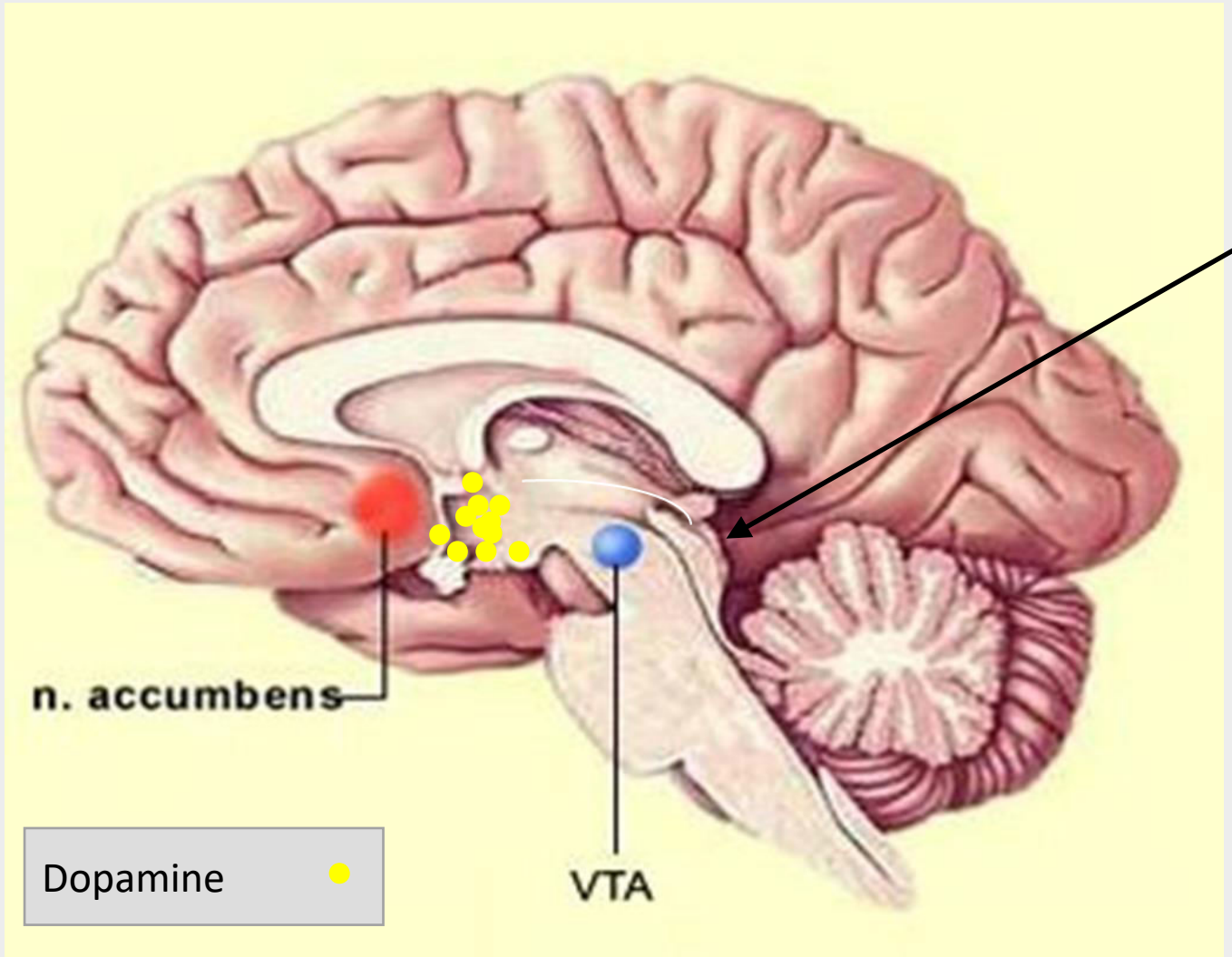
- Approved Sept 2019; OTC (Canada & Europe)
- Faster absorption
- 1-2 to two sprays (140/ container; each 1mg nic). Max 4/ hour, 64/ day (most 10-14/ day)
- No evidence product abuse
- Real world and efficacy trials 2X placebo
- Contains tiny amount ethanol. At 64 doses/d, <one tsp (~ 5ml) of wine with 12% alcohol)
- Side effects: hiccups, headache, nausea, mouth/throat irritation, dyspepsia, dizziness

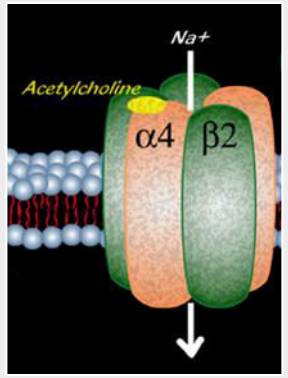
Combination Therapies [71,72]

- Improve abstinence rates
- Decrease withdrawal
- Well tolerated

	OR
Patch + gum or spray	**1.9** (1.3-2.7)
Patch + bupropion	**1.3** (1.0-1.85)

Varenicline: A selective a4B2 nicotinic receptor partial agonist

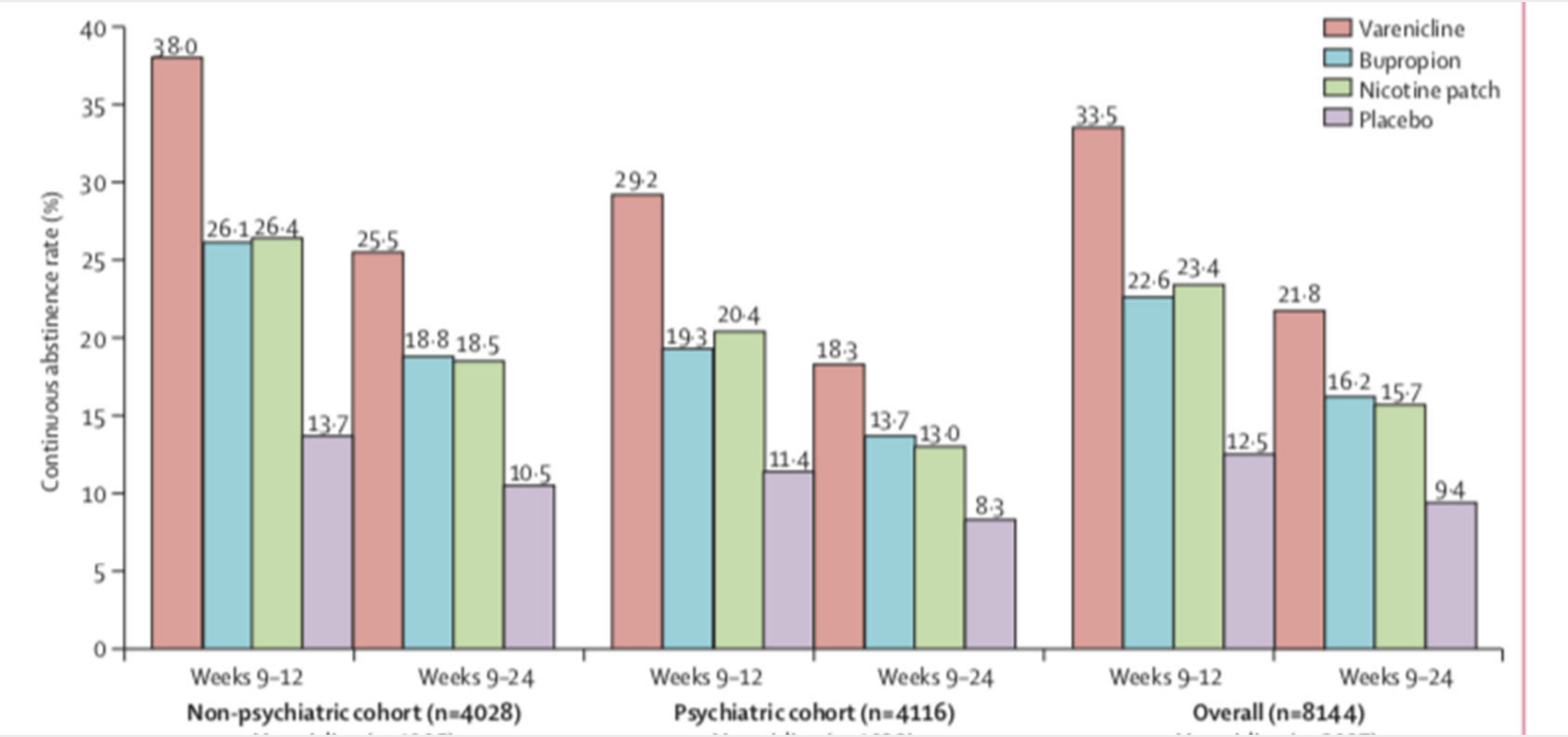




Partial Agonist [73]
- Partially stimulates receptor
- Some dopamine release
- Prevents withdrawal

"Antagonist"
- Blocks nicotine binding

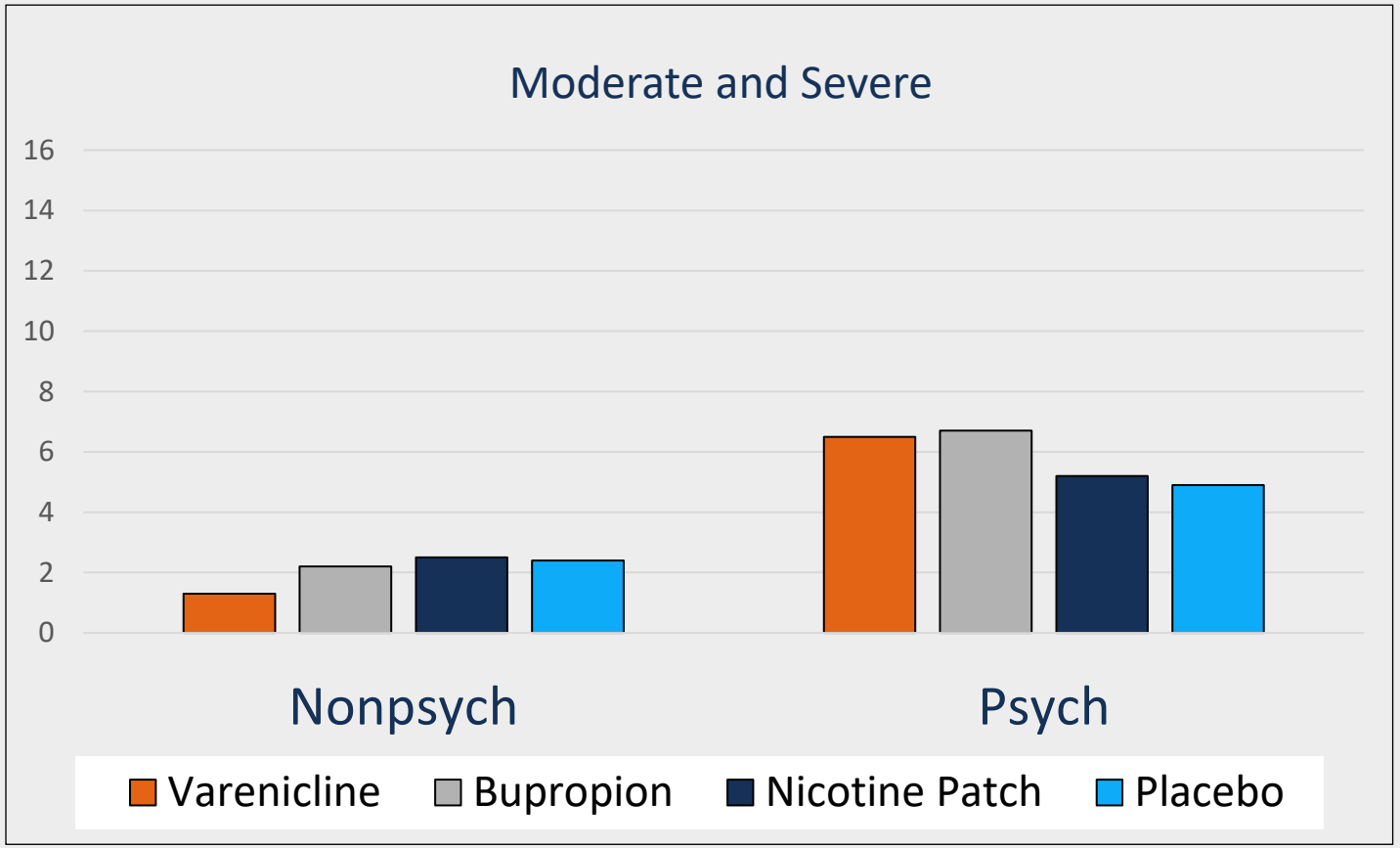
EAGLES study [74]



Results from 2013 Cochrane Review [75]

Medication	Versus Placebo OR (95% Credible Interval)	Versus other medication OR (95% Credible Interval)
NRT	1.84 (1.71-1.99)	Combination outperformed single formulations
Bupropion	1.82 (1.60-2.06)	NRT: 0.99 (0.86-1.13)
Varenicline	2.88 (2.40-3.47)	Nicotine patches: 1.51 (1.22-1.87) Nicotine gums: 1.72 (1.38-2.13) Other NRT: 1.42 (1.12-1.79) Combination NRT: 1.06 (0.75-1.48)

Neuropsychiatric Adverse Events



- FDA Approves Removal of Boxed Warning Regarding Serious Neuropsychiatric Events from CHANTIX® (varenicline) Labeling [90]

- Based on a U.S. Food and Drug Administration (FDA) review of a large clinical trial that we required the drug companies to conduct, we have determined the risk of serious side effects on mood, behavior, or thinking with the stop-smoking medicines Chantix (varenicline) and Zyban (bupropion) is lower than previously suspected. The results of the trial confirm that the benefits of stopping smoking outweigh the risks of these medicines (December 2016) [76]

Varenicline ↑ Side effects: Nausea, insomnia, abnormal dreams, headaches

Summary of Treatment

- All tobacco users should be offered treatment to try to stop
- Counseling + Medications = Best treatment plan
- Better outcomes
  - Education to use medication effectively
  - Combinations of NRT or Varenicline as first line
  - Longer durations (6 mos) effective for relapse prevention

Gender Issues

- In any given quit-attempt, women are less likely to successfully quit smoking than men [77]
  - Negative affect/ depression/ socioeconomic issues/ less likely meds
- Women in placebo group less likely than men to quit
- Varenicline was more effective than TNP for women (OR=1.51; 95%CI=0.12,2.05; p=0.007) but not men (OR=0.92; 95%CI=0.65,1.31; p=0.64). [78]
- The advantage of varenicline over bupropion SR and TN is greater for women than men
- Clinical trials and epidemiologic studies

Combination Therapy Of Varenicline and Bupropion

- Meta Analysis: 4 RCTs with 1230 smokers.
- Compared with varenicline, combination treatment with varenicline and bupropion could significantly improve the abstinence rate at the end of treatment (RR 1.153, 95% CI 1.019 to 1.305, P = 0.024). [79]

Combination Therapy Of Varenicline and Bupropion

- The benefit existed at 6 months follow-up (RR 1.231, 95% CI 1.017 to 1.490, P = 0.033) and was mainly concentrated in highly dependent smokers (RR 1.631, 95% CI 1.290 to 2.061, P < 0.001) and heavy smokers (RR 1.515, 95% CI1.226 to 1.873, P < 0.001) [79]

- For safety outcomes, the combination treatment was associated with more anxiety (RR 1.717, 95% CI 1.176 to 2.505,P = 0.005) and insomnia (RR 1.268, 95% CI 1.076 to 1.494, P = 0.005) symptoms vs varenicline monotherapy. [79]

Medication Interaction Tobacco Treatments [79]

Nicotine	**CYP_2A6**	**None**
Bupropion	**CYP_2B6** **CYP_2D6 inhibitor**	**Many**
Varenicline	**Excreted in urine**	**None**

Special Population: Pregnancy

In 2016, 7.2% of US women who gave birth smoked cigarettes during pregnancy. [80]

Smoking in pregnancy ↑ risks of:

- Spontaneous pregnancy loss
- Placenta abruption
- Ectopic pregnancy
- Placenta previa
- Preterm rupture of membranes
- Low birth weight
- Sudden infant death syndrome
- Low milk volume production and shorter duration of lactation

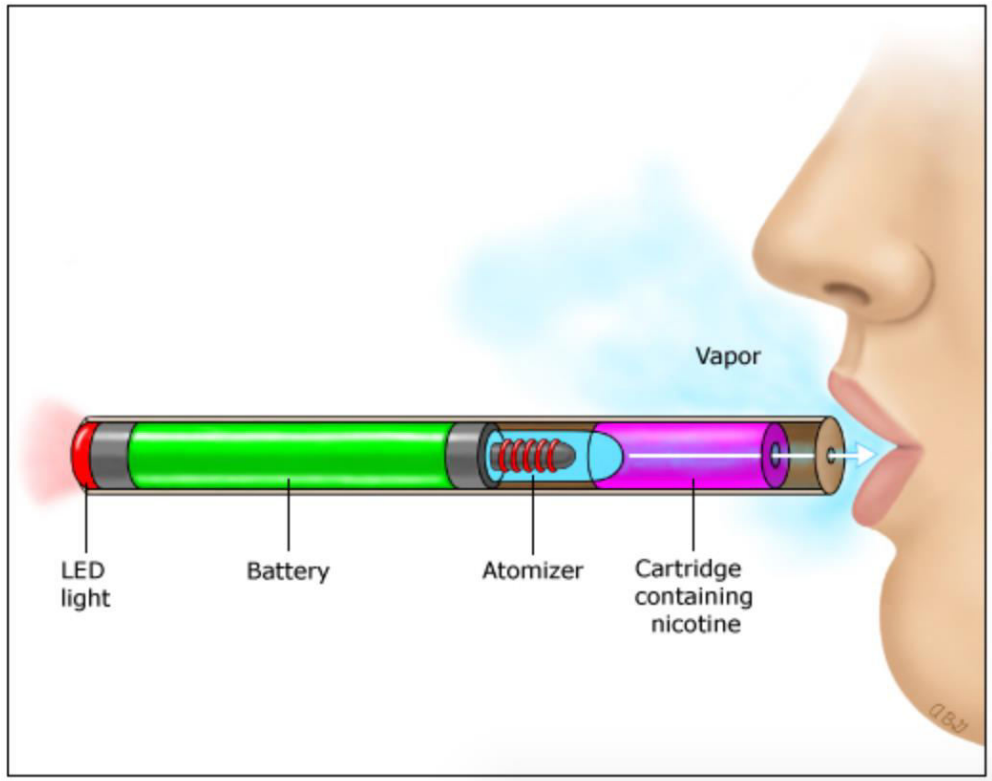
Special Population: Pregnancy [80]

- More likely to quit smoking in pregnancy
- Initiate intervention before conception
- Continue interventions during prenatal care visits
- Counseling is the first-line of treatment
- NRT or bupropion are acceptable second-line options (data lacking but supported by experts comities)
- Limited information regarding safety of varenicline

Special Population: Adolescents

- Early intervention is important
- Counseling is the first-line of treatment
- If counseling fails NRT is an acceptable options
- Insufficient data regarding bupropion and varenicline

E-Cigarettes



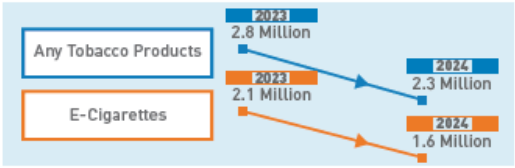
- Battery-operated device
- Heats liquid containing nicotine
- Creates vapor that is inhaled
- Entered US market in 2006 [81]

Image from Rigotti N. et al. E cigarette chapter. Uptodte 2019.

NYTS 2024

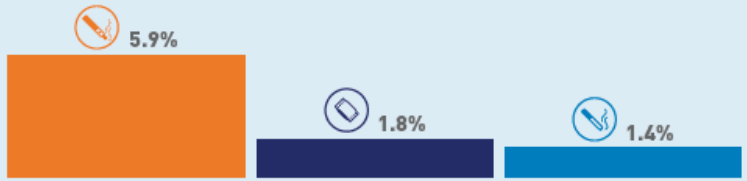
Youth Tobacco Product Use Drops to Lowest Level in Past 25 Years

Half a Million Fewer Students Used Tobacco Products in 2024



The decline in use of all tobacco products is largely attributable to the drop in students who used e-cigarettes.

Most commonly used products among middle and high school students:



E-Cigarettes
Youth e-cigarette use has dropped to a third of its peak in 2019

Nicotine Pouches
Youth nicotine pouch use remains low

Cigarettes
Youth cigarette use reaches all-time historic low

Among those who reported current e-cigarette use:



More than **1 in 4** (26.3%) used them daily

Majority (87.6%) used **flavored e-cigarettes** with fruit flavors being the most popular, followed by candy and mint

Youth use of tobacco products in any form - including e-cigarettes - is unsafe. Keeping tobacco products out of the hands of youth remains a top priority for the FDA.

Note: Current use: use on ≥1 day during the last 30 days. All numbers presented here are estimates.

Source: Jamal A, Park-Lee E, Birdsey J, et al. Tobacco Product Use Among Middle and High School Students — National Youth Tobacco Survey, United States, 2024. MMWR Morb Mortal Wkly Rep 2024;73:817–824.
Park-Lee E, Jamal A, Cowan H, et al. Notes from the Field: E-Cigarette and Nicotine Pouch Use Among Middle and High School Students — United States, 2024. MMWR Morb Mortal Wkly Rep 2024;73:774–778.

CENTER FOR TOBACCO PRODUCTS

CTP-190

FDA

Chemicals in Electronic Cigarettes [82,83]

- Propylene glycol, ethylene glycol and glycerin
- Nicotine
- Flavors (sweeteners)
- Most chemicals found at or below 1% of levels in tobacco smoke, and far below safety limits for occupational exposure.
  - Metals (cadmium, chromium, lead, manganese and nickel)
  - Formaldehyde
  - Other carcinogens
  - Solvents
  - Tobacco alkaloids

Association of Electronic Cigarette Use With Subsequent Initiation of Tobacco Cigarettes in US Youths

- Prospective cohort (6123=N), mean age 13.4
- Cigarette use at wave 3 was higher among prior e-cigarette users (20.5%) vs no prior tobacco (3.8%). 85
- Prior e-cigarette use was associated with more than 4 times the odds of ever cigarette use (odds ratio, 4.09; 95%CI, 2.97-5.63) and nearly 3 times the odds of current cigarette use (odds ratio, 2.75; 95%CI, 1.60-4.73) vs no prior tobacco use.
- Supports that e-cigarette use is associated with increased risk for cigarette initiation and use, particularly among low-risk youths.

E-cigarette or Vaping Associated Lung Injury (EVALI) [86]

- Lung injury cases associated with e-cigarette, or vaping, to CDC
- **Vitamin E acetate** -bronchoalveolar lavage (BAL) fluid samples
- Thickening agent in THC-containing e-cigarette
- **Most (86%) involved THC products**; some (11%) nicotine alone
- 70% of patients are male; 79% are < 35 years old

E-Cigarettes

- More frequently used by Americans than other FDA-approved treatments for smoking cessation
- Safer than combustible products, but long-term effects are unknown
- Controversial whether e-cigarette should be used as a first line of treatment, although this is common in UK

Select the one TRUE statement about nicotine dependence.

A. Smokers that report smoking within 30 minutes of waking are moderately nicotine dependent and may need medications to succeed in quitting

B. Smokers who use less than 10 cigarettes per day are not nicotine dependent

C. Users of electronic cigarettes almost never become addicted to nicotine

D. Treatment for tobacco dependence should not be initiated until the primary mental disorder is in remission and all symptoms have abated

References

- 1. Mathers CD, Loncar D. Projections of global mortality and burden of disease from 2002 to 2030. PLoSMed 2006;3(11):e442.
- 2. Gately I. Tobacco: a cultural history of how an exotic plant seduced civilization. New York: Grove Press, 2002.
- 3. CDC. State-specific prevalence of cigarette smoking and quitting among adults—United States, 2004. MMWR Morb Mortal Wkly Rep 2005;54:1124-1127.
- 4. Cummings, K Michael, and Robert N Proctor. "The changing public image of smoking in the United States: 1964-2014." *Cancer epidemiology, biomarkers & prevention : a publication of the American Association for Cancer Research, cosponsored by the American Society of Preventive Oncology* vol. 23,1 (2014): 32-6. doi:10.1158/1055-9965.EPI-13-0798
- 5. Giovino GA, Schooley MW, Zhu BP, Chrismon JH, Tomar SL, Peddicord JP, et al. Surveillance for Selected Tobacco-Use Behaviors - United States, 1900–1994. Centers for Disease Control and Prevention. CDC Surveillance Summaries, 1994. *MMWR.* 1994;43(SS-3):1–50
- 6. https://www.cdc.gov/tobacco/data_statistics/fact_sheets/fast_facts/index.htm#:~:text=More%20than%2016%20million%20Americans,a%20serious%20smoking%2Drelated%20illness.
- 7. https://www.who.int/news/item/22-09-2020-tobacco-responsible-for-20-of-deaths-from-coronary-heart-disease
- 8. Centers for Disease Control and Prevention. Vital signs: current cigarette smoking among adults aged ≥18 years with mental illness—United States, 2009-2011. MMWR Morb Mortal Wkly Rep 2013;62(5):81-87.
- 9. CDC. Annual smoking-attributable mortality, years of potential life lost, and economic costs: United States, 1995-1999. MMWR Morb Mortal Wkly Rep 2001;51(14):300-303.
- 10. Lawrence, D., Mitrou, F., & Zubrick, S. R. (2009). Smoking and mental illness: results from population surveys in Australia and the United States. *BMC public health*, *9*(1), 1-14.
- 11. Benowitz NL. Basic cardiovascular research and its implications for the medicinal use of nicotine. J Am Coll Cardiol 2003;41(3):497-498.
- 12. National Cancer Institute (NCI). (2001). *Risks Associated with Low Machine-Measured Yields of Tar and Nicotine* (NIH Publication No. 02-5074). Smoking and Tobacco Control Monograph No. 13. Bethesda, MD: U.S. Department of Health and Human Services, National Institutes of Health, National Cancer Institute.
- 13. Hecht SS. Human urinary carcinogen metabolites: biomarkers for investigating tobacco and cancer.
- 14. USDHHS. Cardiovascular diseases. In: How tobacco smoke causes disease: the biology and behavioral basis for smoking-attributable disease. Surgeon General's Report, US Department of Health and Human Services. 2010. http://www.surgeongeneral.gov/library/reports/tobaccosmoke/full_report.pdf:351-434.
- 15. USDHHS. Pulmonary diseases. In: How tobacco smoke causes disease: the biology and behavioral basis for smoking-attributable disease. Surgeon General's Report, US Department of Health and Human Services. 2010. http://www.surgeongeneral.gov/library/reports/tobaccosmoke/full_report.pdf:435-521.

References

- 16. DHHS. Women and Smoking. A Report of the Surgeon General. 2001 (Publication No. 099-6815).
- 17. Pierce, J. P., White, V. M., & Emery, S. L. (2012). What public health strategies are needed to reduce smoking initiation?. Tobacco control, 21(2), 258-264.
- 18. Di Chiara G. Role of dopamine in the behavioural actions of nicotine related to addiction. Eur J Pharmacol 2000;393(1-3):295-314.
- 19. Brody AL, Mandelkern MA, London ED, et al. Cigarette smoking saturates brain alpha 4 beta 2 nicotinicacetylcholine receptors. Arch Gen Psychiatry 2006;63(8):907-915.
- 20. Rose JE. Nicotine and nonnicotine factors in cigarette addiction. Psychopharmacology (Berl) 2006;184(3-4):274-285.
- 21. Palmatier MI, Liu X, Matteson GL, et al. Conditioned reinforcement in rats established with self-administered nicotine and enhanced by noncontingent nicotine. Psychopharmacology (Berl) 2007;195(2):235-243.
- 22. Rose JE, Behm FM, Westman EC. Acute effects of nicotine and mecamylamine on tobacco withdrawal symptoms, cigarette reward and ad lib smoking. Pharmacol Biochem Behav 2001;68(2):187-197.
- 23. Kenny PJ, Markou A. Conditioned nicotine withdrawal profoundly decreases the activity of brain reward systems. J Neurosci 2005;25(26):6208-6212.
- 24. Benowitz NL. Nicotine addiction. N Engl J Med 2010;362(24):2295-2303.
- 25. https://science.education.nih.gov/supplements/nih2/addiction/guide/lesson3-1.html
- 26 - Hukkanen J, Jacob P III, Benowitz NL. Metabolism and disposition kinetics of nicotine. Pharmacol Rev2005;57(1):79-115.
- 27. Henningfield JE, Stapleton JM, Benowitz NL, et al. Higher levels of nicotine in arterial than in venous blood after cigarette smoking. Drug Alcohol Depend 1993;33(1):23-29.
- 28. Dempsey D, Tutka P, Jacob P III, et al. Nicotine metabolite ratio as an index of cytochrome P450 2A6metabolic activity. Clin Pharmacol Ther 2004;76(1):64-72.
- 29. Dempsey D, Jacob P III, Benowitz NL. Accelerated metabolism of nicotine and cotinine in pregnant smokers. J Pharmacol Exp Ther 2002;301(2):594-598.
- 30. Perez-Stable EJ, Herrera B, Jacob P III, et al. Nicotine metabolism and intake in black and white smokers. JAMA 1998;280(2):152-156.
- 31. Haiman CA, Stram DO, Wilkens LR, et al. Ethnic and racial differences in the smoking-related risk of lung cancer. N Engl J Med 2006;354(4):333-342.
- 32. Malaiyandi V, Sellers EM, Tyndale RF. Implications of CYP2A6 genetic variation for smoking behaviors and nicotine dependence. Clin Pharmacol Ther 2005;77(3):145-158.

References

- 33. Benowitz NL. Cotinine as a biomarker of environmental tobacco smoke exposure. Epidemiol Rev 1996;18(2):188-204.
- 34. Jacob P III, Hatsukami D, Severson H, et al. Anabasine and anatabine as biomarkers for tobacco use during nicotine replacement therapy. Cancer Epidemiol Biomarkers Prev 2002;11(12):1668-1673.
- 35. Jarvis M, Tunstall-Pedoe H, Feyerabend C, et al. Biochemical markers of smoke absorption and self-reported exposure to passive smoking. J Epidemiol Community Health 1984;38(4):335-339.
- 36. Benowitz NL, Dains KM, Dempsey D, et al. Estimation of nicotine dose after low-level exposure using plasma and urine nicotine metabolites. Cancer Epidemiol Biomarkers Prev 2010;19(5):1160-1166.
- 37. Jacob P III, Hatsukami D, Severson H, et al. Anabasine and anatabine as biomarkers for tobacco useduring nicotine replacement therapy. Cancer Epidemiol Biomarkers Prev2002;11(12):1668-1673.
- 38. Zevin S, Benowitz NL. Drug interactions with tobacco smoking. An update. Clin Pharmacokinet1999;36(6):425-438.
- 39. https://www.aafp.org/dam/AAFP/documents/patient_care/tobacco/drug-interactions.pdf
- 40. Schiff I, Bell WR, Davis V, Kessler CM, Meyers C, Nakajima S, Sexton BJ. Oral contraceptives and smoking, current considerations: recommendations of a consensus panel. Am J Obstet Gynecol. 1999 Jun;180(6 Pt 2):S383-4.
- 41. DHHS. Women and Smoking. A Report of the Surgeon General. 2001 (Publication No. 099-6815).
- 42. Zevin S, Benowitz NL. Drug interactions with tobacco smoking. An update. Clin Pharmacokinet1999;36(6):425-438.
- 43. Chiolero A, Faeh D, Paccaud F, et al. Consequences of smoking for body weight, body fat distribution, and insulin resistance. Am J Clin Nutr 2008;87(4):801-809.
- 44. Benowitz NL. Pharmacologic aspects of cigarette smoking and nicotine addiction. N Engl J Med1988;319:1318-1330.
- 45. Benowitz NL, Hansson A, Jacob P III. Cardiovascular effects of nasal and transdermal nicotine andcigarette smoking. Hypertension 2002;39(6):1107-1112.
- 46. Mercincavage M, Branstetter SA, Muscat JE, Horn KA. Time to first cigarette predicts cessation outcomes in adolescent smokers. Nicotine Tob Res. 2013 Dec;15(12):1996-2004.
- 47. Balfour D. The neurochemical mechanisms underlying nicotine tolerance and dependence. In: Pratt J, ed. The biological basis of drug tolerance and dependence. London, UK: Academic Press, 1991:121-151.
- 48. Cosgrove KP, Batis J, Bois F, et al. Beta2-Nicotinic acetylcholine receptor availability during acute and prolonged abstinence from tobacco smoking. Arch Gen Psychiatry 2009;66(6):666-676.

References

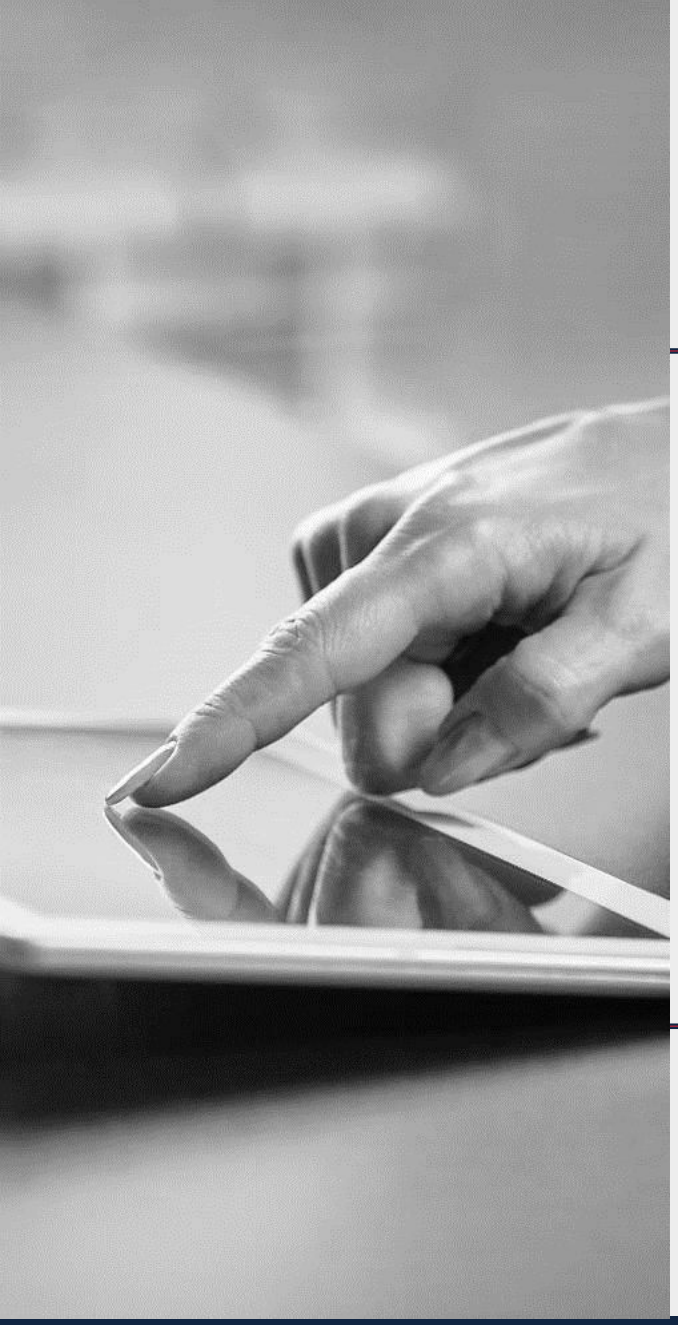
- 49. CDC. State-specific prevalence of cigarette smoking and quitting among adults—United States, 2004. MMWR Morb Mortal Wkly Rep 2005;54:1124-1127.
- 50. Rose JE, Behm FM, Westman EC. Acute effects of nicotine and mecamylamine on tobacco withdrawal symptoms, cigarette reward and ad lib smoking. Pharmacol Biochem Behav 2001;68(2):187-197.
- 51. Kenny PJ, Markou A. Conditioned nicotine withdrawal profoundly decreases the activity of brain reward systems. J Neurosci 2005;25(26):6208-6212.
- 52. George O, Ghozland S, Azar MR, et al. CRF-CRF1 system activation mediates withdrawal-induced increases in nicotine selfadministration in nicotine-dependent rats. Proc Natl Acad Sci U S A 2007;104(43):17198-17203.
- 53. De Biasi M, Dani JA. Reward, addiction, withdrawal to nicotine. Annu Rev Neurosci 2011;34:105-130.
- 54. Fowler JS, Logan J, Wang GJ, et al. Monoamine oxidase and cigarette smoking. Neurotoxicology2003;24(1):75-82.
- 55. Lewis A, Miller JH, Lea RA. Monoamine oxidase and tobacco dependence. Neurotoxicology 2007;28(1):182-195.
- 56. Talhout R, Opperhuizen A, van Amsterdam JG. Role of acetaldehyde in tobacco smoke addiction. EurNeuropsychopharmacol 2007;17(10):627-636.
- 57. Guillem K, Vouillac C, Azar MR, et al. Monoamine oxidase inhibition dramatically increases themotivation to self-administer nicotine in rats. J Neurosci 2005;25(38):8593-8600.
- 58. Jacob P III, Hatsukami D, Severson H, et al. Anabasine and anatabine as biomarkers for tobacco use during nicotine replacement therapy. Cancer Epidemiol Biomarkers Prev 2002;11(12):1668-1673.
- 59. USDHHS. Pulmonary diseases. In: How tobacco smoke causes disease: the biology and behavioral basis for smoking-attributable disease. Surgeon General's Report, US Department of Health and Human Services. 2010. http://www.surgeongeneral.gov/library/reports/tobaccosmoke/full_report.pdf:435-521.
- 59. USDHHS. Pulmonary diseases. In: How tobacco smoke causes disease: the biology and behavioral basis for smoking-attributable disease. Surgeon General's Report, US Department of Health and Human Services. 2010. http://www.surgeongeneral.gov/library/reports/tobaccosmoke/full_report.pdf:435-521.
- 60. Hecht SS. Human urinary carcinogen metabolites: biomarkers for investigating tobacco and cancer.
- 61. USDHHS. Cardiovascular diseases. In: How tobacco smoke causes disease: the biology and behavioral basis for smoking-attributable disease. Surgeon General's Report, US Department of Health and Human Services. 2010. http://www.surgeongeneral.gov/library/reports/tobaccosmoke/full_report.pdf:351-434.
- 62. DHHS. Women and Smoking. A Report of the Surgeon General. 2001 (Publication No. 099-6815).

References

- 63. -Yin L, Morita A, Tsuji T. Skin aging induced by ultraviolet exposure and tobacco smoking: evidence from epidemiological and molecular studies. Photodermatol Photoimmunol Photomed 2001;17(4):178-183.
- 64. Foulds, J., Gandhi, K. K., Steinberg, M. B., Richardson, D. L., Williams, J. M., Burke, M. V., & Rhoads, G. G. (2006). Factors associated with quitting smoking at a tobacco dependence treatment clinic. American Journal of Health Behavior, 30(4), 400-412.
- 65.Ashare, R. L., Wileyto, E. P., Ruparel, K., Goelz, P. M., Hopson, R. D., Valdez, J. N., ... & Lerman, C. (2013). Effects of tolcapone on working memory and brain activity in abstinent smokers: a proof-of-concept study. Drug and alcohol dependence, 133(3), 852-856.
- 66. Twyman, L., Bonevski, B., Paul, C., Bryant, J., West, R., Siahpush, M., ... & Palazzi, K. (2018). What factors are associated with abstinence amongst socioeconomically disadvantaged smokers? A cross-sectional survey of use of cessation aids and quitting approach. Drug and alcohol review, 37(2), 170-179.
- 67. Fiore M, Jaén C, Baker T, et al. Treating tobacco use and dependence: 2008 update. Quick reference guide for clinicians. Rockville, MD: U.S. Department of Health and Human Services. Public Health Service,2009.
- 68. Fiore M, Jaén C, Baker T, et al. Treating tobacco use and dependence: 2008 update. Quick reference guide for clinicians. Rockville, MD: U.S. Department of Health and Human Services. Public Health Service, 2009.
- 69. Piper ME, Smith SS, Schlam TR, et al. A randomized placebo controlled clinical trial of 5 smoking cessation pharmacotherapies. Arch Gen Psychiatry 2009;66(11):1253-1262.
- 70. Ebbert JO, Hays JT, Hurt RD. Combination pharmacotherapy for stopping smoking: what advantages does it offer? Drugs 2010; 70(6):643-650.
- 71. Piper ME, Smith SS, Schlam TR, et al. A randomized placebo controlled clinical trial of 5 smoking cessation pharmacotherapies. Arch Gen Psychiatry 2009;66(11):1253-1262.
- 72. Ebbert JO, Hays JT, Hurt RD. Combination pharmacotherapy for stopping smoking: what advantages does it offer? Drugs 2010; 70(6):643-650.
- 73. Rollema H, Chambers LK, Coe JW, et al. Pharmacological profile of the alpha4beta2 nicotinic acetylcholine receptor partial agonist varenicline, an effective smoking cessation aid. Neuropharmacology 2007;52(3):985-994.
- 74. Anthenelli, R. M., Benowitz, N. L., West, R., St Aubin, L., McRae, T., Lawrence, D., ... & Evins, A. E. (2016). Neuropsychiatric safety and efficacy of varenicline, bupropion, and nicotine patch in smokers with and without psychiatric disorders (EAGLES): a double-blind, randomised, placebo-controlled clinical trial. The Lancet, 387(10037), 2507-2520.
- 75. Cahill, K., Stevens, S., Perera, R., & Lancaster, T. (2013). Pharmacological interventions for smoking cessation: an overview and network meta-analysis. Cochrane database of systematic reviews, (5).

References

- 76. http://www.fda.gov/Drugs/DrugSafety/ucm532221.htm
- 77. Perkins KA. Nicotine discrimination in men and women. Pharmacol Biochem Behav 1999;64(2):295-299.
- 78. Smith, P. H., Zhang, J., Weinberger, A. H., Mazure, C. M., & McKee, S. A. (2017). Gender differences in the real-world effectiveness of smoking cessation medications: Findings from the 2010–2011 Tobacco Use Supplement to the Current Population Survey. Drug and alcohol dependence, 178, 485-491.
- 79. Zhong, Z., Zhao, S., Zhao, Y., & Xia, S. (2019). Combination therapy of varenicline and bupropion in smoking cessation: A meta-analysis of the randomized controlled trials. Comprehensive psychiatry, 95, 152125.
- 80. https://www.cdc.gov/nchs/products/databriefs/db305.htm
- 81. National Center for Chronic Disease Prevention and Health Promotion (US) Office on Smoking and Health. E-Cigarette Use Among Youth and Young Adults: A Report of the Surgeon General [Internet]. Atlanta (GA): Centers for Disease Control and Prevention (US); 2016. Chapter 4, Activities of the E-Cigarette Companies. Available from: https://www.ncbi.nlm.nih.gov/books/NBK538679/
- 82. U.S. Food and Drug Administration (FDA). Summary of results: laboratory analysis of electronic cigarettes conducted by FDA. 2009; http://www.fda.gov/newsevents/publichealthfocus/ucm173146.htm. Accessed November 5, 2012.
- 83. Farsalinos, Konstantinos E, and Riccardo Polosa. “Safety evaluation and risk assessment of electronic cigarettes as tobacco cigarette substitutes: a systematic review.” Therapeutic advances in drug safety vol. 5,2 (2014): 67-86. doi:10.1177/2042098614524430
- 84. https://www.drugabuse.gov/drug-topics/trends-statistics/monitoring-future
- 85. Berry, K. M., Fetterman, J. L., Benjamin, E. J., Bhatnagar, A., Barrington-Trimis, J. L., Leventhal, A. M., & Stokes, A. (2019). Association of electronic cigarette use with subsequent initiation of tobacco cigarettes in US youths. JAMA network open, 2(2), e187794-e187794.
- 86. https://www.cdc.gov/tobacco/basic_information/e-cigarettes/severe-lung-disease.html



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ASAM REVIEW COURSE 2026

Cannabis Use Disorder: Science, Trends, and Clinical Implications

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Financial Disclosure

Mashal Khan, MD

- No relevant disclosures

Learning Objectives

- Increase knowledge about current epidemiological trends in cannabis use in the United States.
- Name the different formulations of cannabis that impact individuals today.
- Review medications that have an evidence base for treating cannabis withdrawal and cannabis use disorder.

Epidemiology

Cannabis Use/Misuse

- In 2024, an estimated 44.3 million Americans- **15.4%** of the population aged 12 years or older had used cannabis in the preceding month.

- In 2015, it was 22.2 million (**8.9%**) Americans aged 12 years and older.

- By the end of 2023, more than half of the U.S. population lived in a state that had legalized recreational (adult-use) cannabis – a major driver of rising use, CUD prevalence, and product potency.

Increased Risk for Use Disorder

- 9% of users develop Cannabis Use Disorder
- Cannabis use peaks in the late teens to early 20s, then declines
- The risk increases to 17% in people who start using in adolescence.
- The risk increases to 25 to 50% in people who are daily users (most of whom started using marijuana early in adolescence).

Cannabis Basics

- The cannabis plant has 104 cannabinoids; only 2 (THC and CBD) have been extensively studied for potential therapeutic applications.
- THC is the most psychoactive component – (*inhaled, ingested*)
- CBD is postulated to have other mechanisms of action (anti-inflammatory, analgesic, etc.).

Cannabis Plant







Natural, Plant - Derived Cannabinoids

- Cannabis
- Sativa, Indica, or Hybrid
- Genus Cannabis; “hemp” = low-THC (<0.3%) cultivars, “marijuana” = higher-THC cultivars

Natural, Plant - Derived Cannabinoids



Most common preparations:

*Marijuana

*Hashish

*Hash Oil

THC Concentrations vary—

For example, extraction of THC with butane (“dabs”) can contain up to 90% THC.

Synthetic Cannabinoids

- Higher affinity for cannabinoid receptors than THC
- Have active metabolites that prolong their durations of action
- Increased potential for toxicity
- “Spice” or “K2”
- Not detected on standard UDS





Synthetic Cannabinoids





Seely et al. Spice Drugs are More than Harmless Herbal Blends: A Review of the Pharmacology and Toxicology of Synthetic Cannabinoids. Prog Neuropsychopharmacol Biol Psychiatry. 2012;39(2):234-243.

Spice/K2, Synthetic Marijuana. dea.gov.

Semi-Synthetic “Hemp-Derived” Cannabinoids

- Delta-8-THC – isomer of Delta-9-THC, psychoactive but less potent; often chemically synthesized from CBD

- THC-O-acetate & HHC – semi-synthetic analogs, higher potency, unregulated production

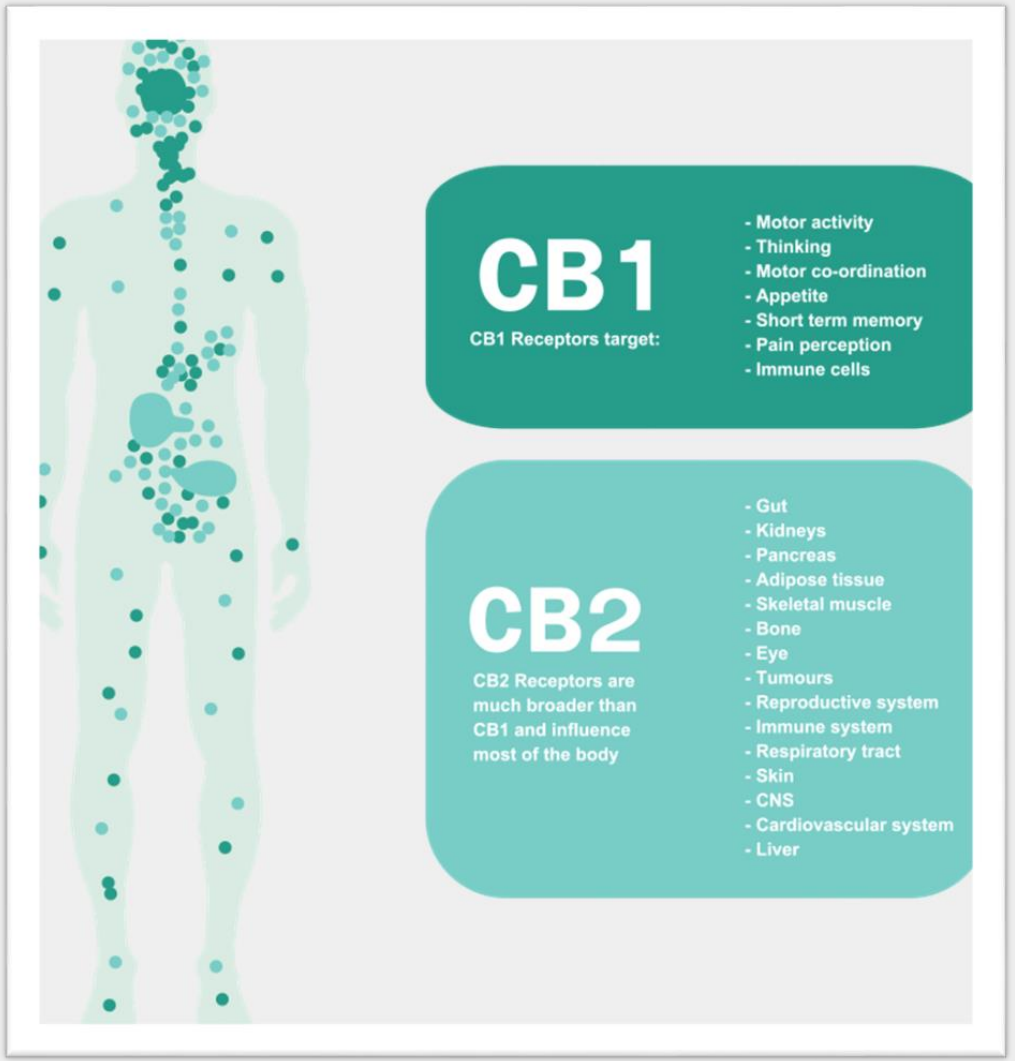
Cannabinoid Receptor Neurobiology

The Cannabinoid System

- THC activates the CB1 and CB2 cannabinoid receptors:
  - CB1 has high density in cerebellum, basal ganglia, hippocampus, cerebral cortex. *G protein mediated system*.
  - CB1 has low density in the brainstem, hence low risk of respiratory depression.
  - CB2 is found in spleen, hematopoietic cell lines, mast cells.

Cannabinoid Receptors

- CB1 – CNS site of CB binding
  - Memory, learning, problem solving, coordination
  - Activated by anandamide, other CBs
  - Modulates neurotransmitters
- CB2 – immune cells outside CNS
  - Anti-inflammatory effects

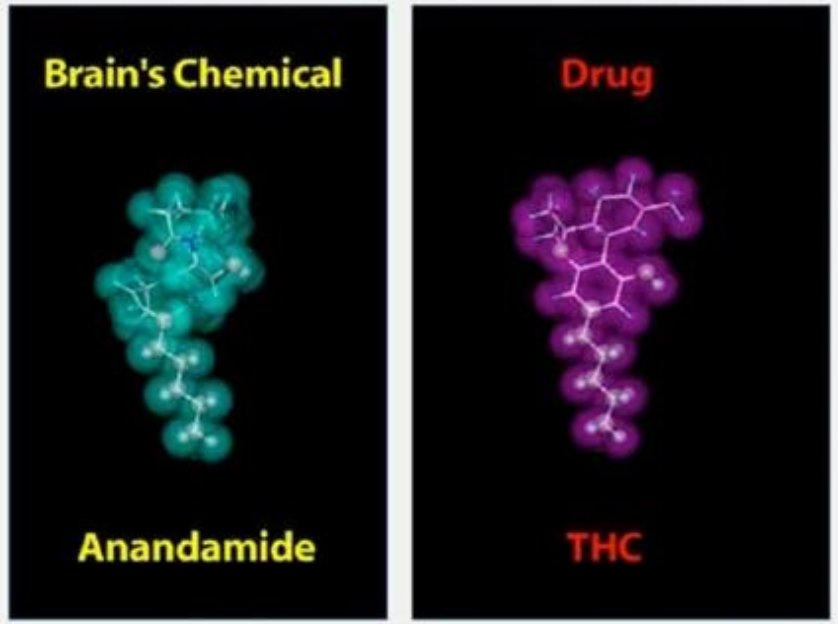


Cannabinoids (CBs)

- > 400 chemicals, ↓ neurotransmitter release
- Natural CBs
  - Endogenous – Anandamide, 2-Arachidonoylglycerol (AEA, 2-AG)
  - Exogenous – Sativa or Indica plant (marijuana)
    - Tetrahydrocannabinol (THC) – psychoactive
    - Cannabidiol (CBD) – non-intoxicating; centrally active (e.g., anticonvulsant)



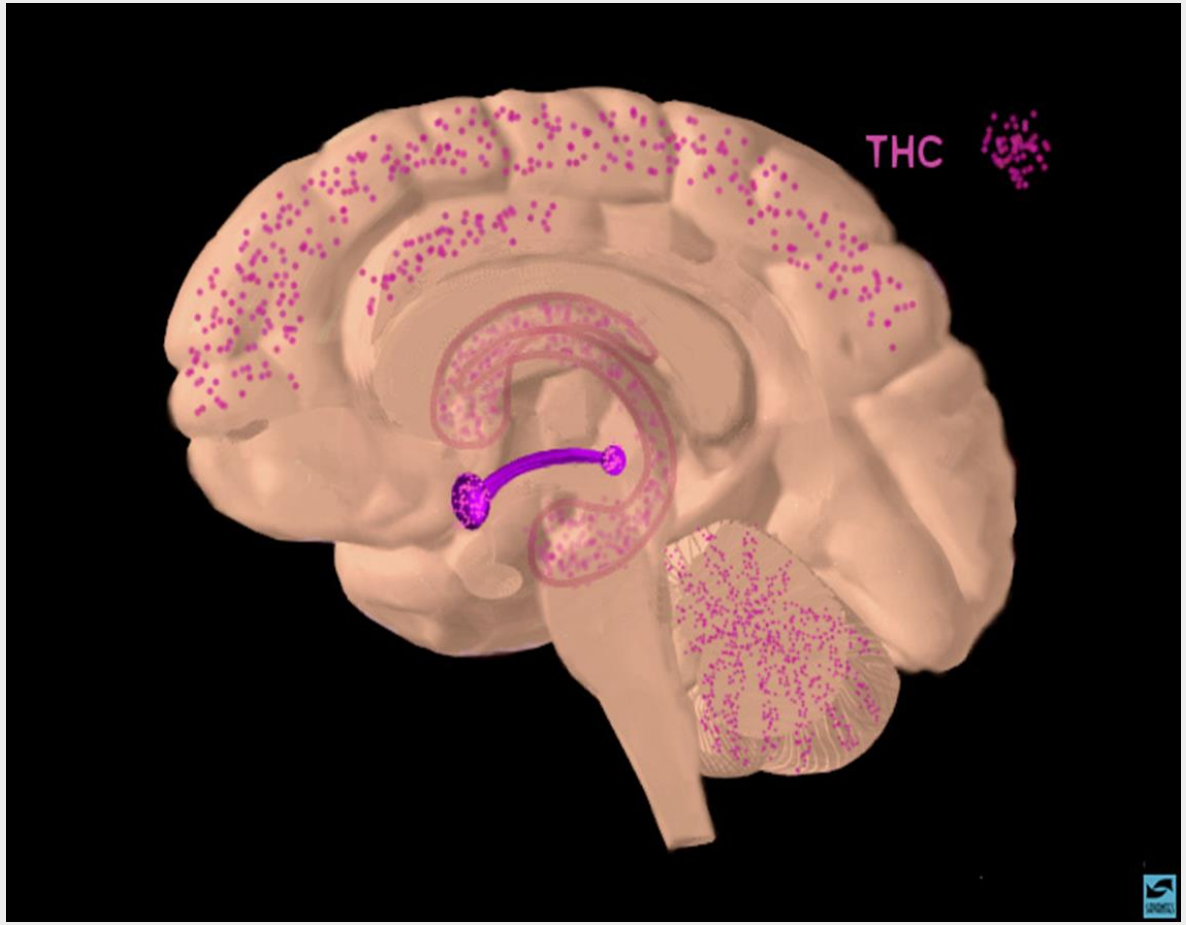
9-tetrahydrocannabinol (THC)

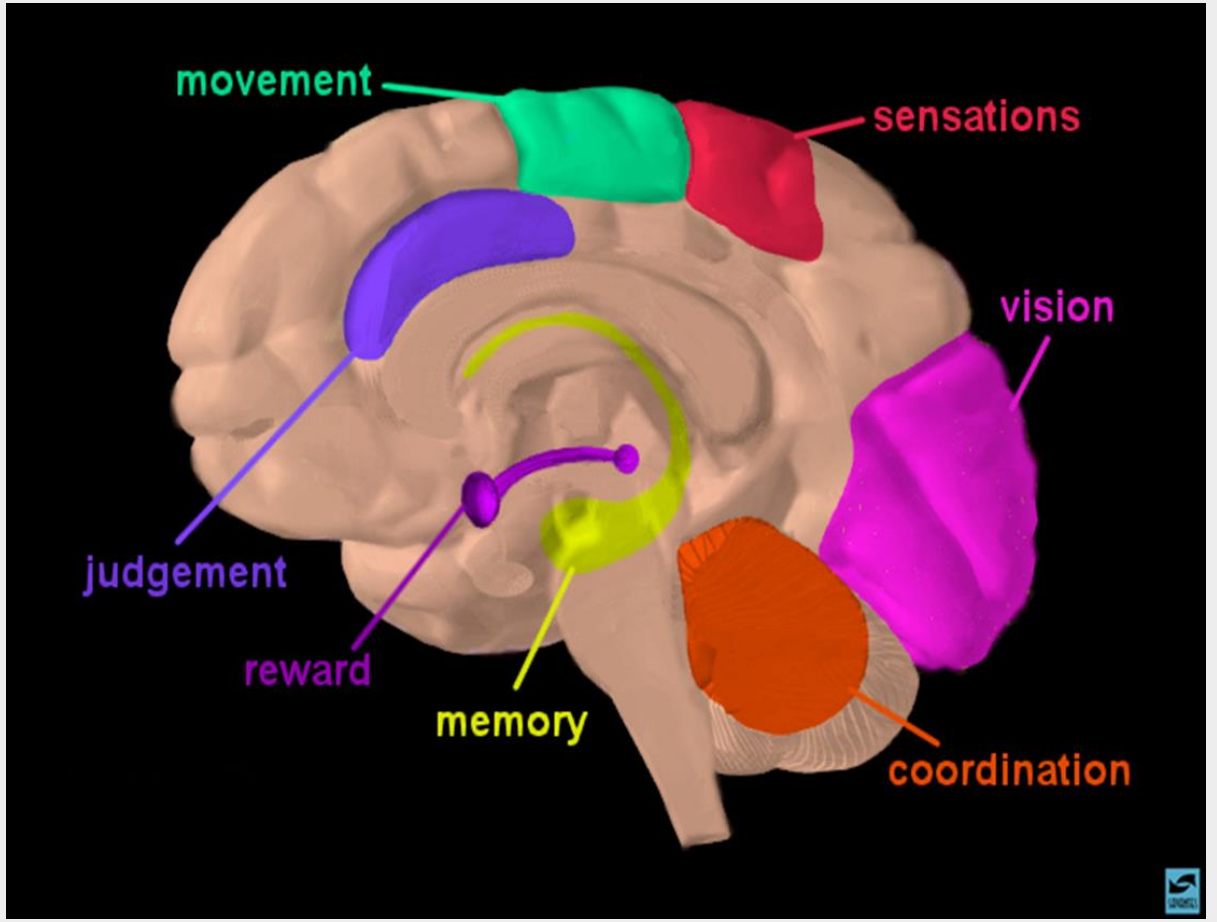




- Primary psychoactive constituent
- Endocannabinoid system
  - Brain development
- Mimics anandamide
  - Dial down neuron activity

CB1 Receptor Locations in the Brain





Neurotransmitter modulation

- Dopamine – euphoria, reward, pleasure
- GABA- muscle relaxation and sleepiness
- ↓ Glutamate- relaxation, ↓ memory

Cannabis Intoxication

- *Desired effects*: relaxation, euphoria, slowed time perception, altered sensory perception, increased appetite.

- *Undesired effects*: impaired concentration, anterograde amnesia, anxiety, panic attacks, paranoia, derealization/depersonalization, acute psychosis (may include hallucinations, which are more commonly visual but can also be auditory).

Synthetic Cannabinoid Toxicity

Central Nervous System	Seizures	*Cardiovascular*	Tachycardia
	Agitation		Hypertension
	Irritation		Chest pain
	Loss of consciousness		Cardiac Ischemia
	Anxiety		
	Confusion	*Gastrointestinal*	Nausea
	Paranoia		Vomiting
Metabolic	Hypokalemia	*Autonomic*	Fever
	Hyperglycemia		Mydriasis
		Other	Conjunctivitis

Seely et al. Marijuana-based Drugs: Innovative Therapeutics or Designer Drugs of Abuse? Mol Interv. 2011;11(1):36-51.

Routes of Administration

- Smoked:
  - Reaches the brain in minutes
  - Effects last 1 - 3 hours
  - Delivers significant amount of THC into the bloodstream

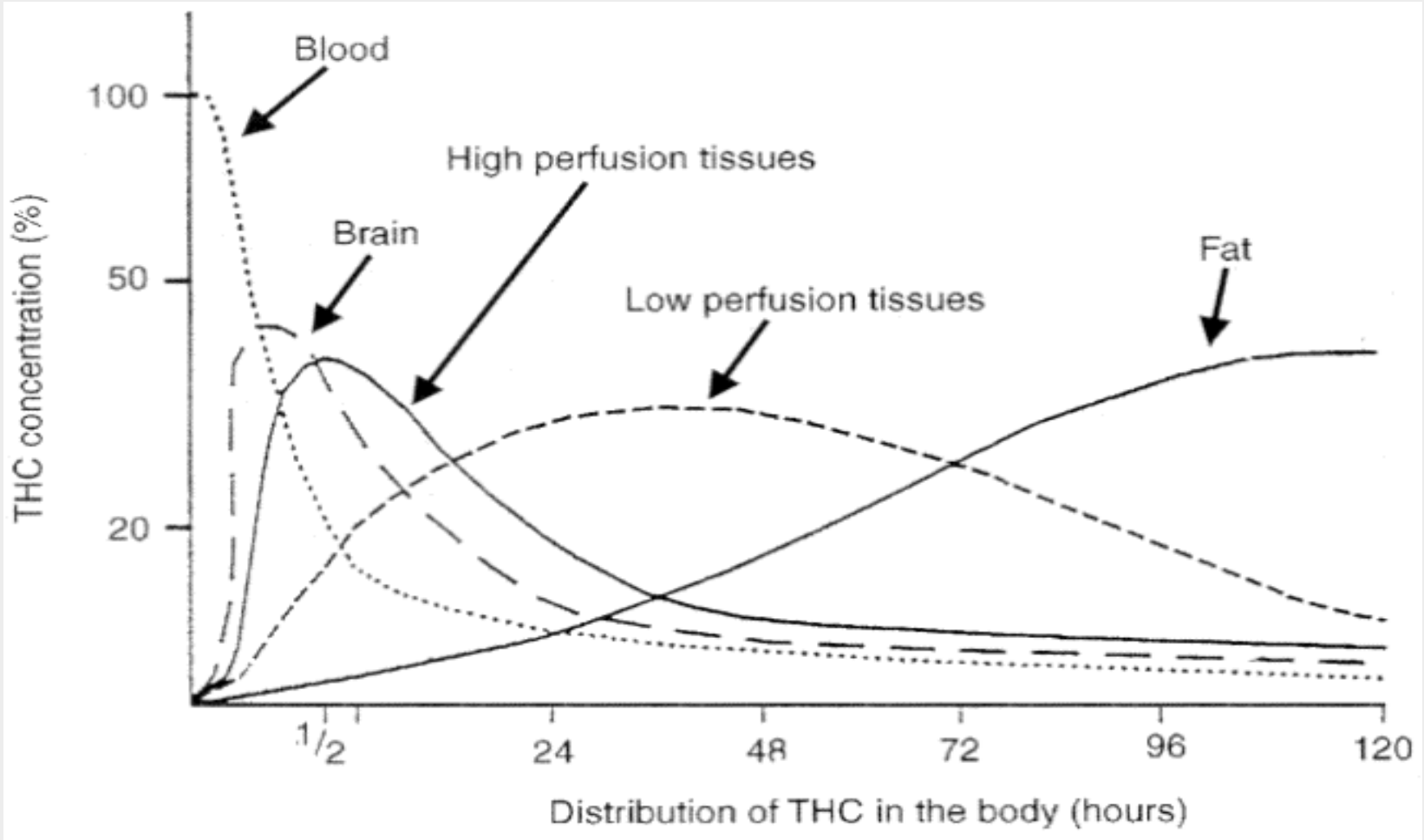
Smoked	*Vaporized*	*Eaten/Drunk*
Smoked in a pipe, bowl, cigarette	Inhaled through machine that converts active compounds into inhalable form	Consumed as ingredient in baked goods, candies, sodas
Rapid effects	Rapid effects	Takes time to reach brain, so effects are delayed

Routes of Administration

- Eating or drinking marijuana:
  - Takes ½ - 1 hour to have an effect
  - Effects last up to 4 hours
  - THC is metabolized by the liver into 11-hydroxy-THC
  - 11-Hydroxy-THC is more lipophilic, potent and has a longer half-life.

Smoked	*Vaporized*	*Eaten/Drunk*
Smoked in a pipe, bowl, cigarette	Inhaled through machine that converts active compounds into inhalable form	Consumed as ingredient in baked goods, candies, sodas
Rapid effects	Rapid effects	Takes time to reach brain, so effects are delayed

Biphasic distribution



2019 National Drug Threat Assessment. US Department of Justice Drug Enforcement Administration. December 2019.

Toxicology Testing

- Casual use:
  - Up to 10 days in urine
  - 50% positive in hair samples
- Heavy use:
  - Up to 30 days in urine
  - 85% positive in hair samples

- Measures THC
- Weight loss gives serial UTox spike
- Dronabinol gives positive test
- Passive inhalation gives negative test

Cannabis Withdrawal

- Reported by up to 1/3 of persons who use cannabis frequently.
- Cannabis withdrawal is recognized by the DSM 5.
- Clinical trials – show reduction of withdrawal symptoms with synthetic THC (dronabinol), nabilone, nabiximol, and gabapentin.

Cannabis Withdrawal

Causing distress & ≥ 3 of the following:

- Irritability
- Anxiety
- Sleep problems
- ↓ Appetite/weight loss
- Depressed Mood
- Restlessness

AND ≥ 1 of the following:

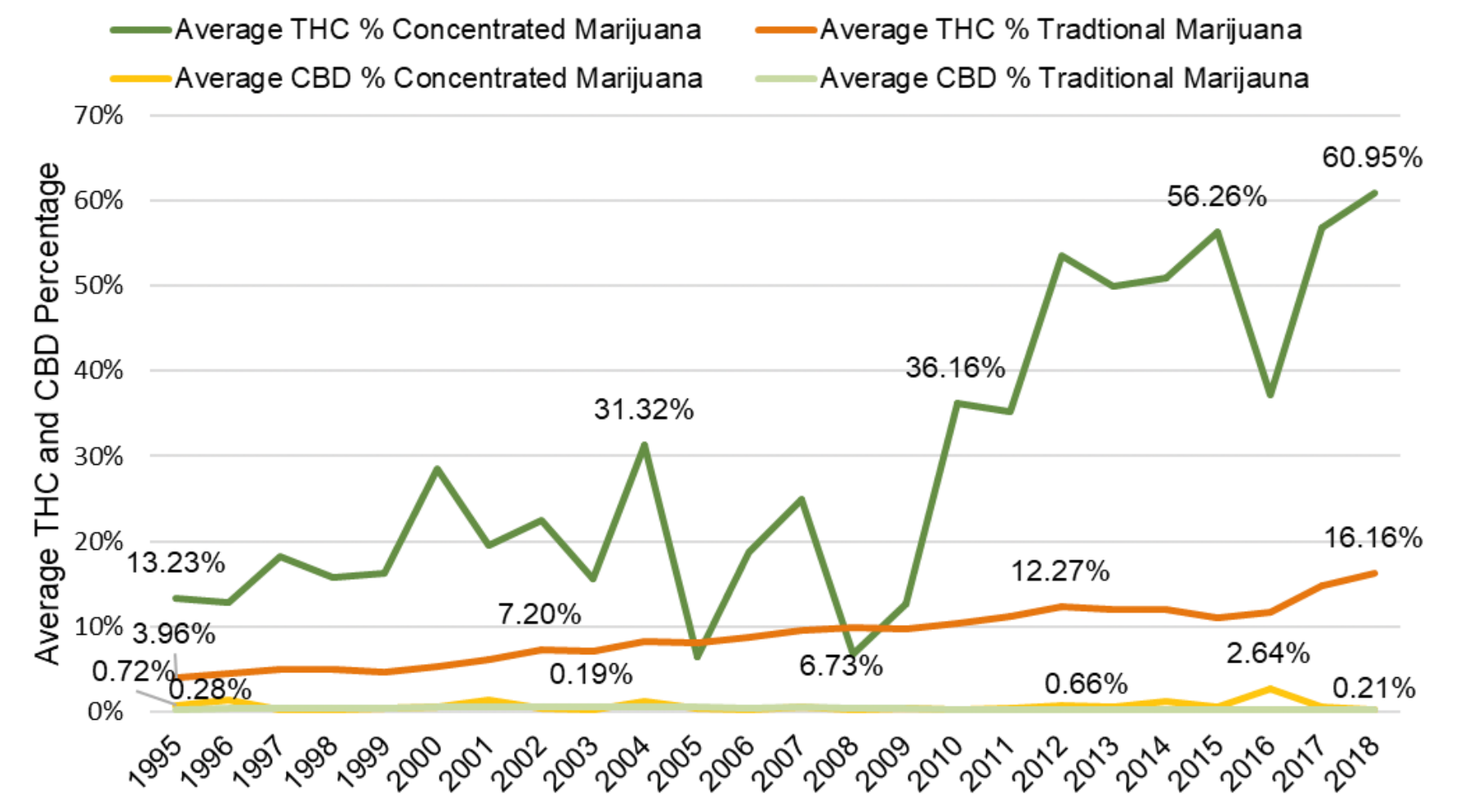
- Abdominal pain
- Sweating
- Shakiness/tremors
- Fever/chills
- Headache

THC Potency is Increasing

- Average flower potency has climbed well past 31% in many legal markets; concentrate products (dabs, wax, shatter, live resin) now routinely exceed 70–90% THC

- Widespread availability of THC edibles (food and beverage products) and butane-extracted hash oil products (“dabs”, “budder”, “shatter”, “wax”)

THC Percent is Increasing



2019 National Drug Threat Assessment. US Department of Justice Drug Enforcement Administration. December 2019.

Special Populations and Cannabis

- Adolescents
- Pregnant persons

Decreased Harm Perception: Adolescents

- 36% of teens think cannabis is harmless
  - 43% favor legalization
  - 80s: 15%
  - 90s-00s: 30%

- Harm perception lowest in 40 yrs
  - Often precedes ↑ prevalence

Rates ↑ Across Adolescence

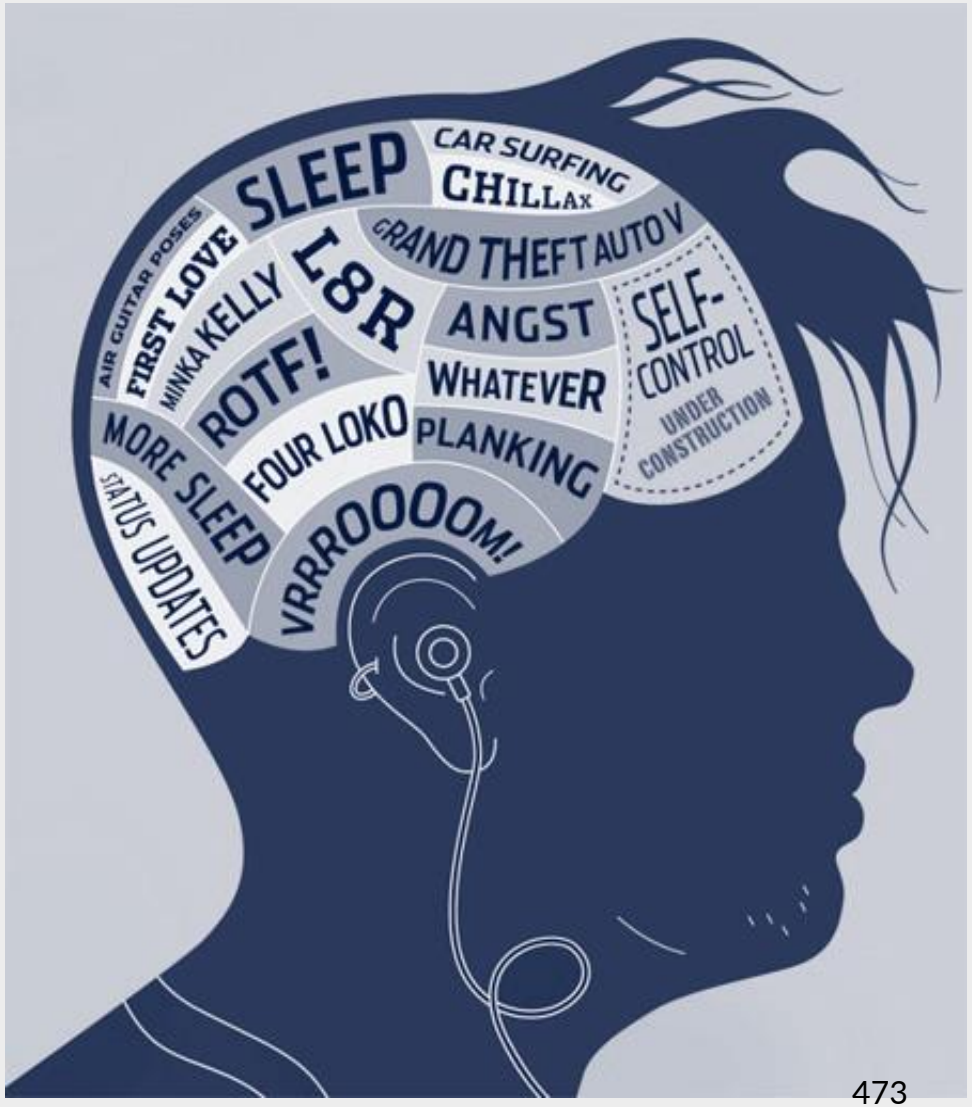
- Ever tried
  - ~17% 8th graders
  - ~50%12th graders
- Past year use
  - 12% 8th graders
  - 35% 12th graders
- Current use (past month)
  - 7% 8th graders
  - 21% 12th graders
  - Surpasses current alcohol and tobacco use

Special Populations: Young Children

- Accidental Pediatric Edible Ingestion
  - Rising ED visits and poison control calls among young children, driven by THC edibles resembling candy, cookies, or gummies
  - Presentation: lethargy, ataxia, somnolence, occasionally respiratory depression in young children (proportionally larger dose per kg)
  - Management is largely supportive; consider child safety/home environment counseling and safe storage

Adolescent Brain

- May be vulnerable to the addictive nature of cannabis and neurotoxic effects, including development of psychiatric disorders.
- One study showed decline in IQ among cannabis users before the age of 18, with much less recovery of neuro-psych functioning.
- NSDUH data: risk for cannabis dependence is higher if use begins before age 16 (17% versus 9%)
- Most and latest change in areas of:
  - Reward and motivation
  - Cognition



Pregnancy

- Endocannabinoid system plays a role in the control of brain maturation, particularly emotional responses

- THC crosses the placenta (also note effect of smoking)

Pregnancy

- Babies exposed to THC:
  - Neurological development effects
  - Reduction in fetal growth, also other negative effects on the infant

Pregnancy

- Children exposed to THC:
  - Problem-solving skills, memory, attention deficit

- THC-specific vs. associated environmental factors hard to sort out; ongoing debate and research.

Effects of Use

Physiological Effects

- Adrenergic look-alike:
  - Tachycardia
  - Hypertension (but orthostatic hypotension)
  - Tachypnea
  - Dry mouth
- Conjunctival injection
- Appetite increase

Impaired Cognition

- ↓ Ability to learn
- ↓ Attention, concentration
- ↓ Abstract reasoning and decision-making
- ↓ Memory

Neurocognitive Effects

- Short-term memory impairment
- Judgment impairment
- Motor coordination impairment (increased risk of MVA)

Impaired Driving

- Acute THC
  - → ↓ Peripheral vision
  - → ↓ Motor coordination
    - → ↑ reaction time
    - → ↓ time/distance judgment
- #1 reported illicit drug in accidents/fatalities
  - 2x accident risk
  - 3-7x risk of causing accident

Physical Health

- Respiratory
  - ↓ Function
  - ↑ Infections
- ↑ Stroke/Temporary brain blood constriction

Cannabinoid Hyperemesis Syndrome (CHS)

- Seen in long-term, frequent (often daily) cannabis users
- Classic features:
  - Cyclic, severe nausea and vomiting
  - Compulsive hot showers/baths for symptom relief
  - Diffuse abdominal pain
  - Resolves with sustained cannabis cessation (key distinguishing feature from cyclic vomiting syndrome)
- **Treatment:** IV fluids, capsaicin cream to the abdomen, haloperidol/droperidol (more effective than typical antiemetics like ondansetron), benzodiazepines as adjuncts, and cessation counseling

Cardiovascular Risk with Cannabis Use

- Acute use: tachycardia and increased myocardial oxygen demand can trigger angina/MI in susceptible patients
- Regular/heavy use: associated with increased risk of MI and stroke, independent of tobacco use
- Cannabis arteritis – rare peripheral arteritis resembling Buerger's disease, seen in young, otherwise healthy heavy cannabis users
- Reversible Cerebral Vasoconstriction Syndrome (RCVS) – thunderclap headache, vasospasm, can cause ischemic/hemorrhagic stroke

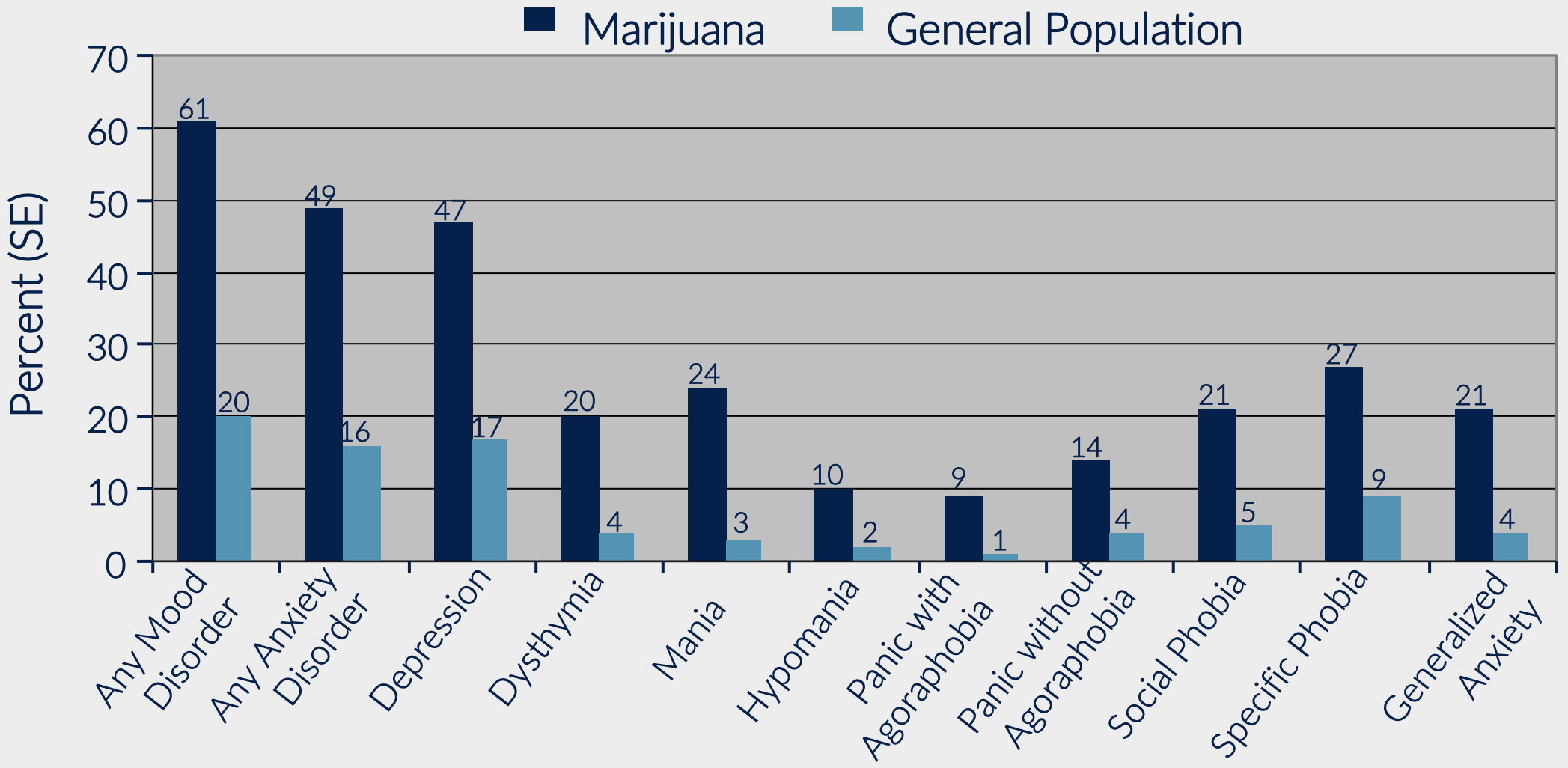
Psychiatric

- Anxiety
  - Acute THC → ↓ anxiety
  - Long-term THC → ↑ anxiety
- ↑ Depression
- ↑ Psychosis

Amotivational Syndrome

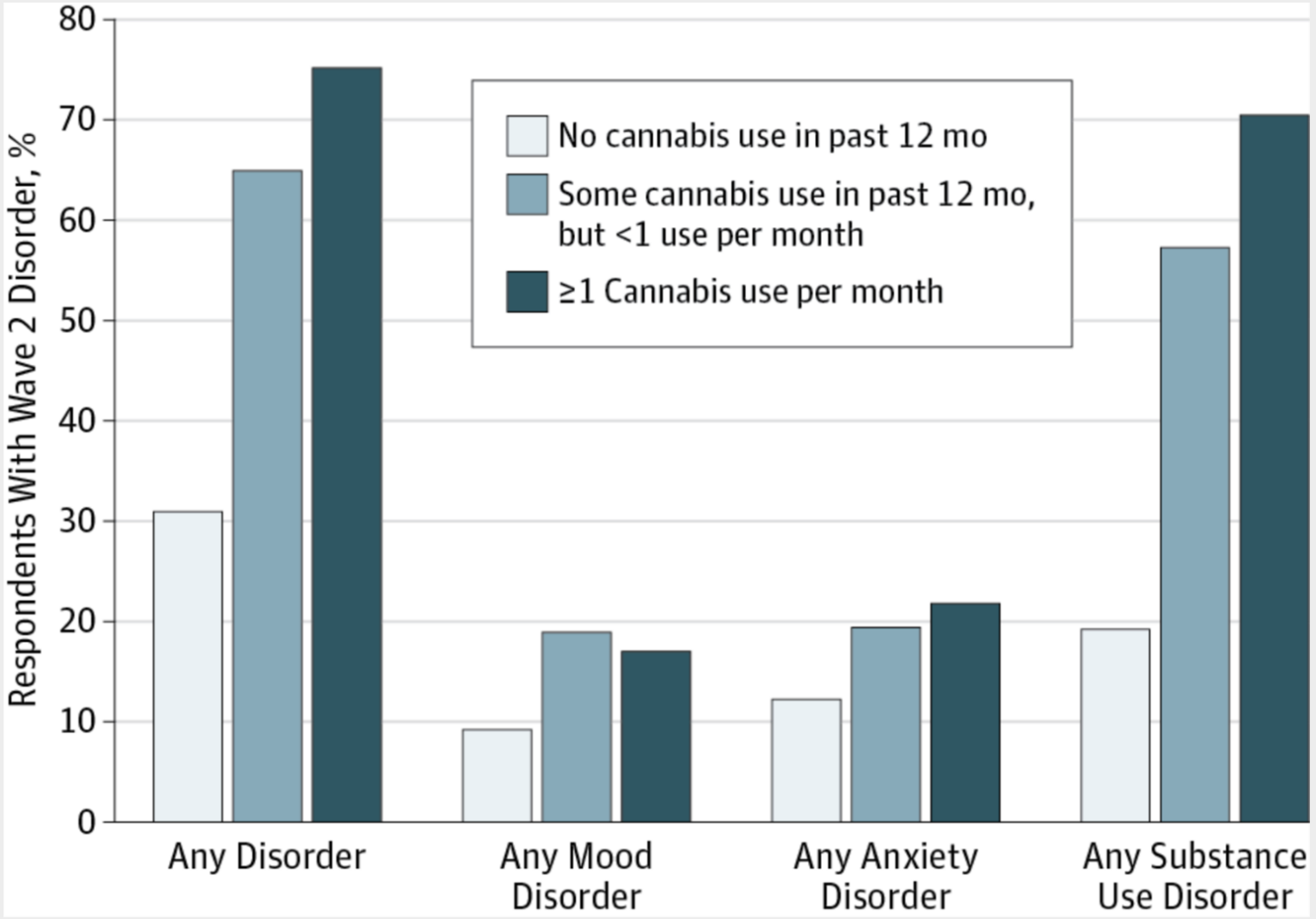
- Mental slowing
- ↓ Planning ability
- ↓ Judgment, concentration, memory
- Apathy, ↓ pursuit of goals

Psychiatric Co-Morbidity



NESARC, 2005; slide courtesy of Dr. Frances Levin.

Psychiatric Co-Morbidity



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Diagnosis

Substance Use Disorder

In Same Year, ≥2 of:

- Tolerance
- Withdrawal
- Use more/longer
- Unable to ↓ use
- Use despite problems
- Craving
- Failed roles
- Hazardous use
- Social problems
- ↓ Activities
- Lots time use

Screening-tools

- CUDIT-R (Cannabis Use Disorder Identification Test – Revised)
  - 8-item, validated self-report screening tool for problematic cannabis use
  - Useful for primary care and addiction settings to identify patients who warrant further diagnostic evaluation

Cognitive Effects

Residual Cognitive Effects

- Memory
  - Learning & retaining new information
- Attention and concentration
  - Response speed & variability
- Executive functioning
  - Working memory
  - Verbal fluency

Likely Reversible with Abstinence

- Biological markers normalize ~4wks
  - CB receptor density in brain
  - Cortical blood volumes
- Especially in cognitive areas

Treatment

Treatment for CUD is Challenging

- Few evidence-based supported approaches
- ~ 50% achieve remission
- ~ 70% return to use
- No FDA-approved medications

Psychosocial Treatments

- Motivational Enhancement Therapy
- Cognitive Behavior Therapy
- Contingency Management
- Family-Based Programs

Pharmacologic Treatment Options

Medication	Mechanism	Comments	Literature in Adolescents?
Atomoxetine	Norepinephrine reuptake inhibitor	• No change in cannabis use • Worsened irritability and GI side effects	• Thurstone et al., 2010[7]
Bupropion	Norepinephrine reuptake inhibitor	• Exacerbated withdrawal (irritability, insomnia)	• Riggs, et al., 2013[8]
Buspirone	Serotonin partial agonist	• Conflicting evidence on cravings and irritability	--
Dronabinol	CB1 receptor agonist	• **Reduced symptoms of withdrawal** • Contains THC	--
Gabapentin	GABA modulation	• **Decrease self-reported cannabis use** • **Reduced withdrawal symptoms**	--
N-acetylcysteine	Correct glutamate dysregulation	• Decreased use in adolescents • Did not show same benefit in adults	• Gray et al., 2012[9]
Naltrexone	Mu-opioid receptor antagonist	• Enhanced subjective effects of cannabis • No change in frequency of cannabis use	--

Medication for CUD

- N-acetylcysteine (NAC)
  - Amino acid derivative, OTC supplement
  - Restores normal glutamate activity
  - Pros: ↓ use in Non-Treatment Seeking adolescents, *not in adults*
  - Cons: did not ↓ craving

N-acetylcysteine (NAC)

Risks	• Nausea/vomiting • Drowsiness/insomnia • Vivid reams • *Anaphylactoid reactions seen with IV admin, not PO*
Pharmacokinetics	• Bioavailability for oral: 9% • Metabolized to cysteine and glutathione • Half-life: ~ 18 hours

Gabapentin

Mechanism of Action	• Blocks alpha-2d subunit of the voltage-gated calcium channel which modulates GABA in the amygdala
Notes	• FDA approved for multiple indications, including partial seizures in ages 3-12
Doses	• Goal of ~1200mg/day Mason (2012) [10]: 50 cannabis-dependent adults (18-65 years old) • Gabapentin 1200mg vs placebo for 12 weeks • Titrated up to 300mg / 300mg / 600mg over the course of 4 days
Clinical benefit	• Increase in negative UDS • Decrease self-reported cannabis use • Reduction in withdrawal symptoms (mood disturbance, craving, and sleep disturbances)

Gabapentin

Risks	Headache, nausea, insomnia and depression

Pharmacokinetics	• Bioavailability: inversely proportional due to saturable absorption
	  • Immediate release
	  • 900mg/day: 60%
	  • 1200mg/day: 47%
	  • 3600mg/day: 33%
	  • 4800mg/day: 27%
	  • Extended release: increased with higher fat content
	• Half-life:
	  • ≤ 12 years old: 5hr
	  • > 12 years: 5-7hr
	  • Longer in patients with decreased renal function

FDA-Approved & Investigational Cannabinoid Medications

Cannabidiol (CBD)
Epidiolex ®

Dronabinol (THC)
Marinol®
Syndros®
Nabilone (THC)
Cesamet®

Nabiximols (THC + CBD)
Sativex® *not FDA approved*

Note: CBD (Epidiolex) is not a CB1 agonist – its mechanism is distinct from THC-based agents (dronabinol, nabilone, nabiximols), which act at CB1.

CB1 Antagonists/Inverse Agonists: Rimonabant

- Rimonabant: a CB1 receptor inverse agonist developed for weight loss and smoking cessation
- Approved in Europe (2006) but never approved in the U.S.; withdrawn from the European market (2008) due to:
  - Significantly increased risk of depression and suicidality
  - Anxiety and other psychiatric adverse effects

Medicinal Uses of Cannabis/Cannabinoids

- Dronabinol: FDA approved for treatment of anorexia associated with weight loss in patients with AIDS, chemotherapy-induced nausea/vomiting.
- Nabilone: FDA approved for treatment of chemotherapy-induced nausea/vomiting.
- Studies also ongoing re: effects on other disease states (epilepsy, MS).

Therapeutic Potential

- Pain (cancer, multiple sclerosis)
- Nausea (cancer)
- Loss of appetite and wasting (HIV/AIDS)
- Increased ocular pressure (glaucoma)
- Inflammation (rheumatoid arthritis, Crohn's disease, ulcerative colitis)
- Epilepsy

In Summary

Cannabis includes plants and synthetic cannabinoids.

Cannabis use is common, risk of a use disorder increases with earlier onset of use.

Cannabis contains more THC now than in the past.

Cannabis can affect cognition, but this is reversible in adults, impacts on adolescents less clear.

Most treatment is psychosocial, but several drug targets are being investigated.

Which of the following trends in youth from the Monitoring the Future study about marijuana use and perception of harm is true?

A. Since the early 1990's, the percentage with perceived risk of harm from marijuana has been higher than past year use of marijuana.
B. Since about 2009, there has been a growing gap between decreased perception of harm and increased past year use of cannabis.
C. The lowest past year cannabis use was in the late 1970's.
D. The perceived risk of harm for cannabis fell throughout the 1980's.

Which of the following medications has a trial supporting efficacy in cannabis use disorder in adolescents?

A. N-acetylcysteine

B. Baclofen

C. Quetiapine

D. Mirtazapine

Cannabis use is reported in greater than 10% of pregnancies. Which correctly lists the reasons cannabis users who are planning to become pregnant should be cautioned against cannabis use:

A. THC does not cross the placenta or pass into breast milk, so the only risk to the fetus or infant is from secondhand smoke exposure after birth.
B. THC easily crosses the placenta and passes into breast milk, but because only the pregnant person is exposed, counseling about prenatal cannabis use is only relevant for female patients.
C. While human data on prenatal THC exposure are still limited, available evidence (consistent with animal studies) shows THC readily crosses the placenta and passes into breast milk, with potential effects on fetal growth and neurodevelopment.
D. Because no human studies have examined prenatal THC exposure, clinicians cannot give any guidance about cannabis use during pregnancy or lactation.

Board Question Answer Key & Rationale

- Q1 (MTF trends): Answer B
  - Since ~2009, a growing gap has emerged between declining perceived harm and sustained/rising past-year cannabis use; verify against the most recent MTF release, as post-pandemic data show shifting adolescent use trends
- Q2 (Medication with adolescent CUD trial): Answer A – N-acetylcysteine
  - Gray et al. (2012) showed NAC reduced cannabis use in non-treatment-seeking adolescents; baclofen, quetiapine, and mirtazapine lack supporting trials in adolescent CUD
- Q3 (Cannabis in pregnancy): Answer C
  - THC readily crosses the placenta and enters breast milk. Human neurodevelopmental data remain limited but are consistent with animal studies showing effects on fetal growth and brain development. Counseling applies to all patients who may become pregnant, not "females only" (A, B incorrect), and limited human data does not preclude clinical guidance (D incorrect)



Get in Touch

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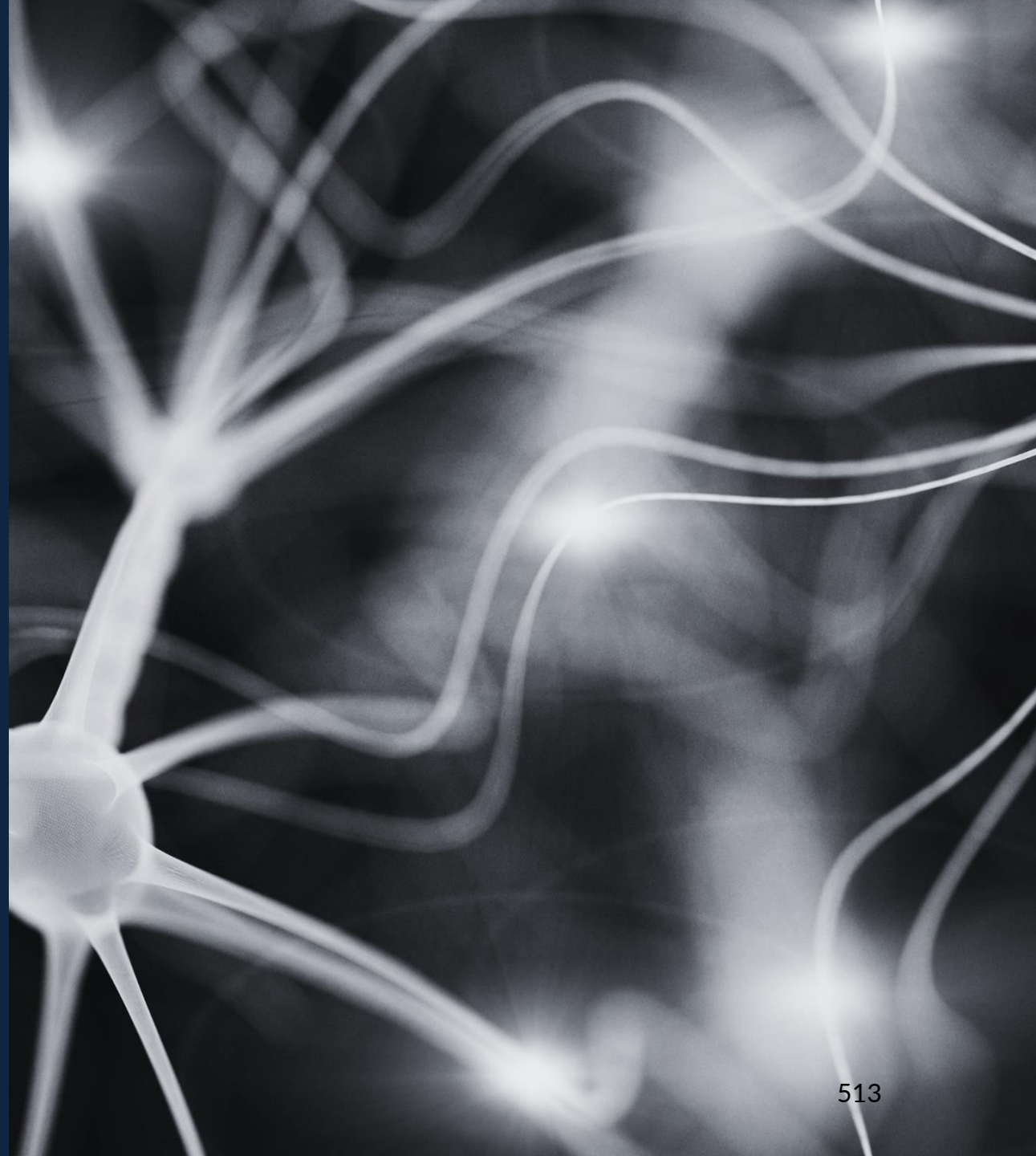
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ASAM REVIEW COURSE 2026

Stimulant Use Disorders: From Neurobiology to Public Health

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Financial Disclosure

Siddarth Puri, MD

- No relevant disclosures

General Outline

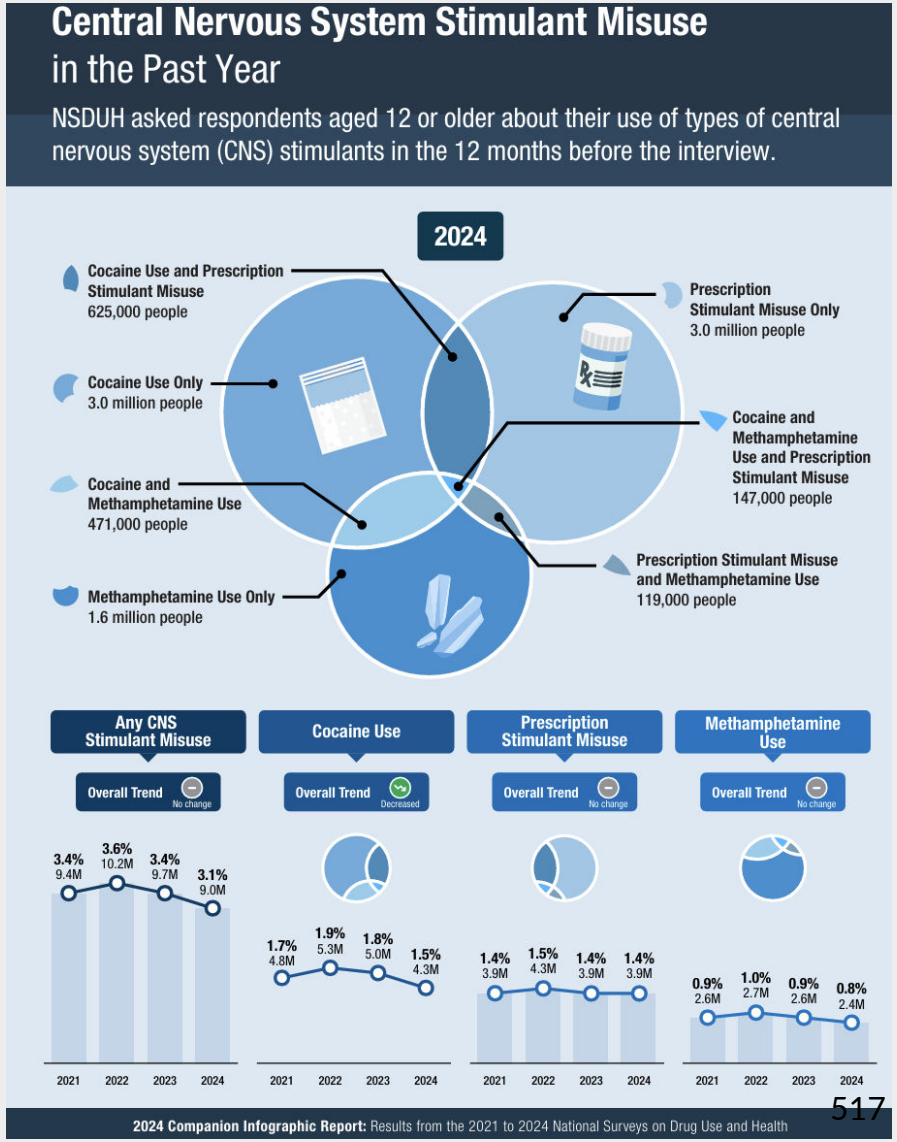
- Cocaine
- Methamphetamine
- MDMA
- Bath Salts

Topics Covered for Each Substance

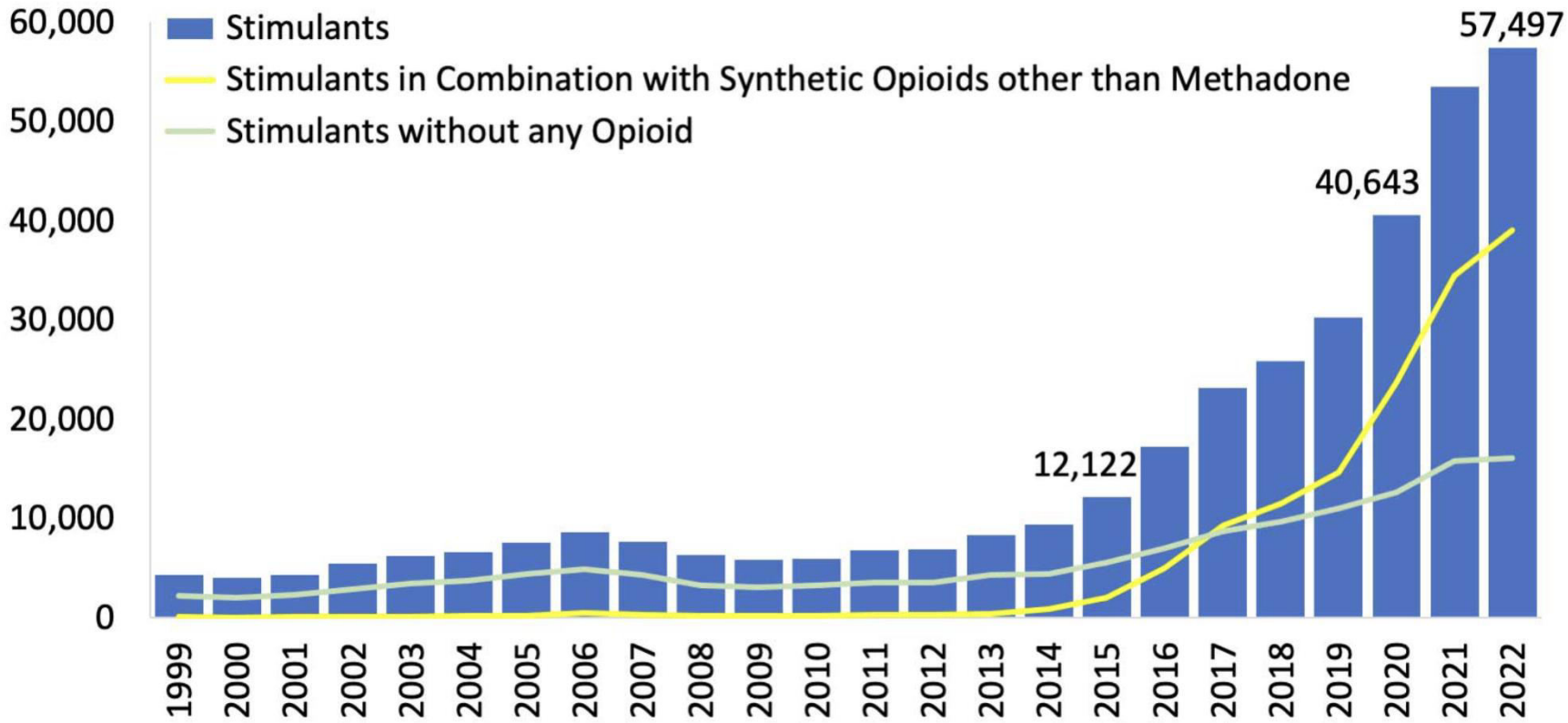
- Formulations and Methods of Use
- Pharmacokinetics and Metabolism
- Desired and Adverse Effects
- Chronic and Withdrawal Effects
- Neurobiology
- Treatments

Epidemiology

- National Survey on Drug Use and Health (NSDUH)
- The majority of people using stimulants are using Cocaine.
- Slight reduction in stimulant misuse.



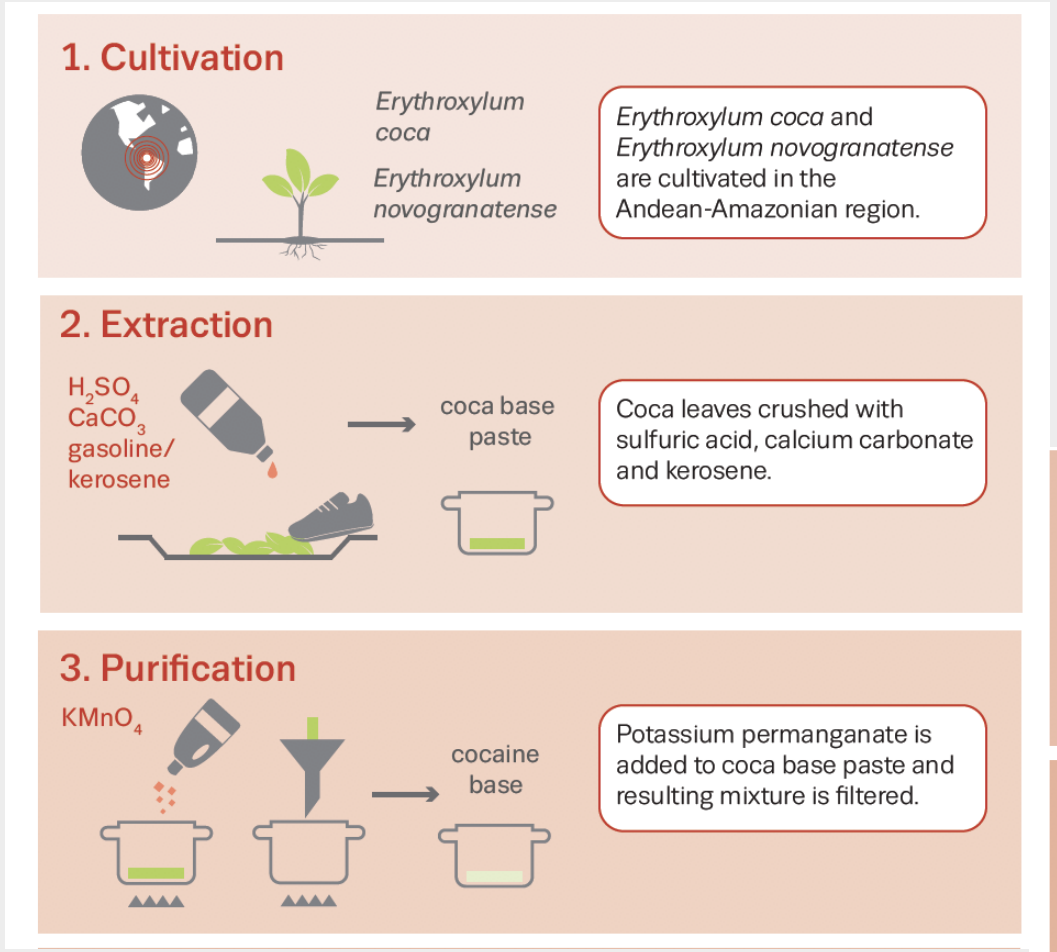
US Overdose Deaths Involving Stimulants (cocaine and psychostimulants)

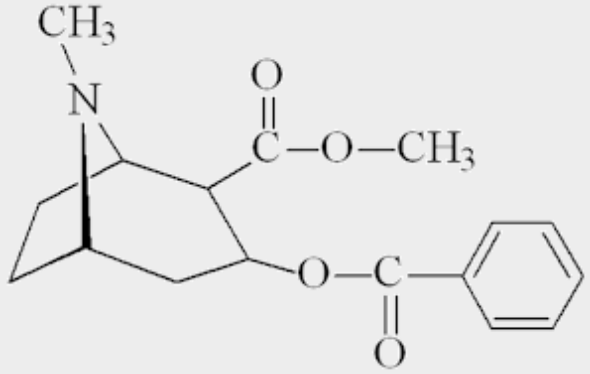


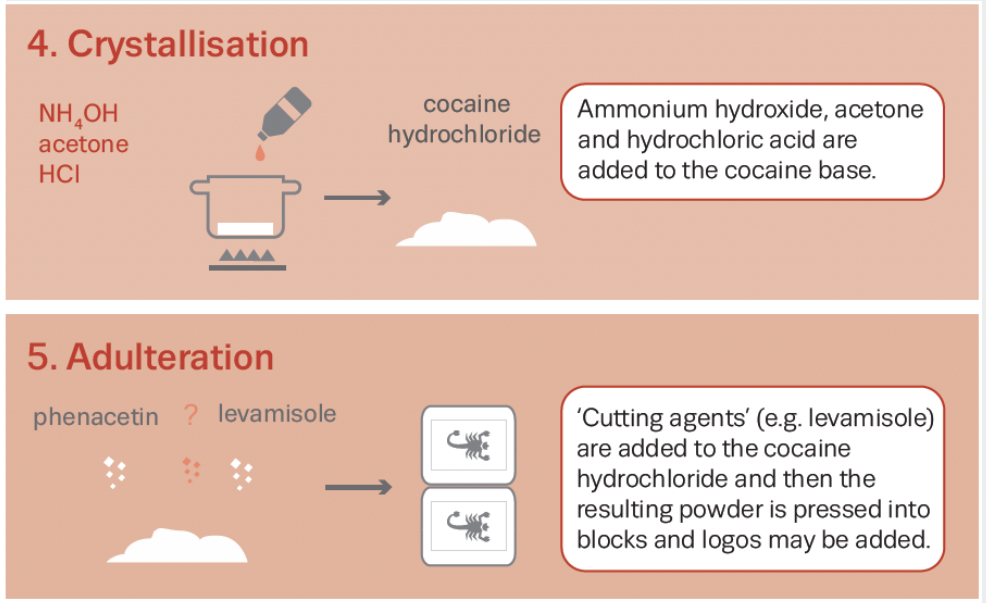
*Among deaths with drug overdose as the underlying cause, the psychostimulants with abuse potential (primarily methamphetamine) category was determined by the T43.6 ICD-10 multiple cause-of-death code. Abbreviated to *psychostimulants* in the bar chart above. Source: Centers for Disease Control and Prevention, National Center for Health Statistics. Multiple Cause of Death 1999-2022 on CDC WONDER Online Database, released 4/2024.

Cocaine

Cocaine: Plant Based Alkaloid



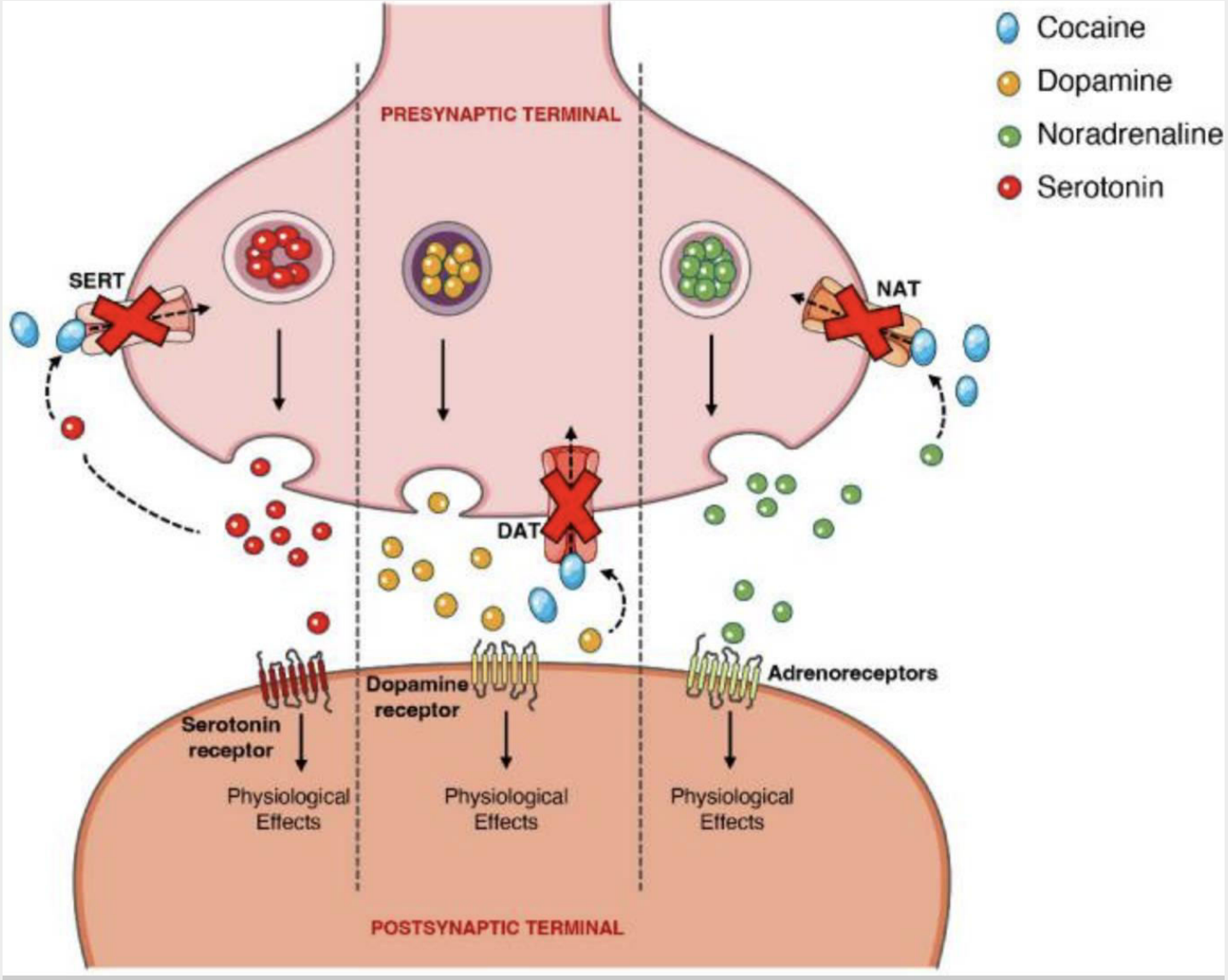




Crack Cocaine vs Cocaine

Category	Crack	Cocaine
Formulation	Powder cocaine mixed with water & baking soda (free base) creating “rocks”	Powder or liquid solution
Method of Use	Smoked	Snorted or Injected
Pharmacokinetics	Instant effects, lasts 5-10 min	Snorting: 3-5 min onset, lasts 15-30 min Injecting: 15-30 sec onset, lasts 20-60 min
Rate Hypothesis and Addiction Potential	Highly psychologically addictive due to **rapid onset**	Less psychologically addictive than crack due to slower onset
Cost depends on location/demand.**	$10-$25 per 1/10 gram ('rock'); $40 per 1/4 gram	$120+ per 1/8 ounce (3.5g) ('8-ball')
Cutting Agents	Glucose, sucrose, talc, inositol, benzocaine, lidocaine, levamisole, ephedrine, Ritalin	Similar to crack; may include boric acid, tetracaine, and procaine

Cocaine: Mechanisms of Action



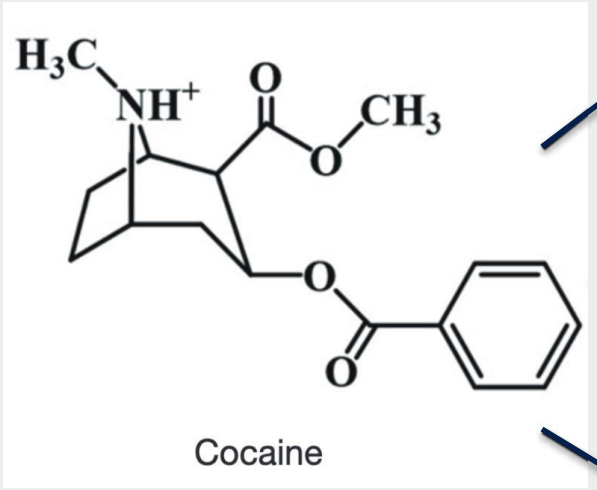
Cocaine: Neurotransmitters

Neurotransmitter	Effect on Neurotransmitter	Impact on Behavior
Dopamine (DA)	Blocks dopamine reuptake in the nucleus accumbens → Increased synaptic dopamine	Euphoria, pleasure, reward, craving
Norepinephrine (NE)	Blocks NE reuptake → Sympathetic nervous system activation	Increased heart rate, blood pressure, energy, alertness
Serotonin (5-HT)	Blocks serotonin reuptake (less pronounced than DA/NE)	Mood elevation, reduced appetite, possible paranoia
Glutamate	Increases glutamate activity in reward circuits	Increased excitability, drug-seeking behavior
GABA	Inhibits GABAergic interneurons, leading to greater dopamine release	Reduced impulse control, heightened stimulation

Cocaine Desired Effects

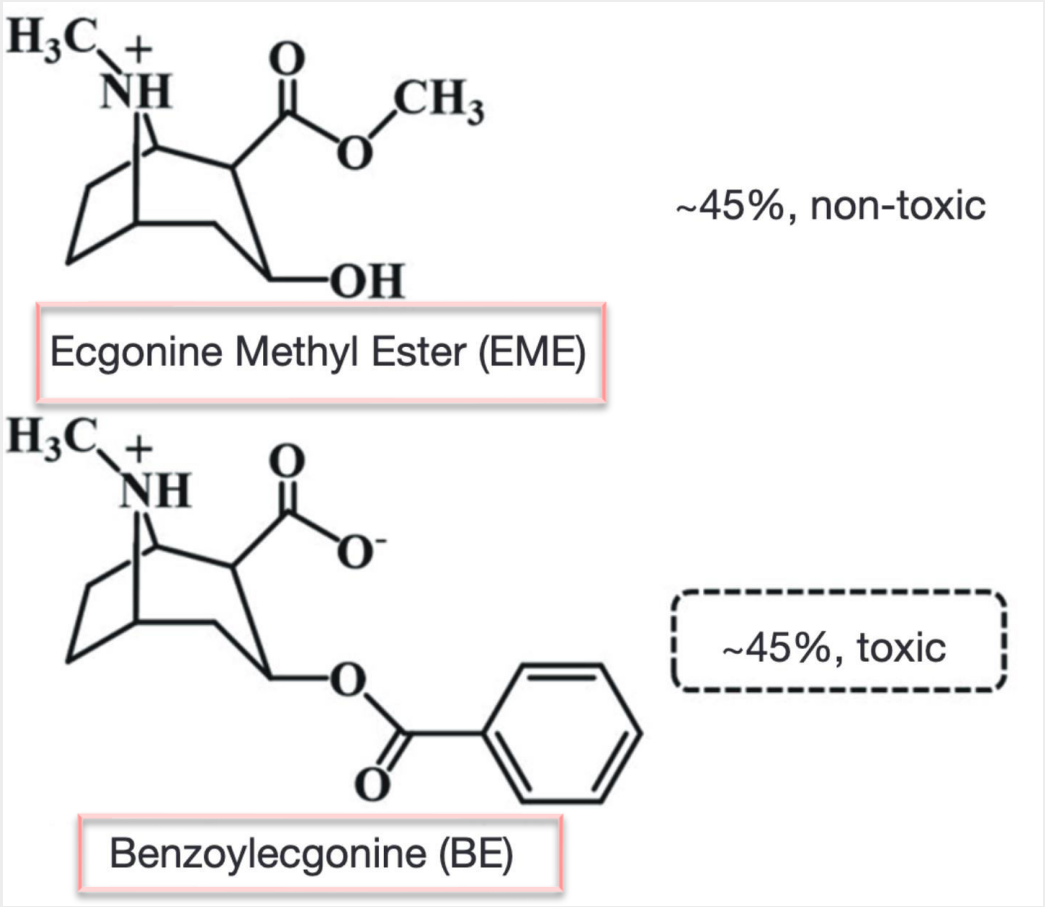
- **Euphoria:** Intense feelings of pleasure, well-being, and confidence.
- **Increased Energy & Alertness:** Reduces fatigue and enhancing wakefulness.
- **Enhanced Focus & Mental Clarity:** Temporary improvements in attention and cognitive function.
- **Increased Sociability & Talkativeness:** Feeling more outgoing, confident, and engaged in conversations.
- **Appetite Suppression:** Reduces hunger and leading to weight loss with chronic use.
- **Improved Physical Performance:** Temporary increase in stamina and strength
- **Heightened Sensory Perception:** Colors may appear brighter, sounds clearer
- **Reduced Need for Sleep:** Prolongs wakefulness
- **Heightened Libido:** Amplifies sexual desire and performance

Cocaine: Metabolism



Plasma cholinesterase

Ester hydrolysis



Other small metabolites: Norcocaine, p-hydroxycocaine, m-hydroxycocaine, p-hydroxybenzoylecgonine

Cocaine Adverse Effects

- Psychological:
  - Paranoia can occur in >50% of heavy users
  - Can persist for hours, even after drug effects wear off.
  - Often includes persecutory delusions, hypervigilance, and tactile hallucinations (e.g., formication, “coke bugs”).
- Tachycardia, Hypertension, MI
- Stroke
- Hyperthermia, Rhabdomyolyses
- Organ Failure

Cocaine: Tolerance

- **Acute Tolerance**: Rapid decrease in response after initial use.
  - **Complete**: Euphoria diminishes with repeated doses in a session.
  - **Incomplete**: Increased heart rate still occurs but to a lesser extent.
- **Reverse Tolerance (Kindling Effect)**: Sensitization to certain CNS effects.
  - **Paranoia, Seizures, Stereotyped Behaviors**: More likely with repeated exposure.

Cocaine and Culture

Affluent & Professional Circles ("High-Functioning" Use)

- Often associated with wealth, power, and status, making it prevalent in corporate, finance, entertainment, and high-income social circles.
- Used to enhance productivity, confidence, and endurance in competitive work environments.
- Often viewed as a "party drug" but can lead to functional dependence over time.

Club , Rave, & Party Scene

- Commonly used with alcohol, MDMA, and ketamine to prolong the party experience.
- Snorted or combined with other drugs, increasing overdose risk.
- Often marketed as a "luxury" stimulant in nightlife settings.

Cocaine and Culture

LGBTQ+ Communities (Club & Chemsex Use)

- Cocaine is popular in gay nightlife and chemsex scenes, though less commonly associated with sexual enhancement than meth.
- Used to increase confidence, social energy, and reduce inhibitions.
- High risk of polysubstance use (alcohol, GHB, poppers, MDMA).

Communities experiencing homelessness/ lower social economic status: Crack Cocaine Use

- Crack cocaine, a cheaper and more potent form of cocaine, is more common in economically disadvantaged populations.
- Crack produces an intense but short-lasting high, leading to frequent re-dosing and compulsive use.
- Historically, racialized drug policies led to disproportionate criminalization of crack cocaine vs. powder cocaine.

Cocaine Intoxication

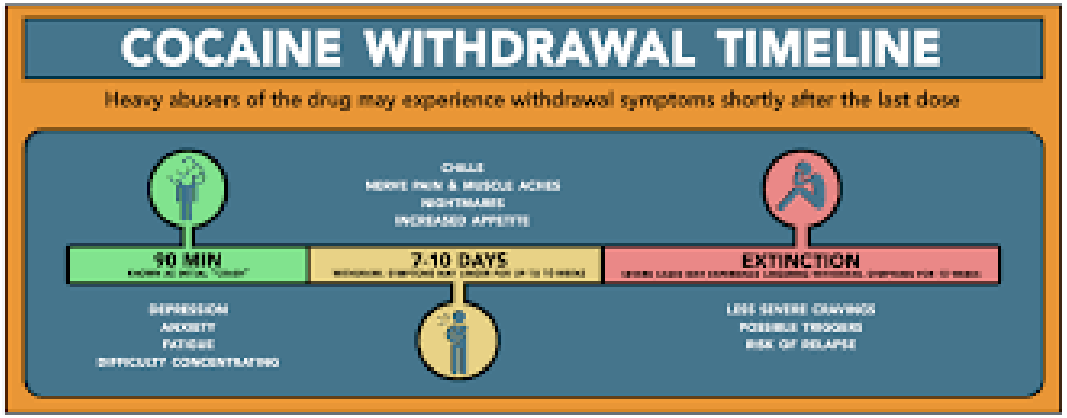
- Recent Stimulant use
- Two or more of the following
  - Tachycardia or bradycardia
  - Pupillary dilation
  - Elevated or lowered blood pressure
  - Perspiration or chills
  - Nausea or vomiting
  - Evidence of weight loss
  - Psychomotor agitation or retardation
  - Muscular weakness, respiratory depression, chest pain or cardiac arrhythmias
  - Confusion, seizures, dyskinesias, dystonia or coma

Cocaine withdrawal

A. Cessation of (or reduction in) prolonged amphetamine-type substance, cocaine or other stimulant use

B. **Dysphoric mood and two (or more)** of the following physiological changes, developing within **hours to several days** after criterion A,

1. **Fatigue**
2. **Vivid, unpleasant dreams**
3. **Insomnia or hypersomnia**
4. **Increased appetite**
5. **Psychomotor retardation, or agitation**

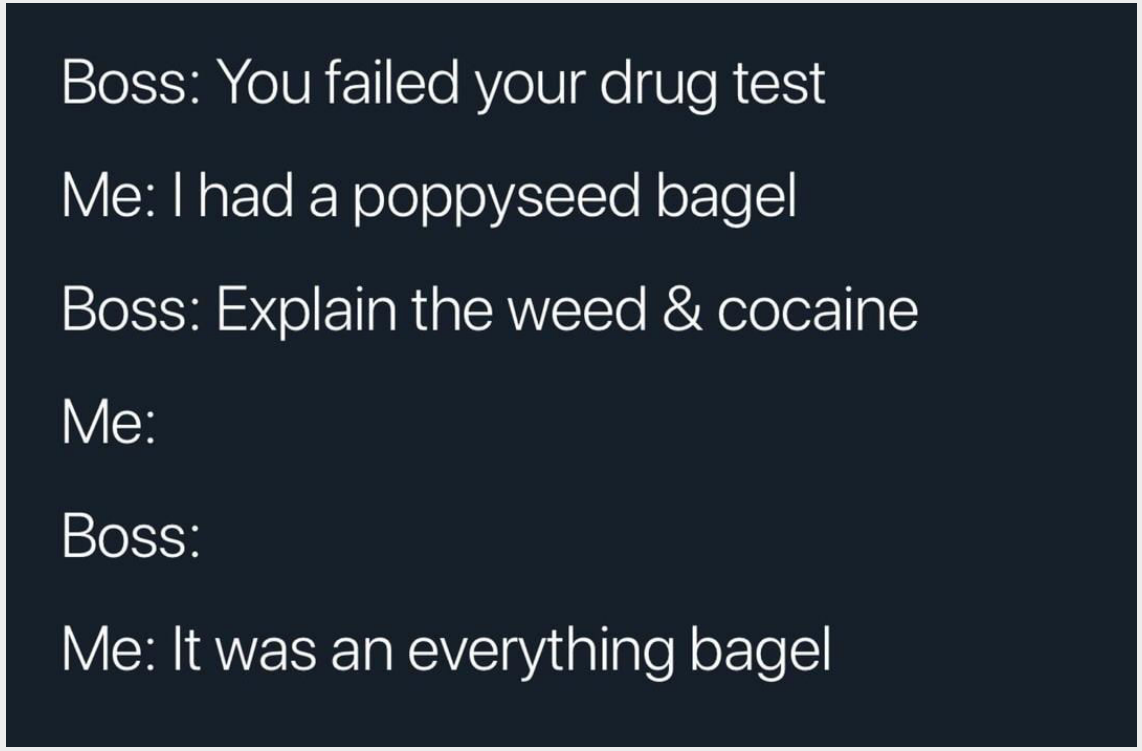


C. Signs and symptoms cause clinically significant distress and impairment in social, occupational, or other important areas of functioning

D. Signs and symptoms not attributable to another medical condition, mental disorder or **intoxication or withdrawal** from another substance

Cocaine Testing: Common False Positive

- Major metabolite, benzoylecgonine, is used in cocaine detection due to longer half-life (t1/2=12 hours) and therefore longer period for detection after use (up to 3-4 days)
- Coca leaf tea or adulterated natural products.
- Generally, cocaine is cocaine +



Cocaine Use Disorder Treatment

- Gold Standard: Behavioral Interventions
  - **<u>Contingency Management:</u>**
    - Based on operant conditioning.
    - Providing positive reinforcement ($$$) for testing without stimulants in a urine drug screen
  - Cognitive Behavioral Therapy
  - Community Reinforcement Approach

Cocaine Use Disorder Treatment

- **Positive Signaling, though low strength evidence for increasing abstinence at 2 weeks or more:**
  - Bupropion
  - Topiramate
  - Dextroamphetamine and mixed amphetamine salts
- **No difference in cocaine use outcomes with or without ADHD**
- **Negative Signals that do not improve abstinence, use, or retention**
  - Antidepressants (SSRIs, SNRIs or TCAS)
  - Anticonvulsants (except topiramate),
  - Neuroleptics
  - SSRIs and disulfiram: lower retention than placebo

JAMA Network | Open

Original Investigation | Substance Use and Addiction

Comparison of Treatments for Cocaine Use Disorder Among Adults
A Systematic Review and Meta-analysis

Brandon S. Bentzley, MD, PhD; Summer S. Han, PhD; Sophie Neuner, BS; Keith Humphreys, PhD; Kyle M. Kampman, MD; Casey H. Halpern, MD

Research Question: What treatments for cocaine use disorder are associated with objective reductions in cocaine use among adults?

	Without imputed data				With imputed data			
	No.				No.			
Treatment category	Studies	Treatment groups	Participants	OR (95% CI)	Studies	Treatment groups	Participants	OR (95% CI)
Anticonvulsants	14	17	570	2.32 (1.15-4.67)[a]	16	20	683	1.39 (0.59-3.29)
Antidepressants	8	15	482	1.96 (0.91-4.25)	11	18	574	1.36 (0.63-2.91)
Antipsychotics	8	11	241	1.59 (0.68-3.71)	9	12	281	1.02 (0.41-2.53)
Contingency management	38	69	2744	2.09 (1.59-2.75)[b]	50	88	3301	2.13 (1.62-2.80)[b]
Dopamine agonists	10	18	645	1.55 (0.80-3.00)	12	20	710	1.04 (0.51-2.14)
Miscellaneous medications	26	38	1455	1.64 (0.88-3.06)	37	54	1751	1.14 (0.60-2.17)
Opioids	49	142	4686	2.32 (1.54-3.49)[b]	55	159	5139	1.70 (0.98-2.94)
Other therapies	12	21	1577	2.19 (1.07-4.49)[c]	15	26	1805	1.35 (0.72-2.53)
Placebo	65	78	2889	1.48 (0.86-2.53)	80	96	3381	1.03 (0.59-1.80)
Psychostimulants	13	19	645	2.48 (1.27-4.85)[d]	17	24	702	1.74 (0.81-3.74)
Psychotherapy	98	258	10 773	1.08 (0.74-1.58)	131	330	13 213	1.18 (0.81-1.73)

Abbreviation: OR, odds ratio.

[a] $P = .02$.

[b] $P < .001$.

[c] $P = .03$.

[d] $P = .008$.

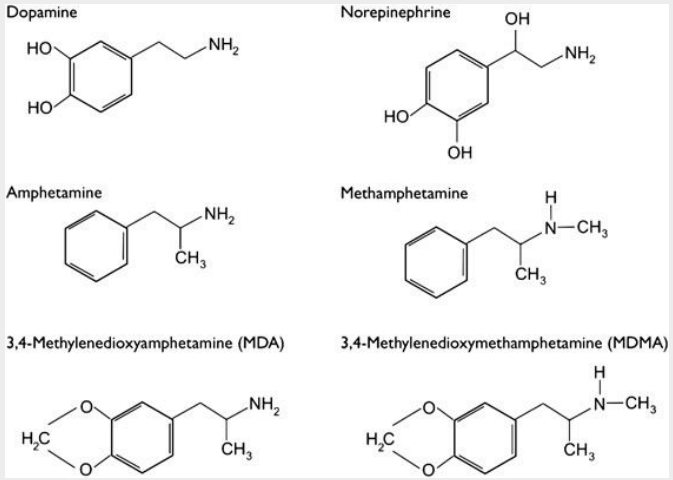
SOURCE: DOI: 10.1001/jamanetworkopen.2021.8049

Methamphetamine

Methamphetamine: Synthetic Amphetamine

- Pseudoephedrine route







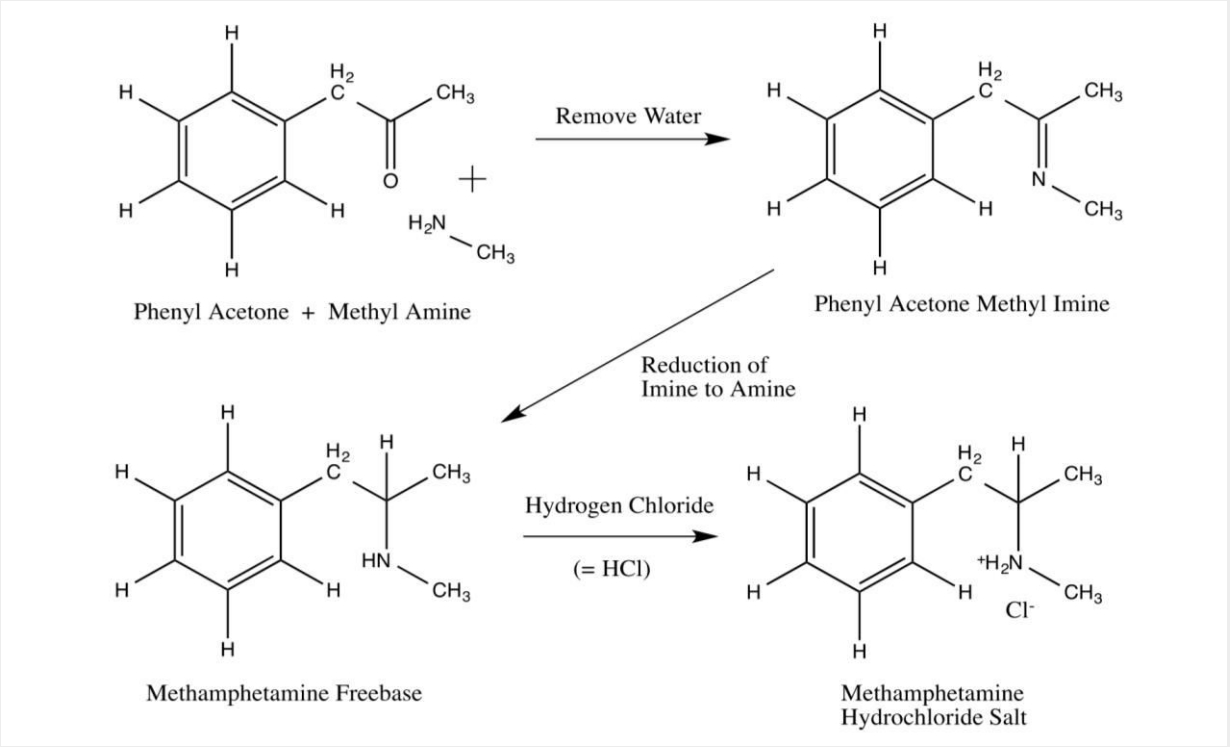
Methamphetamine: Synthetic Amphetamine

- Pseudoephedrine route: "Shake and Bake:" One pot!
  - Pseudoephedrine + ammonium nitrate + organic solvent + lithium mixed together in a cannister. Then add 1 capful of sodium hydroxide (lye). Then add water.
  - Swirl bottle. Take cap off every few minutes (release ammonia)
  - Keep swirly, venting for 1-2 hours
  - Filter fluid, dry filtrate, meth!



Methamphetamine: Synthetic Amphetamine

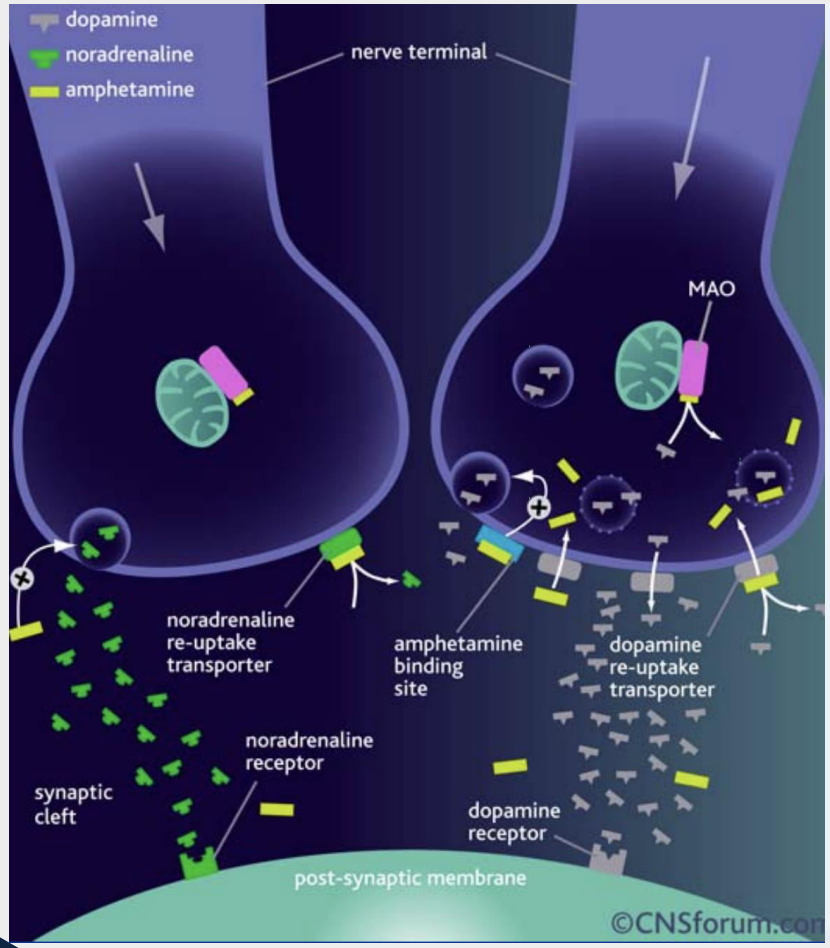
- Phenyl 2 Butane/ Phenyl Acetone Route:
  - Cooked in large laboratories in Mexico with expert chemists

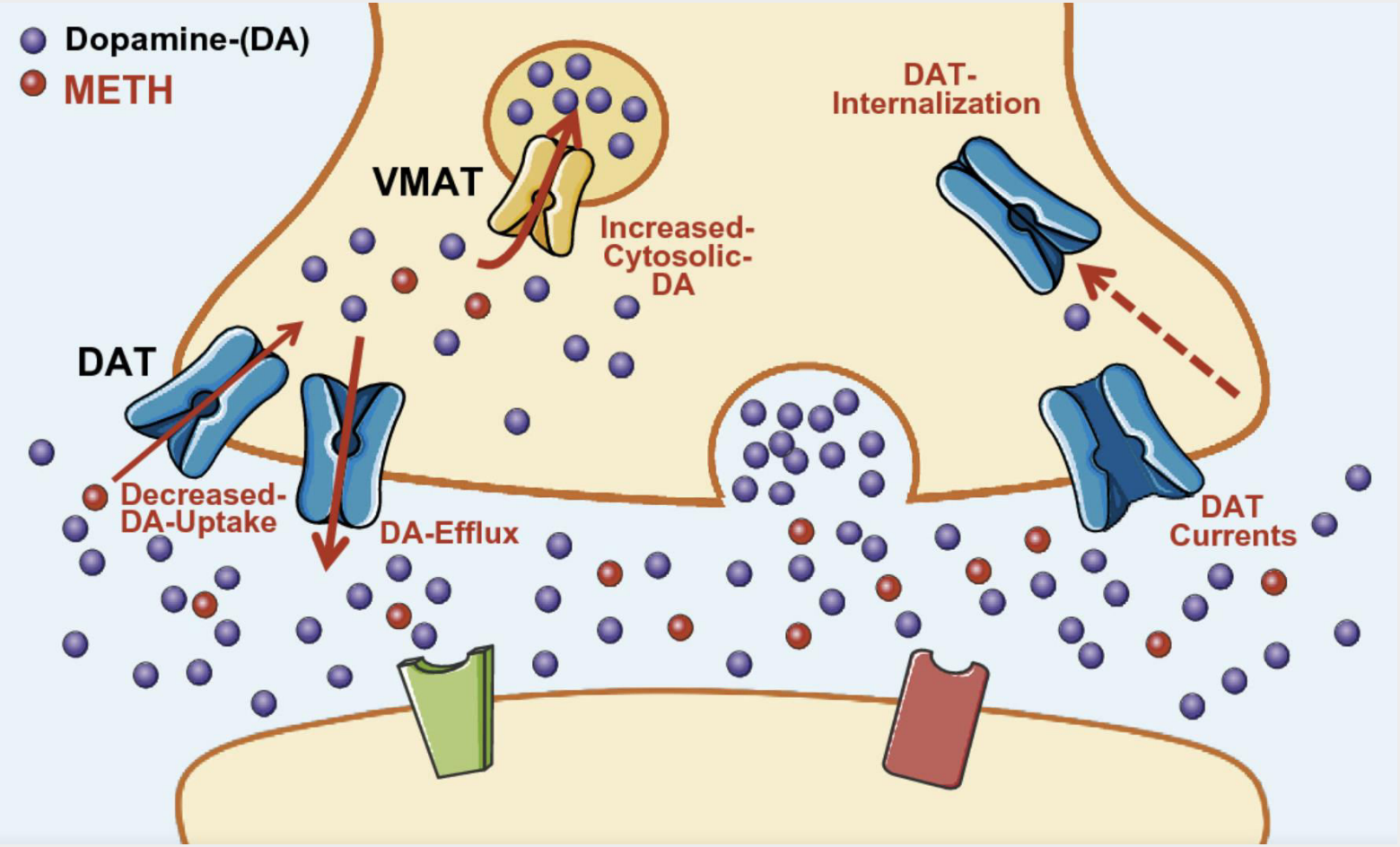


Methamphetamine

Formulation	Synthetic stimulant; crystal (crystal meth) or powder form
Method of Use	Smoked, snorted, injected, or taken orally
Pharmacokinetics	Smoking/Injecting: Immediate intense rush, lasts 6-12 hours Snorting: Effects within minutes, lasts up to 12 hours Oral: Slower onset, effects last up to 24 hours
Rate Hypothesis and Addiction Potential	Extremely addictive due to long duration & high dopamine release
Cost (depends on location/demand)	$20-$80 per gram; varies widely by region
Cutting Agents	Lactose, MSM (methylsulfonylmethane), acetone, ephedrine, pseudoephedrine, lithium, red phosphorus

Methamphetamine: Mechanism of Action





Methamphetamine: Neurotransmitters

Neurotransmitter	Effect on Neurotransmitter	Impact on Behavior
Dopamine (DA)	Releases DA from vesicles & reverses dopamine transporter (DAT)	More intense euphoria than cocaine, addiction, and cravings
Norepinephrine (NE)	Massive NE release from nerve terminals	Extreme energy, alertness, sympathetic overdrive
Serotonin (5-HT)	Releases 5-HT → Longer-lasting effects than cocaine	Elevated mood, hallucinations, possible aggression
Glutamate	Excitotoxicity & synaptic remodeling	Cognitive deficits, compulsive drug-seeking
GABA	Decreased GABAergic inhibition, leading to prolonged stimulant effects	Hyperstimulation, impulsivity, paranoia

Methamphetamine Desired Effects

- **Euphoria** – Intense feelings of pleasure, well-being, and confidence.
- **Increased Energy & Alertness** – Reduces fatigue and enhancing wakefulness.
- **Increased Sociability & Talkativeness** – Feeling more outgoing, confident, and engaged in conversations.
- **Appetite Suppression** – Reduces hunger and leading to weight loss with chronic use.
- **Improved Physical Performance** – Temporary increase in stamina and strength
- **Heightened Sensory Perception** – Colors may appear brighter, sounds clearer
- **Reduced Need for Sleep** – Prolongs wakefulness
- **Heightened Libido** – Meth **amplifies sexual desire and performance**

- **Prolonged Effects (12+ Hours)** – Unlike cocaine (which lasts ~30-60 minutes), **meth effects persist for 6-12 hours**, leading to extended binge use.

Methamphetamine Adverse Effects

- Psychological:
  - Paranoia, agitation, anxiety
  - Hallucinations (visual, tactile, and auditory)
  - Aggression & violent behavior
  - Hyperactivity & restlessness
- Tachycardia, Hypertension, MI
- Stroke
- Hyperthermia, Rhabdomyolyses
- Multiorgan Failure
- Severe teeth grinding and jaw clenching

Methamphetamine Intoxication

- Recent Stimulant use
- Two or more of the following
  - Tachycardia or bradycardia
  - Pupillary dilation
  - Elevated or lowered blood pressure
  - Perspiration or chills
  - Nausea or vomiting
  - Evidence of weight loss
  - Psychomotor agitation or retardation
  - Muscular weakness, respiratory depression, chest pain or cardiac arrhythmias
  - Confusion, seizures, dyskinesias, dystonia or coma

Methamphetamine Withdrawal

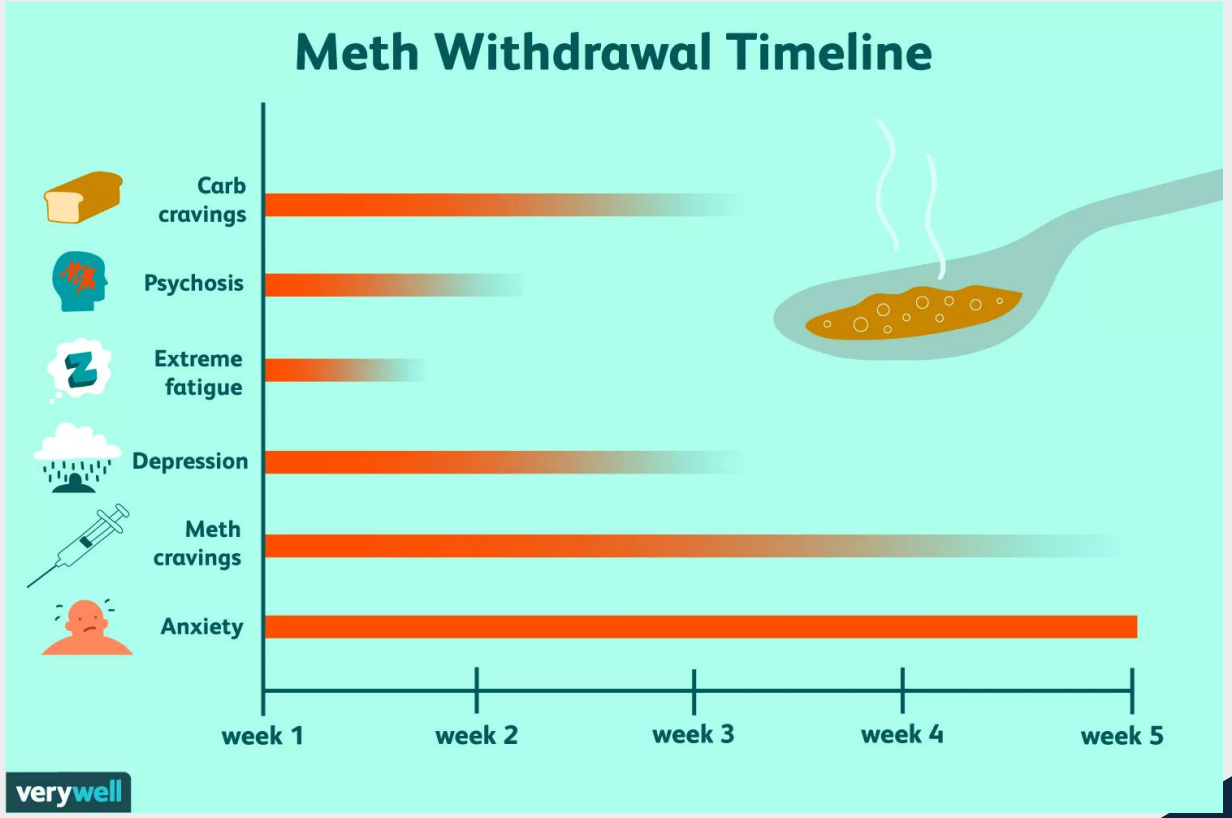
A. Cessation of (or reduction in) prolonged amphetamine-type substance, cocaine or other stimulant use

B. **Dysphoric mood and two (or more)** of the following physiological changes, developing within **hours to several days** after criterion A,

1. **Fatigue**
2. **Vivid, unpleasant dreams**
3. **Insomnia or hypersomnia**
4. **Increased appetite**
5. **Psychomotor retardation, or agitation**

C. Signs and symptoms cause clinically significant distress and impairment in social, occupational, or other important areas of functioning

D. Signs and symptoms not attributable to another medical condition, mental disorder or **intoxication or withdrawal** from another substance



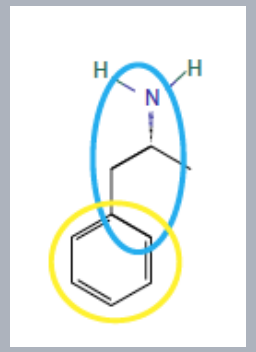
Methamphetamine Testing: Common False Positives

UDS: + Up to 72 hours after use
Confirmation for methamphetamine with Gas Chromatography Mass spectrometry (GC MS)

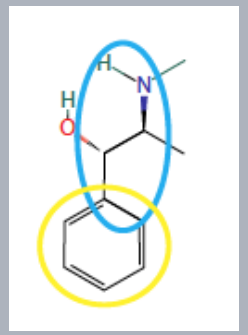
Amine Group Connected with Carbon Chain

Phenyl ring moiety

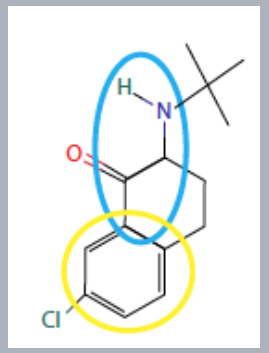
Amphetamine



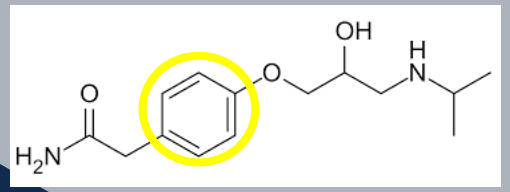
Pseudophedrine



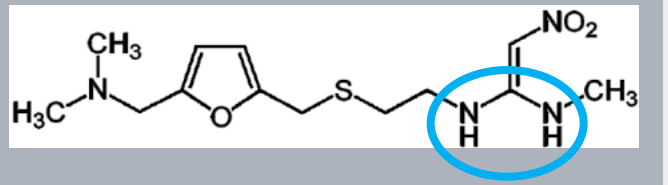
Bupropion



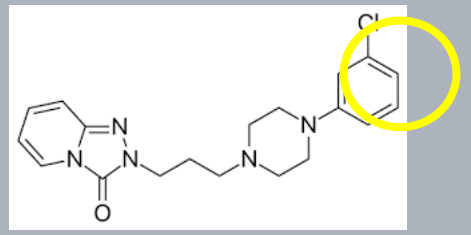
Atenolol



Ranitidine



Trazodone



Methamphetamine and Culture

Rural Communities

- Prevalent due to availability, economic stress, and lack of access to other stimulants (e.g., cocaine).
- Used to sustain long work hours in physically demanding jobs (e.g., agriculture, trucking, manual labor).
- Limited access to healthcare & treatment → Higher rates of meth-related health complications.

LGBTQ+ Communities (Chemsex/Substance Use in Party Scenes)

- Methamphetamine is commonly used in “chemsex” (sexualized drug use) settings, particularly among gay, bisexual, and other men who have sex with men (MSM).
- Reasons for use: Enhanced sexual experiences, increased confidence, prolonged stamina
- High-risk behaviors: Increased likelihood of unprotected sex, multiple partners, and transmission of HIV/STIs.
- Barrier to treatment: Fear of stigmatization from healthcare providers.

Methamphetamine and Culture

Homeless & Marginalized Populations

- Meth is used to stay awake at night for safety (avoiding assault, robbery, or sexual violence).
- Helps cope with trauma, PTSD, and mental illness.
- Commonly smoked or injected, leading to higher risks of infection and dental deterioration.

Club & Rave Scene

- Used as an alternative to MDMA/ecstasy to enhance energy and euphoria.
- Often mixed with other substances (e.g., GHB, ketamine, alcohol), increasing overdose risk.

Methamphetamine Use Disorder Treatment

- Gold Standard: Behavioral Interventions
  - **<u>Contingency Management:</u>**
    - Based on operant conditioning.
    - Providing positive reinforcement ($$$) for testing without stimulants in a urine drug screen
  - Cognitive Behavioral Therapy
  - Community Reinforcement Approach

Methamphetamine Use Disorder Treatment

- Some Positive Results: All considered “off label”
  - **Bupropion** [1]

    Better evidence in low severity/frequency users
  - **Mirtazapine** [2]
  - Methylphenidate [4]
  - **Topiramate** [6]

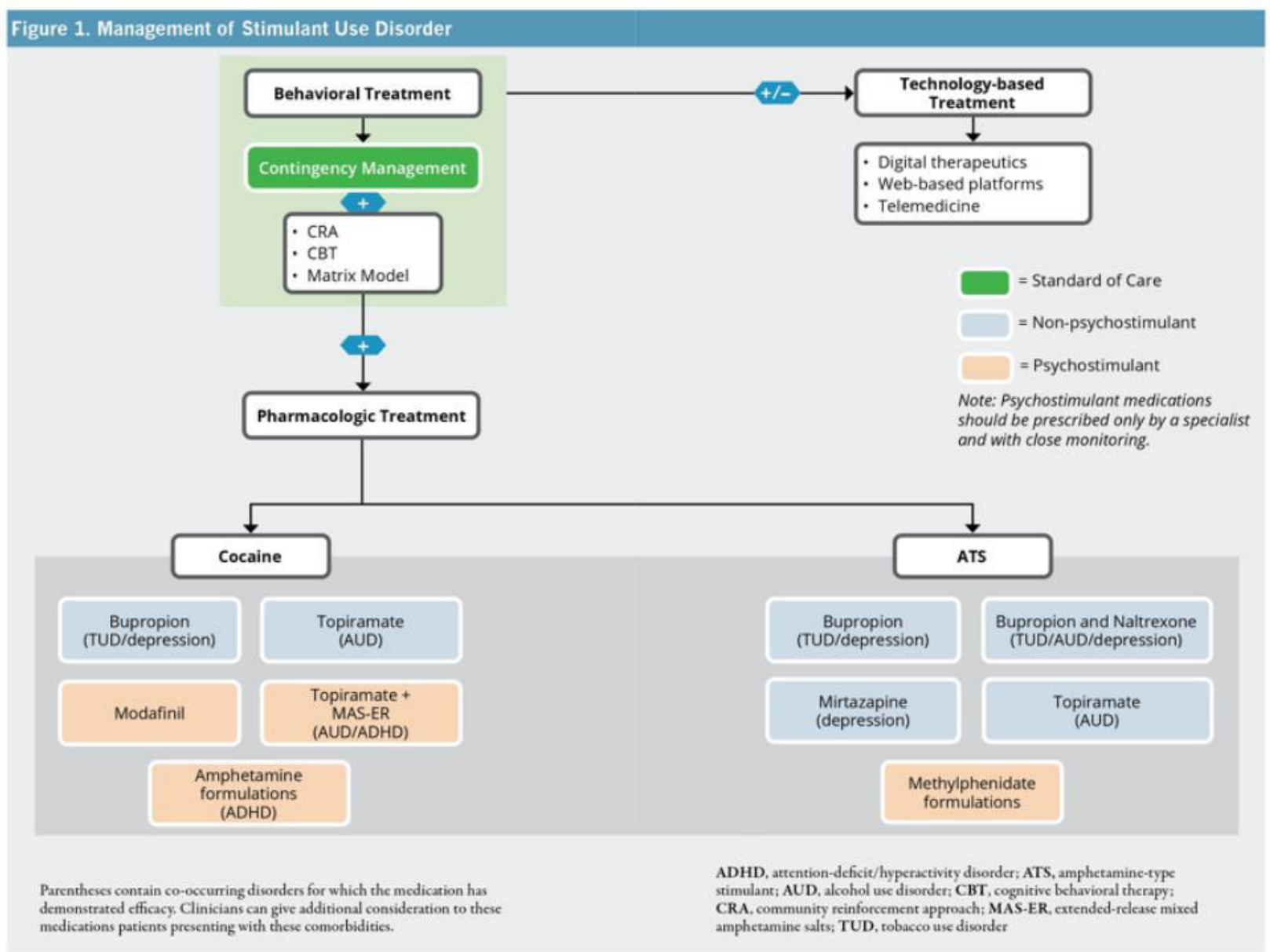
    Better outcomes if abstinent at treatment start
  - **Combination Treatment (Bupropion + Naltrexone)**
- **Mostly Negative Results**
  - Imipramine, Desipramine, Fluoxetine, Sertraline, Paroxetine, Tyrosine, Ondansetron
  - Aripiprazole, Gabapentin
  - N-Acetylcysteine, Varenicline

[1] Elkashaef et al. 2008, Shaptow et al. 2008; Heinzerling et al. 2014; Anderson et al. 2015. [2] Colfax et al. 2012, Coffin et al., 2020; [3] Jayaram-Linstrom et al., 2008; [4] Tiihonen et al., 2007; Ling et al. 2014; [5] Galloway et al. 2011; [6] Elkashef et al., 2011; [7]Heinzerling et al., 2010; Anderson et al., 2012.

Cocaine vs Methamphetamine Summary

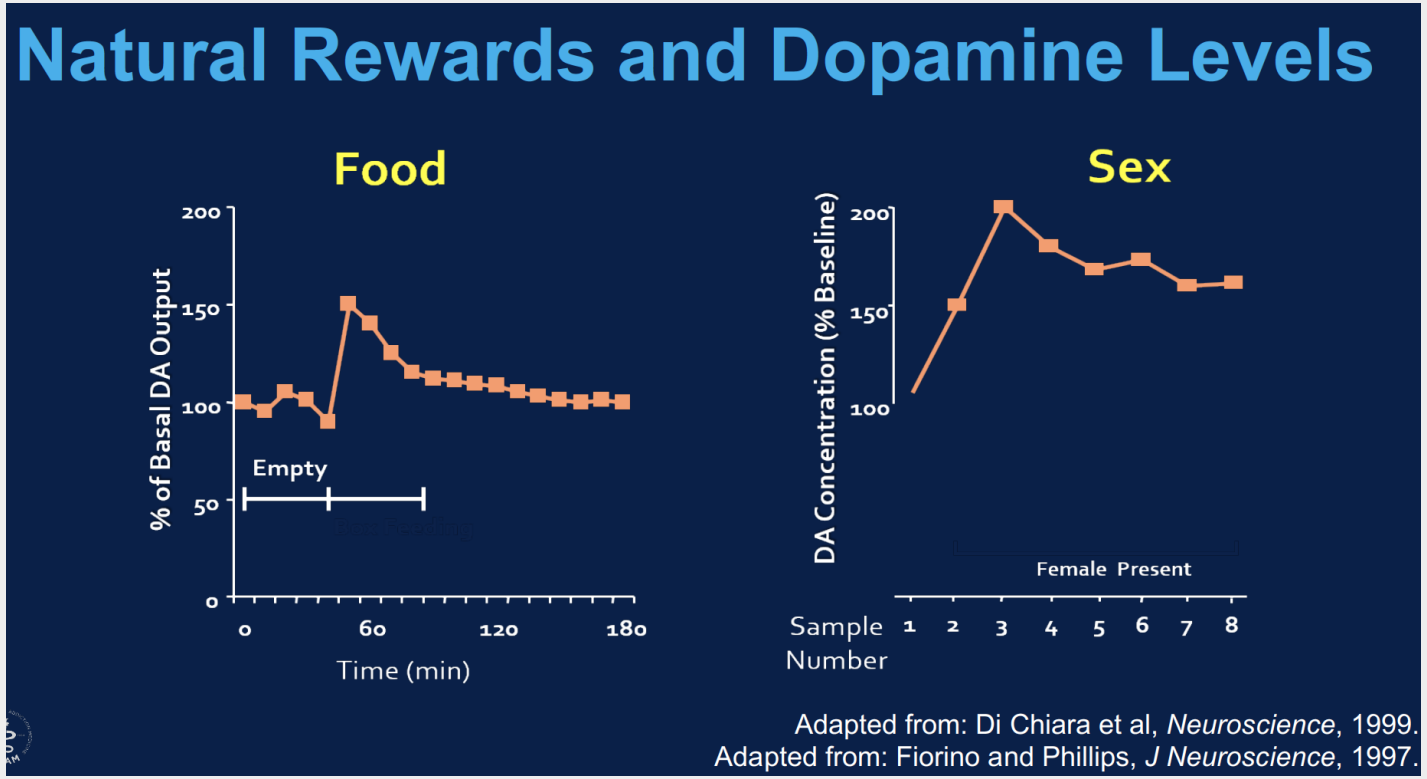
Feature	Cocaine	Methamphetamine
Development	Plant-derived	Synthetic
Length of high	Lasts 10-30 mins	Lasts 8-24 hours
Half-life	1 hour	12 hours
Primary Action	Blocks monoamine reuptake transporters	Increases monoamine release (DA, NE, 5-HT)
Reuptake Inhibition	Prevents neurotransmitter reuptake into presynaptic terminals	Partially blocks reuptake but mainly reverses transporter function
Neurotransmitter Release	No direct release; increases extracellular levels by **blocking reuptake**	Forces neurotransmitters out of vesicles and into synaptic cleft
Effects on Dopamine Transporters (DAT)	Blocks DAT, increasing synaptic DA	Reverses DAT, actively pumping DA out
Effects on Monoamine Oxidase (MAO)	No direct MAO inhibition	Inhibits MAO, preventing neurotransmitter breakdown
Effects on VMAT (Vesicular Monoamine Transporter)	No effect on VMAT (unlike reserpine)	Disrupts VMAT, causing release of stored neurotransmitters
Lipid Solubility & BBB Penetration	Passes BBB quickly, but less lipid-soluble than meth	Highly lipid-soluble, crosses BBB very rapidly
Additional Toxic Effects	Blocks Na+, K+, and Ca2+ channels at high doses (cardiotoxic)	Increases DA synthesis promoting long-term neurotoxicity
Sympathomimetic Effects	Prolonged monoamine accumulation leads to enhanced sympathetic effects (↑HR, ↑BP, ↑alertness)	Prolonged sympathetic activation similar to cocaine, but longer-lasting due to transporter reversal & MAO inhibition
Medical uses:	Vasoconstrictor	Derivatives for ADHD

ASAM Stimulant Use Treatment Guidelines

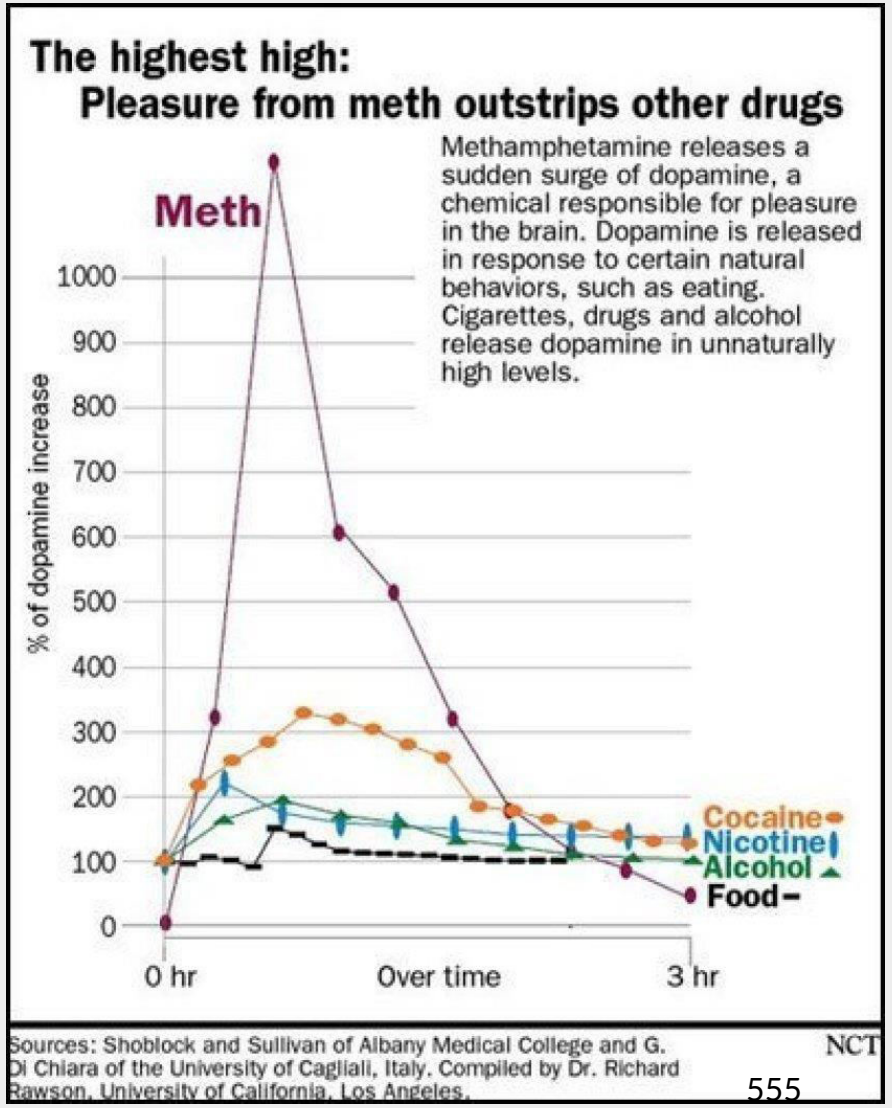


Neurobiology of Stimulant Use

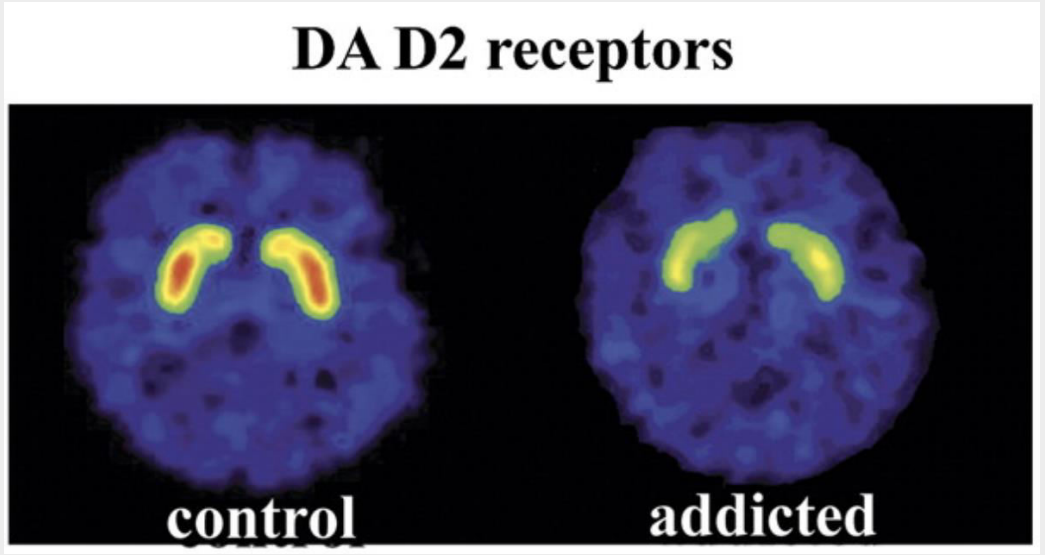
Dopamine Levels

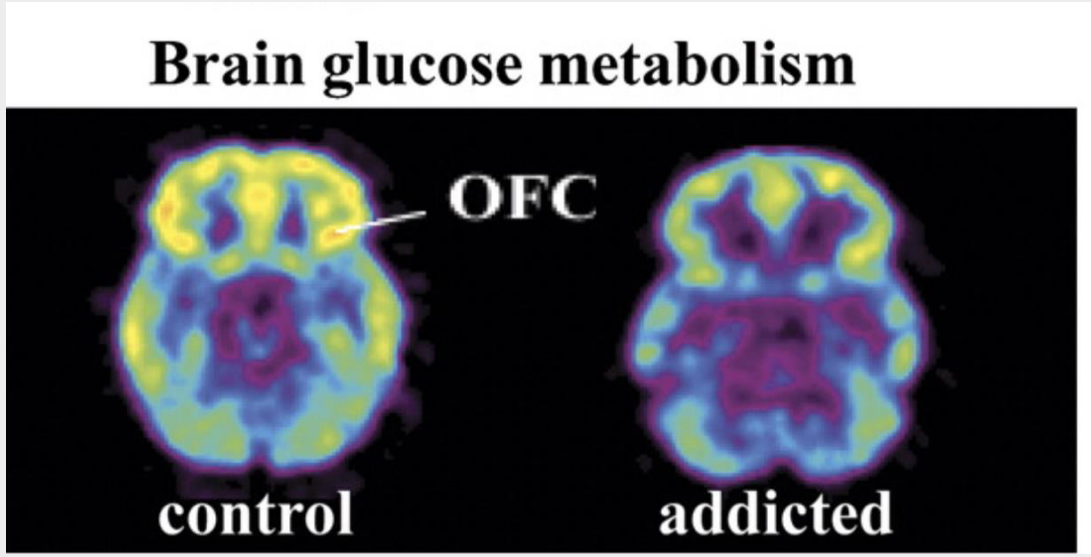


Adapted from: Di Chiara et al, *Neuroscience*, 1999.
Adapted from: Fiorino and Phillips, *J Neuroscience*, 1997.



Impact on Dopamine & Glutamate Pathways



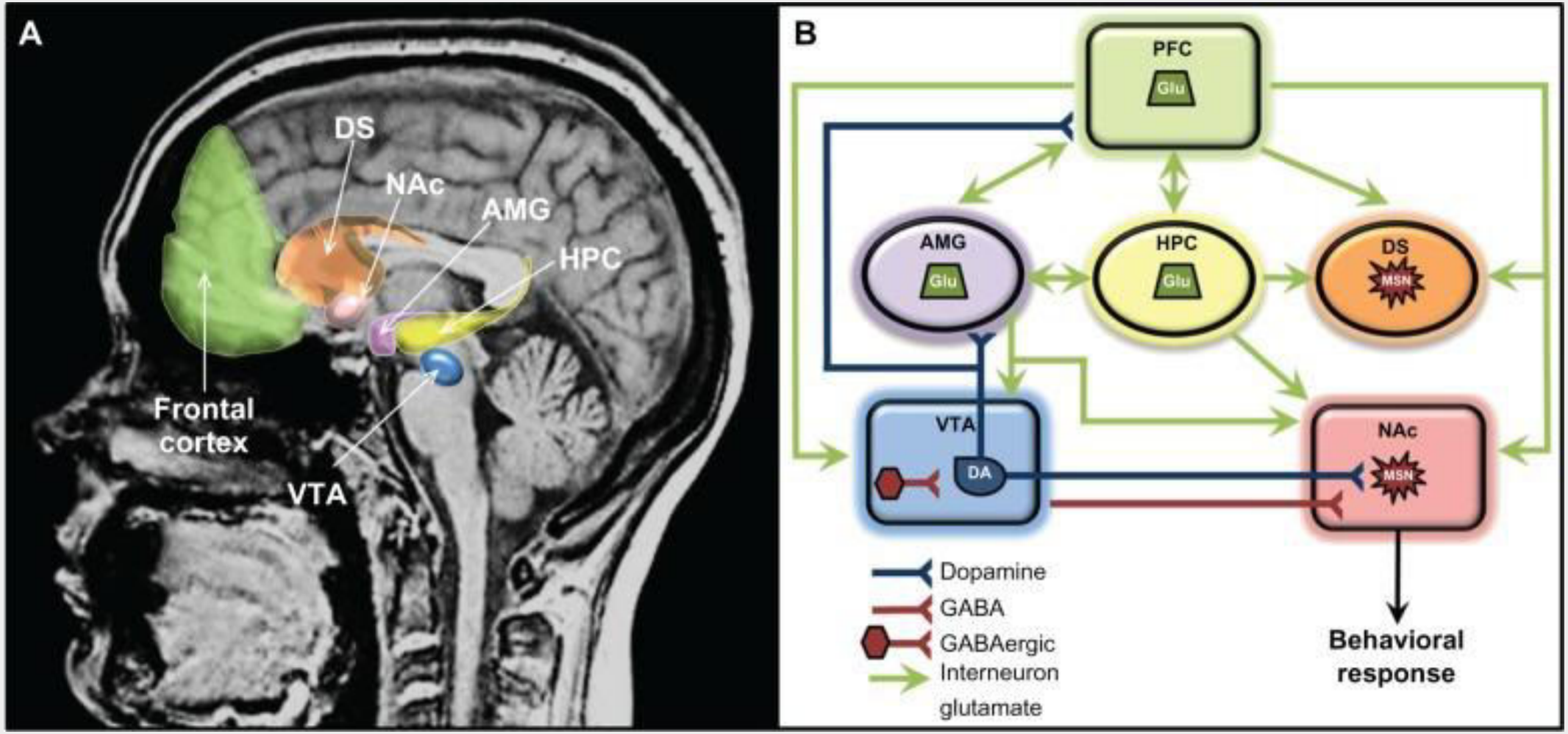


↓ Dopamine transporters:
↓ Ability to respond to non-drug rewards,
↑ impulsivity, immediate>delayed rewards[1]

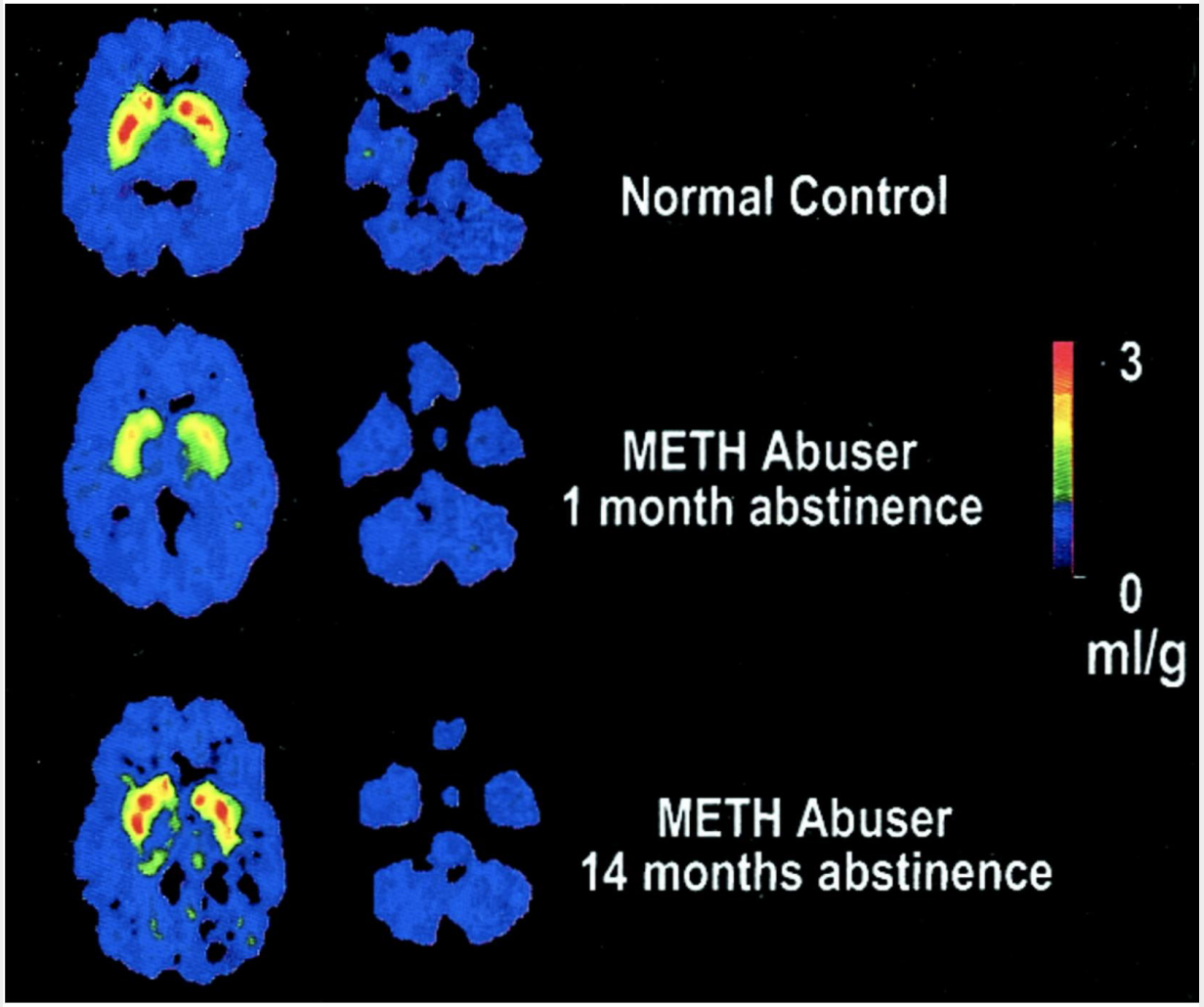
↓ Orbitofrontal Cortex Function, GLUT
- Poor decision making, ↓ resistance to urges[2]

[1]Volkow ND, Am J Psychiatry. 2001 [2] Volkow ND, Nature Review Neuroscience 12/2004

Mesocorticolimbic Reward Pathway



The Brain can Heal!



Volkow, ND. J Neuroscience 2001

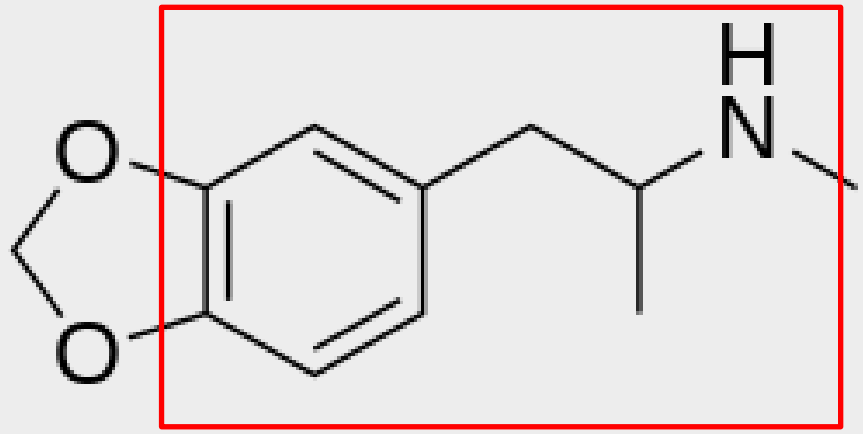
Cocaine vs Methamphetamine Neurobiology

Neuroadaptation	Cocaine	Methamphetamine
Dopamine D2 Receptor Downregulation	Decreased D2 receptors → Blunted reward response & anhedonia	More severe D2 receptor loss → Severe anhedonia & cognitive impairment
Prefrontal Cortex Dysfunction	Reduced PFC activity → Impaired impulse control & decision-making	Greater neurotoxicity in PFC → More severe cognitive & executive function deficits
Glutamate Dysregulation	Increased glutamate in NAc → Stronger drug-seeking behavior	More severe glutamate toxicity → Widespread synaptic damage & cravings
Dendritic Spine Remodeling	Increased Structural changes in NAc & PFC → Persistent drug-seeking	More profound loss of dendritic spines → Contributes to cognitive decline
Neurotoxicity & Brain Damage	Less neurotoxic compared to methamphetamine	Highly neurotoxic → Causes dopaminergic neurodegeneration (like Parkinson's)

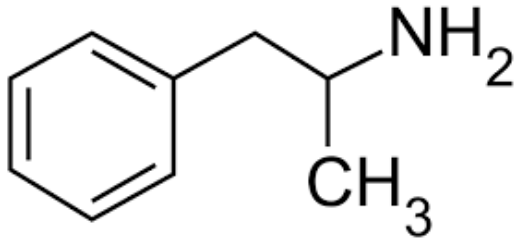
MDMA
3,4-Methylenedioxymethamphetamine

MDMA

- Entactogen/Empathogen
- Synthetic
  - Structurally similar to Amphetamine
  - Started as “Club Drug”
  - Psychedelic Assisted Therapy Agent



Amphetamine



MDMA

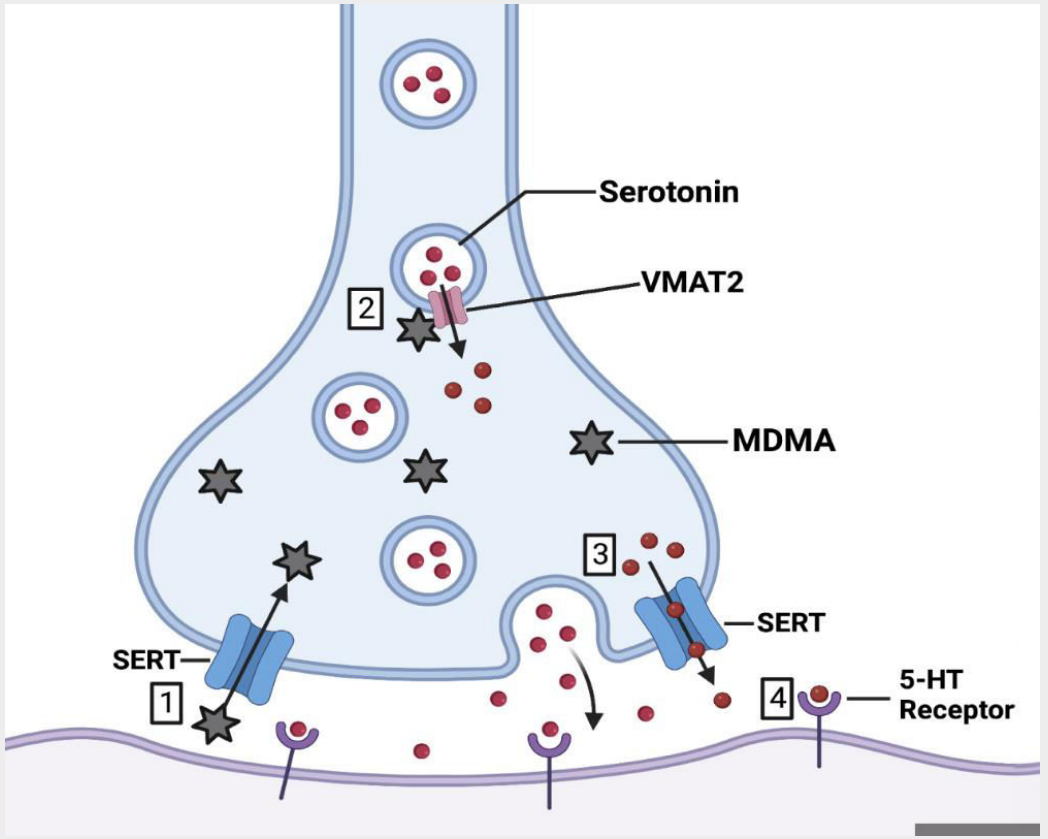
Formulation	**Tablets/Pills (often mixed with adulterants)** **Powder/Crystals (claimed to be "pure" MDMA, but may contain other substances)** **Capsules (powder-filled)**
Method of Use	**Oral (Most Common)** – Swallowed as a pill or capsule **Intranasal** – Powder/Crystal Bumping: Repeated oral or intranasal doses Stacking: Taking multiple doses at the same time
Cutting Agents	Can contain methamphetamine, caffeine, synthetic cathinones ("bath salts"), ketamine, or PMA (para-methoxyamphetamine, a toxic substitute).

MDMA Pharmacokinetics

- **Absorption:** Rapidly absorbed from the gastrointestinal tract or intranasally
- **Peak Effects:** 1-3 hours after ingestion, 15-30 mins after intranasal
- **Half-Life:** ~7-9 hours, but varies due to nonlinear metabolism
- **Duration of Effects:**
  - Psychoactive effects: 3-6 hours
  - Aftereffects ("comedown"): Up to 24 hours
  - Residual mood effects ("Tuesday blues"): Days to a week

MDMA: Mechanism of Action

- Increases release and reuptake inhibition of serotonin (5-HT) (SERT)
- To a lesser extent, dopamine (DA) and norepinephrine (NE).



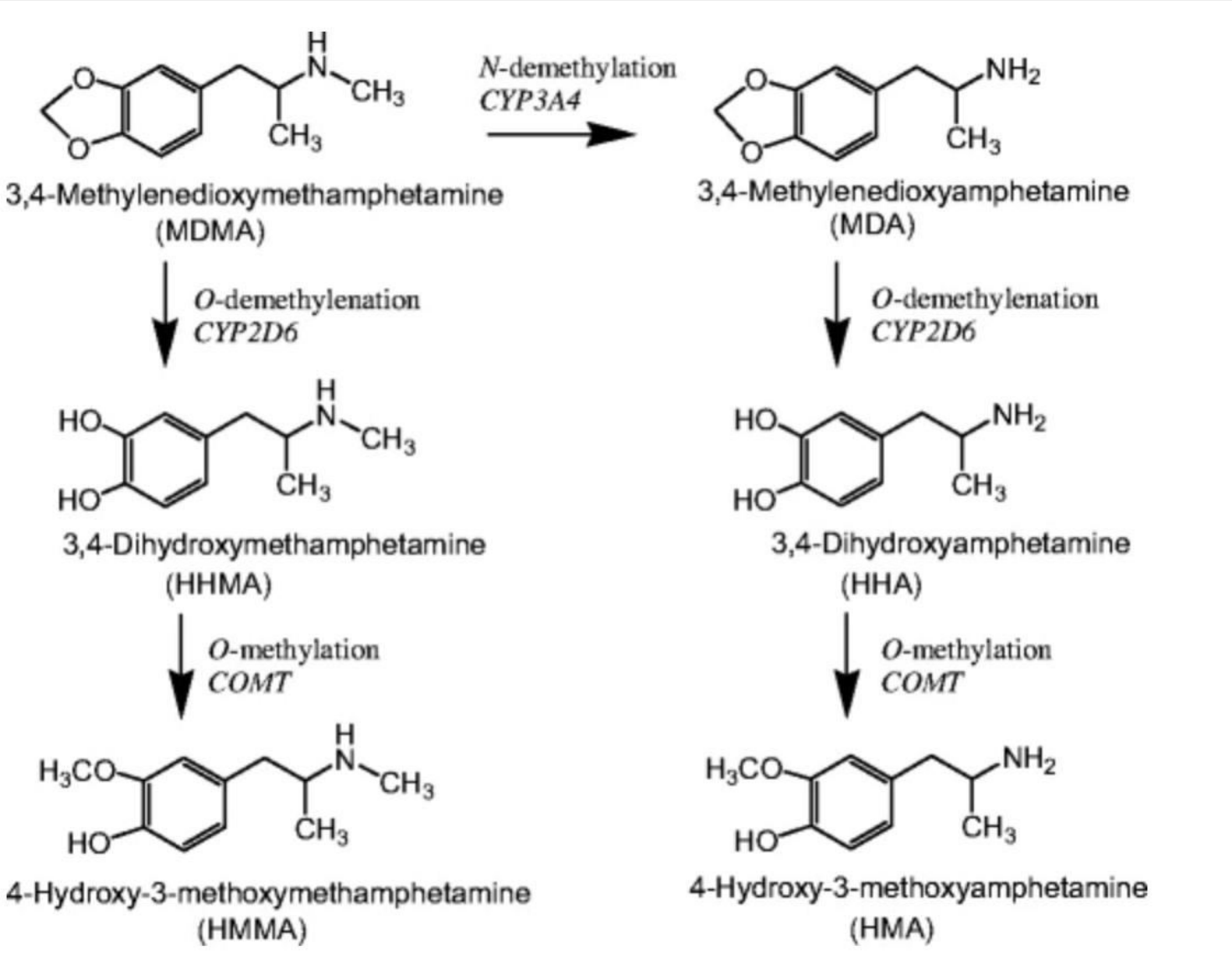
MDMA: Desired Effects

- **Euphoria & Empathy** – Heightened feelings of happiness, emotional openness, and connection with others
- **Increased Energy & Alertness** – Mild stimulant effects, generally less jittery than cocaine/meth
- **Enhanced Sensory Perception** – Brighter colors, increased tactile sensitivity, intensified music appreciation
- **Reduced Anxiety & Increased Sociability** – Promotes relaxation and bonding

MDMA Metabolism

- **Primary Enzyme: CYP2D6** (hepatic metabolism)
- **Major Metabolites:**
  - **3,4-Dihydroxymethamphetamine (HHMA)**
  - **3,4-Methylenedioxyamphetamine (MDA)** (active metabolite with more psychedelic effects)
- **Excretion:**
  - Mainly via **urine**, with **~20-50% excreted unchanged**

MDMA Metabolism



MDMA: Neurotransmitters

Neurotransmitter	Effect on Neurotransmitter	Impact on Behavior
Serotonin (5-HT)	**Massive serotonin release** → Blocks reuptake & reverses transporter function	Elevated mood, hallucinations, possible aggression
Dopamine (DA)	Moderate DA release (less than cocaine/meth)	Mild stimulation, motivation, reward-seeking behaviors
Norepinephrine (NE)	Increased NE	Elevated HR, BP, sweating
Oxytocin	Increased Oxytocin	Emotional warmth, social bonding

MDMA: Desired Effects

- **Euphoria & Well-Being** – Users feel intense happiness, pleasure, and emotional openness.
- **Increased Empathy & Emotional Bonding** – Often described as a "love drug," MDMA enhances feelings of connection and trust.
- **Reduced Anxiety & Fear Response** – Suppresses activity in the amygdala, decreasing social anxiety and emotional distress.
- **Increased Sociability & Talkativeness** – Users feel more outgoing, affectionate, and expressive.
- **Enhanced Self-Awareness & Emotional Processing** – May facilitate introspection and trauma processing, contributing to its therapeutic potential.

MDMA: Adverse Effects

Short-Term Risks

- Jaw Clenching & Teeth Grinding (Bruxism)
- Hyperthermia
- Dehydration & Electrolyte Imbalance (Risk of water intoxication if overhydrated)
- Anxiety, Restlessness, or Agitation
- Blurred Vision & Nystagmus

Long-Term Risks (Frequent Use)

- Serotonin Depletion → "Tuesday Blues" (Depression, fatigue, irritability for days to weeks post-use)
- Cognitive Impairment (Memory, learning deficits with chronic use)
- Neurotoxicity (Potential serotonin system damage with high-dose or frequent use)
- Dysphoria, anhedonia, psychomotor slowing, prolonged fatigue lasting weeks.

MDMA Toxicity

- **Symptoms of MDMA Overdose (Serotonin Syndrome & Hyperthermia)**
  - Severe Hyperthermia (>104°F, 40°C) → Organ failure, rhabdomyolysis
  - Seizures
  - Severe Hypertension & Cardiovascular Collapse
  - Serotonin Syndrome (Agitation, confusion, muscle rigidity, high fever)
- **Factors Increasing Overdose Risk:**
  - High doses or frequent re-dosing ("stacking")
  - Mixing with other stimulants (e.g., meth, cocaine)
  - Overhydration (causing hyponatremia)
  - Genetic CYP2D6 polymorphisms (poor metabolizers have increased risk of toxicity)

MDMA Toxicity Treatment

- **Medical Emergency! Supportive Care & Symptom Management:**
  - **Hyperthermia** → Rapid cooling measures, hydration with electrolyte-balanced fluids (avoid excessive water intake)
  - **Hypertension & Tachycardia** → Benzodiazepines (lorazepam, diazepam)
  - **Serotonin Syndrome** → Cyproheptadine (serotonin antagonist)
  - **Seizures** → Benzodiazepines, supportive care

MDMA: Culture

- **Rave, Club, & Festival Scene**
  - MDMA is deeply associated with electronic dance music (EDM) festivals, raves, and nightclub culture.
  - Used to enhance music appreciation, increase sensory perception, and boost energy for prolonged dancing.
  - Often taken in group settings, reinforcing its reputation as a "social drug."
- **LGBTQ+ & Queer Party Culture**
  - MDMA has been popular in gay nightlife & underground club scenes since the 1980s.
  - Used to promote emotional connection, self-expression, and intimacy.
  - Some crossover with chemsex culture, where it may be mixed with other substances (e.g., GHB, ketamine).

MDMA: Culture

- **Psychedelic & Consciousness Exploration Communities**
  - Some use MDMA for spiritual experiences, introspection, and therapy.
  - Often integrated into psychedelic retreats, Burning Man, and underground therapy sessions.
  - Microdosing MDMA is being explored for mental health benefits.
- **Therapeutic & Research Settings**
  - MDMA-assisted psychotherapy is being studied for PTSD, trauma, and couples therapy.
  - MAPS (Multidisciplinary Association for Psychedelic Studies) is leading clinical trials for FDA approval of MDMA-assisted therapy.
  - Unlike recreational use, therapeutic MDMA is carefully dosed, monitored, and combined with therapy.

MDMA: FDA Update

Background:

- Clinical trials aimed to evaluate the efficacy and safety of MDMA-assisted therapy in alleviating PTSD symptoms.

FDA Advisory Panel Decision (June 2024):

- An 11-member FDA advisory committee reviewed the clinical trial data for MDMA-assisted therapy. The panel voted 9-2 against the therapy's effectiveness and 10-1 against its benefits outweighing the risks. Concerns highlighted included:
  - Potential unblinding of study participants.
  - Adverse cardiovascular effects associated with MDMA.
  - Insufficient data on MDMA's misuse potential within the trial context.

FDA's Official Response (August 2024):

- Following the advisory panel's recommendation, the FDA declined approval of MDMA-assisted therapy for PTSD. The agency requested additional data to address the identified concerns, including the conduct of a third Phase 3 clinical trial.

MDMA Treatment

Long-Term Stimulant Use Disorder Treatment (MDMA Addiction):

- **Psychosocial Interventions**:
  - Cognitive Behavioral Therapy (CBT) – Address impulsivity, relapse prevention
  - Motivational Interviewing (MI) – Enhance motivation to quit
  - Harm Reduction Strategies – Education on hydration safety, avoiding polydrug use, and dosing precautions
- No FDA-Approved Options:
  - Can Consider SSRIs to restore serotonin balance in chronic users and Mirtazapine (5-HT antagonist) to reduce withdrawal symptoms, anxiety

Bath Salts
Synthetic Cathinones

Bath Salts: Formulations

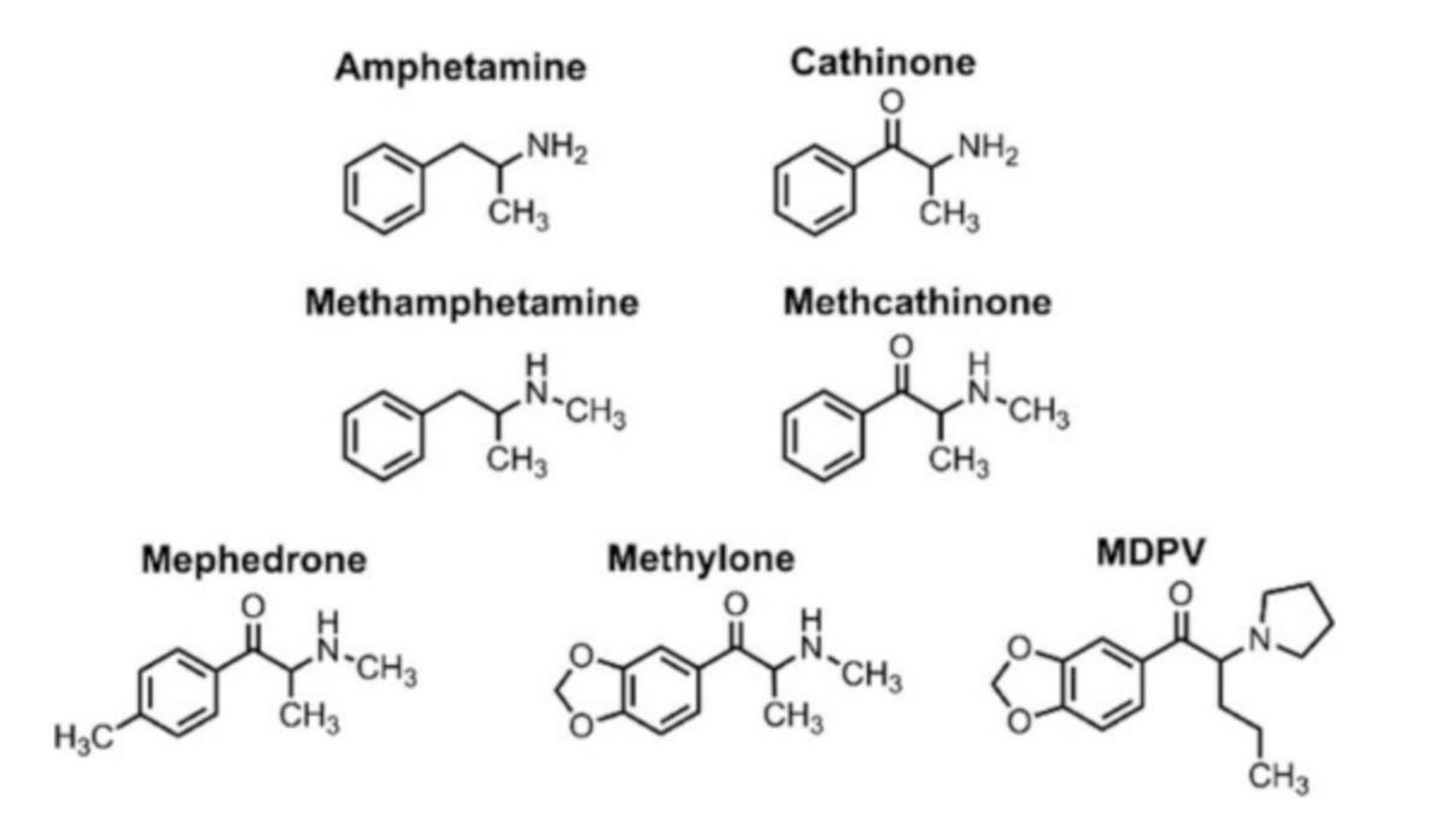
- **Common Names:** "Bath salts," Flakka, Cloud 9, Vanilla Sky, White Lightning
- **Chemical Class: Synthetic Cathinones** (structurally related to cathinone, the active compound in **khat**, a plant chewed for stimulant effects).
- **Common Ingredients:**
  - **Methylenedioxypyrovalerone (MDPV)**
  - **Mephedrone ("Meow Meow")**
  - **α-Pyrrolidinopentiophenone (α-PVP, "Flakka")**
- **Forms:**
  - **White or tan powder**
  - **Crystals, capsules, or pressed pills**
  - **Liquid formulations (e-cigarettes, vaping solutions)**

Bath Salts: Khat Plant Origin

- Khat is a flowering evergreen shrub that has two active ingredients:
  - Cathine and Cathinone.
- Khat is typically chewed like tobacco, then retained in the cheek and chewed intermittently to release the active drug.
- Dried khat leaves can be made into tea or a chewable paste, and khat can also be smoked and even sprinkled on food.
- Desired effects: Increased energy, euphoria.



Bath Salts: Cathinone Family



Bath Salts & Cathinones: Desired Effects

- Euphoria
- Increased energy and alertness
- Boost in confidence or invincibility
- Heightened sociability
- Increased libido

Bath Salts & Cathinones: Adverse Effects

Psychiatric:

- Agitation, Panic attacks
- Psychosis: Paranoia, Auditory or visual hallucinations: Often lasting weeks after use.
- Delirium
- Aggressive behavior

Physical:

- Tachycardia, hypertension
- Hyperthermia
- Seizures
- Muscle breakdown (rhabdomyolysis)
- Kidney failure
- Death (due to overdose, cardiac issues, or behavioral harm)

Bath Salts & Cathinones: Mechanism of Action

- Synthetic cathinones block **reuptake of dopamine, norepinephrine, and serotonin**
- Some (like mephedrone) also increase release of monoamines (like MDMA)
- **MDPV** (3,4-methylenedioxypyrovalerone):
  - Acts as a **potent reuptake inhibitor of dopamine and norepinephrine**
  - **10x more potent than cocaine** in dopamine transporter inhibition
  - Minimal effect on serotonin (unlike MDMA)
  - MDPV is one of the most dangerous cathinones due to its potency and long duration (up to 8 hours).
  - MDPV's mechanism closely resembles cocaine but with much higher affinity for dopamine transporters—leading to intense stimulation and paranoia.

Bath Salts & Cathinones: Metabolism

- Primarily metabolized in the **liver** via **CYP450 enzymes**
- Excreted in **urine**, both as parent compound and metabolites
- Difficult to detect in standard drug screens — requires **specialized testing**
- MDPV has a half-life of around **3-4 hours**, but effects may last longer due to **slow clearance from the brain**
- Some can be detected using advanced GC-MS or LC-MS/MS methods in forensic or toxicology labs.

Bath Salts & Cathinones: Complications and Treatment

- High risk of severe HTN, seizures, kidney injury due to hyperadrenergic states.
- First-line:
  - Benzodiazepines.
  - Supportive care for hypertension and hyperthermia.

High-Yield Board Review Summary

- **Cocaine**:
  - Plant-based stimulant that blocks dopamine reuptake (DAT) → Short-acting stimulant.
- **Methamphetamine**:
  - Synthetic Amphetamine that releases dopamine + Blocks reuptake → Longer-lasting effects.
- **MDMA**:
  - Primarily serotonin release → Hyperthermia risk.
- **Bath Salts**:
  - Potent synthetic cathinones → Severe paranoia, agitation.
- **Treatments**:
  - Psychosocial and Behavioral treatments are gold standard, but off-label medications can be effective, too!

Summary Slide

Category	Cocaine	Methamphetamine	MDMA	Synthetic Cathinones (Bath Salts)
Neurobiology & Mechanisms	Blocks dopamine reuptake (DAT), increasing dopamine in synapse.	Releases dopamine + blocks reuptake via VMAT2, leading to prolonged effects.	Primarily serotonin release (SERT), with lesser dopamine effects.	Potent dopamine/NE reuptake inhibition; severe stimulant-like effects.
Intoxication Effects	Euphoria, increased energy, vasoconstriction, MI risk, paranoia.	Euphoria, hyperthermia, agitation, paranoia, 'meth mouth'.	Empathogenic effects, sensory enhancement, hyperthermia, hyponatremia.	Extreme agitation, paranoia, violent behavior, 'excited delirium'.
Withdrawal Symptoms	Dysphoria, hypersomnia, fatigue, intense cravings.	Severe anhedonia, psychomotor slowing, prolonged fatigue, mood disturbances.	Serotonin depletion → depression, anxiety, fatigue, irritability.	Severe withdrawal symptoms including dysphoria, insomnia, cravings.
Evidence-Based Treatments	No FDA-approved meds; possible benefit from disulfiram, modafinil, and mixed amphetamine salts.	No FDA-approved meds: Bupropion + naltrexone; methylphenidate for stimulant agonist therapy.	Supportive care: benzodiazepines for agitation, cooling measures, hydration.	First-line: Benzodiazepines; supportive care for hypertension, hyperthermia.

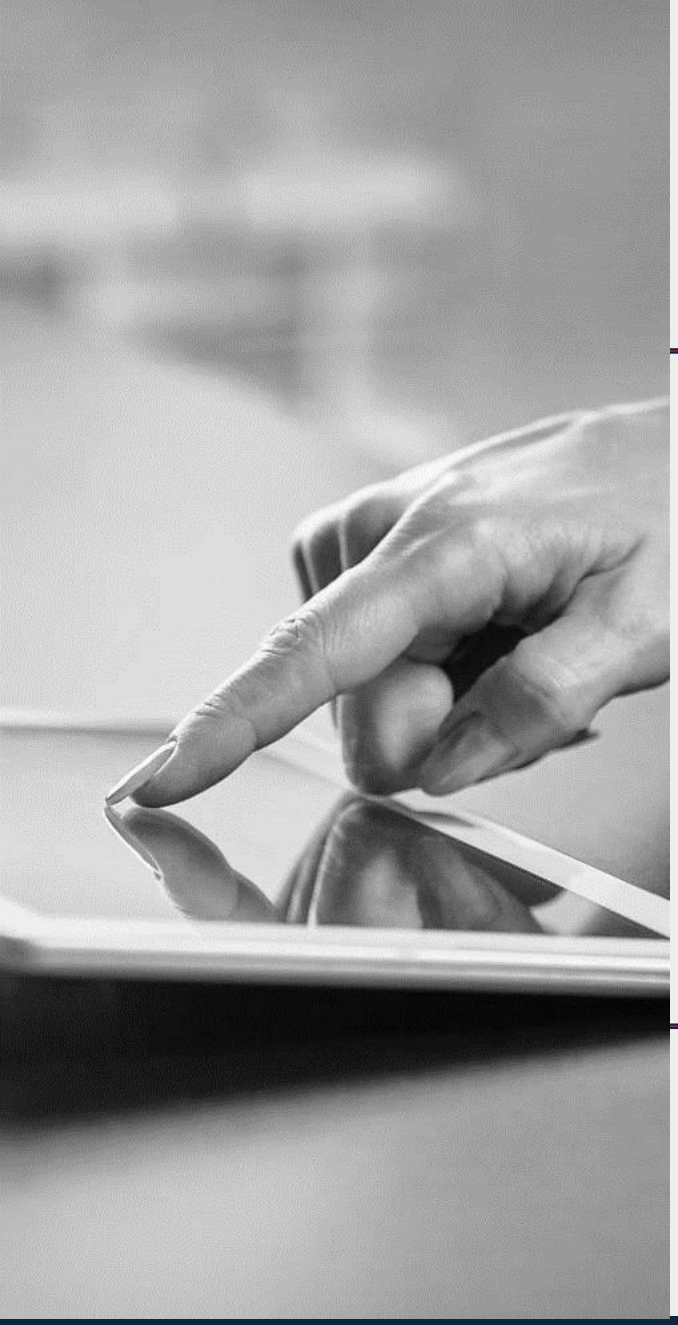
Thank You

References

- Kampman, K. M. (2019). The treatment of cocaine use disorder. *Science advances*, *5*(10), eaax1532.
- Chan, Brian, et al. "Pharmacotherapy for cocaine use disorder—a systematic review and meta-analysis." *Journal of general internal medicine* 34 (2019): 2858-2873.
- Schwartz, E. K., Wolkowicz, N. R., De Aquino, J. P., MacLean, R. R., & Sofuoglu, M. (2022). Cocaine use disorder (CUD): current clinical perspectives. *Substance Abuse and Rehabilitation*, 25-46.
- Paulus, M. P., & Stewart, J. L. (2020). Neurobiology, clinical presentation, and treatment of methamphetamine use disorder: a review. *JAMA psychiatry*, *77*(9), 959-966.
- Han, B., Compton, W. M., Jones, C. M., Einstein, E. B., & Volkow, N. D. (2021). Methamphetamine use, methamphetamine use disorder, and associated overdose deaths among US adults. *JAMA psychiatry*, *78*(12), 1329-1342.
- Potvin, S., Pelletier, J., Grot, S., Hebert, C., Barr, A. M., & Lecomte, T. (2018). Cognitive deficits in individuals with methamphetamine use disorder: A meta-analysis. *Addictive behaviors*, *80*, 154-160.

References

- Paulus, M. P., & Stewart, J. L. (2020). Methamphetamine use disorder: the next addiction crisis. *JAMA psychiatry*, *77*(9), 959.
- Trivedi, M. H., Walker, R., Ling, W., Dela Cruz, A., Sharma, G., Carmody, T., ... & Shoptaw, S. (2021). Bupropion and naltrexone in methamphetamine use disorder. *New England Journal of Medicine*, *384*(2), 140-153.
- Brown, H. D., & DeFulio, A. (2020). Contingency management for the treatment of methamphetamine use disorder: A systematic review. *Drug and Alcohol Dependence*, *216*, 108307.
- Burgess, C., O'donohoe, A., & Gill, M. (2000). Agony and ecstasy: a review of MDMA effects and toxicity. *European psychiatry*, *15*(5), 287-294.
- Quinton, M. S., & Yamamoto, B. K. (2006). Causes and consequences of methamphetamine and MDMA toxicity. *The AAPS journal*, *8*, E337-E337.
- Capriola, M. (2013). Synthetic cathinone abuse. *Clinical pharmacology: advances and applications*, 109-115.
- Wood, D. M., Greene, S. L., & Dargan, P. I. (2011). Clinical pattern of toxicity associated with the novel synthetic cathinone mephedrone. *Emergency medicine journal*, *28*(4), 280-282.



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ASAM REVIEW COURSE 2026

Other Classes of Drugs: Pharmacology and Epidemiology

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Financial Disclosure

Annie Lévesque, MD, MSc

- No relevant disclosures

LEARNING OBJECTIVE

Identify other classes of drugs, their physiological impacts, and treatment considerations.

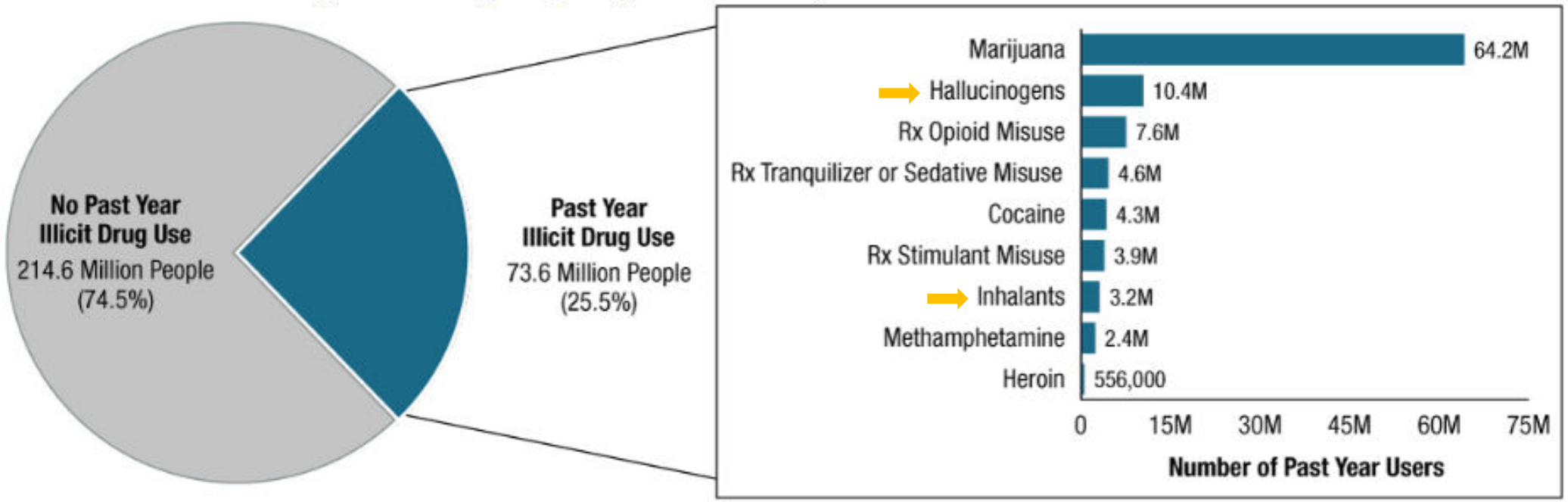


In Summary



1. Hallucinogens
2. Dissociatives
3. Inhalants
4. Anabolic-Androgenic Steroids

Figure 13. Past Year Illicit Drug Use: Among People Aged 12 or Older; 2024



View Figure 13 long description

Rx = prescription.

Note: The estimated numbers of past year users of different illicit drugs are not mutually exclusive because people could have used more than one type of illicit drug in the past year.

TABLE D-54 (continued)

STEROIDS: [o,bb] Trends in Lifetime, Annual, and 30-Day Prevalence of Use in Grades 8, 10, and 12

(Entries are percentages.)

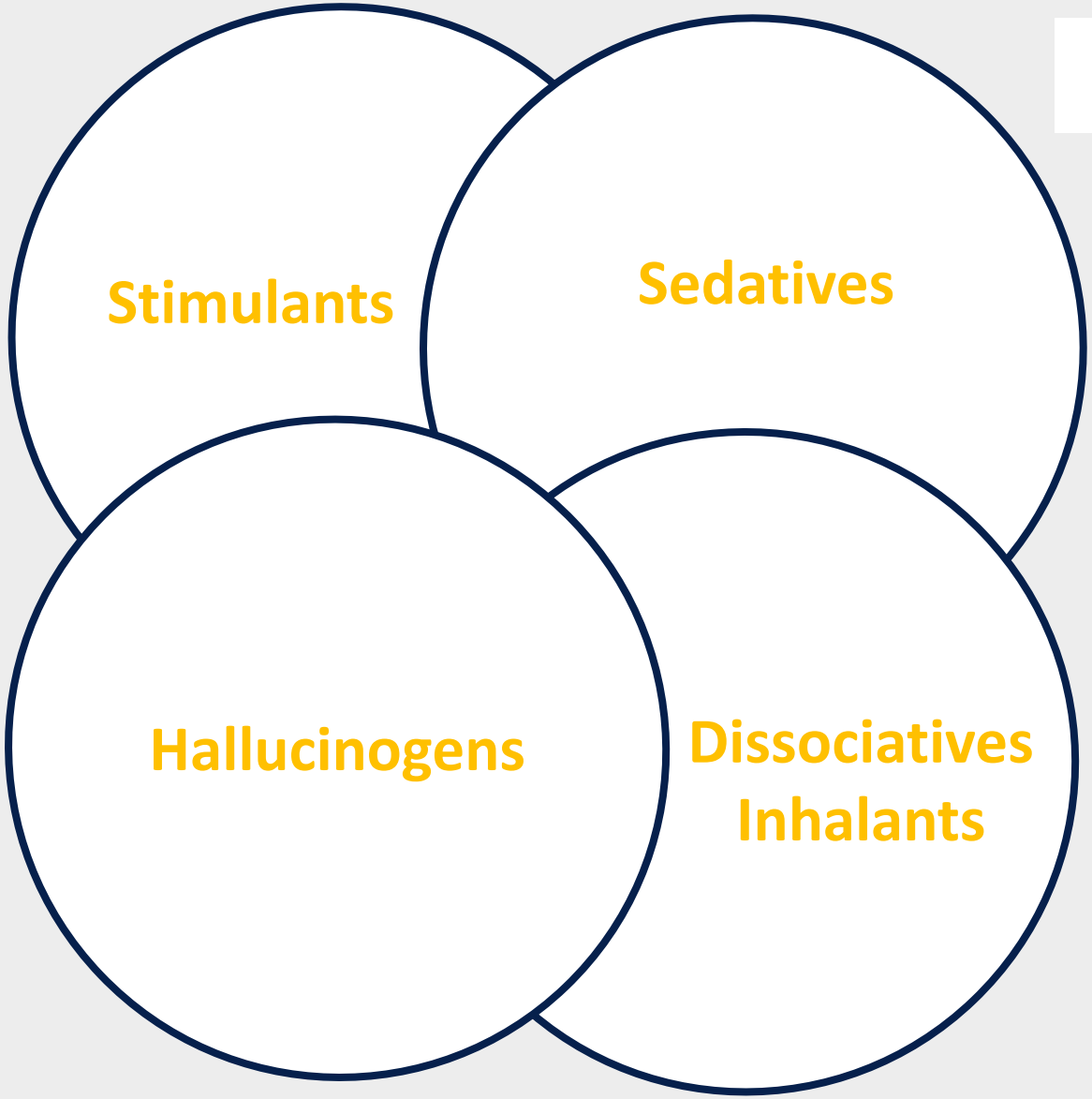
	2018	2019[i]	2020	2021	2022	2023	2022-2023 change	2020-2023 change	2020-2022 change	2020-2021 change	2018-2023 change	Proportional change	Peak year–2023 change	Proportional change	Low year–2023 change	Proportional change
Lifetime																
8th Grade	1.1	1.5	2.0	1.2	1.6	1.2	-0.4	-0.9	-0.4	-0.9 s	+0.1	+7.0	-1.8 sss	-61.0	+0.3	+29.3
10th Grade	1.2	1.6	1.7	0.7	0.9	1.2	+0.2	-0.5	-0.7 s	-0.9 s	0.0	-1.8	-2.3 sss	-66.3	+0.4 s	+59.0
12th Grade	1.6	1.6	2.0	0.8	1.5	0.9	-0.6	-1.1	-0.5	-1.2	-0.6	-40.0	-3.0 sss	-76.3	+0.1	+11.3
Last 12 Months																
8th Grade	0.6	0.8	1.1	0.5	0.8	0.6	-0.1	-0.5	-0.3	-0.7 s	0.0	+1.0	-1.0 sss	-61.2	+0.2	+43.0
10th Grade	0.6	0.8	0.9	0.3	0.5	0.5	0.0	-0.4	-0.4 s	-0.6 sss	-0.1	-18.6	-1.7 sss	-76.3	+0.2 s	+80.3
12th Grade	1.1	1.0	1.2	0.5	1.3	0.7	-0.7	-0.6	+0.1	-0.7	-0.5	-41.3	-1.9 sss	-74.3	+0.1	+26.2
Last 30 Days																
8th Grade	0.3	0.3	0.3	0.2	0.5	0.3	-0.2	0.0	+0.2	-0.2	0.0	+10.0	-0.5 sss	-61.4	+0.2	+99.9
10th Grade	0.4	0.4	0.5	0.1	0.3	0.4	+0.1	-0.1	-0.2	-0.3 ss	0.0	-5.5	-0.7 sss	-64.9	+0.2 s	+150.7
12th Grade	0.8	0.7	1.2	0.5	1.3	0.5	-0.7 s	-0.6	+0.1	-0.7	-0.3	-32.1	-1.0 ss	-65.2	+0.1	+20.0

Source. The Monitoring the Future study, the University of Michigan.

Note. See last four pages for relevant footnotes.

Dopamine
Norepinephrine

GABA



Serotonin

NMDA
Glutamate

Hallucinogens

Hallucinogens

- Serotonin 5HT-2A receptor agonists
- Alterations in cognition, perception, and emotion
- Minimal autonomic side effects or craving



“Illusionogen”



- Illusions = alteration or enhancement of existing sensory perception
- May be more accurate term
  - Reality testing is generally intact
  - Effect varies greatly with expectations and environment

Hallucinogens

Classical Hallucinogens:

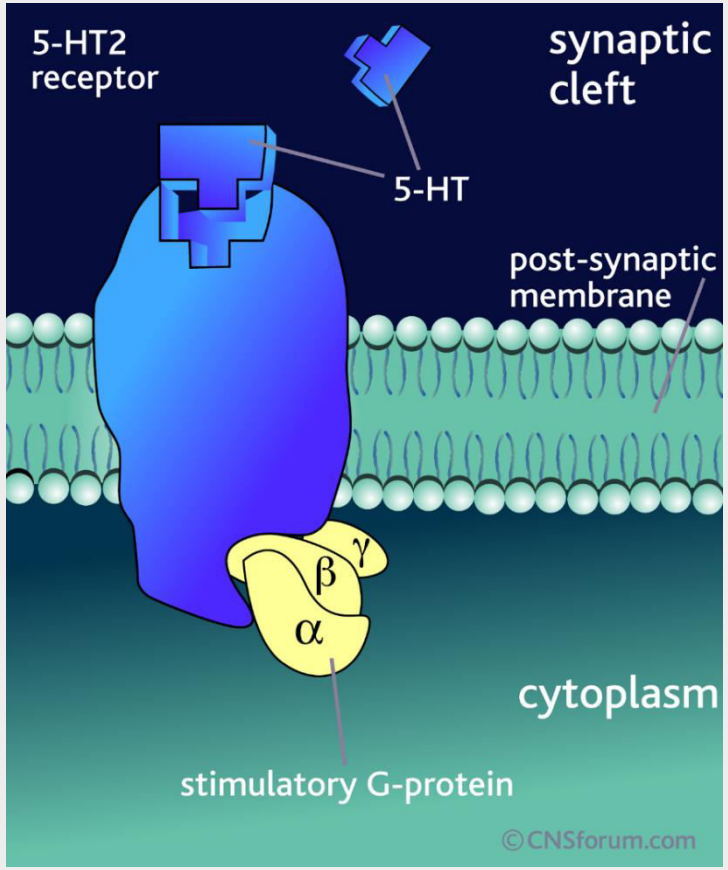
- 5HT-2A agonists or partial agonists
- LSD, DMT, psilocybin, mescaline

Empathogens:

- Creates a sense of connection to others
- MDMA and related substances

Others:

- Salvia, Ibogaine



Effects of Hallucinogens



Altered shapes and colors

Synesthesia

Alterations in mood (can be tension and anxiety)

Distorted sense of time

Depersonalization

Dreamlike feeling

Effects of Hallucinogens
Somatic



Dizziness	Weakness	Tremors	Nausea

Drowsiness	Paresthesias	Blurred Vision

Most hallucinogens induce rapid tolerance

DMT

Naturally occurring (plants, toad)

- Inhalation (smoking) or injection (rare)
- Can be taken orally, but requires MAOI
- Rapid onset (<5 min), short duration of action (30 min)



In contrast to other classical hallucinogens, DMT does not induce tolerance in humans.





Ayahuasca

- Brew containing DMT, MAOIs, and other hallucinogens
- Used ceremonially in some traditional religious ceremonies
- Can cause significant vomiting
- High dose may lead to seizure

Psilocybin

Psilocybin (Pro-drug) → psilocin

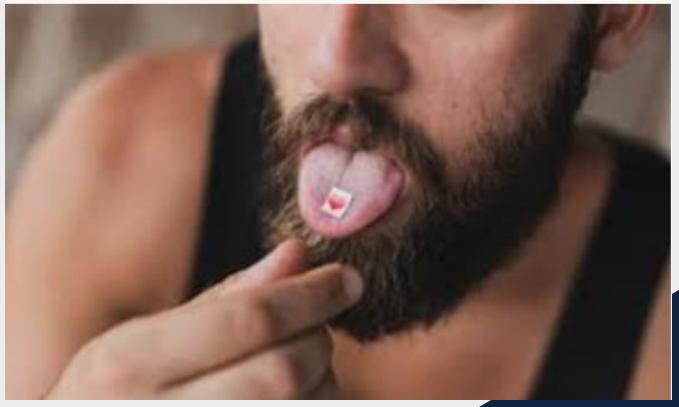
- Found as naturally occurring tryptamine in certain varieties of mushrooms
- Inability to discern fantasy from reality
  - Can lead to panic attacks, psychosis
- Duration: 4-6 hours



Lysergic Acid Diethylamide (LSD)

- First hallucinogen to be synthesized
- Blotter paper with dried solution of LSD
- Breath mints, sugar cubes, pressed into pills or thin gelatin squares
- Onset: 30-60 min, Peak: 2-4 hours, Duration 8-12 hours





Effects

- Altered shapes and colors, heightened sense of hearing
- Depersonalization, visual hallucinations, alterations in mood

Mescaline/Peyote



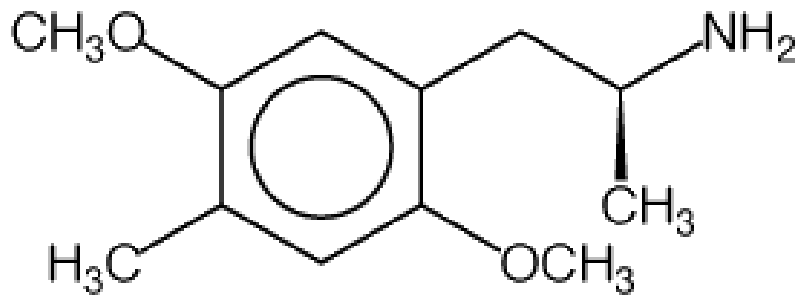
- Buttons from top of peyote cactus
  - 6-10 buttons for intoxication
- Slow onset (30-60 min)
  - **First hour**:
    - Minor perceptual changes
    - Increased respiratory rate,
    - Nausea
  - **Next several hours (5-10):**
    - Visual illusions/hallucinations
    - Synesthesia

DOM

- Results from structural modification of mescaline-like substances
- Extremely potent
- Used as model hallucinogen in drug discrimination studies

DOM

2,5-dimethoxy-4-methylamphetamine



MDA (*Sass*)

- Powder or pill – swallowed or sniffed
- Produces stimulant, empathogen and hallucinogenic effects
- Increases release of serotonin, norepinephrine and dopamine
- Closely related to MDMA (*Ecstazy*)
- Is sometimes used as an adulterant and falsely sold as MDMA



Salvia

- Naturally grows in the US
- Can be ingested or smoked
- Active ingredient: salvinorin A (kappa opioid agonist)
- Changes in visual perception
- Decreased ability to interact with surroundings
- Intense and short-lived
  - Onset < 1 minute, Duration < 30 minutes



Hallucinogen Intoxication

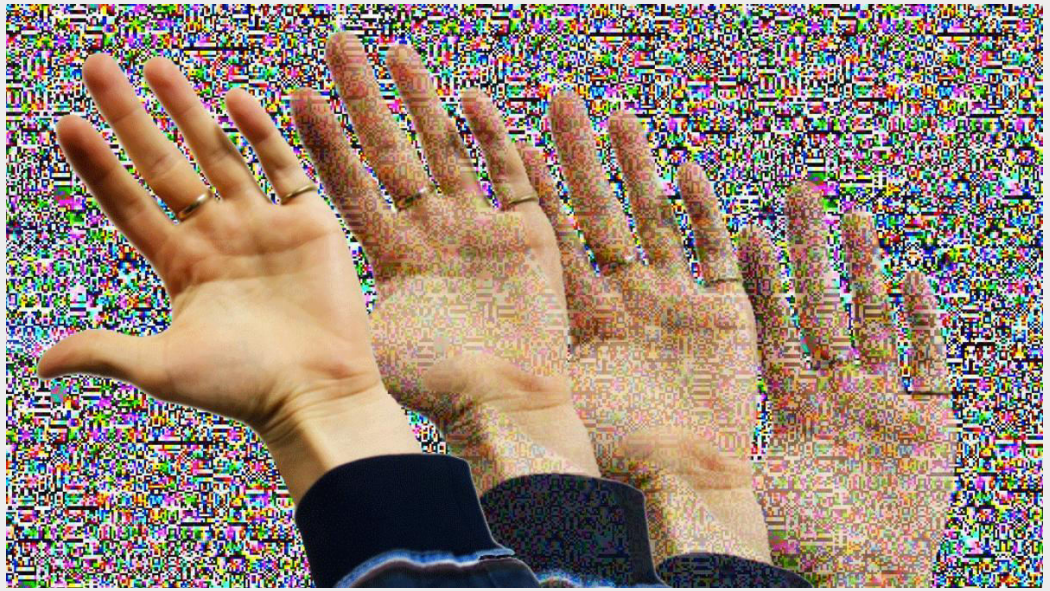
- Anxiety, “Bad Trip”
- Usually self-limited and returns to baseline without treatment
- Treatment
  - First line: Low stimulus environment, reassurance
  - Second line: Benzo
  - Third line: Antipsychotic

Summary: Hallucinogen Intoxication

- Clear Sensorium
- Intact Memory
- Hyperalert
- Tolerance
- Intact reality testing
- Visual Hallucinations >> Auditory

Hallucinogen Persisting Perception Disorder (HPPD)

- Re-experiencing of perceptual symptoms experienced while intoxicated following cessation of use (flashbacks)



Hallucinogen Persisting Perception Disorder (HPPD)

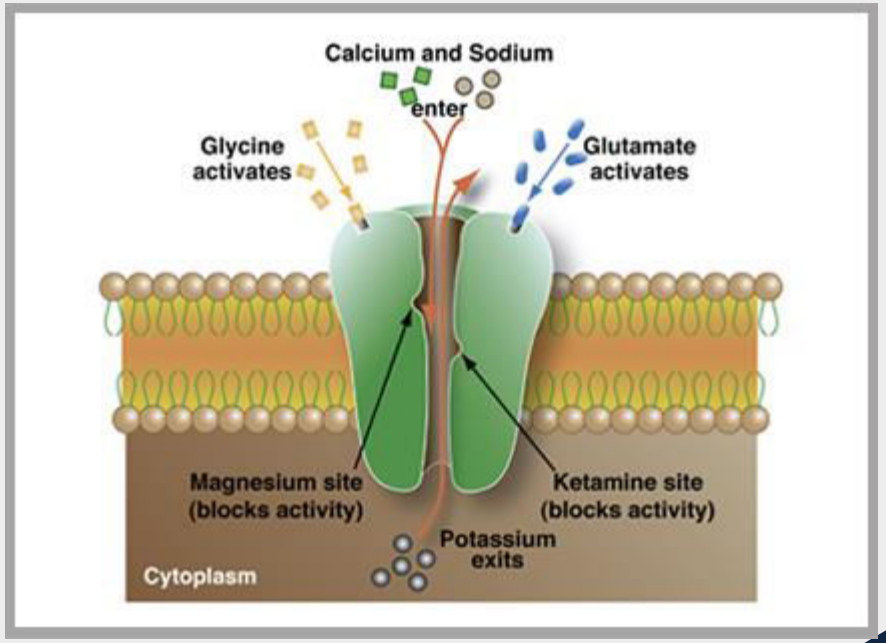
- Unrelated to dose or number of exposures
- Usually resolves within 1-2 years of last use
- Can be triggered by other substance use



Dissociatives

Definition

- NMDA receptor antagonists
  - Glutamate activates NMDA receptors to filter sensory stimuli
  - Dissociatives noncompetitively block NMDA receptors → sensory overflow



Effects



- Dissociation
- Sensory Isolation
- Mental Distortions
- Increased HR, BP, Temp

Members of the Class

- PCP
- Ketamine
- Dextromethorphan (DXM)
- Nitrous Oxide







Phencyclidine (PCP, Angel dust)

- Developed as IV anesthetic
  - No longer FDA-approved
  - Associated with prolonged delirium
  - Risk of seizures or death
- Available as powder, tablets, liquid, and sprayed onto plant leaves and then smoked



PCP Effects

Confusion, delirium, psychosis

↓

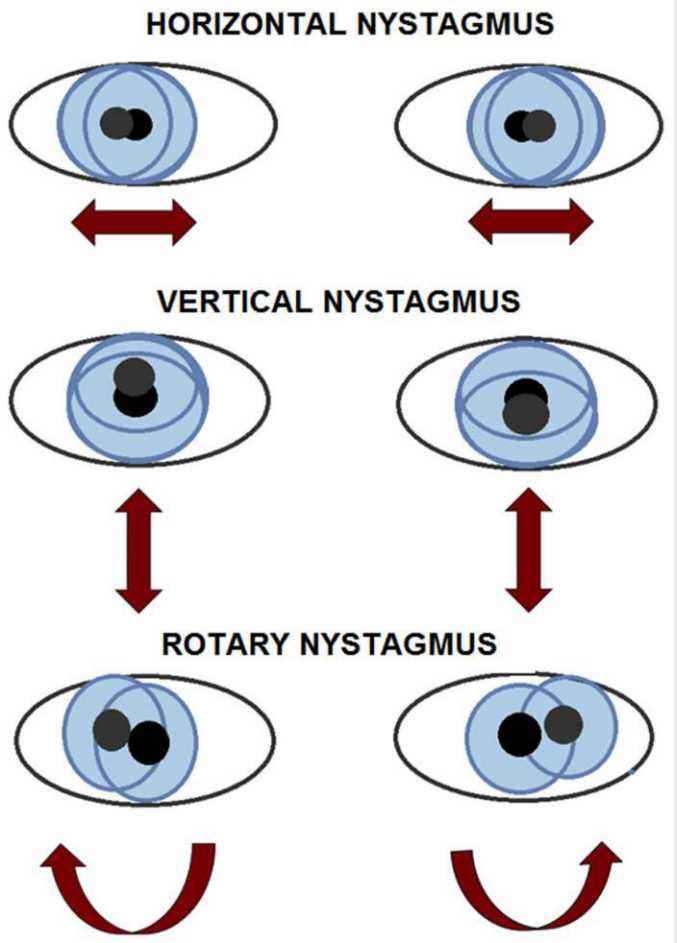
Semi-coma and coma (less common)

↓

Coma with seizures (rare)

PCP

- PCP Intoxication
  - Nystagmus (rotary, vertical, horizontal)
  - Hyperreflexia
  - HTN
  - Feelings of invulnerability
  - Management of intoxication: low stimulus environment, benzos/antipsychotics as indicated



Ketamine (K, Special K)

- FDA-approved for general anesthesia and treatment-resistant depression
- Administered as IV, IM or as nasal spray in medical settings
- Misused by inhalation, smoking, or oral administration
- Less potent, shorter-acting than PCP





Effects of Ketamine

- Analgesia / numbness
- Spacey feeling (“K-hole”)
- Amnesia
- Delirium (higher doses)
- Nystagmus (vertical and/or horizontal)
- Urinary complications

Dextromethorphan (DXM)



- OTC cough medicines
- FDA-approved for the treatment of depression (combo drug with bupropion)
- Anti-tussive dose: <120mg daily; recommended dose 10-20mg q4hours
- 300-1800mg produces PCP-like effects
  - Euphoria and hallucinations
  - Drowsiness, blurred vision, slurred speech
  - N/V, hypertension, diaphoresis

Effects of DXM

- In addition to antagonism at NMDA receptor, DXM has significant serotonergic properties
  - ↑ serotonin synthesis and release
  - ↓ reuptake

- Deaths have been reported with large doses (200x dose)
  - CNS & respiratory depression, seizure, arrhythmias

Therapeutic use of hallucinogens and dissociatives

- Research mostly stopped in the 70s with war on drugs
- More recently:
  - Ketamine for depression
  - MDMA for the treatment for PTSD
  - Research currently conducted to use of some hallucinogen and dissociative drugs for the treatment of SUD but nothing approved

Inhalants

Inhalants



Breathable chemicals that can be self-administered, also known as:

- Whippets
- Poppers
- Huff
- Bang
- Kick
- Sniff

Source of Inhalants: Products



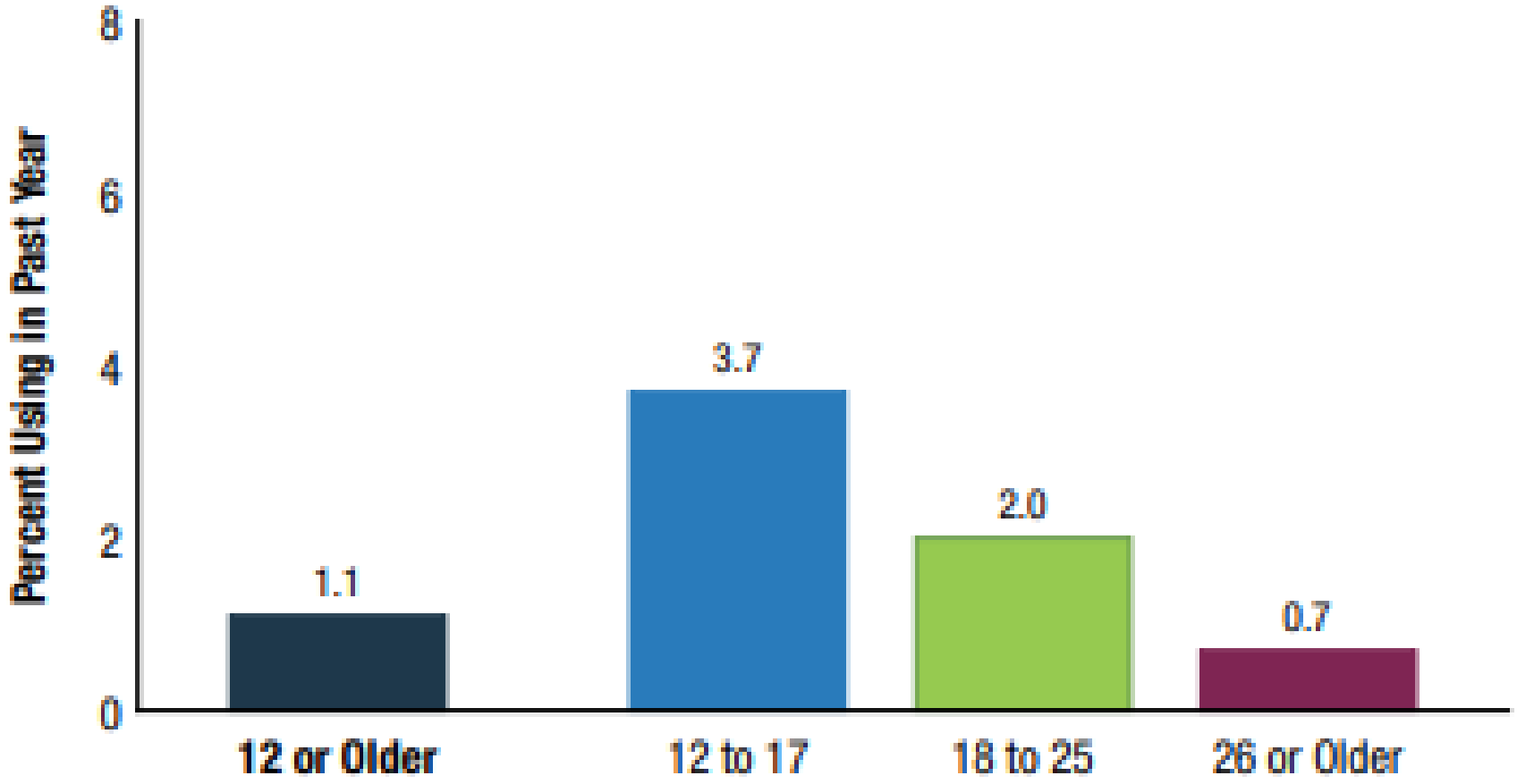
Air freshener	Lighter fluid	Household cleaners	Gasoline
Hair spray	Mothballs	Nail polish remover	Paint thinner
Markers	Refrigerant	Rubber cement	Spray paint
	Video head cleaner	Whipped cream canisters	

Terminology

- **Sniffing** = inhaling from an open container
- **Huffing** = holding fabric soaked in substance to the nose or mouth and inhaling
- **Bagging** = concentrating vapors in a bag and inhaling



Figure 20. Past Year Inhalant Use: Among People Aged 12 or Older; 2024



SAMHSA – NSDUH survey 2024

Abuse Liability

- Number of factors increase abuse potential
  - Free or low cost
  - Readily available
  - Difficult to test for
  - Perceived as low risk

- Inquire about inhalant use, especially when working with adolescent population
- Provide education regarding consequences of use

Inhalant Pharmacology

- Highly lipophilic
- Rapidly absorbed through the lungs
- Crosses blood-brain barrier
- Accumulates in brain, liver and fatty tissue
- Rapid onset, short duration
- Synergistic effect: alcohol, benzos

Effects of Inhalants

Acute Effects

- Euphoria
- Disinhibition
- Dizziness / lightheadedness
- Slurred speech
- Ataxia

Toxic Effects and Overdose

- Respiratory depression
- Arrhythmias
- Asphyxia, cardiac arrest and death can occur

Chronic Effects of Inhalants

CARDIAC

arrhythmia

cardiomyopathy

DERMATOLOGICAL

perioral infection

rash

GASTROINTESTINAL

hepatorenal failure

MUSCULOSKELETAL

Rhabdomyolysis

Chronic Effects of Inhalants

PULMONARY

emphysema

hypoxia

aspiration pneumonia

GENITOURINARY

glomerulonephritis

hypokalemia

HEMATOPOIETIC

aplastic anemia

leukemia

bone marrow suppression

NEUROLOGICAL

peripheral neuropathy

delirium/dementia

cerebellar atrophy

irreversible white matter changes

Treatment Considerations

- User may experience prolonged residual effects because chemicals are stored in fatty tissue
- Neurological impairment is often present
  - Talk therapy / group therapy may not be appropriate

Anabolic-androgenic Steroids

Anabolic - Androgenic Steroids (AAS)







- Anabolic = skeletal muscle-building
- Androgenic = masculinizing
- Includes testosterone and related synthetic substances
- Enhance performance and/or improve physical appearance
- May be taken at 10-100x the intended dose

Medical Indications for AAS

- Hypogonadism
- Hereditary angioedema prophylaxis
- Acquired aplastic anemia and myelofibrosis treatment
- Muscle wasting secondary to starvation, weight loss following extensive surgery, chronic infections (advanced HIV), or severe trauma
- Secondary treatment of bone metastases from breast cancer in postmenopausal women
- Menopause with methyltestosterone combined with estrogen to alleviate symptoms
- Patients on dialysis to increase lean body mass
- Female-to-male gender change

Addiction Liability

- Rarely seek treatment
- Not euphorigenic; no immediate high
- Goal is long-term reward associated with physical changes
- May be seen as socially acceptable or positive
- Often missed by clinicians

Epidemiology

3 most common populations:

- Athletes
  - Performance enhancement
- Aesthetes
  - Improve physical appearance (often adolescents)
- Fighting Elite
  - Increase aggression and/or job performance (security, law enforcement)

Terminology

Stacking: use of combinations of multiple drugs at the same time

Cycling: use of steroid combinations for weeks to months with abstinent rest periods before resumption of different steroid or combinations in order to avoid tolerance

Pyramiding: starting with a low dose and gradually increasing the dose until peak levels are achieved a number of weeks before a competition and then tapering so the individual will be drug free when tested

Steroid Side Effects

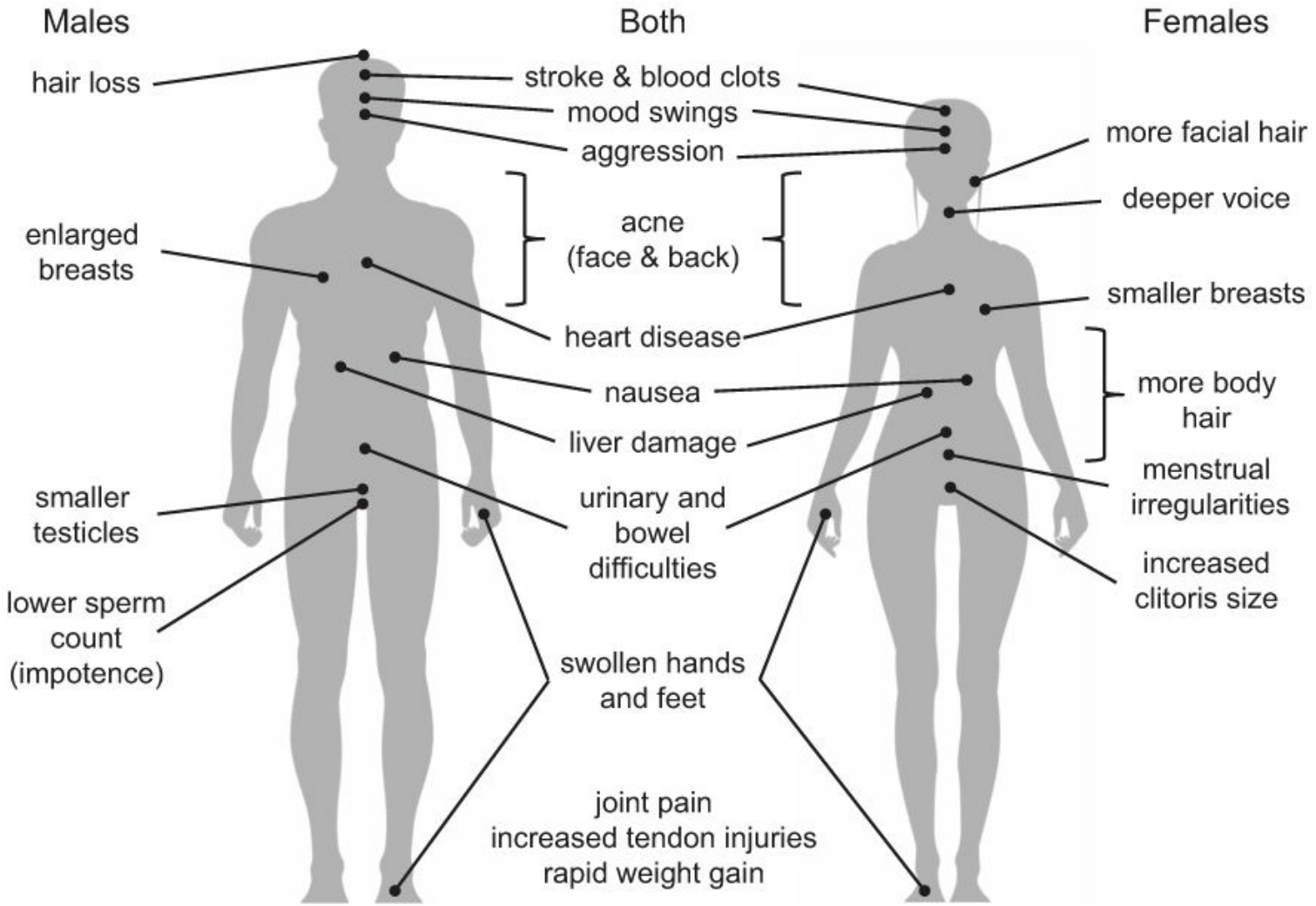


Figure 21-1. Side effect profiles of AAS in male and female persons with substance use disorder.

Miller et al. The ASAM Principles of Addiction Medicine 7th edition

Steroid Side Effects

Acne	Liver damage	↑LDL, ↓HDL	Complications of Injections
Tendon rupture	Cardiac complications	Sexual dysfunction	Polycythemia

Psychiatric Side Effects

- Aggressive / violent behavior
- Hypomania or Mania (high doses)
- Paranoia
- Extreme irritability
- Impaired judgment
- Delusions

Treatment:

- Remove AAS
- Use mood stabilizers or anti-psychotics as needed
- Generally, resolves within 1-2 weeks after cessation

Other Associated Syndromes & Treatment

- Steroid Withdrawal-Associated Depression
  - Can be responsive to SSRIs
- Comorbid SUD, especially opioid
- Body Dysmorphic Disorder / Muscle Dysmorphia



In Summary

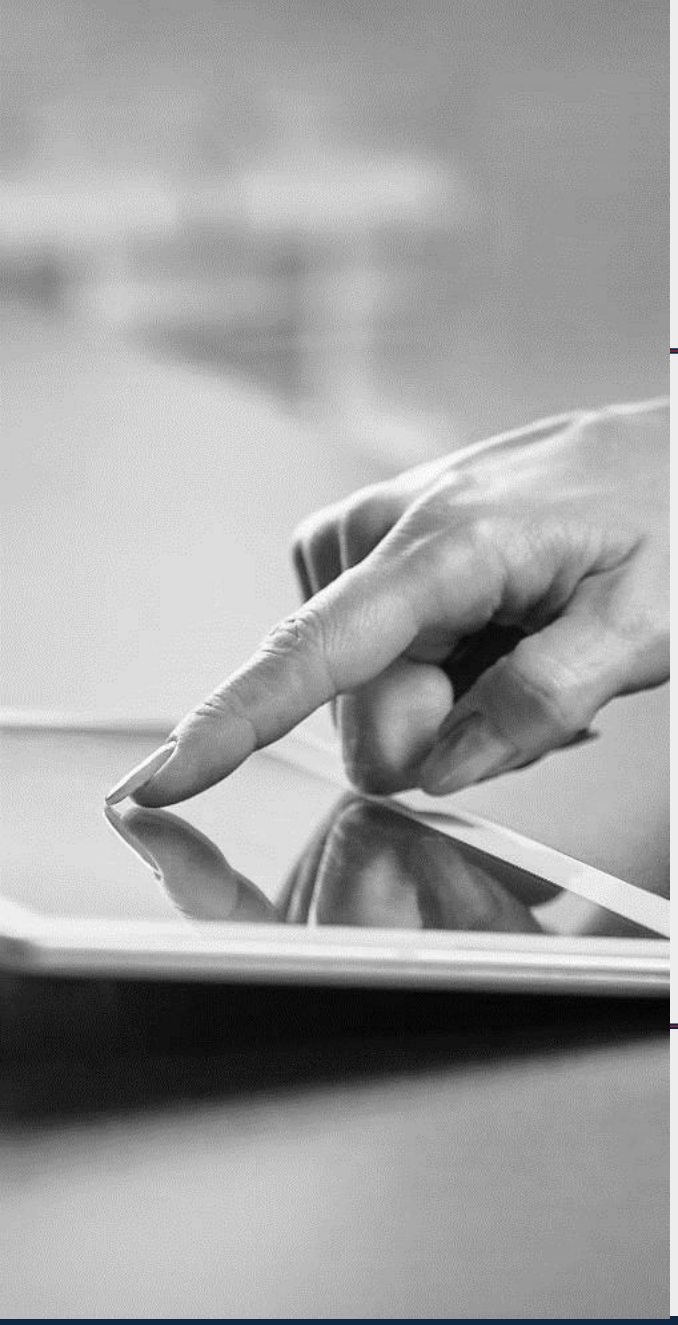


1

Diverse group of substances with relatively low prevalence, but high abuse liability

2

Varied but significant effects from use and misuse, including long-term consequences



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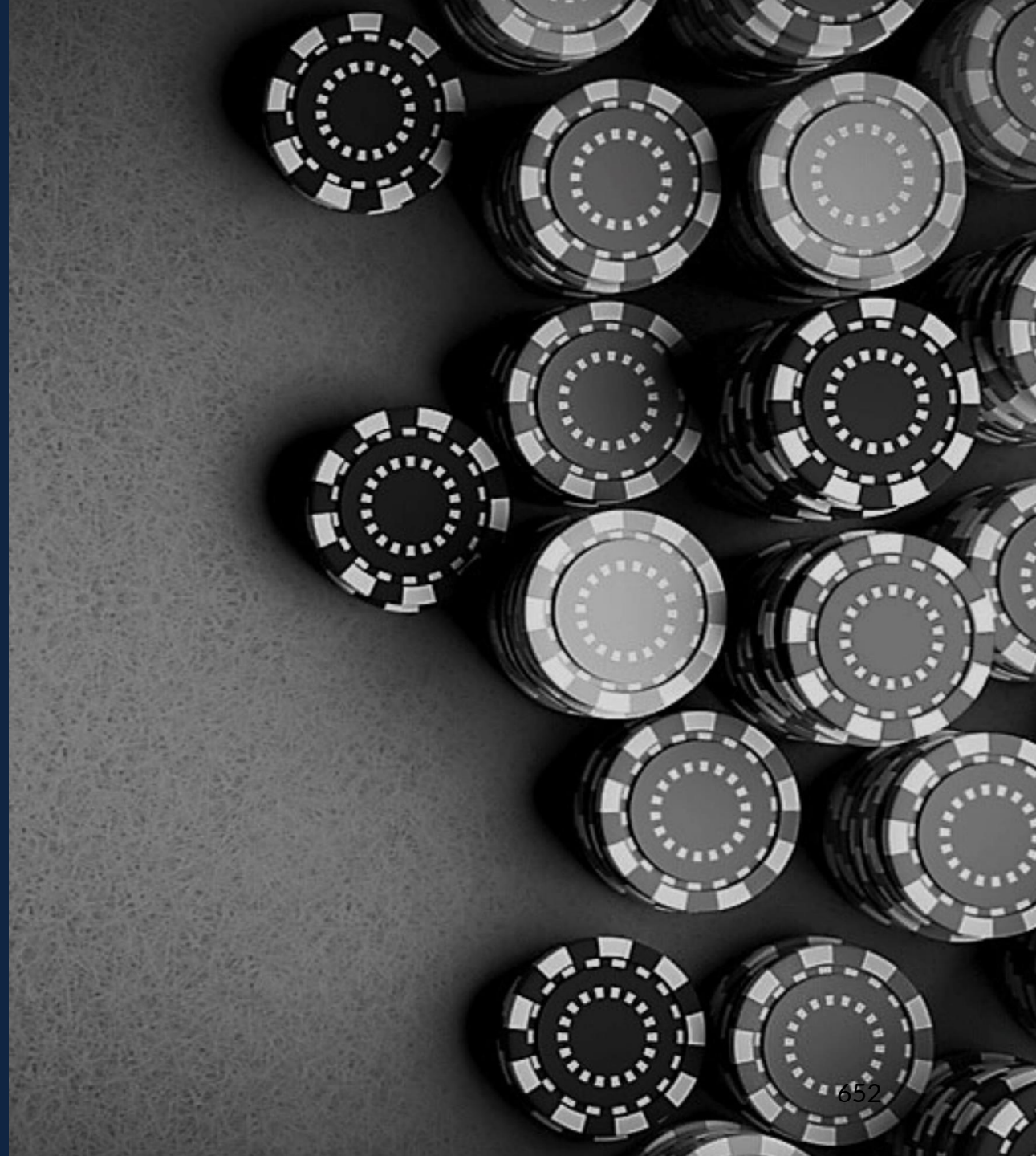
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ASAM REVIEW COURSE 2026

Behavioral Addiction: Criteria, Challenges and Considerations

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Financial Disclosure

Faye Chao, MD

- No relevant disclosures

LEARNING OBJECTIVE

Describe the theoretical framework for behavioral addiction, criteria for diagnosis and evidence-based treatment strategies.



Presentation Outline

- Historical background
- Gambling Disorder (including sports betting)
- Internet Gaming Disorder

Essential Features

- Failure to resist an . . .
  - impulse
  - drive
  - temptation

. . . to perform an act that is harmful to oneself or others.

Potenza, M: Non-substance addictive behaviors in the context of DSM-5. Addict Behav 2014.

Impulsivity vs. Compulsivity

- Both show inability to refrain from repetitive behaviors.
- Impulsivity is driven by an effort to obtain arousal and gratification.
- Compulsivity is driven by an effort to reduce anxiety.

History of diagnosis

- Classified as:
  - Obsessive-compulsive spectrum disorders
  - Impulse-control disorders
  - By-products of mood disorders
  - Now: substance-related and addictive disorder

DSM-5

- Substance-related and Addictive Disorders
  - Gambling disorder
- Conditions for Further Study
  - Internet gaming disorder
- Not included at all (“insufficient evidence”)
  - Other internet or technology-related behaviors (social media, TV, etc.)
  - Sex, exercise, shopping, food, etc.

Potenza, M: Non-substance addictive behaviors in the context of DSM-5. Addict Behav 2014.

Gambling Disorder

Gambling Disorder

DSM-IV-TR

Pathological Gambling

as

Impulse-Control Disorder



DSM-5

Gambling Disorder

as

Substance-Related and Addictive Disorder

American Psychiatric Association: Diagnostic and Statistical Manual of Mental Disorders, 5th Edition. Washington, DC: American Psychiatric Association, 2013.

Clinical Presentation for GD

- *Five DSM-5 Addiction Criteria*

Plus

- "Chases" one's losses
- Lies to conceal the extent of their gambling
- Relies on others for money
- Gambles when feeling distressed (Specifiers: episodic or persistent)

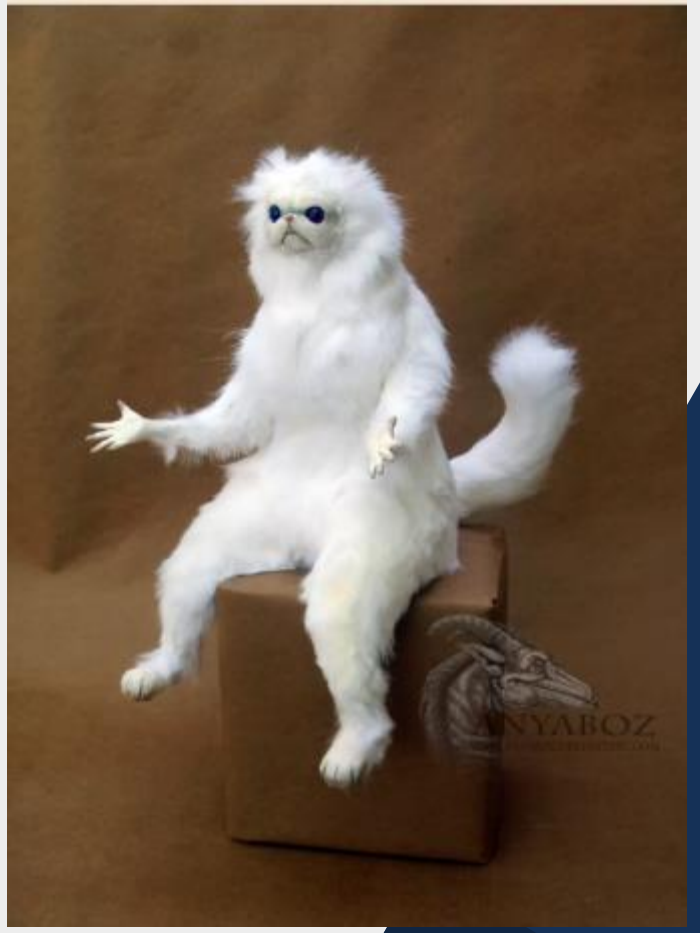
Phases

- Winning Phase
- Loss Phase
- Desperation Phase
- Hopelessness Phase

Blanco C, Cohen O, Luján JJ, et al: Pathological gambling and substance use disorders, in Substance Dependence and Co-Occurring Psychiatric Disorders: Best Practices for Diagnosis and Treatment. Edited by Nunes EV, Selzer J, Levounis P, Davies CA. New York, Civic Research Institute, 2010.

Screening Tools

- Questions about gambling behaviors should be included in addiction assessments
- Several validated screening tools exist
  - South Oaks Gambling Screen (SOGS)
  - Problem Gambling Severity Index (PGSI)
  - Massachusetts Gambling Screen
  - Lie-Bet Questionnaire



The Lie/Bet Questionnaire

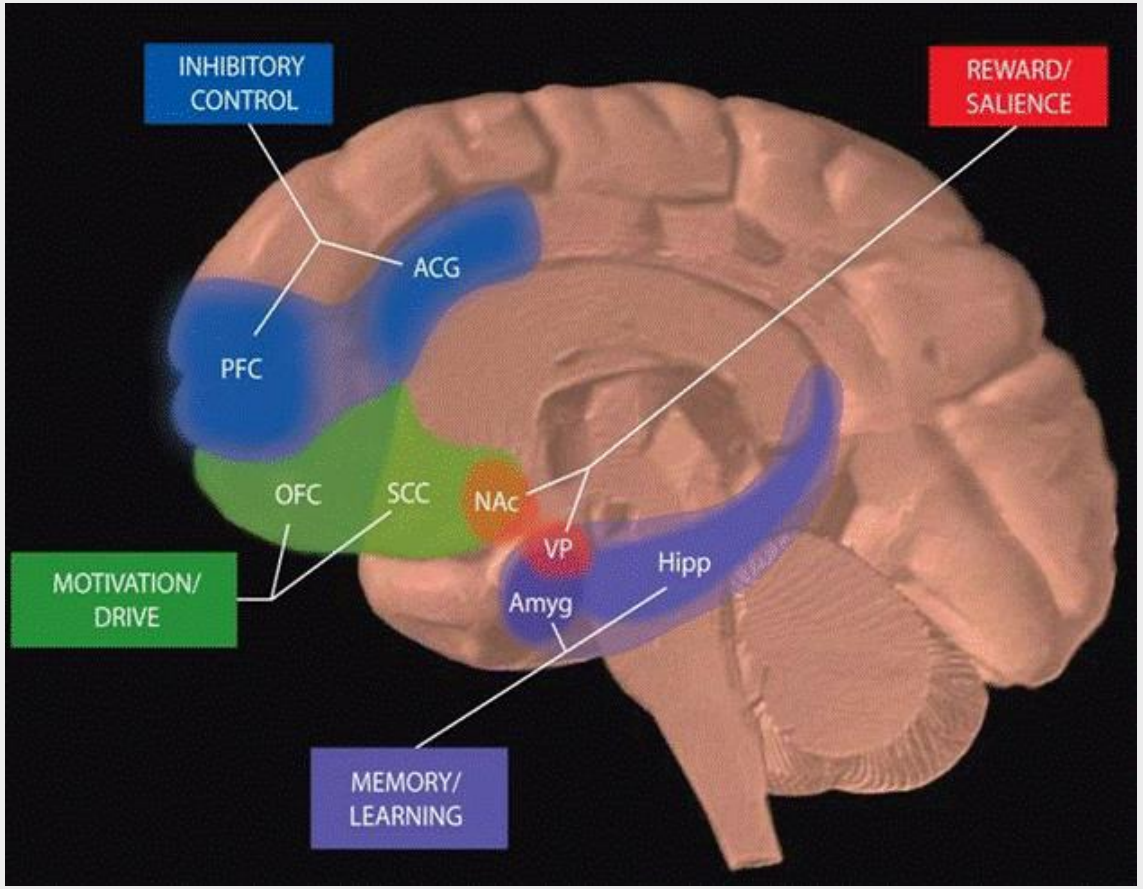
- The Lie/Bet Questionnaire
  - Have you ever felt the need to bet more and more money?
  - Have you ever had to lie to people important to you about how much you gambled?
    - *99% sensitivity, 91% specificity*



Johnson EE, Hamer R, Nora RM, et al: The lie/bet questionnaire for screening pathological gamblers. Psychological Reports 80:83-88, 1997.

Neurobiology of GD

- Gambling affects:
  - DA
  - NE
  - Cortisol
  - 5HT
- Neurobiological similarities with substance use disorders



Epidemiology

- US Gambling Statistics:
  - $78.7 billion commercial gaming revenue in 2026
    - Does not include revenue from casinos on tribal land ($43.9 billion in 2024)
    - $18.09 billion in revenue from gambling taxes
  - 57% of US residents participated in some form of gambling in 2026
    - 30% at physical casino, 21% placed a sports bet
  - ~1 % (range 0.5-3%) of the US adult population meets criteria for GD

www.americangaming.org;
National Indian Gaming Commission FY2024 Gross Gaming Revenue Report;
Stefanovics E, Potenza M: Update on Gambling Disorder. Psych Clin of N Am 45(3): 483-502, 2022.
https://www.ncpgambling.org/news/national-council-on-problem-gambling-survey-shows-drop-in-problem-gambling-risk-highlights-ongoing-challenges/

Epidemiology

- High rate of co-occurrence with other psychiatric disorders
  - 96% of individuals with GD have one or more co-occurring psychiatric disorders
  - 64% have 3 or more
  - Substance use disorders, mood disorders, anxiety disorders, and impulse control disorders are most common
  - Co-occurring disorders may help guide treatment



Kessler RC, et al: DSM-IV pathological gambling in the National Comorbidity Survey Replication. Psych Med 38(9): 1351-1360, 2008.

What's Available in Your State?



- Opportunities in US:
  - Land-based casinos
  - Internet gambling
  - Nonregulated gambling
  - Sports betting
  - Prediction markets
- More available and accessible now than ever before

Sports Betting

Sports Betting: History

- Traditional: Bookmakers ("bookies") make a "book" (ledger of bets) specifically to make a profit regardless of outcome
  - Adjusting the odds
  - Spread betting
- Sports contests
- Fantasy sports



Sports Betting: History

- Professional and Amateur Sports Protection Act (PASPA) passed in 1992 (supported by NFL and NBA at the time)
- In 2018, PASPA was overturned by the Supreme Court
- Sportsbooks currently legal in 39 states and online sports betting legal in 30 states
  - LOOPHOLE! Prediction markets (e.g. Kalshi, Polymarket)



Sports Betting: Changes

- App-based betting
  - Live, in-game betting
  - Ability to bet continuously
- More sophisticated bookmaking
  - AI-powered predictions
  - Continuous odds calibration
  - Analysis of user behavior to tailor promotions
- Further abstraction of monetary investment
- Enmeshment with sports leagues/broadcasts themselves

Sports Betting: Epidemiology

- National Survey on Gambling Attitudes and Gambling Experiences (NGAGE 3.0) from Apr 2024
  - After rising from 20% in 2018 to 26% in 2021, sports betting participation leveled off at 23% of the population in 2024
  - The greatest predictors of risk for problematic gambling included:
    - participation in many different gambling activities
    - gambling weekly or more often
    - agreeing that gambling is a good way to make money
    - **participating in sports betting** (either traditional sports betting or fantasy sports)
    - **gambling online**
    - **being male and/or under the age of 35**
  - The number of sports bettors making **parlay bets** has almost doubled, from 17% of sports bettors in 2018, to 30% in 2024

National Survey on Gambling Attitudes and Gambling Experiences 3.0 (2024); *www.americangaming.org;*

Problem Sports Betting: Epidemiology

- Tend to be younger (<35) and more likely to be male
- More likely to be highly educated and tech-savvy
    - Perceive their gambling to be more determined by their own skills, knowledge, and analysis than by luck or chance
- More likely to be single
- 50% of men 18-49 have an account with at least one online sportsbook (SCRI poll 2026)



Auer, M., & Griffiths, M. D. (2017). Self-reported losses versus actual losses in online gambling: An empirical study. Journal of Gambling Studies, 33, 795–806.
Hing, N et al. (2016). Demographic, behavioural and normative risk factors for gambling problems amongst sports bettors. Journal of Gambling Studies, 32, 625–641.
Hing, N. et al. (2015). Maintaining and losing control during Internet gambling: A qualitative study of gamblers' experiences. New Media and Society, 17, 1075–1095.
Mestre-Bach G et al. Sports-betting-related gambling disorder: Clinical features and correlates of cognitive behavioral therapy outcomes. Addict Behav. 2022 Oct;133:107371.
Mercier, J., Sévigny, S., Jacques, C., Goulet, A., Cantinotti, M., & Giroux, I. (2018). Sports bettors: A systematic review. Journal of Gambling Issues, 38, 203–236.

Sports Betting and Alcohol

- Grubbs et al 2024 collected a census-matched sample of 4363 US adults with an oversample of adults who wager on sports
- 75% of daily (or almost daily) sports bettors engaged in binge drinking.
  - ♦ This is 4 TIMES more than gamblers who do not engage in sports betting.
- 66% of weekly sports bettors engaged in binge drinking.
  - ♦ This is 3 TIMES more than gamblers who do not engage in sports betting.
- 59% of monthly sports bettors engaged in binge drinking.
  - ♦ This is 2.5 TIMES more than gamblers who do not engage in sports betting.

Grubbs JB, Kraus SW. Binge Drinking Among Sports Gamblers. JAMA Netw Open. 2024;7(4):e245473. doi:10.1001/jamanetworkopen.2024.5473

Sports Betting Legalization Amplifies Emotional Cues & Intimate Partner Violence

40 Pages • Posted: 27 Sep 2024 • Last revised: 30 Oct 2024

Kyutaro Matsuzawa
San Diego State University

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University of Oregon - Department of Economics

Date Written: August 27, 2024

- Found that when sports gambling is legalized, there is a 10% increase in IPV with NFL home-team upset losses
- Effects are larger
  - In states where mobile betting is legalized
  - In locations where higher bets were placed
  - Around paydays
  - For teams who were on a winning streak

Gambling Cognitive Distortions

The Odds are Never in Your Favor

- "The house always wins"
- House edge is the ratio of the average loss to the initial bet, essentially the average gross profit the casino expects to make from each game
  - Keno – house edge 25-29%
  - Any craps – 11.11%
  - Ultimate Texas Hold 'Em – 2.19%
  - Blackjack (liberal Vegas rules) – 0.28%
- The longer you play, the greater the odds are that the result of your play will match up with the house edge



www.wizardofodds.com/gambling/house-edge

Interpretative Biases



- Attributing wins to skill, losses to flukes
- Wrongly believing that a series of losses increases the chance of subsequent win
- Near misses (“*I was only one number away!*”)

The “Sunk-Cost” Effect



Superstitious Beliefs

- Believing in:
  - Good luck objects (like animal parts)
  - Behaviors
  - Routines



Gaboury A, Ladouceur R: Erroneous perceptions and gambling. Journal of Social Behaviors and Personality 4:411-420, 1989.

Selective Memory



- Remembering wins while ignoring losses
- Totaling wins without correcting for amounts lost

Treatment Options

Treatment

- Evidence-based therapies
  - CBT, Motivational Interviewing, Imaginal Desensitization all appear efficacious
- NO FDA-approved medication for GD
  - opioid antagonists, SSRIs, and lithium show some positive effect
- Mutual-help groups (Gamblers Anonymous)



Treatment: Opioid Antagonists

- Naltrexone and Nalmefene
- GD conceptualized as an impulsive disorder
- Block opioid receptors, decrease dopamine function, and reduce "reward cravings"



Treatment: Opioid Antagonists

- Reductions in gambling outcomes and urges to gamble with daily naltrexone
- Results for “as-needed” use of naltrexone more mixed
- Naltrexone 50 mg PO daily seems to be as effective as higher doses though some studies dose up to 250 mg PO daily
- Appears to work best in patients with either a personal or family history of alcohol use disorder

Grant JE, Kim SW, Hollander E, et al: Predicting treatment response to opiate antagonists and placebo in the treatment of pathological gambling. Psychopharmacol 200:521-527, 2008.

Grant JE, Potenza MN: Pathological Gambling: A Clinical Guide to Treatment. Washington, DC, American Psychiatric Publishing, 2004.

Ward S, Smith N, Bowden-Jones H: The use of naltrexone in pathological and problem gambling: A UK case series. J of Behav Addictions 7(3): 827-833, 2018

Treatment: Lithium

- Mood stabilizer
- GD conceptualized as an impulsive disorder
- Shown to decrease both urges to gamble and gambling behavior in people with co-morbid bipolar-spectrum illness
- May also have some efficacy for those with GD but no bipolar illness



Pallanti S, Querceoli L, Sood E, Hollander E: Lithium and valproate treatment of pathological gambling: A randomized single-blind study. J Clin Psych 63: 559-564, 2002.
Hollander E et al: Does sustained-release lithium reduce impulsive gambling and affective instability versus placebo in pathological gamblers with bipolar spectrum disorders? Am J Psychiatry 162(1): 137-145, 2005.

Treatment: SSRIs



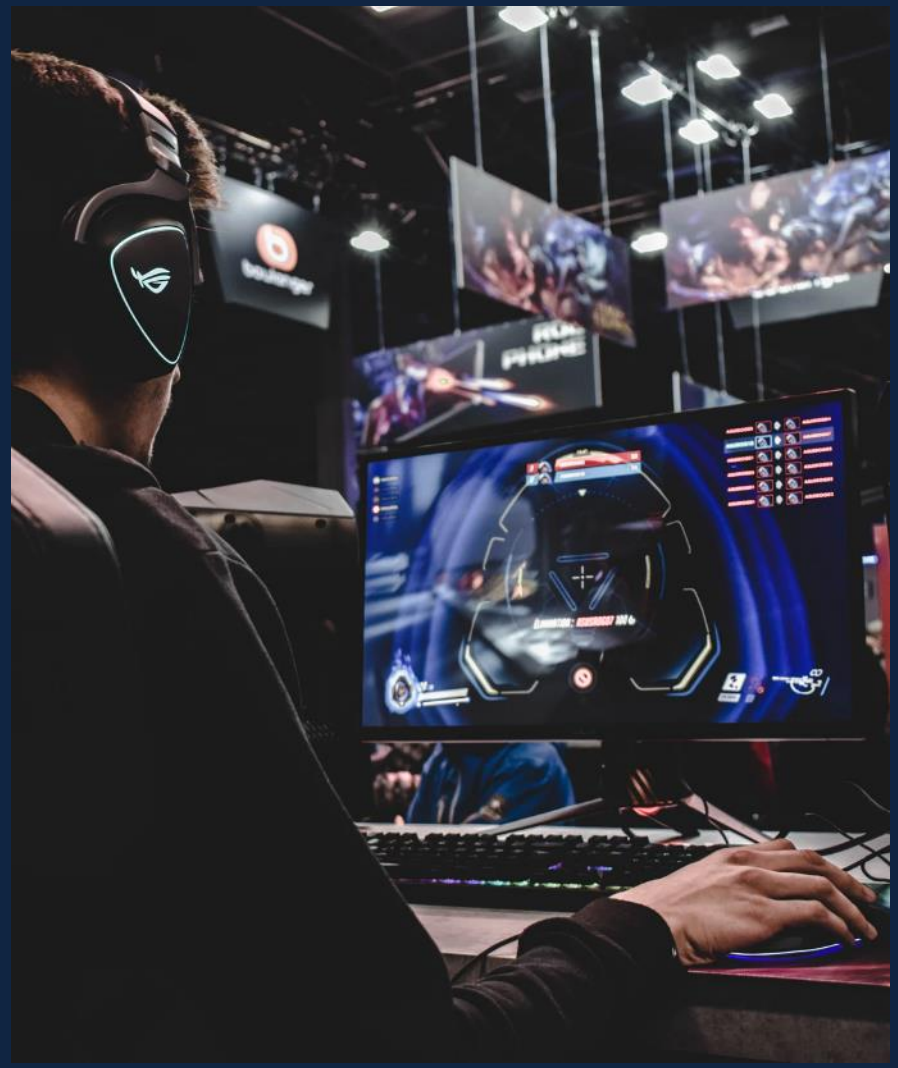
- Frequently investigated for compulsive disorders (e.g. OCD, hoarding, trichotillomania)
- Gambling conceptualized as a compulsive disorder
- Block serotonin reuptake, increase serotonin function, used for treatment of mood and anxiety disorders

Hollander E, Sood E, Pallanti S, et al: Pharmacological treatments of pathological gambling. Journal of Gambling Studies 21:101-110, 2005.

Treatment: SSRIs

- Fluvoxamine, paroxetine, escitalopram most studied
- Unclear if they help decrease urges but may reduce “self-medication” behavior
- May require higher-than-usual doses
- Work best with co-occurring depression or anxiety

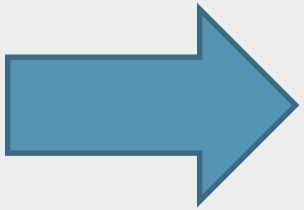
Grant JE, Kim SW. Medication management of pathological gambling. Minn Med. 2006 Sep;89(9):44-8.



Internet Gaming Disorder

The Evolution of IGD

DSM-IV-TR	DSM-5
Not Found	Conditions for Further Study



American Psychiatric Association: Diagnostic and Statistical Manual of Mental Disorders, 5th Edition. Washington, DC: American Psychiatric Association, 2013.

Proposed Criteria

- Seven DSM-5 Addiction Criteria, plus
  - Has deceived family, therapists or others about the amount of gaming
  - Uses games to escape/relieve negative mood
    - (*Excludes Internet gambling, recreational/social Internet use, sexual websites*)

American Psychiatric Association: Diagnostic and Statistical Manual of Mental Disorders, 5th Edition. Washington, DC: American Psychiatric Association, 2013.

ICD-11 Criteria

- A pattern of persistent or recurrent gaming behavior ('digital gaming' or 'video-gaming'), which may be online (i.e., over the internet) or offline, manifested by:
  - 1) impaired control over gaming (e.g., onset, frequency, intensity, duration, termination, context)
  - 2) increasing priority given to gaming to the extent that gaming takes precedence over other life interests and daily activities
  - 3) continuation or escalation of gaming despite the occurrence of negative consequences.
  - The behavior pattern is of sufficient severity to result in significant impairment in personal, family, social, educational, occupational or other important areas of functioning.
- Modifiers are "predominantly online" and "predominantly offline."
- "Hazardous gaming" also exists as a diagnosis

World Health Organization: International Statistical Classification of Diseases and Related Health Problems, 11th Edition. Retrieved from https://icd.who.int/, 2019.

Who's Playing?

- ESA (Entertainment Software Association) 2024 survey
  - 205.1 million Americans play video games
  - 64% of the U.S. population reports playing 1+ hours a week
  - 55% of gamers play with others on-line or in person at least weekly



2024 Essential Facts about the Computer and Video Game Industry. Entertainment Software Association. https://www.theesa.com/. Published May 2026. Accessed June 2026.

The Average Player

- Is white (75%)
- 52% identify as male, 47% identify as female (1% identify as “non-binary/prefer not to say”)
- Is age 36
  - 77% of players are 18 years or older
  - 28% of those who play video games are over the age of 50.

2024 Essential Facts about the Computer and Video Game Industry. Entertainment Software Association. https://www.theesa.com/. Published May 2026. Accessed June 2026.

Clinical Presentation of IGD

- Has more to do with life impact than amount of time played (though this is controversial)
- Often, but not always, occurs in patients with other co-morbidities (especially SUDs and mood disorders)
- Prevalence: Global prevalence appears to be ~2-3% and males 2.5 times as likely to be diagnosed
  - More common in Asian countries esp. China, Taiwan, South Korea



Problematic Play

- Risk factors include:
  - Personality traits (neuroticism, aggression and hostility, and sensation seeking)
  - Motivations for play (escapism, control, avoiding dissatisfaction)
  - Structural game characteristics (online games, ability to customize virtual game persona, game reinforcement structure).
    - MMORPGs a particular area of interest



Imaging studies

- Executive control networks are altered
  - Internet gaming addicts showed lower resting-state functional connectivity between VTA and mOFC (Han 2018)
  - Impaired task performance in Stroop test (Dong 2015)
- Decreased gray matter volume in brain regions involved in self-control and motivation in patients with gaming disorder (Yao 2017)

Imaging studies

- Several studies show increased activity in the ACC and mOFC in response to gaming cues in subjects with gaming disorder (Han 2010, Ko 2009)

Bottom Line

- Imaging studies suggest that the brains of people with problematic play are similar to those of people with substance use disorders
  - Gaming and gaming-related cues trigger activation of reward pathway
  - Gaming cues acquire increased salience over other activities
- Clinically this may manifest in other impulse control problems
- Problematic play is frequently co-morbid with other psychiatric disorders including mood disorders and substance use disorders

Treatment

- Therapy modalities consist mainly of CBT, behavior therapy, and 12-Step approaches
- Psychopharmacologic management is off-label and has poor to middling evidence base for efficacy
  - Potential agents mainly selected from the same medications that are researched for SUDs
- Treatment centers initially arose in Asia and then Europe but now exist in North America as well

In Summary



- Behavioral addictions fall within an impulsivity-compulsivity spectrum of illness.
- DSM-5 only recognizes one disorder officially though one other is included as a condition for further study.
- Psychosocial treatments work.
- Medications have fallen short so far.



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ASAM REVIEW COURSE 2026

Evolution of Addiction and Treatment: History and Impact

Timothy K. Brennan, MD, MPH
Chief of Clinical Services in Addiction, Icahn School of Medicine at Mount Sinai





Financial Disclosure

Timothy K. Brennan, MD, MPH

- No relevant disclosures

Colonial and Early America

- Native American tribes offer earliest systematic approach as alcohol-related problems arise in colonial America.
  - Hop tea = suppress cravings
  - Trumpet vine root = aversion to alcohol
- 1774-1829: physicians, clergy, family, social activists recognize addiction as a “disease state”
- Opium introduced by Chinese laborers building transcontinental railroad
- 1828: Dr. Eli Todd called for creation of physician-directed asylums to treat alcohol problems.

Early America

- In 1784, Dr. Benjamin Rush Published: *Inquiry into the Effects of Ardent Spirits on the Human Mind and Body*
  - Chronic intoxication was a “disease induced by a vice”
  - Claimed that persons with alcohol addiction could be restored to health through proper medical treatment
  - Called for the creation of a facility (a “sober house”) to care for these persons

Proposed Treatments from Dr. Benjamin Rush

Dr. Benjamin Rush: multiple pathway

- Christian conversion
- Acute guilt or shame
- The linking of drink with some painful impression
- Vegetarianism
- Cold baths
- Acute disease
- Blistering the ankles
- Witnessing the death of a drunkard
- Swearing an oath of abstinence



Mid to Late 1800s

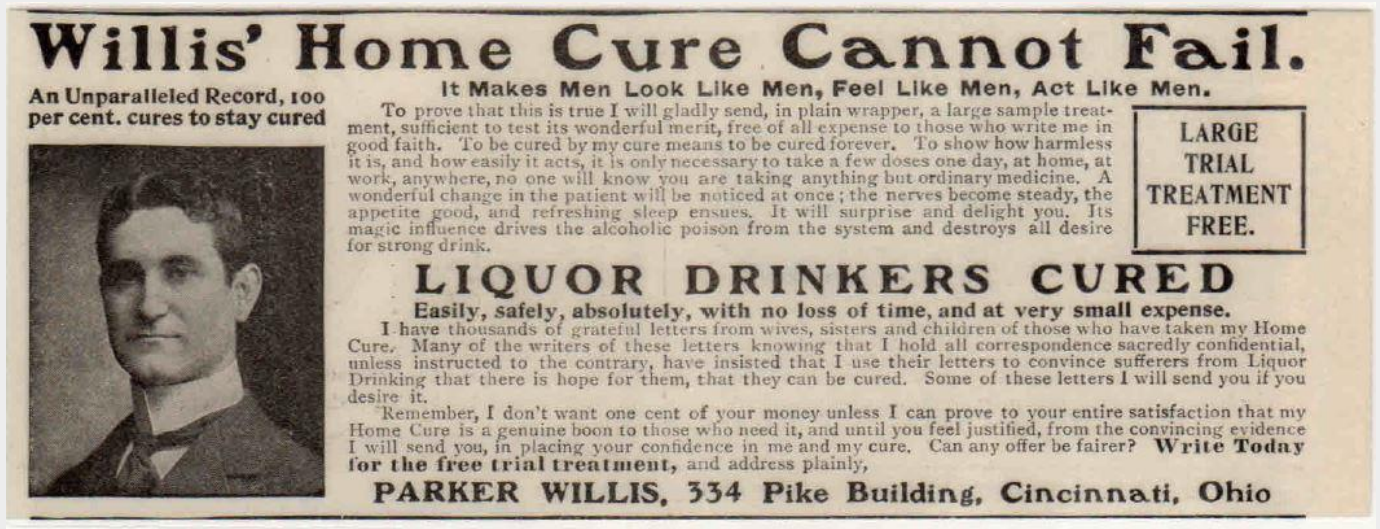
- 1849: Magnus Huss describes “alcoholism” as a clinical condition
- 1864: New York State Inebriate Asylum opens in Binghamton
- 1870: American Association for Cure of Inebriety established, publishes Journal of Inebriety
- 1881: Dr. Carl Wernicke notes ophthalmoplegia, ataxia and altered mental status as a triad occurring in thiamine deficient states.
- 1897: Dr. Sergei Korsakoff presents “On a special form of mental illness combined with degenerative polyneuritis” in Moscow
- Morphine syringes are being used on Civil War battlefields
- Culture begins to shift to a temperate/abstinent stance, "Prohibition Era”

Idea of “Inebriety”

- Disease had different pathways, there was need to individualize treatment
- Asylum vs Private addiction cure institutes
  - Asylum: Years not weeks, enforced
  - Private: Weeks not years, paid in advance, not-enforced


STEP 1.
A glass with a Friend.
STEP 2.
A glass to keep the cold out.
STEP 3.
A glass too much.
STEP 4.
Drunk and rioteus.
STEP 5.
The summit attained
Jolly companions
A confirmed drunkard.
STEP 6.
Poverty and Disease.
STEP 7.
Forsaken by Friends.
STEP 8.
Desperation and crime.
STEP 9.
Death by suicide.
THE DRUNKARDS PROGRESS
FROM THE FIRST GLASS TO THE GRAVE.

Early 1900s: Bogus Cures from Profiteers Create a "Wild West" of Addiction Treatment



Willis' Home Cure Cannot Fail.

An Unparalleled Record, 100 per cent. cures to stay cured

It Makes Men Look Like Men, Feel Like Men, Act Like Men.

To prove that this is true I will gladly send, in plain wrapper, a large sample treatment, sufficient to test its wonderful merit, free of all expense to those who write me in good faith. To be cured by my cure means to be cured forever. To show how harmless it is, and how easily it acts, it is only necessary to take a few doses one day, at home, at work, anywhere, no one will know you are taking anything but ordinary medicine. A wonderful change in the patient will be noticed at once; the nerves become steady, the appetite good, and refreshing sleep ensues. It will surprise and delight you. Its magic influence drives the alcoholic poison from the system and destroys all desire for strong drink.

LARGE TRIAL TREATMENT FREE.

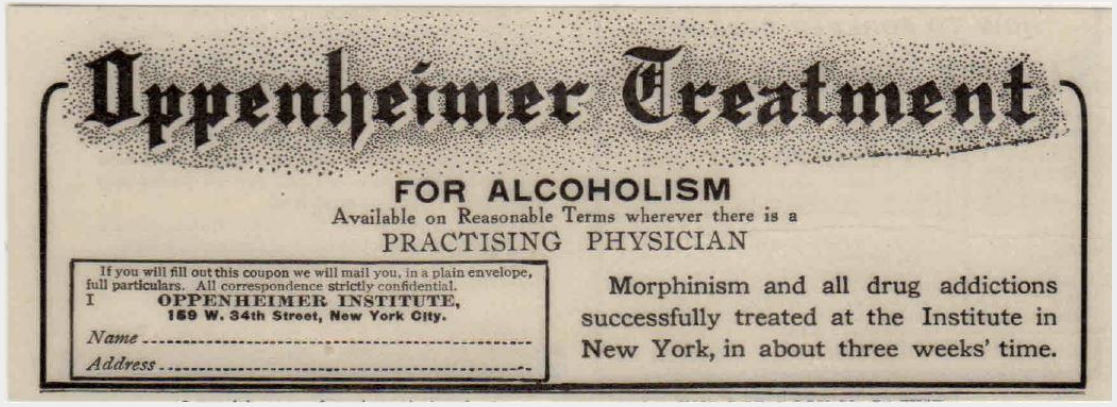
LIQUOR DRINKERS CURED

Easily, safely, absolutely, with no loss of time, and at very small expense.

I have thousands of grateful letters from wives, sisters and children of those who have taken my Home Cure. Many of the writers of these letters knowing that I hold all correspondence sacredly confidential, unless instructed to the contrary, have insisted that I use their letters to convince sufferers from Liquor Drinking that there is hope for them, that they can be cured. Some of these letters I will send you if you desire it.

Remember, I don't want one cent of your money unless I can prove to your entire satisfaction that my Home Cure is a genuine boon to those who need it, and until you feel justified, from the convincing evidence I will send you, in placing your confidence in me and my cure. Can any offer be fairer? **Write Today for the free trial treatment,** and address plainly,

PARKER WILLIS, 334 Pike Building, Cincinnati, Ohio



Oppenheimer Treatment

FOR ALCOHOLISM

Available on Reasonable Terms wherever there is a PRACTISING PHYSICIAN

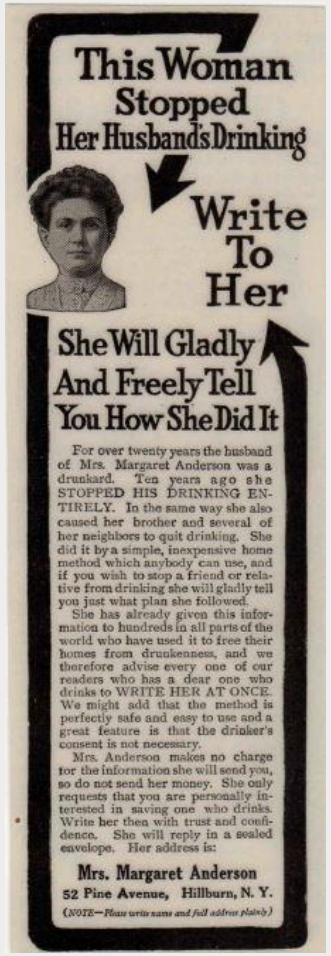
If you will fill out this coupon we will mail you, in a plain envelope, full particulars. All correspondence strictly confidential.

I OPPENHEIMER INSTITUTE, 159 W. 34th Street, New York City.

Name .....

Address .....

Morphinism and all drug addictions successfully treated at the Institute in New York, in about three weeks' time.



This Woman Stopped Her Husband's Drinking

Write To Her

She Will Gladly And Freely Tell You How She Did It

For over twenty years the husband of Mrs. Margaret Anderson was a drunkard. Ten years ago she STOPPED HIS DRINKING ENTIRELY. In the same way she also caused her brother and several of her neighbors to quit drinking. She did it by a simple, inexpensive home method which anybody can use, and if you wish to stop a friend or relative from drinking she will gladly tell you just what plan she followed.

She has already given this information to hundreds in all parts of the world who have used it to free their homes from drunkenness, and we therefore advise every one of our readers who has a dear one who drinks to WRITE HER AT ONCE. We might add that the method is perfectly safe and easy to use and a great feature is that the drinker's consent is not necessary.

Mrs. Anderson makes no charge for the information she will send you, so do not send her money. She only requests that you are personally interested in saving one who drinks. Write her then with trust and confidence. She will reply in a sealed envelope. Her address is:

Mrs. Margaret Anderson
52 Pine Avenue, Hillburn, N. Y.
(NOTE—Please write name and full address plainly)

Charles B Towns Hospital – America's Finest "Jitter Joint"

- 293 Central Park West
- Founded in 1909
- Private pay only ($350 for 5 day stay, had to pay in advance)
- $350 is $10,500 in 2022 dollars
- Mr. Towns was a life insurance salesman from Georgia
- Met Dr. Alexander Lambert, President Roosevelt's personal MD, told him about a "cure" he heard about in Georgia known as "belladonna" (anti-cholinergic, anti-spasmodic properties)
- Claimed 90% success rate (based on percentage of people who would not return)
- Closed 1965



Pure Food and Drug Act 1906

- Signed into law by Roosevelt
- Gained momentum due to pediatric poisonings from morphine elixirs
- Did not ban use of alcohol, morphine, opium, cocaine, heroin, chloroform, cannabis, chloral hydrate in patent medicine, but labels required
- Eventually became the FDA

Harrison Anti-Narcotic Act 1914

Restricted use of opiates and cocaine to legitimate medical purposes.

- Control now in hands of physicians only
- Treasury Dept Decision 2200, May 11, 1915, physicians had to write progressively decreasing doses. Morphine maintenance clinics begin to close
- 1916, U.S. v. Jin Fuey Moy, possession of smuggled drugs illegal
- 1919 U.S. v. Doremus, Court ruled Act constitutional
- 1919 Webb v. U.S., Court ruled physician prescribing to keep patient comfortable was illegal.
- 1922 U.S. v. Behrman, violation of Act to prescribe at all regardless of “good faith.”
- Congress passes Jones-Miller Act in 1922-narcotic violation $5,000 and up to 10 years imprisonment.
- 13 years later Dr Ratigan would be arrested

Consequences of Harrison Act

- Doctors stopped treating addiction
- Most “inebriate homes” close
- shift toward solving addiction problems through legal restraint, punishment and sequestration—>criminalization of addiction.
- 25,000 physicians indicted, 20,000 fined, 3000 jailed
- Addiction moves from a medical issues to a criminal issue
- The only “treatment” for OUD becomes continuing to buy illegal drugs from dealers

Voices of Reason

- 1921: Dr. Charles Terry: “Any activity which tries to handle individuals as ‘addicts’ instead of as ‘patients’ will fail”
- Dr. Henry Smith Williams (brother indicted) writes Drug Addicts are Human Beings (1938).
  - Turned law-abiding citizens into outcasts/criminals
  - Created a billion-dollar-a-year illicit-drug industry
  - Punished physicians whose only crime was to relieve suffering
  - Filled federal prisons with those who did not deserve to be there, nor could they be cared for there.
  - Claimed nothing inherently more immoral in use of morphine than in use of cigarettes or alcohol.

Federal Narcotic Farms

- 1929, Porter Act allocates funds to US Public Health Service to construct two “farms” to house offenders of drug laws
- Lexington, Kentucky and Fort Worth, Texas (1935,1938)
- Kentucky passes "blue grass" law making narcotic use a crime, removing voluntary admissions to the farm.
- Was it a hospital or prison?

Meanwhile…in New York City on December 11, 1934

- After 4 admissions to Towns Hospital, a man named Bill W stops drinking



1940s: More Glimmers of Hope

- Yale and National Committee on Education for Alcoholism (NCEA) present new models of care
- City of Toledo opens alcoholic counseling clinic with $10,000 state grant
- 1943: OR and UT legislate sponsorship of activities to treat alcohol use disorder.
- 1945: CT first state to create formal state-level division to address alcohol problems.
- 1946: AA members prepare bill that passes Utah legislature to provide $50,000 for public education/treatment.

1950s

- Heroin use rising in urban areas, cities organize narcotics bureaus within police depts.
- Narcotic courts created
- 1951: disulfiram receives FDA approval
- 1951: Boggs Act = mandatory minimum sentences, eliminated option of probation/parole.
- 1954: President Eisenhower declares a “new war on narcotic addiction.”
- 1956: Narcotic Control Act = establishes death penalty for certain drug offenses.
- AA members quietly meeting throughout America

1960s – Gaining Ground

- NIMH suggests decriminalization of drug offenses.
- Comprehensive community mental health centers provided funds for alcohol/drug problems
- 1964: Dole/Nyswander open methadone maintenance at Rockefeller Univ
- 1966: Economic Opportunity Amendment = funding treatment and legal advice to avoid incarceration.
- 1966: President Johnson "The alcoholic suffers from a disease which will yield eventually to scientific research and adequate treatment."
- 1966: Narcotic Addict Rehabilitation Act supported diversion from criminal justice system
- 1968: 400 patients in US are on methadone maintenance
- 1969: Congress appropriates $28 million for national efforts

Sunday, May 16, 1971



"All the News That's Fit to Print"

The New York Times

LATE CITY EDITION

Weather: Rain today; clearing and cool tonight. Partly sunny tomorrow. Temp. range: today 50-60; Saturday 49-66. Full U.S. report on Page 111.

SECTION ONE

VOL. CXX . No. 41,385 © 1971 The New York Times Company. NEW YORK, SUNDAY, MAY 16, 1971 BQLI 50 CENTS

The New York Times/Michael Evans

ARMED FORCES DAY: Adm. Thomas H. Moorer, Chairman of the Joint Chiefs of Staff, saluting cadets from the United States Military Academy during parade down Fifth Ave.

TRIBUTE PAID HERE TO ARMED FORCES

10,000 Parade on 22d Day Honoring Military Units —Admiral Takes Salute

With their flags flapping in a

Go-Ahead on Rail Links To 2 Airports Announced

By FRANK J. PRIAL

Governor Rockefeller of New York and Gov. William T. Cahill of New Jersey announced jointly yesterday that the Port of New York Authority would "finance and construct" direct, high-speed rail links from mid-

ity Trans Hudson service, is owned and operated by the authority.

The Newark line would be extended to Cranford, N.J., a decision that represents a substantial victory for Governor

Nixon Wins Wide Backing On Troop Total in Europe

President Asserts a Withdrawal Would Be 'Error of Historic Dimensions' —Johnson Among 24 Supporters

By ROBERT B. SEMPLE Jr.
Special to The New York Times

KEY BISCAYNE, Fla., May 15—The White House today won the endorsement of 24 former high ranking public servants — including former President Lyndon B. Johnson—of a Presidential statement asserting that the unilateral withdrawal of American troops from Europe would constitute "an error of historic dimensions."

In yet another stage of the Administration's offensive against a Congressional move to reduce by half the United States forces assigned to the North Atlantic Treaty Organization, the White House press office made public a statement from President Nixon reasserting his commitment to present troop levels, and a separate list of 23 former Government officials, who, it said, supported Mr. Nixon's position.

Mansfield Leads Drive

Minutes after the release of both documents, word came from the L.B.J. Ranch in Johnson City, Tex., that Mr. Nixon's predecessor wished to be recorded as "totally in accord with the statement," and opposed to any move that "would endanger what we have achieved in the past and shatter our hopes for the future."

The move to reduce American forces in Europe has been spearheaded by Senator Mike Mansfield, Democrat of Montana, the Senate majority leader. He proposed early last week that a bill extending the military draft be amended to ob-

Reportedly taken by surprise when Senator Mansfield introduced his amendment, the White House has since marshaled its considerable resources to defeat the move. On Wednesday, the White House press secretary, Ronald L. Ziegler, announced that the President was "totally opposed" to the amendment, and on Thursday Mr. Nixon met with a dozen former high-ranking officials, who announced afterward that they would exercise their influence to persuade the Senate to reject Mr. Mansfield's proposal.

Former Secretary of State Dean Acheson, a Democrat, agreed to coordinate the effort to change sentiment in the Senate, while the White House, at Mr. Nixon's explicit instructions, rapidly gathered its own resources. Not only has Mr. Ziegler kept up steady criticism of the Mansfield move, but Clark MacGregor, Mr. Nixon's principal adviser on Congres-

Continued on Page 22, Column 1

Canonero II Triumphs

Canonero II, winner of the Kentucky Derby, captured the $189,000 Preakness Stakes for 3-year-olds yesterday at Pimlico in Baltimore. He won by 1½ lengths in the track-record time of 1 minute 54 seconds for 1 3/16 miles. Eastern Fleet ran second and Jim French third. The Venezuelan horse paid $8.80 for $2 to win at Pimlico and

G.I. Heroin Addiction Epidemic in Vietnam

By ALVIN M. SHUSTER
Special to The New York Times

SAIGON, South Vietnam, May 15—The use of heroin by American troops in Vietnam has reached epidemic proportions.

The United States military command, the American Embassy and the South Vietnamese Government have been slow to awaken to the crisis. Now they are intensifying their efforts to curtail the easy flow of heroin to the soldiers, punish the sellers and rehabilitate the soaring numbers of Americans who use what they and Vietnamese sellers call "scag."

So serious is the problem considered that Ambassador Ellsworth Bunker and Gen. Creighton W. Abrams, the military commander, recently met with President Nguyen Van Thieu on measures to be taken by the Saigon Government, including agreement on a special task force that will now report directly to Mr. Thieu.

John Ingersoll, the Director of the Bureau of Narcotics and Dangerous Drugs, also conferred with Mr. Thieu and other officials and returned to Washington, reportedly alarmed at the ease with which heroin circulates and fearful of the danger to American society when the addicted return craving a drug that costs many times more in

Continued on Page 20, Column 4

The New York Times/Denis Cameron

American soldier going through drug withdrawal at a rehabilitation center in South Vietnam.

Saigon Reports New Push Into Parrot's Beak Region

By CRAIG R. WHITNEY
Special to The New York Times

SAIGON, South Vietnam, region of Cambodia, about

THRONGS IN CAIRO CHEER PRESIDENT AND BERATE FOES

Emotions Aroused by Sadat's Report of a Conspiracy to Overthrow Regime

TRIALS APPEAR POSSIBLE

Leader's Hand Strengthened by Collapse of Challenge From Ousted Colleagues

By RAYMOND H. ANDERSON
special to The New York Times

CAIRO, May 15—Their emotions aroused by President Anwar el-Sadat's dramatic narration last night of a conspiracy to overthrow him, tens of thousands of Egyptians demonstrated today in the streets of Cairo.

They shouted Mr. Sadat's name and demanded punishment for Cabinet Ministers and leading officials of the Arab Socialist Union, the country's only political organization, accused by the President of having intrigued to bring about his downfall.

For the first time since he took power after the death of Gamal Abdel Nasser last Sept. 28, large portraits of President Sadat were carried through the streets by the demonstrators.

Banners Are Displayed

Banners were hung over Kasr el Nil Street in downtown Cairo proclaiming, "Long Live Anwar el-Sadat, a Son of the People!" and "Our Great Army in the Front Line Is Behind You!"

"Hang Aly Sabry!" shouted

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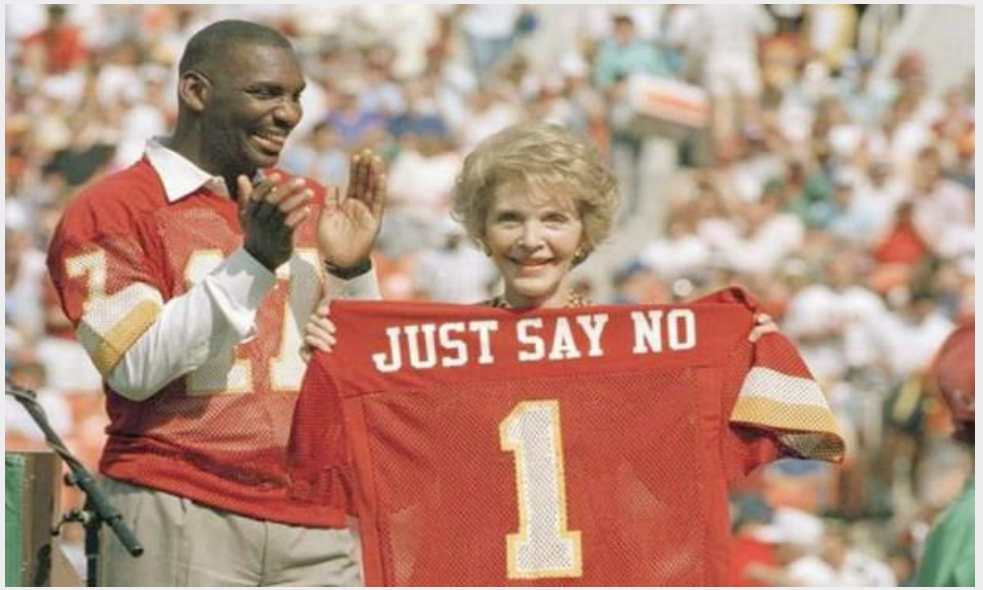
1970s: Compassion vs Criminalization

- 1970: Comprehensive Alcoholism Prevention and Treatment Act creates National Institute on Alcohol Abuse and Alcoholism (NIAAA) to research, educate and train a national network of treatment centers
- 1971: President Nixon declares “War on Drugs” and creates Special Action Office for Drug Abuse Prevention
- 1972: Drug Abuse Treatment Act creates National Institute of Drug Abuse (NIDA)
- 1973: Congress appropriates $386 million in 1973
- 1973: President Nixon creates the Drug Enforcement Administration (DEA)
- 1973: Gov Rockefeller signs law setting MINIMUM penalty for selling 57 grams or more of heroin, morphine, cocaine, or cannabis at 15 years in prison (removed by Gov Patterson in 2009)
- 1976: 80,000 patients in methadone maintenance programs

1980s

- First Lady Reagan asked by a child at Longfellow Elementary in Oakland what to do if she was offered drugs by her peers
- First Lady Reagan responds, “Just say no”
- First Lady Reagan appears on 23 talk-shows, travels 250,000 miles promoting “Just Say No”
- Diff’rent Strokes and Punky Brewster episodes devoted to “Just Say No”
- Mixed legacy




JUST SAY NO
1



Late 1980s: Return to Criminalization

- 1988 White House Conference for a Drug Free America
  - Recommendation 2: “Additional funds must be appropriated for prison construction.”
  - Recommendation 3: “Criminal justice personnel should test all persons in their custody for illicit drug use, and the results of those tests should be used to make determinations regarding pretrial release, probation, and parole.
  - Recommendation 10: “Judges must recognize all persons (adult and juvenile) found guilty of drug trafficking as serious offenders and sentence them accordingly.”
  - Recommendation 14: “Law enforcement agencies should adopt aggressive street-level enforcements of antidrug laws”
  - Recommendation 16: “Persons found to be using drugs while incarcerated should not be eligible for early release.”

1990s

- 50% of people entering prison meet criteria for a substance use disorder.
- 1992: Congress creates Substance Abuse and Mental Health Services Administration (SAMHSA) to direct efforts at state level to implement evidence-based treatment for addiction and mental health
- 1994: Naltrexone receives FDA approval for AUD
- 1996: OxyContin released by Purdue Pharma

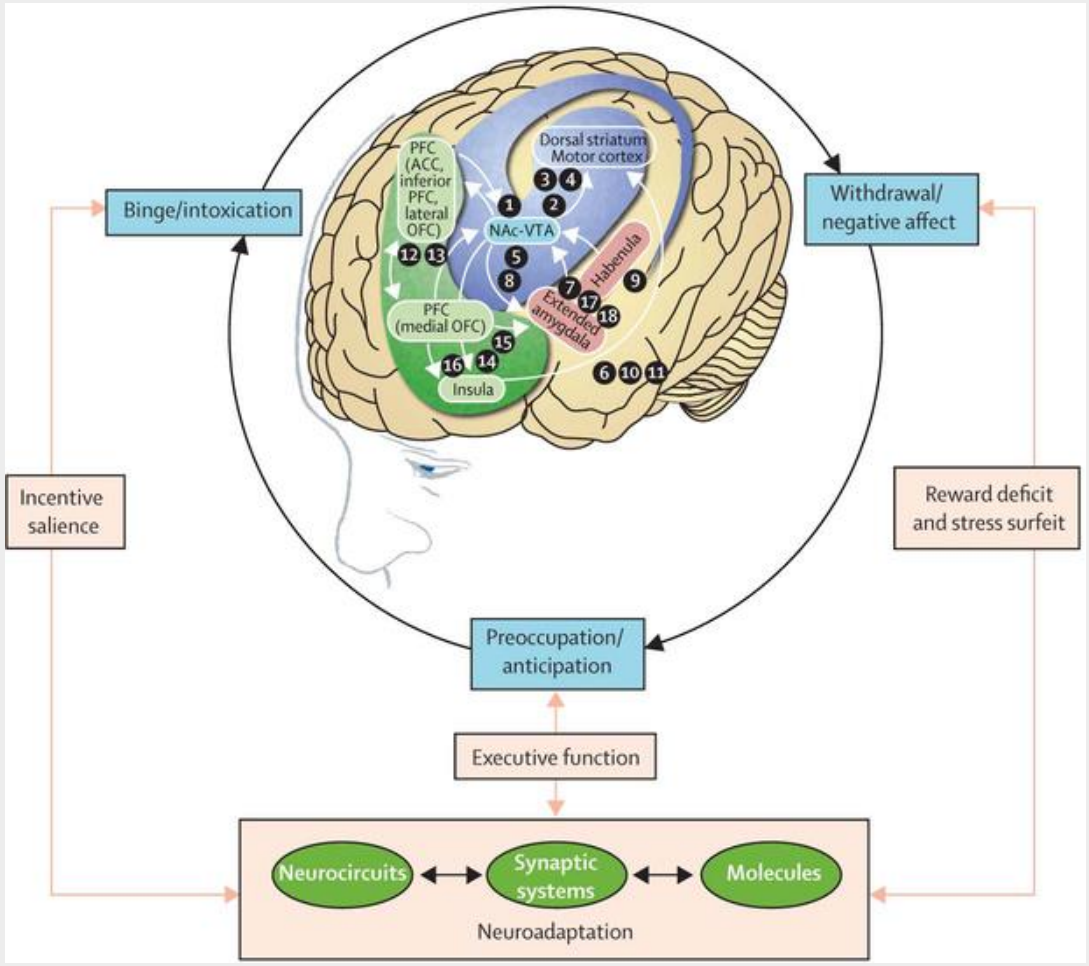
2000s

- 2000: buprenorphine/naloxone receives FDA approval for OUD
- 2005: George Koob and Michel Moal publish “Neurobiology of Addiction” describing a neurobiological framework for the disease
- 2006: Extended-release naltrexone receives FDA approval for OUD
- 2008: Wellstone and Domenici Mental Health and Addiction Equity Parity Act requires insurers to provide coverage for addiction treatment on par with other medical or surgical services

Koob/Volkow 2016

"Drug addiction can be defined as a chronically relapsing disorder, characterized by compulsion to seek and take the drug, loss of control in limiting intake, and emergence of a negative emotional state (eg, dysphoria, anxiety, irritability) when access to the drug is prevented."

- Lancet Psychiatry 2016 Aug



Today


THE COLLEGE ON PROBLEMS OF DRUG DEPENDENCE
EST
1929


AMERSA


AMERICAN SOCIETY OF ADDICTION MEDICINE
FOUNDED
1954
ASAM


AMERICAN COLLEGE of ACADEMIC ADDICTION MEDICINE
ACAAM


NIH
National Institute
on Alcohol Abuse
and Alcoholism


NIH
National Institute
on Drug Abuse



Get in Touch

301.656.3920

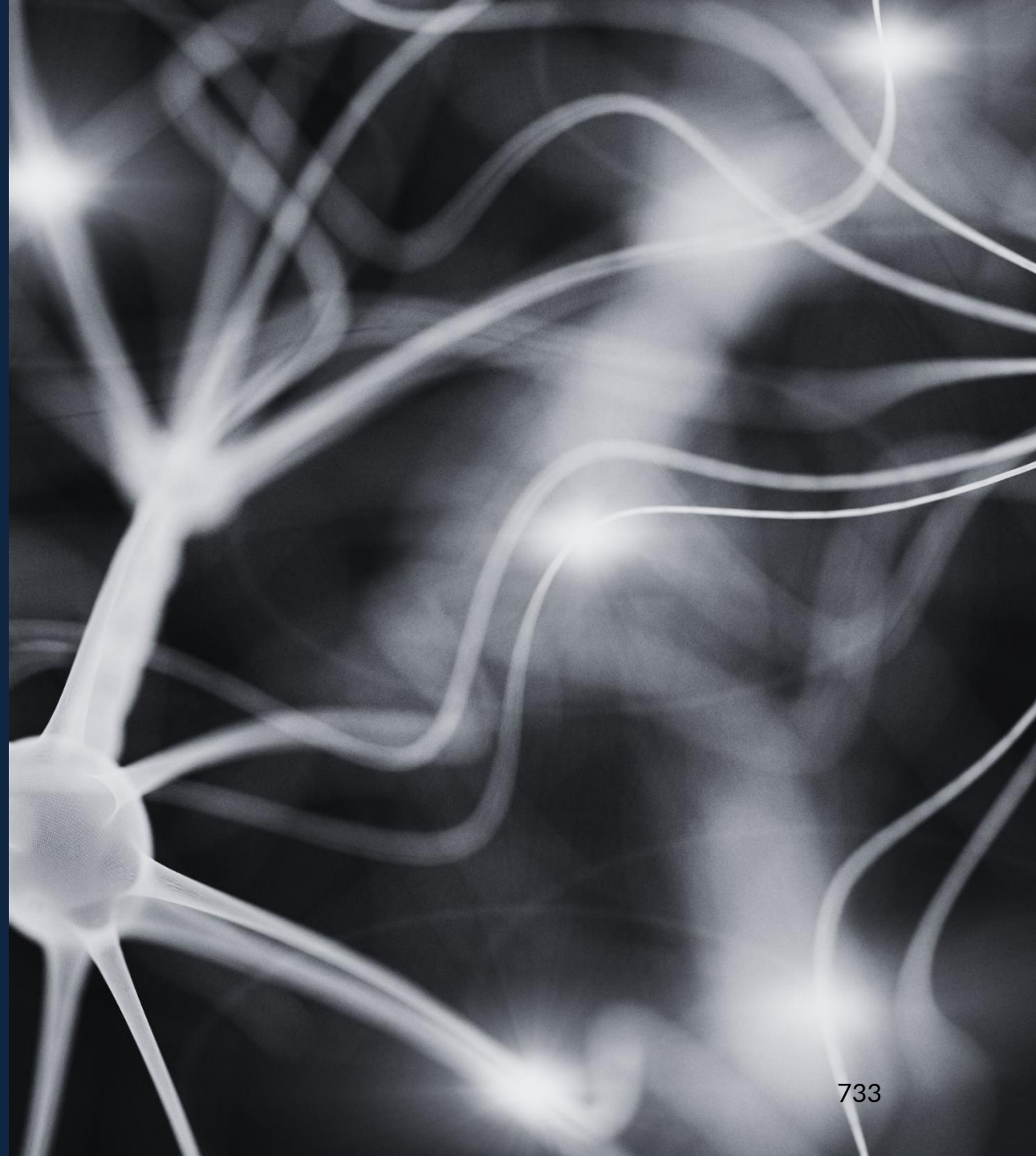
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www.asam.org

ASAM REVIEW COURSE 2026

Epidemiology: Core Concepts and Applications

Jeffrey J. DeVido, MD, MTS
Chief, Addiction Services, Marin County Dept. of Health and Human Services
Behavioral Health Clinical Director, Partnership HealthPlan of California
Assistant Clinical Professor—Volunteer, UCSF Dept. of Psychiatry and Behavioral Sciences, UCSF Weill Institute for Neurosciences





Disclosures

Jeffrey J. DeVido, MD, MTS

Equity shareholder: Altria/Philip Morris/Merck

The opinions expressed in this talk are mine and they do not represent the opinions of my employing institutions or those with whom I am professionally affiliated.

I will not be talking about off or on label medications for the treatment of any condition.

This talk was prepared without the assistance of AI.

Learning Objectives

Review the dimensions of epidemiology covered in the ABPM exam: 1) basic trends, and 2) epidemiologic concepts.

Establish different approaches for (re)learning epidemiology as necessary for ongoing professional acumen as well as (unfortunately) those things needed to regurgitate on an exam.

Demonstrate epidemiologic concepts in action through 2 different common addiction epidemiological questions.

Guide participants towards resources for ongoing review of epidemiologic data

Presentation Outline

- Consider ways of thinking about and learning about epidemiology
- Cheat sheets vs. enduring learning patterns
- Highlight some important epidemiological trends AND how to find them yourselves…
- Follow two common questions in addiction medicine as a springboard for reviewing key concepts in epidemiology

Two Ways to Think about Epidemiology

- What do I need to know for the test?

- What might I need to know professionally?

The ABPM Exam and Epi

Core Content Areas

25%	01 – Definitions 02 – Genetics 03 – Pharmacokinetic and pharmacodynamic principles 04 – Pharmacology 05 – [illegible] of addiction
20%	06 – Epidemiological concepts 07 – Epidemiological trends of substance use disorders 08 – Prevention
40%	[illegible] Screening, assessment, and brief intervention 10 – Overview of addiction treatment 11 – Management of inpatient and outpatient intoxication and withdrawal 12 – Pharmacologic interventions for addictions 13 – Behavioral interventions 14 – Co-occurring and medical disorders among patients with alcohol and other drug use and addiction 15 – Co-occurring psychiatric disorders among patients with alcohol and other druge use and addiction 16 – Pain and addiction
15%	17 – Ethical, legal, and liability issues in addiction practice

Addiction	Target Percentage
01 – Alcohol	15-20%
02 – Sedatives	7-10%
03 – Stimulants	7-10%
04 – Opioids	10-15%
05 – Cannabinoids	7-10%
06 – Nicotine	15-20%
07 – Hallucinogens	0.5-3%
08 – Dissociatives	0.5-3%
09 – Inhalants	0.5-3%
10 – Anabolic steroids	0.5-3%
11 – Other substances	1-3%
12 – Nonsubstance addiction	1-3%
13 – General / All substances combined	1-5%

https://www.theabpm.org/become-certified/exam-content/addiction-medicine-content-outline/

For the Test Strategy:

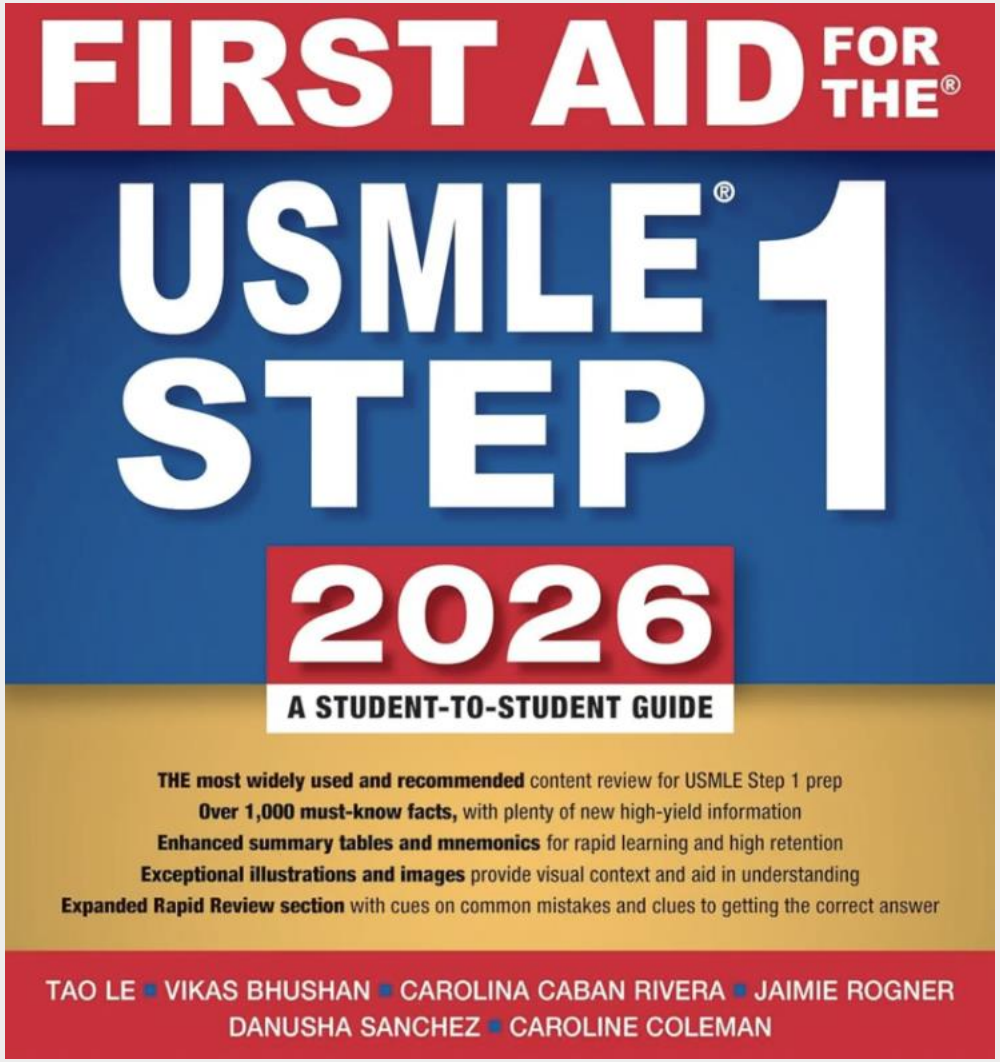
Some assumptions:

- All of you have had some rudimentary epidemiology/biostatistics
- Most of you have seen these concepts multiple times
- For the most part, you don't use these concepts as much as they come up on tests
- You scribble some notes on a cheat sheet to remind yourself as you're studying
- When you've been taught these concepts before, it has been shoveled to you in large amounts in short lectures

For the Test Strategy:



http://www.bishopmikelowry.com/wp-content/uploads/2013/03/drinking-from-the-firehose.jpg



https://www.amazon.com/First-USMLE-Step-2021-Thirty/dp/126046752X/ref=asc_df_126046752X/?tag=hyprod-20&linkCode=df0&hvadid=459537678676&hvpos=&hvnetw=g&hvrand=12792418851990343229&hvpone=&hvptwo=&hvqmt=&hvdev=c&hvdvcmdl=&hvlocint=&hvlocphy=9032089&hvtargid=pla-1113406220592&psc=1

So…



https://memegenerator.net/instance/26662134/med-student-meerkat-stay-on-your-toes

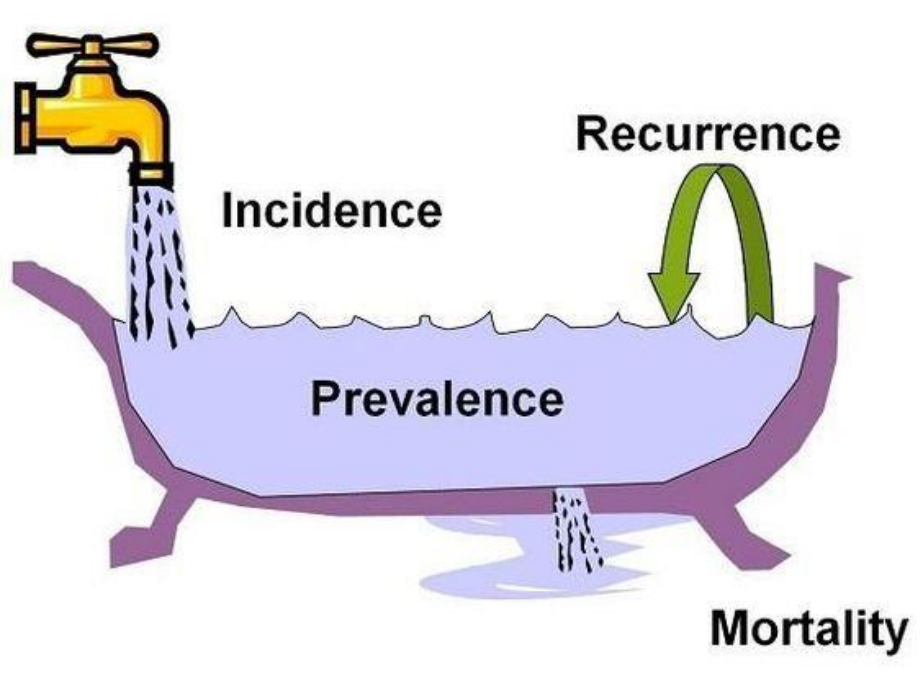
Let's Do A Quick Matching Exercise:

- Incidence
- Prevalence

- #of existing cases/Total #of people (at a point in time)
- Rate: #new cases/#people at risk (during a specified time period)

Incidence:

- Represents the RISK of a disease: new cases coming into a population in time
- Have to see people longitudinally (in time) so these data are harder to find for SUDs—PROSPECTIVE studies
  - Example: follow-ups on Epidemiologic Catchment Area study (1980s)
    - Highest incidence in youngest population (18-29 y/o)



http://image.slidesharecdn.com/measurementinepidemiology-141121024727-conversion-gate01/95/measurements-in-epidemiology-15-638.jpg?cb=1416559706

Let’s Start with A Quick Matching Exercise:

- Incidence
- Prevalence

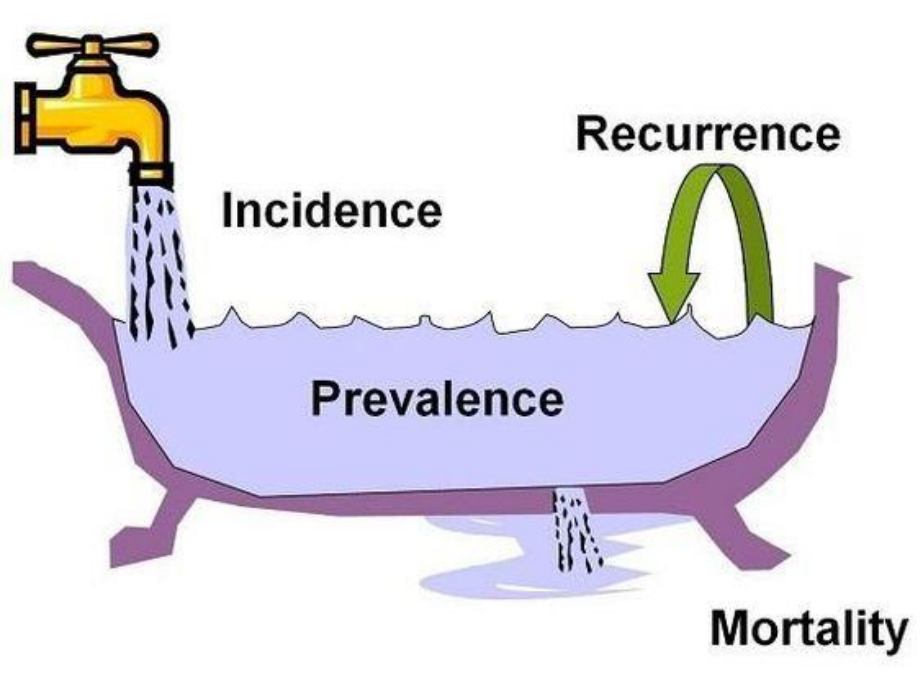
- #of existing cases/Total #of people (at a point in time)
- Rate: #new cases/#people at risk (during a specified time period)

Prevalence:

- Represents the *public health burden* of a disease at a particular time

- CROSS SECTIONAL SURVEYS

  - Example: annual National Survey on Drug Use and Health (NSDUH)
    - Tobacco products, alcohol, illicit drugs



http://image.slidesharecdn.com/measurementinepidemiology-141121024727-conversion-gate01/95/measurements-in-epidemiology-15-638.jpg?cb=1416559706

Let's Start With Some Useful Basics:

Primary Prevention

Interventions designed to prevent the onset or future incidence of a specific problem

Secondary Prevention

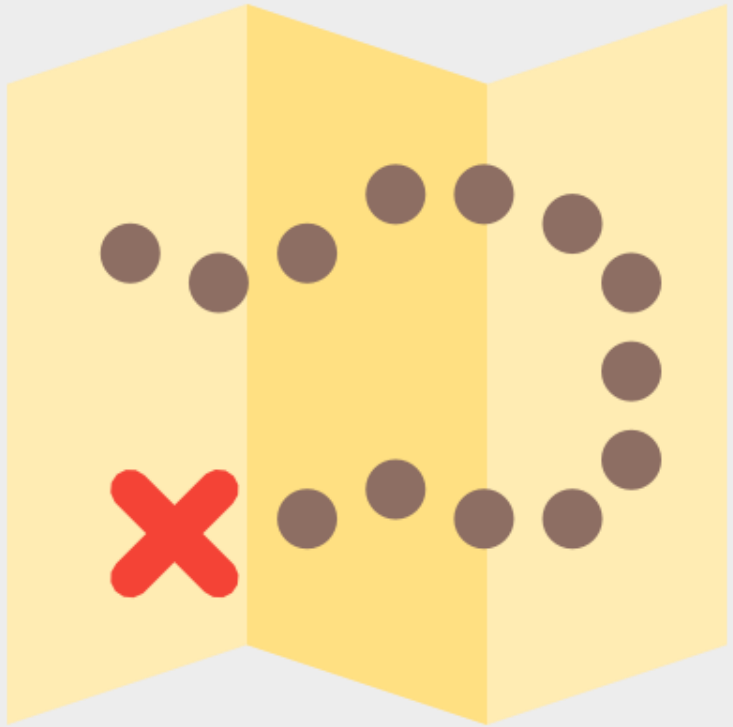
An early intervention that decreases the prevalence of a specific problem

Tertiary Prevention

Treatment designed to improve quality of life and reduce the symptoms after a disease or disorder has developed
Does not reduce incidence or prevalence

https://press.rebus.community/introductiontocommunitypsychology/chapter/prevention-and-promotion/

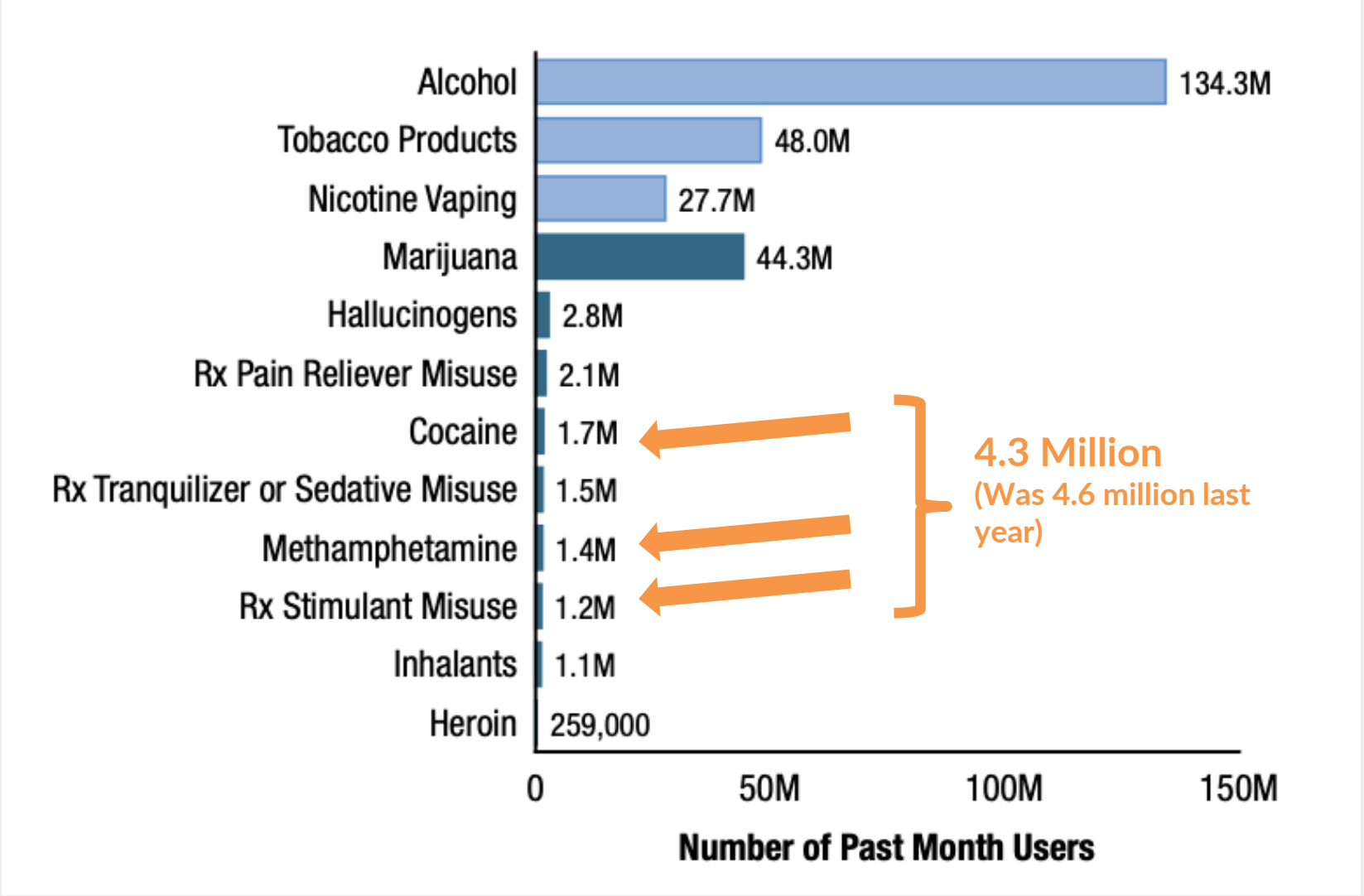
Let’s take a quick tour of some prevalence data and important trends to help us put the story together:



First: Big Picture

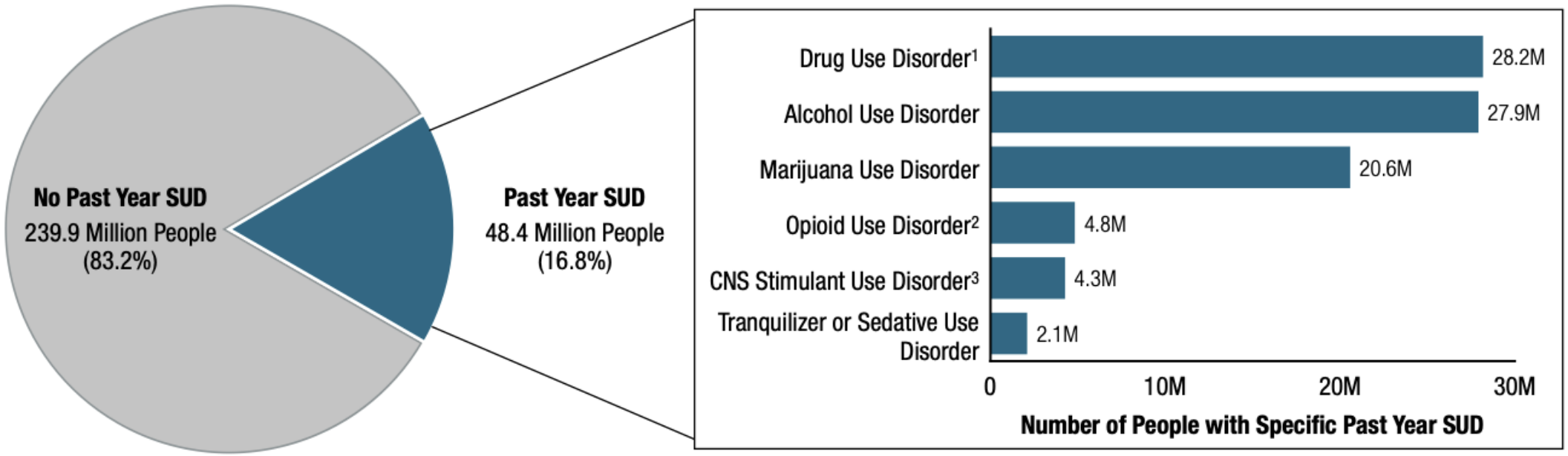


2024 NSDUH Prevalence: Past Month General Substance Use and Nicotine Vaping: Among People Aged 12 or Older; 2024



https://www.samhsa.gov/data/sites/default/files/reports/rpt56287/2024-nsduh-annual-national-report.pdf

People Aged 12 or Older with a Past Year Substance Use Disorder (SUD); 2024



CNS = central nervous system.

Note: The estimated numbers of people with SUDs are not mutually exclusive because people could have use disorders for more than one substance.

[1] Includes data from all past year users of marijuana, cocaine, heroin, hallucinogens, inhalants, methamphetamine, or prescription psychotherapeutic drugs (i.e., pain relievers, tranquilizers, stimulants, or sedatives). See footnote 2 for more information about opioid use disorder.

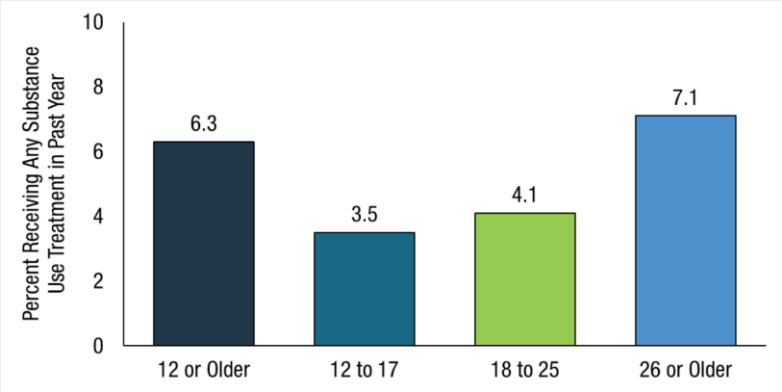
[2] Includes data from all past year users of heroin or prescription opioids. Respondents were not included if they used only nonopioid pain relievers and did not use heroin in the past year.

[3] Includes data from all past year users of cocaine, methamphetamine, or prescription stimulants.

https://www.samhsa.gov/data/sites/default/files/reports/rpt56287/2024-nsduh-annual-national-report.pdf

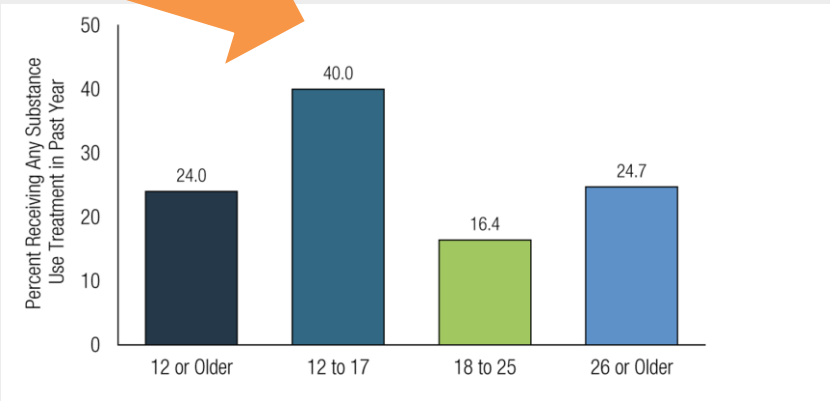
But do people get treatment?

2021

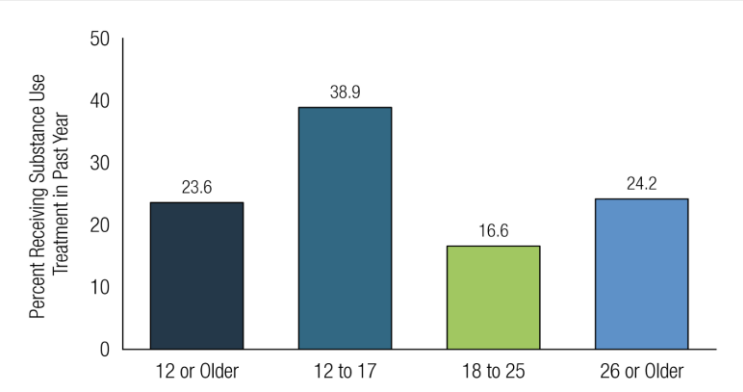


?

2022

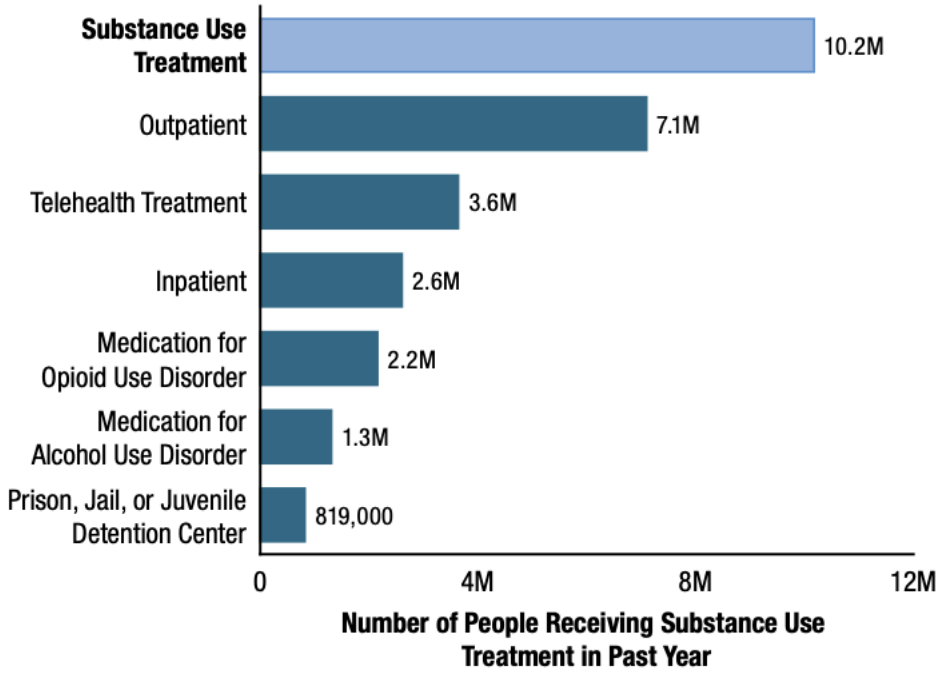


2023



https://www.samhsa.gov/data/data-we-collect/nsduh-national-survey-drug-use-and-health/national-releases#highlights

For the people who do get “treatment” where do people get it (2024)?



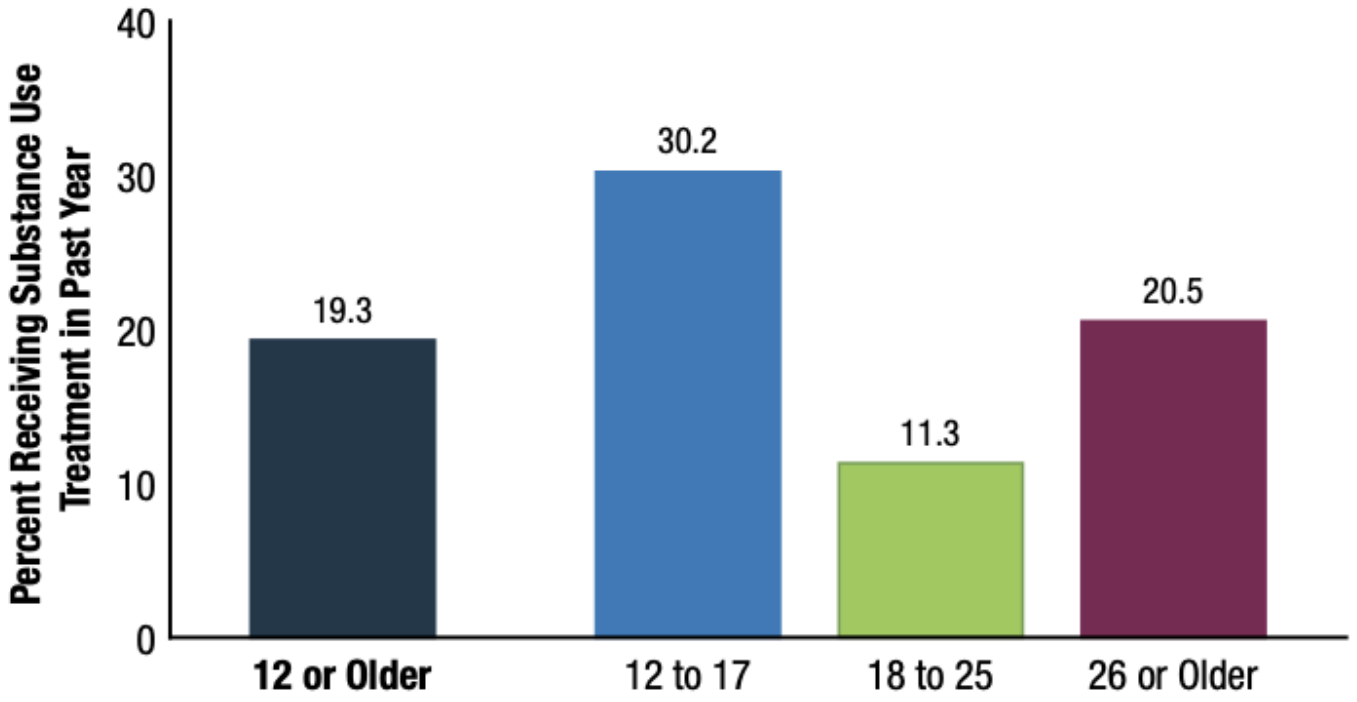
Note: Types of substance use treatment and locations where people received substance use treatment are not mutually exclusive because respondents could report that they received treatment in more than one setting in the past year.

Note: Substance use treatment includes treatment for drug or alcohol use through inpatient treatment/counseling; outpatient treatment/counseling; medication for alcohol use disorder or opioid use disorder; telehealth treatment; or treatment received in a prison, jail, or juvenile detention center.

Note: Because respondents who used prescription pain relievers or heroin in their lifetime were shown a list of medications that are prescribed to treat opioid use disorder, respondents who used prescription pain relievers but not heroin in their lifetime and who reported use of these medications were assumed to have received medication for opioid use disorder.

https://www.samhsa.gov/data/sites/default/files/reports/rpt56287/2024-nsduh-annual-national-report.pdf

Received Substance Use Treatment in the Past Year: Among People Aged 12 or Older Who Needed Substance Use Treatment in the Past Year (2024)

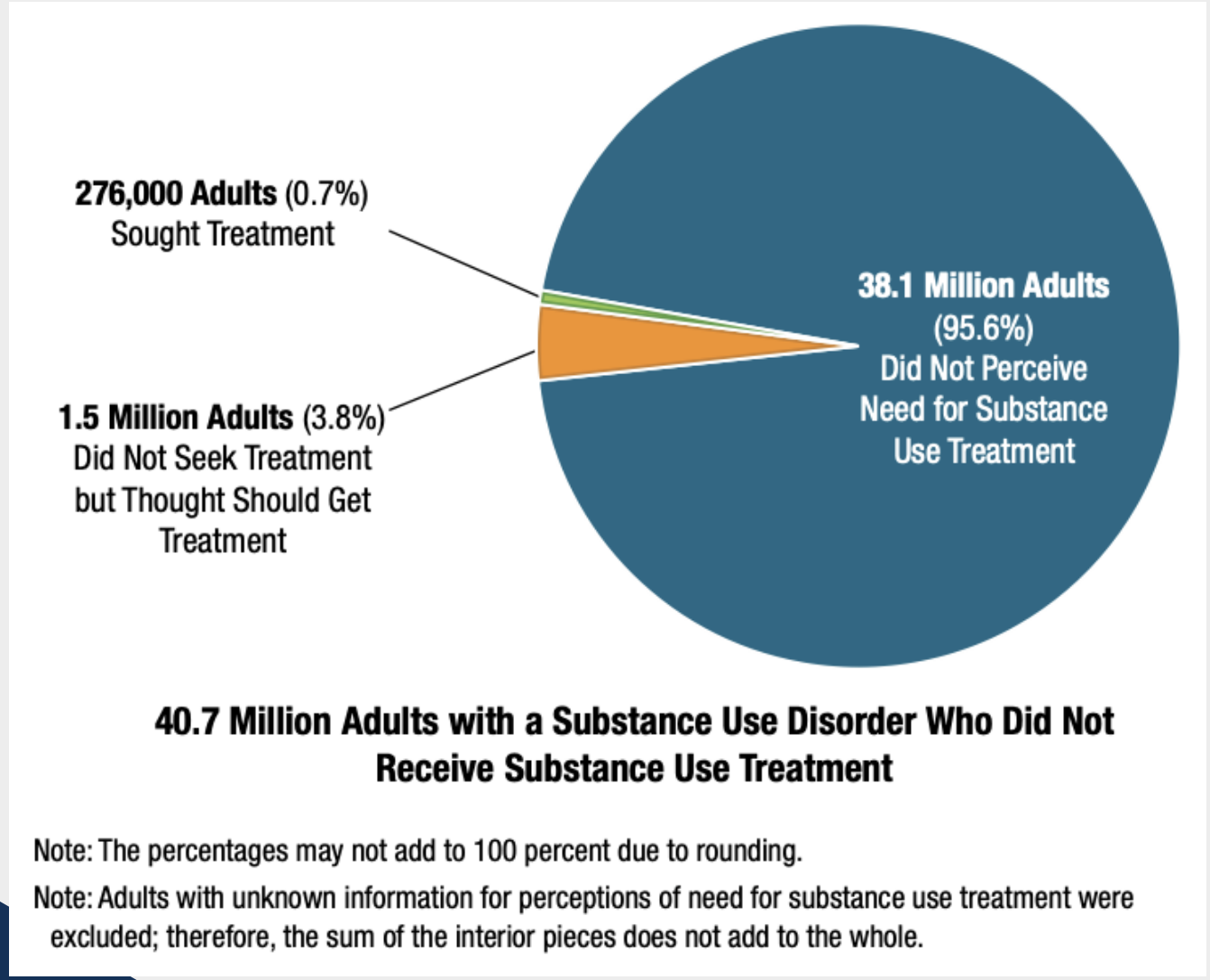


Note: Substance use treatment includes treatment for drug or alcohol use through inpatient treatment/counseling; outpatient treatment/counseling; medication for alcohol use disorder or opioid use disorder; telehealth treatment; or treatment received in a prison, jail, or juvenile detention center.

Note: Need for Substance Use Treatment is defined as having a substance use disorder in the past year or receiving substance use treatment in the past year.

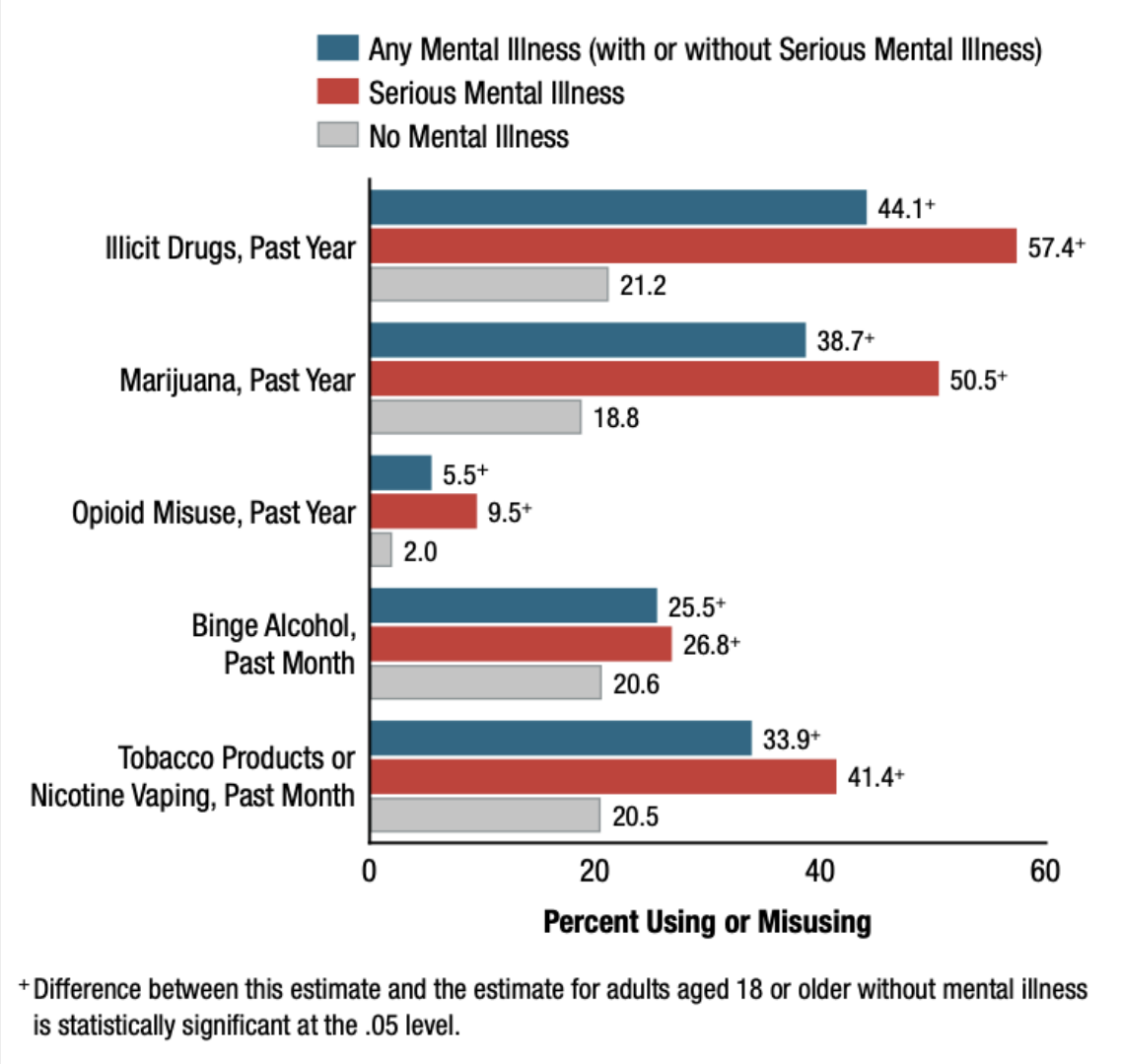
https://www.samhsa.gov/data/sites/default/files/reports/rpt56287/2024-nsduh-annual-national-report.pdf

Perceived NEED for treatment (2024): 18 or older with past year SUD who did NOT receive SU treatment in past year



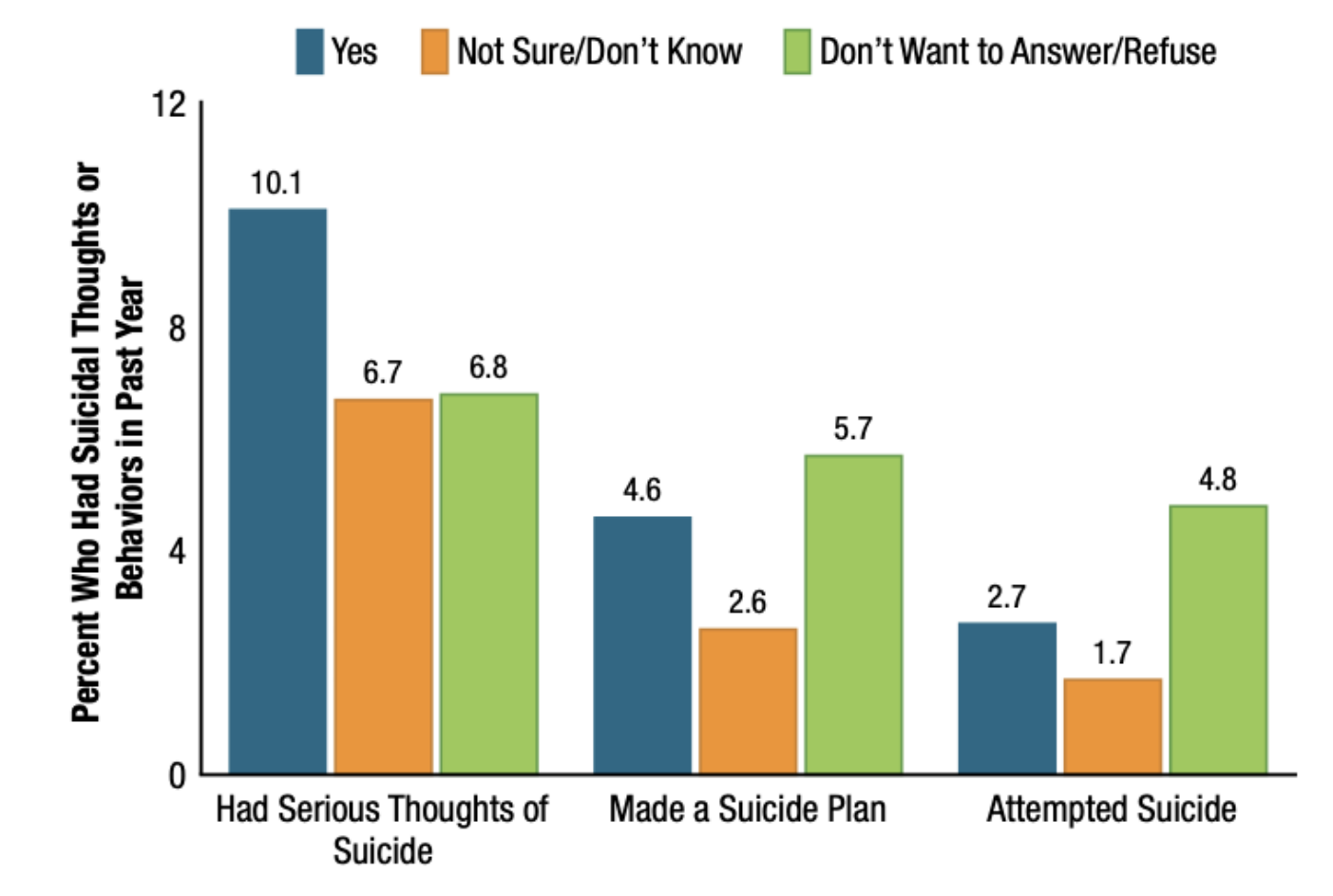
https://www.samhsa.gov/data/sites/default/files/reports/rpt56287/2024-nsduh-annual-national-report.pdf

Past Year or Past Month Substance Use: Among Adults Aged 18 or Older; by Mental Illness Status, 2024



https://www.samhsa.gov/data/sites/default/files/reports/rpt56287/2024-nsduh-annual-national-report.pdf

Had Serious Thoughts of Suicide, Made a Suicide Plan, or Attempted Suicide in the Past Year: Among Youths Aged 12 to 17; 2024



https://www.samhsa.gov/data/sites/default/files/reports/rpt56287/2024-nsduh-annual-national-report.pdf

Second: Looking a little closer by substance



Past Month Tobacco/Nicotine; 12 and older, 2023

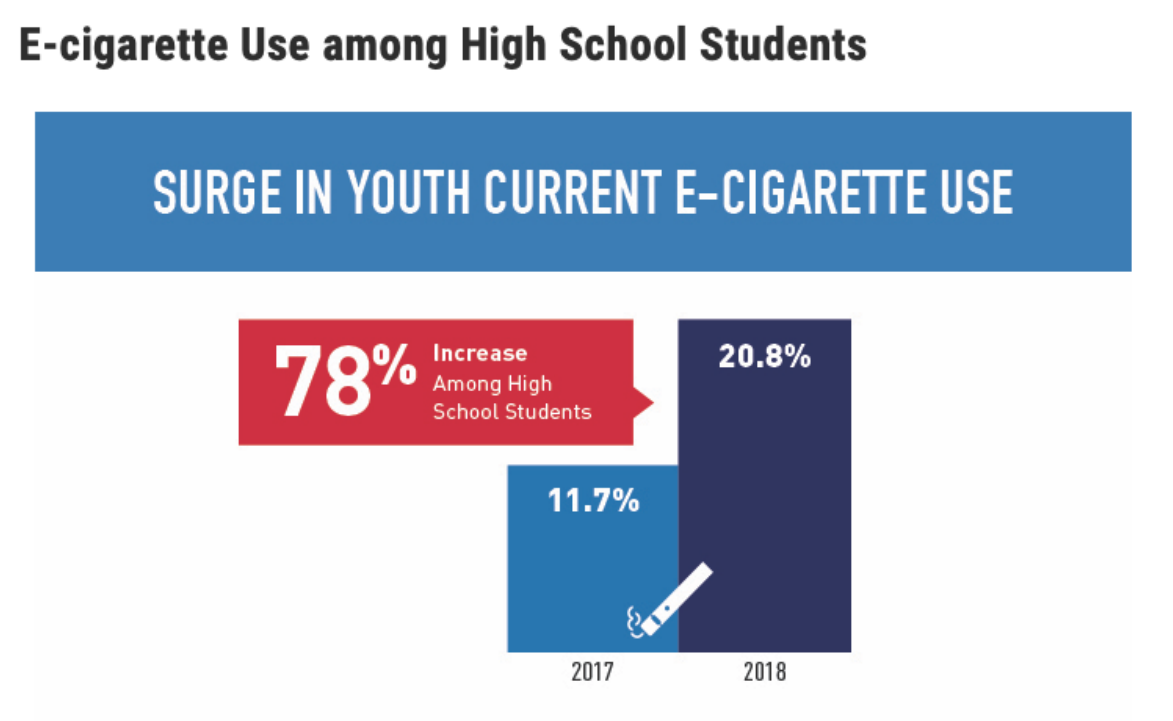


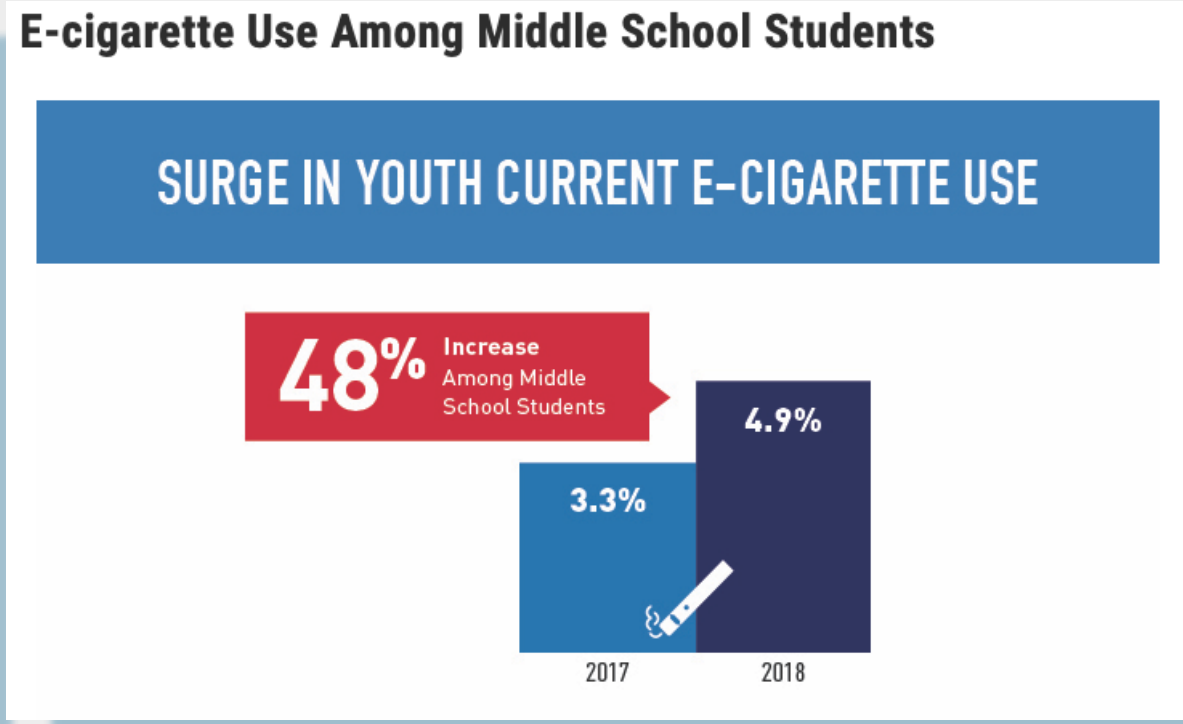
	1991	1993	1995	1997	1999	2001	2003	2005	2007	2009	2011	2013	2015	2017	2019	2021
9th Grade	23.2	27.8	31.2	33.4	27.6	23.9	17.4	19.7	14.3	13.5	13	10.2	7.6	5.2	3.8	2.2
10th Grade	25.2	28	33.1	35.3	34.7	26.9	21.8	21.4	19.6	18.3	15.6	13.2	8.8	7.6	5.2	3.8
11th Grade	31.6	31.1	35.9	36.6	36	29.8	23.6	24.3	21.6	22.3	19.3	21.1	13.1	9.5	5.9	4.1
12th Grade	30.1	34.5	38.2	39.6	42.8	35.2	26.2	27.6	26.5	25.2	25.1	19.2	14.1	13.4	9	5.2

https://medicalxpress.com/news/2024-01-decline-cigarette-teens-decades.html

https://www.samhsa.gov/data/sites/default/files/reports/rpt56287/2024-nsduh-annual-national-report.pdf

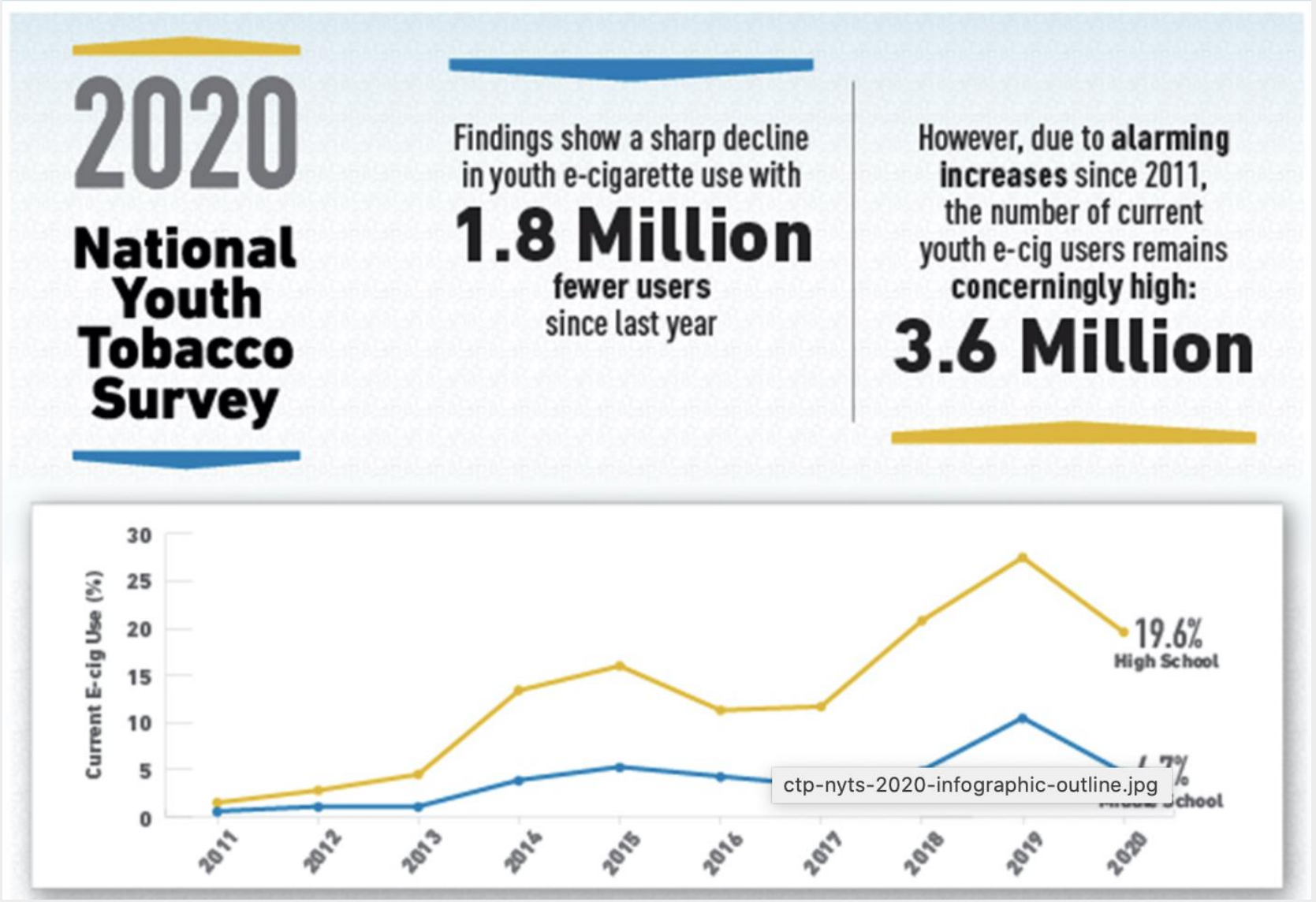
E-Cigarettes





https://www.fda.gov/tobacco-products/youth-and-tobacco/2018-nyts-data-startling-rise-youth-e-cigarette-use

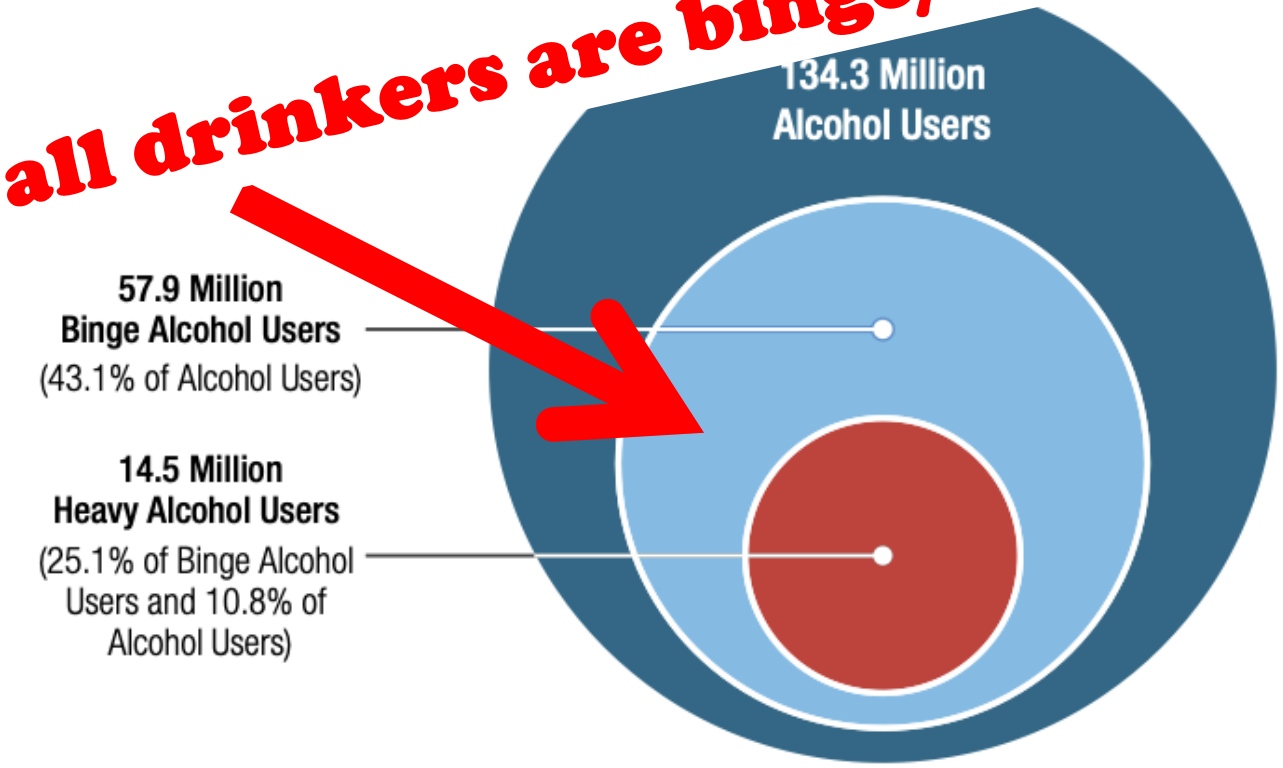
But(t):



https://www.fda.gov/tobacco-products/youth-and-tobacco/youth-tobacco-use-results-national-youth-tobacco-survey

Current, Binge, and Heavy Alcohol Use: Among People Aged 12 or Older; 2024 (

~Half of all drinkers are binge/heavy drinkers



Note: Binge Alcohol Use is defined as drinking five or more drinks (for males) or four or more drinks (for females) on the same occasion on at least 1 day in the past 30 days. Heavy Alcohol Use is defined as binge drinking on the same occasion on 5 or more days in the past 30 days; all heavy alcohol users are also binge alcohol users.

~60% of all SUDs in US are Alcohol (may be overlap)

https://www.samhsa.gov/data/sites/default/files/reports/rpt56287/2024-nsduh-annual-national-report.pdf

Alcohol deaths increase dramatically during pandemic, especially for younger

CDC: ~178,000 people die annually from excessive alcohol use
Increasing 29% from 2016-2021 (27% men, 35% women)
(2024)

mbers:
ng More
People Than the

Federal Estimates: $249 billion annually (lost productivity & health costs
(2024)

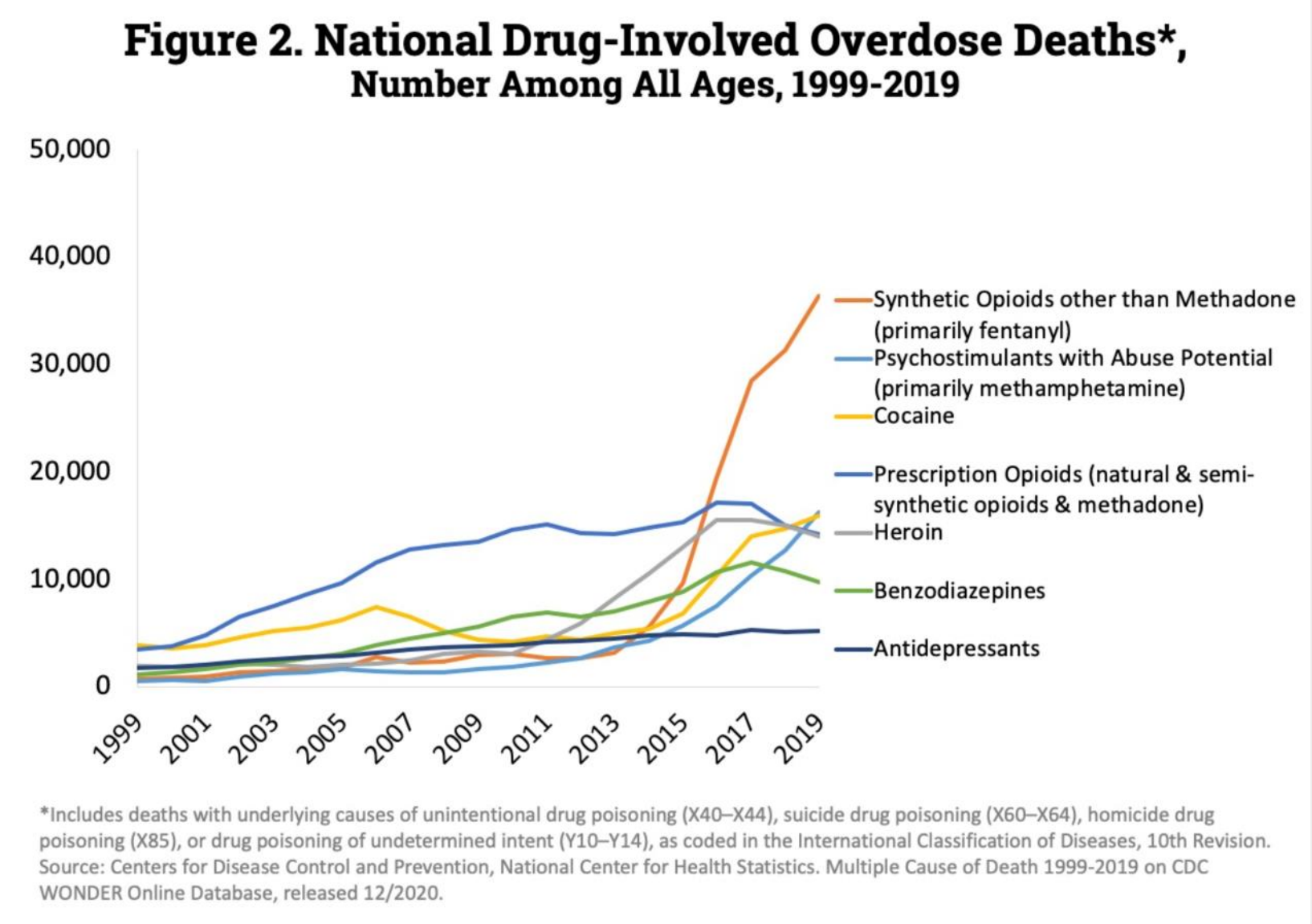
younger-adults-research/story?id=84496498

https://www.caron.org/blog/alcohol-is-killing-more-people-than-the-opioid-epidemic

Overdose Deaths Statistics Rollercoaster

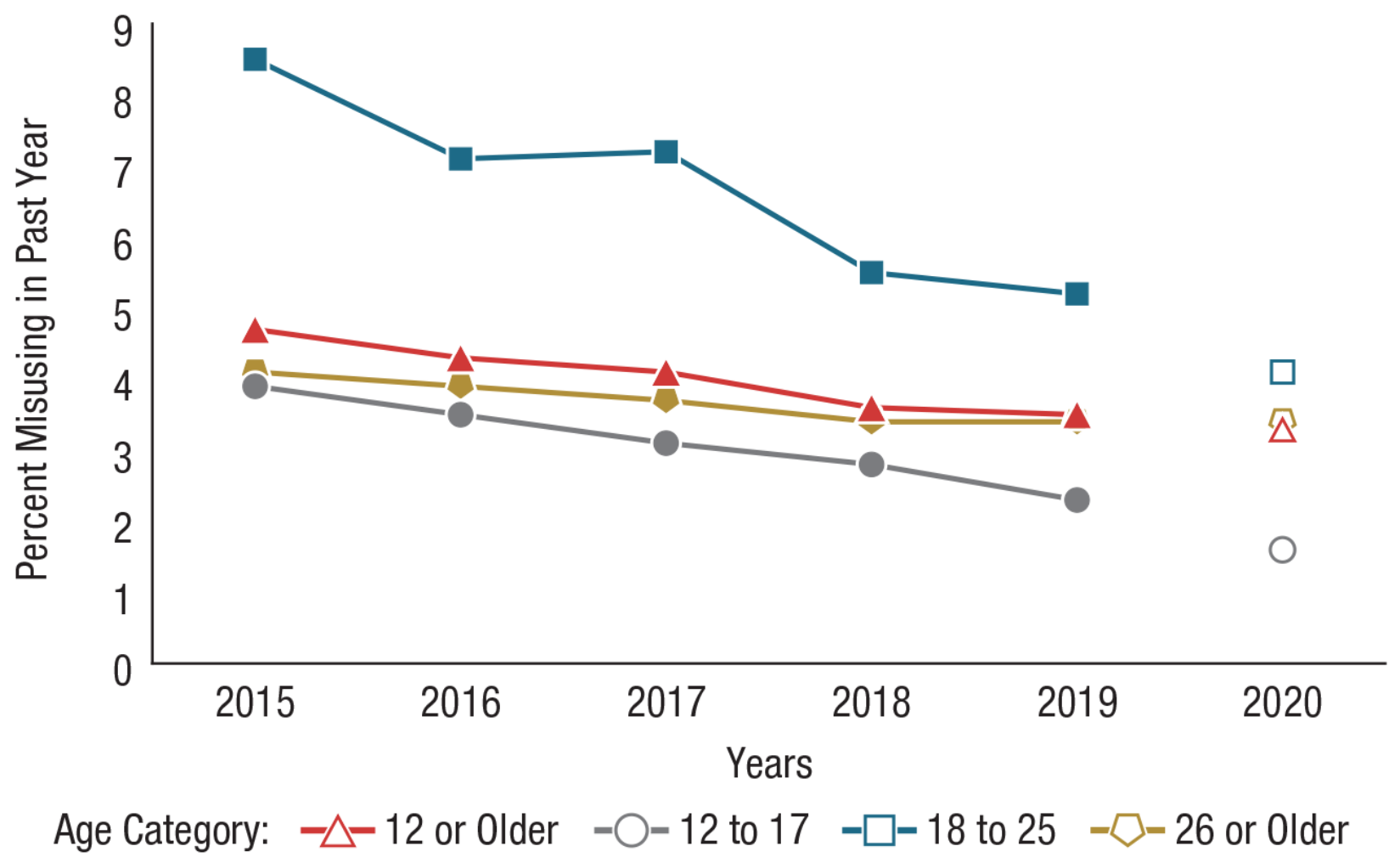


Four Waves of the Overdose Crisis…



https://www.drugabuse.gov/drug-topics/trends-statistics/overdose-death-rates

Wave 2: Past Year Prescription Pain Reliever Misuse: Among People Aged 12 or Older; 2015-2020



https://www.samhsa.gov/data/data-we-collect/nsduh-national-survey-drug-use-and-health

Wave 3-4: HPSO…

Society

The Guardian

Number of fentanyl-filled pills seized by US law enforcement up 4,850%

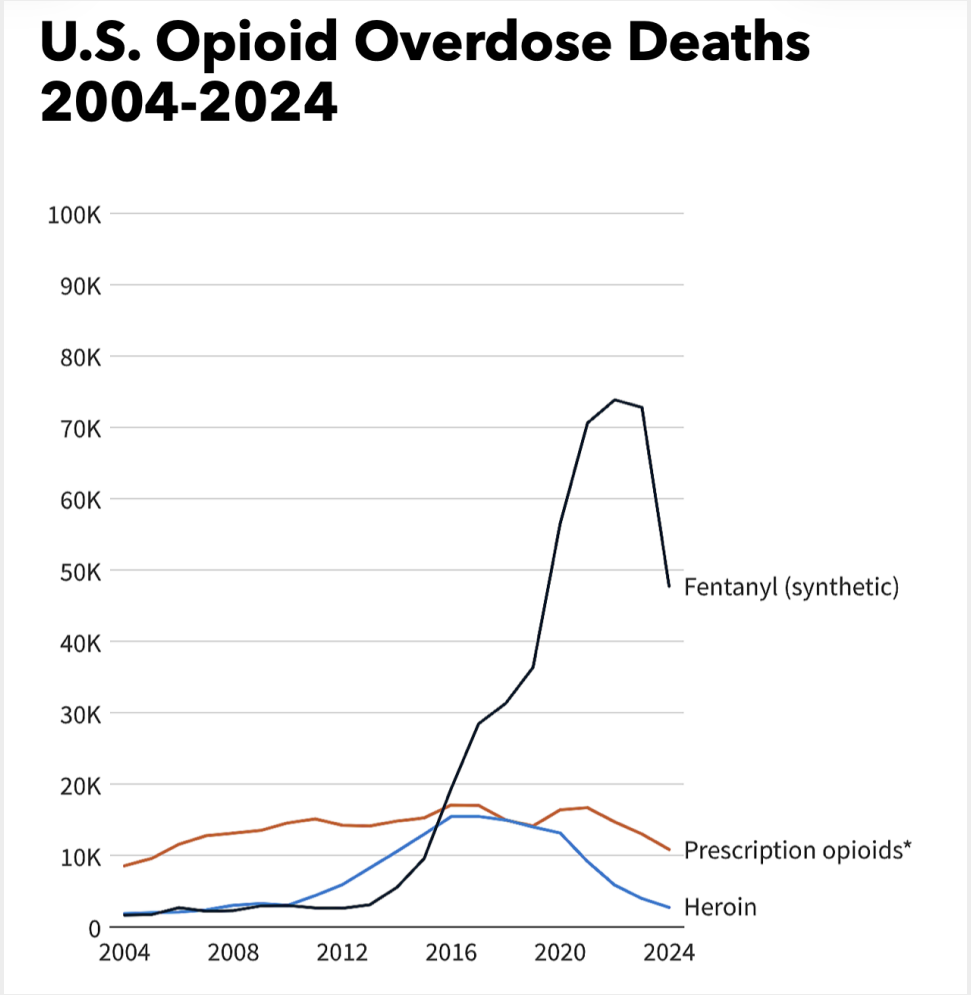
A study found that more than 2m counterfeit pills were confiscated in the last quarter of 2021 alone



Erin McCormick

12:00 UTC Thursday, 31 March 2022

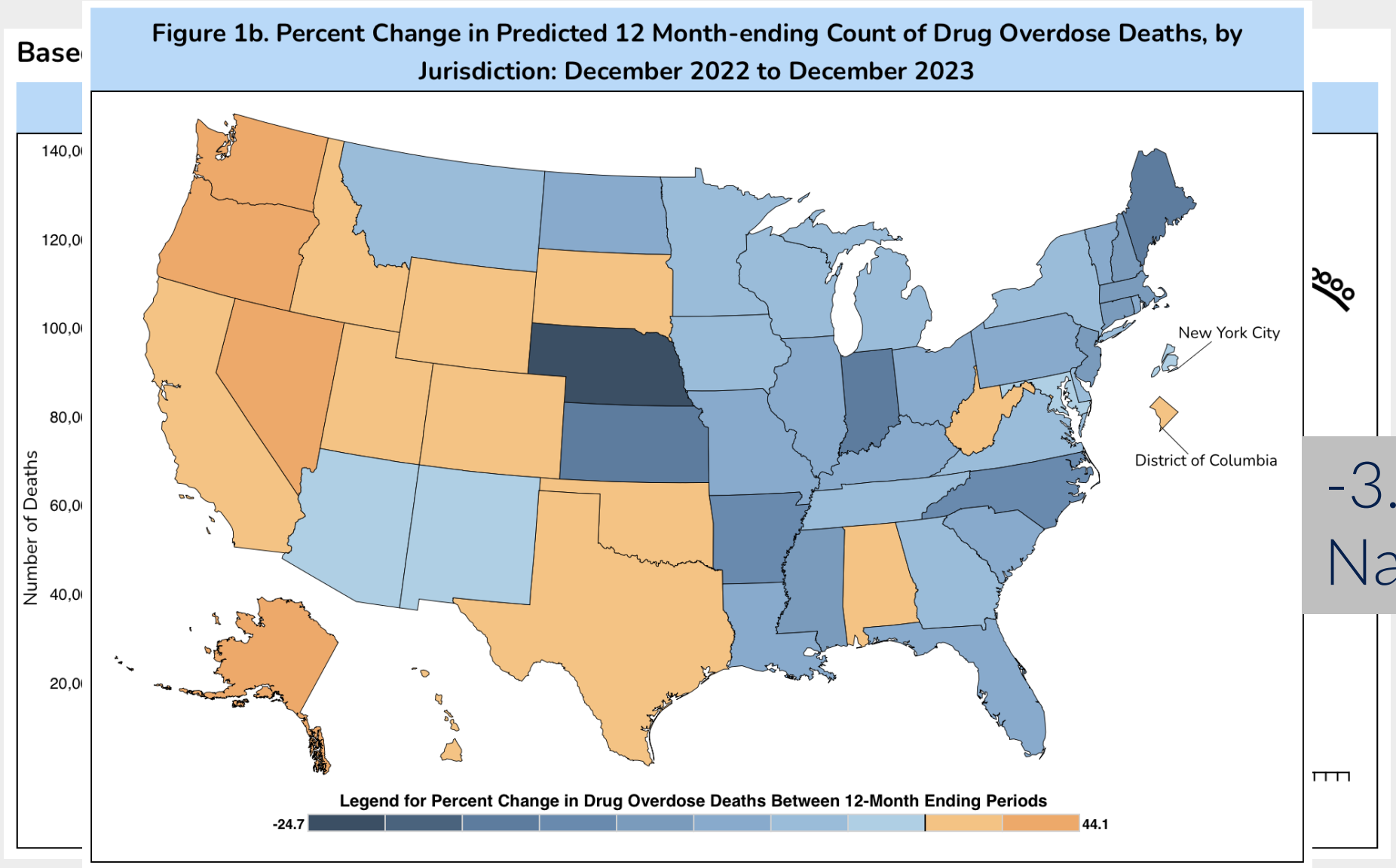
https://www.theguardian.com/society/2022/mar/31/fentanyl-overdose-us-law-enforcement



https://apple.news/ALwQLj1rlRtq6iL467t3jSw

https://www.drugabuse.gov/drug-topics/trends-statistics/overdose-death-rates

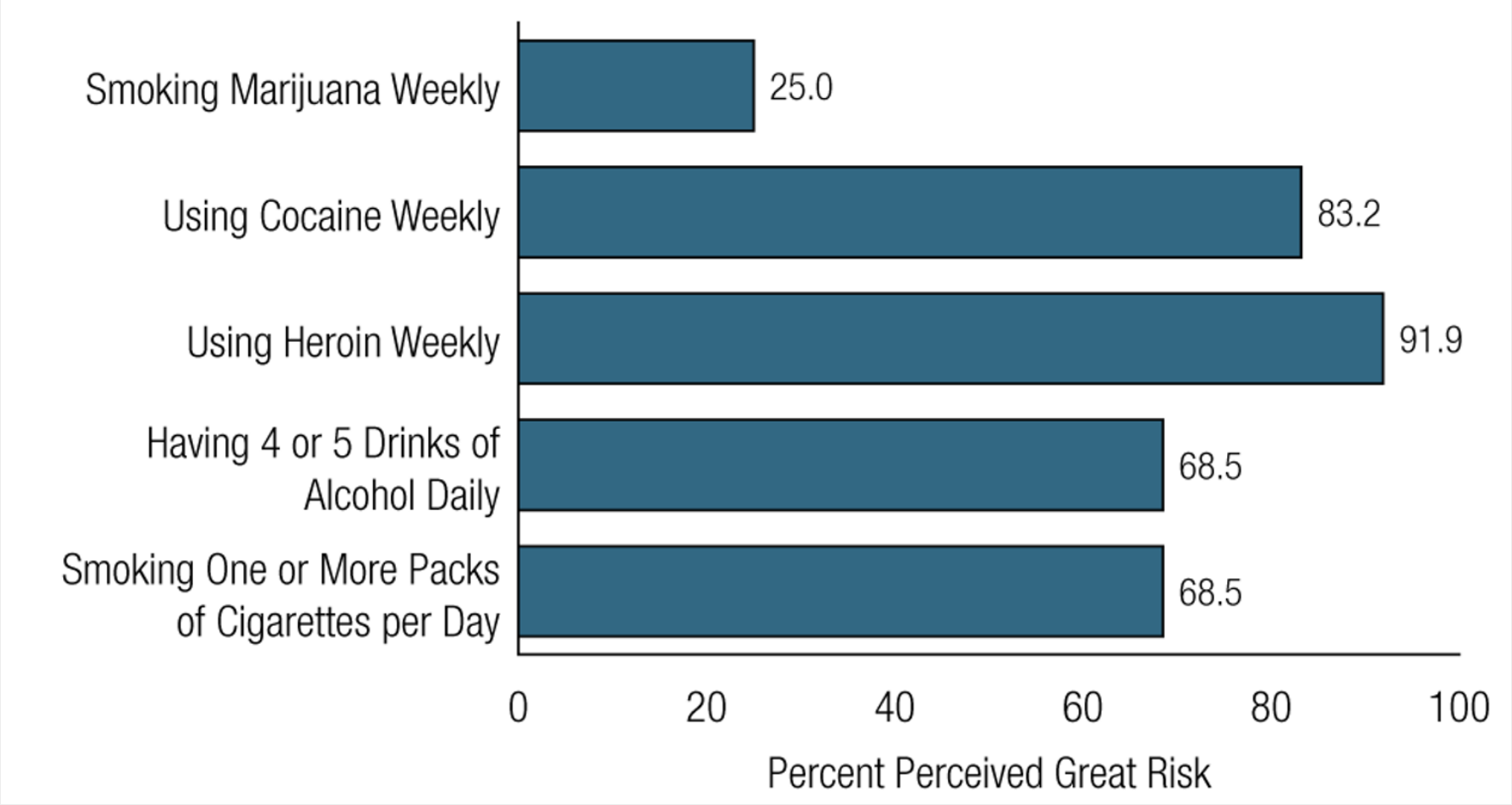
Fortunately (?)…



-3.1% Nationwide

https://www.cdc.gov/nchs/nvss/vsrr/drug-overdose-data.htm

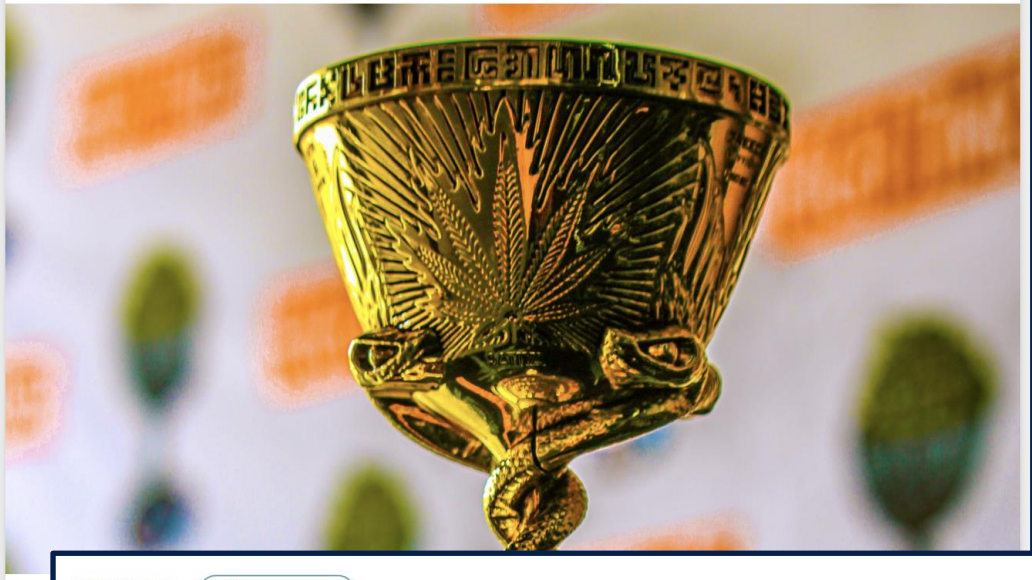
Perceived Great Risk from Substance Use: Among People Aged 12 or Older; 2022



https://www.samhsa.gov/data/release/2022-national-survey-drug-use-and-health-nsduh-releases#highlighted-pop-slides

You can become a judge in High Times' "Cannabis Cup" and pick your favorite product!

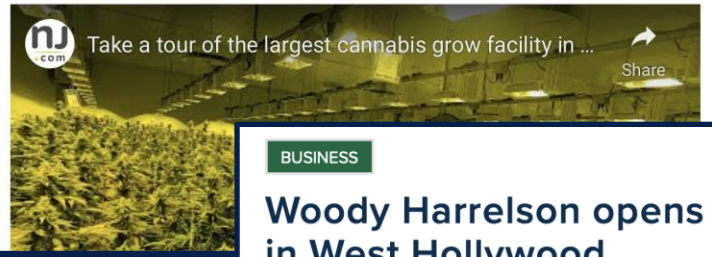
by Mason Carroll | Friday, May 13th 2022



htt
car

A beginner's guide to weed: How to choose the right strain for you

Updated: Apr. 15, 2022, 11:51 a.m. | Published: Apr. 15, 2022, 9:02 a.m.



Advertisement

RITE AID

https://www.nj.c
to-choose-the-rig

BUSINESS

Woody Harrelson opens The Woods cannabis dispensary in West Hollywood

BY SUSAN CARPENTER | WEST HOLLYWOOD
PUBLISHED 5:00 PM PT MAY. 13, 2022

WEST HOLLYWOOD, Calif. — With a waft of marijuana swirling around him and an adoring crowd of fans, Woody Harrelson cut the ribbon on his new cannabis dispensary in West Hollywood Friday. Part retail, part lounge and 100% dedicated to selling the best marijuana grown under the California sun, The Woods opened for business Friday.

"Hopefully we've added more beauty and more good times here," Harrelson told an eclectic group that had packed onto the sidewalk on Santa Monica Blvd. moments before The Woods opened its doors. "Hopefully we can help make the West Hollywood citizens a little bit higher."

https://www.hollywoodreporter.com/lifestyle/lifestyle-news/woody-harrelson-opens-cannabis-dispensary-the-woods-west-hollywood-

HEALTH NEWS ✓ Fact Checked

FDA Warns Companies to Stop Making False Claims for THC and CBD Products



Written by Julia Ries on May 13, 2022 — Fact checked by Jennifer Chesak

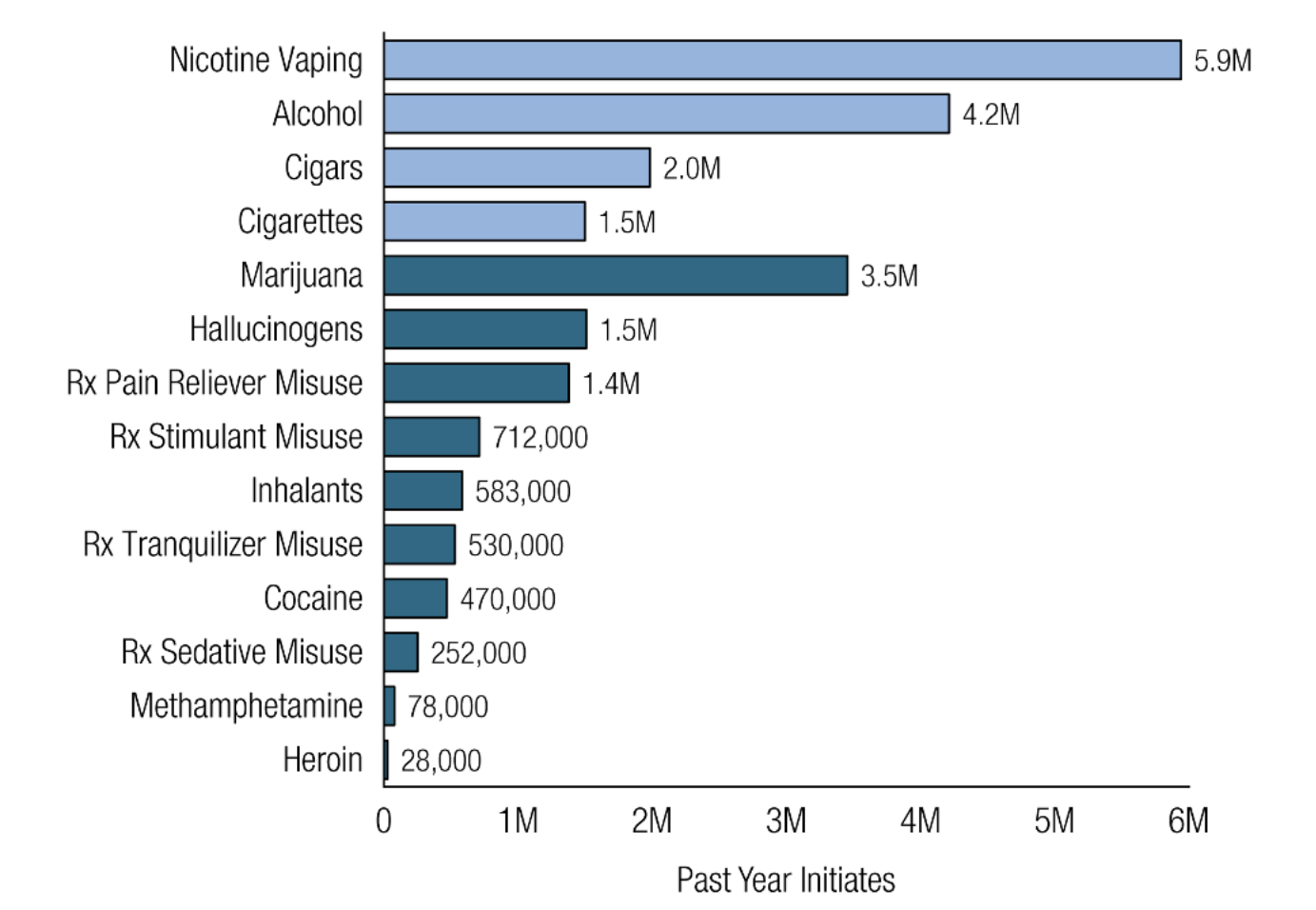
ADVERTISEMENT



https://www.healthline.com/health-news/fda-warns-companies-to-stop-making-false-claims-for-thc-and-cbd-products

healthline

Past Year Initiates of Substances: Among People Aged 12 or Older; 2023



https://www.samhsa.gov/data/data-we-collect/nsduh-national-survey-drug-use-and-health/national-releases#highlights



NEWS

Abuse of party drugs ecstasy and ketamine soar by more than 200% in last four years

Boffins analysed samples of waste water from England's sewers and found a 229 per cent increase in the amount of residue from ketamine between 2021 and last year.

By David Barrett Home Affairs Editor at 2:50 PM UTC on 13 April 2026

Illegal use of ketamine as a party drug has more than tripled in just four years, according to experimental scientific tests carried out for the Home Office.

Past year hallucinogen use reached historically high prevalence among adults 35 to 50 years old, reported by **4% in 2022**. The prevalence reported in 2022 was also a substantial increase compared to the year before (**2% in 2021**) and five and 10 years ago (**no greater than 1%** in both 2017 and 2012).

https://nida.nih.gov/news-events/news-releases/2023/08/marijuana-and-hallucinogen-use-binge-drinking-reached-historic-highs-among-adults-35-to-50#:~:text=Past%2Dyear%20hallucinogen%20use%20reached,in%20both%202017%20and%202012).

People who used 'magic mushrooms' less likely to develop opioid use disorder, study finds

USA TODAY

ADRIANNA RODRIGUEZ | USA TODAY
Updated 2:58 pm EDT Apr. 7, 2022

A "shroom craze" may get even wilder after a new study that suggests a psychedelic drug found in some mushrooms may have protective benefits against addiction.

Harvard University researchers found opioid use disorders were 30% less likely among people who used psilocybin compared with those who never had it, according to the study published Thursday in Scientific Reports.

Every item on this page was chosen by a Town & Country editor. We may earn commission on some of the items you choose to buy.

Why Is Everyone Smoking Toad Venom?

How an illegal amphibian-venom-derived psychedelic became the loudest whisper at a dinner party near you.



BY ALEX KUCZYNSKI — JAN 20, 2022

BOXING

Mike Tyson Says He 'Died' After Smoking Psychedelic Toad Venom

ANDREW GASTELUM • NOV 17, 2021

https://www.townandcountrymag.com/leisure/arts-and-culture/a38687510/toad-venom-bufo-illegal-psychedelic-drug/

https://www.si.com/boxing/2021/11/17/mike-tyson-says-he-died-smoking-psychedelic-toad-venom

“Synthetic Soup”

npr

Historic decline in U.S. overdose deaths threatened by changing street drug supply

Drug overdose deaths are plummeting in th
U.S. in ways never seen before. Experts wor
new, toxic "synthetic" street drugs could de
the recovery.

Brian Mann · April 14, 2026 01:03 PM EDT



AP apnews.com

Weapons-grade chemical carfentanil surges as dangerous substitute for fentanyl



BY HALLIE GOLDEN AND JIM MUSTIAN
Published 11:57 PM EDT, April 17, 2026

Third: Other Important Parts of the Story



Race/Ethnicity 2023

	National Average (%)	Black (%)	Asian (%)	American Indian/Alaska Native (%)	Hispanic (%)	NH Multiracial (%)
Past Month Binge Alcohol Use (12+)	21.7	21.6	10.7	19.1	22.9	22.2
Past Month Heavy Alcohol Use (12+)	5.8	4.2	2.0	5.6	4.5	7.6
Past Year Illicit Drug Use (12+)	24.9	27.7	12.4	36.7	21.6	36.2
Past Year Marijuana Use (12+)	21.8	24.5	10.0	30.2	18.2	32.9
Past Year SUD (12+)	17.1	17.6	9.2	25.3	15.7	24.3
Suicidal Thinking Past Year (18+)	5.0	4.0	4.2	4.7	5.0	12.0

BLACK = national average
RED = ABOVE national average
BLUE = BELOW national average

https://www.samhsa.gov/data/data-we-collect/nsduh-national-survey-drug-use-and-health/national-releases#highlights

Sexual Minority* 2023

	Straight (%)	Bisexual (%)	Gay (%)	Lesbian (%)	Some Other Term (%)
Binge Alcohol Use Past Month (12+)	22.5	24.4	28.4	25.5	19.9
Illicit Drug Use Past Month (12+)	16.1	35.8	33.9	28.7	26.3
Marijuana Use Past Month (12+)	14.8	32.6	27.1	27.8	23.2
Opioid Misuse Past Month (12+)	0.8	1.7	0.7	0.3	1.8
SUD Past Year (12+)	16.6	28.9	32.2	24.7	30.3
Suicidal Thoughts Past Year (18+)	4.1	16.7	8.1	11.7	16.7

RED = higher than national average

BLUE = Lower than national average

* Defined by SAMHSA as people who identify as lesbian, gay, or bisexual:
NSDUH began collecting data on this specific population in 2015

https://www.samhsa.gov/data/sites/default/files/reports/rpt53159/2023-nsduh-pop-slides-lbgplus.pdf

Women vs. Men…

- Women tend to initiate substance use later than men
- Women have accelerated course of disorder → "telescoping" (alcohol, marijuana, cocaine, prescription opioids)
- Women with SUDs → more severe impairment in employment, social/family, medical and psychiatric functioning
- Women have LOWER rates (2023) than men for binge drinking, illicit drug use, cannabis/opioid use, SUD
- Women have HIGHER rates (2023) than men for MDE, any mental illness, receipt of MH services

McHugh RK, et al. Sex and gender differences in substance use disorder. Clin Psychol Rev. 2017 Nov 10.

https://www.samhsa.gov/data/sites/default/files/reports/rpt53159/2023-nsduh-pop-slides-female.pdf

Let's Look at a Study…

- Question: Does Marijuana use cause psychosis?

Schizophrenia Bulletin vol. 42 no. 5 pp. 1262–1269, 2016
doi:10.1093/schbul/sbw003
Advance Access publication February 15, 2016

Meta-analysis of the Association Between the Level of Cannabis Use and Risk of Psychosis

Arianna Marconi[1], Marta Di Forti[1], Cathryn M. Lewis[2], Robin M. Murray[1], and Evangelos Vassos[*,2]

[1]Department of Psychosis Studies, King's College London, Institute of Psychiatry Psychology & Neuroscience, London, UK; [2]King's College London, Institute of Psychiatry Psychology & Neuroscience, MRC SGDP Centre, London, UK

*To whom correspondence should be addressed; King's College London, Institute of Psychiatry Psychology & Neuroscience, MRC SGDP Centre, Box P082, De Crespigny Park, London SE5 8AF, UK; tel: +44-20-7848-5433, fax: +44-20-7848-0866, e-mail: evangelos.vassos@kcl.ac.uk

What Is This Study?

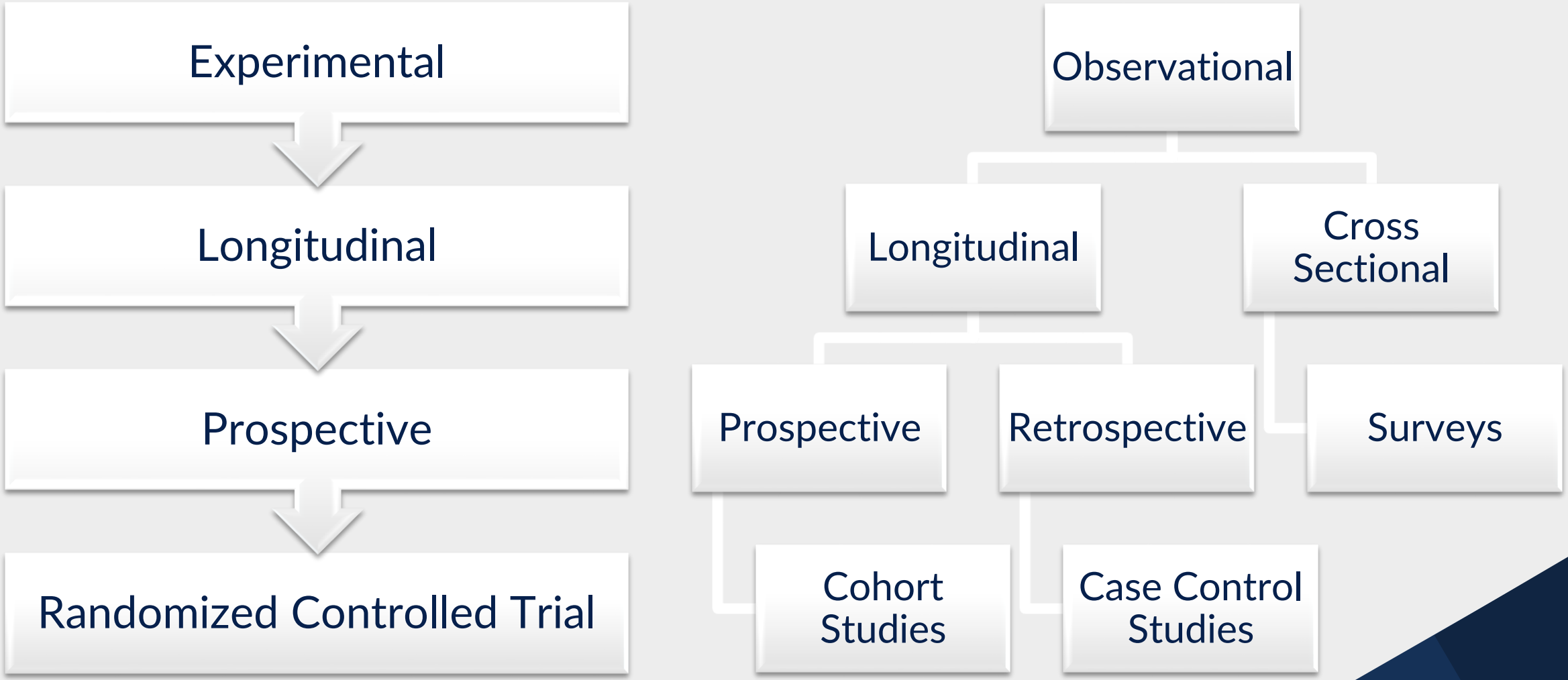
- Performed a systematic review and a meta-analysis
- Included: provided data on cannabis consumption prior to the onset of psychosis
  - 18 for systematic review and 10 for meta-analysis (66,816 individuals)
  - Continuous variable → amount of exposure
  - Cohort and cross-sectional studies included
- Findings:
  - Odds ratio 3.90 (95% confidence interval 2.84 to 5.34) for risk of schizophrenia and other psychosis-related outcomes among the heaviest cannabis users compared to non-users

What can we say about this study?

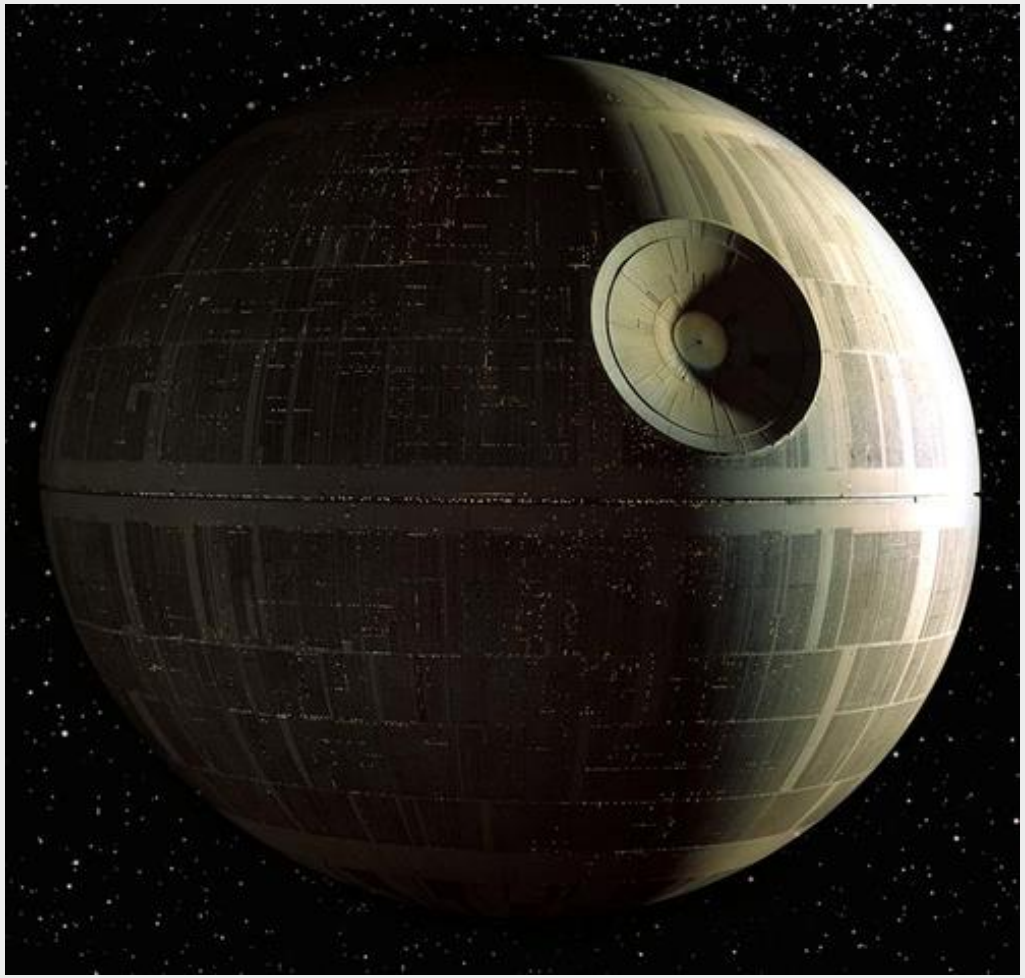
1) Quality of evidence, based on study design.



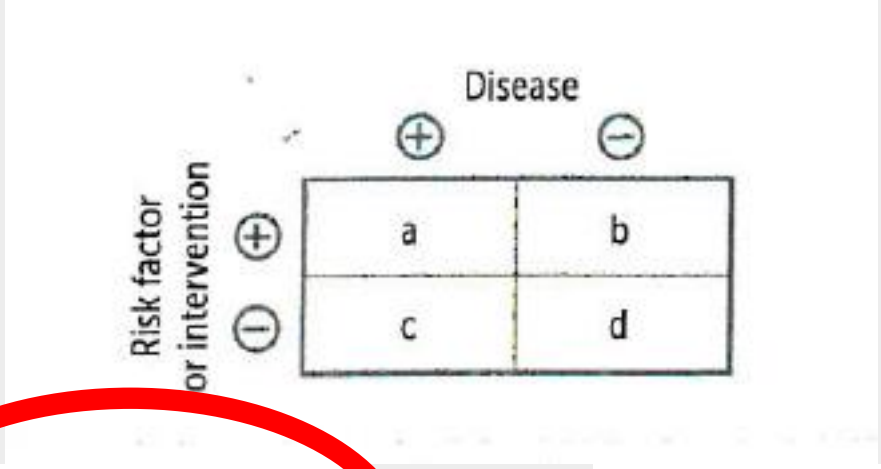
Types of Studies



Quantifying Risk…



Quantifying Risk…



$$AR = \frac{a}{a+b} - \frac{c}{c+d}$$

$$NNH = 1/AR$$

$$OR = \frac{a/c}{b/d} = \frac{ad}{bc}$$

$$RR = \frac{a/(a+b)}{c/(c+d)}$$

$$ARR = \frac{c}{c+d} - \frac{a}{a+b}$$

$$NNT = 1/ARR$$

Odds Ratio--more

- What is an odds ratio?

Ratio of Odds

- Higher the Odds Ratio, stronger the association between the exposure and the outcome appears to be

- If Odds Ratio is 1, then that means that the ratio of the odds shows NO ASSOCIATION between the exposure and the outcome

- (those with disease who were exposed/those with disease not exposed)/(those without disease exposed/those without disease not exposed)

Odds Ratio—An Example

- Imagine: relationship between getting breast cancer and driving an American car vs. not
  - If no correlation between these two, then the ratio of those with disease who drove American cars/those with disease who didn't would be likely close to 1, and ratio of those without disease who drove American cars/those without disease who did not drive American cars would also be close to 1, and the ratio of those two would be one = no relationship

Back To The Cannabis Paper…
2) An ASSOCIATION Was Found

- Odds ratio 3.90 (95% confidence interval 2.84 to 5.34) for risk of schizophrenia and other psychosis-related outcomes among the heaviest cannabis users compared to non-users
  - Dose-response effect seen such that increasing exposure to cannabis increases risk of psychosis-related outcomes

What about Confidence Interval?

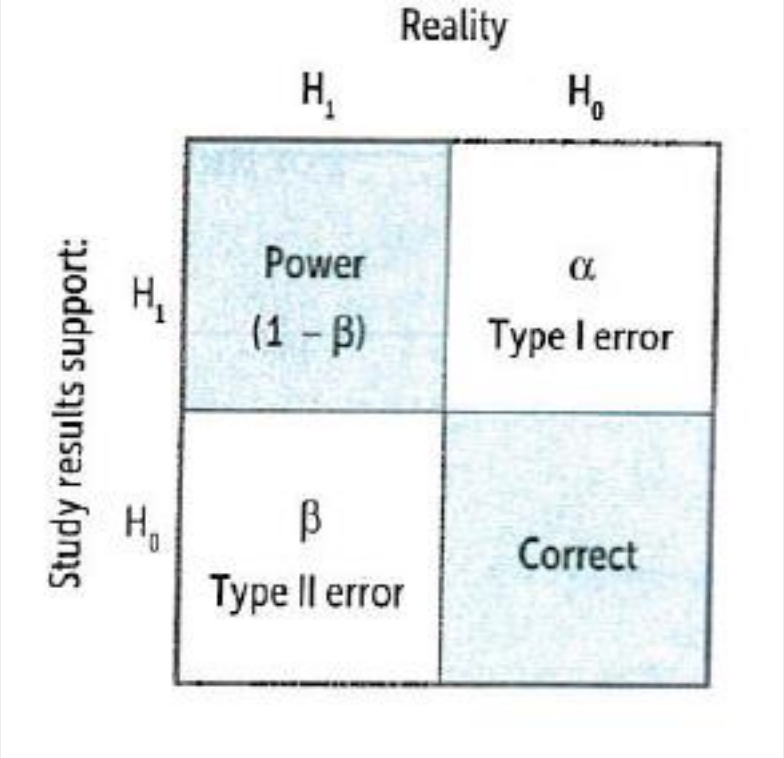
- (95% confidence interval 2.84 to 5.34)

  - This is the range of values within which the true mean of the population is expected to fall, with a specified probability
  - Probability: 95% CI basically corresponds to p=0.05
  - If this includes 1, for odds ratio or relative risk, null hypothesis is NOT rejected (no significant difference)

Oh No, Not the “Null Hypothesis”!!!

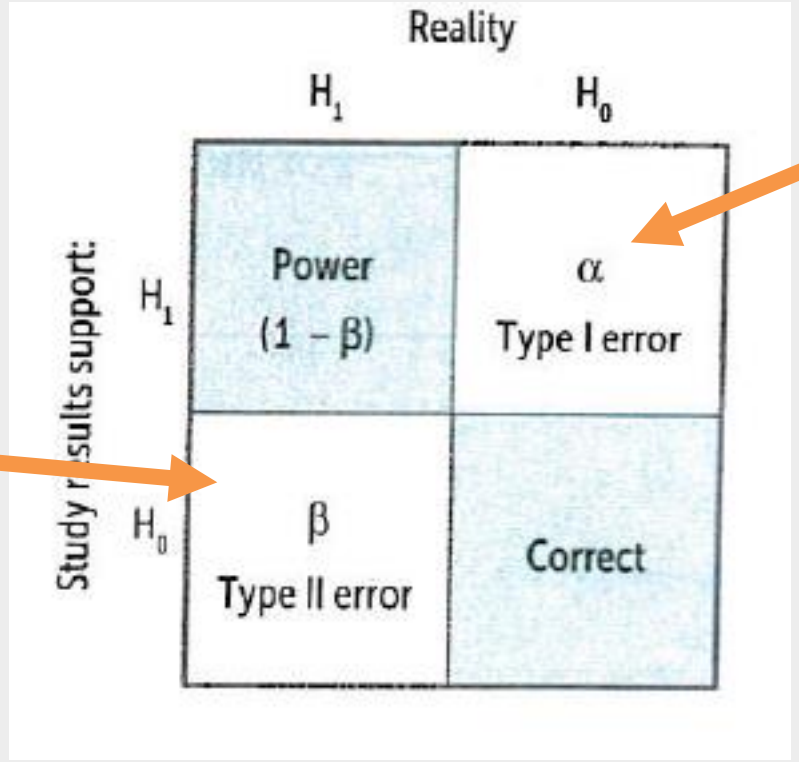


Oh No, Not the “Null Hypothesis”!!!



Oh No, Not the “Null Hypothesis”!!!

Stating that there is not an effect when one does exists:
False negative error



Stating that there is an effect when none exists:
False positive error

2) An Association Was Found

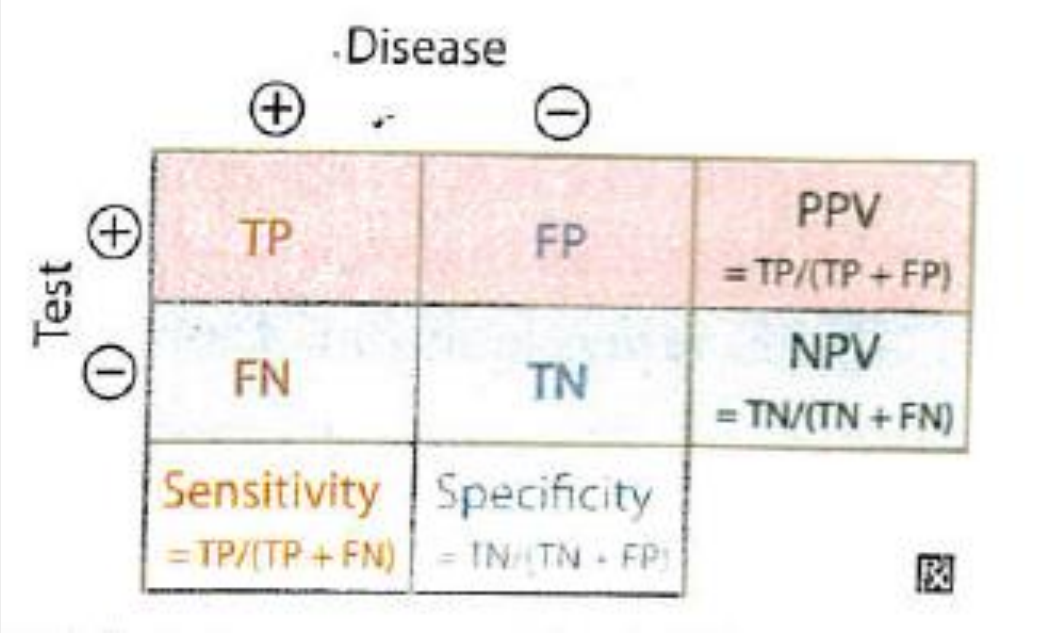
- Does this mean that cannabis CAUSES psychosis, based on this paper?

Why the heck is his urine toxicology screen negative?

Question:

Patient's ED urine drug screen came back negative for opiates, so he must not have used the methadone he claims to be taking?

Sensitivity vs. Specificity



High sensitivity screen for opiates (those metabolized to morphine), but low sensitivity for synthetic opioids (methadone)

What We've Done

- Briefly reviewed scope of epidemiology covered on ABPM exam
- Examined trends in addictions and explored ways to find that data for future professional or personal use
- Followed two common questions in addiction medicine as a springboard for reviewing key concepts in epidemiology

Whew!....



https://animals.sandiegozoo.org/animals/meerkat

3 CME Questions

A cross sectional survey is conducted to assess how many people at a given time in a particular population have moderate amphetamine use disorder. The survey has not been previously conducted. The total population is 50,000, and the survey reveals that 5,000 people report meeting criteria consistent with moderate amphetamine use disorder. What is the incidence of moderate amphetamine use disorder in this population?

A. 10,000
B. 45,000
C. 0.5
D. Incidence cannot be calculated from single cross-sectional surveys

Which of the following is TRUE regarding epidemiologic trends in addictive disorders?

A. Tobacco use has had an overall incline from 2002 to 2019, in large part due to the spike in use of e-cigarettes (especially among younger Americans)
B. Prescription opioid use has modestly increased from 2018-2019 (heroin and prescription pain relievers)
C. Despite **decreases** in opioid use in the years leading up to 2025, substance related overdose deaths INCREASED, but since 2025 there has been a DECREASE in overdose deaths nationwide, with regional variations
D. Substance related overdose deaths have increased largely because of the increase in serious mental illness and alcohol use

A case control study finds an odds ratio of 5.5 (95% CI 0.5 to 7.5) regarding the association between an exposure and development of a condition. Which is true regarding the above comment?

A. The odds ratio of 5.5 reflects a strong association between the exposure and the development of the condition
B. The high odds ratio here conclusively means that the exposure causes the development of the condition
C. The 95% confidence interval crosses 1, meaning there is an intolerable risk that the perceived relationship (OR 5.5) is due to chance—a type 1 error (no effect/relationship exists)
D. Since case control studies generally "look forward" (i.e. are prospective), this study is likely to have a low chance of asserting a Type II (Beta) error.

A toxicology test for xylazine is found to be 100% sensitive and 80% specific. Based on these findings, this test would function best as:

A. A screening test
B. A confirmatory test
C. Neither a confirmatory nor a screening test
D. Both a screening and confirmatory test

Of the following types of studies, which is considered to be of the “highest quality” (if done properly and ethically):

A. Double Blind Placebo Controlled Trial
B. Cohort Study
C. Case Control Study
D. Systematic Reviews and Meta Analyses



Get in Touch

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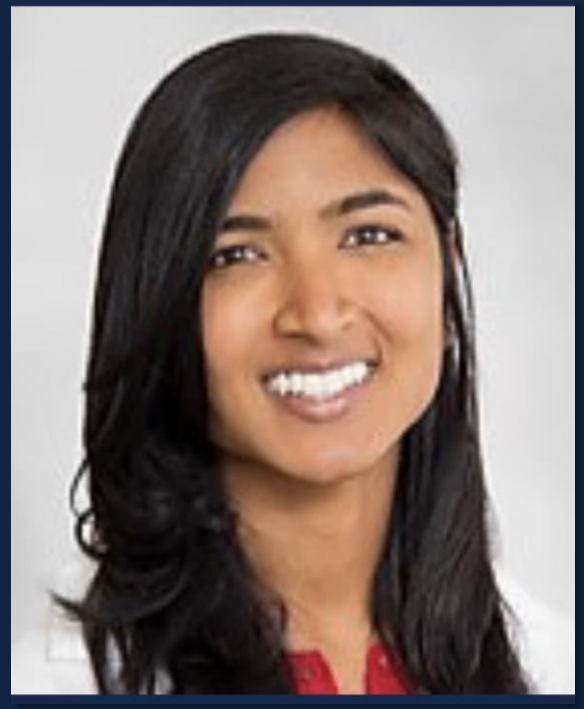
www.asam.org

ASAM REVIEW COURSE 2026

Prevention and Public Health: From Theory to Practice

Amutha Rajagopal, MD, MPH
Addiction Medicine, Infectious Diseases, Public Health and General Preventive Medicine
Oregon Health & Sciences University





Financial Disclosure

Amutha Rajagopal, MD, MPH

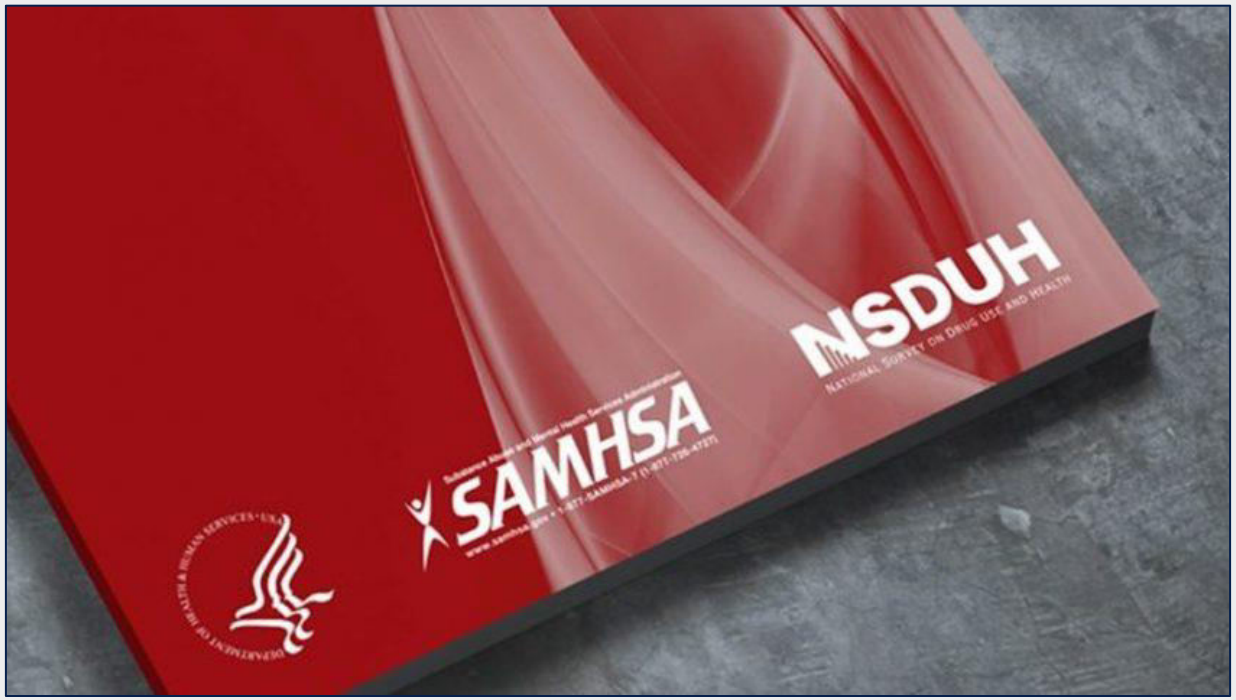
- No relevant disclosures

Learning Objectives

- Describe the importance of preventing unhealthy substance use
- Describe risks and protective factors for the development of substance use disorders
- Describe a public health approach to addressing unhealthy substance use
- Describe evidence-based prevention interventions

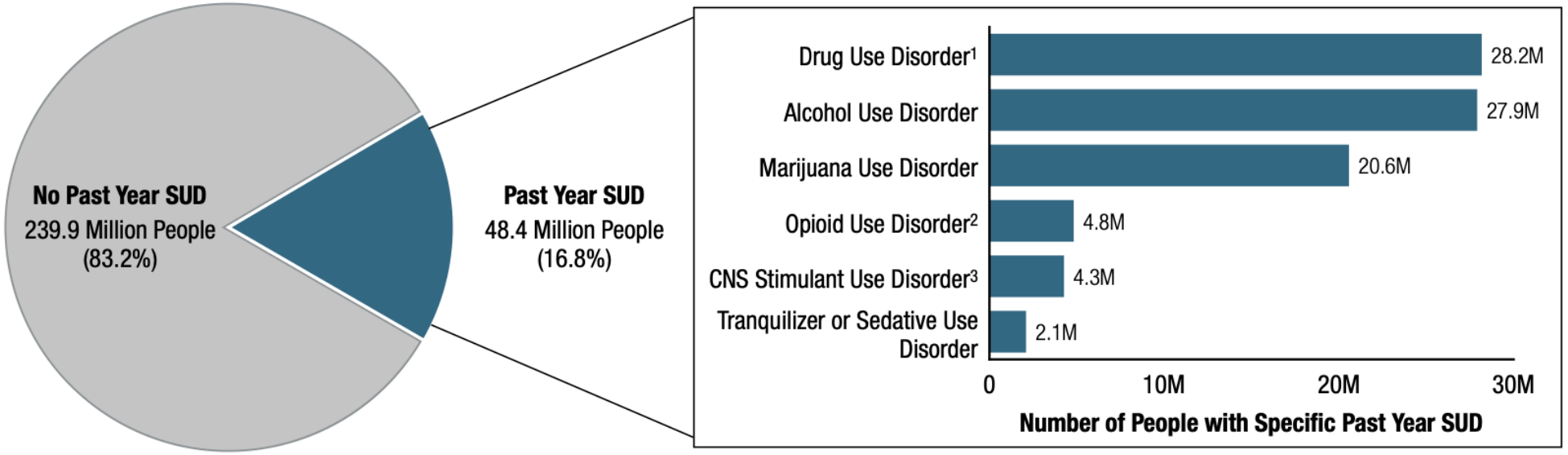
National Survey on Drug Use and Health (NSDUH)

- Provides nationally representative data on the use of tobacco, alcohol, and illicit drugs, SUD, and receipt of treatment among the non-institutionalized US population 12 years and older



2024 National Survey of Drug Use and Health (NSDUH) releases. SAMHSA.gov.

Figure 35. Past Year Substance Use Disorder (SUD): Among People Aged 12 or Older; 2024



CNS = central nervous system.

Note: The estimated numbers of people with SUDs are not mutually exclusive because people could have use disorders for more than one substance.

[1] Includes data from all past year users of marijuana, cocaine, heroin, hallucinogens, inhalants, methamphetamine, or prescription psychotherapeutic drugs (i.e., pain relievers, tranquilizers, stimulants, or sedatives). See footnote 2 for more information about opioid use disorder.

[2] Includes data from all past year users of heroin or prescription opioids. Respondents were not included if they used only nonopioid pain relievers and did not use heroin in the past year.

[3] Includes data from all past year users of cocaine, methamphetamine, or prescription stimulants.

2024 National Survey of Drug Use and Health (NSDUH) releases. SAMHSA.gov.

FACING ADDICTION IN AMERICA

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

A Vision for the Future

Substance Abuse and Mental Health Services Administration SAMHSA

#FacingAddiction

NATIONAL DRUG CONTROL STRATEGY

THE WHITE HOUSE
EXECUTIVE OFFICE OF THE PRESIDENT
OFFICE OF NATIONAL DRUG CONTROL POLICY

MAY 2024

Surgeon General Issues Landmark Report on Alcohol, Drugs and Health

Announcement

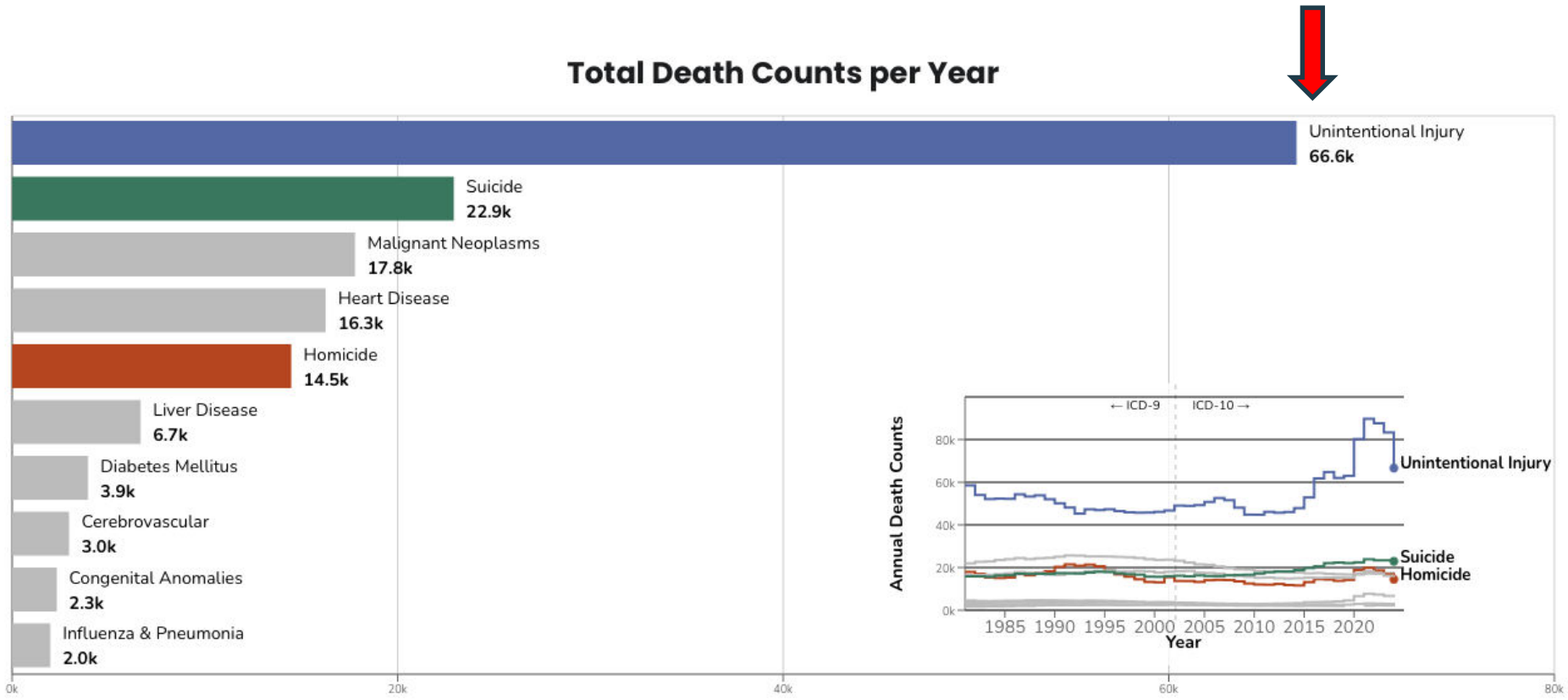
Thursday, November 17, 2016

"How we respond to this crisis is a test for America"
A new Surgeon General's report finds alcohol and drug misuse and severe substance use disorders, commonly called addiction, to be one of America's most pressing public health concerns. Nearly 21 million Americans – more than the number of people who have all cancers combined – suffer from substance use disorders.



"Alcohol and drug addiction take an enormous toll on individuals, families, and communities," said U.S. Surgeon General Dr. Vivek Murthy. "Most Americans know someone who has been touched by an alcohol or a drug use disorder. Yet 90 percent of people with a substance use disorder are not getting treatment. That has to change."

Top Ten Leading Causes of Death in the U.S. for Ages 1-44 from 1981-2024



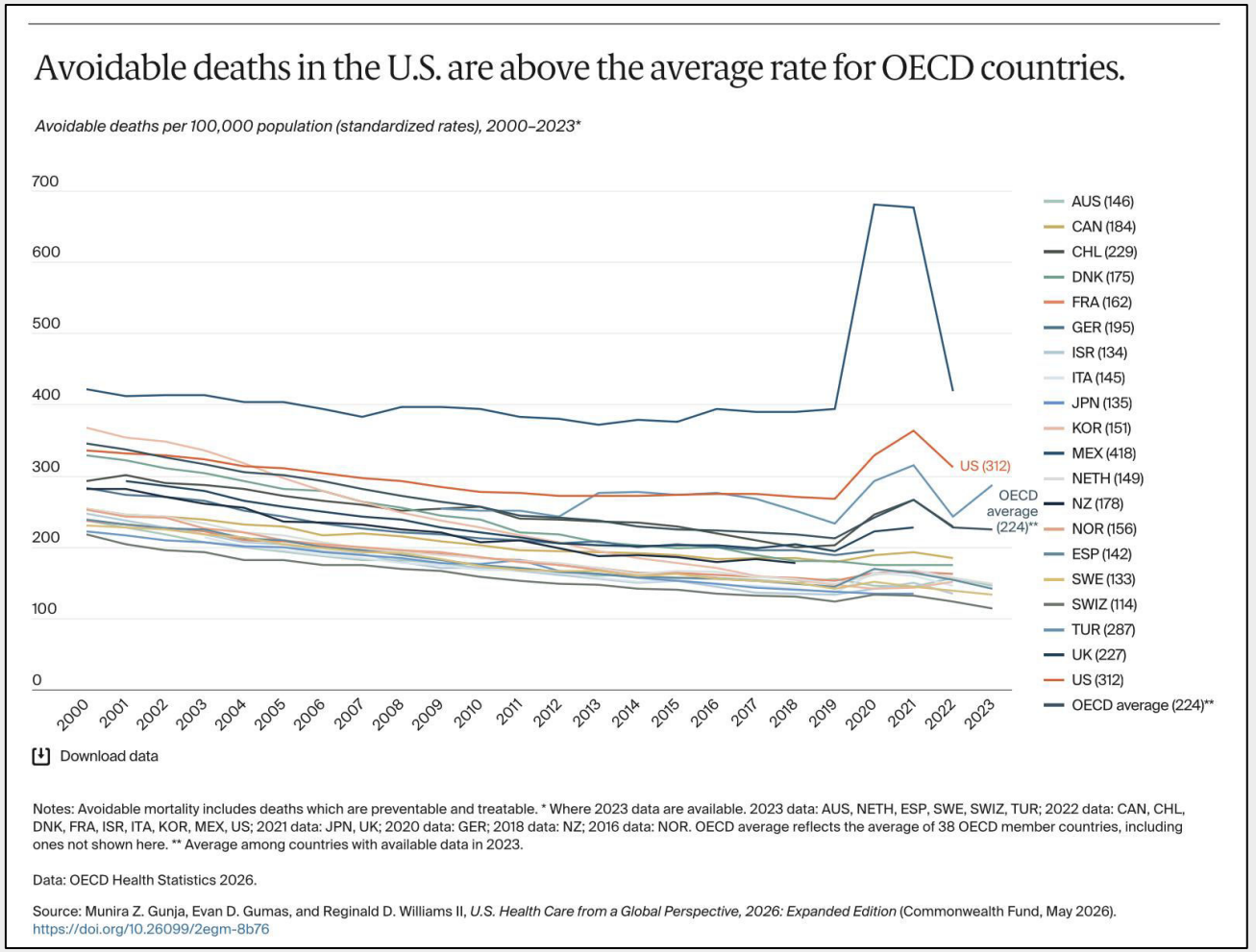
Unintentional injuries are the leading cause of death for Americans age 1-44 years, and most are drug overdoses

https://wisqars.cdc.gov/animated-leading-causes/

Costs of Unhealthy Substance Use

- Data from CDC show that opioid use disorder and opioid overdose alone cost the United States >$1 trillion annually





Florence C., et al. J Alcohol Depend. 2021.

Evidence-Based Prevention

- Evidence- based prevention interventions, carried out before the need for treatment, can delay early use and stop the progression from use to problematic use



SAMHSA. Facing Addiction in America: The Surgeon General's Report on Alcohol, Drugs, and Health. 2016

Table 3.1: Risk Factors for Adolescent and Young Adult Substance Use

Risk Factors	Definition	Adolescent Substance Use	Young Adult Substance Use
Individual/Peer			
Early initiation of substance use[46,47]	Engaging in alcohol or drug use at a young age.	✔	✔
Early and persistent problem behavior[48,49]	Emotional distress, aggressiveness, and "difficult" temperaments in adolescents.	✔	
Rebelliousness[48,50]	High tolerance for deviance and rebellious activities.	✔	✔
Favorable attitudes toward substance use[51,52]	Positive feelings towards alcohol or drug use, low perception of risk.	✔	✔
Peer substance use[53-55]	Friends and peers who engage in alcohol or drug use.	✔	✔
Genetic predictors[56]	Genetic susceptibility to alcohol or drug use.	✔	✔

SAMHSA. Facing Addiction in America: The Surgeon General's Report on Alcohol, Drugs, and Health. 2016

Table 3.1: Risk Factors for Adolescent and Young Adult Substance Use

Risk Factors	Definition	Adolescent Substance Use	Young Adult Substance Use
Family			
Family management problems (monitoring, rewards, etc.)[57-60]	Poor management practices, including parents' failure to set clear expectations for children's behavior, failure to supervise and monitor children, and excessively severe, harsh, or inconsistent punishment.	✔	✔
Family conflict[61-63]	Conflict between parents or between parents and children, including abuse or neglect.	✔	✔
Favorable parental attitudes[64,65]	Parental attitudes that are favorable to drug use and parental approval of drinking and drug use.	✔	✔
Family history of substance misuse[66,67]	Persistent, progressive, and generalized substance use, misuse, and use disorders by family members.	✔	✔

SAMHSA. Facing Addiction in America: The Surgeon General's Report on Alcohol, Drugs, and Health. 2016

Risk Factors for Adolescent and Young Adult Substance Use

Risk Factors	Definition	Adolescent Substance Use	Young Adult Substance Use
School			
Academic failure beginning in late elementary school[68,69]	Poor grades in school.	✔	✔
Lack of commitment to school[70,71]	When a young person no longer considers the role of the student as meaningful and rewarding, or lacks investment or commitment to school.	✔	✔

SAMHSA. Facing Addiction in America: The Surgeon General's Report on Alcohol, Drugs, and Health. 2016

Risk Factors for Adolescent and Young Adult Substance Use

Risk Factors	Definition	Adolescent Substance Use	Young Adult Substance Use
Community			
Low cost of alcohol[30,72]	Low alcohol sales tax, happy hour specials, and other price discounting.	✔	✔
High availability of substances[73,74]	High number of alcohol outlets in a defined geographical area or per a sector of the population.	✔	✔
Community laws and norms favorable to substance use[75,76]	Community reinforcement of norms suggesting alcohol and drug use is acceptable for youth, including low tax rates on alcohol or tobacco or community beer tasting events.	✔	✔
Media portrayal of alcohol use[77-79]	Exposure to actors using alcohol in movies or television.	✔	
Low neighborhood attachment[80,81]	Low level of bonding to the neighborhood.	✔	
Community disorganization[82,83]	Living in neighborhoods with high population density, lack of natural surveillance of public places, physical deterioration, and high rates of adult crime.	✔	
Low socioeconomic status[84,85]	A parent's low socioeconomic status, as measured through a combination of education, income, and occupation.	✔	
Transitions and mobility[80,86]	Communities with high rates of mobility within or between communities.	✔	

SAMHSA. Facing Addiction in America: The Surgeon General's Report on Alcohol, Drugs, and Health. 2016

Table 3.2: Protective Factors for Adolescent and Young Adult Substance Use

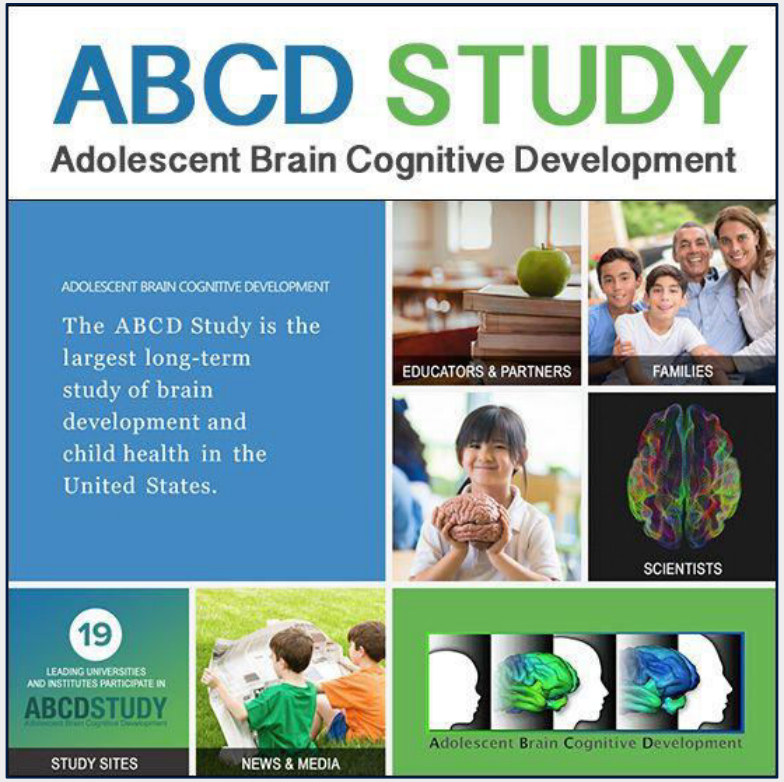
Protective Factors	Definition	Adolescent Substance Use	Young Adult Substance Use
Individual			
Social, emotional, behavioral, cognitive, and moral competence[87,88]	Interpersonal skills that help youth integrate feelings, thinking, and actions to achieve specific social and interpersonal goals.	✔	✔
Self-efficacy[89,90]	An individual's belief that they can modify, control, or abstain from substance use.	✔	✔
Spirituality[91,92]	Belief in a higher being, or involvement in spiritual practices or religious activities.	✔	✔
Resiliency[88]	An individual's capacity for adapting to change and stressful events in healthy and flexible ways.	✔	✔
Family, School, and Community			
Opportunities for positive social involvement[93,94]	Developmentally appropriate opportunities to be meaningfully involved with the family, school, or community.	✔	✔
Recognition for positive behavior[51]	Parents, teachers, peers and community members providing recognition for effort and accomplishments to motivate individuals to engage in positive behaviors in the future.	✔	✔
Bonding[95-97]	Attachment and commitment to, and positive communication with, family, schools, and communities.	✔	✔
Marriage or committed relationship[98]	Married or living with a partner in a committed relationship who does not misuse alcohol or drugs.		✔
Healthy beliefs and standards for behavior[51,99]	Family, school, and community norms that communicate clear and consistent expectations about not misusing alcohol and drugs.	✔	✔

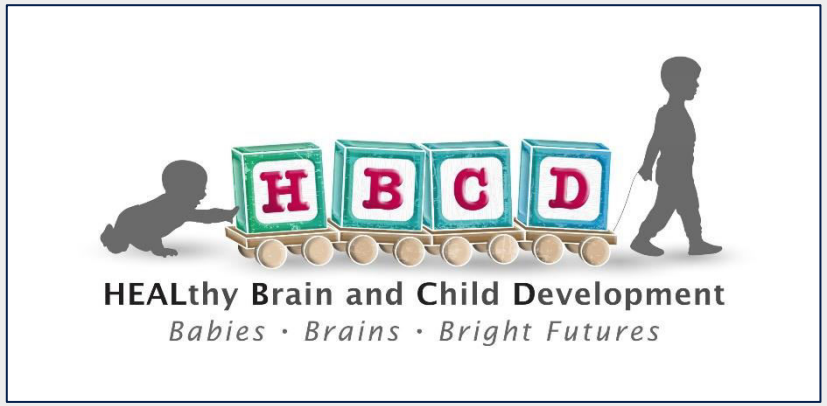
Note: These tables present some of the key risk and protective factors related to adolescent and young adult substance initiation and misuse.

SAMHSA. Facing Addiction in America: The Surgeon General's Report on Alcohol, Drugs, and Health. 2016

Evidence-Based Prevention

- Most risk factors and protective factors are modifiable through preventive programs and policies that reduce vulnerability at multiple levels: federal, state, community, family, school, and individual levels







SAMHSA. Facing Addiction in America: The Surgeon General's Report on Alcohol, Drugs, and Health. 2016

The Public Health Systems Approach



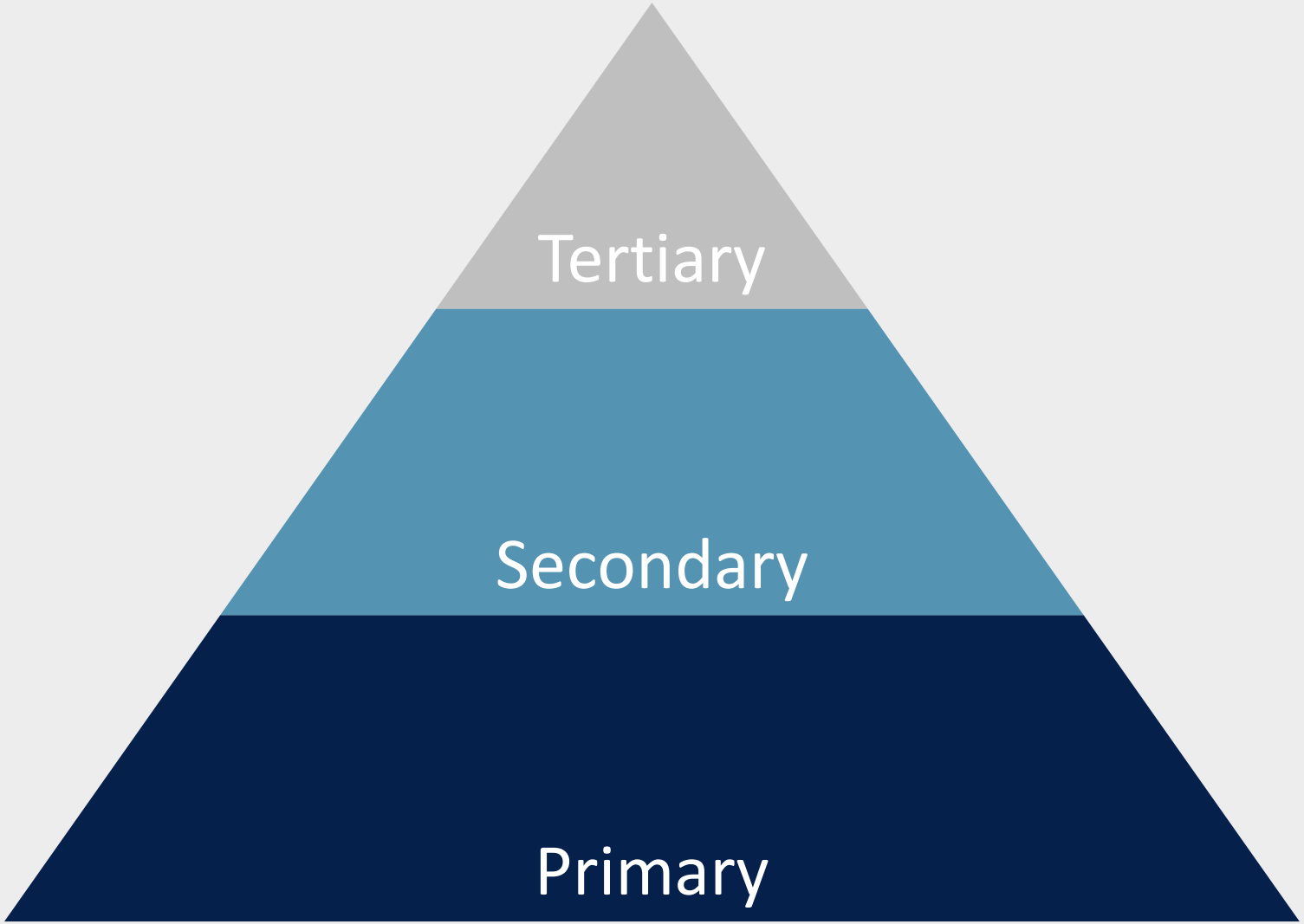
SAMHSA. Facing Addiction in America: The Surgeon General's Report on Alcohol, Drugs, and Health. 2016

Priorities of Research on Prevention of Substance Use Problems

- Identifying and targeting biological factors
- Identifying risk and protective factors for substance use and misuse, substance use disorders, and related health and safety problems
- Enhancing people's resilience and buffering against stressors to help prevent substance use and promote healthy behaviors across the lifespan.
- Developing strategies to prevent substance use and the progression of substance use to harmful use
- Understanding why and how effective prevention approaches work and improving their uptake and reach.
- Developing tailored prevention strategies to help underserved or low-resource populations with risk factors for substance use and related health problems.
- Supporting research to evaluate effective harm reduction approaches
- Addressing stigma towards people who use drugs.
- Including local partners, end users, and potential funders in the research process, including the development and testing of potential strategies, and ways to communicate findings.

https://nida.nih.gov/research-topics/prevention#nida-advancing-science

Public Health Frameworks: Tiers of Prevention



https://www.iwh.on.ca/what-researchers-mean-by/primary-secondary-and-tertiary-prevention

Levels of Prevention

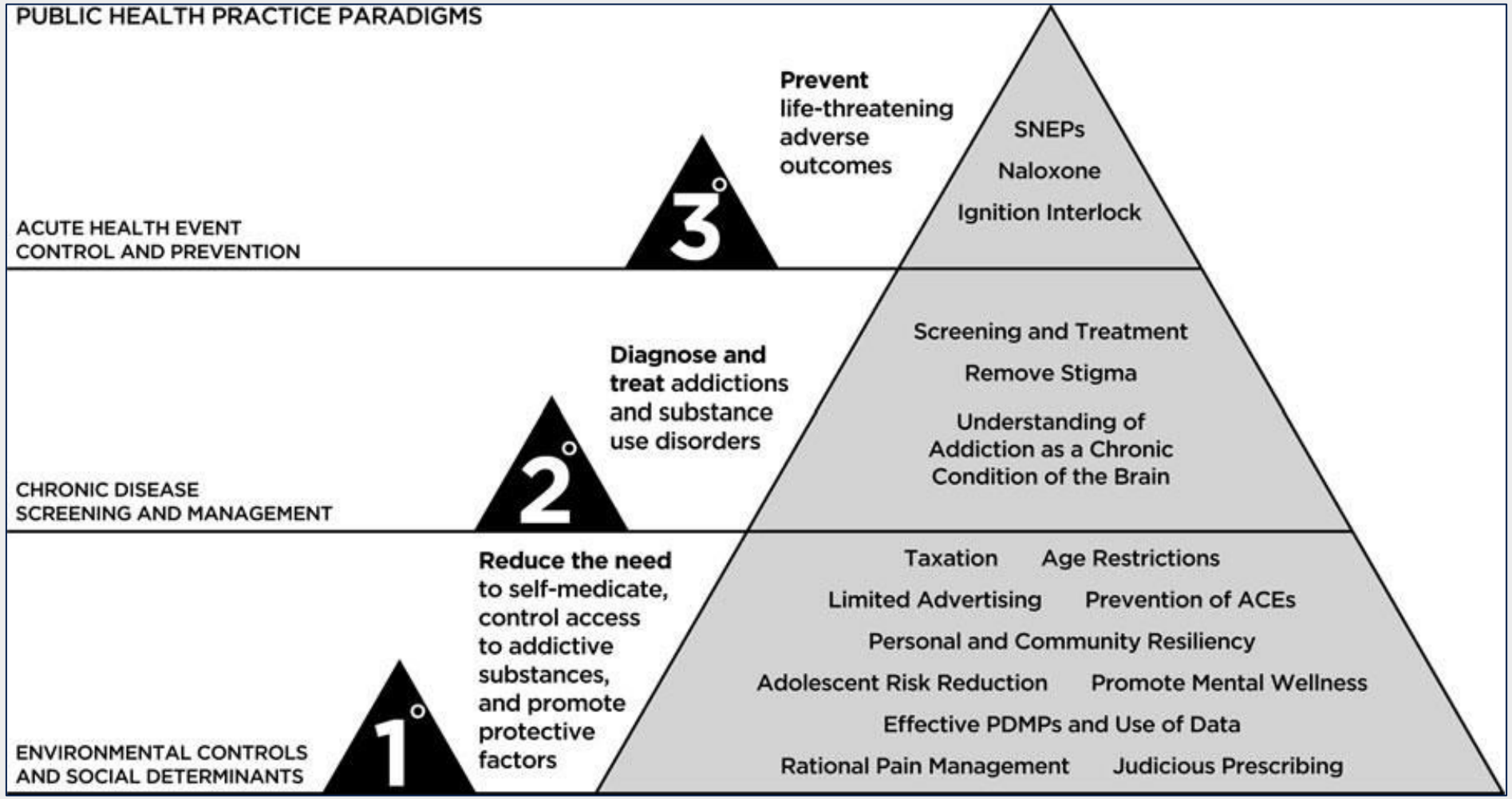
- **Primary prevention** aims to prevent disease or injury before it ever occurs

- **Secondary prevention** aims to reduce the impact of a disease or injury that has already occurred

- **Tertiary prevention** aims to soften the impact of an ongoing illness or injury that has lasting effects

https://www.iwh.on.ca/what-researchers-mean-by/primary-secondary-and-tertiary-prevention

Public Health Approaches to Preventing Substance Use Problems



Butler JC. 2017 ASTHO President's Challenge: Preventing Substance Misuse and Addiction. J Public Health Manag Pract. 2017;23(5):531-536.

Institute of Medicine Intervention Classifications

- **Universal:** broad approaches for the public or everyone
- **Selective:** strategies aimed at a subgroup determined to be at the highest risk for substance use
- **Indicated:** strategies designed to prevent the onset of substance use problems in individuals who are showing early danger signs

SAMHSA. Facing Addiction in America: The Surgeon General's Report on Alcohol, Drugs, and Health. 2016

Harm Reduction

- Programs aimed toward minimizing negative health, social and legal impacts associated with drug use while grounded in human rights



https://www.hri.global/what-is-harm-reduction, Health, Rights, and Drugs & AIDS 2019

Harm Reduction Services	Harm Reduction Supplies
• Overdose reversal education and training services • Navigation services to ensure linkage to HIV and viral hepatitis prevention, testing, treatment and care services, including antiretroviral therapy for HCV and HIV, pre-exposure prophylaxis (PrEP), post-exposure prophylaxis (PEP), prevention of mother to child transmission and partner services • Referral to hepatitis A and hepatitis B vaccinations to reduce risk of viral hepatitis infection • Provision of education on HIV and viral hepatitis prevention, testing, and referral to treatment services • Provision of information on local resources and/or referrals for PrEP	• Overdose reversal supplies, including the purchase of naloxone kits (this may include syringes for the purpose of administering injectable naloxone only) • Substance test kits, including fentanyl test strips • Safer sex kits, including condoms • Sharps disposal and medication disposal kits • Wound care supplies • Medication lock boxes • Supplies to promote sterile injection and reduce infectious disease transmission through injection drug use, exclusive of sterile needles, syringes, and other drug paraphernalia* • Safer smoking kits to reduce infectious disease transmission, excluding pipes/pipettes and other drug paraphernalia**

https://www.samhsa.gov/find-help/harm-reduction

Evidence-Based Prevention Interventions

- Programs and policies supported by research that reduce unhealthy substance use and related threats to public health
- Long-term and cost saving benefits
- Prevent other undesirable outcomes among youth: delinquency, psychiatric conditions, violence, and school dropout
- Vast majority of studies have been conducted on children, adolescents, and young adults
- Remain underutilized

SAMHSA. Facing Addiction in America: The Surgeon General's Report on Alcohol, Drugs, and Health. 2016

School-Based Interventions

- Strong study habits, academic support, bonding to school, self-efficacy and assertiveness, social problem-solving, emotional awareness and strong communication skills are correlated with decreasing risk of future drug use among youth

- Focus on building social, emotional, cognitive, and substance refusal skills and provide accurate information on rates and amounts of peer substance use

SAMHSA. Facing Addiction in America: The Surgeon General's Report on Alcohol, Drugs, and Health. 2016

School-Based Interventions

- Good Behavior Game
- Classroom-centered Intervention
- The Fast track Program
- Life Skills Training



- Delayed and lowered rates of alcohol, tobacco, and other substance use in adulthood

SAMHSA. Facing Addiction in America: The Surgeon General's Report on Alcohol, Drugs, and Health. 2016

Family-Based Interventions

- Focus on enhancing parenting skills
  - Nurse-Family Partnership
  - Strengthening Families Program: for Parents and Youth
  - Coping power
  - I Hear What You're Saying
  - Parent Handbook
- Reduce early alcohol and substance use

SAMHSA. Facing Addiction in America: The Surgeon General's Report on Alcohol, Drugs, and Health. 2016

Healthcare-Based Interventions

- Brief alcohol screening:
  - associated with significant reductions in alcohol consumption and alcohol-related problems in both adults and adolescents
  - recommended by USPSTF and American Academy of Pediatrics
- Motivational interviewing
  - associated with reductions in drinking

SAMHSA. Facing Addiction in America: The Surgeon General's Report on Alcohol, Drugs, and Health. 2016

Community Coalition-Based Interventions

- Change community-level physical, social and economic risk and protective factors
- Composed of representatives from multiple community sectors or organizations- government, law enforcement, health, and education
- Achieve community- wide reductions in substance use by planning and implementing prevention strategies

SAMHSA. Facing Addiction in America: The Surgeon General's Report on Alcohol, Drugs, and Health. 2016

Community Coalition-Based Interventions

- Communities that Care: community coalition tailors interventions to results of high school survey
  - associated with lower rates of alcohol and tobacco initiation in high school

- Communities Mobilizing for Change on Alcohol: aimed at reducing youth access to alcohol, increased enforcement of underage drinking laws, reduced availability of alcohol at community events, and media campaigns against underage drinking
  - associated with significant reductions in alcohol-related problem behaviors in young adults including DUIs

SAMHSA. Facing Addiction in America: The Surgeon General's Report on Alcohol, Drugs, and Health. 2016

Drinking-Oriented Interventions

- Policies that reduce alcohol availability and increase the costs of alcohol have immediate benefits in reducing drinking and harms from alcohol use:
  - Decrease morbidity
  - Decrease mortality
  - Decrease crime and violence

- Drinking-oriented policies include:
  - Raising alcohol taxes
  - Reducing alcohol production
  - Reducing alcohol sales
  - Preventing alcohol sales to minors

SAMHSA. Facing Addiction in America: The Surgeon General's Report on Alcohol, Drugs, and Health. 2016

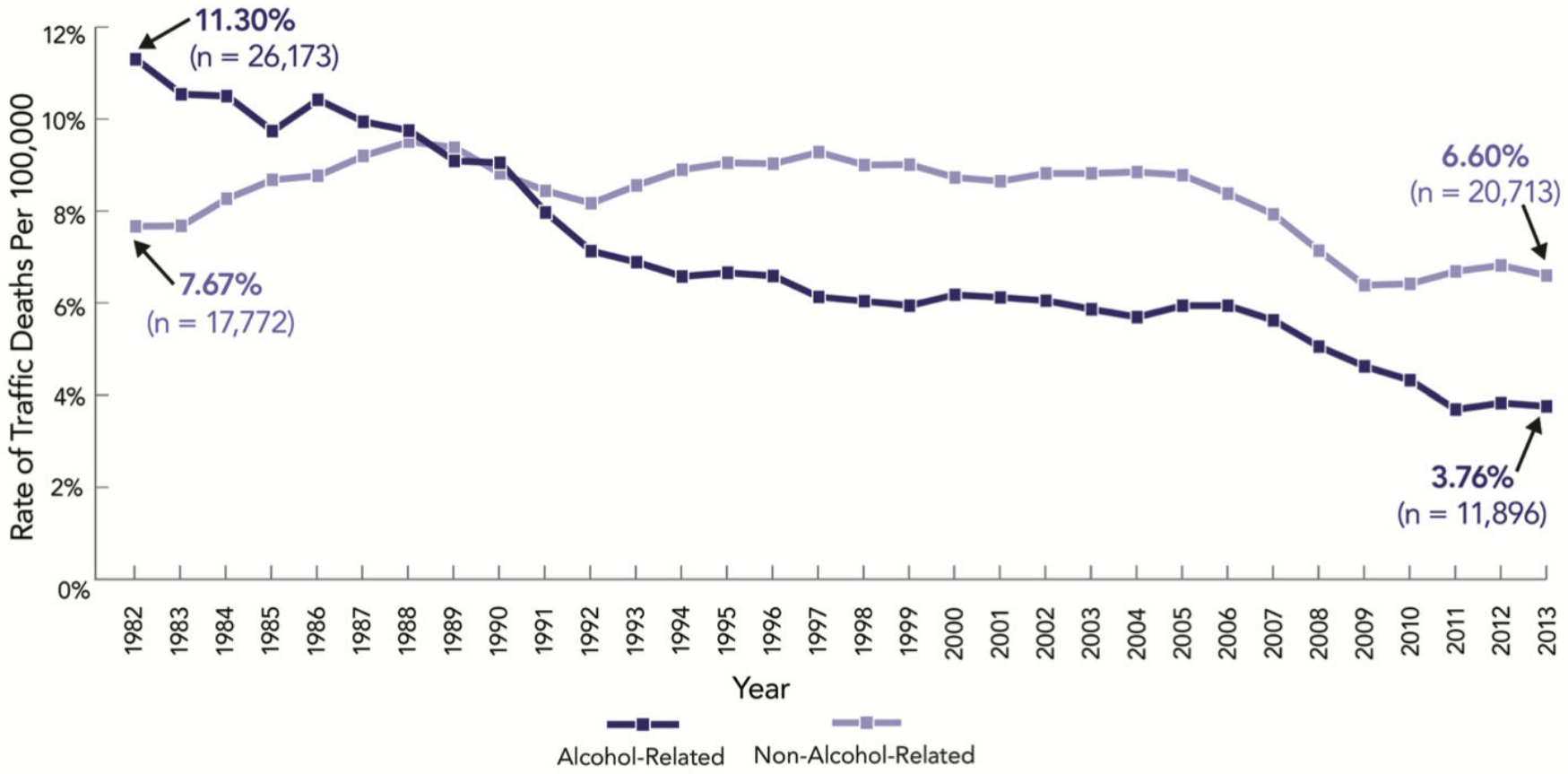
Driving-Oriented Interventions

- Policies that prevent an intoxicated person from driving have been found to:
  - Reduce rates of drinking and driving
  - Traffic crashes
  - Injuries
  - Deaths
- Driving-oriented policies include:
  - Driving under influence (DUI) blood alcohol content (BAC) limits
  - Sobriety checkpoints
  - Lower BAC limits for people convicted of DUI
  - Mandatory assessment and treatment of persons convicted of DUI
  - Raising minimum legal drinking age
  - Zero tolerance laws
  - Use/lose laws

SAMHSA. Facing Addiction in America: The Surgeon General's Report on Alcohol, Drugs, and Health. 2016

Driving-oriented Prevention Policies

Figure 3.2: Alcohol- Versus Non-alcohol-related Traffic Deaths, Rate per 100,000, All Ages, United States, 1982-2013

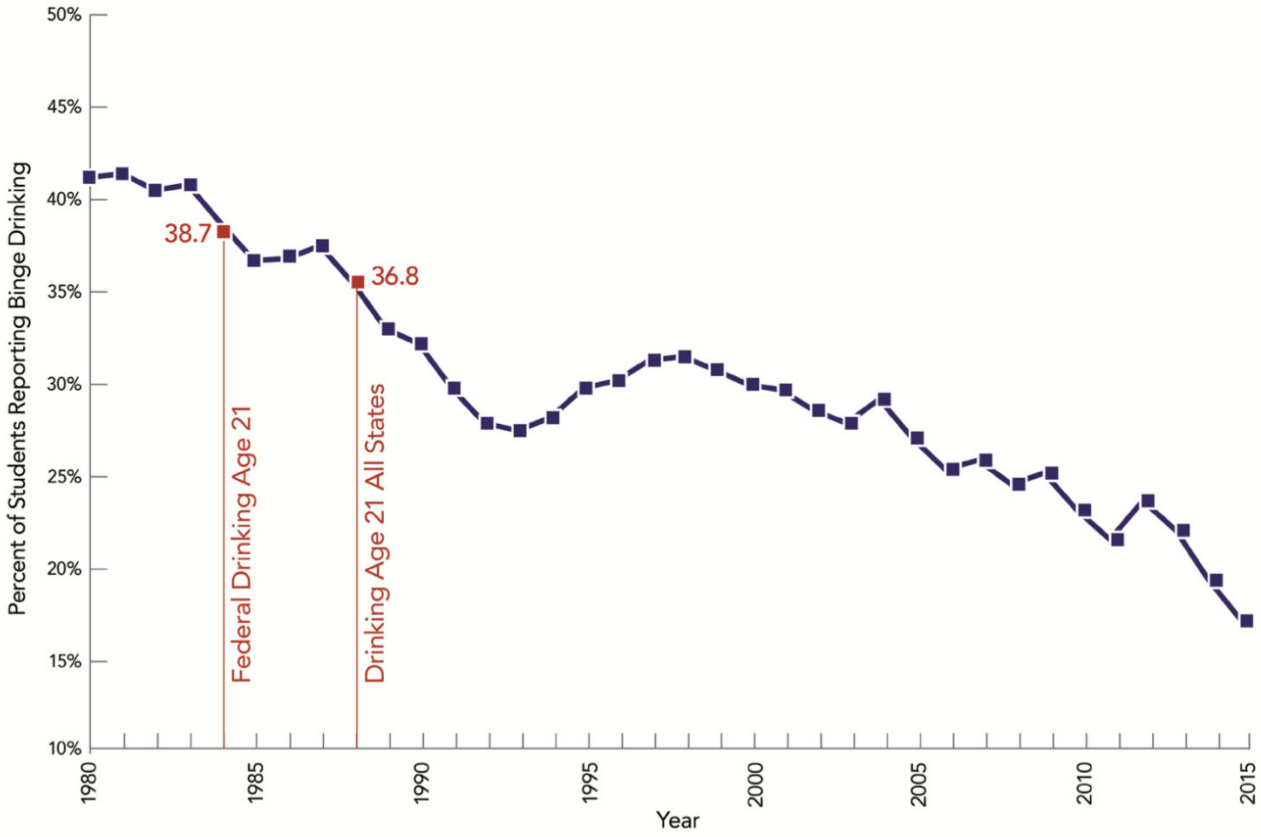


Source: Adapted from Hingson and White, (2014).[213]

SAMHSA. Facing Addiction in America: The Surgeon General's Report on Alcohol, Drugs, and Health. 2016

Driving-oriented Prevention Policies

Figure 3.3: Trends in 2-Week Prevalence of 5 or More Drinks in a Row among 12th Graders, 1980-2015



Note: The first vertical bar indicates institution of the MLDA 21 policy change in 7 states in 1984. The second vertical bar indicates federal passage of the MLDA 21 policy in all states in 1988.

Source: Adapted from Hingson and White, (2014).[213]

SAMHSA. Facing Addiction in America: The Surgeon General's Report on Alcohol, Drugs, and Health. 2016

Overall Benefits of Prevention Interventions

- Cost saving benefits for personal and public health
- Long-term positive effects that can last for generations

Economics of Prevention

The Washington State Institute for Public Policy developed a standardized model using scientifically rigorous standards to estimate the costs and benefits associated with various prevention programs. Benefit-per-dollar cost ratios for EBIs ranged from small returns per dollar invested to more than $64 for every dollar invested. These estimates are illustrated below in Table 3.3.

Table 3.3: Cost-Benefit of EBIs Reviewed by the Washington State Institute for Public Policy, 2016

Program	Benefit per Dollar Cost
Nurse-Family Partnership	$1.61
Raising Healthy Children/SSDP	$4.27
Good Behavior Game	$64.18
LifeSkills Training	$17.25
keepin' it REAL	$11.79
Strengthening Families Program 10-14	$5.00
Guiding Good Choices	$2.69
Positive Family Support/ Family Check Up	$0.62
Project Towards No Drug Abuse	$6.54
BASICS	$17.61

*Cost estimates are per participant, based on 2015 United States dollars.

Note: This is a general indication of the potential health and social value of EBIs. It is not possible to estimate specific cost-benefit for every EBI due to challenges in calculating accurate intervention effect sizes, the failure to document costs, the variation of methods used, and few mandates or incentives to complete this research. Reaching a consensus on standards for cost-benefit analyses and making them a routine part of prevention program evaluation could help policymakers choose EBIs that both prevent substance misuse and ensure that investments return benefits over the life course.

Source: Washington State Institute for Public Policy, (2016).[176]

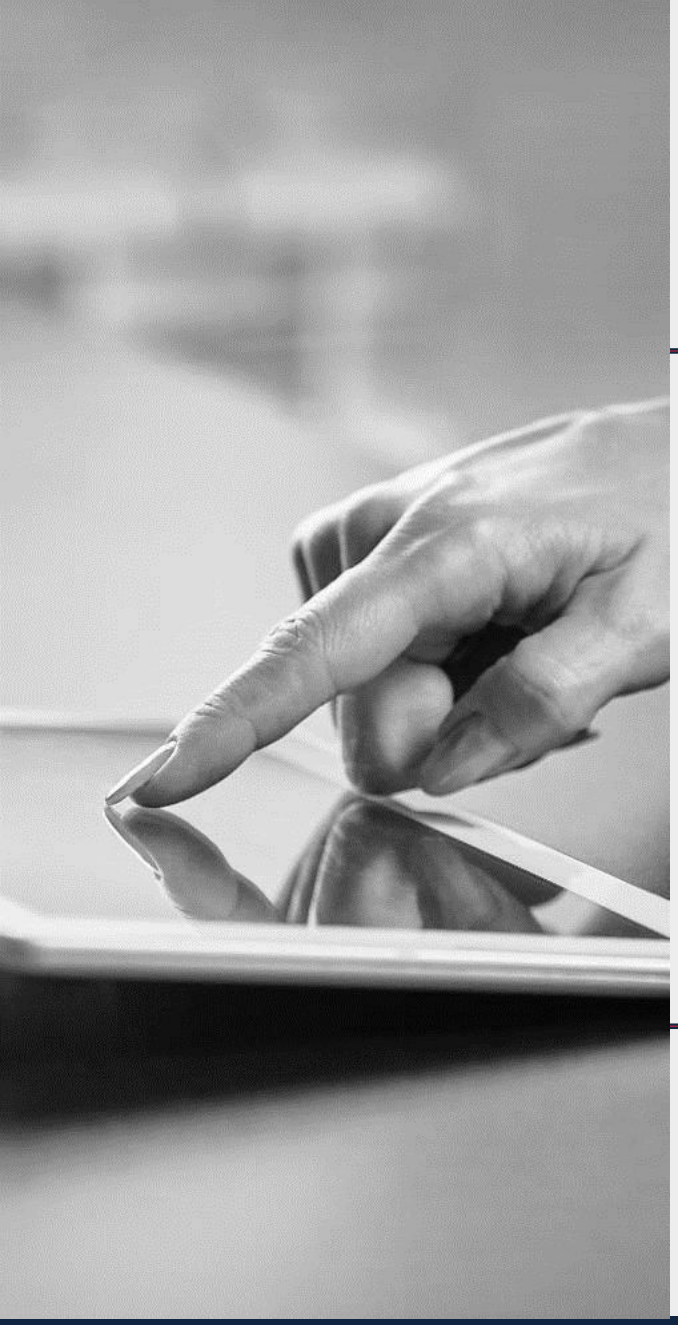
SAMHSA. Facing Addiction in America: The Surgeon General's Report on Alcohol, Drugs, and Health. 2016

Conclusions

- A well-established body of evidence-based interventions exists
- More implementation, systematic monitoring and research are needed

Thank You!

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ASAM REVIEW COURSE 2026

Genetics and Gender: Impacts on Diagnosis and Care

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Financial Disclosure

Leslie Hayes, MD

- No relevant disclosures

Genetics and Substance use disorder

- Overview
- Pharmacogenetics
  - Pharmacokinetics
  - Pharmacodynamics
- Epigenetics
- Polygenic risk scores

Disclaimer for genetics portion of talk

- Almost all the research done on addiction and genetics has been done on persons of European ancestry.

*Gerring, Z.F., Thorp, J.G., Treur, J.L. et al. The genetic landscape of substance use disorders. Mol Psychiatry **29**, 3694–3705 (2024). https://doi.org/10.1038/s41380-024-02547-z*

Second disclaimer for genetics portion of talk

- December 2024 SAMHSA Advisory:
- Genetic testing should be used only as part of a comprehensive evaluation, and practitioners need to be aware of the limitations and risks.

Genetics of substance use disorder

Nature vs nurture better phrased as nature and nurture for substance use disorder. [1]

SUD is likely polygenic. Multiple genes, each having a small effect contribute to risk of developing SUD.[2]

1. *Genetics and Epigenetics of Addiction. in DrugFacts. https://www.drugabuse.gov/publications/drugfacts/genetics-epigenetics-addi*

2. *Prom-Wormley EC, Ebejer J, Dick DM, Bowers MS. The genetic epidemiology of substance use disorder: A review. Drug Alcohol Depend. 2017 Nov 1;180:241-259. doi: 10.1016/j.drugalcdep.2017.06.040. Epub 2017 Aug 1. PMID: 28938182; PMCID: PMC5911369*

Genetics of substance use disorder

Environment has stronger influence on initiation, whereas genetic factors are more important in progression and development of SUD.[1]

Heritabilities of SUD's range from 0.39 for hallucinogens to 0.72 for cocaine.[2]

1.. Deak JD, Johnson EC. Genetics of substance use disorders: a review. Psychol Med. 2021 Oct;51(13):2189-2200. doi: 10.1017/S0033291721000969. Epub 2021 Apr 21. Erratum in: Psychol Med. 2022 Mar 02;:1. PMID: 33879270; PMCID: PMC8477224.

2. 2. Bevilacqua and Goldman. Genes and Addictions. Clin Pharmacol Ther. 2009 APril; 85(4) pp 359-361

Twin studies – direct effect of genes

- Both the Swedish and Vietnam twin studies showed significantly higher concordance rates for substance use disorder in monozygotic twins than in dizygotic twins.[1,2]

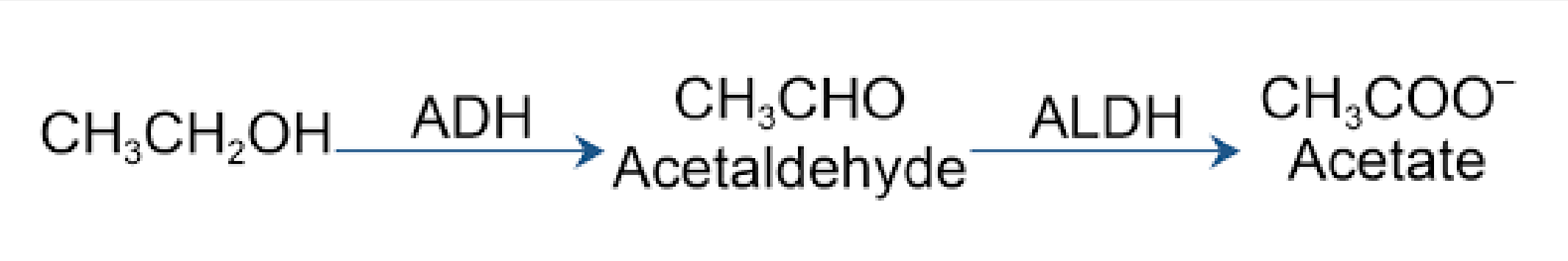
[1]*Gelernter et Kranzler. Chapter 2. Genetics of Addiction in Galanter et al. Textbook of Substance Abuse Treatment. The American Psychiatric Publishing 2015 pp. 26-45*

[2]*Bevilacqua and Goldman. Genes and Addictions. Clin Pharmacol Ther. 2009 April; 85(4) pp 359-361*

Pharmacogenetics

Pharmacokinetics

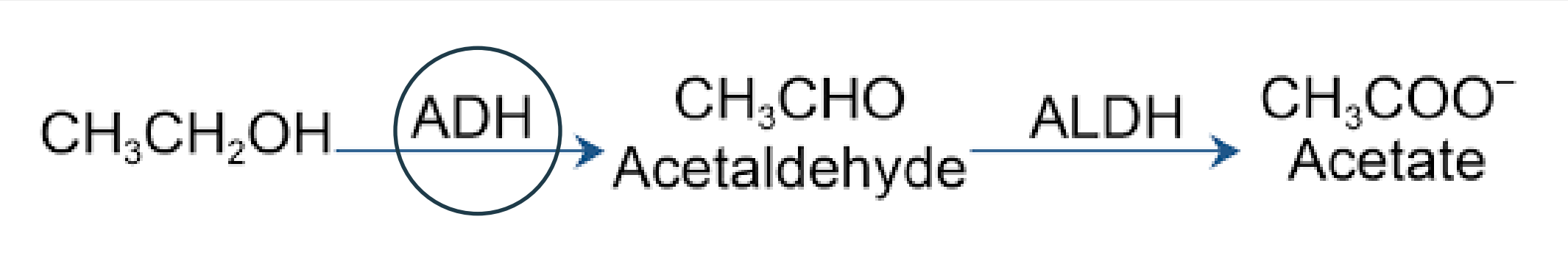
- Metabolism of alcohol



https://www.niaaa.nih.gov/publications/alcohol-metabolism accessed 4/14/2024

Pharmacokinetics

- Metabolism of alcohol

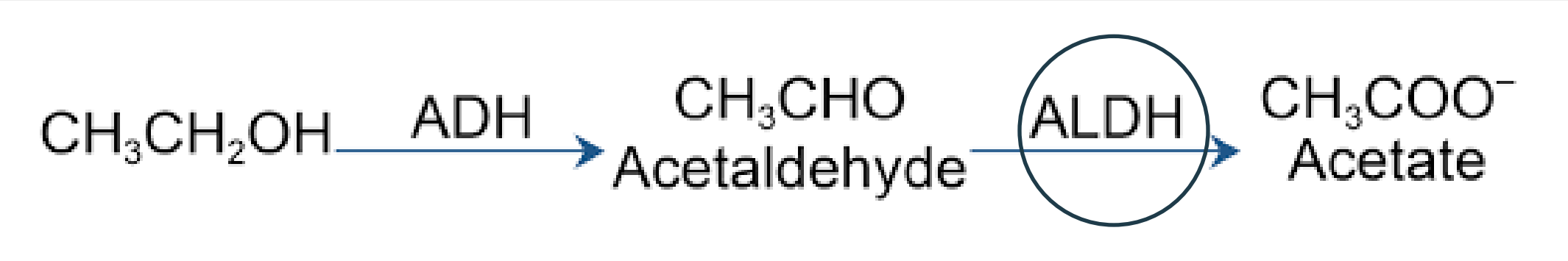


Alcohol dehydrogenase that metabolizes rapidly will cause high levels of acetaldehyde

https://www.niaaa.nih.gov/publications/alcohol-metabolism *accessed 4/14/2024*

Pharmacokinetics

- Metabolism of alcohol



Acetaldehyde dehydrogenase that metabolizes too slowly will lead to high levels of acetaldehyde

https://www.niaaa.nih.gov/publications/alcohol-metabolism accessed 4/14/2024

Pharmacokinetics

Both the ADH1 B2-His47 ARG allele of Alcohol Dehydrogenase 1B and ALDH-Glu487 Lys allele of Aldehyde Dehydrogenase 2 can cause flushing, nausea, and headache with alcohol, due to accumulation of acetaldehyde.[1]

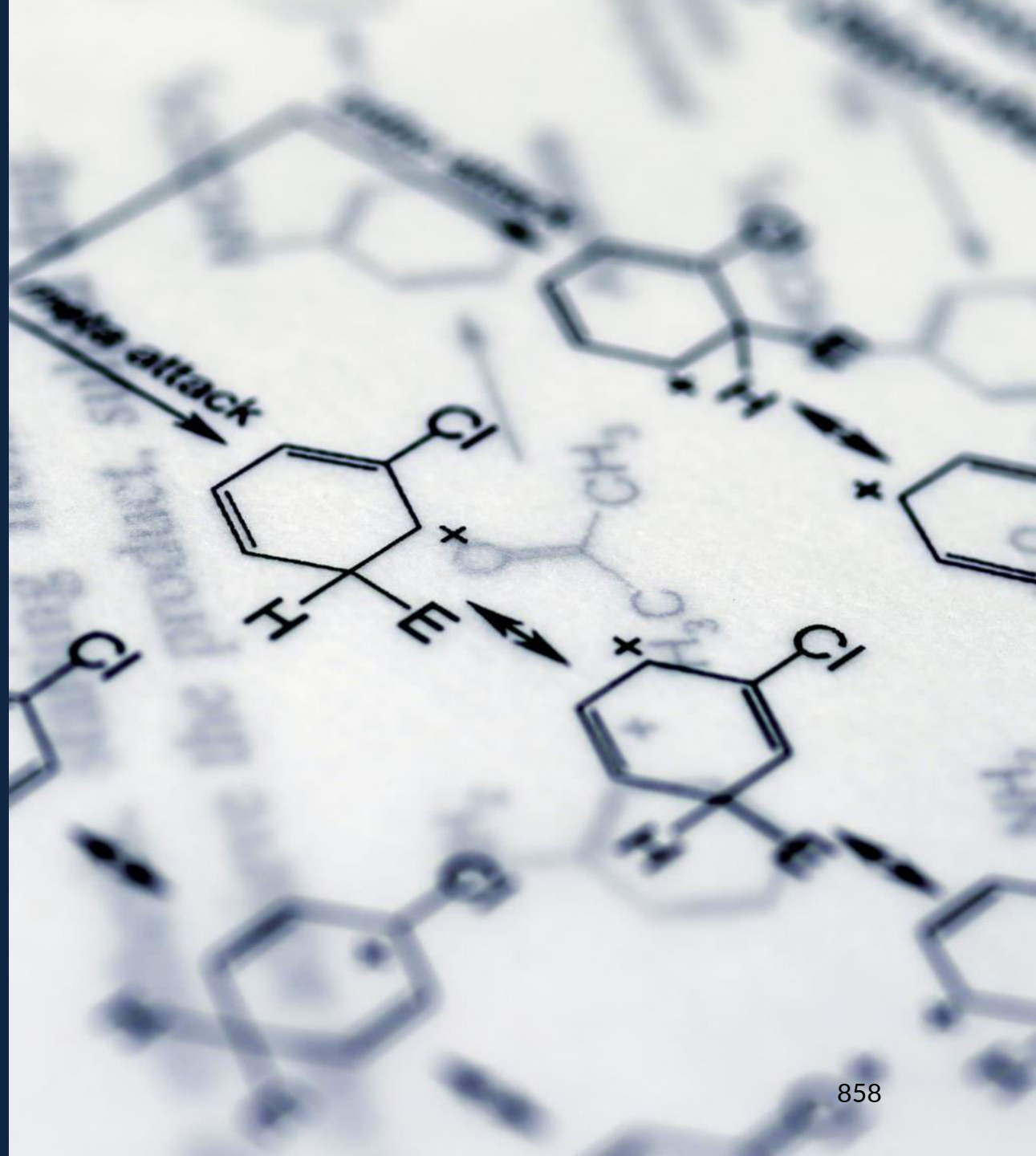
More common in person of South Asian descent and those of Jewish ancestry.

Homozygotes nearly completely protected from alcoholism.

[1]*Zajicek and Karan. Pharmacokinetic and Pharmacodynamic Principles in Miller et al. The ASAM Principles of Addiction Medicine. Wolters Kluwer 2019. p. 97-98*

Pharmacodynamics

Genes that code for the receptor for various substances can affect the likelihood of substance use disorder for that substance



Pharmacodynamics -- Nicotine

- CHRNA and CHRNB = family of genes that encode subunits of nicotinic acetylcholine receptors
- The gene cluster encoding the neuronal acetylcholine receptor (CHRNA3-CHRNA5-CHRNB4) seems to be closely related to quantity and frequency of cigarette use.

Gelernter J, Polimanti R. Genetics of substance use disorders in the era of big data. Nat Rev Genet. 2021 Nov;22(11):712-729. doi: 10.1038/s41576-021-00377-1. Epub 2021 Jul 1. PMID: 34211176; PMCID: PMC9210391.



Pharmacodynamics – opioid receptor

- The mu-1 opioid receptor gene (OPRM1) codes for the mu opioid receptor.
  - The G allele of the OPRM1 is related to a lower pain threshold and higher opioid consumption in the post-op period.
- The catchol-O-methyltransferase (COMT) gene regulates the expression of the mu-opioid receptor.

Bugada D, Lorini LF, Fumagalli R, Allegri M. Genetics and Opioids: Towards More Appropriate Prescription in Cancer Pain. Cancers (Basel). 2020 Jul 18;12(7):1951. doi: 10.3390/cancers12071951. PMID: 32708424; PMCID: PMC7409018.

Epigenetics

- Epigenetics is the study of epigenomes which are markers that turn genes on or off or express them more or less strongly.
  - Changes to the epigenomes can be passed down anywhere from 2-12 generations.
  - Environmental factors like diet, stress, and prenatal drug use can cause epigenetic changes which predispose to substance use disorder.

Polygenic risk scores for alcohol use disorder

- Polygenic risk scores were useful for showing a predisposition.
  - In a recent JAMA study, the 5% of samples with the highest polygenic risk score were approximately twice as likely to develop AUD as the rest of the sample (OR 1.96, [95% CI, 1.78-2.16] [1]
  - The 5% of samples with the lowest polygenic risk score were approximately twice as likely to develop AUD as the rest of the sample (OR 0.57 [95% CI, 0.39-0.84][1]
- Another study showed an increase in psychological distress in people as score increased, but also an increased likelihood to engage in follow-up behaviors such as seeking additional information, talking to a healthcare provider, and reducing drinking behaviors.[2]

Lai D, Zhang M, Abreu M, et al. Alcohol Use Disorder Polygenic Score Compared With Family History and ADH1B. JAMA Netw Open. 2024;7(12):e2452705. doi:10.1001/jamanetworkopen.2024.52705

Driver MN, Kuo SI, Dron JS, Austin J, Dick DM. The impact of receiving polygenic risk scores for alcohol use disorder on psychological distress, risk perception, and intentions to reduce drinking. Am J Med Genet B Neuropsychiatr Genet. 2023 Jul-Sep;192(5-6):93-101. doi: 10.1002/ajmg.b.32933. Epub 2023 Mar 1. PMID: 36856135

Gender and Substance use disorder outline

Gender differences in presentation of substance use disorder

Differences in medical problems for males and females

LGBTQ and SUD

Incarceration and SUD

Sex work and SUD

Differences in treatment for SUD

A word about terminology

- None of the studies I found looking at gender and substance use disorder specified cis- or trans-gender.
- I have generally used the terms (female/male or woman/man) the study did. I have also used the terms for substance use disorder (addiction, dependence, SUD) from the study.

Social stigma and substance use disorder

- Women are less likely to develop problems as a results of substance use because they are less likely to use substances. However, because of this, when they do develop problems, they deviate more from the female norm compared with a man with an addiction.

Dorte H., Morten H., (2009), Women and Substance Use Disorders. In: Some Issues in Women's Studies, and Other Essays (A.R. Singh and S.A. Singh eds.), MSM, 7, Jan - Dec 2009, p50-62

Different presentations of Substance Use Disorder in Men and Women

Gender differences and substance use disorder

Men are more likely than women to use almost all types of illicit drugs.[1,2]

- Women use prescription drugs at greater rates than men and have higher rates of prescription drug use disorder.[2]
- Otherwise, men have higher rates of drug use disorder.[2]

Men have higher rates of alcohol use, including binge drinking, than women[1,2], except for teens and young adults, where rates were similar until recently.

- Female teens currently use more alcohol than males.[3]
- Young adult women binge drink more than young adult men.[4]

Substance Use in Women Research Report Sex and Gender Differences in Substance Use https://www.drugabuse.gov/publications/research-reports/substance-use-in-women/sex-gender-differences-in-substance-use Accessed 2/18/2021

Center for Behavioral Health Statistics and Quality. (2023). Results from the 2022 National Survey on Drug Use and Health: Detailed tables. Substance Abuse and Mental Health Services Administration. https://www.samhsa.gov/data/report/2022-nsduh-detailed-tables

Hoots BE, Li J, Hertz MF, et al. Alcohol and Other Substance Use Before and During the COVID-19 Pandemic Among High School Students — Youth Risk Behavior Survey, United States, 2021. MMWR Suppl 2023;72(Suppl-1):84–92. DOI: http://dx.doi.org/10.15585/mmwr.su7201a10

Gender differences and substance use disorder

- Women are more likely to be introduced to injection drug use by their male sexual partner, whereas men are more likely to be injected by a friend.[1]

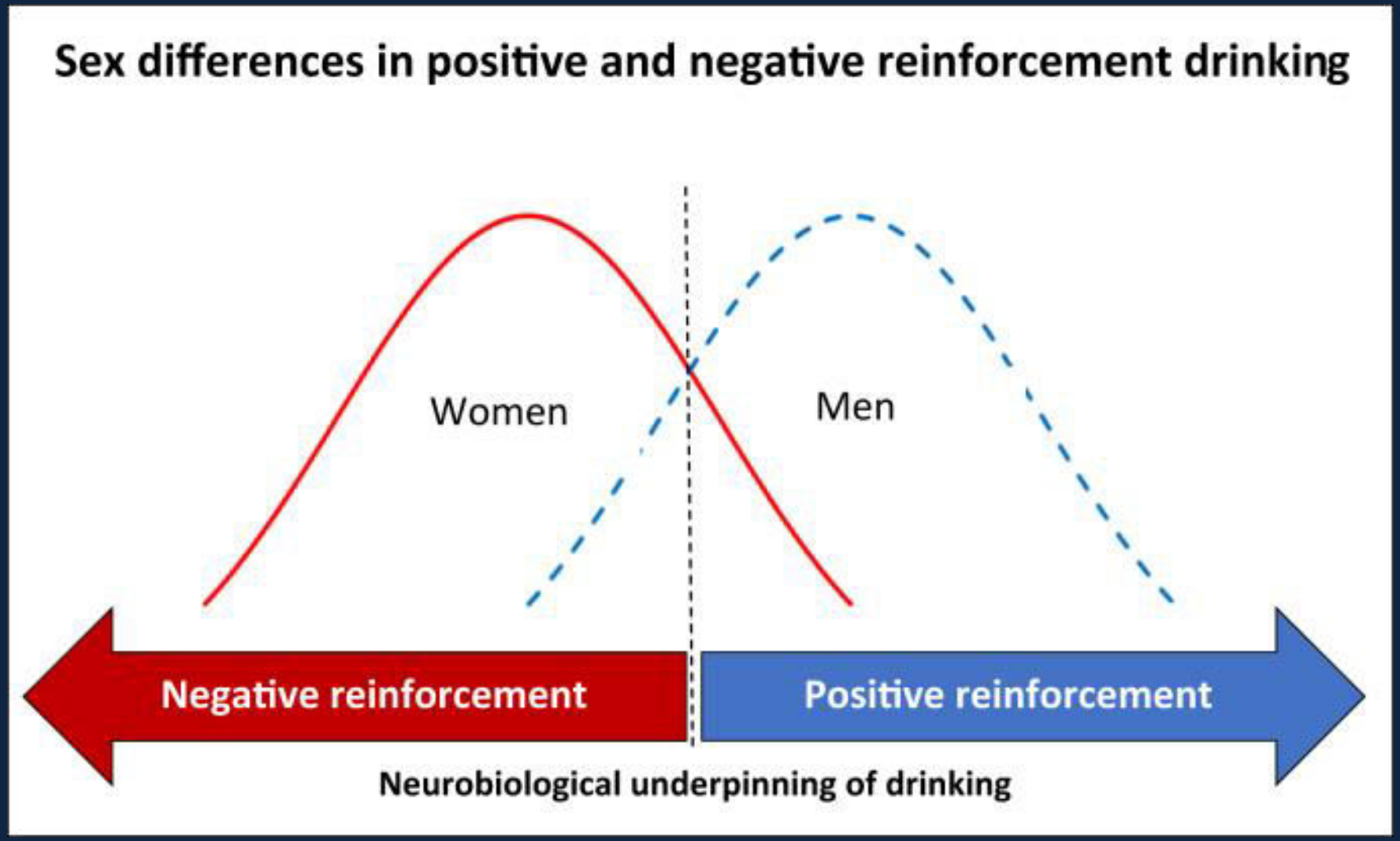
1. *Greenfield et al. Substance Abuse in Women. Psychiatr Clin Nort Am. 2010 June; 33(2): 339-355*

Gender differences and substance use disorder

- Women are more likely to use prescription opioids [1] and to drink[2] to self-medicate for anxiety or stress.
- Men are more likely to use prescription opioids for experimentation or to get high.[2] Men are more likely to drink to enhance positive emotions or conform to a group.[3]

1. Final Report: Opioid Use, Misuse, and Overdose in Women.. Office on Women's Health. July 19, 2017

2. Greenfield et al. Substance Abuse in Women. Psychiatr Clin Nort Am. 2010 June; 33(2): 339-355



Peltier MR, Verplaetse TL, Mineur YS, Petrakis IL, Cosgrove KP, Picciotto MR, McKee SA. Sex differences in stress-related alcohol use. Neurobiol Stress. 2019 Feb 8;10:100149. doi: 10.1016/j.ynstr.2019.100149. PMID: 30949562; PMCID: PMC6430711.

Mental illness and substance use disorder

- Men and women have different co-occurring mental illness with substance use disorder

Rhee TG, Rosenheck RA. Gender Differences in Psychiatric and Behavioral Health Burden Among Adults With Alcohol and Other Substance Use Disorders in the United States. J Addict Med. 2022 May-Jun 01;16(3):295-302. doi: 10.1097/ADM.0000000000000890. PMID: 34310435.

Mental illness and substance use disorder

	No alcohol use disorder or substance use disorder	Alcohol use disorder only	Substance use disorder +/- alcohol use disorder
Past year depression-- males	5.7%	10.2%	21.4%
Past year depression--females	11.9%	21.2%	35.9%
Past year antisocial personality d/o --males	4.5%	11.6%	22.0%
Past year antisocial personality d/o -- females	1.7%	5.8%	13.2%
Lifetime suicide attempt -- males	2.7%	5.5%	11.8%
Lifetime suicide attempt-- females	5.6%	11.1%	24.7%

Rhee TG, Rosenheck RA. Gender Differences in Psychiatric and Behavioral Health Burden Among Adults With Alcohol and Other Substance Use Disorders in the United States. J Addict Med. 2022 May-Jun 01;16(3):295-302. doi: 10.1097/ADM.0000000000000890. PMID: 34310435.

Women have increased levels of mortality at lower levels of intake

- A 2023 systematic review and meta-analysis of 107 cohort studies involving more than 4.8 million participants found a significantly increased risk of all-cause mortality among female drinkers who drank 25 or more grams per day and among male drinkers who drank 45 or more grams per day.
- They also have a “telescoped” course and develop the effects more rapidly.

1. *Zhao J, Stockwell T, Naimi T, Churchill S, Clay J, Sherk A. Association Between Daily Alcohol Intake and Risk of All-Cause Mortality: A Systematic Review and Meta-analyses. JAMA Netw Open. 2023;6(3):e236185. doi:10.1001/jamanetworkopen.2023.6185*
2. *Zweben. Special Issues in Treatment: Women in Miller et al. The ASAM Principles of Addiction Medicine, Sixth Edition. Wolters Kluwer 2019 p. 529*

Men die at higher rates than women from alcohol

- Despite the higher risk for alcohol-related problems for women if they do drink, men still have much higher death rates from alcohol because they drink at higher rates
- A study from 2023 of alcohol-related deaths in the United states showed that the mortality burden was higher among male individuals than female individuals, with male individuals being 2.88 (95% CI, 2.86-2.89) times more likely to die compared with female individuals.

Karaye IM, Maleki N, Hassan N, Yunusa I. Trends in Alcohol-Related Deaths by Sex in the US, 1999-2020. JAMA Netw Open. 2023;6(7):e2326346. doi:10.1001/jamanetworkopen.2023.26346

CDC guidelines for risky drinking



- Excessive drinking (or risky drinking or at risk drinking) is defined as the following:
- Binge drinking, the most common form of excessive drinking, is defined as consuming
  - For women, 4 or more drinks during a single occasion.
  - For men, 5 or more drinks during a single occasion.

https://www.cdc.gov/alcohol/fact-sheets/alcohol-use.htm *accessed 11/10/19*

CDC guidelines for risky drinking

- Excessive drinking (or risky drinking or at risk drinking) is defined as the following:
- Heavy drinking is defined as consuming
  - For women or men > 65, 8 or more drinks per week.
  - For men < 65, 15 or more drinks per week.



https://www.cdc.gov/alcohol/fact-sheets/alcohol-use.htm accessed 11/10/19

LGBTQ Persons and Substance Use

LGBTQ People have higher rates of SUD

- Data from the 2020 National Survey on Drug Use and Health (NSDUH) suggest sexual minority adults report increased consumption and substance use disorders compared to heterosexual adults.
  - (In this survey, sexual minority adults include individuals who describe themselves as lesbian, gay, or bisexual.)
- Sexual minority adults had roughly double the rate of marijuana use, misuse of opioids, and alcohol use disorder compared to heterosexual adults.

https://nida.nih.gov/research-topics/substance-use-suds-in-lgbtq-populations Accessed 11/12/2023

This rate is high for LGBTQ youths, especially if they are not accepted

- Youths experiencing “conversion therapy,” or physical harm due to their LGBTQ identity have higher rates of drug and alcohol use.[1]
- Rates are higher for LGBTQ youth overall.[2]

https://www.thetrevorproject.org/research-briefs/substance-use-and-suicide-risk-among-lgbtq-youth-jan-2022/ Accessed 11/12/2023

Hoots BE, Li J, Hertz MF, et al. Alcohol and Other Substance Use Before and During the COVID-19 Pandemic Among High School Students — Youth Risk Behavior Survey, United States, 2021. MMWR Suppl 2023;72(Suppl-1):84–92. DOI: http://dx.doi.org/10.15585/mmwr.su7201a10

Reasons for increased substance use and misuse among LBGTQ persons

- High levels of stress
- Lack of cultural competency and health care discrimination in the medical community
- Targeted marketing efforts by alcohol and tobacco companies
- Discrimination in employment
- Discrimination in housing

https://www.americanprogress.org/article/why-the-gay-and-transgender-population-experiences-higher-rates-of-substance-use/ Accessed 11/12/2023

Sex Hormones and Substance Use Disorder

Menstrual cycle and substance use disorder

- Women who attempt to quit smoking during the luteal phase of their menstrual cycle had more favorable outcomes than women who attempted to quit during the follicular phase.[1]
- Response to stimulants, such as cocaine and methamphetamine, is higher in the follicular than the luteal phase.[2]

Allen et al. Menstrual phase effects on smoking relapse. Addiction. Volume 103. Issue 5. April 14, 2008.

Terner et al. Menstrual cycle phase and responses to drugs of abuse in humans.Drug Alcohol Depend. 2006 Sep 1;84(1):1-13.

Testosterone and substance use

- Testosterone levels in men are suppressed by both alcohol[1] and opioids[2].

1. *Malabanan and Jack. Endocrine and Reproductive Disorders Related to Alcohol and Other Drug Use. The ASAM Principles of Addiction Medicine. Sixth Edition. Wolters Kluwer 2019 p. 1298*
2. *Bawor et al. Testosterone suppression in opioid users: A systematic review and meta-analysis. Drug and Alcohol Dependence 149 (2015) 1–9*

Gender differences in incarceration and substance use disorder

Incarceration and substance use disorder

- An estimated 65% percent of the United States prison population has an active SUD.
- Another 20% percent did not meet the official criteria for an SUD, but were under the influence of drugs or alcohol at the time of their crime.

https://nida.nih.gov/publications/drugfacts/criminal-justice Accessed 8/6/2023

Incarceration and substance use disorder

- Men with substance use disorder are much more likely to have a history of incarceration than women with substance use disorder. Both are more likely to have a history of incarceration than persons without substance use disorder.

Rhee TG, Rosenheck RA. Gender Differences in Psychiatric and Behavioral Health Burden Among Adults With Alcohol and Other Substance Use Disorders in the United States. J Addict Med. 2022 May-Jun 01;16(3):295-302. doi: 10.1097/ADM.0000000000000890. PMID: 34310435.

Incarceration and substance use disorder

	No history of alcohol or substance use disorder	Alcohol use disorder without other substance use disorder	Any substance use disorder +/- alcohol use disorder
History of incarceration -- females	4.9%	13.9%	27.5%
History of incarceration -- males	15.5%	28.1%	45.5%

Rhee TG, Rosenheck RA. Gender Differences in Psychiatric and Behavioral Health Burden Among Adults With Alcohol and Other Substance Use Disorders in the United States. J Addict Med. 2022 May-Jun 01;16(3):295-302. doi: 10.1097/ADM.0000000000000890. PMID: 34310435.

Incarceration and gender differences

- Blacks and Latinos are far more likely to be incarcerated for drug law violations than whites, even though rates of drug use and drug selling are similar.[1]

1. http://www.drugpolicy.org/resource/drug-war-mass-incarceration-and-race-englishspanish *Accessed 11/15/19*

Sex work and substance use disorder

There is a significant correlation between sex work and substance use disorder

- A 2021 meta-analysis looked at 86 studies in 46 countries[1]
  - Most studies reported lifetime drug use among female sex workers (32 studies from 20 countries), and pooled prevalence in this sub-group was 29% (95% CI 24–34%).
  - There was insufficient data for estimates for male and transgender sex workers.
- A 2008 cross-sectional, secondary data analysis of 1606 women and 3001 men entering substance use treatment in the United States found a high incidence of sex work among people entering treatment.[2]
  - 50.8% of women and 18.5% of men reported prostitution in their lifetime. 41.4% of women and 11.2% of men reported prostitution in the past year
  - Women who engaged in prostitution had far more episodes than the men did.

1. *Iversen J, Long P, Lutnick A, et al.* ***Patterns and Epidemiology of Illicit Drug Use Among Sex Workers Globally: A Systematic Review.*** *2021 Apr 29. In: Goldenberg SM, Morgan Thomas R, Forbes A, et al., editors. Sex Work, Health, and Human Rights: Global Inequities, Challenges, and Opportunities for Action [Internet]. Cham (CH): Springer; 2021. Chapter 6. Available from: https://www.ncbi.nlm.nih.gov/books/NBK585687/ doi: 10.1007/978-3-030-64171-9_6*
2. *Burnette ML, Lucas E, Ilgen M, Frayne SM, Mayo J, Weitlauf JC.* ***Prevalence and Health Correlates of Prostitution Among Patients Entering Treatment for Substance Use Disorders.*** *Arch Gen Psychiatry. 2008;65(3):337–344. doi:10.1001/archpsyc.65.3.337*

There is a significant correlation between sex work and substance use disorder

- It is often assumed that women who use drugs and participate in sex work began sex work to pay for drugs, but it is often the other way around, that they began using drugs to cope with the trauma of sex work.[1]
  - A study in Chicago that interviewed 222 women doing sex work found that women on the streets, in drug houses, and in hotels reported high rates of forced sex and physical violence, with almost one-fourth of women in drug houses being raped more than 10 times.
- Sex workers who are sexually assaulted do not get good support from the medical system, the legal system, or family and friends.
  - It is often believed that they deserve sexual assault because of their work.
  - It is also commonly believed that they are not traumatized by sexual assault because of their work.

https://www.caase.org/mental-health-impacts-of-sex-trade/ accessed 12/9/2023

Raphael J. and Shapiro D. Sisters speak out: the lives and needs of prostituted women in Chicago a research study Center for Impact Research. www.impactresearch.org August 2002

Natalie West with Tina Horn. We Too. Essays on Sex Work and Survival. Feminist Press. 2021

Relationship of violence to Substance Use Disorder

“Trauma is both a risk factor for and a consequence of substance use.”

Substance Abuse and Mental Health Services Administration. (2021). Addressing the Specific Needs of Women for Treatment of Substance Use Disorders. Advisory. Publication No. PEP20-06-04-002

Women and violence and SUD

- Girls with a history of childhood sexual abuse are 3 times as likely to develop an addictive disorder as girls without that history.[1]
- One study showed lifetime intimate partner violence victimization was reported by 46.7% of women and 9.5% of men entering SUD treatment.

1. Zweben. Special Issues in Treatment: Women in Miller et al. The ASAM Principles of Addiction Medicine. Wolters Kluwer 2019 p. 532
2. Schneider et al. Violence and Victims, Volume 24, Number 6, 2009 744 © 2009 Prevalence and Correlates of Intimate Partner Violence Victimization Among Men and Women Entering Substance Use Disorder Treatment

Gender Differences in Treatment

Treatment Differences

- Women have been found to do better in treatment programs that reduce barriers to treatment or address women's needs.
  - Provision of childcare
  - Prenatal care
  - Treatment for co-occurring mental health problems
  - Comprehensive approach to treatment
  - Supplemental services that address women-focused topics
- Actual treatment for substance use disorder probably doesn't vary

McCrady BS, Epstein EE, Fokas KF. Treatment Interventions for Women With Alcohol Use Disorder. Alcohol Res. 2020 Jul 30;40(2):08. doi: 10.35946/arcr.v40.2.08. PMID: 32742894; PMCID: PMC7384374

Gender Differences in Treatment – Different Responses to Medication

- Male smokers have been found to respond better to nicotine replacement therapy than female smokers.
- Women may respond less favorably to bupropion for tobacco.
- Naltrexone was found to reduce the stimulating effects of alcohol in women but not men.

Polak K, Haug NA, Drachenberg HE, Svikis DS. Gender Considerations in Addiction: Implications for Treatment. Curr Treat Options Psychiatry. 2015 Sep;2(3):326-338. doi: 10.1007/s40501-015-0054-5. PMID: 26413454; PMCID: PMC4578628.

Take Home Messages:

- Genetic risk for substance use disorder is usually polygenic.
- Some of the genes that may affect risk include the genes affecting metabolism of alcohol to aldehyde to acetate, the genes affecting the receptor (CHRNA and CHRNB and OPRM1) and epigenetic changes

Take Home Messages:

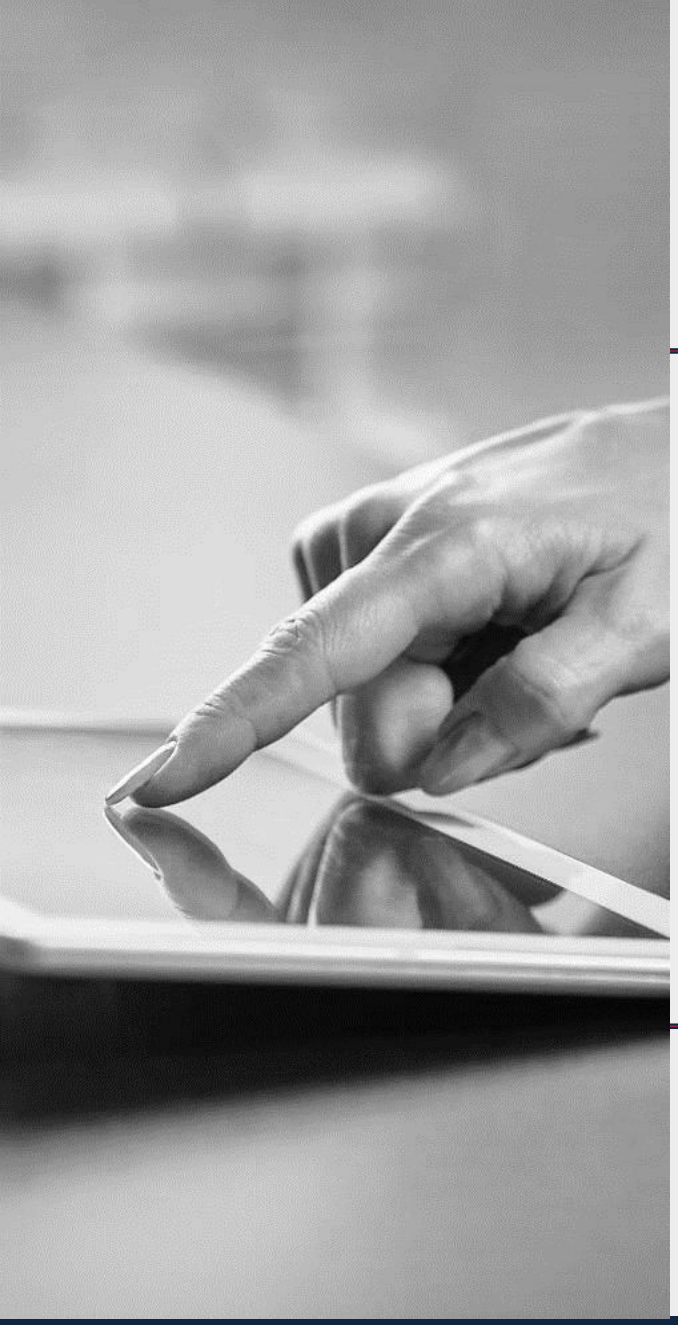
- Women are less likely to use substances or have a substance use disorder, but when they do, the consequences are usually more severe.
- Be aware of the correlation between violence and substance use disorder.
- Recognize that women with SUD may have substantially different co-morbidities and social factors than men do, and address those. There may not be much difference in actual substance use disorder treatment.

Which of the following is true about genetics and substance use disorder?

A. Some alleles of the ADH2 gene will cause flushing and nausea with alcohol ingestion. People who are homozygous for these alleles are protected against alcohol use disorder
B. There has been one gene found that completely determines the likelihood of developing SUD
C. Genetic factors influence whether people start using drugs, whereas environment influences how likely they are to continue.
D. Epigenetic changes affect only the individual and are not passed down.

Which of the following is true regarding gender differences with respect to substance use disorder?

A. Men are less likely to use illicit drugs than women are
B. Women are more likely to use drugs to celebrate, whereas men are more likely to use to cope with physical or emotional pain
C. Women will suffer adverse effects from their use of similar levels of alcohol much sooner than men will
D. Women with substance use disorder are more likely to have a history of incarceration than men are



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ASAM REVIEW COURSE 2026

Pharmacology and Toxicology: Principles, Applications, and Limitations

Lewis S. Nelson, MD, MBA, FASAM
Dean, Chief of Health Affairs and Professor of Emergency Medicine and Medical Toxicology
Florida Atlantic University





Financial Disclosure

Lewis S. Nelson, MD, MBA, DFASAM

- No relevant disclosures

Learning Objectives



1

Explain the differences between and clinical relevance of tolerance, dependence, and hyperalgesia.

2

Describe the pharmacologic principles of pharmacokinetics and pharmacodynamics and how each impacts addiction risk and addiction treatment.

3

Discuss the interpretation pitfalls of screening and confirmatory urine drug tests in the management of patients with substance use.

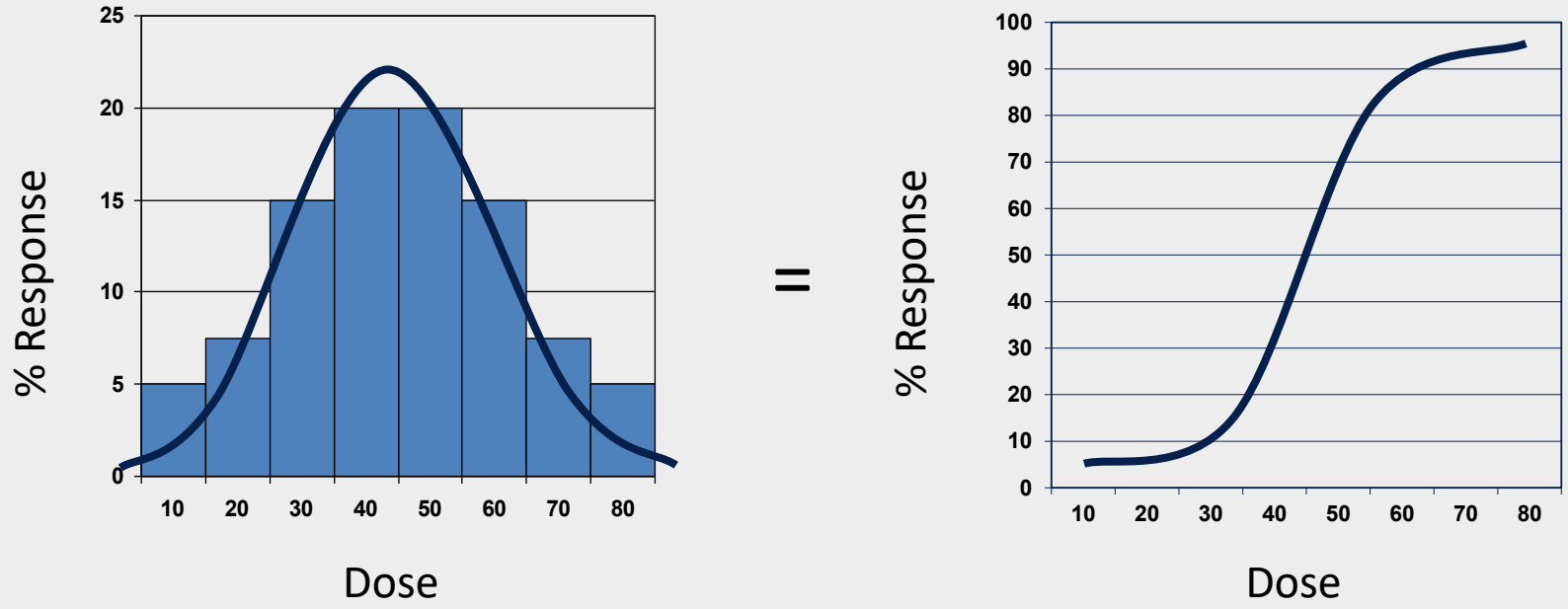
Addiction Medicine IS Pharmacology

- Drugs have to get to the brain to elicit a response.
  - Blood brain barrier is an effective barrier
- Euphoria – rate of rise
- Dependence – duration of exposure

Pharmacokinetics and Pharmacodynamics

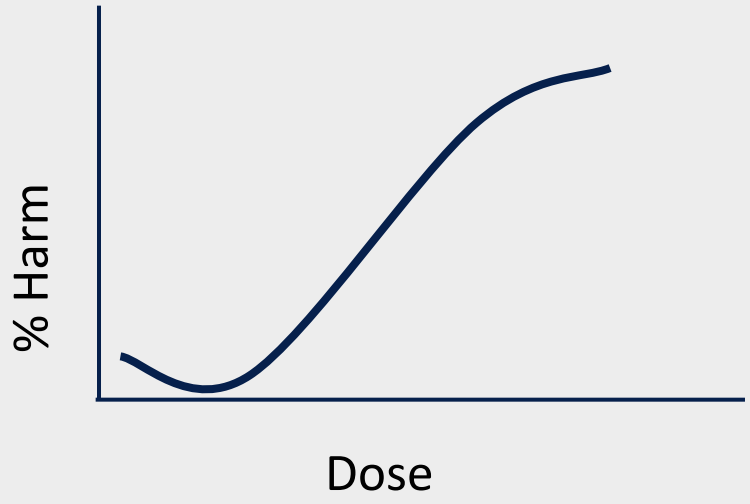
Absorption (Bioavailability)	Distribution	Elimination
Biotransformation	Dose Response (Clinical Effect)	Potency
Drug interaction	Tolerance	Dependence

Dose-Response

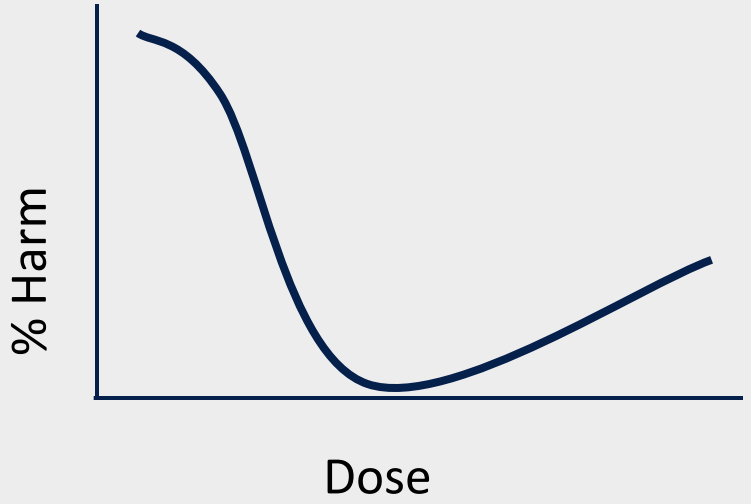


Response = Anything (Blood pressure, Euphoria, Death)

Dose-Response



Vitamins



Oxygen
Water

Potency

Rank order the potency at causing death:

Agent	LD50 (approx.)
Ethanol	5,000 (mg/kg)
Nicotine	2 (mg/kg)
Morphine	1 (mg/kg)
Fentanyl	0.01 (10 µg/kg)
Botulinum	0.000001 (2 ng/kg)

Don’t confuse potency with clinical effect

Which has more potent THC?

1980’s weed

Trick question:

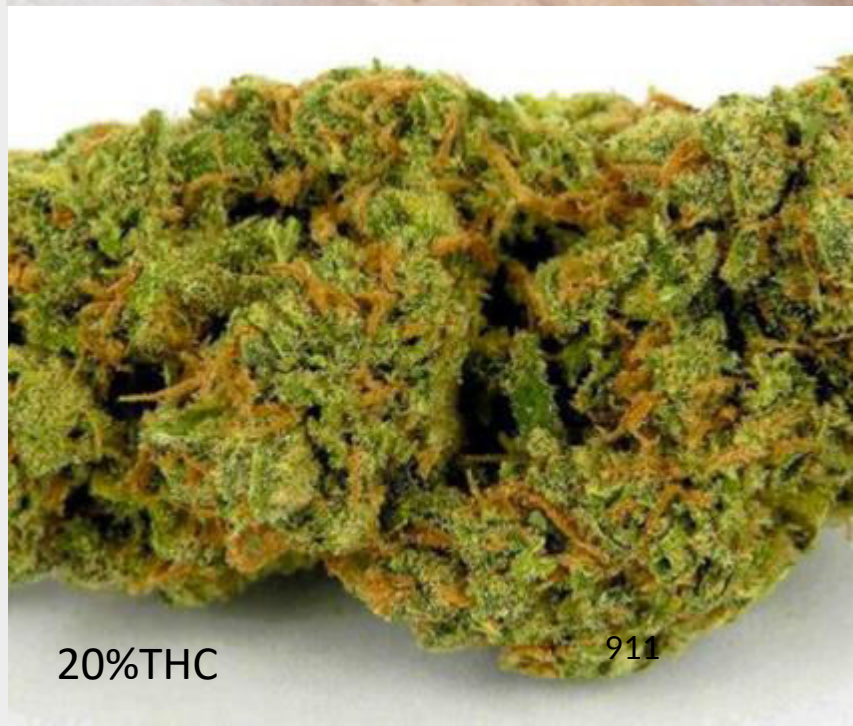
The THC is the same potency

The higher concentration product is more “potent”

Don’t confuse potency of a drug with its concentration

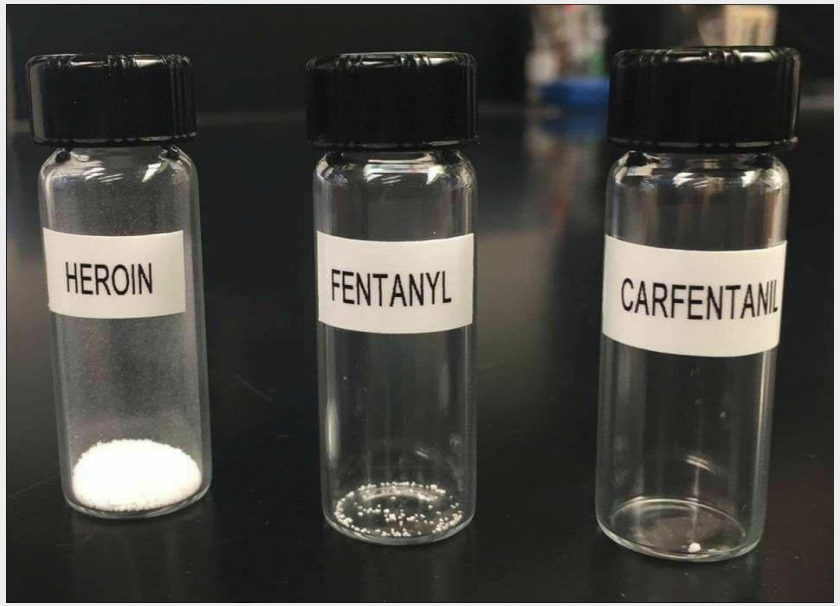
2026 weed





Potency doesn't really matter

Agent	Potency (vs morphine)
Tramadol	0.2
Morphine	1
Oxycodone	1.3
Methadone	4
Heroin	4
Buprenorphine	30
Fentanyl	100
Carfentanil	10,000



Any of these drugs will kill you if you take enough



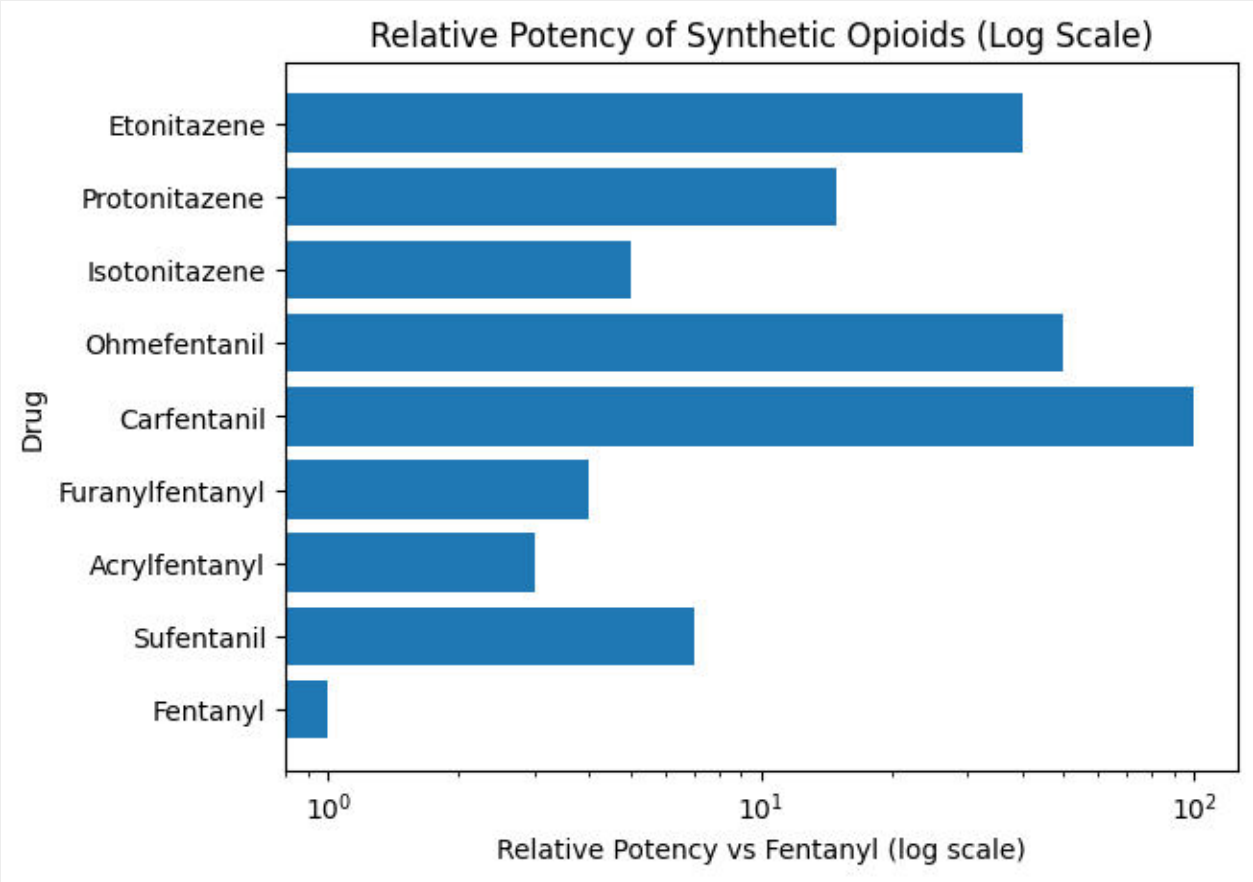
Dose Makes The Poison

"What is there that is not poison? All things are poison and nothing [is] without poison. Solely the dose determines that a thing is not a poison"

Paracelsus (1493-1541)
in *Third Defense*

Philip Theophrastus Bombast von Hohenheim
aka PARACELSUS (1493-1541)

Why potency may matter….



Absorption

Routes of Administration

- Oral
  - Potentially extensive first-pass
- IV, IN, IM, SC, SL, buccal, inhalational, rectal
  - Bypass hepatic first-pass
- Intrathecal
  - Unique –bypass Blood Brain Barrier
- Transdermal
  - Bypass hepatic first-pass
  - Depot in skin/body fat can influence absorption
- Intranasal
  - May directly access CNS (nose-to-brain)

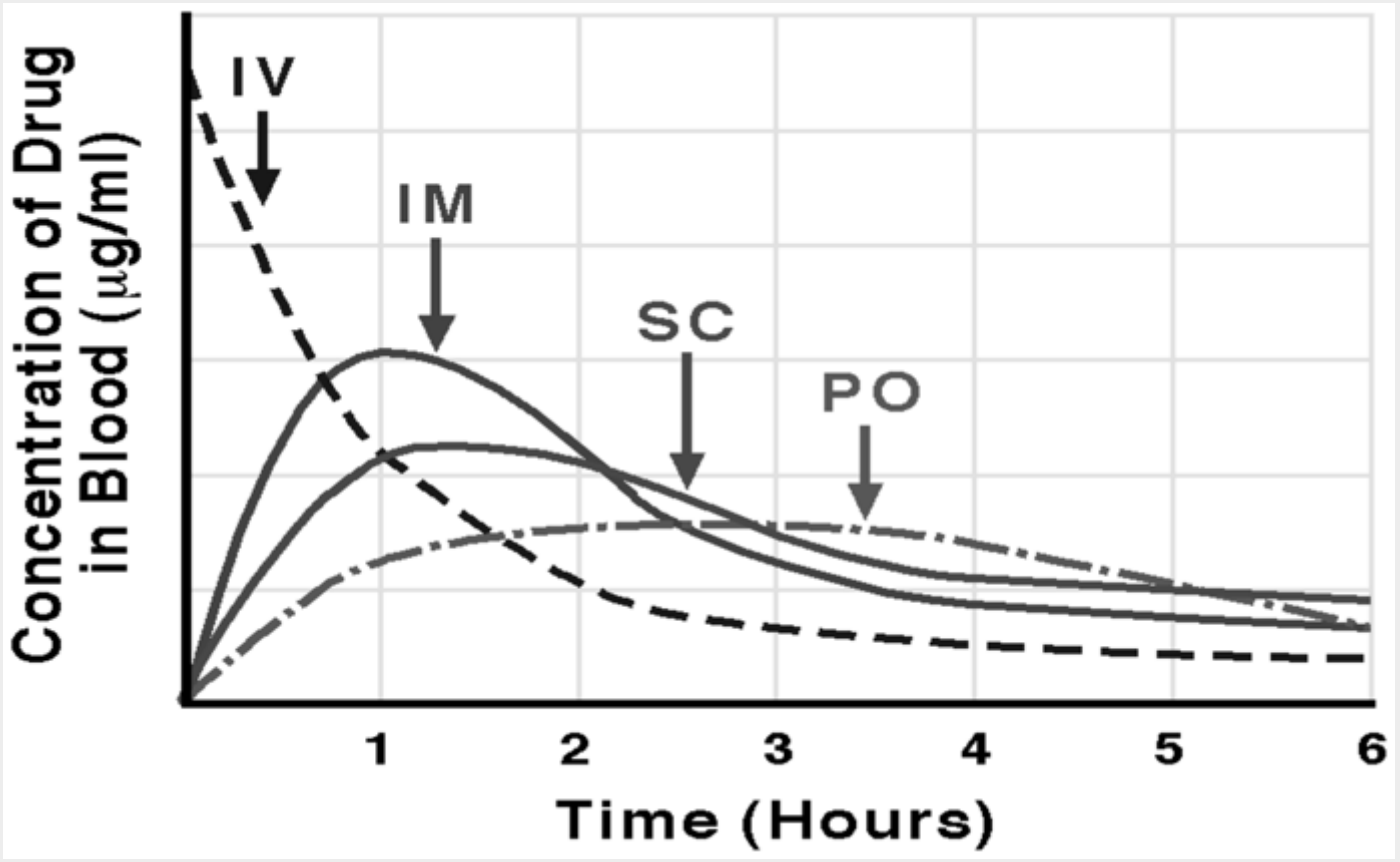
Bioavailability

- The amount of unchanged drug reaching systemic circulation after administration is the bioavailability (F).
- F depends upon:
  - Route (IV is 100%)
  - Site specific membrane permeability
  - Drug transporter activity (p-glycoprotein)
  - First-pass metabolism (hepatic)

	Route		
	Oral	**Sublingual**	**Buccal**
Buprenorphine	10%	40%	50%
	Oral	**Sublingual**	**Intranasal**
Naloxone	1%	10%	50%
	Oral		
Morphine	33%		
Oxycodone	75%		

Kuhlman JJ, et al. J Anal Toxicol 1996;20(6):369–78.

Area Under the Curve (AUC)



Wolff K, et al. The SAGE Handbook of Drug & Alcohol Studies

Q12h

OxyContin® CII

(OXYCODONE HCl CONTROLLED-RELEASE) TABLETS

10mg 20mg 40mg 80mg 160mg

Small, color-coded tablets (actual size)

OxyContin 80 and 160 mg Tablets for use
tolerant patients requiring daily oxycodone
dosages of 160 mg and 320 mg respective

OxyContin® Tablets are to be
are not to be broken, chewed or
broken, chewed or crushed OxyCont
lead to the rapid release and absorption
toxic dose of oxycodone.

One OxyContin 160 mg Tablet is comparable
two 80 mg tablets when taken on an empty stomach.
With a high fat meal, however, there is a 25% greater
peak plasma concentration following one 160 mg
tablet. Dietary caution should be taken when patients
are initially titrated to 160 mg tablets.

OxyContin® Tablets are to be swallowed whole, and are not to be broken, chewed or crushed. Taking broken, chewed or crushed OxyContin Tablets could lead to the rapid release and absorption of a potentially toxic dose of oxycodone.

section in package insert.)

For more information about pain management and prevention, visit our Web site: www.partnersagainstpain.com

Please read attached professional prescribing information.

©2001, Purdue Pharma L.P., Stamford, CT 06901-3431

B6571



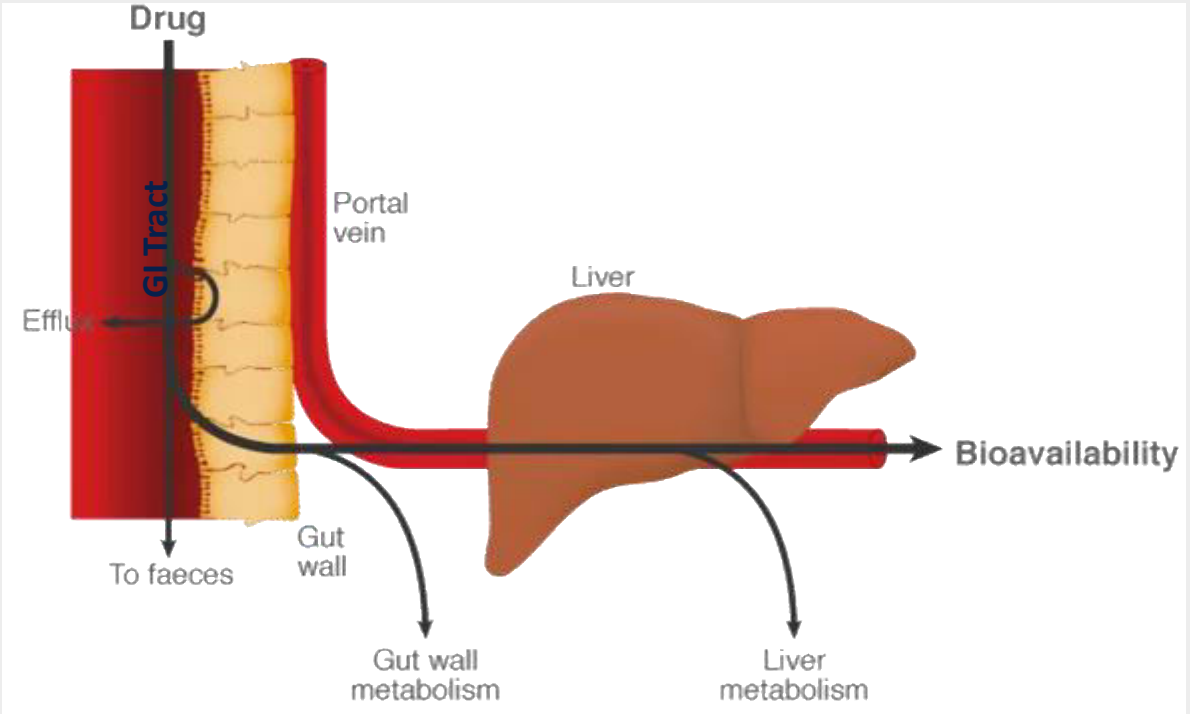
Distribution

First Pass Hepatic Metabolism

Bypass first pass

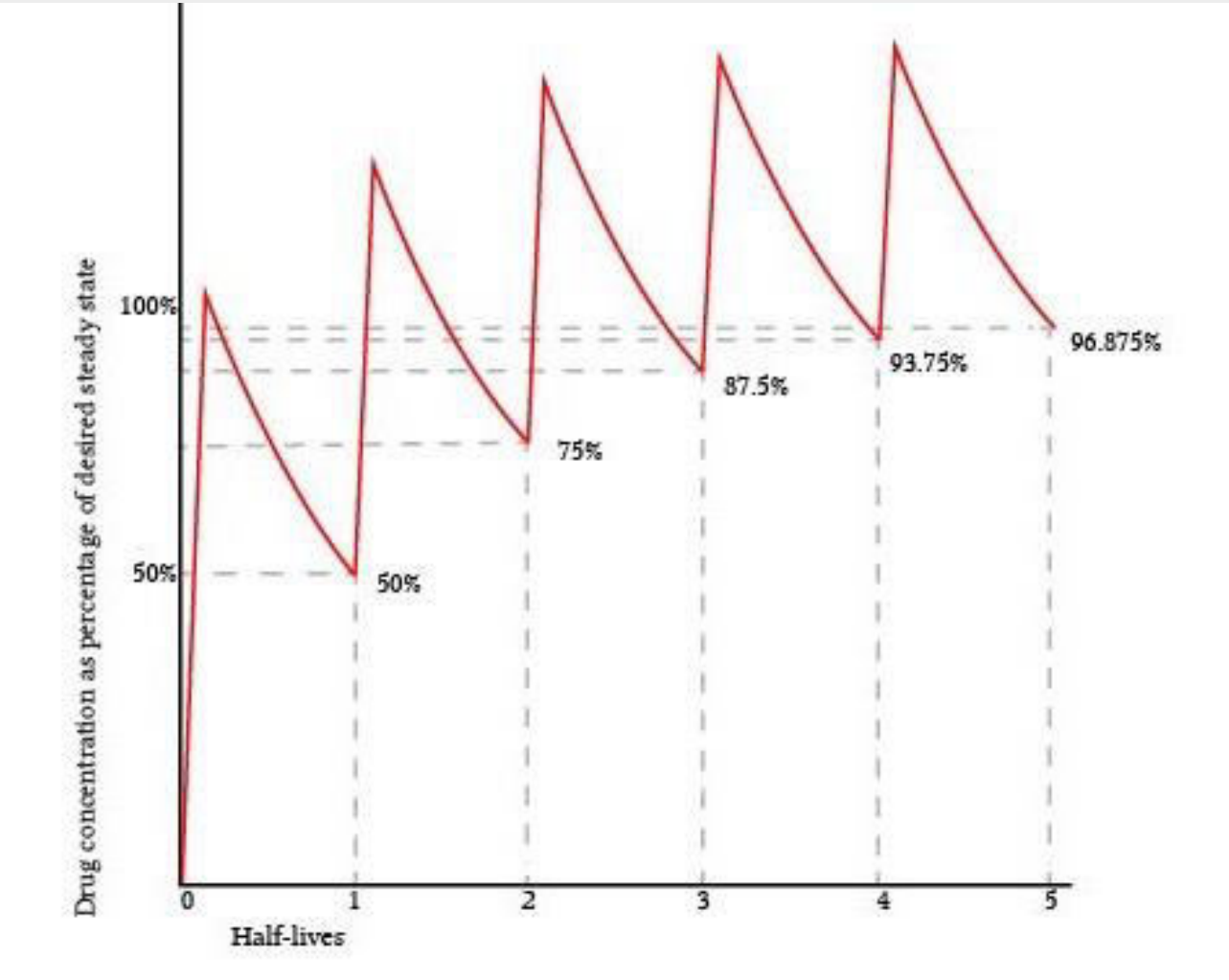




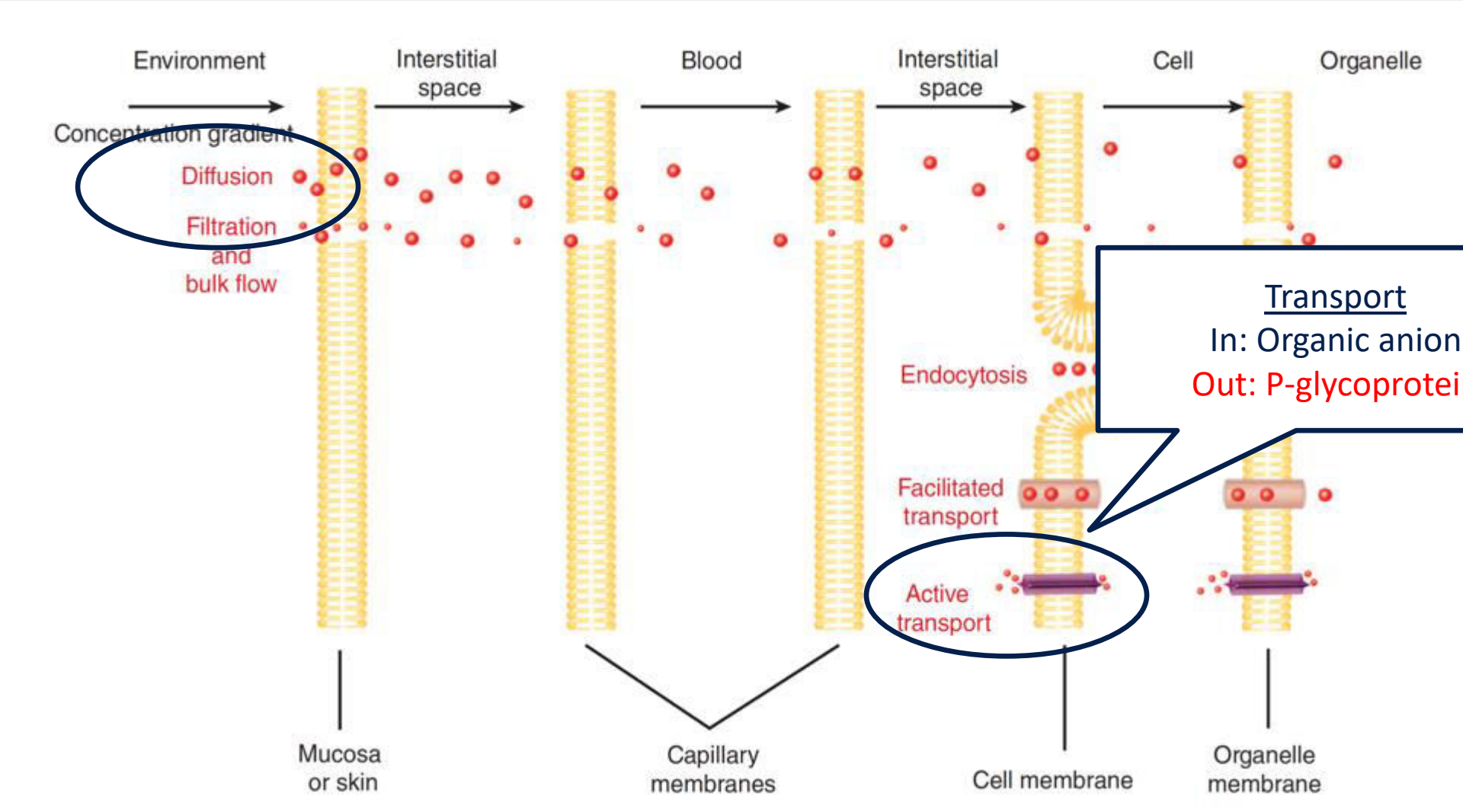


www.doctoralerts.com

Steady State



- Requires approximately 5 half-lives
  - Regardless of the compound's half-life
- Explains (in part) the risk and difficulty of methadone induction
  - T½ ~24 hr (12-36 hr)



Transport

In: Organic anion

Out: P-glycoprotein

Goldfrank's Toxicologic Emergencies, 11th

P-Glycoprotein



Loperamide the OTC fentanyl (reason for no CNS activity) [A...
www.bluelight.org/vb/archive/index.php/t-217933.html
Aug 21, 2005 - 50 posts - 30 authors
I have found many commonly available items (herbal extracts, supplements or food items) which are **p-glycoprotein inhibitors**, but inhibition at ...

Immodium, BBB, and PGp inhibition [Archive]	8 posts	Jan 12, 2013
(**Loperamide**/cimetidine/quinine) Veteran. Wasn't a ...	13 posts	Oct 2, 2012
Forcing **Loperamide** through the BBB [Archive] - Page 2	30 posts	Jun 21, 2011
Forcing **Loperamide** through the BBB [Archive]	50 posts	May 23, 2006

More results from www.bluelight.org

Loperamide and P-glycoprotein inhibition: assessment of ...
www.ncbi.nlm.nih.gov/... National Center for Biotechnology Information
by J Vandenbossche - 2010 - Cited by 12 - Related articles
Loperamide and P-glycoprotein inhibition: assessment of the clinical relevance. ... coadministration of **loperamide** with a **P-glycoprotein inhibitor** or substrate.

Combinations - **Loperamide** Potentiation + **p-glycoprotein** in...
www.drugs-forum.com › ... › DRUG-FORUMS › Opiates & Opioids
Mar 2, 2012 - 3 posts - 2 authors
SWIM is going to be performing an experiement with **Loperamide**, he is ... SWIM is aware of the dangerous of **inhibiting p-glycoprotein** but is not ...

Addiction - metabolite of **loperamide** is possible PGP ...	4 posts	Feb 28, 2013
Combinations - Cheap Opiate High-potential ...	22 posts	Dec 27, 2012
Experiences - **Loperamide** Report	22 posts	Jan 16, 2012
Blood brain barrier permeation	17 posts	Dec 4, 2010

More results from www.drugs-forum.com

Pepper **Inhibits P-Glycoprotein** (just add **loperamide**??) [Ar...

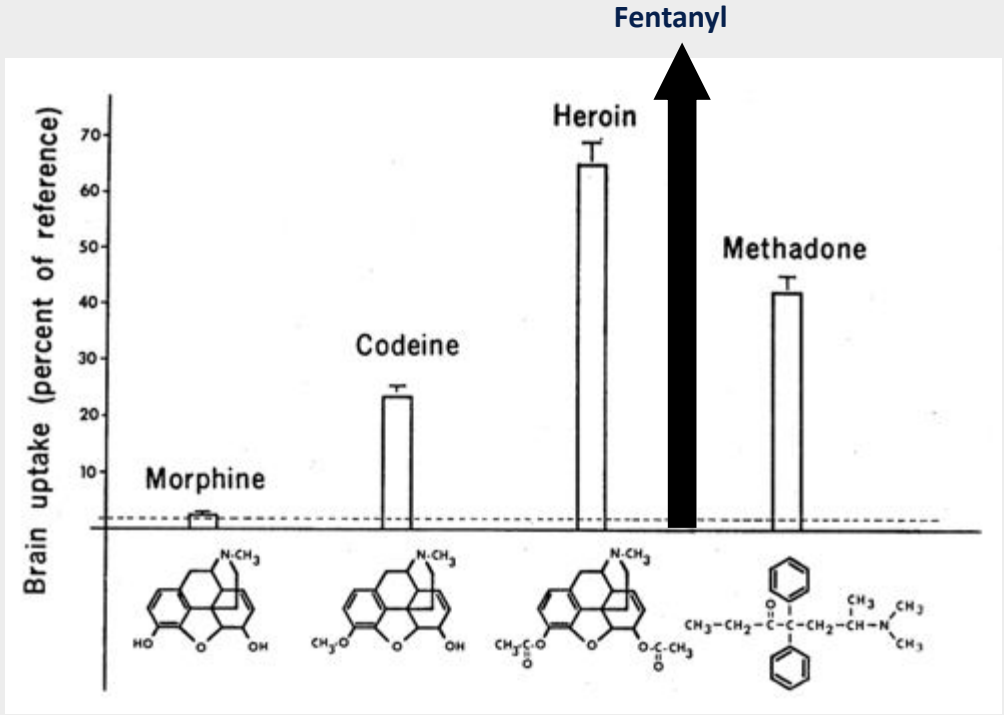
"Street pharmacologists" understand these principles

Loperamide and p-glycoprotein inhibitors

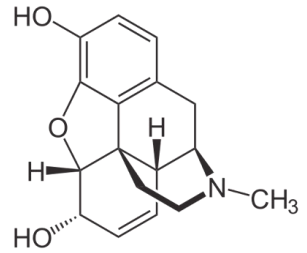
Lipophilicity

Lipophilicity = Reward = Abuse liability

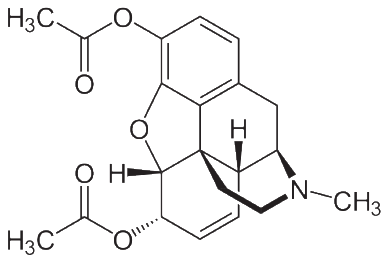
Drug	LogP
Buprenorphine	4.98
Fentanyl	4.05
Methadone	3.93
Naloxone	2.09
Hydromorphone	1.65
Heroin	1.58
Morphine	0.89
Oxycodone	0.85



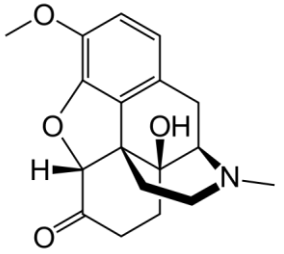
Oldendorf WH. Science. 1972



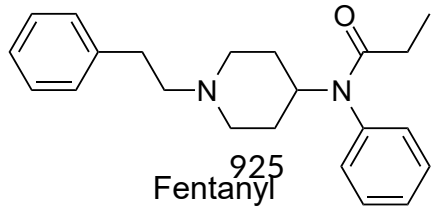
Morphine



Heroin
(diacetyl morphine)



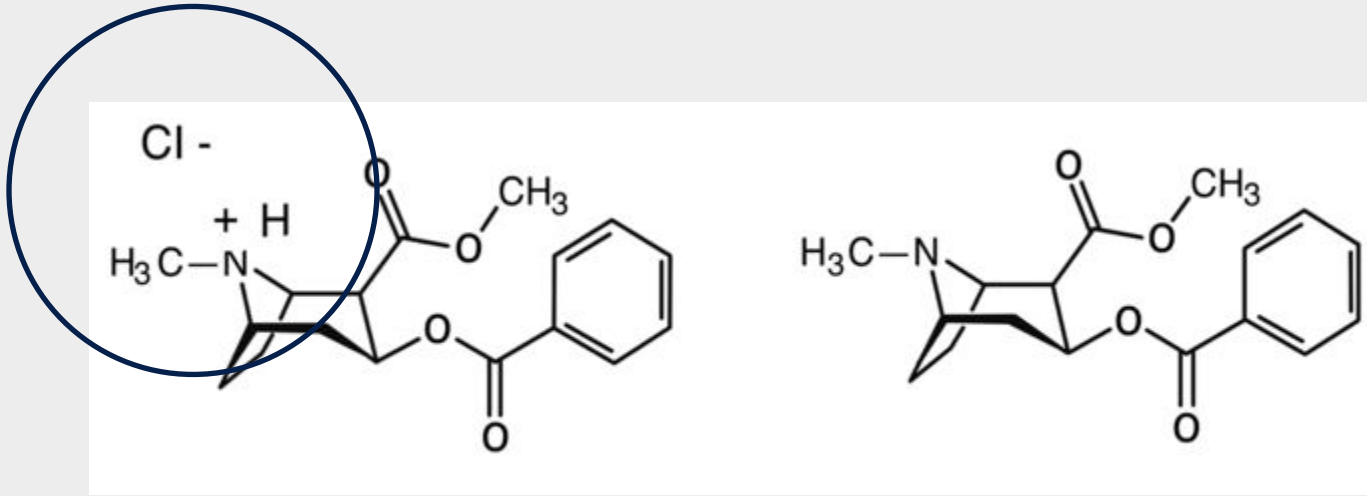
Oxycodone



Fentanyl

Addiction Medicine IS Pharmacology



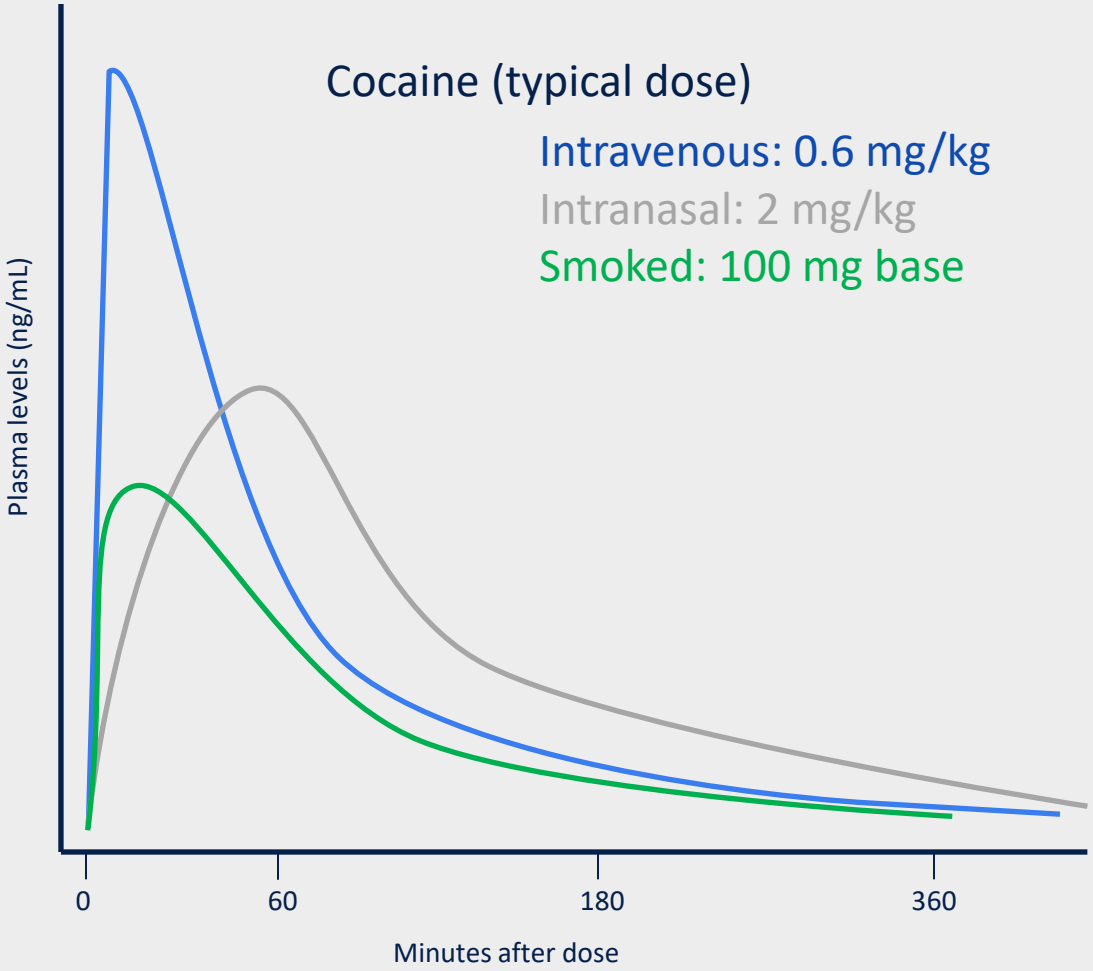


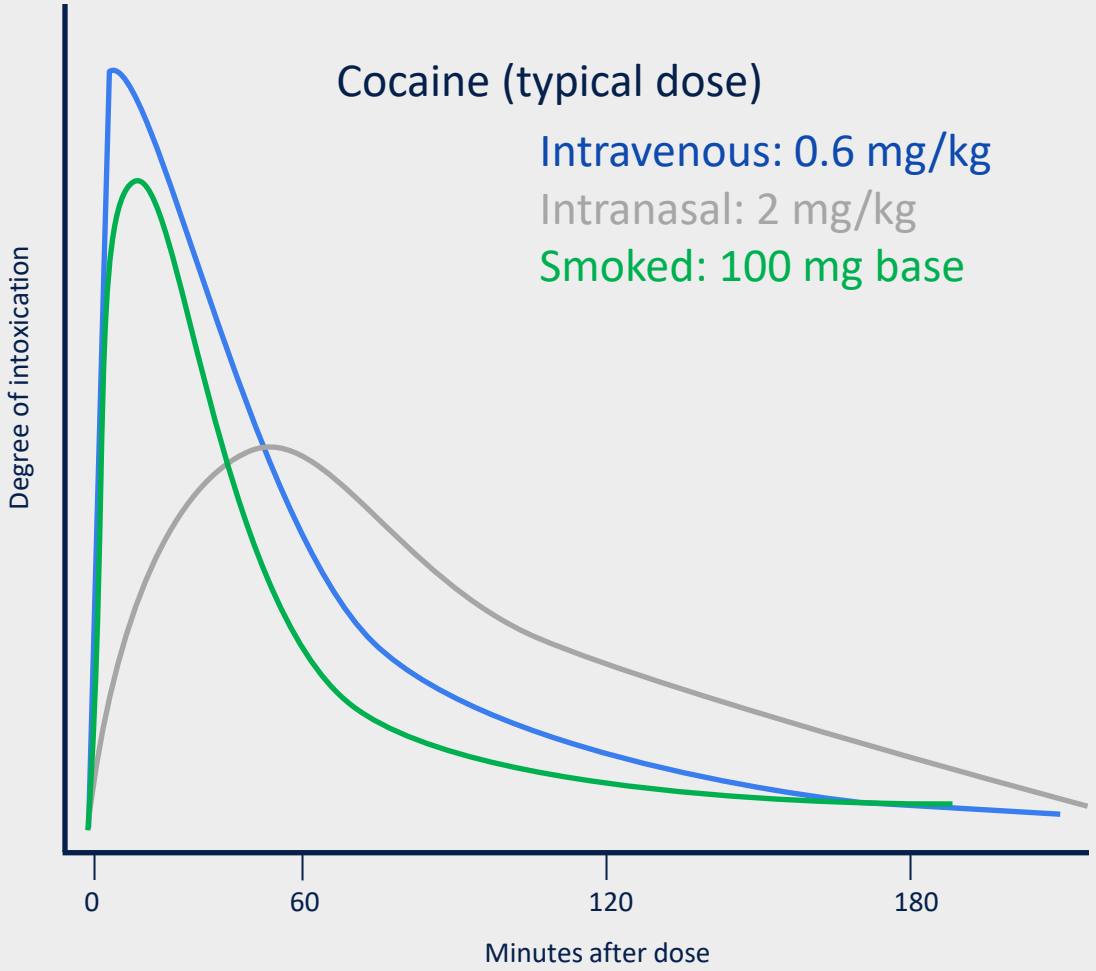


Cocaine hydrochloride
(salt)



Cocaine base
(alkaloidal)





C_{max} and T_{max} depend on route of administration and dose
(C_{max} : IV → *Nasal* → *Smoked*)
(T_{max} : IV = *Smoked* → *Nasal*)

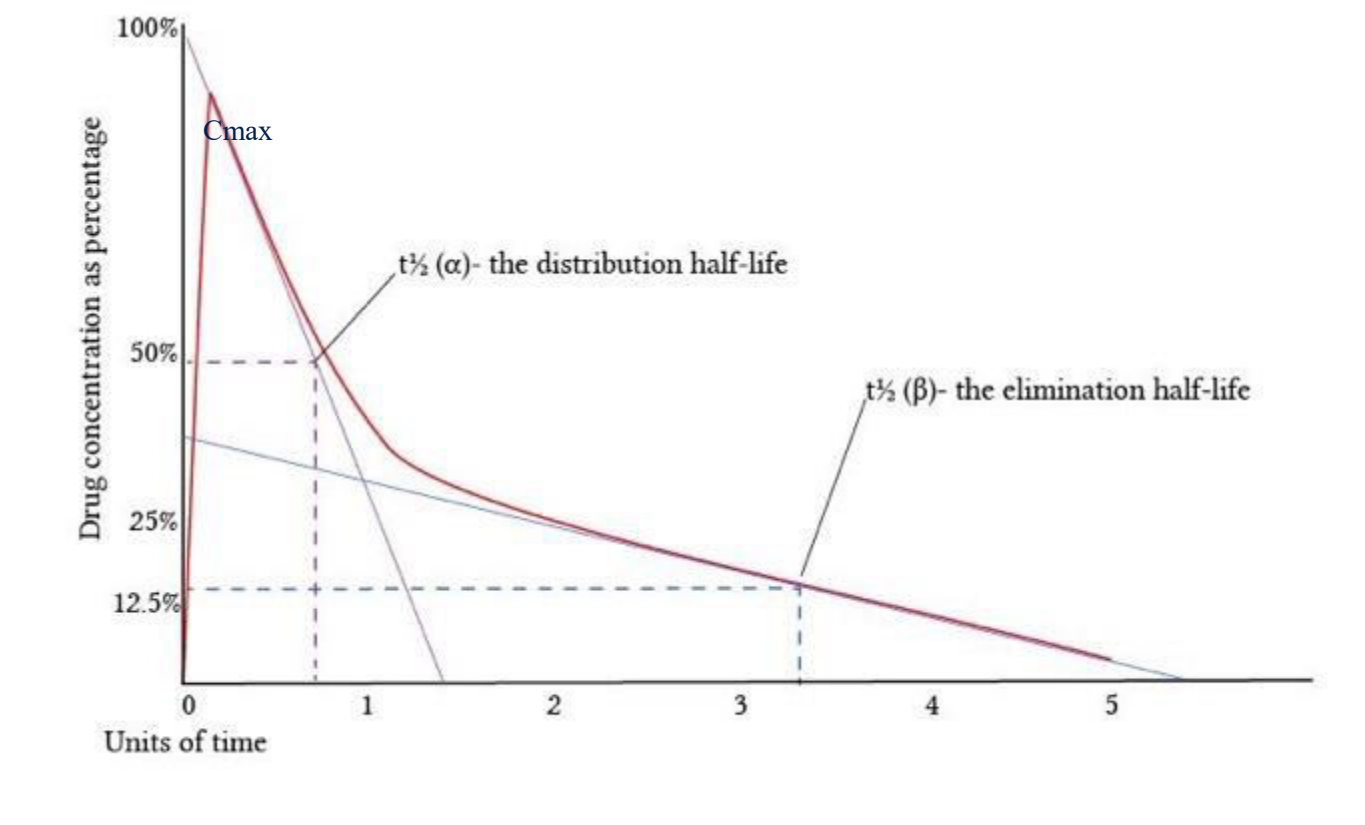
Subjective 'high' (0-100) by route
(*IV* → *Smoked* → *Nasal*)

NIDA Research Monograph 1992, 120

Elimination

T1/2 (Half-life)

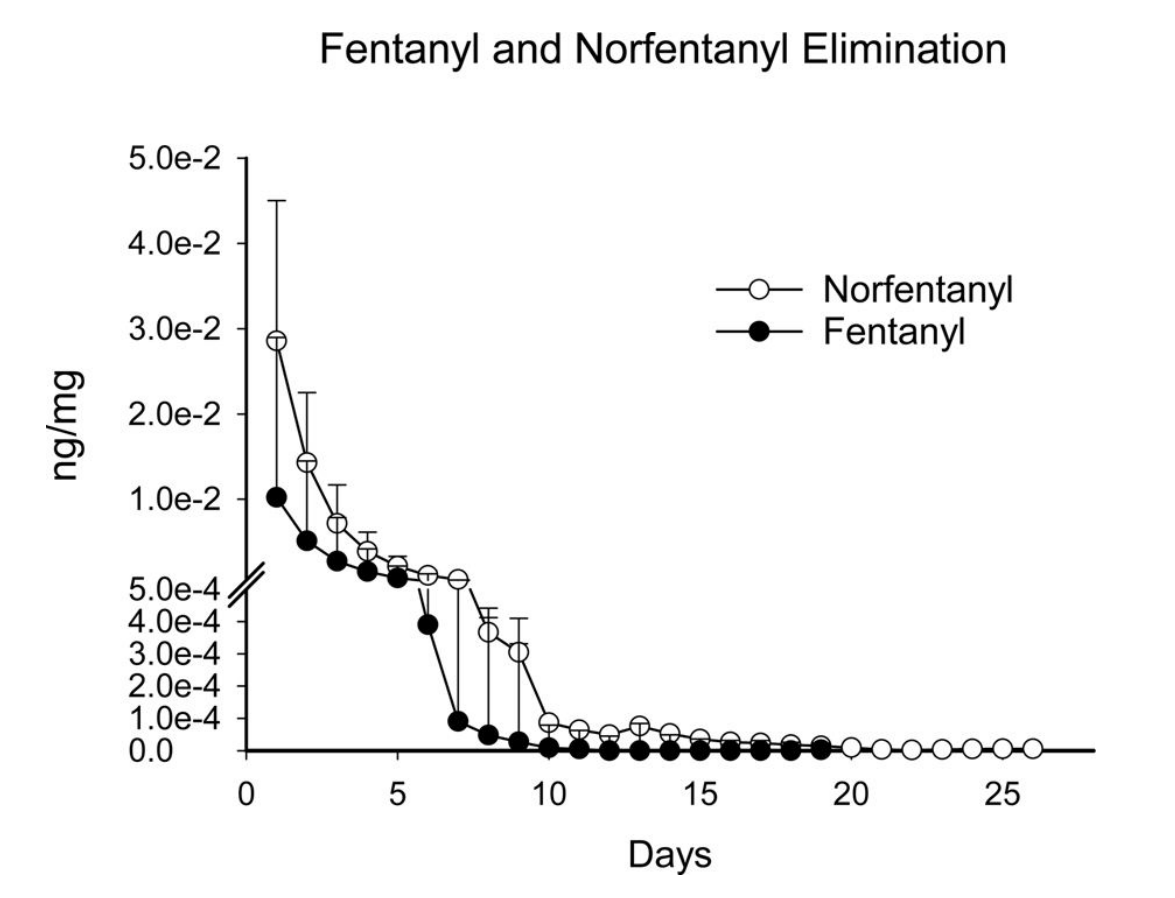
The Time For Cmax to Fall by Half



- Distribution t½
  - Redistribution t½
- Terminal elimination t½
  - Apparent t½
    - Oxycodone ER
  - Context sensitive t½
    - Fentanyl

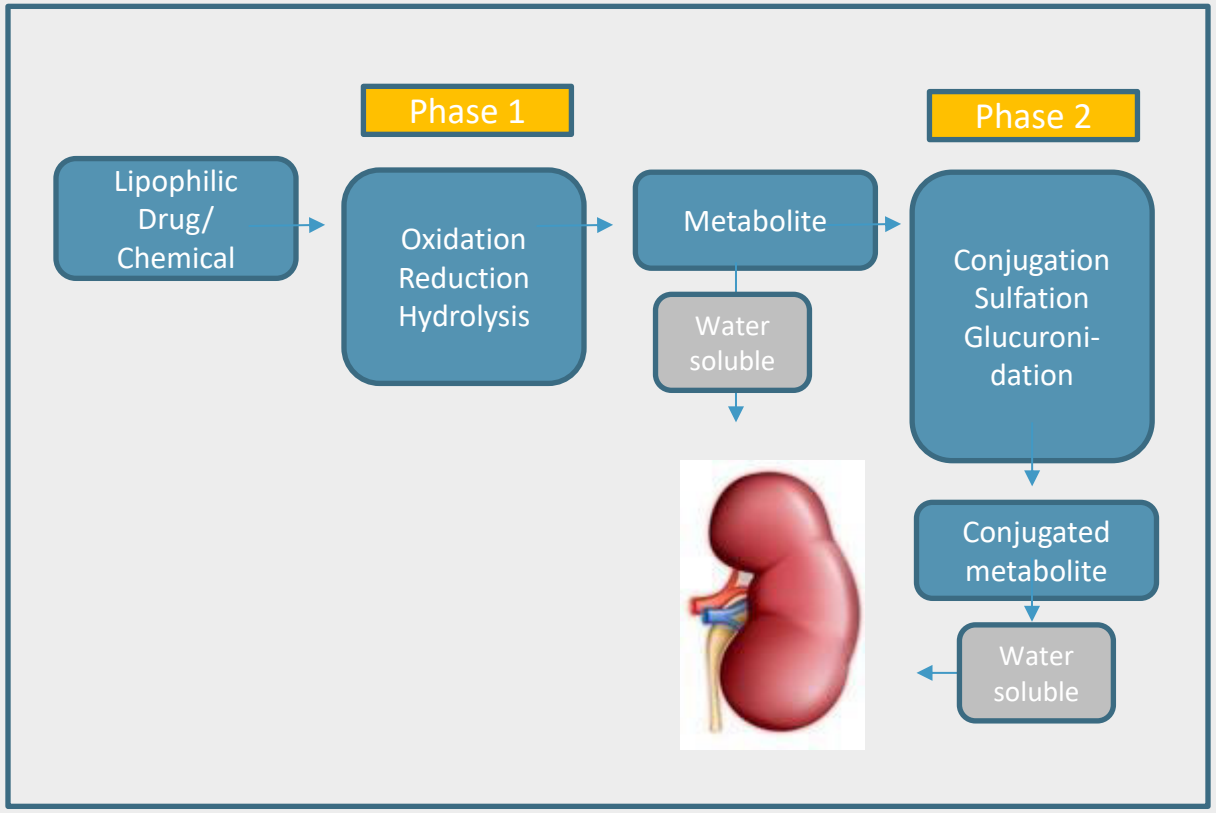
Fentanyl

	Half life (distribution)	Half life (redistribution)	Half life (termal)
Fentanyl	2 min	12 min	480 min

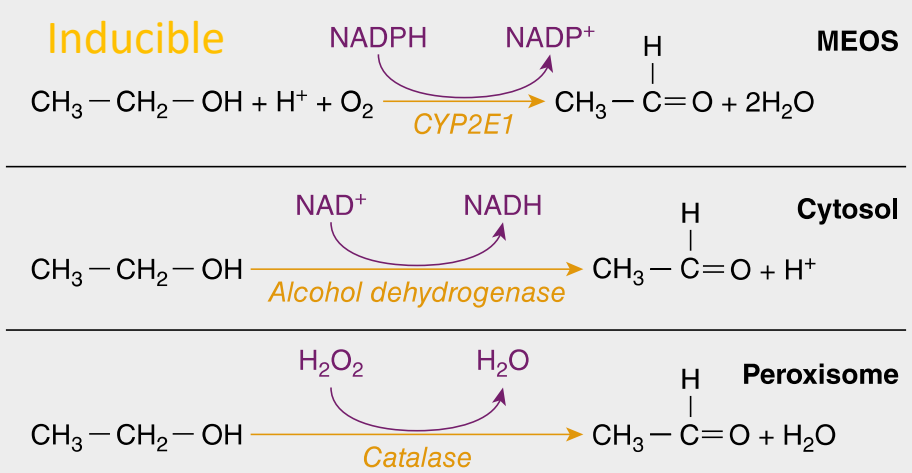


Huhn AS, et al. Drug Alcohol Depend 2020;108:147

Biotransformation



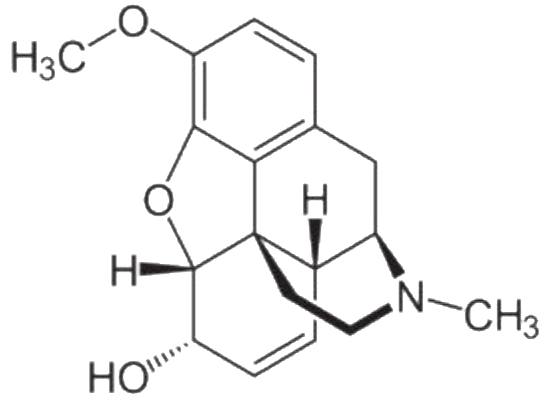
Ethanol Metabolism



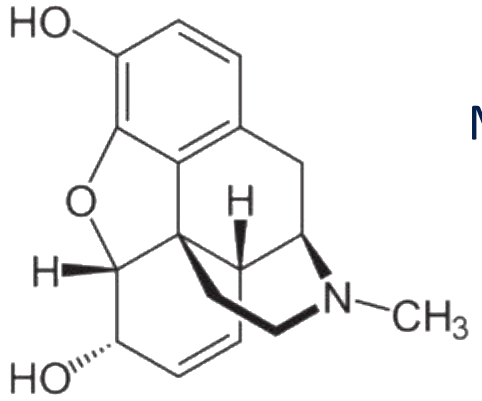
Activation through Biotransformation

- Codeine is demethylated in the liver to morphine
  - Occurs via CYP2D6
  - Codeine is a “pro-drug” (drug undergoes hepatic biotransformation or ‘metabolism’ to its active component
  - Lisdexamfetamine (Vyvanse™) is another example of a pro-drug

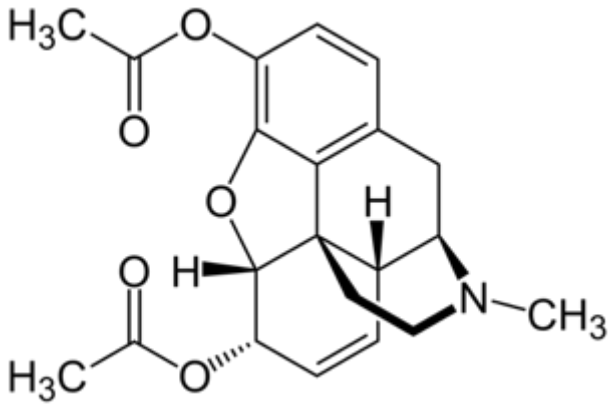
Fun pharm fact: *heroin does not bind to the mu receptor. Metabolism occurs in the CSF. Heroin is a pro-drug for morphine.*



Codeine



Morphine



Heroin

Biotransformation

TABLE 11–1 Characteristics of Different Cytochrome P450 Enzymes[26,33,123]

CYP Enzyme	*1A2*	*2B6*	*2C9*	*2C19*	*2D6*	*2E1*	*3A4*
Percent of liver CYPs	4%–16%	2%–5%	5%–29%	1%–4%	1%–4%	6%–17%	15%–37%
Contribution to enterocyte CYPs	None	None	Minor	Minor	Minor	Minor	70%
Organs other than liver with enzyme	Lung	Kidney	Small intestine, nasal mucosa, heart	Small intestine, nasal mucosa, heart	Small intestine, kidney, lung, heart	Lung, small intestine, kidney	Much in small intestine; some in kidney, nasal mucosa, lung, stomach
Percent of metabolism of typically used pharmaceuticals	9%	7%	13%	7%	20%	3%	30 %
Polymorphisms[a]	No	Yes	Yes	Yes	Yes	No	No
Allelic Frequency							
Decreased Activity							
African American		38%–62%	0%–3%	10%–17%	14%–30%		
Asian	—	14%–25%	2%–8%	25%–39%	47%–94%	—	—
Caucasian		23%–39%	16%–23%	6%–16%	31%–45%		
Increased Activity							
African American		0%–25%		15%–27%			
Asian	—	5%–15%	—	0%–2%	1%	—	—
Caucasian		6%		21%–25%	1%–9%		
Ethiopian					30%		

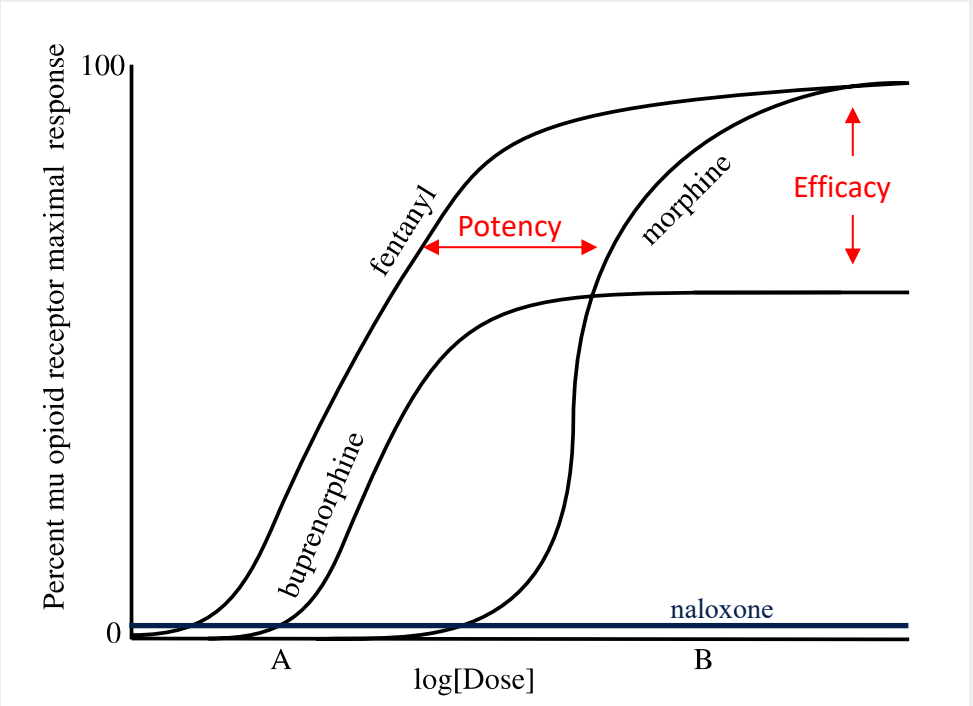
[a] Polymorphism is a genetic change that exists in at least 1% of the human population. Interpersonal allelic variations exist even in those listed as "No" for polymorphism.

Goldfrank's Toxicologic Emergencies, 11th

Receptor Pharmacology

Efficacy

Ligand	% Efficacy
Full agonist	E = 100
Partial agonist	0 < E < 100
Antagonist	E = 0
Inverse agonist	E < 0



Affinity

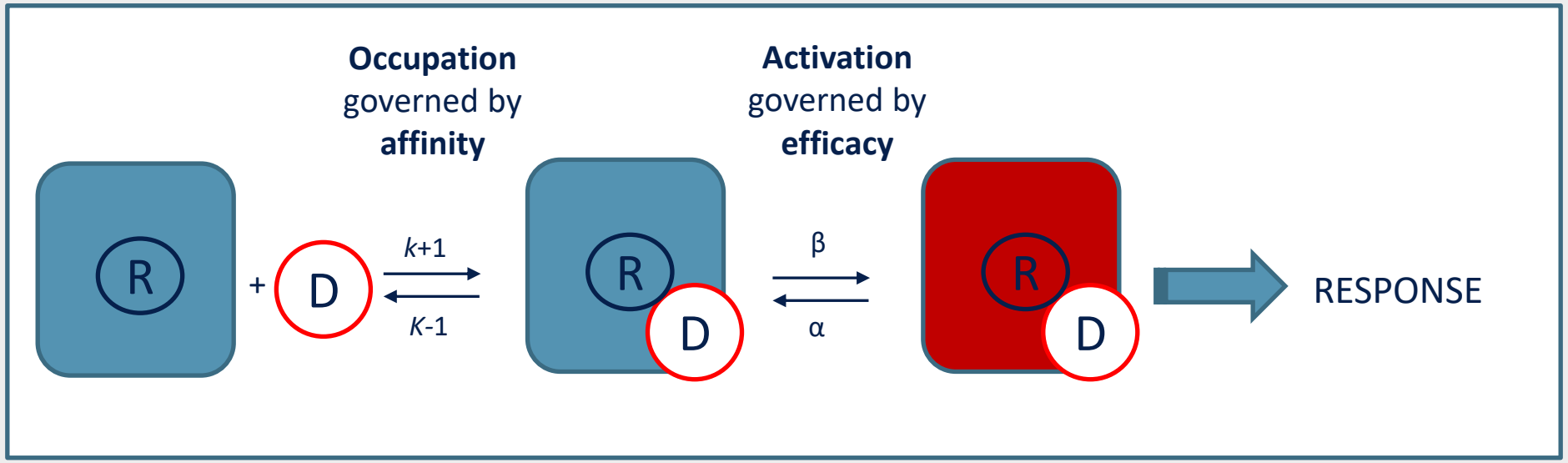


Lower is higher

Ligand	Ki (Affinity) (nmol)
Hydrocodone	41.58
Oxycodone	25.87
Heroin	9.6
Methadone	3.38
Fentanyl	1.35
Morphine	1.14
Naloxone	1.1
Hydromorphone	0.6
Buprenorphine	0.21

Volpe DA. Uniform assessment and ranking of opioid Mu receptor binding constants for selected opioid drugs. Reg Toxicol Pharmacol 2011

Receptor kinetics
On-off



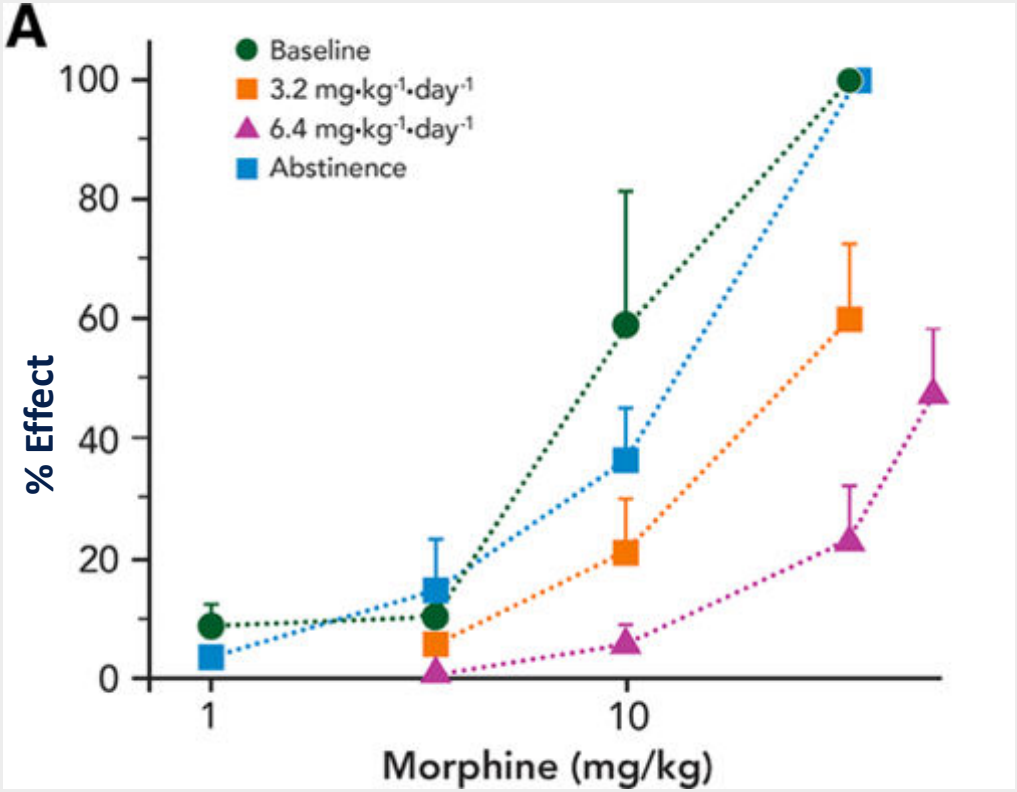
Pharmacodynamics

Tolerance

- Tolerance is the reduction in response to a drug after its repeated administration
- Tolerance shifts the dose-response curve to the right
  - Higher doses than initial doses to achieve the same effect

  Or
  - The same dose provides less effect

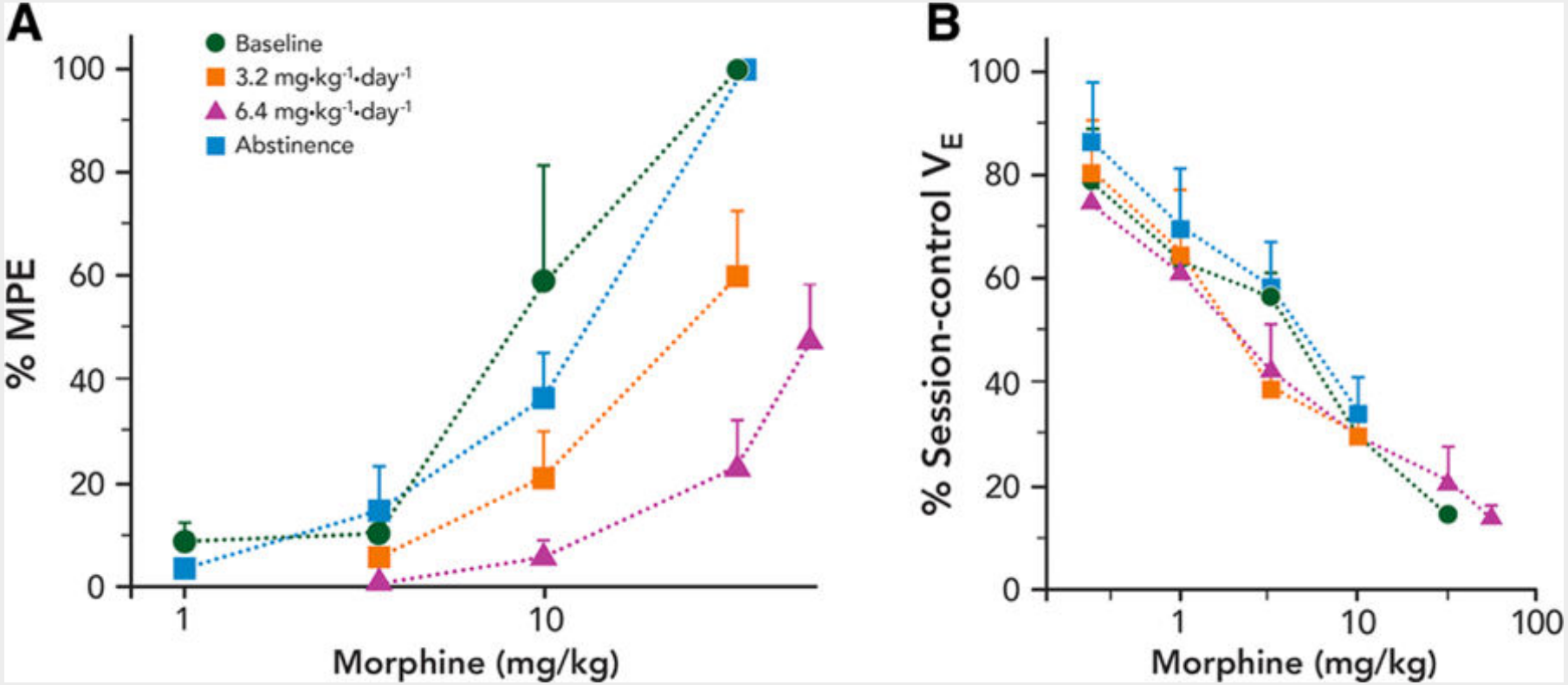
Analgesia



Differential Tolerance

Analgesia

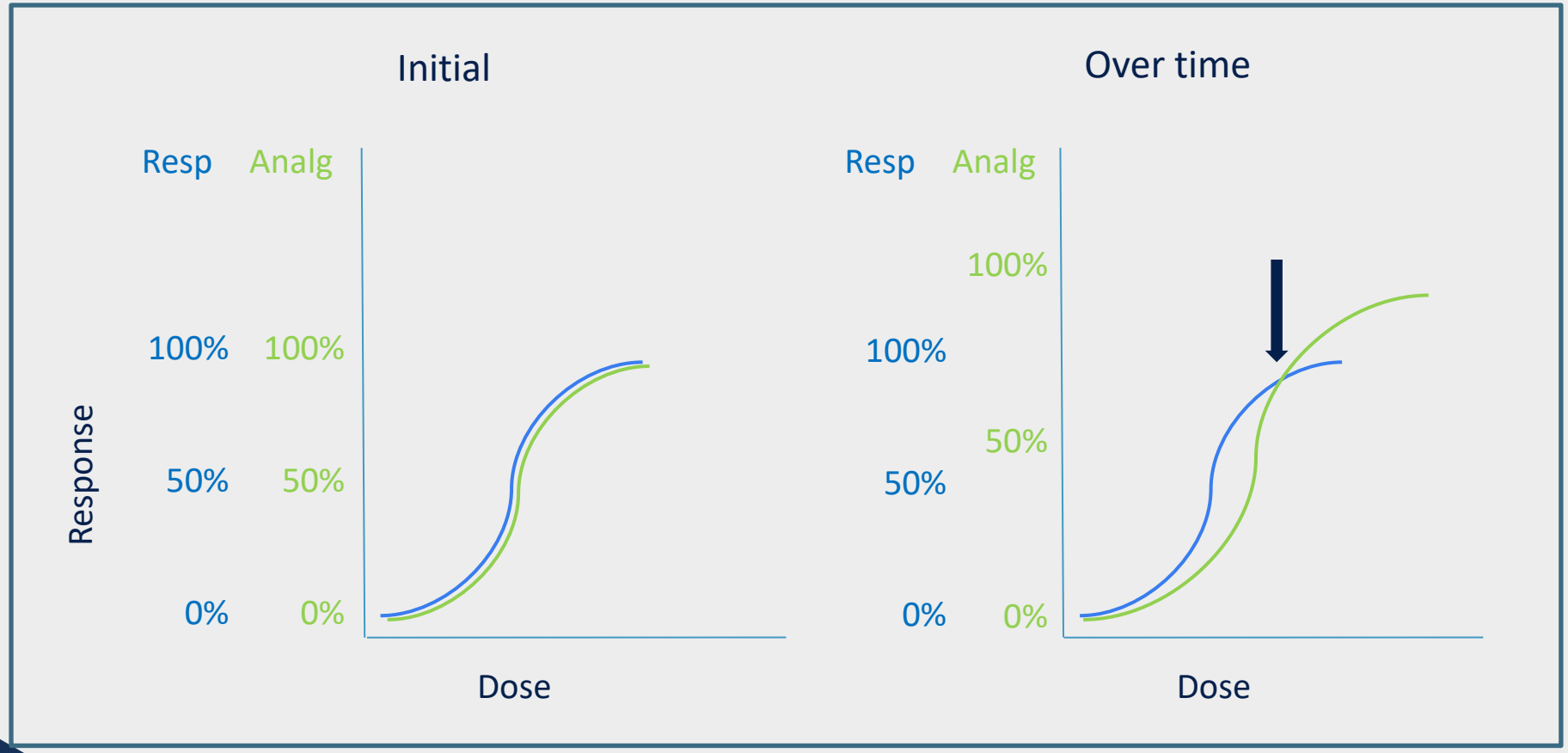
Respiratory depression*



*limited development of tolerance

Hayhurst. Anesthesiology 2016;124:483-8

The Paradox of Differential Tolerance

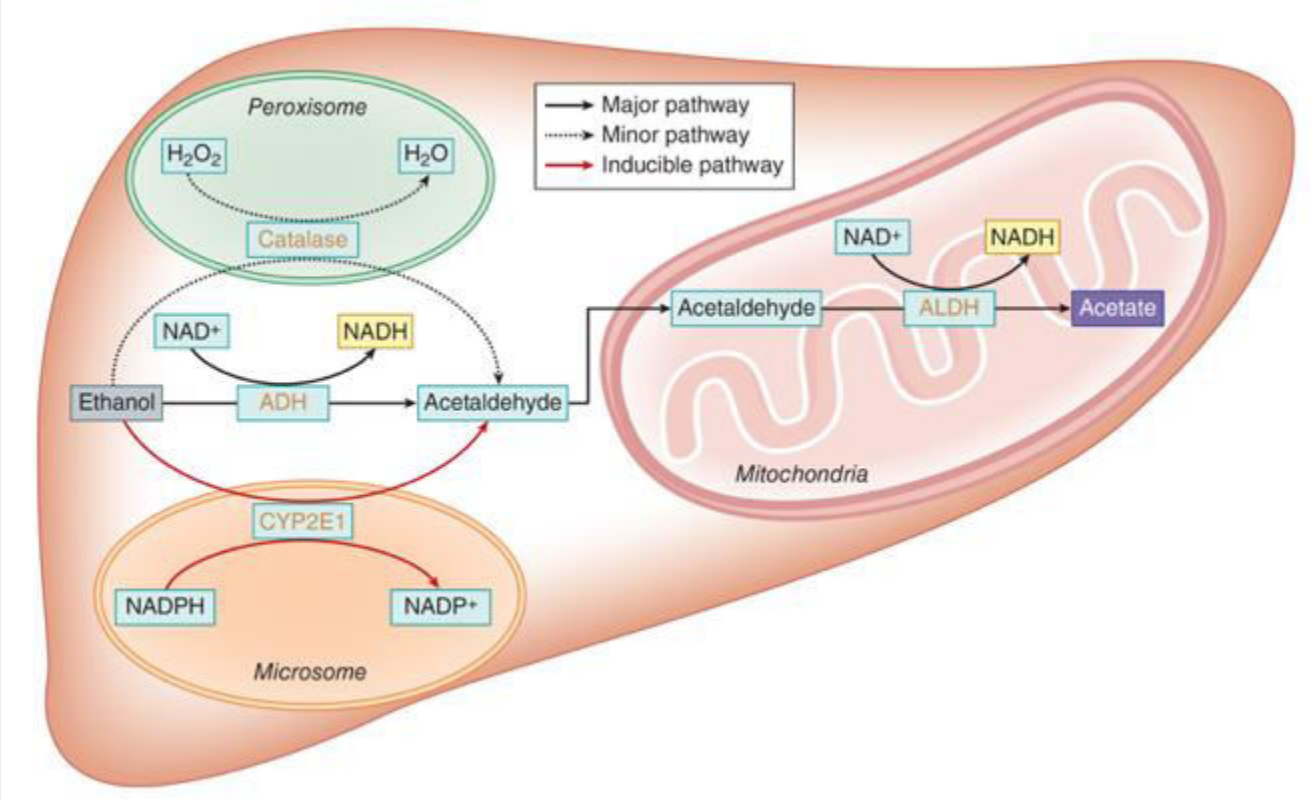


Tolerance to analgesia is rapid

Tolerance to respiratory depression is slow

Pharmacokinetic Tolerance

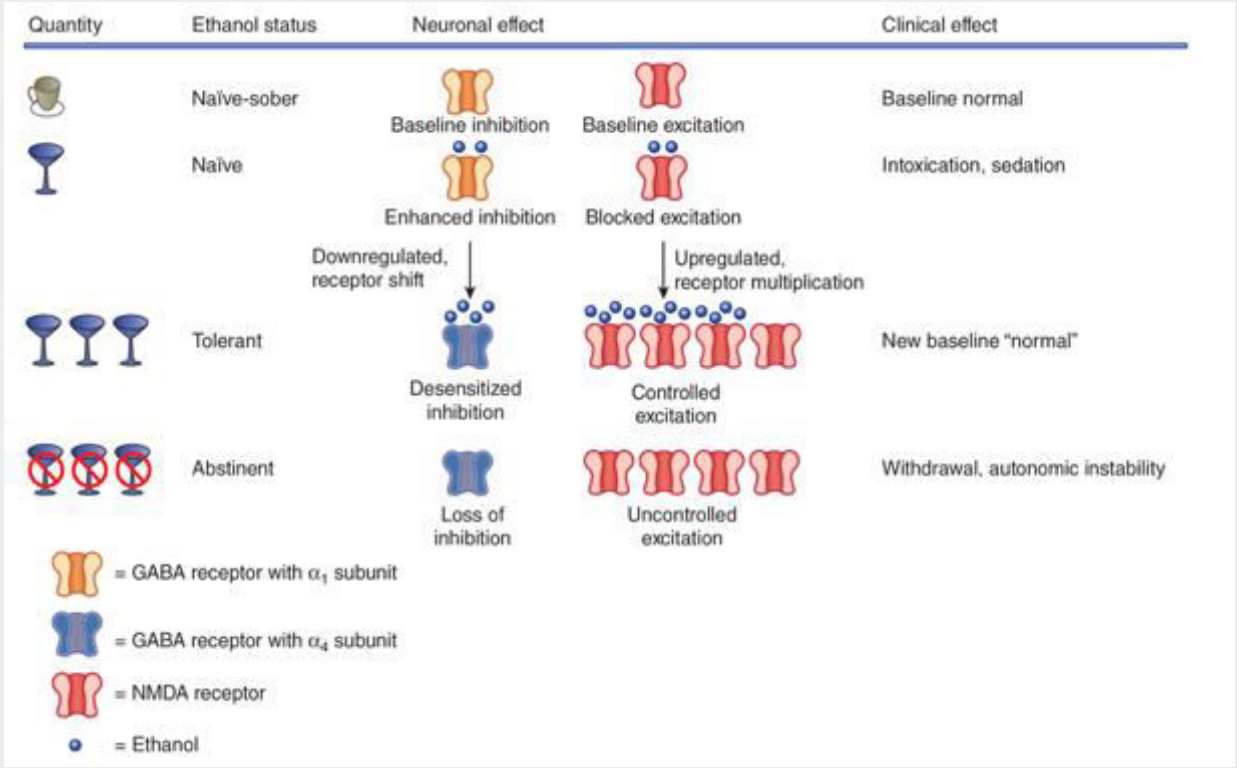
- A consequence of increased metabolism after a drug is repeatedly administered
- Results in less drug being available at the receptor for drug activity.
- Ethanol
  - Although ADH is not inducible, CYP2E1 is
  - Accounts for more rapid elimination of alcohol in heavy, chronic users



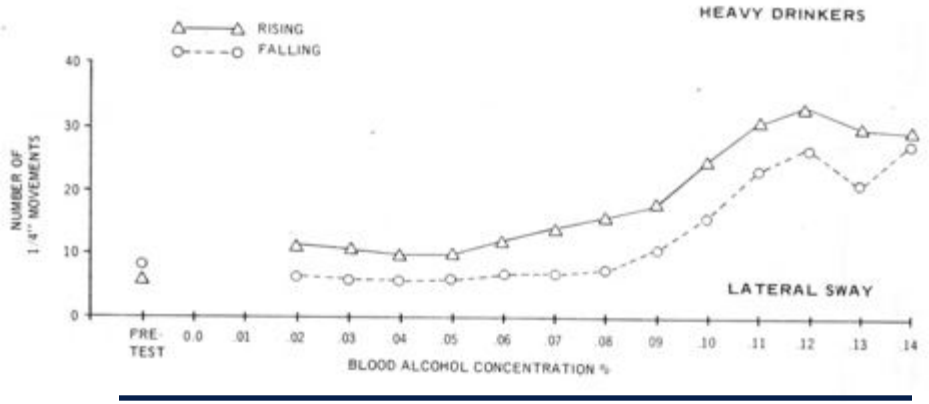
Goldfrank's Toxicologic Emergencies, 11th

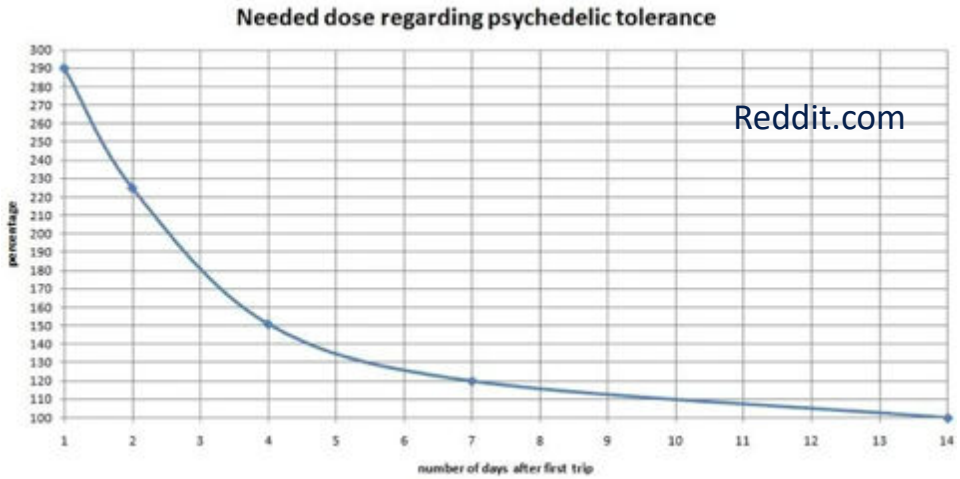
Pharmacodynamic Tolerance

- Down-regulation of receptors (higher drug concentration needed)
  - Desensitization of GABA (ethanol)
    - Receptor conformation
  - Desensitization of MOR (opioid)
    - Signal transduction
    - Decreased density (internalization)
- Up-regulation of receptors
  - Increased number of NMDA (ethanol)



Goldfrank's Toxicologic Emergencies, 11th





Reddit.com





Tachyphylaxis (acute tolerance)

- Mellanby effect
  - Less “intoxicated” on descending limb of BAC curve
- MDMA, psilocybin, and LSD
  - Serotonin receptor
- BZD resistant alcohol withdrawal from IV (less with PO) diazepam

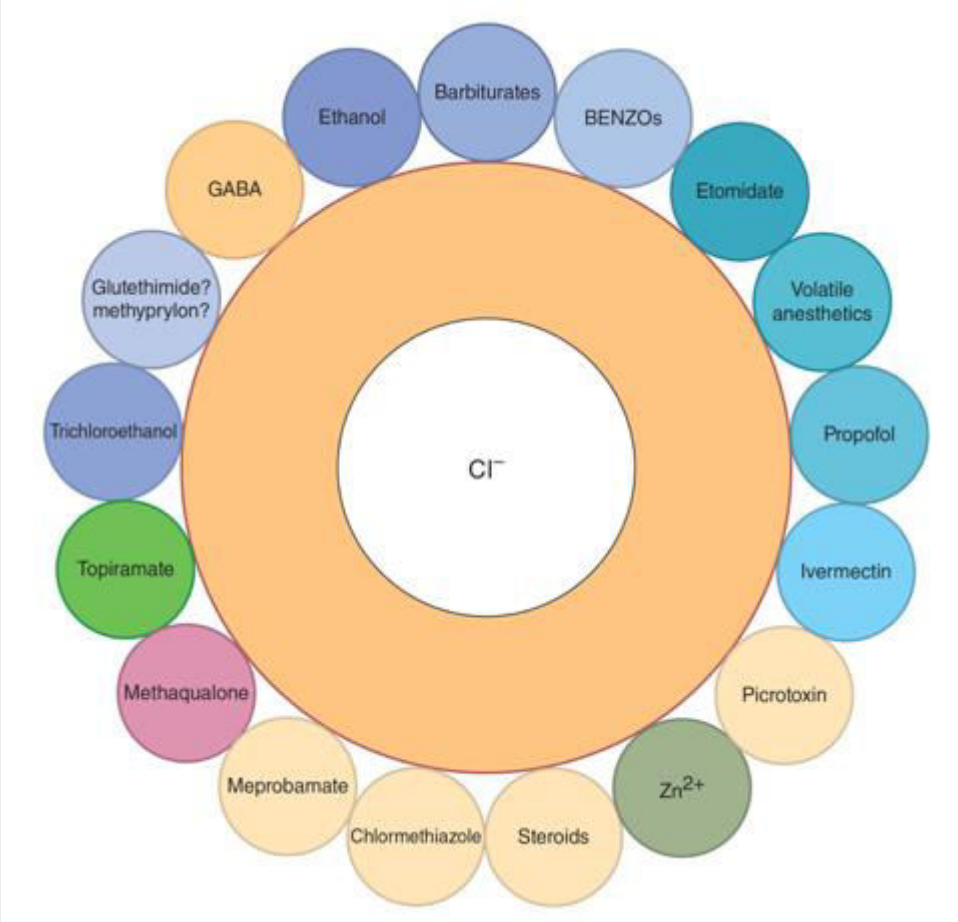
Mellanby E. Medical Research Committee. Special Report Series No 31, 1919.

Conditioned Tolerance

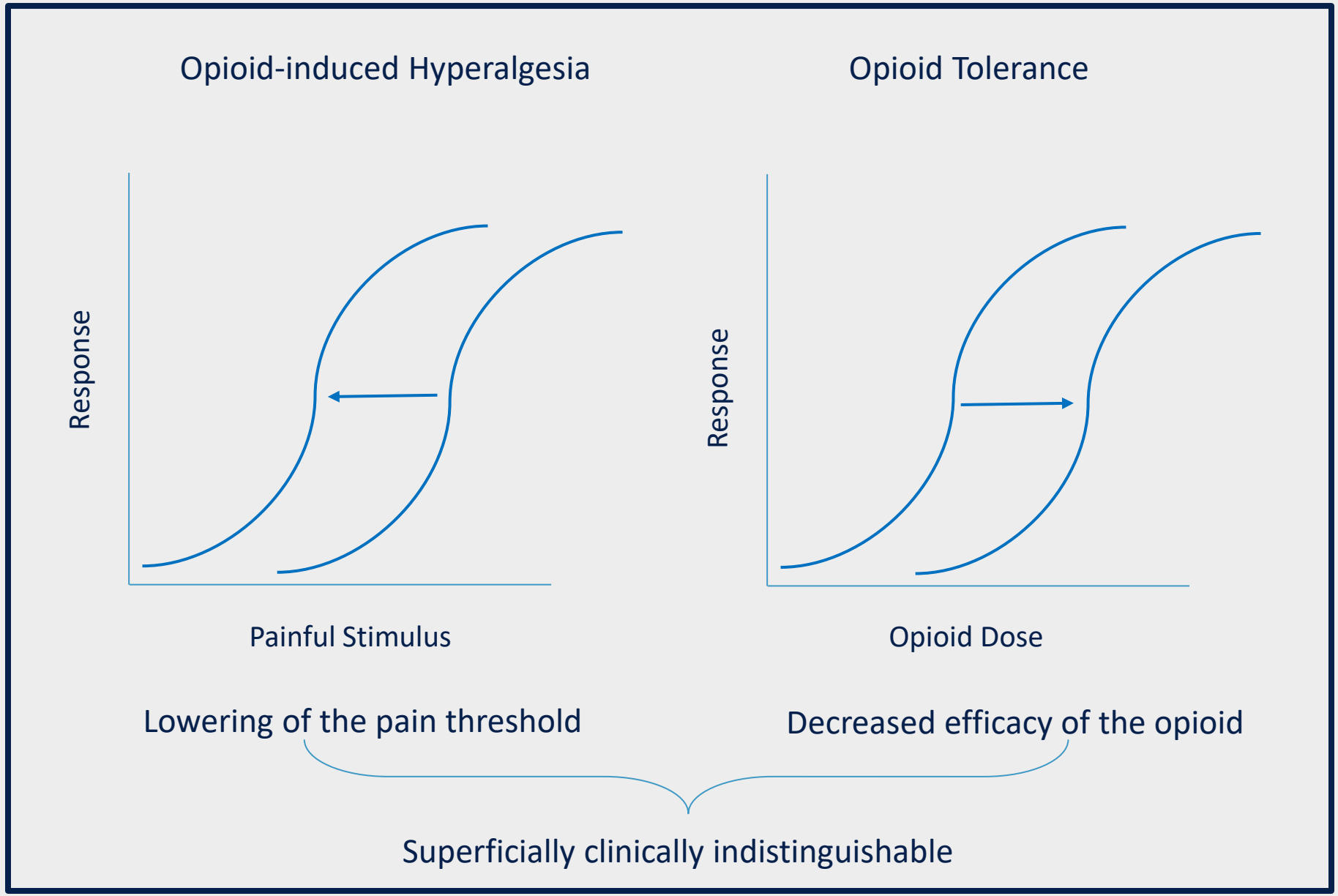


Cross-Tolerance

- Tolerance to the repeated use of a specific drug in a given category is generalized to other drugs with the same structural or mechanistic category.



Goldfrank's Toxicologic Emergencies, 11th

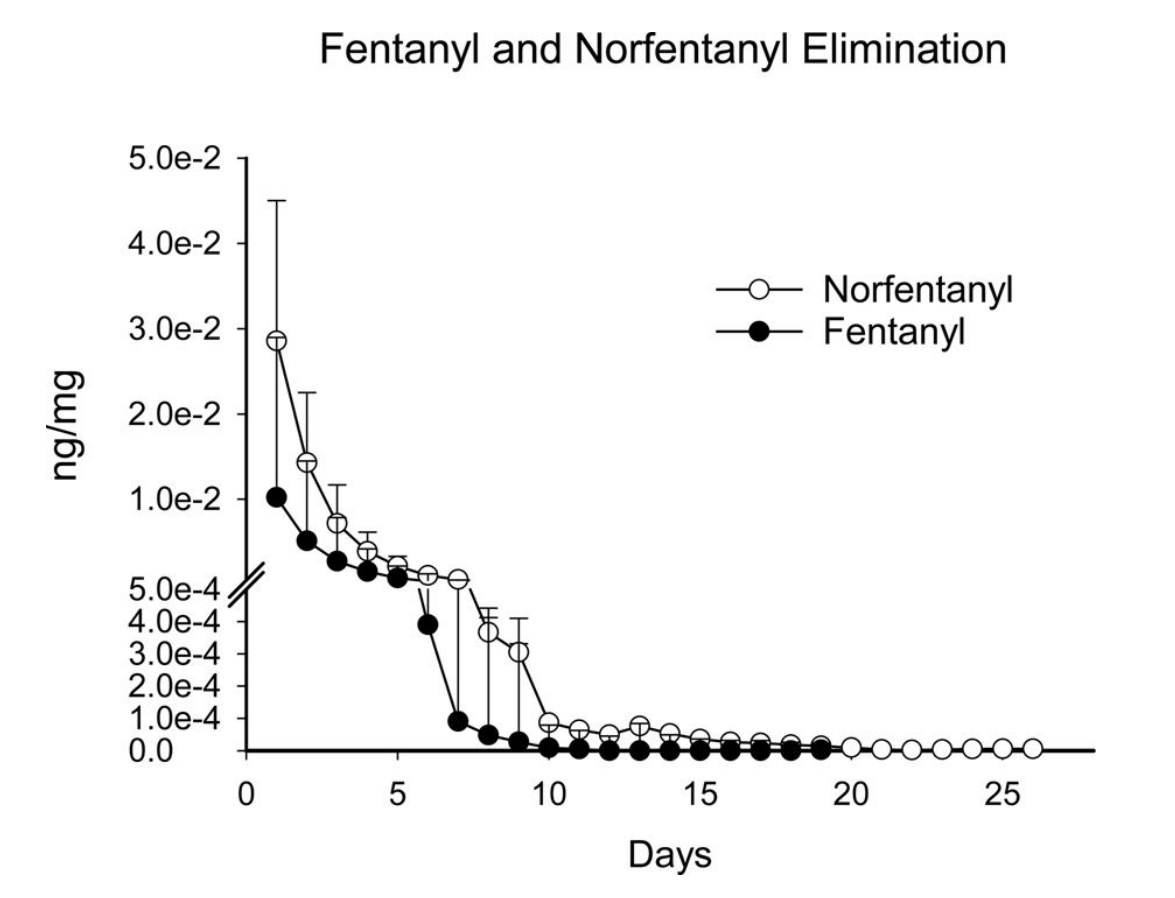

Opioid-induced Hyperalgesia
Response
Painful Stimulus
Lowering of the pain threshold
Opioid Tolerance
Response
Opioid Dose
Decreased efficacy of the opioid
Superficially clinically indistinguishable

Physical Dependence

- A state that develops as a result of adaptation and the resetting of homeostatic mechanisms
- Withdrawal syndrome can occur in physically dependent person when the drug is abruptly stopped or dose reduced
  - Typically improves on restarting the drug
  - There can be a “point of no-return”
- Can occur with both addictive and non-addictive use of drugs
  - Caffeine, nicotine
- And with therapeutic use
  - Clonidine

Physical Dependence
Withdrawal Severity

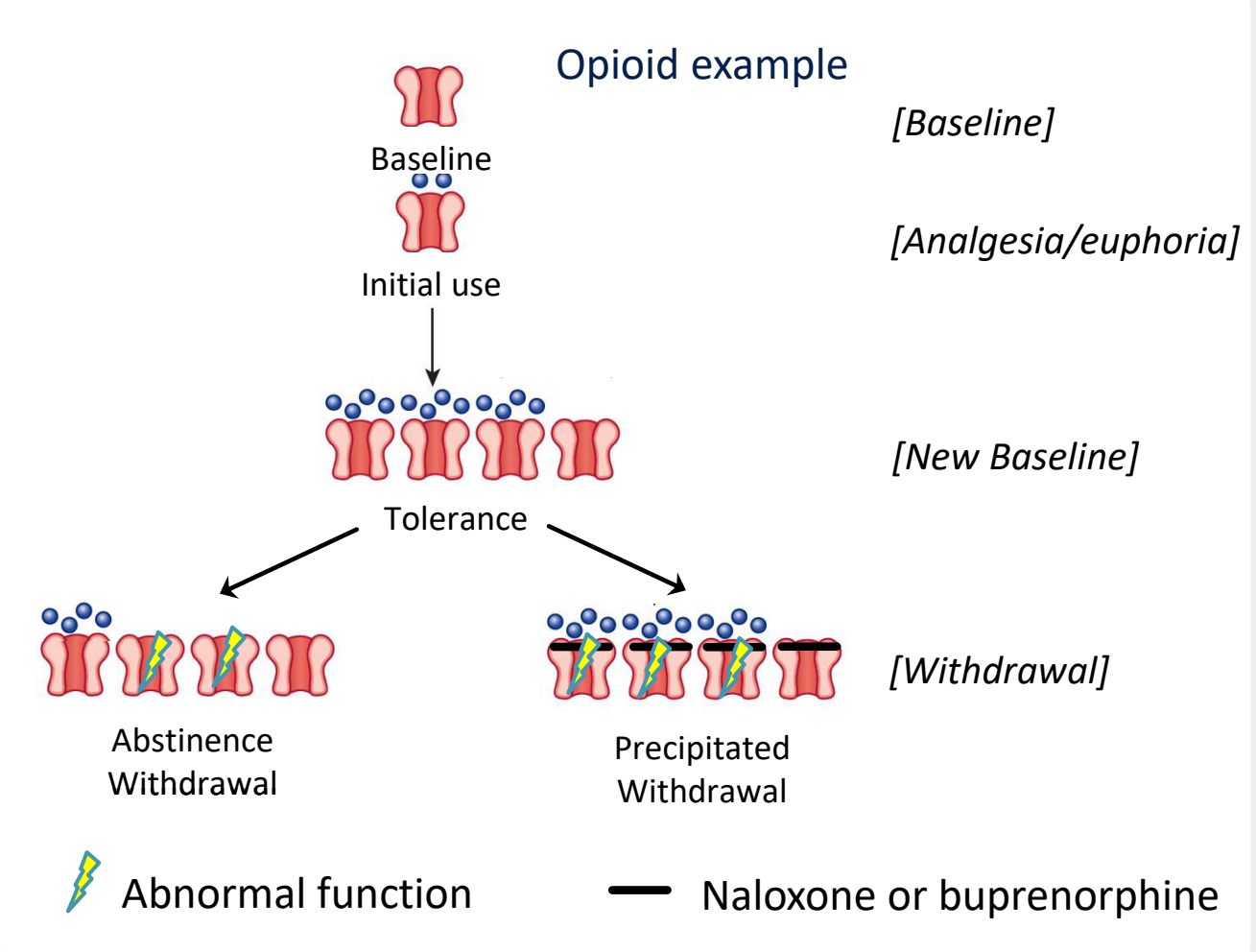
- Depth of dependence is related to extent and duration of exposure
  - Receptor adaptation



Huhn AS, et al. Drug Alcohol Depend 2020;108:147

Physical Dependence
Withdrawal Severity

- Related to rapidity of development of withdrawal



Drug Interactions

Physiological Drug Interactions (Pharmacodynamic)

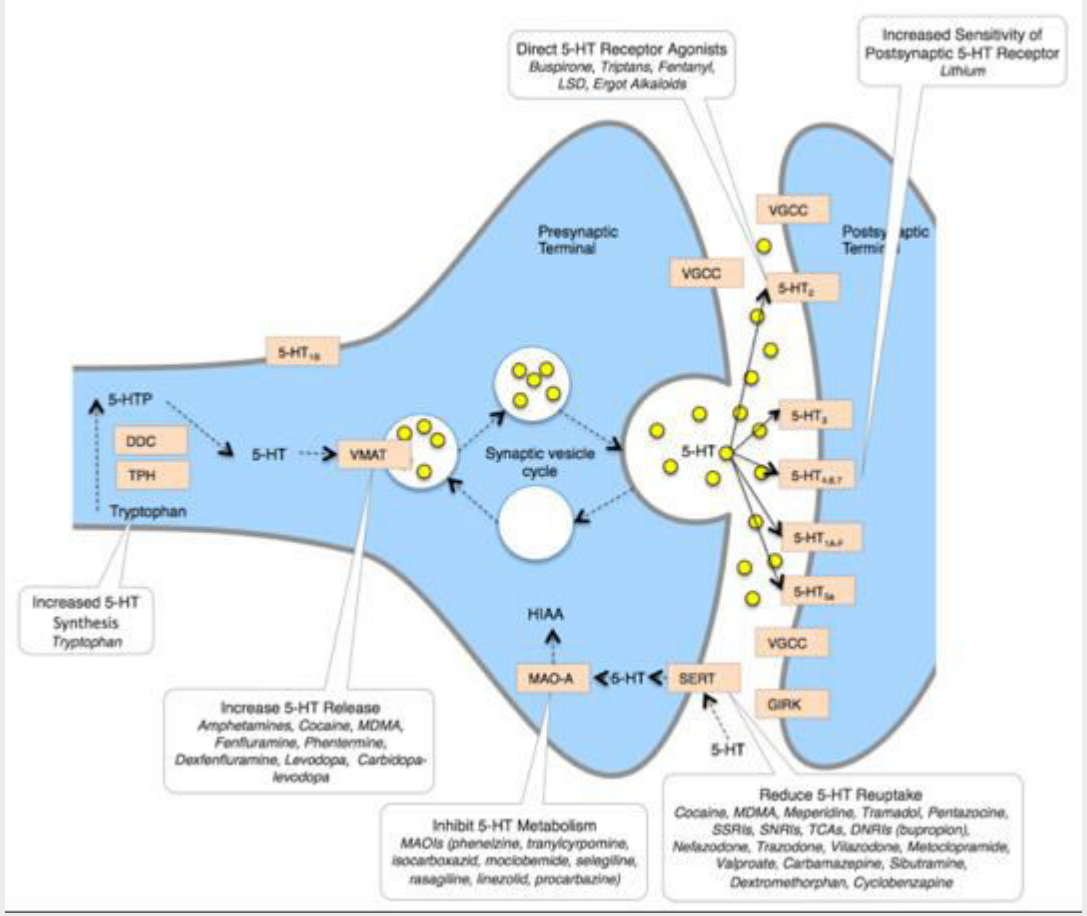


Heroin
and cocaine



Medetomidine
and fentanyl

PK/PD Drug Interactions



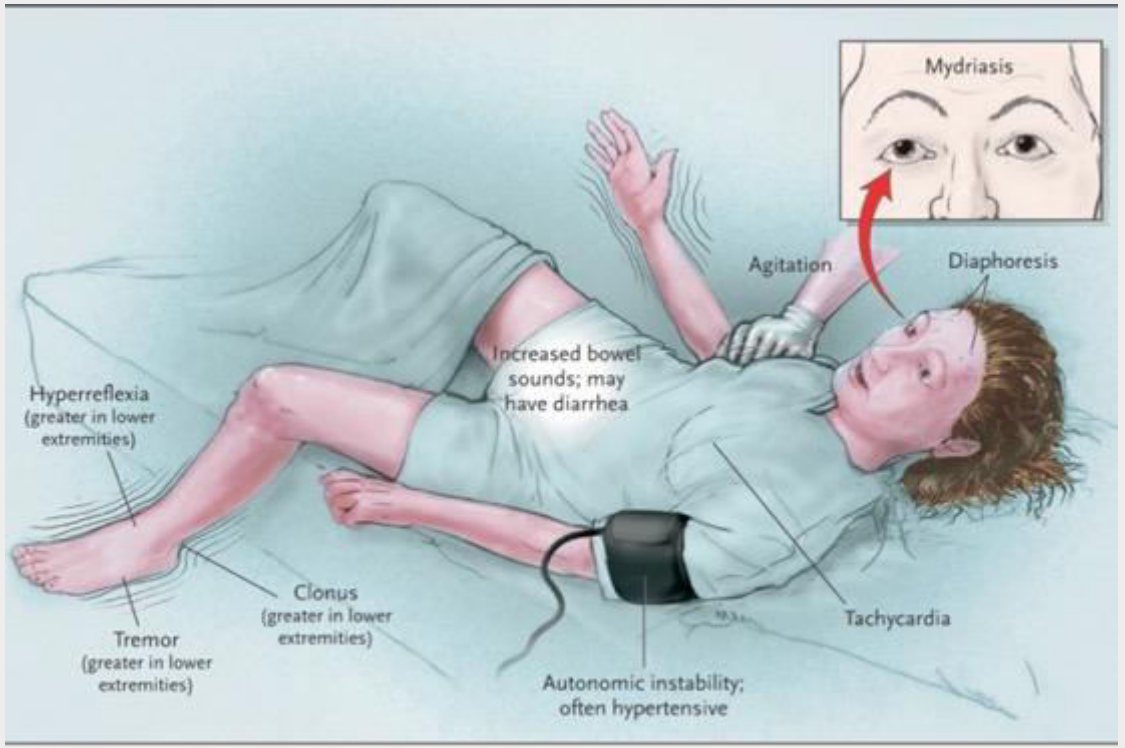


Figure 2. Findings in a Patient with Moderately Severe Serotonin Syndrome.
Hyperkinetic neuromuscular findings of tremor or clonus and hyperreflexia should lead the clinician to consider the diagnosis of the serotonin syndrome.

www.real-psychiatry.blogspot.com

Boyer E. NEJM 2005

CONSENSUS STATEMENT

Appropriate Use of Drug Testing in Clinical Addiction Medicine



Effective Date: January 1, 2020
Rev. 0722

Medical Review Officer Guidance Manual for Federal Workplace Drug Testing Programs







Department of Health and Human Services
Substance Abuse and Mental Health Services Administration
Center for Substance Abuse Prevention
Division of Workplace Programs

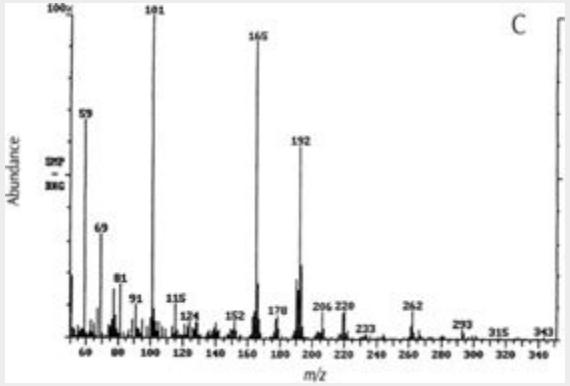
Philosophical Considerations (for substance use)

- Testing is not meant to "catch" the patient
  - Testing identifies recent use it does NOT identify addiction or impairment
  - A positive finding suggests need to talk with patient and/or review treatment plan
    - Not to prevent, limit, or punitively change treatment
- Tests must be interpreted in the context of patient self-report and other information from observed behaviors or reliable sources



Screening and Confirmatory Tests





Screening (Presumptive) Assays – indicate the presumptive presence of drugs

Highly sensitive

Rapid, inexpensive

Cutoff - Yes/No

Confirmatory (Definitive) Assays – specifically identify the drug detected in the screening assay

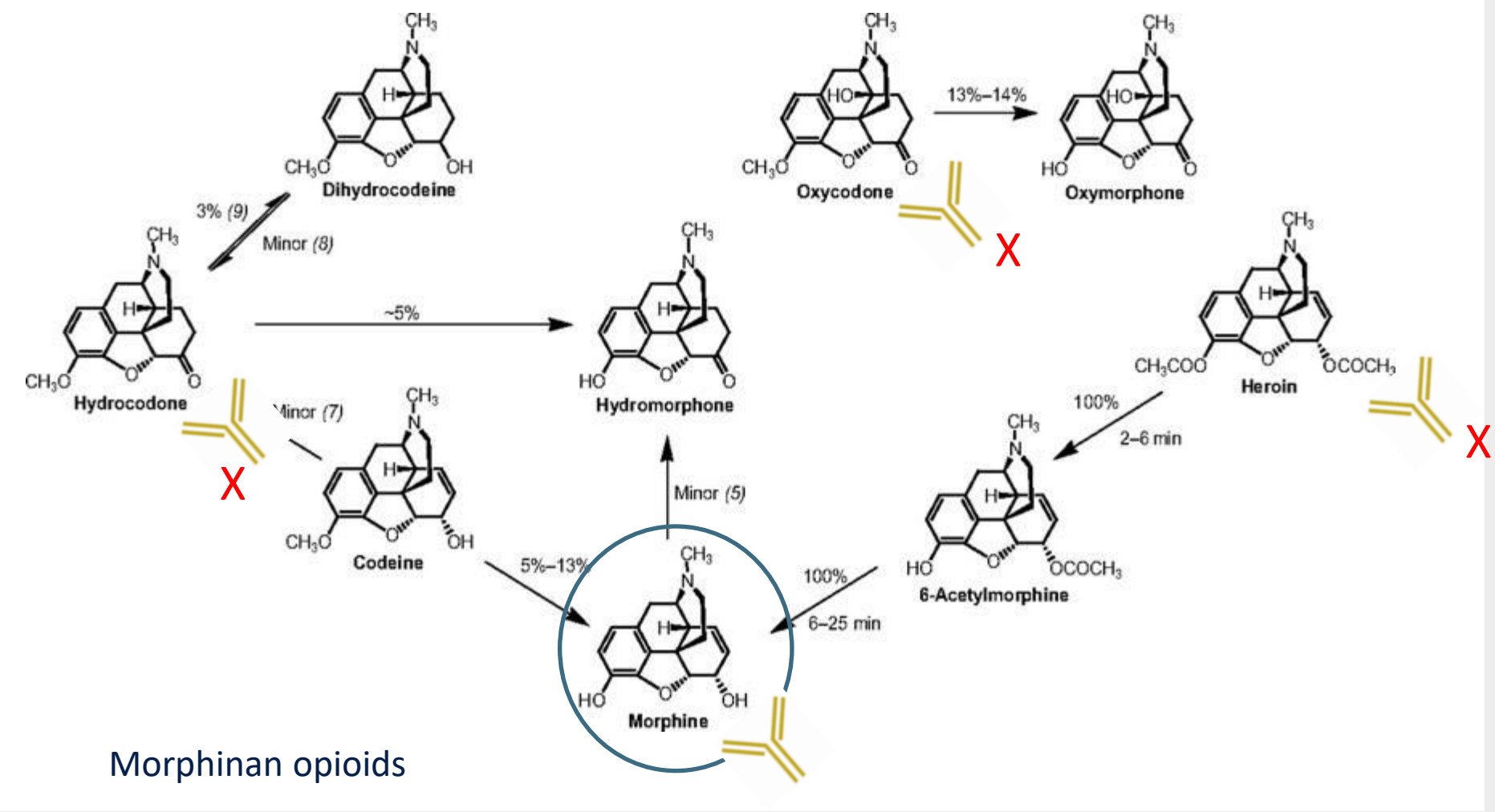
Highly specific

Quantitative

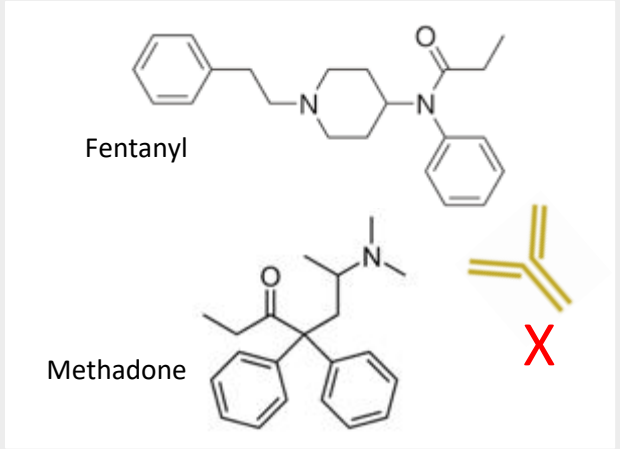
Complicated, expensive

Screening Tests for “Drugs of Abuse”

- Enzyme immunoassay
  - Based on a substance’s structure.
  - Relatively inexpensive, easily automated
- Analytical false positives are possible (e.g., amphetamine assay identifies pseudoephedrine)
  - Confirm “unconfirmed” positive screens in some clinical situations
- Analytical false negatives are uncommon (i.e., assay completely misses an expected analyte)
  - Clinical false negatives occur (e.g., opiate assay doesn’t detect an opioid)



Morphinan opioids



Non-morphinan opioids

The “Opiate” Assay: Not So Good for “Opioids”

TABLE 7–4 Performance Characteristics of Common Urine Drug Screening Immunoassays[a]

Drug/Class	*Detection Limits (ng/mL)[b]*	*Confirmation Limits (ng/mL)[b]*	*Detection Interval[c]*	*Comments*
Amphetamine/ methamphetamine	500	500	1–2 days (2–4 days)	Decongestants, ephedrine, L-methamphetamine, selegiline, and bupropion metabolites are reported to give false-positive test results with some assays; MDA, MDEA, and MDMA are variably detected.
Barbiturates	200		2–4 days	Phenobarbital detection interval is up to 4 weeks.
Benzodiazepines	100–300		1–30 days	Benzodiazepines vary in reactivity and potency. Hydrolysis of glucuronides increases sensitivity. False-positive test results are reported with oxaprozin.
Cannabinoids	50	15	1–3 days (1 month)	Screening assays detect inactive and active cannabinoids; confirmatory assay detects inactive metabolite THCA. Duration of positivity is highly dependent on screening assay detection limits.
Cocaine	150	100	2 days (1 wk)	Screening and confirmatory assays detect inactive metabolite BE. False-positive test results caused by cross-reactive compounds are unlikely.
Opiates			1–2 days (1 week)	Semisynthetic opioids derived from morphine show variable cross-reactivity. Fully synthetic opioids (eg, fentanyl, meperidine, methadone, tramadol) have minimal cross-reactivity. Quinolones are known to cross-react with some assays.
Codeine/morphine	2,000	2,000		
Hydrocodone/hydromorphone	300	100		
Oxycodone/oxymorphone	100	50		
6-Acetylmorphine	10	10		
Methadone	300		1–4 days	Doxylamine is reported to cross-react with some assays.
Phencyclidine	25	25	4–7 days (1 month)	Dextromethorphan, diphenhydramine, ketamine, and venlafaxine is reported to cross-react with some assays.

[a]Performance characteristics vary with manufacturer and may change over time. For the most accurate information, consult the package insert of the current lot or contact the manufacturer. [b]Substance Abuse and Mental Health Services Administration recommendations[10] are shown for amphetamines/methamphetamines, cannabinoids, cocaine, opiates, and phencyclidine immunoassays. Other commercial immunoassay cutoffs are also listed. Other cutoffs may be set by individual laboratories. [c]Values are after typical use; values in parentheses are after heavy or prolonged use.

BE = benzoylecgonine; MDA = methylenedioxyamphetamine; MDEA = methylenedioxyethylamphetamine; MDMA = methylenedioxymethamphetamine; THCA = tetrahydrocannabinolic acid.





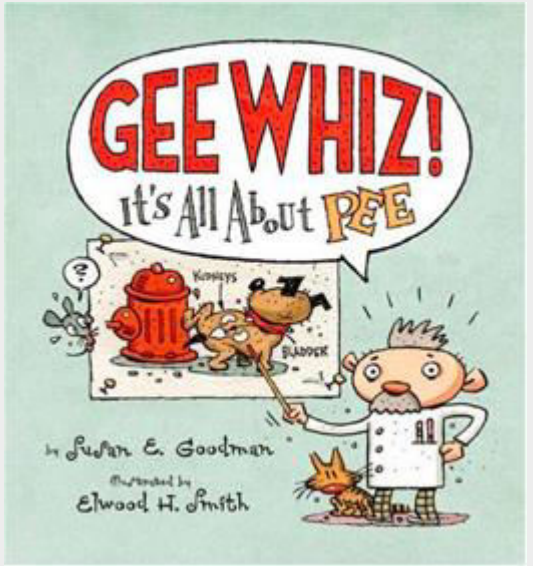
The Gold Standards for Confirmation

- Gas Chromatography/Mass Spectrometry
  - Gold standard for confirmation
  - Chemical “fingerprint” of drugs
  - Sensitive and specific
  - Legally defensible

- Liquid Chromatography/Tandem Mass Spectrometry (LC/MS/MS)
  - Emerging Standard for Confirmation
  - Less sample preparation

Interpretation of a Negative Opioid Assay

- Patient is not using (e.g., diversion)
- Clinical false negative
  - Collection/Lab error
  - Wrong screening assay used
    - e.g.: “Opiate” assay for oxycodone
  - Cutoffs are often used
  - Detection periods are short
  - Adulteration



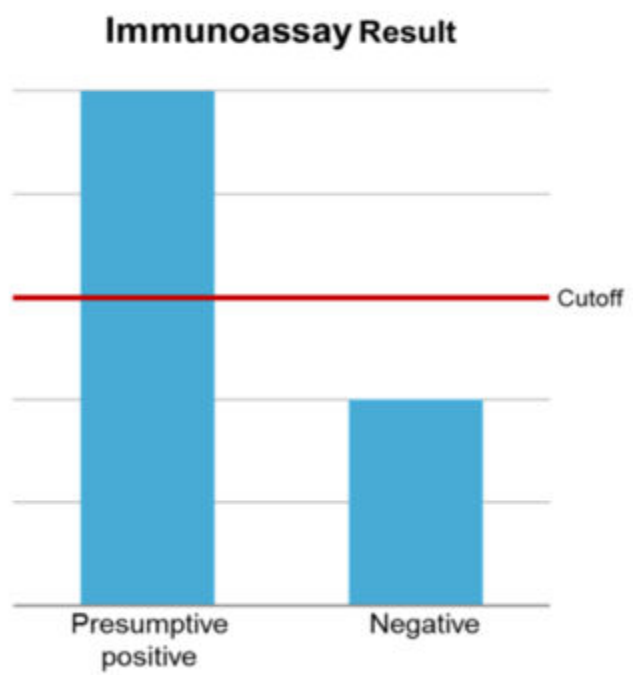


TABLE 2. **Length of Time Drugs of Abuse Can Be Detected in Urine**

Drug	Time
Alcohol	7-12 h
Amphetamine	48 h
Methamphetamine	48 h
Barbiturate	
Short-acting (eg, pentobarbital)	24 h
Long-acting (eg, phenobarbital)	3 wk
Benzodiazepine	
Short-acting (eg, lorazepam)	3 d
Long-acting (eg, diazepam)	30 d
Cocaine metabolites	2-4 d
Marijuana	
Single use	3 d
Moderate use (4 times/wk)	5-7 d
Daily use	10-15 d
Long-term heavy smoker	>30 d
Opioids	
Codeine	48 h
Heroin (morphine)	48 h
Hydromorphone	2-4 d
Methadone	3 d
Morphine	48-72 h
Oxycodone	2-4 d
Propoxyphene	6-48 h
Phencyclidine	8 d

Data from references 7 through 12.

Buprenorphine analysis

- Can only generalize about expected levels
  - No credible way to say “X” dose should give “Y” level
  - Patients tend to stay within a certain range over time unless dose change
    - Trending helpful and can detect aberrancy
- Adulterated specimen
  - Bup without metabolite (always)
  - Bup >1000 ng/mL, even with metabolite (suggestive)
- Higher Bup levels than Norbup levels due to:
  - Dosing shortly before urine test
  - CYP 3A4 inhibitor or substrate which slows conversion to metabolite

Matrix Considerations

- Window of detection
- Time to obtain results (availability of POCT)
- Ease of collection (need for trained personnel, collection facilities)
- Invasiveness/unpleasantness of collection
- Availability of the sample (e.g., renal health, shy bladder, baldness, dry mouth)
- Susceptibility of the sample to tampering

Where Can I Get Help with Interpretation?



- Medical or forensic toxicologist
- Staff at the testing laboratory
- A physician with MRO certification

What property of fentanyl accounts for its enhanced psychoactive effects compared to morphine?

A. Charge
B. Lipophilicity
C. Molecular weight
D. Potency

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D. Potency

A patient started on opioids requires increasing doses of medication to get adequate pain relief. At the same time, painful stimuli elicit more pain that they previously did. What does this represent?

A. Hyperalgesia
B. Pharmacodynamic tolerance
C. Pharmacokinetic tolerance
D. Withdrawal

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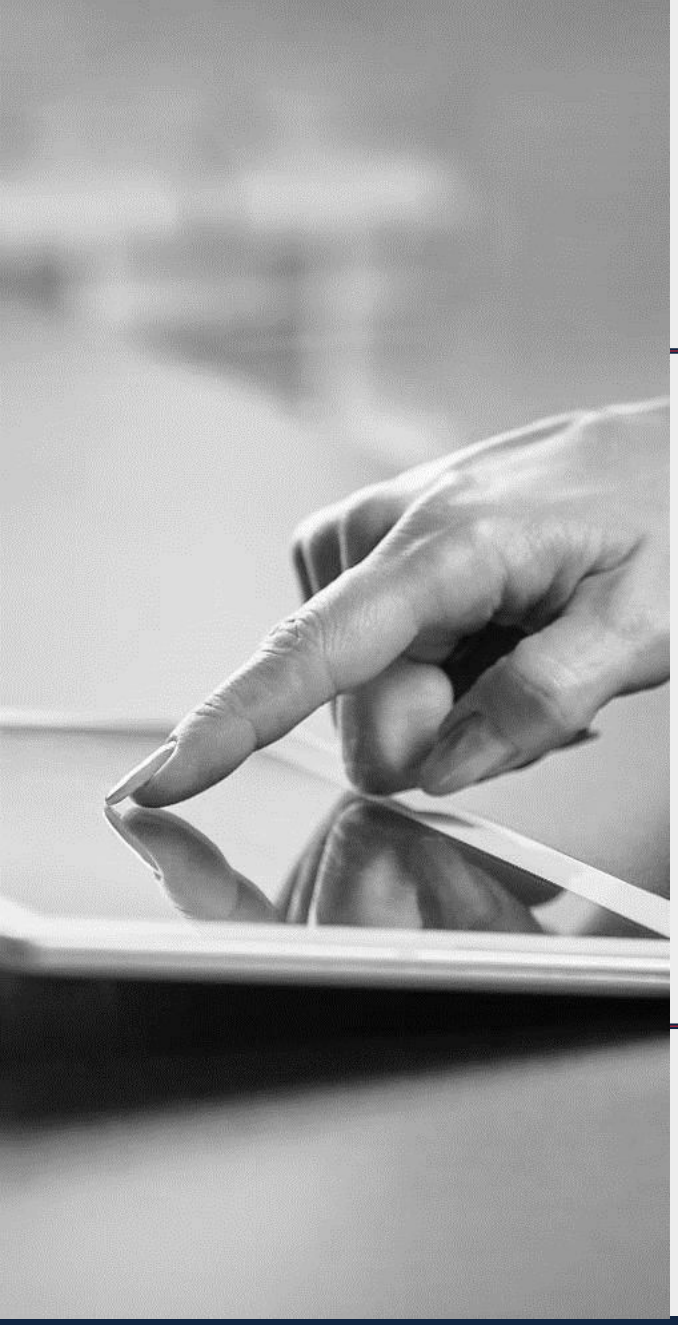
D. Withdrawal

Which of the following drug screening tests is associated with the lowest rate of false positive results?

A. Amphetamine
B. Cocaine
C. Opioids
D. Phencyclidine

Which of the following drug screening tests is associated with the lowest rate of false positive results?

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B. Cocaine
C. Opioids
D. Phencyclidine



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ASAM REVIEW COURSE 2026

Medical Co-Morbidities: Diagnosis, Prevention and Complications

Carolyn Warner-Greer, MD, MSc, FASAM
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Bowen Health
Fort Wayne, IN





Financial Disclosure

Carolyn Warner-Greer, MD, MSc, FASAM

- No relevant disclosures

Learning Objectives



1

Conduct an appropriate history and physical exam for persons with substance use disorder.

2

Identify key medical co-morbidities that can occur with substance use disorder.

Presentation Outline

Routine and Preventive Care

- History
- Physical examination
- Labs
- Preventative Care
- Preconception Care

Medical Consequences of Alcohol and Drug Use

- Alcohol
- Tobacco
- Opioids
- Stimulants
- Injection Drug Use
- Cannabis

SUD = Poor Medical Care

- Reasons
- Barriers
- Consequences

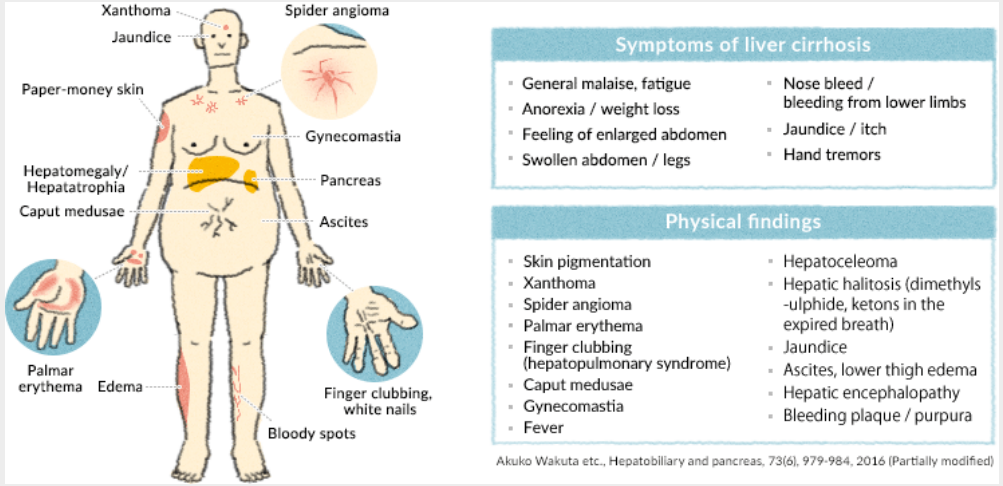
Chan Carusone, S., Guta, A., Robinson, S. et al. "Maybe if I stop the drugs, then maybe they'd care?"—hospital care experiences of people who use drugs. Harm Reduct J 16, 16 (2019).

General Medical Evaluation

- Medical History
- Physical Examination
- Tests
- Preventative Counseling
- Preventative Screening
- Immunizations
- Chemoprophylaxis

Alcohol

- Affects every organ system
- Women>>Men
- Is any ETOH safe?
- Physical Exam Findings:

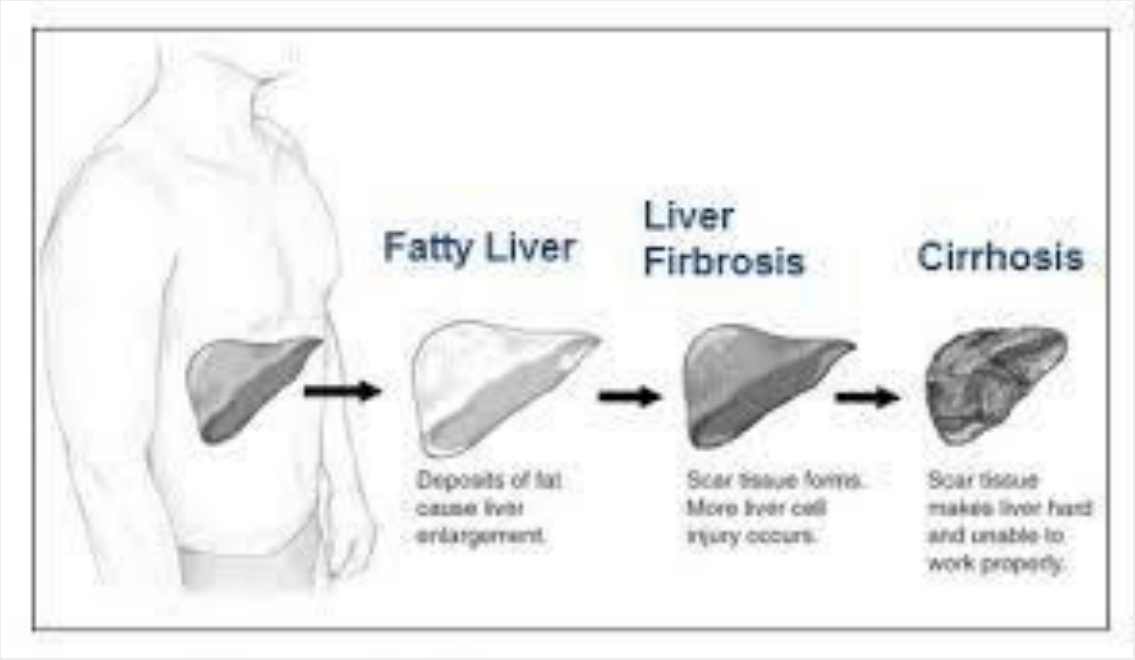


- Spider angiomas
- Palmar Erythema

- Jaundice
- Ascites

Alcohol

- GI-
  - Esophagitis/gastritis, Mallory-Weiss tears, esophageal varices
  - Pancreatitis (dose-related toxic effect)
  - Alcohol-related liver disease
    - AST/ALT >2
    - Fatty liver
    - Alcohol related hepatitis (ALH)
    - Cirrhosis-10-20%



Alcohol

- Respiratory
  - Aspiration
  - OSA
- Infectious
  - Hepatitis
  - SBP
  - TB
- Nutrition-vitamin and mineral deficiencies
  - B1, B6, riboflavin, niacin, Vit D, Mg2+, Ca2+, folate, PO4, zinc

Alcohol

- CV
  - HTN-dose dependent
  - Cardiomyopathy-dilated
  - Atrial Fibrillation “Holiday Heart”
- Heme/Oncology
  - Anemia-macrocytic
  - Thrombocytopenia/pancytopenia
  - Coagulopathy
  - Increase CA: breast, oral, GI, hepatic (no safe threshold)

Zhao J, Stockwell T, Naimi T, Churchill S, Clay J, Sherk A. Association Between Daily Alcohol Intake and Risk of All-Cause Mortality: A Systematic Review and Meta-analyses. JAMA Netw Open. 2025;6(3)

Alcohol

- Neurological
  - Neuropathy-peripheral/autonomic
  - Sleep
  - Cognition
  - Cerebellar dysfunction
  - Trauma

Wernicke Encephalopathy	Korsakoff's Syndrome
C-Confusion	R-Retrograde amnesia
O-Ophthalmoplegia	A-Anterograde amnesia
A-Ataxia	C-Confabulation
T-Thiamine Deficiency	K-Korsakoff psychosis

Medical Maestro

Alcohol

- Endocrine
  - Hypogonadism
    - Direct testicular effect
    - Hepatic dysfunction → reduction in gonadal hormones
  - Decreased fertility
  - Hyperlipidemia
- Musculoskeletal
  - Prolonged immobilization
  - Gout
  - Osteonecrosis

Tobacco

- Leading cause of preventable death
- CV
  - HTN
  - CAD (multifactorial)
  - Peripheral vascular disease
- GI
  - GERD/PUD
  - Pancreatitis
  - Inflammatory Bowel Disease
  - Malignancy

Tobacco

- Respiratory
  - COPD
  - Malignancy
  - Asthma
  - PTX
  - Pulmonary HTN
  - Pneumonia/bronchitis

Tobacco

- Heme/Onc
  - 49% of cancer deaths related to tobacco use
  - Oral, gastric, lung, breast, cervical, bladder, kidney
  - DVT/PE
- Neurological
- Infectious Disease
- Reproductive/Endocrinology
  - Grave's Disease/hypothyroidism
  - Erectile Dysfunction/infertility
  - Osteoporosis


I didn't survive drugs & alcohol
so I could die from lung cancer.
I had to stop smoking.
CIGARETTES ARE MY GREATEST ENEMY

Tobacco Cessation and Recovery?

- Continued tobacco use predicted return to all substance use
- Should residential treatment programs allow nicotine use?
- Will patients leave prematurely?
- Philadelphia, California, NY experiences

Weinberger AH, et al. Cigarette Smoking Is Associated With Increased Risk of Substance Use Disorder Relapse: A Nationally Representative, Prospective Longitudinal Investigation. J Clin Psychiatry. 2017 Feb;78(2)

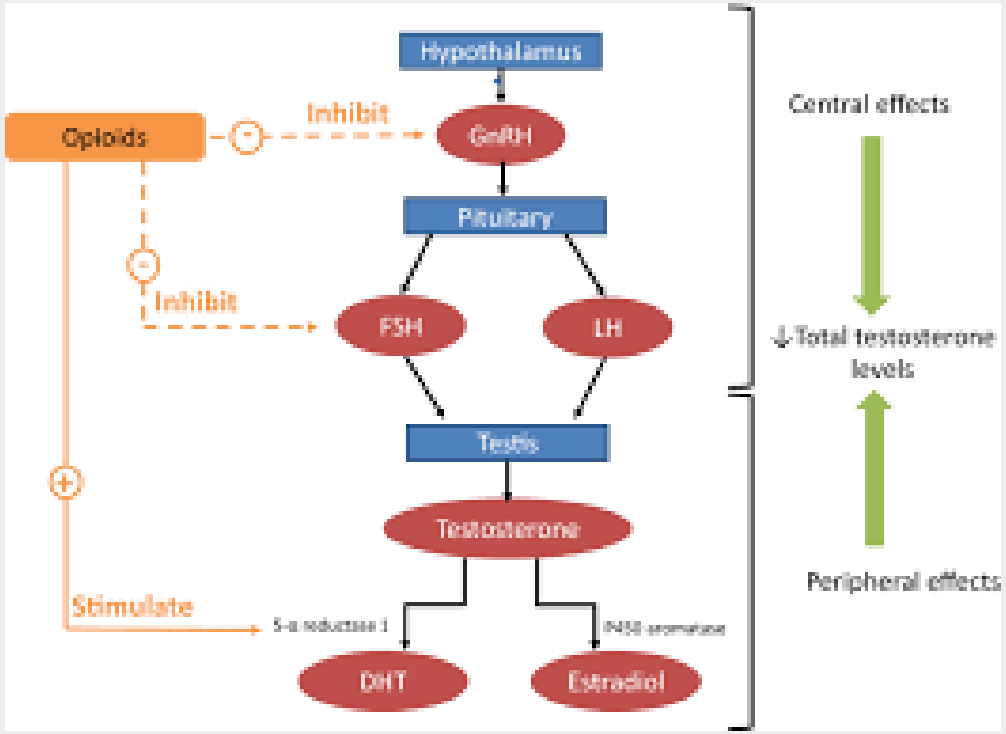
Pagano A, et al Evaluating a Tobacco-free Policy Intervention in Residential Substance Use Disorder Programs. J Drug Issues. 2025 Feb 24;56(3):482–501

Opioids

- ID
  - IVDA-endocarditis, osteomyelitis, Hep C and HIV
  - STD
- Respiratory-overdose, chest wall rigidity with FENT, pulmonary edema
- Endocrine-reduction in steroid hormones
- Trauma-rhabdomyolysis, compartment syndrome
- Respiratory-OSA,
- GI-constipation

Opioid Induced Hypogonadism

- Low libido
- Muscle wasting
- Increased adiposity
- Depression
- Osteoporosis
- Treatment:
  - Testosterone replacement



Mayo Clinic Proceedings: Innovations, Quality & Outcomes, ISSN: 2542-4548, Vol: 3, Issue: 3, Page: 276-284

QT Prolongation

- DX:
  - Men-460-469 ms (borderline) 470+ prolonged
  - Women-460-479 ms (borderline) 480+ prolonged
- Medications: methadone, quinolones, ondansetron, macrolides, hydroxyzine, citalopram
- ↓Mg2+, K+, Ca2+
- Screening:
  - Good family and medical history-look at all medicines
  - Genetic testing
  - EKG at higher doses of methadone?
- Flockhart Table/APP-IUSOM
- Credible Meds/APP

Treece JM, Al Madani M, El Khoury G, Khraisha O, Martin JE, Baumrucker SJ, et al. Comprehensive review on methadone induced QT prolongation and torsades. J Pharmacol Pharmacother 2018;9:66-7511-12-2017 R

Risk Factors for TdP

Risk Factors for Torsades de Pointes	
Nonmodifiable	**Modifiable**
Female sex	Multiple QT-prolonging medications
Older age	Drug toxicity
Structural or functional heart disease	Drug-drug interactions
Congenital long-QT syndrome	Severe acute illness
Personal history of drug-induced QT prolongation	Bradycardia
Family history of sudden (or aborted) cardiac death	Hypokalemia, hypomagnesemia, hypocalcemia
Poor metabolizer at CYP enzymes	Hepatic or renal impairment

Adapted from Funk MC et al, Am J Psychiatry *2020;177(3):273–274*

“My dentist says Suboxone caused my tooth loss!”

- Many drugs cause dental problems!
  - Reduction in saliva-xeromastia
  - Tooth grinding-bruxism
  - Periodontal disease
- Active addiction
  - Poor oral hygiene
  - Poor nutrition/high sugar intake
  - Lack of access to prophylactic care

Screening Questions for Dental Problems

- Do you experience dry mouth?
- Do you notice pain in your teeth or gum bleeding when brushing?
- When did you last see a dentist?
- Have you been told you grind your teeth or have you noticed wear or chipping?
- How often do you brush your teeth and floss?
- Do you frequently consume simple carbs and sugary drinks?

Yazdanian M, Armoon B, Noroozi A, Mohammadi R, Bayat AH, Ahounbar E, et al. Dental caries and periodontal disease among people who use drugs: a systematic review and meta-analysis. BMC Oral Health 2020;20:44.

How To Discuss With Patients

- 2022-FDA warning
- AR very low
- Practical measures
  - Regular dental care
  - Tobacco cessation (all forms)
  - Rinse mouth, delay brushing

Suzuki J, Mittal L, Woo SB. Sublingual buprenorphine and dental problems: a case series. Prim Care Companion CNS Disord 2013;15:PCC.13l01533.

LFT’s and Naltrexone

- Indication OUD/AUD-baseline higher risk of hepatic disease
- No need to check LFT’s prior to initiating treatment
- HCV, HBV not a contraindication
- Elevated LFT’s no greater than placebo

Springer, Sandra A., “Monitoring of Liver Function Tests in Patients Receiving Naltrexone or Extended-Release Naltrexone,” PCSS clinical guidelines, Update 2022

Stimulants

- CNS
  - CVA-5X increased risk hemorrhagic (METH), also ischemic (COC)
- CV
  - MI
  - HTN
  - Aortic dissection
  - Ventricular arrhythmia
  - Supportive treatment: β1blocker not associated with unopposed α activity
- GI
  - Ischemic bowel
  - Colitis

Arenas DJ, Beltran S, Zhou S, Goldberg LR. Cocaine, cardiomyopathy, and heart failure: a systematic review and meta-analysis. Sci Rep. 2020 Nov 13;10(1):19795

Stimulants

- Renal
  - AKI
  - CKD
- Pulmonary
  - PAH
- Dermatological
- Dental

Tanz LJ, Miller KD, Dinwiddie AT, Gladden RM, Asher A, Baldwin G, Nesbit B, O'Donnell J. Drug Overdose Deaths Involving Stimulants - United States, January 2018-June 2024. MMWR Morb Mortal Wkly Rep. 2025 Aug 28;74(32):491-499.

Do I get an EKG prior to starting a prescribed stimulant?

- Kids, young adults-no
  - Low pretest probability
  - Look at EKG if one is available
- Older Adults-poor data
  - Risk of RX stimulants is hypertension, tachycardia, vasospasm
  - BP and HR every 6 months
  - EKG annually? Look for QRS widening, ventricular conduction delay, arrhythmia

Medical Complications of Inhalants-Acute

- Acute
  - Sudden Sniffing Death-fatal cardiac arrhythmia
  - Seizures
  - Hypoxia
  - Aspiration
  - Accidents

Berling I and Isbister GK, Addiction 2025;120(9):1884–1888

Medical Complications of Inhalants-Chronic

- Neuropsychiatric
  - White matter changes-cognition loss
  - Cerebellar dysfunction
  - Peripheral neuropathy
  - Mood disorders
- Pneumonitis
- Hepatoxicity
- Bone marrow suppression
- Hematologic malignancies
- Congenital defects
- Nitrous Oxide-Vitamin B 12

Lubman DI et al, Br J Pharmacol 2008;154(2):316–326

Medical Complications of IVDU

- HIV
  - PWID=10% of new HIV cases since 2012
  - Reduction:
    - SSP-reduction in HIV by 50%
    - PrEP, overdose prevention sites
- Hepatitis
  - 65% PWID-->anti HCV +
  - SSP, MOUD-reduction in HCV
  - DAA regardless of stage of recovery
  - IVDU most common risk factor for new HBV

www.cdc.gov/hepatitis/php/npr-2025/hep-c-reduce-infections-pwid.html

PrEP

- Public Health Goal: reduce new HIV infections by 75% by 2025 and 90% by 2030
- CDC, FDA endorse PrEP as effective strategy to reduce new HIV infections among PWID
- Fewer than 2% PWID filled RX for PrEP
- LAI forms of PrEP- every two months and every six months
- All forms if PrEP appropriate in pregnancy and lactation

Streed CG, Morgan JR, Gai MJ, Larochelle MR, Paasche-Orlow MK, Taylor JL. Prevalence of HIV Preexposure Prophylaxis Prescribing Among Persons With Commercial Insurance and Likely Injection Drug Use. JAMA Netw Open. 2022;5(7):e2221346

Medical Complications of IVDU

- Serious Bacterial Infections
  - Osteomyelitis
  - Endocarditis
    - S. aureus (often methicillin resistant)
    - Osler nodes, Roth spots, splinter hemorrhages, Janesway lesions
    - Vasculitis
    - Standard of care is multidisciplinary approach

Appa A, et al; Patient-Directed Discharges Among Persons Who Use Drugs Hospitalized with Invasive Staphylococcus aureus Infections: Opportunities for Improvement. Am J Med. 2022 Jan;135(1):91-96



Splinter hemorrhage



Osler node



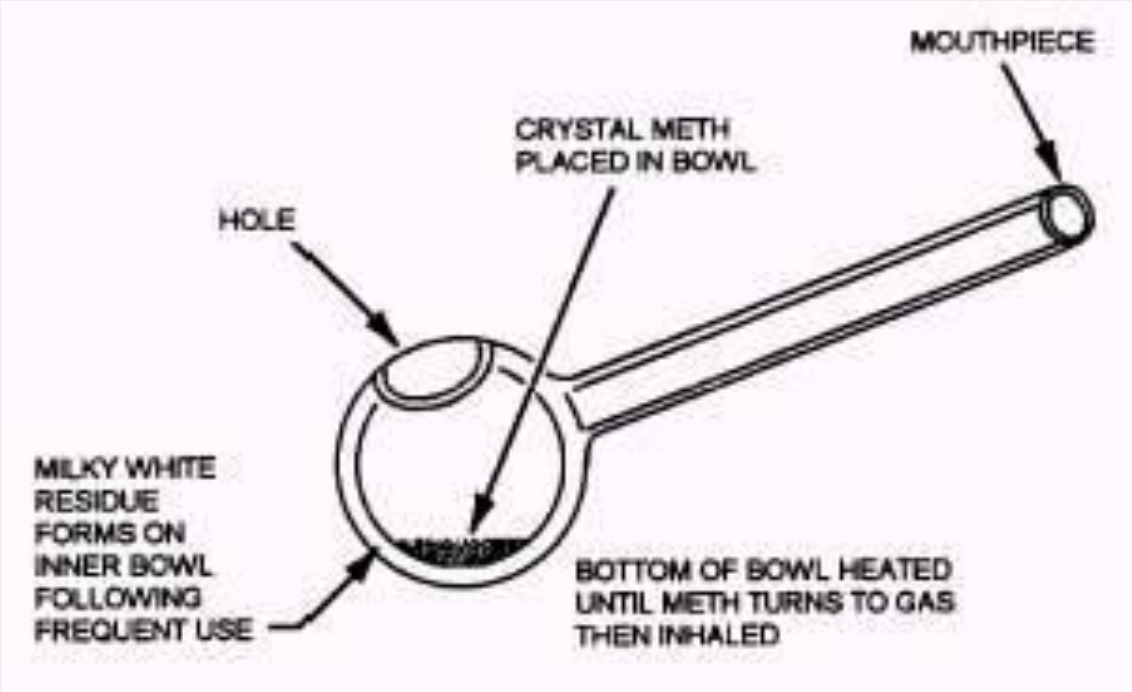
Roth's spot



Janeway lesion

Medical Complications of Inhaling Drugs

- Inhalation and insufflation
- Shared equipment-->risks of ID
- Poor adherence to barriers during SI
- Trauma-burns, cuts
- Harm reduction



Best Practices Recommendations for Canadian Harm Reduction Programs-CATIE, 2020

Cannabis

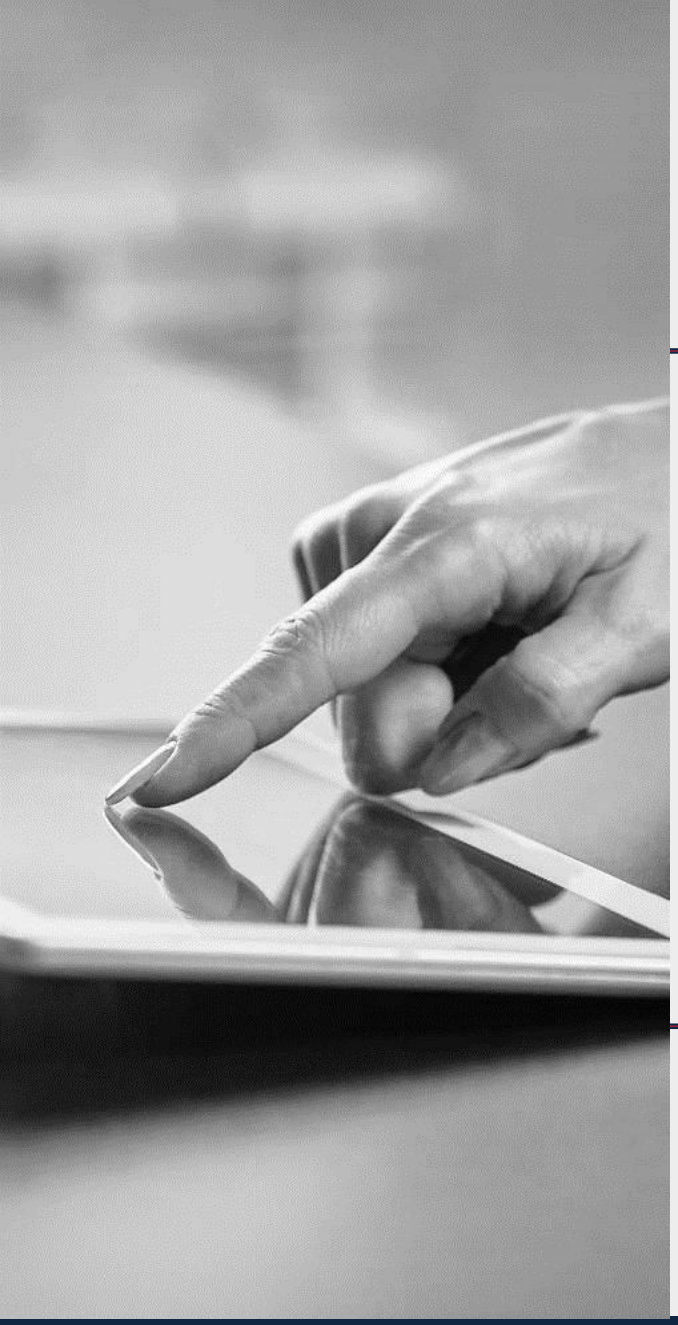
- Hyperemesis Syndrome
  - Downregulation of CNS CBD R and upregulation of gut CBD R
  - Chronic cannabis use-Rome V Criteria
  - Relieved with hot showers
  - Resolved with cessation
- Medical Cannabis
  - Medical condition with RCT suggests response to THC
  - Symptoms refractory to pharmacotherapy
  - No SUD/psychological morbidity

Gabriel P. A. et al. (2024) The impact of cannabis on non-medical opioid use among individuals receiving pharmacotherapies for opioid use disorder: a systematic review and meta-analysis of longitudinal studies, The American Journal of Drug and Alcohol Abuse, 50:1, 12-26, DOI: 10.1080/00952990.2025.2287406

Swartz JA, Franceschini D. Cannabinoid Hyperemesis Syndrome, 2016 to 2022. JAMA Netw Open. 2025 Nov 3;8(11):e2545310. doi: 10.1001/jamanetworkopen.2025.45310. PMID: 41284293; PMCID: PMC12645340.

Conclusion

- Targeted history and physical exam
- Physical health
- Teach patients to advocate for themselves
- Tobacco and alcohol most toxic substances
- Partnership with primary care colleagues



Get in Touch

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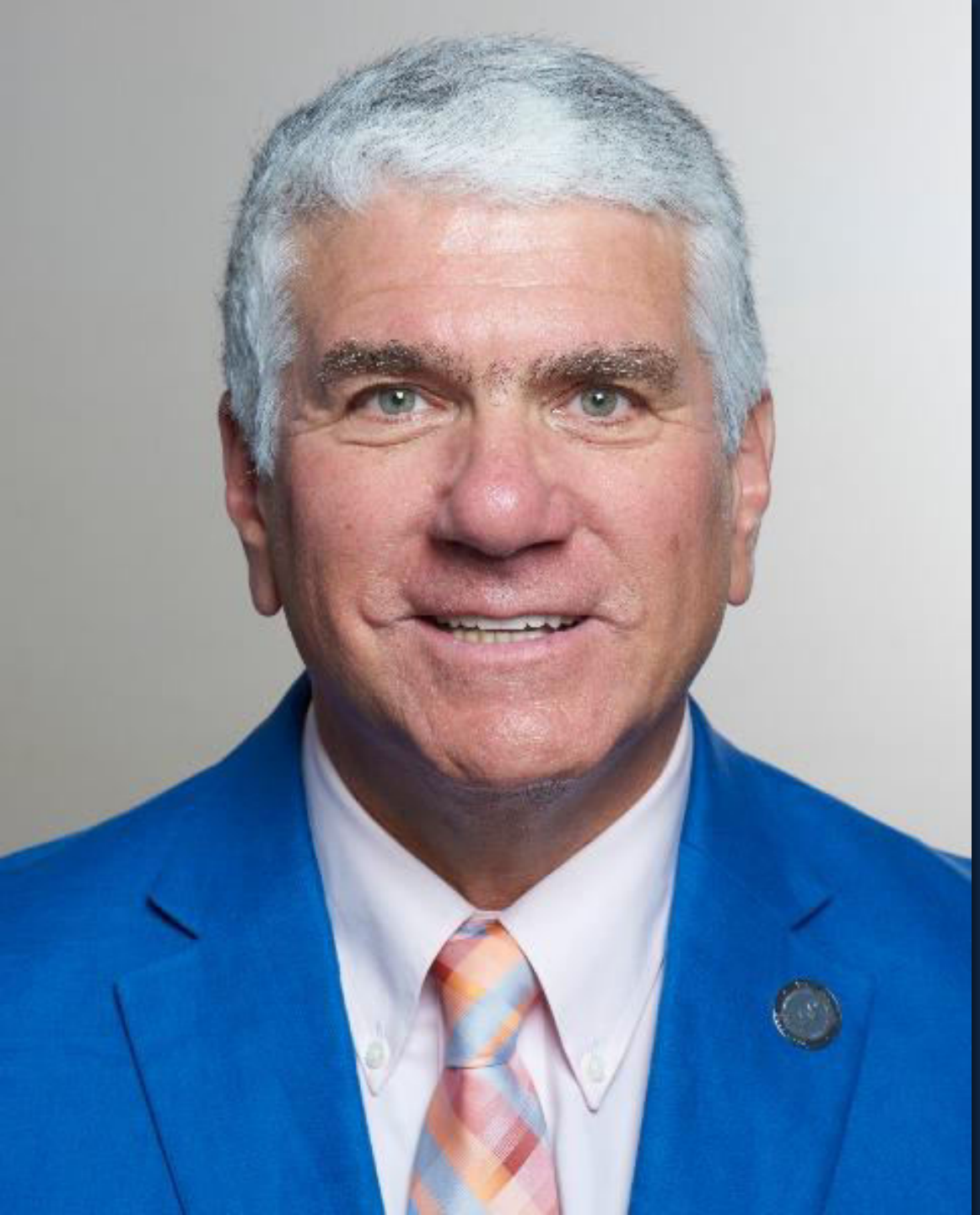
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ASAM REVIEW COURSE 2026

Interesting Cases: Applying Concepts to Unexpected Real-Life Scenarios

Edwin A. Salsitz, MD, DFASAM
Associate Clinical Professor
Mount Sinai Beth Israel
New York, NY





Financial Disclosure

Edwin A. Salsitz, MD, DFASAM

- No relevant disclosures

Name the Event

Patient : 64-year-old Female

- Admitted to rehab for treatment of AUD following a “detox” protocol. MMTP 60mg for many years-OUD in Remission
- Married: Spouse no SUD
- F: +EtOH M: No EtOH 4S: No EtOH 2Children: No EtOH
- HS Graduate: Employed in Sales
- Social, Occasional EtOH until age 56
- **? Event** → ↑↑ EtOH one year after event → **AUD**
- PE: unremarkable
- Labs: Normal CMP, CBC, Lipids
- UDT: + Methadone

What was the event?

Bariatric Surgery

64-year-old Female with AUD

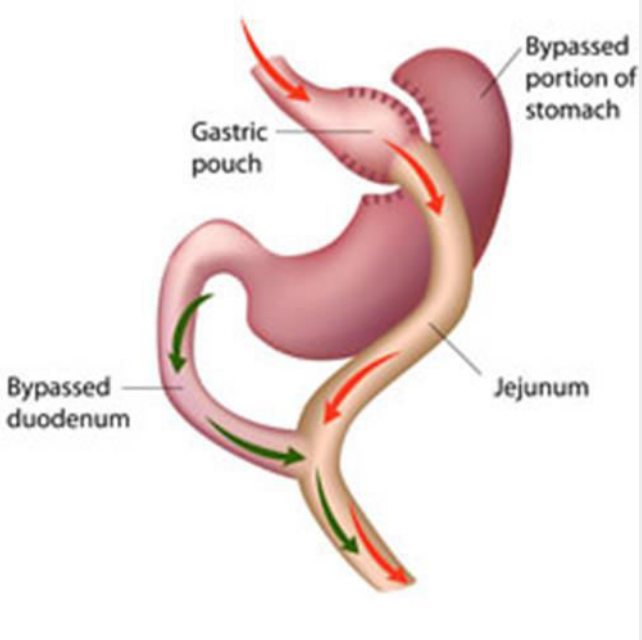
- Age 56: Bariatric Surgery: 5’ 4’’ 240lbs. BMI= 41
- ? Type of Bariatric Surgery?
- ? RYBS, SG, LAGB
- SG
- Current BMI: 24
- 2 liters Vodka day

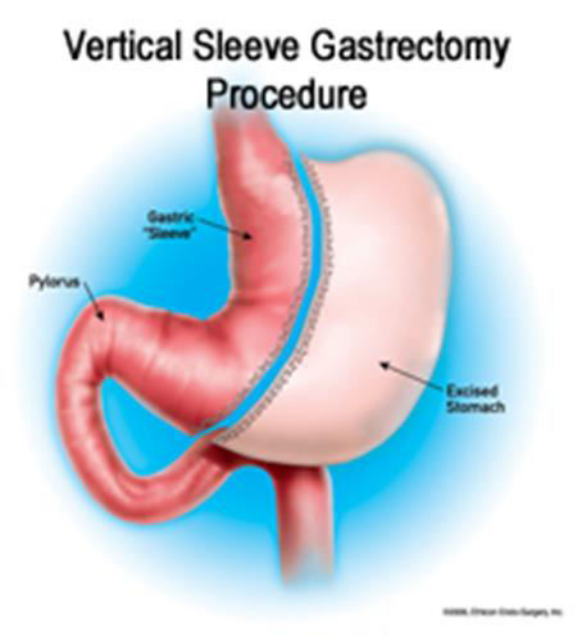
RYGB

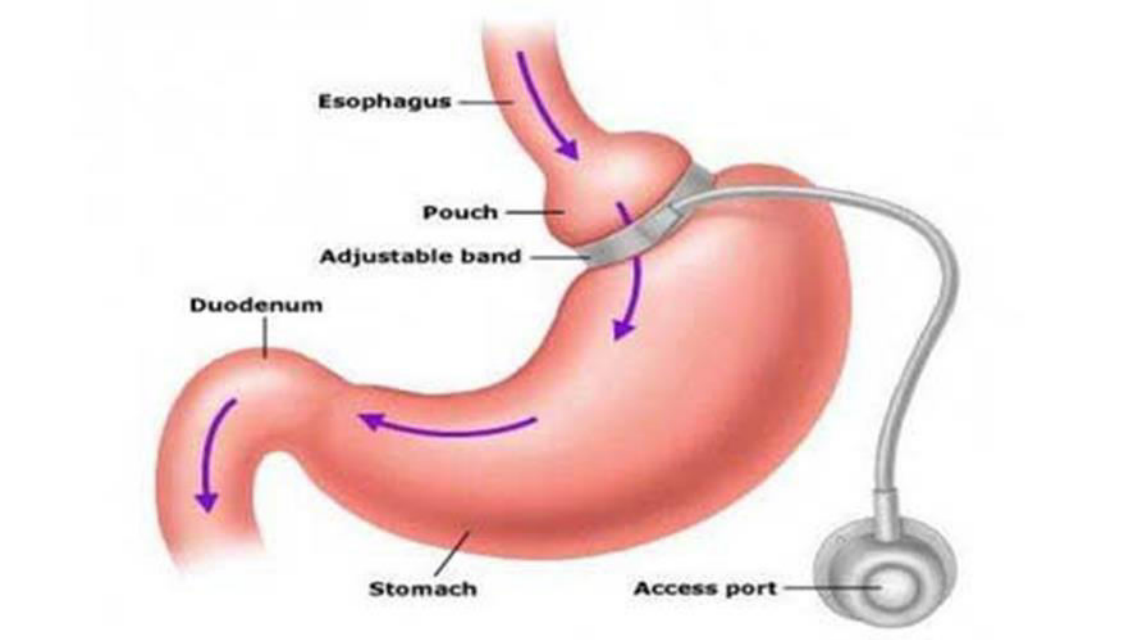
SG

LAGB

Roux-en-Y





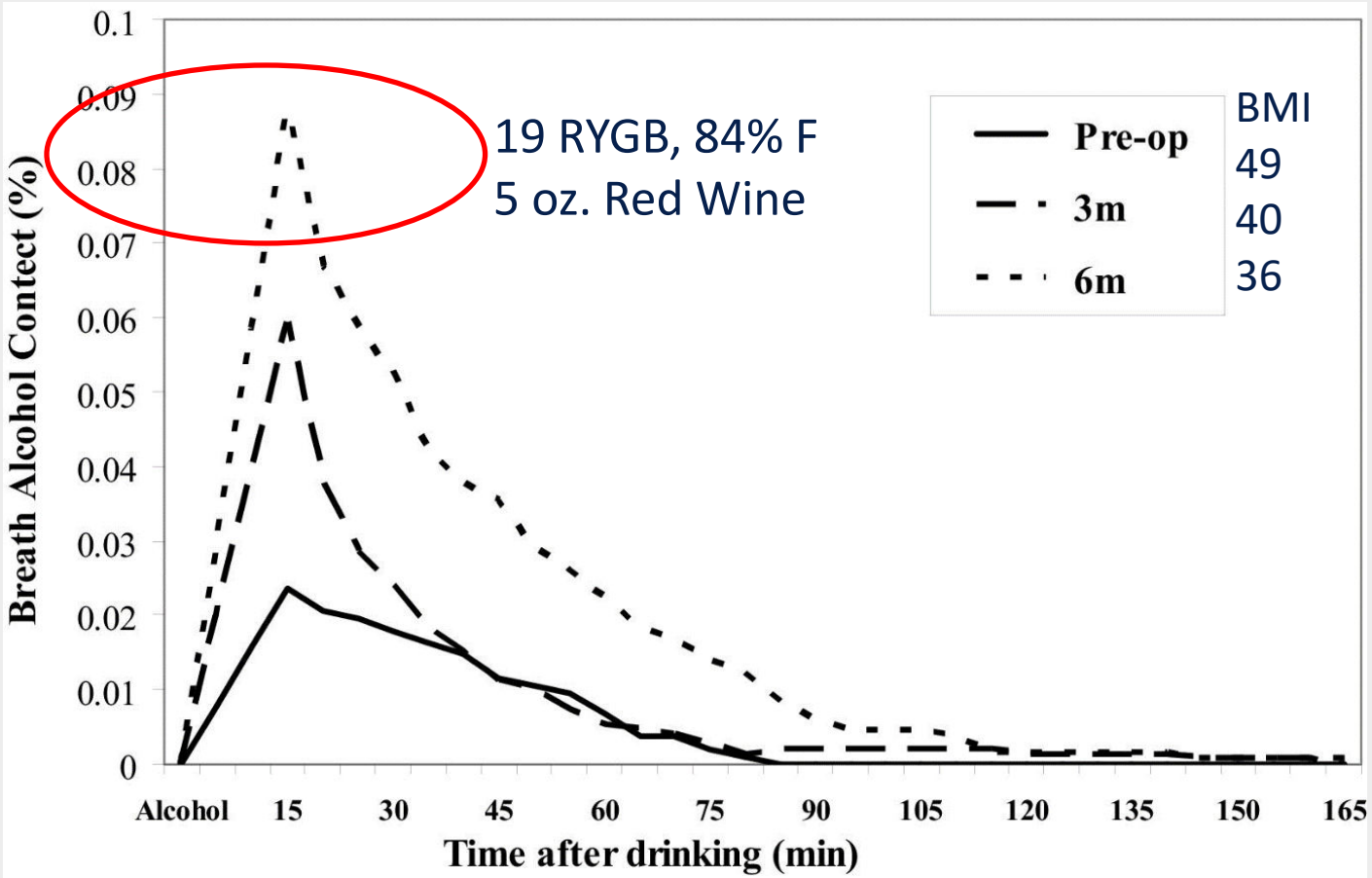


Roux-en-Y, is an end-to-side surgical anastomosis of bowel used to reconstruct the gastrointestinal tract. The name is derived from the surgeon who first described it César Roux and the stick-figure representation.

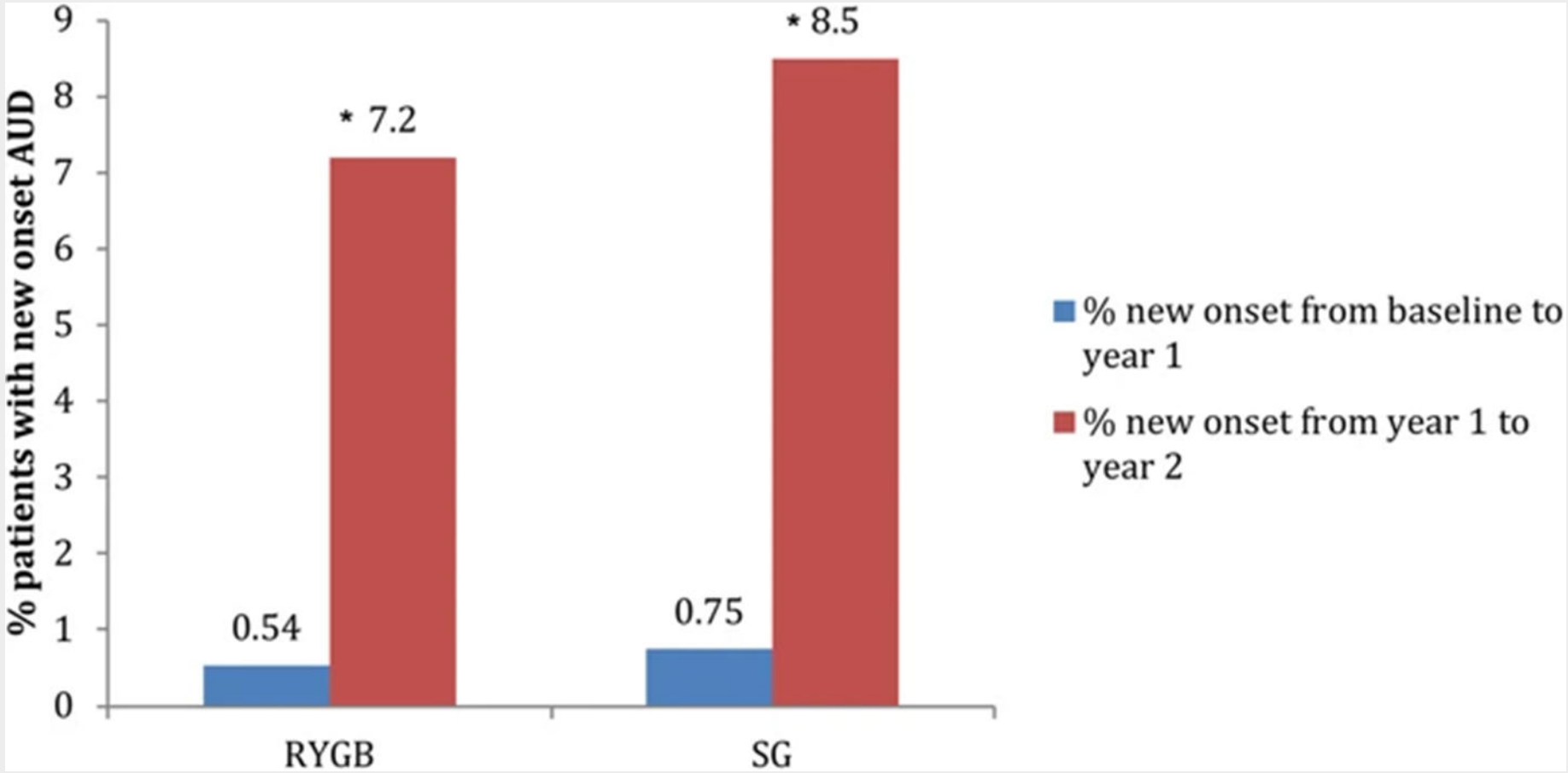
Impaired Alcohol Metabolism after Gastric Bypass Surgery: A Case-Crossover Trial

Gavitt A Woodard, BS, John Downey, MD, Tina Hernandez-Boussard, PhD, MPH, John M Morton, MD, MPH, FACS

J Am Coll Surg 2011;212;209-214



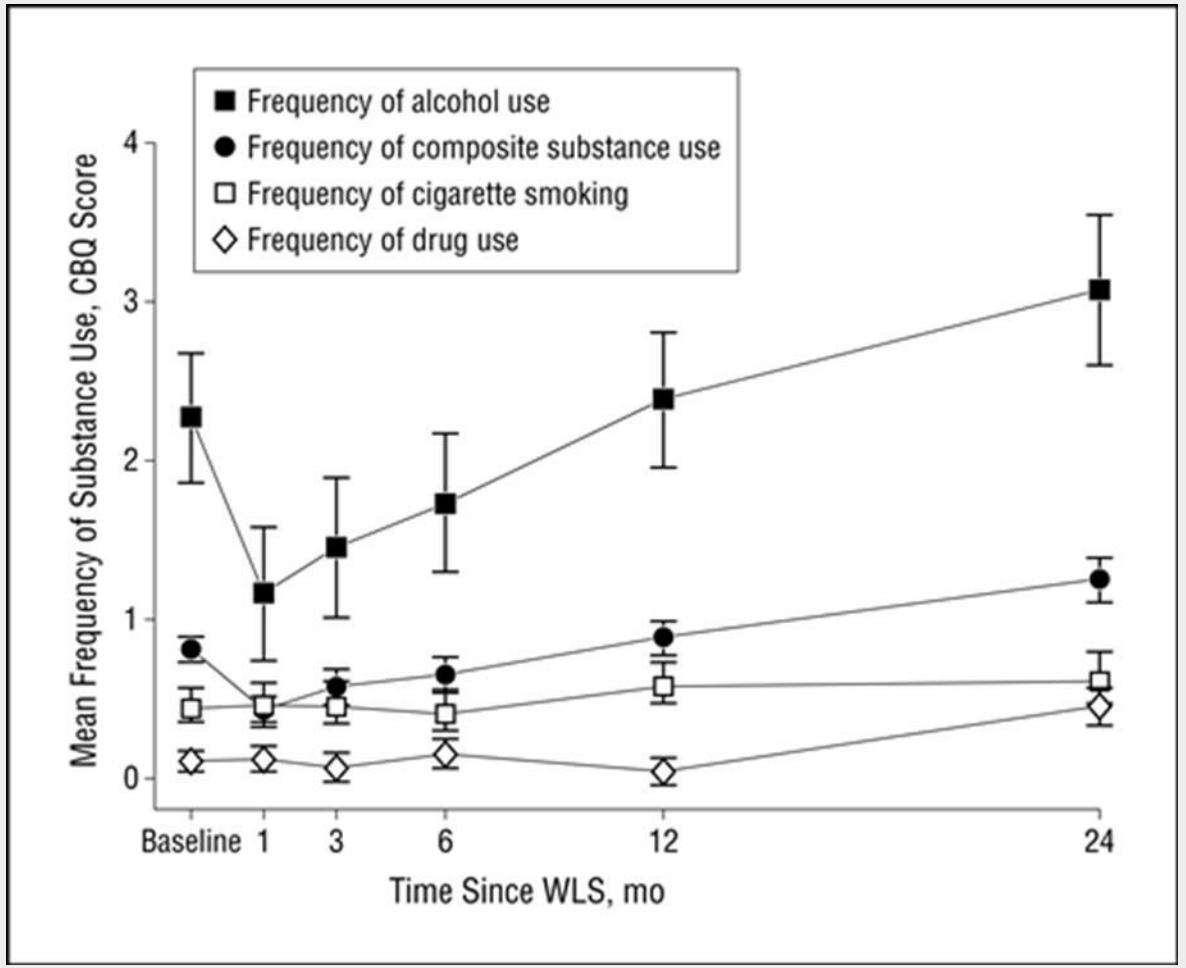
Comparison of patients screening positive for AUD between baseline and year 1 and year 1 to year 2 following surgery



Ibrahim, N., Alameddine, M., Brennan, J. et al. New onset alcohol use disorder following bariatric surgery. Surg Endosc 33, 2521–2530 (2019)

Substance Use Following Bariatric Weight Loss Surgery

Alexis Conason, PsyD; Julio Teixeira, MD; Chia-Hao Hsu, PhD; Lauren Puma, MS; Danielle Knafo, PhD; Allan Geliebter, PhD



JAMA Surg. 2013;148(2):145-150

Addiction Transfer/Substitution

- Why the ~ 2-year delay?
- Why procedure-dependent?
- Occurs In Patients with Gastrectomy for peptic ulcer and CA with nl BMI
- Rodent Model: ↑EtOH after RYGB

Pharmacokinetics/Pharmacodynamics

- Explains Difference RYGB, SG, LAGB
- ↓ Gastric ADH (Cimetidine H2 Blocker)
- ↓Weight → ↑ Socialization
- ↑ Absorption, ↑ Cmax, earlier Tmax
- Feeling More Intoxicated
- AUD>> Other SUDs
- Cocaine Analogy: I.N. → Smoked (Crack Cocaine)

Predictors of AUD Post WLS

- Type of Weight Loss Surgery
- Male: Women More WLS
- Younger Age, FH
- EtOH use Pre-Op
- Tobacco, Illicit Drug Use
- ADHD
- Lower Sense of Belonging, Depression, Minimal Weight Loss
- More Weight Loss → ↑ Socialization → ↑ EtOH

Key Takeaways

- New Onset EtOH related problems occur in ~ 10% of WLS Pts.
- More likely with RYGB & SG than with LAGB.
- Some WLS patients ↓ EtOH intake.
- EtOH problems increase over time. Usually begins ~2 years after WLS.
- Inform and Monitor all WLS patients about the risk of AUD/SUD over time.
- Special Thanks to Allan Geliebter PhD, for alerting me to the relationship between Bariatric Surgery and Alcohol

ASAM REVIEW COURSE 2026

Mental Health and Psychiatric Co-Morbidities

Mason Turner, MD, DFASAM
Senior Medical Director for the Behavioral Health Clinical Program
Intermountain Health, Las Vegas, NV

President-Elect
California Society of Addiction Medicine



1024



Financial Disclosure

I, Mason Turner, MD, DFASAM, have nothing to disclose, and in this presentation, I have indicated where proposed use of “off label” drugs is mentioned.

Educational Objectives

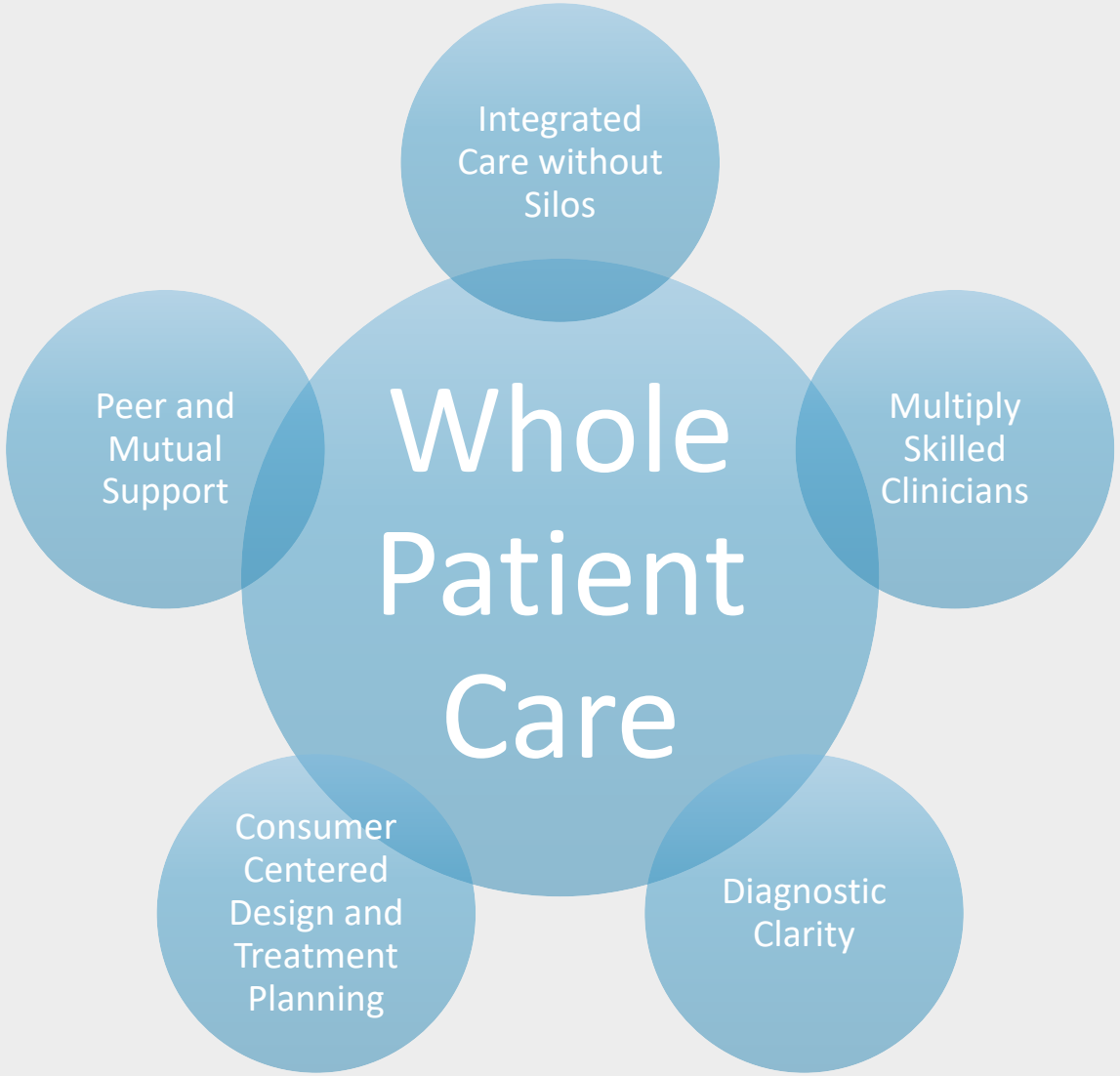
After attending this presentation, participants will be able to:

- Formulate a diagnostic assessment approach for differentiating substance-induced and primary mental health conditions.
- Describe the epidemiology of major mental health conditions relative to substance use disorders
- Apply treatment approaches for co-morbid disorders in their practice environment
- Describe inequities in healthcare delivery for those with co-morbid disorders and understand one method by which they can address those inequities.

Make Sure to Check the Appendix for Additional Information

Importance of Mental Health Co-Morbidities

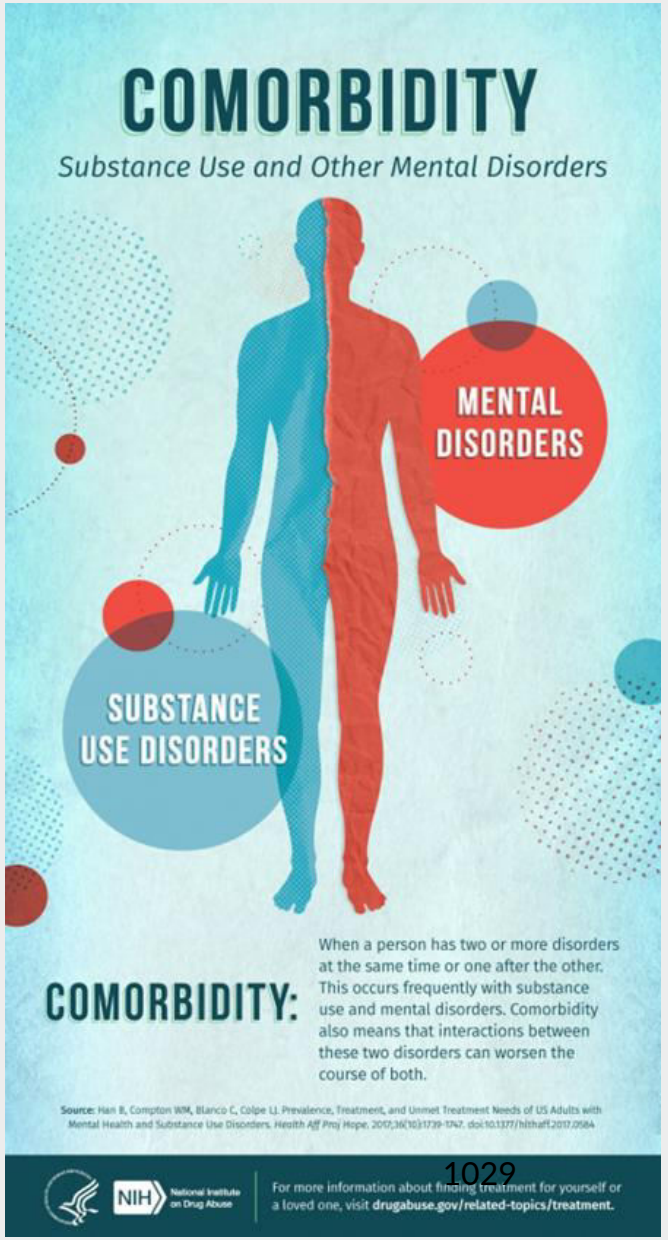
Importance of Mental Health Co-Morbidities



Importance of Mental Health Co-Morbidities

Co-occurring: The co-existence of both a mental illness and a substance use disorder. May also apply to other illness states as well (i.e., pain, medical illness, etc.).

Co-morbidity: The existence of two or more disorders at the same time or one after the other. Interactions worsen the course of both.



Importance of Mental Health Co-Morbidities

Specialized Treatment Approaches in Co-Morbid Disorders

Current State	• Severity Based
Evolving Concepts	• Co-Morbidity Approach • PTSD • ADHD
Emerging Therapies	• Individualized Treatment • Personality Disorders • Eating Disorders

Importance of Mental Health Co-Morbidities

Current model

- Level of severity indicates primary treatment location
- If both conditions are of high severity, combined or concurrent treatment is indicated, but collaboration, coordination and integration rarely available.
- Often assumes one illness predominates over another and that treatment for one condition will not worsen the other

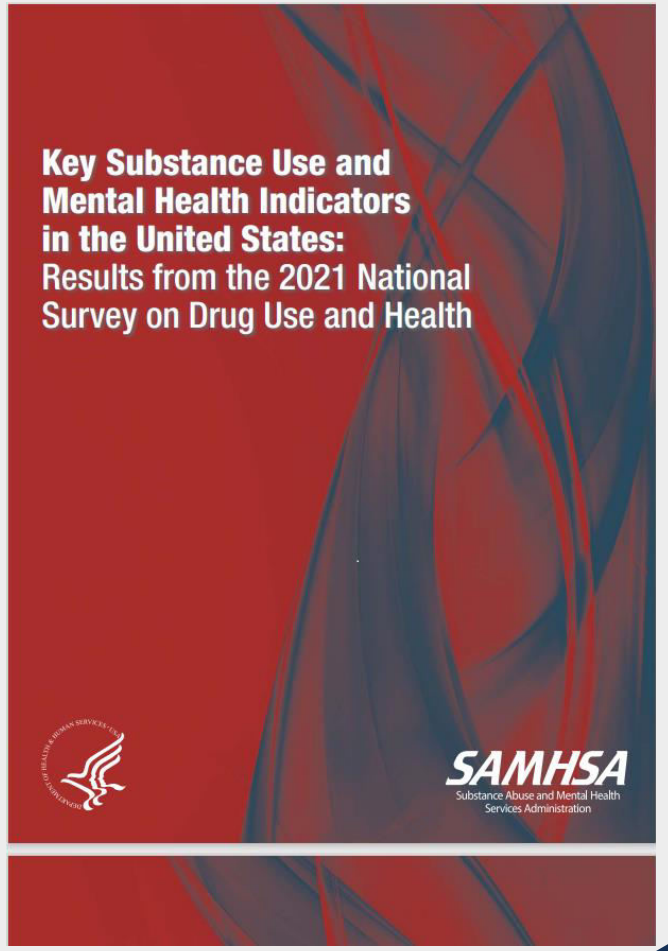
Evolving model

- Focuses on a co-morbidity, rather than a co-occurring, model
- Integrated treatment approaches in primary care and other medical specialties
- Multi-modal skilling amongst all staff
- Specialized treatment programs with recognition that whole person recovery rarely occurs in a linear fashion.

Epidemiology and Barriers to Treatment Access

Epidemiology and Barriers to Treatment Access

- According to the 2022 National Survey on Drug Use and Health, 46.3 million people aged 12 or older (or about 16.5% of the US population), reported symptoms consistent with an SUD in the last year.
- Of those, 19.4 million people (or 41.9%) also had a co-occurring mental health condition.
- Rates of lifetime prevalence are much higher

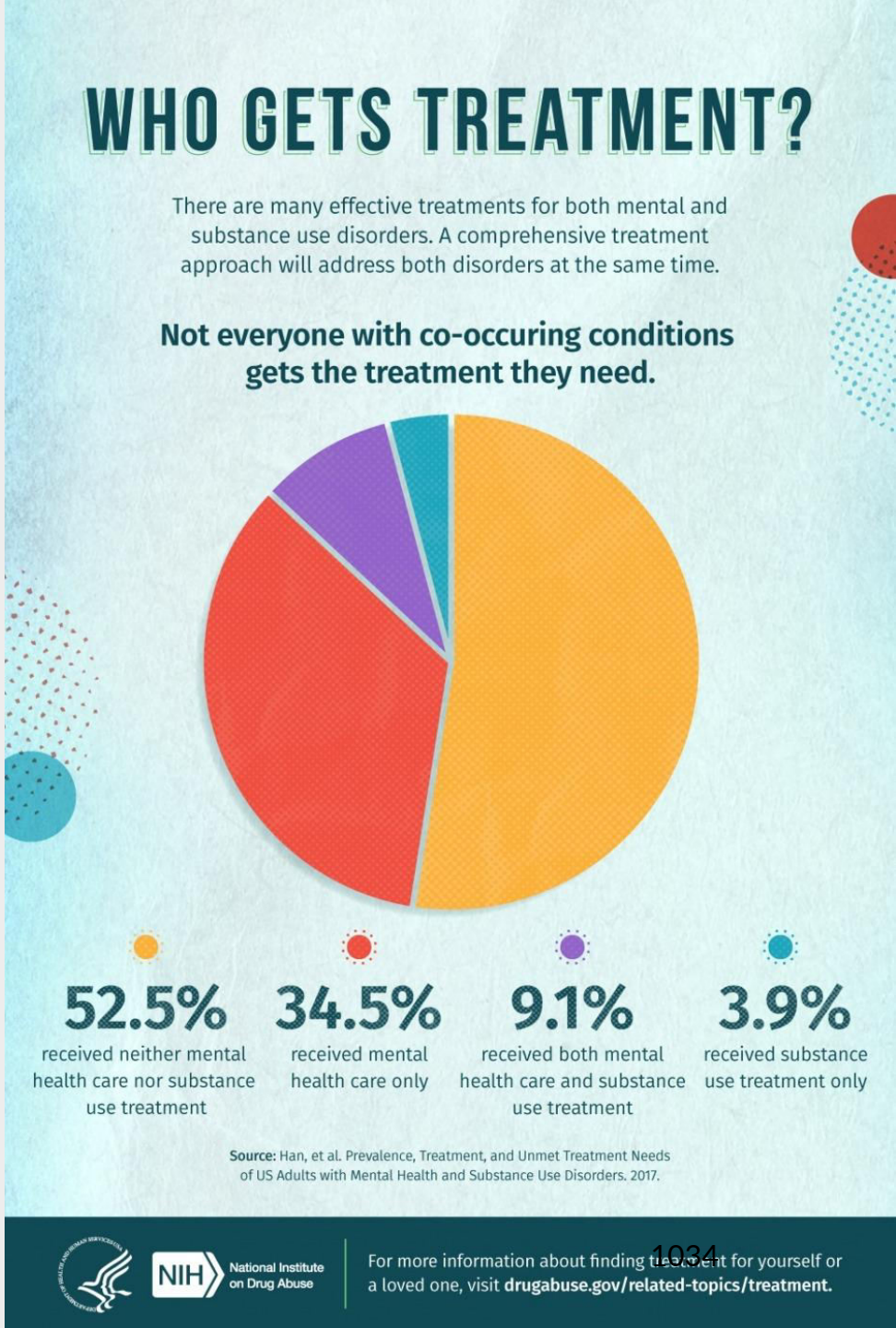


https://www.samhsa.gov/data/sites/default/files/reports/rpt39443/2021NSDUHFFRRev010323.pdf

Epidemiology and Barriers to Treatment Access

Of those with co-occurring disorders…

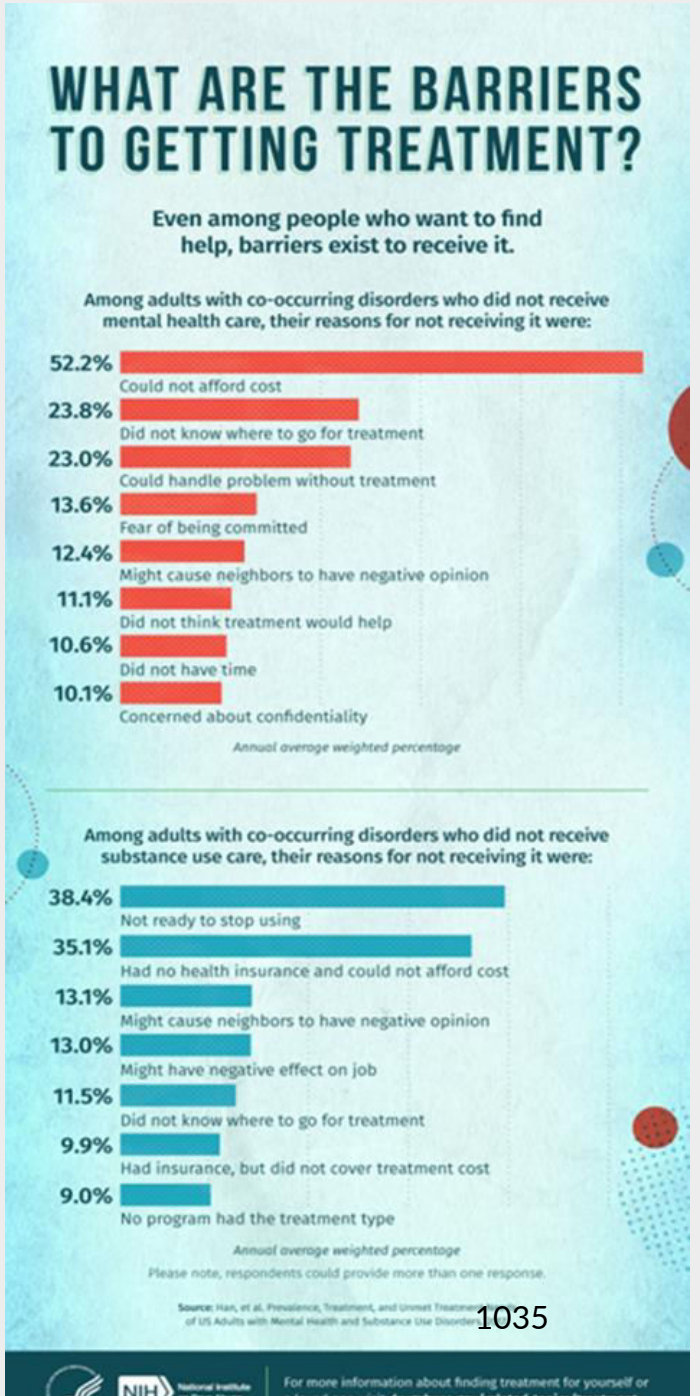
- 52.5% received ***neither*** mental health care nor substance use treatment.
- 34.5% received ***mental health care only.***
- 9.1% received ***both*** mental health care and substance use treatment.
- 3.9% received ***substance use disorder treatment only.***
- More recent data suggests increasing access to mental health and combined treatment but regression for SUD treatment only



Epidemiology and Barriers to Treatment Access

Among adults with co-occurring disorders who did not receive mental health care, their reasons for not receiving it were as follows:

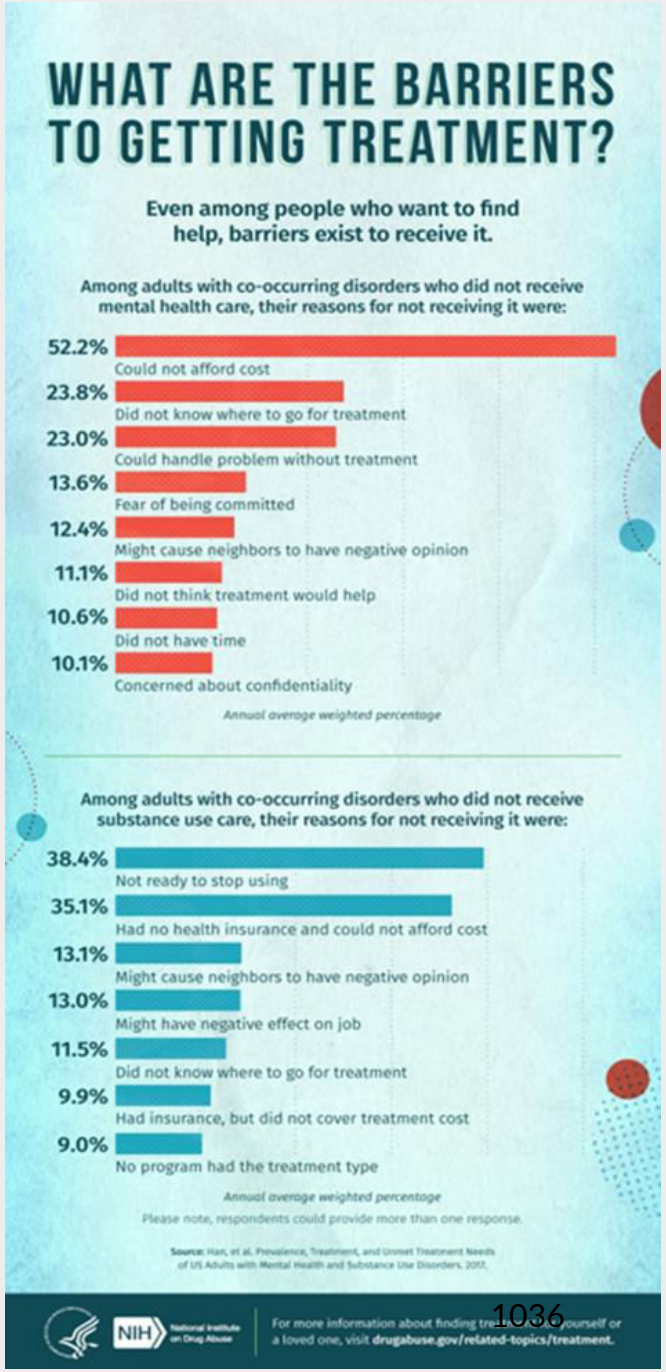
- 52.2% could not afford the cost.
- 23.8% did not know where to go for treatment.
- 23.0% said they could handle the problem without treatment.
- 13.6% feared being committed.
- 12.4% said it might cause their neighbors to have a negative opinion of them.
- 11.1% did not think treatment would help.
- 10.6% did not have the time.
- 10.1% were concerned about confidentiality.



Epidemiology and Barriers to Treatment Access

Among adults with co-occurring disorders who did not receive substance use care, their reasons for not receiving it were as follows:

- 38.4% were not ready to stop using.
- 35.1% could not afford the cost.
- 13.1% said it might cause their neighbors to have a negative opinion of them.
- 13.0% said it might have a negative effect on their job.
- 11.5% did not know where to go for treatment.
- 9.9% had insurance but could not afford the co-insurance/co-payments.
- 9.0% said no program had the treatment type.



Equity Considerations

Equity Considerations

Between 2016 and 2020, 116,000 premature deaths occurred because of disparities in how mental health and addiction concerns were addressed among racial/ethnic minorities and indigenous groups. Likely a vast underestimate because the study excluded high risk groups such as incarcerated and unhoused populations.

Secondary, in large part, to minority stress, rates of problematic substance use and progression to use disorders are higher among minoritized groups across the spectrum.

Engagement in addictions treatment, particularly with medications for opioid use disorder (MOUD), is far less for minoritized populations, particularly black men/tribal populations.

Equity Considerations

- Among minoritized groups, the total excess cost burden (relative to non-minoritized groups) for mental illness, addiction and suicide was $278 billion from 2016-2020.
- Multiple explanations
  - Access to care
  - Discriminatory local, state and federal policies
  - Disparities in social determinants of health
  - Lack of culturally aware/sensitive therapeutic approaches
  - Lack of diversity in the workforce
- Take Home Message: Addressing healthcare inequity is a massive issue but start small by looking for even small disparities and address them within you sphere of influence.

Principles of Triage, Assessment and Treatment

Triage and Assessment

- Consumer- and patient-centric with no wrong door
- Presenting Problem: Most likely of greatest concern to patient and is the initial starting point
- Standard of care is no longer “let’s wait and see how you feel after 30, 60 or 90 days of sobriety.”
- Special considerations for severe mental illness
- Full risk assessment is essential
- Consider entire ecosystem of care and patient’s environment
- Beware of screening in early abstinence

Triage and Assessment

Mental Health History

- Symptoms during periods of abstinence or (preferred) prior to initiation of use
- Relationship between cessation or reduction of use and psychiatric symptoms
- Patient's subjective experience of substance use to self-medicate (use caution)

Substance Use History

- Early substance use can indicate a primary mental health condition
- Substance use prior to onset of psychiatric illness does not imply the addiction is primary
- Progression of use and functional consequences can be helpful

Comprehensive treatment history

The complex role of trauma/traumatic sequelae and PTSD

DSM5 diagnostic criteria

Principles of Treatment

- As severity increases, likelihood of engagement in treatment does as well.
- From Flynn 2008, monotherapy was typically in mental health (20.7%) not addiction (7.6%) treatment programs. This trend has continued to widen over time, with current estimates that about 48.6% of monotherapy is in mental health, 19.2% in combined treatment and 2.3% in addiction treatment only.
- Psychotherapy versus psychopharmacology.
- Access to evidence-based practices for psychotherapy, including motivational interviewing, and multi-modal treatment is extremely limited in many areas.

Principles of Treatment

Risk of Inaction or Delayed Treatment

- Cycle of use, return to use and remission from co-occurring disorders
- Escalating functional consequences

Defining Success and Treating to Target

- Engagement
- Abstinence
- Functional improvement
- Symptom reduction
- Individualized treatment outcomes

Flexible treatment approaches

Shared decision-making re: treatment planning and goals

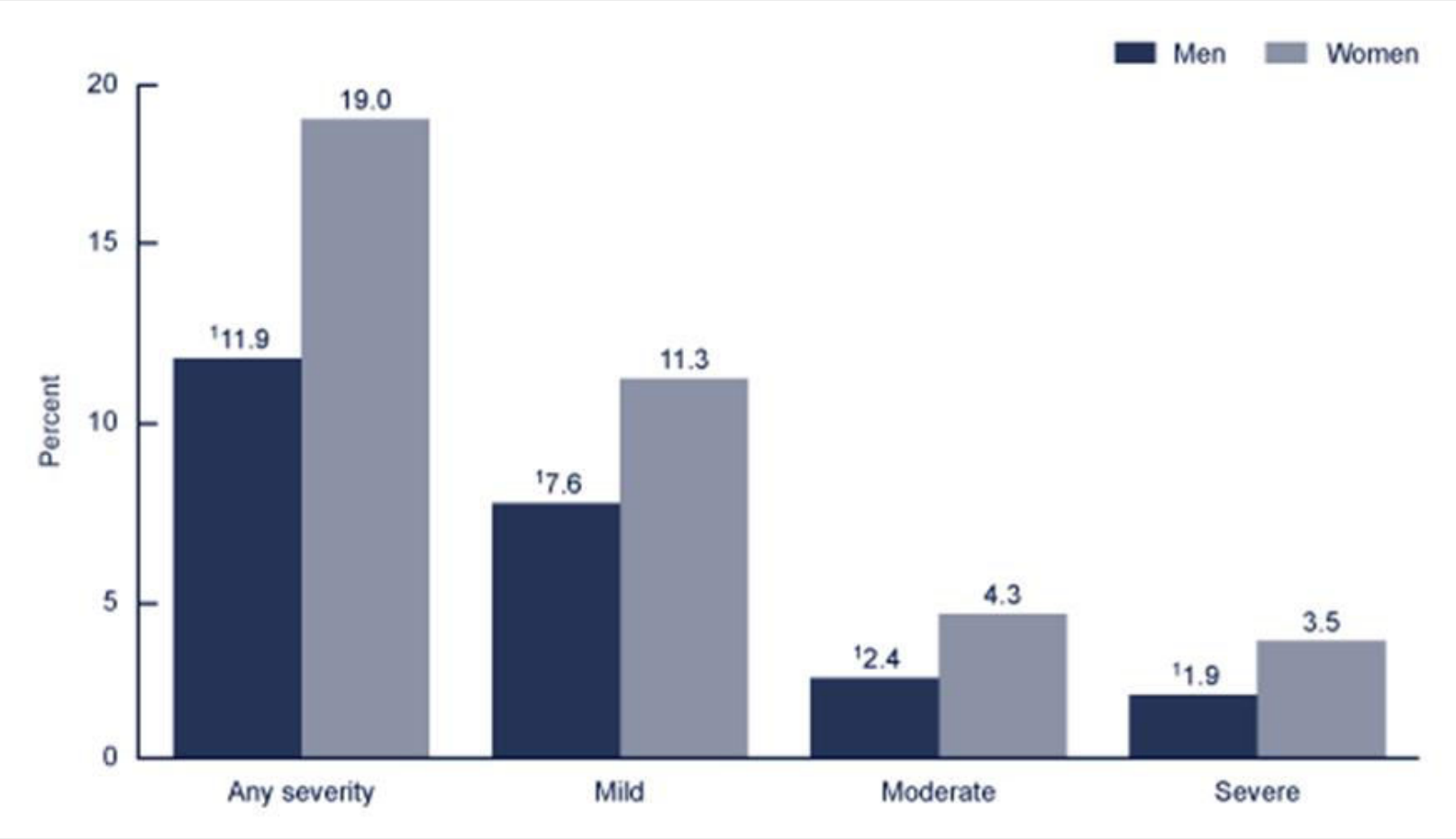
Mental Health Conditions: A Lightning Review



Co-Morbid Anxiety Disorders

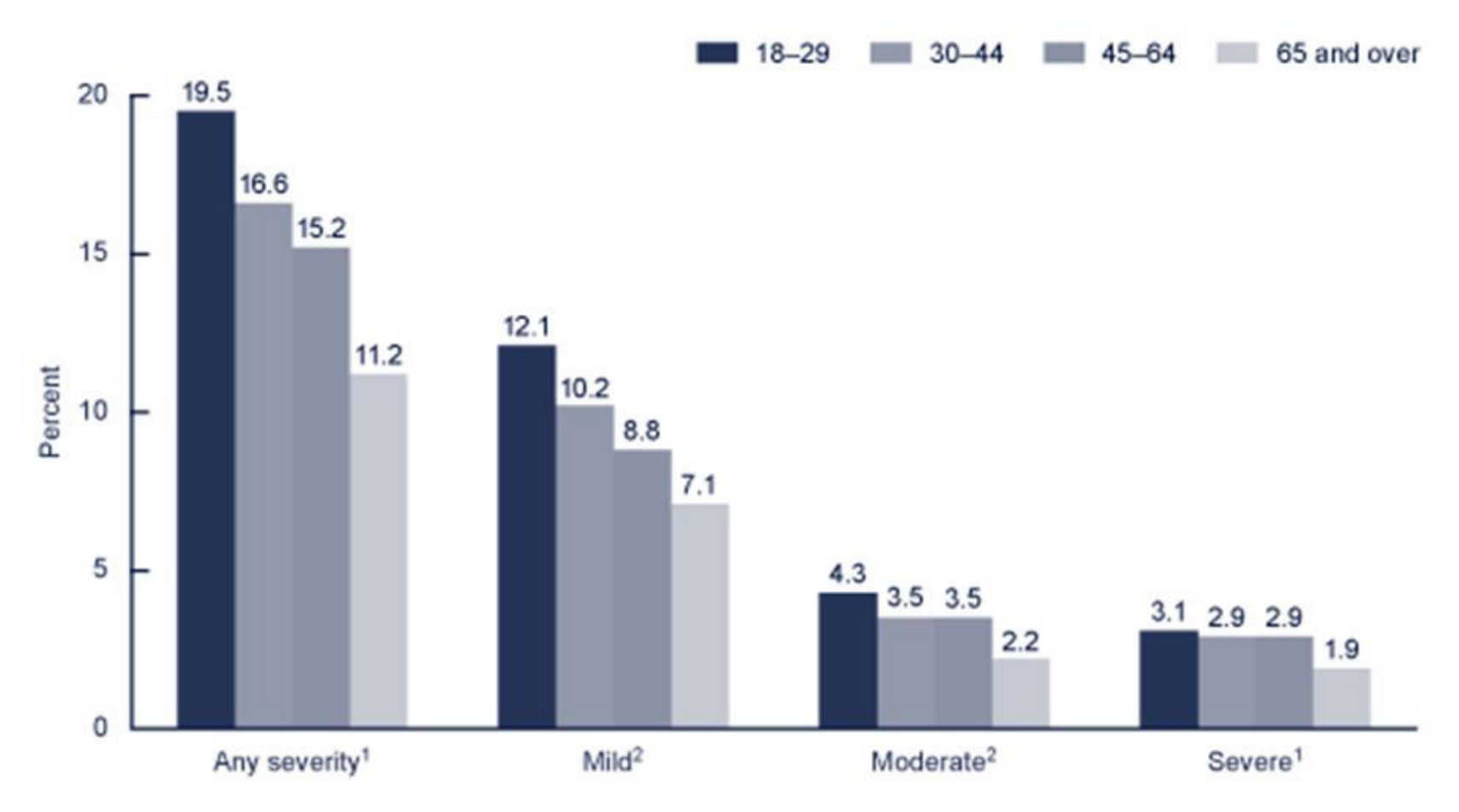
Co-Morbid Anxiety Disorders

Percentage of adults aged 18 and over who experienced symptoms of anxiety in the past 2 weeks, by symptom severity and age group: United States, 2019

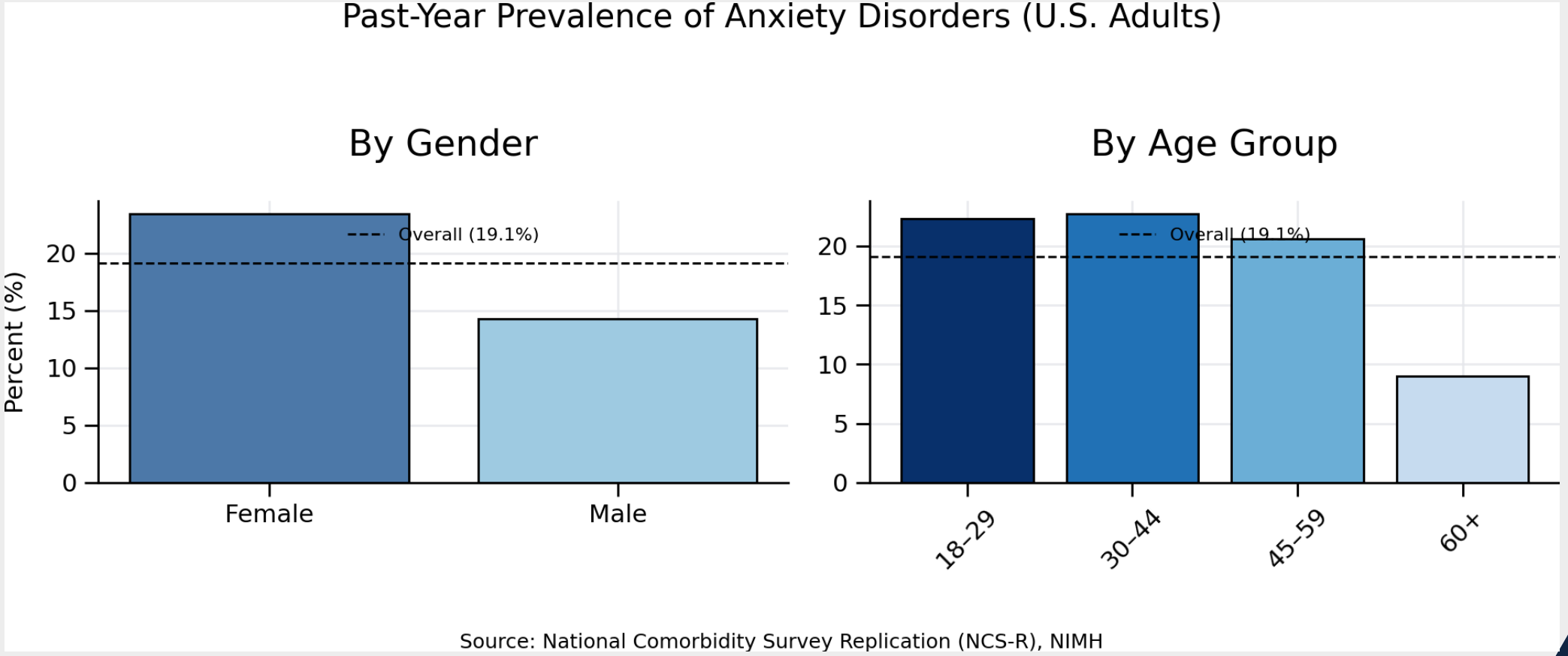


Co-Morbid Anxiety Disorders

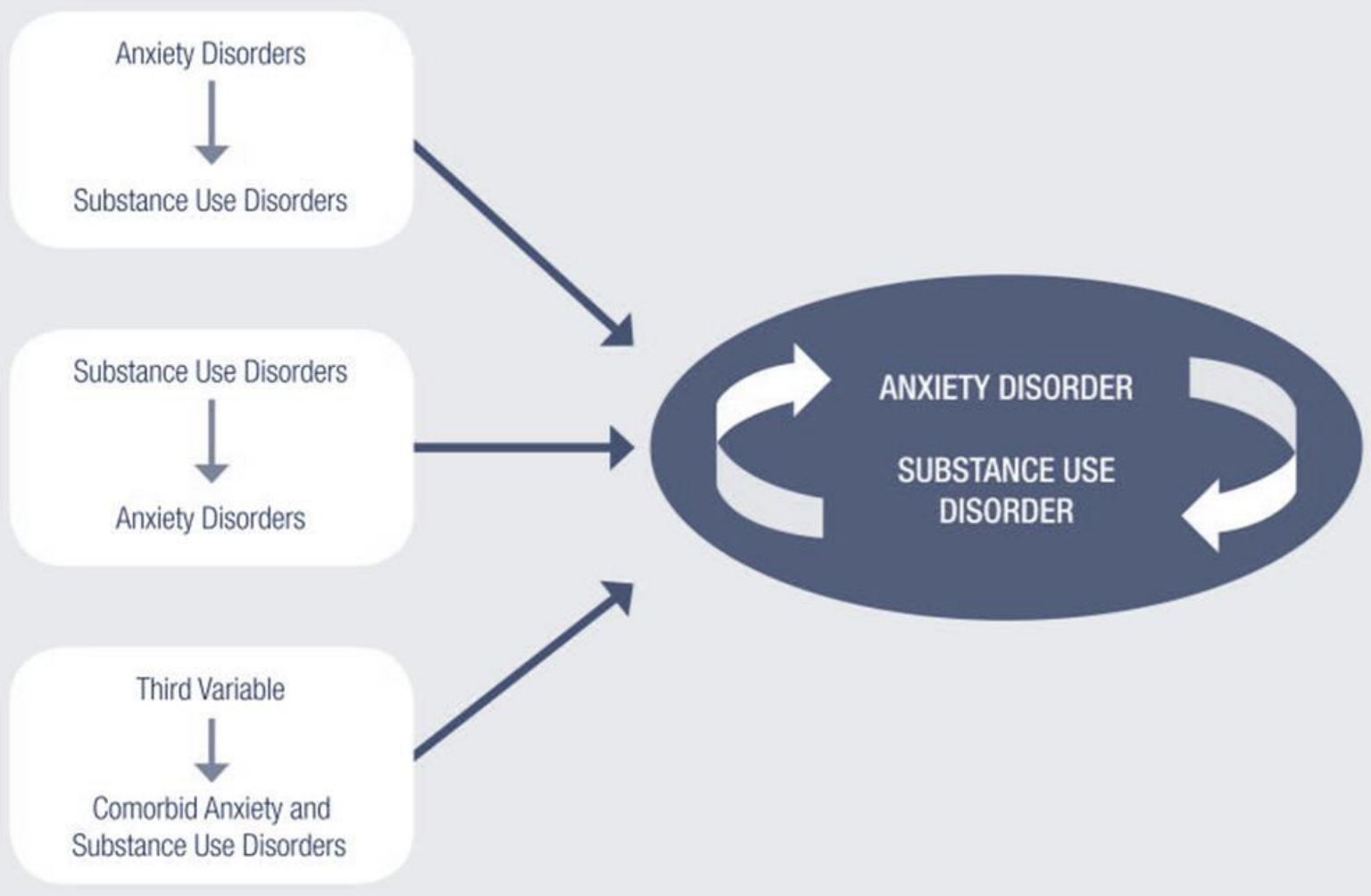
Percentage of adults aged 18 and over who experienced symptoms of anxiety in the past 2 weeks, by symptom severity and age group: United States, 2019



Co-Morbid Anxiety Disorders



Co-Morbid Anxiety Disorders



Smith JP and Book SW. Anxiety and Substance Use Disorders: A Review. Psychiatry Times. 2008 Oct; 25(10): 19–23.

Co-Morbid Anxiety Disorders

Lifetime prevalence of anxiety disorders is over 30%. The pandemic led to an increase in this number which may be returning to baseline.

Mild substance use disorders likely not associated with anxiety disorders, but moderate and severe substance use disorders are highly related.

Traditionally, alcohol use disorder is associated with anxiety disorders, but in fact, all substance use disorders are implicated.

Substance-induced anxiety disorders are rare (<1%) with anxiety disorders usually preceding the substance use disorder.

Co-Morbid Anxiety Disorders

Diagnosis

Generalized anxiety and panic disorders: Most strongly associated with substance use disorders

- Generalized Anxiety Disorder: Significant worry and ruminations
- Panic Disorder: Panic attacks with or without agoraphobia
- Specific Phobias (i.e., fear of heights)
- Social Phobia: Spectrum from mild anxiety to full avoidance
- Obsessive-Compulsive Disorder: Not technically an anxiety disorder

Treatment

The presence of either generalized anxiety or panic disorder is likely to predict a higher degree of severity of the substance use disorder.

- Evidence-based psychotherapy, typically cognitive-behavioral therapy, is first-line
- Medications
  - SSRI's/SNRI's, typically only for generalized anxiety disorder or severe panic disorder
  - Benzodiazepines
    - Blunts psychotherapeutic effects
    - Risk of addiction is low, but misuse is common
    - Physiological dependence is a difficult issue
    - Long-term risk is equivocal

Co-Morbid Mood Disorders

Co-Morbid Depressive Disorders

- Relationship between depression and substance use disorders is bidirectional: Odds ratio of 1.3 to 2.6.

- Adolescents: 2017 study found a doubling of the incidence of substance use disorders in adolescents with a major depressive episode in the last year (29.3% versus 14.3%).

- Substance-induced depression is also common
  - Direct physiological effects of substances
  - Psychosocial sequelae
  - Medical co-morbidities with depressive disorders and SUDs (i.e., diabetes and chronic pain)

Co-Morbid Depressive Disorders

- Dysfunction in frontal-limbic reward pathways.
- Altered reward systems lead to compulsive use of substances and anhedonia.
- Repeated cycles of intoxication and withdrawal complicate any *de novo* diagnosis of major depressive disorder in the acute phase of addictions treatment.
- Symptoms of depressive disorders usually precede initiation of substance use or progression to a use disorder.

Co-Morbid Depressive Disorders

Diagnosis

- Major depressive disorder
- Persistent depressive disorder
- Substance-induced mood disorder
- Caution re: bipolar disorder

Major Depressive Episode versus Persistent Depression

- Major depressive episode (MDE): Usually intermittent with inter-episode recovery
- Persistent depressive disorder: Long term, chronic, mild depressed mood. May co-occur with an MDE

Substance-Induced Mood Disorders

- Over half of patients with alcohol and opioid use disorders.
- Usually, symptoms resolve quickly after cessation or reduction of use
- Persistent symptoms can occur and require medical treatment.

Co-Morbid Depressive Disorders

Treatment (Severity Based on Objective Instrument)

- Mild depression: Self-care + psychotherapy first line
- Moderate depression: Psychotherapy ± pharmacotherapy
- Severe depression: Pharmacotherapy + Psychotherapy ± interventional/neuromodulation treatments

Medical/Interventional

- Standard algorithm
- SSRI's first line
- SNRI's and atypical anti-depressants
- Neuromodulation (ECT, TMS, MST)
- Emerging role of ketamine/psychedelics

Evidence-Based Psychotherapies

- Cognitive-Behavioral Therapy
- Interpersonal Therapy
- Supportive/Non-Directive Therapy not effective
- Access to EBP's is challenged

Co-Morbid Bipolar Disorder

- Bipolar disorder affects 1%-4% of the US population with most studies/surveys consistent with a 4% lifetime prevalence rate for the combination of bipolar 1 and 2 disorders (2% for each).

- Eliciting symptom reports from patients can be challenging (see later patient education graphics)

- Bipolar 1 disorder
  - High correlation with SUD's with lifetime SUD prevalence rate of 50-60%. Some studies found rates as high as 90%.
  - Significant functional impairment, often with hospitalization.

- Bipolar 2 disorder
  - Likely under/mis-diagnosed (as major depressive disorder) with some key opinion leaders noting up to an 11% prevalence.
  - Correlation with substance use disorders is less well studied.

Co-Morbid Bipolar Disorder

- Age of onset: Teens to early 20's with rare onset after age 40.
- Onset often, but not always, prior to substance initiation/progression.
- Substance intoxication can mimic mania. While ruling out substance-induced mania is important, treatment is largely the same for both conditions.
- Treat with a low suspicion given the bi-directionality of bipolar and substance use disorders and improved outcomes for both conditions with treatment of either.
- Use provisional diagnosis when unsure to avoid later confusion.

Bipolar Disorder Symptoms

Manic Episodes:



Feeling Overly Happy for Long Periods of Time



Talking very Fast with Racing Thoughts



Becoming Easily Distracted



Having Overconfidence in Abilities



Engaging in Risky Behavior

Depression Episodes:



Feeling Sad or Hopeless for Long Period of Time



Significant Change in Appetite



Thinking About or Attempting Suicide



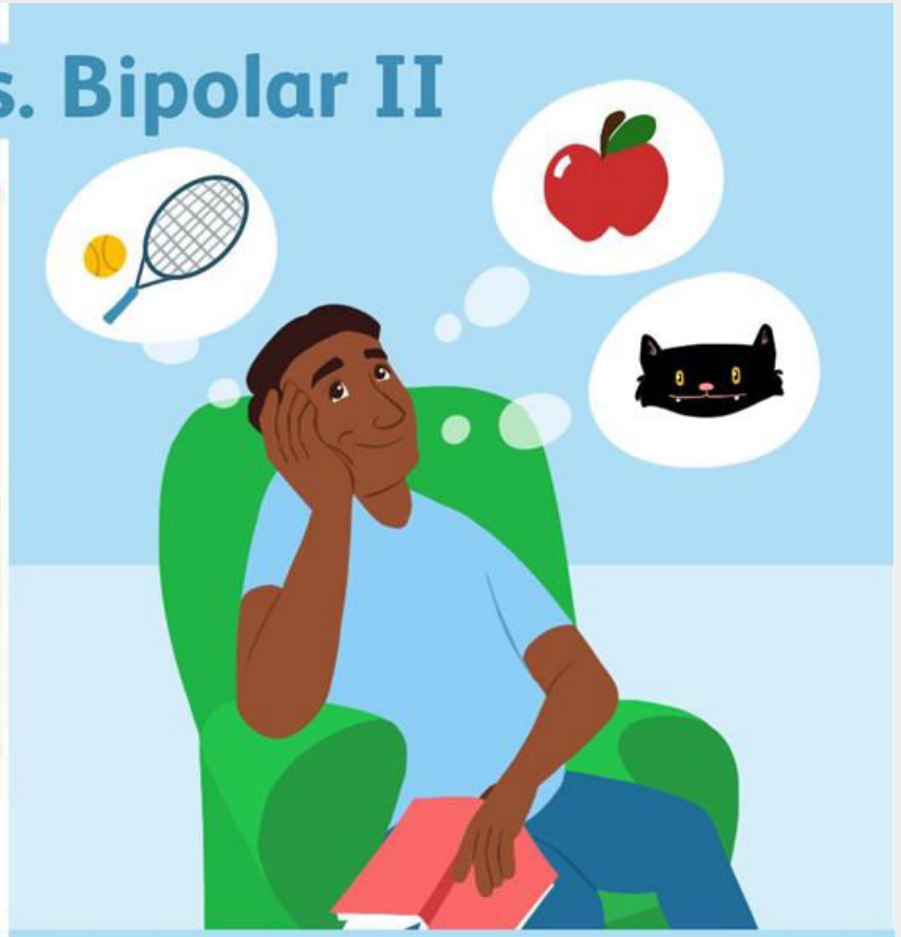
Feeling Fatigue or Lack of Energy



Problems with Memory and Concentration

Bipolar I vs. Bipolar II





- Symptoms interfere with daily life
- Extreme elevation in mood and energy during manic episodes

- Elevated mood during hypomanic episodes
- Symptoms are shorter and less intense

VeryWell Health

Co-Morbid Bipolar Disorder

Diagnosis

- Bipolar 1: Manic episode ± Major depressive episode with or without psychosis
- Bipolar 2: Hypomania + Major depressive episode
- Cyclothymic disorder (rare in treatment-seeking populations): Hypomania + Dysthymia
- In general, any hospitalization during an elevated mood episode is likely mania, not hypomania

Treatment

- Pharmacotherapy
  - Mood stabilizers/Anti-manic agents
  - Anti-psychotics
  - Use caution with anti-depressants in bipolar 1, but acceptable with bipolar 2.
- Psychotherapy
  - Cognitive-behavioral therapy
  - Family-focused therapy
  - Interpersonal therapy
  - Social-rhythm therapy

Co-Morbid Post-Traumatic Stress Disorder

Co-Morbid Post-Traumatic Stress Disorder

- Patients with PTSD are 2-4 times more likely to have an SUD in general, but among treatment seeking populations, those who present with PTSD are 14 times more likely to have an SUD.
- Severity of trauma correlates with substance use in general and overall development of an SUD.
- Trauma cue-induced cravings and use are a major challenge.
- Trauma, independent of PTSD, is also correlated with substance use and progression to a use disorder. Less than 10% of those exposed to significant trauma will develop PTSD but may have addictions sequelae.

Co-Morbid Post-Traumatic Stress Disorder

Theories of etiology/correlation

- ***Self-medication hypothesis***: Reduction of autonomic symptoms as well as psychological distress with ongoing substance use
- ***High-risk hypothesis***: Substance use leads to presence in higher risk environments and situations that predispose to trauma and development of PTSD
- ***Susceptibility hypothesis***: Chronic hyperarousal from substance use predisposes to PTSD rather than non-pathological reactions after traumatic events
- ***Shared risk model***: Genetics, neurophysiological systems, recurrent trauma
- ***Possible direct effect of substance***: Cannabis may lead suppression of negative memories but unclear as to whether this leads to disordered use.

Trauma without PTSD

- Minority stress
- Forced resilience
- Social determinants of health
- Sequelae related to other mental health conditions

Co-Morbid Post-Traumatic Stress Disorder

- Comprehensive diagnostic evaluation and treatment planning to include social determinants of health and safety/risk assessment
- Focus on safety and stabilization
- Treatment of single-episode versus recurrent PTSD requires differential approaches

Co-Morbid Post-Traumatic Stress Disorder

Specialized Evidence-Based Psychotherapies (First Line)

- Seeking Safety (SUD + PTSD)
- Prolonged exposure (Use in caution in early recovery)
- Eye movement desensitization and reprocessing
- Cognitive processing therapy

Pharmacotherapy

- Typically, less effective than for other co-morbid conditions.
- SSRI's and SNRI's are the best studied and most effective
- α-Adrenergic receptor antagonists important for symptom management.
- Anti-psychotics and benzodiazepines should generally be avoided due to risk and side effect profiles.

Co-Morbid Attention-Deficit Hyperactivity Disorder

Co-Morbid Attention-Deficit Hyperactivity Disorder

- 15.2% of adults with attention-deficit hyperactivity disorder (ADHD) have a substance use disorder (SUD) compared with 5.6% of those without ADHD.
- Among adolescents, the rate of ADHD in those with an SUD is 24% versus 11.5% in the general adolescent population.
- Substance use begins earlier, and remission rates are lower or take longer to achieve, in those patients with ADHD.
- ADHD + SUD = Higher risk of attempted suicide
- Early *and* adequate treatment of ADHD in childhood is one of the only primary prevention strategies for SUDs.
- Evidence supports use of psychostimulants in this population with appropriate monitoring and safe storage practices.

Co-Morbid Attention-Deficit Hyperactivity Disorder

Inattention/Poor Concentration

- Target symptom for most medications
- Can be independent of, or foundational to, other functional domains

Executive Dysfunction

- Poor impulse control
- Lack of long-term reward and consequence orientation
- Decreased academic and occupational functioning
- Improvement with medications is limited

Impaired Reward System

- Increased risk-taking behaviors
- Need for a higher degree of stimulation
- Does not improve with medications

Co-Morbid Attention-Deficit Hyperactivity Disorder

Retrospective global study of 4.4 million people prescribed medications for ADHD versus 6.1 million prescribed asthma medications (low risk of diversion): Abuse, misuse and diversion of stimulants was 4 times more likely with stimulants

In those patients who were dispensed stimulants rather than non-stimulants, those with ADHD were 8 times more likely to engage in “doctor shopping” behaviors.

In a Swedish national registry study, 7.6% of those prescribed methylphenidate abused, misused or diverted the medication. The 46-65 age group was 17 times more likely to engage in these behaviors than the 6–12-year-old age group. Those with SUDs were twice as likely to misuse/divert.

Co-Morbid Attention-Deficit Hyperactivity Disorder

Diagnostic Challenges

- Contemporary lifestyle promotes short attention spans: Easy to confuse with ADHD
- Diagnosis of ADHD with active substance use/early recovery: Extraordinarily challenging without pre-morbid diagnostic verification in childhood.
- Inattentive symptoms are common across a range of behavioral health conditions.
- Malingering to obtain psychostimulants is common.
- Engaging in extensive history-gathering can be difficult and time-consuming.
- *De novo* ADHD diagnoses: Only with significant reduction or abstinence from substances and with objective verification.

Co-Morbid Attention-Deficit Hyperactivity Disorder

Treatment Considerations

- ***Treatment of ADHD in childhood/adolescence is one of the few primary prevention strategies in addiction medicine***
- 2021 meta-analysis by Özgen and collaborators: Adolescents with concomitant ADHD + SUD did not respond as well to medications as those with only ADHD. Higher doses of psychostimulants may be required and more effective in the co-morbid population.
- Psychosocial treatments are poorly studied and open for innovation. Are these safer approaches?
- Dopamine dysregulation, particularly with stimulant use disorders, may mean that higher doses of stimulants are required to achieve similar effects. As such, safety considerations are important.

Summary and Key Takeaways

- Co-occurring mental health and substance use disorders are common with a wide range of severity levels impacting clinical outcomes.
- Consider co-morbidity, not just co-occurrence.
- Diagnosis of co-occurring/co-morbid conditions is essential in order to create effective individualized treatment plans.
- Treatment of co-occurring/co-morbid disorders requires specialized approaches that integrate addictions and mental health treatment together rather than provides in silos or according to the severity of the presenting problem.
- Know key diagnostic criteria for the most common mental health conditions.

Appendix

Co-Morbid Psychotic Disorders

Co-Morbid Psychotic Disorders

Initial presentation of psychotic illness: Usually mental health

However, up to 50% co-occurrence of substance use disorders in those with psychotic disorders: Cross-skilling is essential when treating this population.

Typical substances and use disorders with a primary psychotic disorder include cannabis and alcohol

Substance-induced psychosis can be common and persistent with repeated use of certain substances, particularly methamphetamine.

Co-Morbid Psychotic Disorders

- Continued use of substances is associated with increased symptoms, adjustment difficulties, treatment nonadherence, relapses, and hospitalizations, even with intensive treatment.
- Individualized treatment plans are essential
- May require treatment in specialized integrated programs.
- Role of family and caregivers is important to recognize.
- Aggressive medication management initially can help to reduce symptoms and increase engagement.

Co-Morbid Psychotic Disorders

Diagnosis

- Schizophrenia
- Mood disorders with psychotic features
- Schizoaffective disorder
- Delusional disorder
- Substance-induced psychosis (particularly methamphetamine-induced psychosis/intoxication)
- Unspecified

Co-Morbid Psychotic Disorders

Pharmacotherapy

- Anti-psychotics are first line but often poorly tolerated
- Mood stabilizers and/or anti-depressants for mood symptoms
- Consider clozapine early. Evidence indicates superior effects for both psychotic and substance use disorders with use of clozapine and superior reduction in suicide risk.
- Long-acting injectables provide significant advantages but cost is a factor

Non-medical therapies

- Cognitive-behavioral therapy for psychosis
- Family psychoeducational and interventional therapies
- Mutual support groups (NAMI, Mental Health America)

Outcomes should focus on functional improvement, not necessarily symptom reduction or abstinence

Co-Morbid Eating Disorders

Co-Morbid Eating Disorders

- Approximately 10% of patients with eating disorders will also have an active substance use disorder, but evidence is mixed:
  - **Anorexia Nervosa:** 16% comorbidity with the binge/purge subtype > restrictive subtype
  - **Bulimia Nervosa** : Less studied, with some evidence that 30% of those with an SUD have bulimia nervosa
  - **Binge Eating Disorder:** Up to 60% may have co-occurrence
- Alcohol, tobacco and caffeine are the most common substances used in those with eating disorders, but evidence also demonstrates increased use of sedative/hypnotics in those with anorexia and hallucinogens/MDMA in those with bulimia
- Evidence for best practice in diagnosis and treatment is lacking

Co-Morbid Eating Disorders

Shared Etiologies

- Maladaptive activation of reward pathways
- Appetite suppression with certain substances can lead to increase in disordered eating
- Shared, but temporary, sense of well-being
- Management of chaotic inner experiences and response to one's environment
- Avoidance of negative feeling states

Treatment Challenges

- Motivation
- Retention
- Concurrent treatment is ideal, but sequential treatment is the norm
- No widely accepted standard of care for concurrent treatment
- Often, one condition worsens as the other improves

Co-Morbid Personality Disorders

Co-Morbid Personality Disorders

- Borderline and anti-social personality disorders carry the highest co-morbidity/co-occurrence with SUDs, and patients with borderline personality disorder have the highest treatment-seeking behavior. As such, most treatment efforts will focus on that disorder.

- Overall prevalence of personality disorders
  - General population: 10-14.8%
  - Substance use disorders: 34.8-73%.

- Personality pathology often precedes substance initiation/disordered use.

- Poor treatment response and outcomes relative to those without the co-morbidity.

Co-Morbid Personality Disorders

- Psychotherapy is first-line treatment
  - Unlike for other co-morbid disorders, treatment may need to be sequential, especially for a first episode, to help patients learn skills to manage emotions in the treatment milieu and as abstinence progresses.
  - Dialectical behavioral therapy (DBT), dynamic deconstructive therapy and dual-focused schema therapy have the greatest evidence, but DBT is most prevalent.
- Disruptions in the milieu environment are common and lead to issues of discharge and lack of engagement.
- Pharmacotherapy should be limited to acute crises and treatment of co-morbidities only.

References

REFERENCES

https://nida.nih.gov/research-topics/comorbidity/comorbidity-substance-use-other-mental-disorders-infographic

https://www.nimh.nih.gov/health/statistics/any-anxiety-disorder

Aryan, N., Banafshe, H. R., Farnia, V., Shakeri, J., Alikhani, M., Rahimi, H., ... & Omidi, A. (2020). The therapeutic effects of methylphenidate and matrix-methylphenidate on addiction severity, craving, relapse and mental health in the methamphetamine use disorder. *Substance Abuse Treatment, Prevention, and Policy*, *15*(1), 1-9.

Bordoloi, Meelie, Geetha Chandrashekar, and Naveen Yarasi. "ADHD in adults and its relation with methamphetamine use: national data." *Current Developmental Disorders Reports* 6 (2019): 224-227.

Brookfield S, Fitzgerald L, Selvey L, Maher L. Turning points, identity, and social capital: A meta-ethnography of methamphetamine recovery, International Journal of Drug Policy, Volume 67, 2019, Pages 79-90

Brunette MF, Drake RE, Xie H, McHugo GJ, Green AI. Clozapine Use and Relapses of Substance Use Disorder Among Patients With Co-occurring Schizophrenia and Substance Use Disorders. Schizophrenia Bulletin. October 2006 32(4): 637–643.

Chan, B., Freeman, M., Kondo, K., Ayers, C., Montgomery, J., Paynter, R., & Kansagara, D. (2019). Pharmacotherapy for methamphetamine/amphetamine use disorder—a systematic review and meta-analysis. *Addiction*, *114*(12), 2122-2136.

Emmerik-van Oortmerssen et al. Prevalence of attention-deficit hyperactivity disorder in substance use disorder patients: A meta-analysis and meta-regression analysis. Drug and Alcohol Dependence April 2012 (1-2) 11-19.

Farone et al. The World Federation of ADHD International Consensus Statement: 208 Evidence-based conclusions about the disorder. Neurosci Biobeh Rev 2021 Sep;128:789-818. doi: 10.1016/j.neubiorev.2021.01.022.

Flynn PM and Brown BS. Co-Occurring Disorders in Substance Abuse Treatment: Issues and Prospects. J Subst Abuse Treat. 2008 Jan; 34(1): 36-47

Gemma M-B, Fernández-Aranda F. Co-occurring Substance Use and Eating Disorders. Psychiatric Times. 10 April 2023. 40(4).

Iqbal MN, Levin CJ, Levin FR. Treatment for Substance Use Disorder With Co-Occurring Mental Illness. FOCUS (Am Psychiatr Publ). Spring 2019 17(2): 88–97.

REFERENCES

McCauley JL, Killeen T, Gros DF, Brady KT, Back SE. Posttraumatic stress disorder and co-occurring substance use disorders: Advances in assessment and treatment. Clinical Psychology: Science and Practice. 2012.19(3): 283–304

Morefield H. There Remain Startling Health Inequities in the Treatment of Substance Use Disorder. Pharmacy Times. 22 Feb 2023.

Neelambika Revadigar; Vikas Gupta. Substance-Induced Mood Disorders. Stat Pearls Publishing, Treasure Island, FL. 2023 Jan.

Obermeit, L. C., Cattie, J. E., Bolden, K. A., Marquine, M. J., Morgan, E. E., Franklin Jr, D. R., ... & Translational Methamphetamine AIDS Research Center (TMARC) Group. (2013). Attention-deficit/hyperactivity disorder among chronic methamphetamine users: frequency, persistence, and adverse effects on everyday functioning. *Addictive behaviors*, *38*(12), 2874-2878.

Özgen et al. *Treatment of Adolescents with Concurrent Substance Use Disorder and Attention-Deficit/Hyperactivity Disorder: A Systematic Review.* J Clin Med. 2021 Sep; 10(17): 3908.

Parmar A and Kaloiya G. Comorbidity of Personality Disorder among Substance Use Disorder Patients: A Narrative Review. Indian J Psychol Med. 2018 Nov-Dec; 40(6): 517–527

Potvin, S., Pelletier, J., Grot, S., Hebert, C., Barr, A. & Lecomte, T. (2018) Cognitive deficits in individuals with methamphetamine use disorder: a meta-analysis. Addictive Behaviors, 80(1), 154– 160

Smith JP and Book SW. Anxiety and Substance Use Disorders: A Review. Psychiatr Times. 2008 Oct; 25(10): 19–23.

Substance Abuse and Mental Health Services Administration. Advisory: Adults With Attention Deficit Hyperactivity Disorder and Substance Use Disorders (2015)

Terlizzi EP and Villaroel MA. Symptoms of Generalized Anxiety Disorder Among Adults: United States, 2019. NCHS Data Brief No. 378. September 2020.

Wisdom JP, Manuel JI, Drake RE. Substance use disorder among people with first-episode psychosis: a systematic review of course and treatment. Psychiatric Services. 2011 Sep. 62(9):1007-12.

ASAM REVIEW COURSE 2026

Pregnancy and Newborns: Considerations from Science to Systems

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Espanola, NM





Financial Disclosure

Leslie Hayes, MD

- No relevant disclosures

Presentation Outline

Pregnancy and the postpartum period

Neonatal opioid withdrawal syndrome

Effects of substance use during pregnancy on the newborn

Learning objectives

- Understand the effect of alcohol and illicit drugs on pregnancy.
- Discuss the rationale behind use of medication treatment for opioid use disorder during pregnancy.
- Realize the importance of the postpartum period.
- Be able to discuss neonatal opioid withdrawal syndrome and child protective services involvement with patient.

Definition of terms for providers not regularly doing obstetric care

- G = Gravida = total number of pregnancies
- P = Para = total number of deliveries
- XX weeks = weeks since last menstrual period or weeks since conception + 2
- Full-term = 37-41 weeks gestation
- IUGR = Intrauterine growth restriction = fetal weight by ultrasound < 10th percentile
- SGA = small for gestational age = weight of newborn baby < 10th percentile for gestational age

Definition of terms for providers not regularly doing obstetric care

- Preterm labor = labor at < 37 weeks
- Preterm delivery = delivery at < 37 weeks
- Placental abruption = placenta pulls away from the wall of the uterus. Small abruptions can cause IUGR or preterm labor. Large abruptions can be fatal for mother and baby.



Case Study

33 yo G4P3 had been stable on buprenorphine-naloxone for 4 years. Presented to her buprenorphine provider for routine appointment and was discovered to be pregnant. Her buprenorphine provider did not give her a script because of this. She relapsed to heroin. She presented to our clinic at 25 weeks gestation, but because of transportation difficulties, she was unable to get restarted on buprenorphine and delivered a premature infant at 31 weeks. She restarted buprenorphine postpartum, and both she and baby did well.



Case Study

22yo G1P0 presents @ 9 weeks gestation. Actively using heroin. Desperately wanted to keep this pregnancy and this child. Started on buprenorphine maintenance, did well. Child with no signs of Neonatal Opioid Withdrawal Syndrome at birth. Currently 10 years old, doing well.

Substance use in pregnancy

- Use of alcohol, tobacco, and drugs during pregnancy is the leading preventable cause of mental, physical, and psychological impairments in children.
- Opioid-dependent pregnant women have an unintended pregnancy rate of 86%.[1]
  - Please provide or refer for contraception if you are treating patients with OUD who can get pregnant and don't want to do so.
  - Also, please start them on folate, 0.4 – 0.8 mg daily, even if they are not planning to get pregnant.[2]

Weaver et al. Alcohol and Other Drug Use During Pregnancy: Management of the Mother and Child in Miller et al. The ASAM Principles of Addiction Medicine. Wolters Kluwer 2019 P. 1315

https://www.uspreventiveservicestaskforce.org/uspstf/recommendation/folic-acid-for-the-prevention-of-neural-tube-defects-preventive-medication accessed 4/14/2024

Perinatal SBIRT: 4 Ps Plus

Parents	Did either of your parents ever have a problem with alcohol or drugs?
Partner	Does your partner have a problem with alcohol or drugs?
Past	Have you ever had a problem with alcohol or drugs in the past?
Past 30 days	In the past month, have you drunk any alcohol or used any substances?

[1]*ACOG committee opinion 711, 2017*

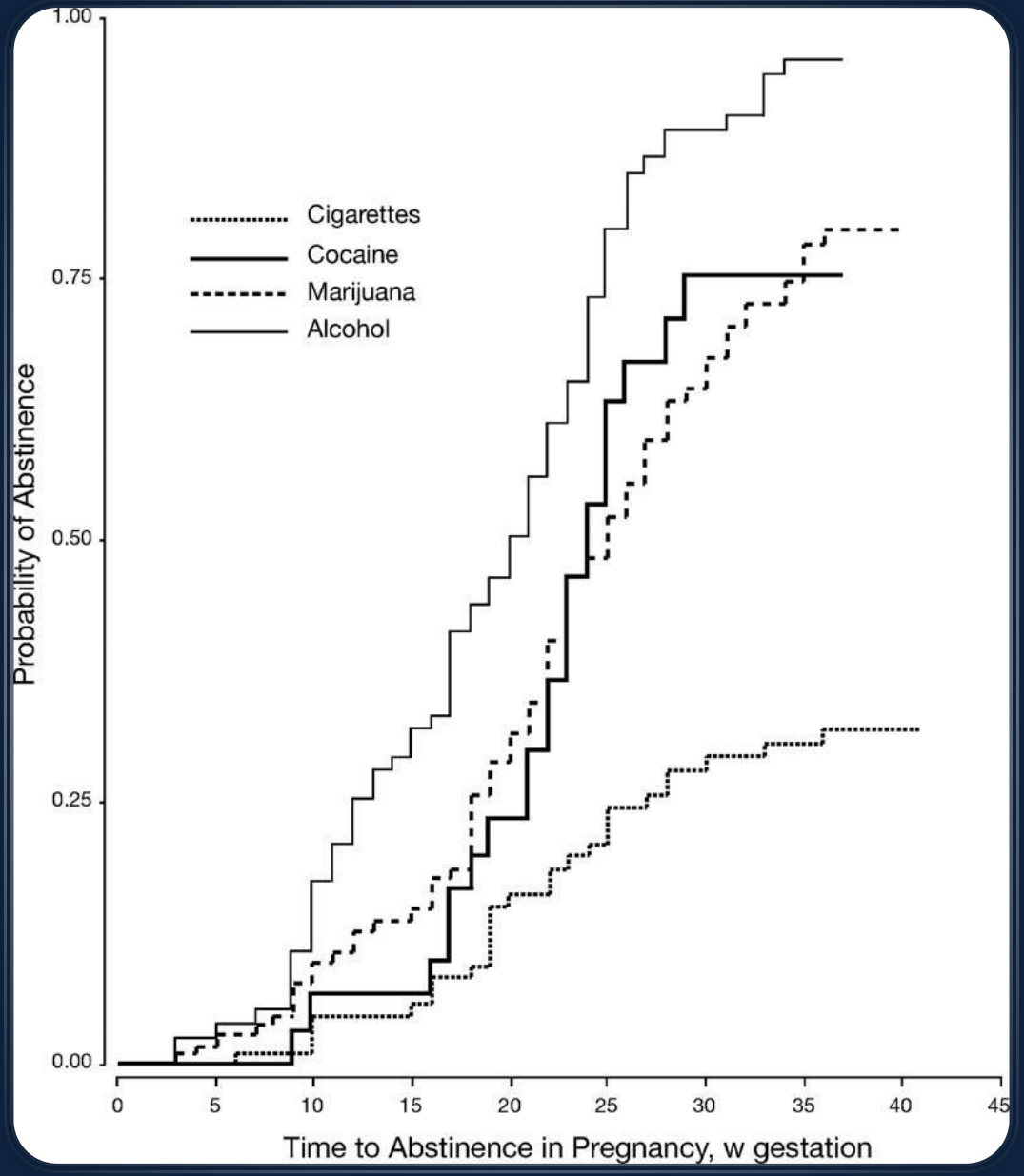
[2] *J Perinatol. 2005 Jun;25(6):368-74.*

- What are medical implications of substance use disorder with pregnancy?
- What is the significance of pregnancy for any substance use disorder?

Pregnant patients are likely to achieve abstinence during pregnancy, but relapse rate postpartum is high

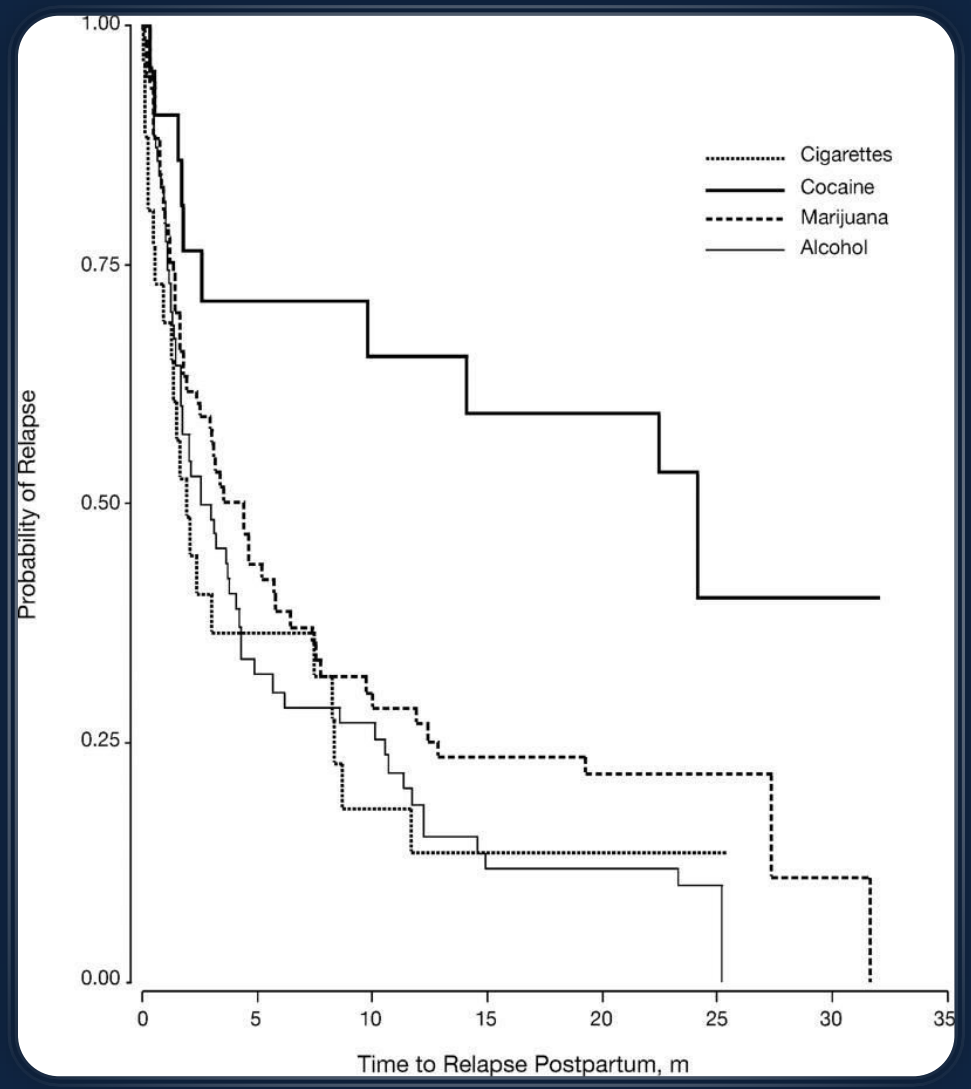
- A 2015 prospective study found that 83% of all women using cigarettes, alcohol, marijuana, and cocaine achieved abstinence from at least one substance.
- Postpartum, 80% of women abstinent in the last month of pregnancy relapsed to at least one substance.

Forray A, Merry B, Lin H, Ruger JP, Yonkers KA. Perinatal substance use: a prospective evaluation of abstinence and relapse. Drug Alcohol Depend. 2015 May 1;150:147-55. doi: 10.1016/j.drugalcdep.2015.02.027. Epub 2015 Mar 3. PMID: 25772437; PMCID: PMC4387084.



Pregnant patients are likely to achieve abstinence during pregnancy

Forray A, Merry B, Lin H, Ruger JP, Yonkers KA. Perinatal substance use: a prospective evaluation of abstinence and relapse. Drug Alcohol Depend. 2015 May 1;150:147-55. doi: 10.1016/j.drugalcdep.2015.02.027. Epub 2015 Mar 3. PMID: 25772437; PMCID: PMC4387084.



Relapse rate postpartum is high

Forray A, Merry B, Lin H, Ruger JP, Yonkers KA. Perinatal substance use: a prospective evaluation of abstinence and relapse. Drug Alcohol Depend. 2015 May 1;150:147-55. doi: 10.1016/j.drugalcdep.2015.02.027. Epub 2015 Mar 3. PMID: 25772437; PMCID: PMC4387084.

Birth defects with substances

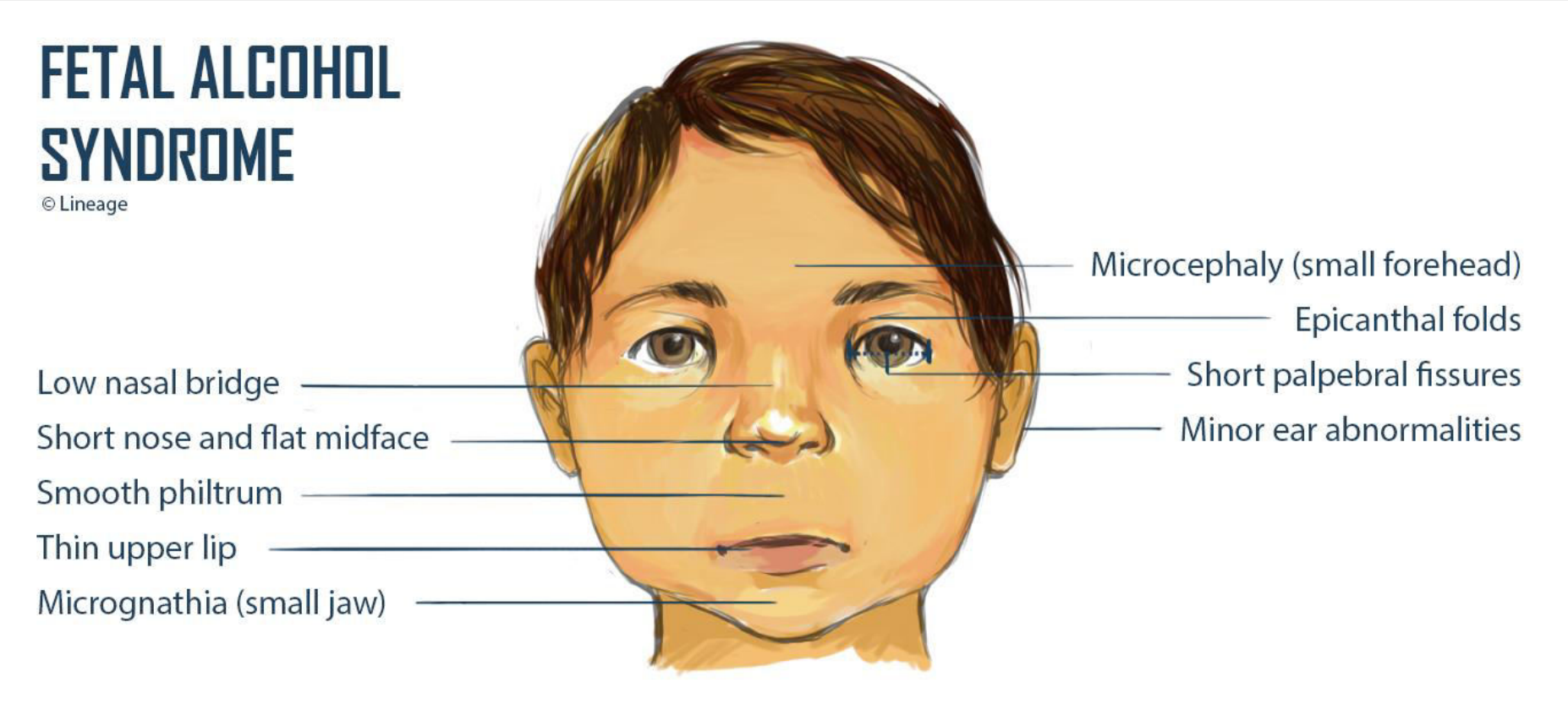
- The drug with the most teratogenic potential is alcohol. [1]

[1] *Weaver et al. Alcohol and Other Drug Use During Pregnancy: Management of the Mother and Child in Miller et al. The ASAM Principles of Addiction Medicine. Wolters Kluwer 2019 P 1317*

Fetal alcohol syndrome

- Evidence of growth restriction (prenatal and/or postnatal)
  - Height and/or weight <= 10th percentile
- Evidence of deficient brain growth and/or abnormal morphogenesis
  - Structural brain anomalies or head circumference <=10th percentile
- Characteristic pattern of minor facial anomalies
  - Short palpebral fissures, thin vermillion border upper lip, smooth philtrum

Fetal alcohol syndrome



Tobacco and pregnancy

- Neonates born to mothers who smoke weigh an average of 200 gm less than neonates born to mothers who don't smoke. [1]
- 22% of SUIDs (Sudden Unexpected infant deaths) can be directly attributed to maternal smoking during pregnancy. [2]

[1]*Weaver et al.* ***Alcohol and Other Drug Use During Pregnancy: Management of the Mother and Chil****d in Miller et al. The ASAM Principles of Addiction Medicine. Wolters Kluwer 2019P 1318*

[2]*Anderson TM, Lavista Ferres JM, Ren SY, et al.* ***Maternal Smoking Before and During Pregnancy and the Risk of Sudden Unexpected Infant Dea****th. Pediatrics. 2019; 143(4):e20183325*

Cannabis and pregnancy



- Many potential confounders:
  - Concurrent use of alcohol/tobacco
  - Income/age/education
  - Co-occurring psychiatric conditions
- Cannabis use is common – the prevalence of self-reported marijuana use is 2-5%, and it increased from 2.37% in 2002 to 3.85% in the 2014 NSDUH. [1]

[1] *Thompson R, DeJong K, Lo J. Marijuana Use in Pregnancy: A Review. Obstet Gynecol Surv. 2019 Jul;74(7):415-428*

Cannabis and pregnancy

- Most common reasons to use cannabis in pregnancy are morning sickness, to manage anxiety/depression and to relax/sleep
  - Use of cannabis for morning sickness can lead to cannabinoid hyperemesis syndrome. [1]



[1] *Badowski S, Smith G.* ***Cannabis use during pregnancy and postpartum****. Can Fam Physician. 2020;66(2):98-103.*

Cannabis and pregnancy

- Data is mixed on effect of cannabis on fetus.[1]
  - A recent Cochrane review showed both low birth weight and small for gestational age in infants exposed to cannabis.[2]
  - Studies have been mixed for birth defects[3]
  - There does seem to be a pattern of neurobehavioral effects on the fetus, with hyperactivity and sleep problems in toddlers, ADHD in pre-teens, and emotional dysregulation in adolescents.[4,5,6,7]

1. *Sheryl A. Ryan, et al, COMMITTEE ON SUBSTANCE USE AND PREVENTION, SECTION ON BREASTFEEDING, Lucien Gonzalez et al;* ***Marijuana Use During Pregnancy and Breastfeeding: Implications for Neonatal and Childhood Outcomes.*** *Pediatrics September 2018; 142 (3): e20181889. 10.1542/peds.2018-1889*
2. *Avalos LA, Adams SR, Alexeeff SE, et al.* ***Neonatal outcomes associated with in utero cannabis exposure: a population-based retrospective cohort****.* Am J Obstet Gynecol. *2024;231(1):132.e1-132.e13.*
3. *Conner et al. Maternal* ***Marijuana Use and Adverse Neonatal Outcomes: A Systematic Review and Meta-analysis****. Obstet Gynecol. 2016 Oct;128(4):713-23. doi: 10.1097/AOG.0000000000001649.*
4. *Weaver et al.* ***Alcohol and Other Drug Use During Pregnancy: Management of the Mother and Child*** *in Miller et al. The ASAM Principles of Addiction Medicine. Wolters Kluwer 2019P 1325*
5. *Thompson R, DeJong K, Lo J.* ***Marijuana Use in Pregnancy: A Review****. Obstet Gynecol Surv. 2019 Jul;74(7):415-428*
6. *Nashed et al.* ***Cannabinoid Exposure: Emerging Evidence of Physiological and Neuropsychiatric Abnormalities*** *Frontiers in Psychiatry. 11/2021*
7. *Roncero et al.* ***Cannabis use during pregnancy and its relationship with fetal developmental outcomes and psychiatric disorders. A systematic review****. Reprod Health. 2020;17(1):25. 2020 Feb 17.*

Cannabis and pregnancy –what we need to tell our patients

- Pregnant patients complain about hearing mixed messages from healthcare providers. They also state that want more research on the safety and effects of cannabis with pregnancy.[1]
- There is no recognized “safe” amount of cannabis with pregnancy.
  - Although marijuana hasn’t been found definitively to be dangerous, it has also most definitely not been found to be safe.
  - It is also likely much more dangerous if combined with tobacco and alcohol.
- There is very likely a risk of long-term neurocognitive effects.
- While it may help with morning sickness, it can lead to cannabinoid hyperemesis syndrome, which is way worse, and there are better treatments.

Barbosa-Leiker et al. Daily Cannabis Use During Pregnancy and Postpartum in a State With Legalized Recreational Cannabis, Journal of Addiction Medicine: November/December 2020 - Volume 14 - Issue 6 - p 467-474

Stimulant use and pregnancy

- Methamphetamine[1] and cocaine[2] use are associated with the following:
  - Preterm delivery
  - Low birth weight
  - Small for gestational age infants



Kalaitzopoulos et al. Effect of Methamphetamine Hydrochloride on Pregnancy Outcome: A Systematic Review and Meta-analysis, Journal of Addiction Medicine: May/June 2018 - Volume 12 - Issue 3 - p 220-226

Smid MC et al. Stimulant Use in Pregnancy: An Under-recognized Epidemic Among Pregnant Women. Clin Obstet Gynecol. 2019;62(1):168-184.

Implications of opioid use disorder with pregnancy

- Medication: Both use and withdrawal have fetal effects. Withdrawal effects usually considered more serious.
  - Withdrawal causes a hyperadrenergic state which causes constriction of blood vessels in placenta. Exacerbated by cocaine and methamphetamine use. Can cause preterm labor and placental abruption.
  - Biggest direct effect of opioid use is Neonatal Opioid Withdrawal Syndrome at birth.

  Opioid use substantially increases the risk of maternal complications.[1]

1. Maeda, Ayumi et al. "Opioid abuse and dependence during pregnancy: temporal trends and obstetrical outcomes." Anesthesiology vol. 121, 6 (2014): 1158-65. doi:10.1097/ALN.0000000000000472

Case Study
Pregnancy and Substance Use Disorder



28 yo G5P4, on methadone maintenance, disappeared from care at about 20 weeks, returned at 38 weeks in labor. Stated she had been at a methadone clinic in another community, but urine was negative for methadone, + for opiates. Baby went into horrible withdrawal at birth, child protective services involved and took child. Mother was arrested when she and her cousin, who was foster mother, got in fight on OB floor.

- What are psychosocial implications of substance use disorder with pregnancy?

Implications of substance use disorder with pregnancy

- Co-occurring disorders
  - Depression and other mental illness[1,2]
    - Both substance use disorder and depression cause poor self-care.
  - Intimate partner violence
    - Homicide is the leading cause of death for women during pregnancy and the first 6 weeks postpartum[3]



1. Metz et al. ***Maternal Deaths from Suicide and Overdose in Colorado, 2004-2012***. Ob Gyn. Vol 128. No. 6. December 2016. pp 1233-1240
2. Schiff et al. ***Fatal and Nonfatal Overdose Among Pregnant and Postpartum Women in Massachusetts***. Obstet Gynecol. 2018
3. Wallace M et al. ***Homicide During Pregnancy and the Postpartum Period in the United States, 2018-2019***. Obstet Gynecol. 2021 Nov 1;138(5):762-769. doi:

Implications of substance use disorder with pregnancy

- Psychosocial:
  - Most mothers have a high motivation to change.
  - Lot of guilt/shame for many women
  - Legal implications around custody of baby and older children
  - Often have history of childhood sexual abuse or physical abuse (with implications for parenting)
  - Cis women who use drugs often start using because their male partners use drugs. If they are still with that partner, it can be difficult for them to quit unless he quits as well.



Medical Conditions Case Study Pregnancy and Opioid Dependence

25 yo G2P1 presents at 26 weeks, stating, “I’m addicted to fentanyl.” Scared that she will lose baby to child protective services or have medical complications. She wants to get into treatment.

- Is medication therapy an option for the patient?
- Which is better, buprenorphine or methadone?
- What about weaning off the fentanyl and using abstinence-based therapy?
- Do they need any special care for their pregnancy?

Prenatal Care

- In a study in the Journal of Perinatology, it was found that pregnant people with illicit drug use and no prenatal care had the highest risk for prematurity, low-birth weight and small for gestational age infants. As prenatal care increased, risk for prematurity, low birth weight and small for gestational age babies dropped. [1]
- Pregnant people will often delay or not get prenatal care because of stigma and fear of consequences, including being reported to child protective services. [2]

[1]*El-Mohandes et al. Prenatal Care reduces the Impact of Illicit Drug use on Perinatal Outcomes. Journal of Perinatology. 2003; 23:354-360*

[2]*Bishop et al. Pregnant Women and Substance Use. Overview of Research and Policy in the United States. Bridging the Divide: A Project of the Jacobs Institute of Women's Health. February 2017*

Medication therapy and pregnancy

- Medication therapy for opioid use disorder (MOUD) is standard of care for pregnancy

SAMHSA Advisory. Evidence-Based, Whole-Person Care for Pregnant People who have Opioid Use Disorder. March, 2024

Benefits of MOUD during pregnancy

- A recent study of 10,741 pregnant persons with OUD on Medicaid with 13,320 pregnancies showed the following benefits to Medication for Opioid Use Disorder:
  - Decreased rate of overdose
  - Decreased preterm birth
  - Decreased low birthweight
- All of the above outcomes improved with longer duration of MOUD during the pregnancy

Krans EE, Kim JY, Chen Q, Rothenberger SD, James AE 3rd, Kelley D, Jarlenski MP. Outcomes associated with the use of medications for opioid use disorder during pregnancy. Addiction. 2021 Dec;116(12):3504-3514. doi: 10.1111/add.15582. Epub 2021 Jun 9. PMID: 34033170; PMCID: PMC8578145.

Benefits of MOUD during pregnancy

- In addition to the medical benefits, infants with NOWS are significantly (odds ration 3.9) more likely to be discharged to the parent, rather than foster or relative, care if the mother received prenatal MOUD

Singleton, Rosalyn et al. "Assessing the Impact of Prenatal Medication for Opioid Use Disorder on Discharge Home With Parents Among Infants With Neonatal Opioid Withdrawal Syndrome." Journal of addiction medicine vol. 16,6 (2022): e366-e373. doi:10.1097/ADM.0000000000000987

Access to buprenorphine and methadone while pregnant

- A 2020 study of obstetricians showed that only a third of obstetricians always recommend MOUD and a fourth never recommend it.[1]
- MOUD providers are less likely to accept pregnant patients than non-pregnant patients.[2, 3]
  - Methadone 97% vs 91% and Buprenorphine 83% vs 51% in a 2018 study[2]
  - Methadone no difference and buprenorphine 73.9% vs 61.4% in a 2020 study[3]

Ko, J.Y., Tong, V.T., Haight, S.C. et al. Obstetrician–gynecologists' practice patterns related to opioid use during pregnancy and postpartum—United States, 2017. J Perinatol 40, 412–421 (2020).

Stephen W. Patrick et al. (2018): Barriers to accessing treatment for pregnant women with opioid use disorder in Appalachian states, Substance Abuse

Patrick SW, Richards MR, Dupont WD, et al. Association of Pregnancy and Insurance Status With Treatment Access for Opioid Use Disorder. JAMA Netw Open. 2020;3(8):e2013456. doi:10.1001/jamanetworkopen.2020.13456

Buprenorphine vs methadone in Pregnancy

- 2022 study of 11,272 pregnant patients who were exposed to buprenorphine and 5056 to methadone showed significantly lower rates of NOWS in babies exposed to buprenorphine than methadone.

Suarez et al. ***Buprenorphine versus Methadone for Opioid Use Disorder in Pregnancy*** *NEJM* ***Vol 387 12/1/2022 Pages: 2033-2044***

Medication therapy and pregnancy

- However, if buprenorphine does not work for patient, it is essential to switch them to methadone quickly. Having the patient on a successful treatment for Opioid Use Disorder is the most essential part of treatment.
- “ANY OPIOID AGONIST THERAPY IS RECOMMENDED OVER UNTREATED OPIOID USE DISORDER IN PREGNANCY.”[1]

1. *Suarez et al.* ***Buprenorphine versus Methadone for Opioid Use Disorder in Pregnancy*** *NEJM* ***Vol 387 12/1/2022 Pages: 2033-2044***

Starting buprenorphine in a pregnant person

- Very little data or consensus recommendation, although most providers are leaning towards rapid low dose dosing in an inpatient setting or low dose dosing in an outpatient setting
- Macrodosing may be considered if the patient presents in active withdrawal

Morning sickness and methadone

- Both ondansetron and methadone cause QT prolongation, so use other treatments first.
- Lifestyle changes:
  - Small frequent meals
  - Avoid fluids with meals
  - Eat something before getting out of bed
  - Popsicles
- Ginger
- Pyridoxine, 10 mg + Doxylamine, 10mg tid

Split dosing recommended for both buprenorphine and methadone during pregnancy

- A recent SAMHSA alert stressed the importance of split dosing of both methadone and buprenorphine during pregnancy to help manage the impact of metabolic changes.[1]

1. https://www.samhsa.gov/sites/default/files/split-dose-guidance-sotas-csat.pdf accessed 4/24/2023

What about medically monitored withdrawal?

Medically monitored withdrawal

- THERE ARE NO GOOD STUDIES ON MEDICALLY MONITORED WITHDRAWAL. THE AVAILABLE STUDIES ARE OF POOR TO FAIR QUALITY AND HAVE CONFLICTING RESULTS.
- Recent meta-analysis reviewed 15 studies with 1,997 participants, of whom 1,126 went detoxification
  - Study quality was fair to poor with no randomized control trials
  - Mostly inpatient or residential setting with 3 incarceration studies
- Detoxification completion ranged from 9-100%.
- Relapse ranged from 0-100%
- 2 maternal deaths from postpartum overdose in one study

Terplan M, Laird HJ, Hand DJ, Wright TE, Premkumar A, Martin CE, Meyer MC, Jones HE, Krans EE. Opioid Detoxification During Pregnancy: A Systematic Review. Obstet Gynecol. 2018 May;131(5):803-814. doi: 10.1097/AOG.0000000000002562. PMID: 29630016; PMCID: PMC6034119.

Medically monitored withdrawal

- Rates of fetal demise and birthweights were similar between women who underwent detoxification and comparison group
- Rates of neonatal abstinence syndrome ranged from 0-100%

Terplan M, Laird HJ, Hand DJ, Wright TE, Premkumar A, Martin CE, Meyer MC, Jones HE, Krans EE. Opioid Detoxification During Pregnancy: A Systematic Review. Obstet Gynecol. 2018 May;131(5):803-814. doi: 10.1097/AOG.0000000000002562. PMID: 29630016; PMCID: PMC6034119.

Medically Monitored withdrawal

- No study of medically monitored withdrawal has examined maternal outcomes postpartum1

1. Jones et al. Medically Assisted Withdrawal (Detoxification): Considering the Mother-Infant Dyad. J Addict Med 2017 DOI 10.1097

- The previous patient has made it to term and is about to go into labor.
- Do you need to do anything special to manage their labor?
- What can you expect for the baby?
- Can they breast-feed?
- What can they expect post-partum?

Labor and delivery

- Method of delivery should be based solely on obstetric considerations.
- Epidural is preferred method of pain relief.



Comorbid Medical Conditions Case Study: Pregnancy and Opioid Dependence

34 yo G2P1 had been on buprenorphine-naloxone for heroin use disorder. She moved away and got pregnant and weaned herself off the buprenorphine. Moved back and declined to restart buprenorphine because “I am not going to ever go back to drugs.” NSVD of healthy baby with negative urine drug screens throughout pregnancy. Died of an overdose about 1 year post-partum.

MATERNAL MORTALITY AND OPIOID USE DISORDER

Studies from Maryland[1], Tennessee[2], Colorado[3], Utah[4], Ohio[5], Massachusetts[6], California[7], Michigan[8], Virginia[9], Philadelphia[10], New York City[11], New Mexico[12] , South Dakota[13], New Hampshire[14], Nevada[15], Michigan[16], Maine[17], Louisiana[18], Indiana[19], Illinois[20], Alaska[21], and Alabama[22] have found that overdose is one of the top causes of pregnancy-associated deaths, causing 14.7-34.5% of deaths.

MATERNAL MORTALITY AND OPIOID USE DISORDER

1. Maryland Maternal Mortality Review. 2022 Annual Review. Health – General Article 13-1212.
2. Maternal Mortality in Tennessee Annual Report 2024 Tennessee Department of Health | Family Health and Wellness | December 2024
3. Metz et al. Maternal Deaths from Suicide and Overdose in Colorado, 2004-2012. Ob Gyn. Vol 128. No. 6. December 2016. pp 1233-1240
4. Smid et al. Pregnancy-Associated Death in Utah: Contribution of Drug-Induced Deaths. Obstet Gynecol. 2019 Jun; 133(6): 1131-1140
5. Hall et al. Pregnancy-Associated Mortality Due to Accidental Drug Overdose and Suicide in Ohio, 2009-2018. Obstetrics and Gynecology. Vol 136, No 4 October 2020
6. Schiff et al. Fatal and Nonfatal Overdose Among Pregnant and Postpartum Women in Massachusetts. Obstet Gynecol. 2018
7. Goldman-Mellor S, Margerison CE. Maternal drug-related death and suicide are leading causes of postpartum death in California. Am J Obstet Gynecol 2019;221:489.e1-9
8. :Kountanis JA, Roberts M, Admon LK, et al. Maternal deaths due to suicide and overdose in the state of Michigan from 2008 to 2018. Am J Obstet Gynecol MFM 2023;5:100811.
9. Virginia Maternal Mortality Review Team Annual Report. Report To The Governor And The General Assembly 2023
10. Mehta PK, Bachhuber MA, Hoffman R, Srinivas SK. Deaths From Unintentional Injury, Homicide, and Suicide During or Within 1 Year of Pregnancy in Philadelphia. Am J Public Health. 2016 Dec;106(12):2208-2210. doi: 10.2105/AJPH.2016.303473. Epub 2016 Oct 13. PMID: 27736205; PMCID: PMC5105012
11. 2024 Health Advisory #31: Overdose is the Leading Cause of Pregnancy-Associated Death in NYC. NEW YORK CITY DEPARTMENT OF HEALTH AND MENTAL HYGIENE
12. New Mexico Maternal Mortality Review Committee. Pregnancy-Associated Deaths 2015 – 2020. New Mexico Department of Health. Prepared March 2025

MATERNAL MORTALITY AND OPIOID USE DISORDER

13. South Dakota Department of Health. **The Silent Toll: A 10-year review of pregnancy-associated deaths in South Dakota: 2015-2024.**

14. New Hampshire Department of Health and Human Services. **2025 Annual Report on Maternal Mortality in New Hampshire.**

15. Office of Analytics. Nevada Department of Health and Human Services**. Maternal Mortality Review Committee Report and Maternal Mortality and Severe Maternal Morbidity Data Report Nevada, 2022-2023.** November 2024

16. Michigan Department of Health and Human Services. **A Maternal Mortality Message for Providers. Substance Use Disorder.**

17. Maine Department of Health and Human Services**. Maine's Maternal, Fetal, and Infant Mortality Review Panel 2024 Annual Report**

18. Louisiana Department of Health. **Louisiana Pregnancy-Associated Review 2020 Report.**

19. Indiana Department of Health. **Indiana Maternal Mortality Review Committee 2024 Annual Report.**

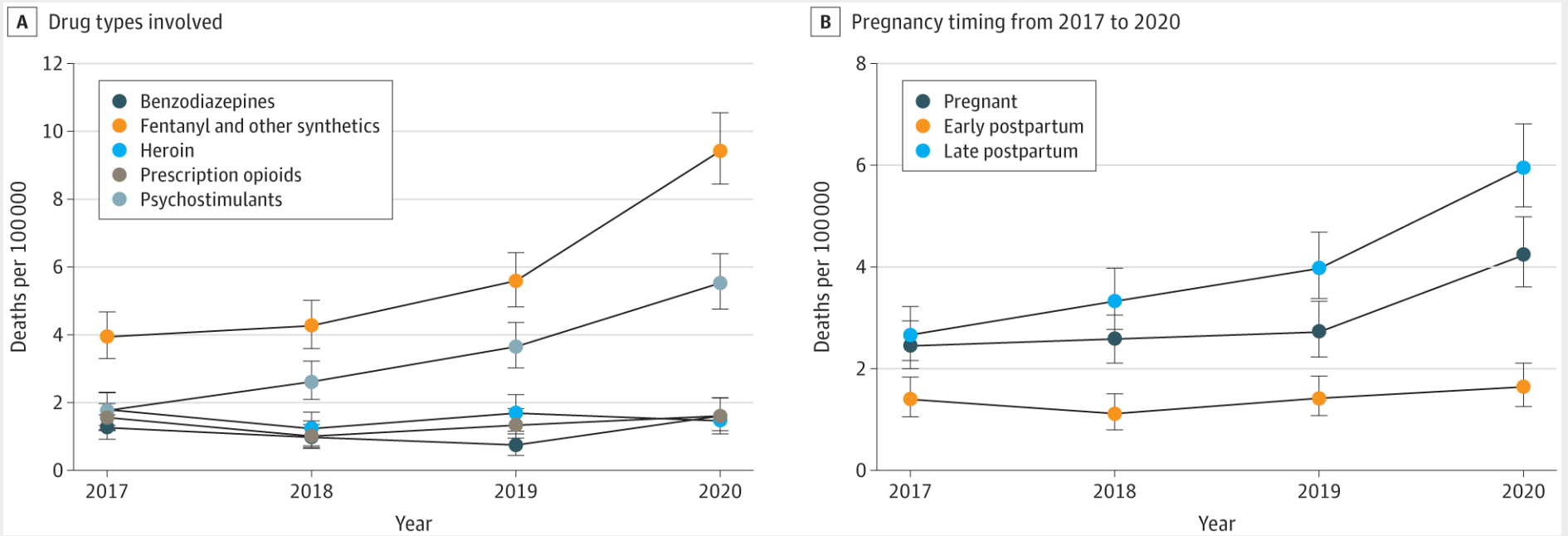
20. Illinois Depart of Public Health. **Illinois Maternal Mortality Data Report. November 2024**

21. Alaska Maternal Child Death Review. **Pregnancy-Associated Mortality in Alaska, 2019-2023**

22. Alabama Department of Public Health. **Alabama Maternal Mortality Review Report for 2020-2021**

From: **US Trends in Drug Overdose Mortality Among Pregnant and Postpartum Persons, 2017-2020**

JAMA. 2022;328(21):2159-2161. doi:10.1001/jama.2022.17045



Maternal mortality and opioid use disorder

- Suicide is also a substantial contributor to postpartum mortality.[1]
- Risk factors for postpartum opioid overdose and postpartum suicide have significant overlap. [2]
  - Three of the most common include depression, intimate partner violence, and substance use disorder.
- Screen for depression postpartum. Use Edinburgh Postpartum Depression Screen or another tool.

1Campbell et al. Pregnancy- Associated Deaths from Homicide, Suicide, and Drug Overdose: Review of Research and the Intersection with Intimate Partner Violence. Journal of Women's Health. Volume 30, Number 2, 2021.

2Mangla et al. Maternal self-harm deaths: an unrecognized and preventable outcome. American Journal of Obstetrics and Gynecology. October 2019.

Maternal mortality and opioid use disorder

- Studies in New Mexico and Philadelphia found that about half of maternal deaths were connected to substance use.[1,2]
- Around 40% are associated with serious mental illness.[1,2]
- About 20% are associated with Intimate Partner Violence.[1,2]
  - 54.3% of suicides and 45.3% of homicides involved IPV.[3]

New Mexico Maternal Mortality Review Committee. Pregnancy-Associated Deaths 2015 – 2018. New Mexico Department of Health.

Mehta PK, Bachhuber MA, Hoffman R, Srinivas SK. Deaths From Unintentional Injury, Homicide, and Suicide During or Within 1 Year of Pregnancy in Philadelphia. Am J Public Health. 2016 Dec;106(12):2208-2210. doi: 10.2105/AJPH.2016.303473. Epub 2016 Oct 13. PMID: 27736205; PMCID: PMC5105012

Glazer, Kimberly B, and Elizabeth A Howell. "A way forward in the maternal mortality crisis: addressing maternal health disparities and mental health." Archives of women's mental health vol. 24,5 (2021): 823-830. doi:10.1007/s00737-021-01161-0

Maternal mortality and opioid use disorder

- Social stressors can also be significant risk factors,[1] including unemployment, divorce, and homelessness.
  - Removal of custody of an infant can significantly destabilize a postpartum patient.[2,3]
- Discontinuing psychiatric medications is associated with suicide.[2,3]
  - Roughly half of women on psychiatric medications discontinue them with pregnancy[1]

Metz et al. Maternal Deaths from Suicide and Overdose in Colorado, 2004-2012. Ob Gyn. Vol 128. No. 6. December 2016. pp 1233-1240

Smid MC, Maeda J, Stone NM, Sylvester H, Baksh L, Debbink MP, Varner MW, Metz TD. Standardized Criteria for Review of Perinatal Suicides and Accidental Drug-Related Deaths. Obstet Gynecol. 2020 Oct;136(4):645-653. doi: 10.1097/AOG.0000000000003988. PMID: 32925616; PMCID: PMC8086704.

Trost et al. Preventing Pregnancy-Related Mental Health Deaths: Insights From 14 US Maternal Mortality Review Committees, 2008–17 Health Affairs 2021 40:10, 1551-1559

Maternal mortality and opioid use disorder

- Prior overdose is predictive of death by overdose in the postpartum period.[1]
- High unscheduled health-care utilization (emergency room visits or hospitalizations) predictive of overdose and suicide.[1,2, 3]
- Not taking or discontinuation of MOUD is a significant risk factor for overdose.[4,5]
  - Methadone discontinuation rate in the first six months postpartum was found to be 56% in one systematic review.[4]

Nielsen T, et al. Maternal and infant characteristics associated with maternal opioid overdose in the year following delivery. Addiction. 2020 Feb;115(2):291-301. doi: 10.1111/add.14825. Epub 2019 Nov 13. PMID: 31692133; PMCID: PMC7066531.Use Edinburgh Postpartum Depression Screen or another tool.

Goldman-Mellor S, Margerison CE. Maternal drug-related death and suicide are leading causes of postpartum death in California. Am J Obstet Gynecol 2019;221:489.e1-9

Kountanis JA, Roberts M, Admon LK, et al. Maternal deaths due to suicide and overdose in the state of Michigan from 2008 to 2018. Am J Obstet Gynecol MFM 2023;5:100811.

Wilder et al Medication assisted treatment discontinuation in pregnant and postpartum women with opioid use disorder. Drug and Alcohol Dependence 149 (2015) 225–231

Trost et al. Preventing Pregnancy-Related Mental Health Deaths: Insights From 14 US Maternal Mortality Review Committees, 2008–17 Health Affairs 2021 40:10, 1551-1559

Substance use and mental health deaths during pregnancy and postpartum are preventable

- The New York State Maternal Mortality Review found that 92.9% of pregnancy associated deaths due to substance use disorder were potentially preventable.

New York State Maternal Mortality Review Report on Pregnancy-Associated Deaths, 2018-2020. Albany, NY: New York State Department of Health. 2023.

Increased maternal mortality continued for many years after delivery in 2019 study

Mothers in Ontario and England with babies who had neonatal abstinence syndrome have a mortality rate that is over ten times as high as mothers who did not have an affected baby.

Roughly 1 in 20 mothers died over the next decade.

Top cause of death was unintentional injuries, but there were also high rates of murder and suicide, drug-related deaths, and unavoidable deaths.

Guttmann A et al. Long-term mortality in mothers of infants with neonatal abstinence syndrome: A population-based parallel-cohort study in England and Ontario, Canada. PLoS Med 16(11): e1002974. November 26, 2019.

What can be done

- Screen for depression postpartum. Use Edinburgh Postpartum Depression Screen or another tool.
- Screen for relapse.
- Screen for intimate partner violence
- Talk about seatbelts.
- Distribute Narcan.
- Make sure every postpartum patient has a follow up appointment with primary care, postpartum care, and addiction medicine.
- Use home nursing liberally.

Neonatal Opioid Withdrawal Syndrome

Neonatal Opioid Withdrawal Syndrome definition

- Neonatal Opioid Withdrawal Syndrome = physical withdrawal.
- Neonatal Opioid Withdrawal Syndrome baby ≠ addicted to drugs.

Clinical definition of opioid withdrawal in the neonate from the AAP

- Presence of clinical elements 1 and 2
- (1)In utero exposure to opioids with or without other psychotropic substances (recommended to be collected via confidential maternal self-report; toxicology testing also acceptable with maternal informed consent)
- (2)Clinical signs characteristic of substance withdrawal; any 2 of the following 5 signs qualify:
  - Excessive crying (easily irritable)
  - Fragmented sleep (<2-3 h after feeding)
  - Tremors (disturbed or undisturbed)
  - Increased muscle tone (stiff muscles)
  - Gastrointestinal dysfunction (hyperphagia, poor feeding, feeding intolerance, loose or watery stools)

Non-pharmacologic treatment of Neonatal Opioid Withdrawal Syndrome

- Non-pharmacologic treatment includes the following:
  - Small, frequent feeds.
  - Quiet, dim light.
  - Swaddling or skin-to-skin.
  - Prenatal education for parents.
- Studies from Dartmouth [1] and Yale [2] showed substantial improvements in cost and length of stay using non-pharmacologic treatment.

1Holmes et al. Rooming-In to Treat Neonatal Opioid Withdrawal Syndrome: Improved Family-Centered Care at Lower Cost. Pediatrics 2016; pp 2015-2029

2Grossman et al. An Initiative to Improve the Quality of Care of Infants with Neonatal Opioid Withdrawal Syndrome. Pediatrics 2017;139(6)

Breastfeeding

- The recommendations from the Academy of Breastfeeding Medicine are the most recent. They recommend mothers breastfeed if they have discontinued use by the or during the delivery hospitalization.
  - Women who were using at the time of delivery or who relapse should express and discard milk. There should be a multidisciplinary discussion about risks and benefits in this situation and when to start or restart breastfeeding.

Harris et al. Academy of Breastfeeding Medicine Clinical Protocol #21: Breastfeeding in the Setting of Substance Use and Substance Use Disorder (Revised 2023). BREASTFEEDING MEDICINE Volume 18, Number 10, 2023

Breastfeeding

- The Academy of Breastfeeding Medicine, the American Academy of Pediatrics, the American College of OB-GYN, the Substance Abuse and Mental Health Services Administration, and the American Society for Addiction Medicine recommend breastfeeding for women with substance use disorder who are in a treatment program and have had negative drug screens for 2 months prior to delivery. [1-5]
  - This includes women on MOUD.

[1]*Jansson, L. et al*, ***Methadone Maintenance and Breastfeeding in the Neonatal Period*** *PEDIATRICS Vol. 121 No. 1 January 2008, pp. 106-114*

2 Harris et al. ***Academy of Breastfeeding Medicine Clinical Protocol #21: Breastfeeding in the Setting of Substance Use and Substance Use Disorder (Revised 2023).*** *BREASTFEEDING MEDICINE Volume 18, Number 10, 2023*

[3]***Substance Use, Misuse, and Use Disorders During and Following Pregnancy, with an Emphasis on Opioids.*** *ASAM Policy Statement. January 18, 2017*

[4]***Clinical Guidance for Treating Pregnant and Parenting Women with Opioid Use Disorder and Their Infants.*** *SAMHSA. HHS Publication No. (SMA) 18-5054*

[5]***ACOG Committee Opinion. Opioid Use and Opioid Use Disorder in Pregnancy.*** *Number 711. August 2017.*

Child protective services and mental health

Study in Manitoba showed that losing custody of a child-to-child protective services is associated with significantly worse maternal mental health outcomes than experiencing the death of a child

Risk of depression was 1.90 times greater for women who had lost a child to child protective services.

Risk of substance use was 8.54 times greater for women who had lost a child to child protective services.

Wall-Wieler, Elizabeth et al. Maternal Mental Health after Custody Loss and Death of a Child: A Retrospective Cohort Study Using Linkable Administrative Data. The Canadian Journal of Psychiatry. 2018, Vol. 63(5) 322-328.

Child protective Services

- Discuss child protective service involvement during pregnancy
  - What will trigger a referral
  - What will likely happen with a referral
- Discuss with your patient what to do if a referral is made:
  - Be honest with child protective services
  - Have a plan for SUD treatment
  - Have a plan to ensure the baby is safe



From the AMERICAN INDIAN HEALTH COMMISSION ADDENDUM TO THE WASHINGTON STATE DEPARTMENT OF HEALTH'S MATERNAL MORTALITY REVIEW PANEL REPORT TO THE LEGISLATURE,

Tribal and Urban Indian Leadership Recommendations September 2022

"Help is not taking the baby from the parents. What we need is laundry cleaned, dishes washed, and some good heartwarming food."

Take home messages

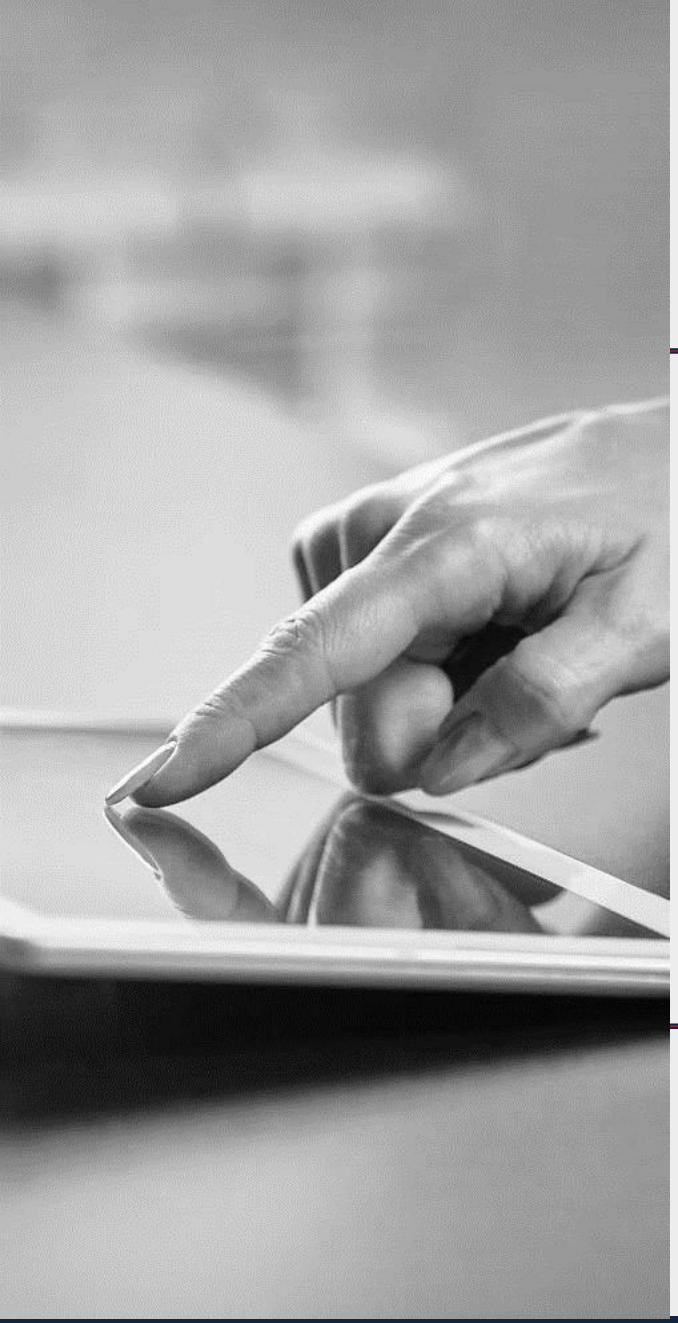
- Substance use disorder is common with substantial risks during pregnancy.
- Medication treatment is recommended for opioid use disorder in pregnancy.
- The postpartum period and after is a risky time for relapse and death in women with SUD
- Use non-medical treatments first for neonatal opioid withdrawal syndrome.

Which of the following is correct about opioid use disorder and pregnancy?

A. The highest risk time for relapse is postpartum
B. Medically-assisted withdrawal should be done during the second trimester to reduce the risk of neonatal opioid withdrawal syndrome
C. C-section is recommended for anyone actively using opioids
D. There is a high risk of congenital anomalies with opioid use

Which of the following are typical symptoms of neonatal opioid withdrawal syndrome?

A. Lethargy, high-pitched cry, constipation
B. Diarrhea, tremor, inability to sleep
C. Bradycardia, poor feeding, excessive sleep
D. Seizures, poor muscle tone, jaundice



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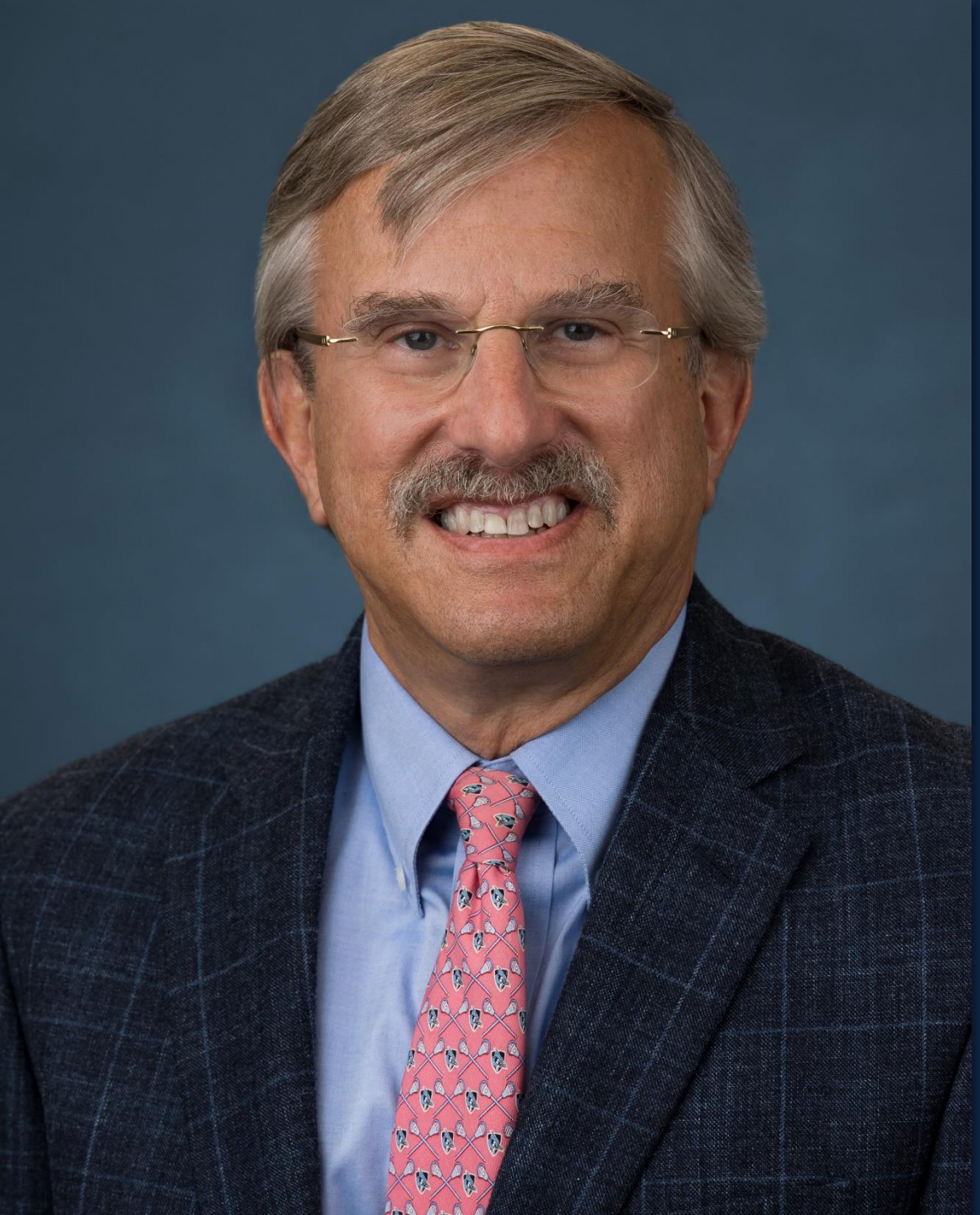
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ASAM REVIEW COURSE 2026

Treatment for Different Stages of Life: Adolescents, Young Adults, and the Elderly

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Financial Disclosure

Michael Fingerhood, MD, FACP, DFASAM

- No relevant disclosures

LEARNING OBJECTIVE

Describe how the different life stage of a patient can impact the development, diagnosis, and treatment of addiction.



Outline



1

Adolescents (10-19) and Young Adults (20-24 per World Health Organization)

2

Older adults (someone much older than yourself)

Adolescence

- Biologic growth and development
- Increased social pressures
- Increased decision making
- Search for self





Substances

- Cannabis
- Alcohol
- Nicotine/vaping
- Opioids
- Cocaine
- Lots of experimenting- inhalants (nitrous and others), MDMA, synthetic cannabinoids, PCP, canthinones, stimulants, kratom, salvia, psilocybin

Adolescents Are Vulnerable

- Early substance use = high risk of addiction
- Adolescent immaturity during critical development period = vulnerability
  - Impulsiveness and excitement seeking
  - Difficulty delaying gratification
  - Poor executive function and inhibitory control

Associated Factors

- Having a parent with substance use disorder
- Mood disorder
- Learning disorder/poor school performance
- Low self-esteem
- Early sexual activity
- Substance using peers
- Availability of substances in community
- Poor family dynamics; family conflict

Recent Trends in Adolescents

Monitoring the Future Survey 2025

- Alcohol use remained stable among all three grade levels, with 11% of eighth graders, 24% of 10th graders, and 41% of 12th graders reporting use in the past 12 months.
- Nicotine vaping remained stable among all grades, with 9% of eighth graders, 14% of 10th graders, and 20% of 12th graders reporting use in the past 12 months.
- Cannabis use remained stable among all grades, with 8% of eighth graders, 16% of 10th graders, and 26% of 12th graders reporting use in the past 12 months.

Patrick, M. E., Miech, R. A., Johnston, L. D., & O'Malley, P. M. (2025). Monitoring the Future Panel Study annual report: National data on substance use among adults ages

Recent Trends for High School Students

In 2023, prevalence of current substance use:

- 22% drank alcohol in the past 30 days
- 17% used marijuana in the past 30 days (19%F and 15%M)
- 10% had ever used an illicit drug and 12% had ever misused a prescription opioid (14%F and 9%M)
- For all substances, students who identified as LGBTQ+ had higher prevalence of substance use than those who identified as cisgender and heterosexual

Centers for Disease Control and Prevention. Youth Risk Behavior Survey Data Summary & Trends Report: 2013–2023. U.S. Department of Health and Human Services; 2025.

Random Tidbits

- Stimulant involved drug overdoses rising among youth; greatest rise in 11-14 year olds
- Inhalant use associated with violence, criminal activity, other substance use disorder, school dropout
- Cannabis related ED visits increased from 2018 to 2023
- College students
  - depressive symptoms associated with non-medical prescription drug use
  - past year non-medical use of prescription medication - prevalence 20%; higher among males and members of fraternities and sororities

Renny MH, Stecher Y, Vargas-Torres C, Zebrowski AM, Merchant RC. Trends in substance use-related emergency department visits by youth, 2018-2023. Am J Emerg Med. 2025 Feb 22;92:1-9.

CRAFFT: A Brief Screening Test for Adolescent Substance Use*

- C - Have you ever ridden in a CAR driven by someone (including yourself) who was "high" or had been using alcohol or drugs?
- R - Do you ever use alcohol or drugs to RELAX, feel better about yourself, or fit in?
- A - Do you ever use alcohol/drugs while you are by yourself, ALONE?
- F - Do your family or FRIENDS ever tell you that you should cut down on your drinking or drug use?
- F - Do you ever FORGET things you did while using alcohol or drugs?
- T - Have you gotten into TROUBLE while you were using alcohol or drugs?

*2 or more yes answers suggests a significant problem

CRAFFT 2.1 + N

Ask about use of vaping device containing nicotine and/or flavors, or any tobacco products.

1. Ever tried to QUIT
2. Use NOW because hard to quit
3. Felt ADDICTED
4. CRAVINGS
5. Felt like NEEDED to vape/use tobacco
6. Hard to keep from using in PLACES where you shouldn't
7. When you HAVEN'T used
   a. Hard to CONCENTRATE
   b. IRRITABLE
   c. NEED/urge
   d. NERVOUS, restless, anxious

Do We Care About Cannabis?

- Vulnerable populations: youth, psychiatric illness, other substance use disorders
- Consequences of intoxication, e.g. MVCs
- Impact on learning
- Psychiatric consequences of use
- Progression to cannabis use disorders and other substance use disorders

Vulnerability in Youth

- Conditional risk of use disorder in adolescents as high as 40%
- Daily use of cannabis <age 17 associated with substantially increased risk of:
  - Later cannabis use disorder (OR=18)
  - High school drop out (OR=3)
  - Use of other drugs (OR=8)
  - Suicide attempts (OR=7)

Pooled longitudinal studies. N =2537 to N=3765.
Silens et al. Lancet Psychiatry, 1,: 286 – 293, 2014S

Messaging – Overcoming Societal Attitudes

- Cannabis is addictive (but not everyone gets addicted)
- Cannabis can be harmful (but not everyone gets harmed)
- Broader use leads to broader problem use through access and decreased perceived harm
- This is a huge problem for youth and other vulnerable populations

Features of Adolescent Treatment

- Developmental barriers to treatment engagement
  - Invincibility
  - Immaturity
  - Motivation and treatment appeal
  - Salience of burdens of treatment
- Variable effectiveness of family leverage (or not)
- Pushback against sense of parental dependence and restriction
- Prominence of co-morbidity

Developmentally Informed Treatment - 1

- Adolescents rely on the support of adults, but also strive for autonomy
- Emphasize rewards and praise
- Emphasize adolescent learning styles, using energetic and fun activities while preserving therapeutic content
- Emphasize social alternatives to drug use
- Acknowledge normative attraction of thrill-seeking, risk, deviance
- Weave a safety net of supports: families (or surrogates), but expect some disdain

Developmentally Informed Treatment - 2

- Encourage adolescents to formulate their own solutions
- Natural consequences: Give some rope (but not too much) and don't enable
- Emotion regulation training
- Address sleep deprivation
- Treatment = habilitation, not rehabilitation
- Not effective- "Just grow up!", "Just say no"

Motivational Approaches

- Do you know other kids who have been in trouble?
- What are the pro's and con's for you?
- How much do you think is too much?
- What do you know about health risks?
- If it did become a problem in the future, how would you know?
- Do you know why I or your parents might think it's a problem?
- If you can stop anytime, would you be willing to see what it's like…
- Let's schedule you to come back and see how it's going…

Vignette

- 17M began prescription opioids at 15, progressing to daily use with withdrawal within 8 months; nasal heroin age 16, injection heroin 6 months later
- 3 episodes residential tx, 2 self-directed discharge, 1 completed
- Presents in crisis seeking detox (“Can I be out of here by Friday?”)
- How should you care for him?

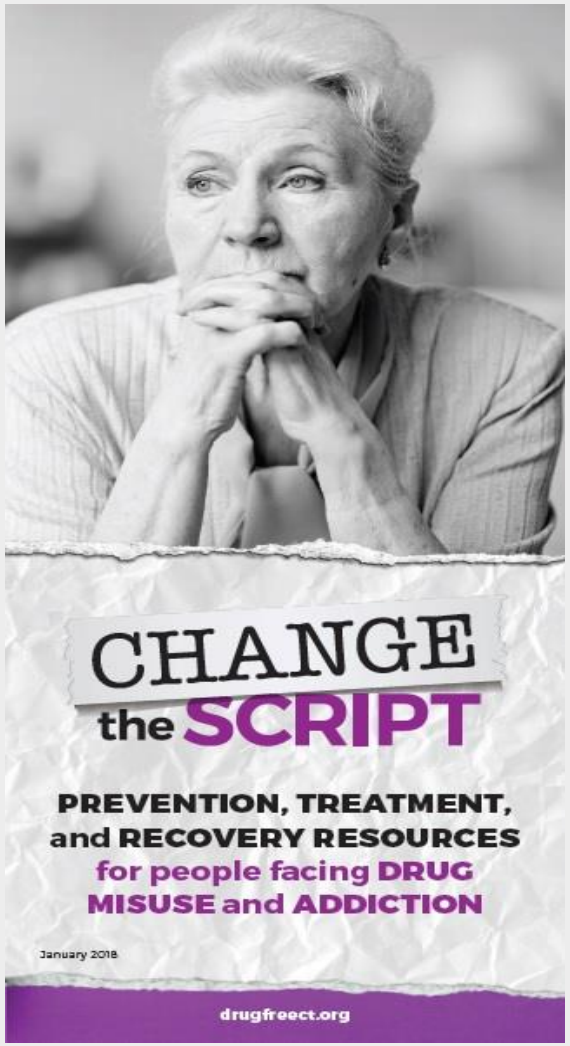
Adolescents and Treatment of OUD

- Medications feasible and effective (buprenorphine better than no buprenorphine)
- Availability of programs offering MOUD limited
- Use of buprenorphine for OUD declined between 2020 and 2023
- Adolescents with non-fatal opioid overdose should be strongly considered for buprenorphine treatment
- Naltrexone requires acceptance with concern over retention
- Longer duration buprenorphine better
- XR buprenorphine should be strongly considered

Oldfield B, Chen K, Joudrey PJ et al. Availability of Specific Programs and Medications for Addiction Treatment to Vulnerable Populations: Results from the Addiction Treatment Locator, Assessment, and Standards (ATLAS) Survey. J Adddict Med 2023 Mar 17. doi: 10.1097/ADM.0000000000001158

Lee E, Rikard SM, Guy G, Terranella A. Trends in Buprenorphine Dispensing Among Adolescents and Young Adults in the US. JAMA. 2025;333(5):425–427.

Older Adults



Older Adults-“Hidden Problem”

- Lack of screening in primary care
- Lack of guidelines for assessing older adults
- Signs and symptoms of harmful use overlap with other conditions
- Ageist bias

Challenges in Detecting Problematic Use

- Relying on older patient's report of frequency and quantity of substance use can lead to underestimation of the problem
- Older adults and family members may not appreciate deleterious consequences of long-time patterns of drinking or drug use
- Harm can come from lower amounts of substances

Detecting Problematic Substance use

Lehmann & Fingerhood. NEJM 2018;379:2351-60

Table 2. Signs of Possible Problematic Substance Use in Older Adults.

Psychiatric symptoms: sleep disturbances, frequent mood swings, persistent irritability, anxiety, depression
Physical symptoms: nausea, vomiting, poor coordination, tremors
Physical signs: unexplained injuries, falls, or bruises; malnutrition; evidence of self-neglect, such as poor hygiene
Cognitive changes: confusion and disorientation, memory impairment, daytime drowsiness, impaired reaction time
Social and behavioral changes: withdrawal from usual social activities, family discord, premature requests for refills of prescription medications

Patient Vignette

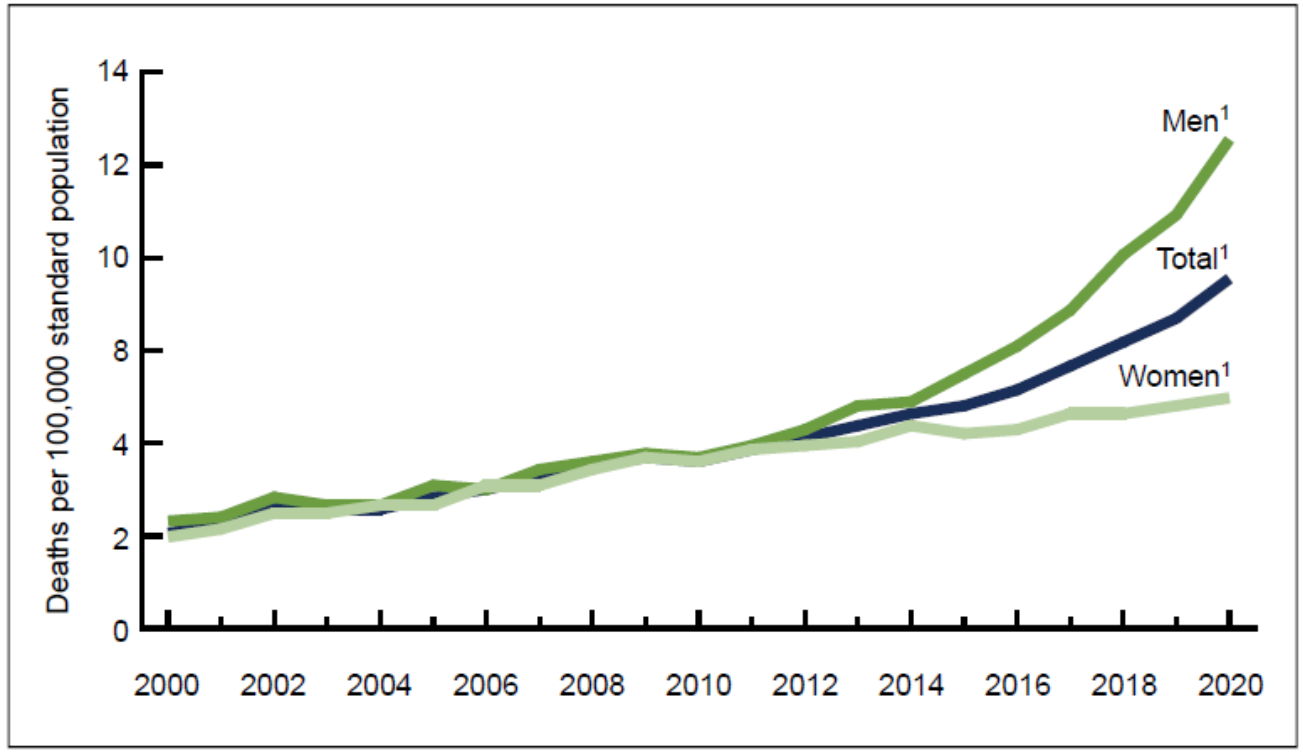
- EB is a 72 F seen for initial visit. She has a history of chronic pain in hips and knees. Her previous provider will no longer prescribe oxycodone as for the past 2 months her 30-day script ran out after 2 weeks. Tearful and fearful that providers won't help her. Cannot take NSAIDs. She admits that she often takes oxycodone when she is upset.
- She lives alone in senior housing apartment; 2 daughters- both with difficulties (medical and social). Non-smoker; no alcohol.
- How should you care for her?

Themes in Older Adults with Opioid (substance) Use Disorder

- Living alone
- Sense of isolation (despite family)
- Opioid as a “friend”
- Shame
- Fear of how to live without opioid (substance)

Older adult overdose death rate based on gender

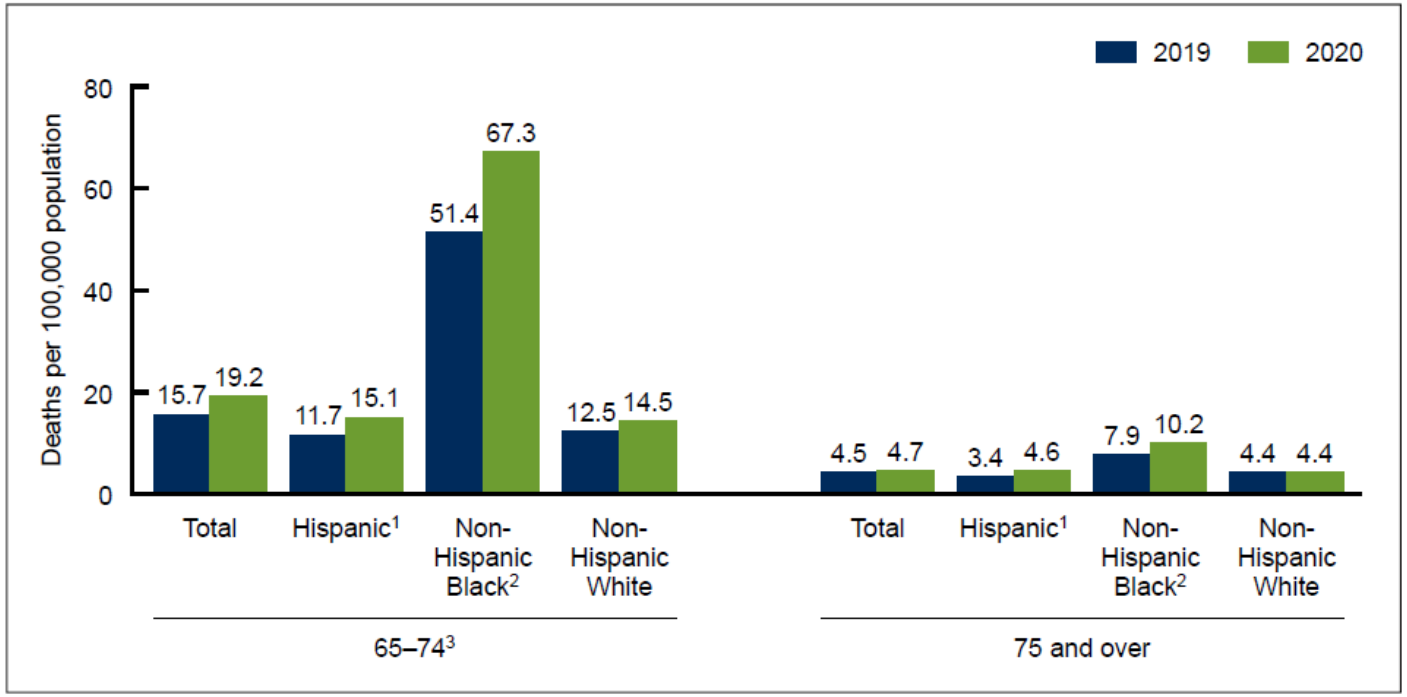
Figure 1. Age-adjusted drug overdose death rate for adults aged 65 and over, by sex: United States, 2000–2020



[1]Significant increasing trend from 2000 through 2020 with different rates of change over time; $p < 0.05$.
NOTES: Drug overdose deaths are identified using the *International Classification of Diseases, 10th Revision* underlying cause-of-death codes X40–X44, X60–X64, X85, and Y10–Y14. Access data table for Figure 1 at: https://www.cdc.gov/nchs/data/databriefs/db455-tables.pdf#1.
SOURCE: National Center for Health Statistics, National Vital Statistics System, Mortality.

Older adult overdose death rate by race

Figure 2. Drug overdose death rate for men aged 65 and over, by age group, race and Hispanic origin, and year: United States, 2019–2020



[1]Rates were significantly lower than rates for non-Hispanic Black men in 2019 and 2020; $p < 0.05$.
[2]Rates were significantly higher than rates for non-Hispanic White men in 2019 and 2020; $p < 0.05$.
[3]Rates for 2020 were significantly higher than 2019 for all groups; $p < 0.05$.
NOTES: Total includes races and origins not shown separately. Data for categories other than non-Hispanic White and non-Hispanic Black should be interpreted with caution because of inconsistencies in reporting race and ethnicity on death certificates, censuses, and surveys. Drug overdose deaths are identified using the *International Classification of Diseases, 10th Revision* underlying cause-of-death codes X40–X44, X60–X64, X85, and Y10–Y14. Access data table for Figure 2 at: https://www.cdc.gov/nchs/data/databriefs/db455-tables.pdf#2.
SOURCE: National Center for Health Statistics, National Vital Statistics System, Mortality.

American Geriatrics Society Beers Criteria

- Avoid chronic NSAIDs, muscle relaxants and use tramadol with caution (added 2019)
- Avoid opioids if history of falls or fracture

American Geriatrics Society 2019 Updated AGS Beers Criteria® for Potentially Inappropriate Medication Use in Older Adults. J Am Geriatr Soc. 2019 Apr;67(4):674-694. doi: 10.1111/jgs.15767. Epub 2019 Jan 29. PMID: 30693946.

Patient Vignette

- BR is a 82F brought to the ER by neighbor with “syncope”, but it is noted that she has alcohol on her breath and her BAL is 228 mg/dl. When confronted she becomes tearful. Her son goes to her home and finds hidden miniatures throughout her apartment.
- How do you approach caring for her?

Short Michigan Alcoholism Screening Test-Geriatric Version (SMAST-G)

In the past year:

1. When talking with others, do you ever underestimate how much you actually drink?
2. After a few drinks, have you sometimes not eaten or been able to skip a meal because you didn't feel hungry?
3. Does having a few drinks help decrease your shakiness or tremors?
4. Does alcohol sometimes make it hard for you to remember parts of the day or night?
5. Do you usually take a drink to relax or calm your nerves?

Short Michigan Alcoholism Screening Test-Geriatric Version (SMAST-G)

6. Do you drink to take your mind off your problems?
7. Have you ever increased your drinking after experiencing a loss in your life?
8. Has a doctor or nurse ever said they were worried or concerned about your drinking?
9. Have you ever made rules to manage your drinking?
10. When you feel lonely, does having a drink help?

*2 or more “yes” responses indicative of alcohol problem.

Alcohol: the Most Commonly Used Substance

- Alcohol Use Disorder in Older Adults
  - Early Onset: 2/3 of older adults; Men>Women
  - Late Onset: more likely to be triggered by stressful life event (loss of spouse, retirement, medical disability, pain, sleep problem); Women>Men

Increased Risks of Alcohol Even at "Low Consumption"

- Increased vulnerability to physiological effects
  - Decreased lean muscle mass
  - Decreased total body water
  - Less efficient liver enzymes that metabolize alcohol
  - Increased effective concentration of alcohol, higher and longer lasting blood alcohol levels

- Additional risks
  - Alcohol-medication interactions
  - Co-morbid chronic illnesses
  - Bariatric surgery

Patient Vignette

- CR is 82M with HTN and GERD and with recurrent depression which is being treated with 2 different antidepressants. His depression is much improved, but he continues to experience anxiety and stress, primarily related to worries about his wife's cancer and her poor health. He reports that he has decided to go to a marijuana dispensary and try cannabis to see if it can help his mood and his anxiety

- How do you respond?

Cannabis use and emergency visits among older adults in California

- Cannabis related ED visit rate for adults ≥ age 65, increased from 20.7/100,000 visits in 2005 to 395.0 per 100,000 ED visits in 2019, a 1804% increase.

Han BH, Brennan JJ, Orozoco, et al. Trends in emergency department visits associated with cannabis use among older adults in California, 2005-2019. J Am Geriatr Soc 2023 Jan 9. doi: 10.1111/jgs.18180

Impact of Cannabis on Physical and Mental Health

- Older adults often see cannabis as “safer” alternative to alcohol, opioids, or pharmaceutical medications
- Short term use is associated with
  - Impaired short-term memory, impaired judgment/motor coordination, worse driving skills
  - Increased anxiety
  - Paranoia and psychosis have dose-response effect

Patient Vignette

- LK is an 80F with long history of episodic anxiety and low mood and insomnia- prescribed temazepam for 30 years. She has 6 month history of low mood, panicky feelings, crying spells, anxiety, poor appetite; can't multitask or concentrate. Medications are- temazepam 30mg qhs, trazodone 50mg qhs, tramadol 50mg prn pain, gabapentin 2400mg daily

Benzodiazepine Prescribing in Older Adults

- What are the reasons?
  - Anxiety symptoms, anxiety disorders, depression with anxiety, sleeplessness

- What are the problems?
  - Often prescribed for years, without good indication of continuing need
  - Often prescribed for symptoms, without recognition of the true underlying cause: e.g. depression, normal worry, cognitive impairment
  - Increased frequency of adverse effects with aging, polypharmacy and use of meds with long half-lives

Deprescribing

- Emphasize that you will not withdraw appropriate care: “I understand that I need to treat your symptoms, but we need to do so without causing you other problems.”

- Reassure that you will monitor closely for symptoms recurrence: “We’ll reduce the medicine very slowly and will stay in close contact to watch for returning symptoms.”

Benzodiazepine tapering (use ASAM guideline)

Initial Considerations

- Use scheduled rather than prn dosing
- Consider switching to a longer-acting benzodiazepine
- Schedule follow-ups every 2-4 weeks- can be telemedicine or phone call

Tapering Considerations

- Reduce total daily dose (TDD) by 10-25% to start
- Continue reducing TDD by 10-25% every 2-4 weeks
- For patients on supra-therapeutic doses consider initial reduction of 25-30%

Treatment Approach for Older Adults

- Don’t minimize
- Confront with compassion
- Remove shame
- Build self-esteem
- Give encouragement/hope
- Undo isolation
- Work on coping skills
- Facilitate finding new ways to stay busy with use of peers

Some Conclusions:
Treatment for Youth and the Elderly is Effective, but …

- We need to learn to improve it
- There isn't enough of it
- Access and engagement is a problem

- Treatment works!

References

1. American Geriatrics Society Beers Criteria® Update Expert Panel. American Geriatrics Society 2023 updated AGS Beers Criteria® for potentially inappropriate medication use in older adults. J Am Geriatr Soc. 2023 Jul;71(7):2052-2081. doi: 10.1111/jgs.18372. Epub 2023 May 4. PMID: 37139824
2. Centers for Disease Control and Prevention. Youth Risk Behavior Survey Data. 2019
3. Choi NG, DiNitto DM, Marti CN. Older adults who use or have used marijuana: Help-seeking for marijuana and other substance use problems. J Subst Abuse Treat. 2017 Jun;77:185-192. doi: 10.1016/j.jsat.2017.02.005. Epub 2017 Feb 16. PMID: 28216197
4. Friedman J, Godvin M, Shover CL, Gone JP, Hansen H, Schriger DL. Trends in Drug Overdose Deaths Among US Adolescents, January 2010 to June 2021. *JAMA*. 2022;327(14):1398–1400. doi:10.1001/jama.2022.2847
5. Johnston, L. D., Miech, R. A., O'Malley, P. M., Bachman, J. G., Schulenberg, J. E., & Patrick, M. E. (2022). Monitoring the Future national survey results on drug use 1975-2021: Overview, key findings on adolescent drug use. Ann Arbor: Institute for Social Research, University of Michigan
6. Lehman S, Fingerhood M. Substance use disorders in later life. New England Journal of Medicine 2018; 378:2351-60
7. Silins E, Horwood LJ, Patton GC, Fergusson DM, Olsson CA, Hutchinson DM, Spry E, Toumbourou JW, Degenhardt L, Swift W, Coffey C, Tait RJ, Letcher P, Copeland J, Mattick RP; Cannabis Cohorts Research Consortium. Young adult sequelae of adolescent cannabis use: an integrative analysis. Lancet Psychiatry. 2014 Sep;1(4):286-93. doi: 10.1016/S2215-0366(14)70307-4. Epub 2014 Sep 10. PMID: 26360862
8. www.crafft.org
9. www.niaaa.nih.gov/alcohols-effects-health/special-populations-co-occurring-disorders/older-adults



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ASAM REVIEW COURSE 2026

Psychosocial Interventions: Cognitive Behavioral Therapy and Motivational Interviewing

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Financial Disclosure

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- No relevant disclosures

Prevalence in 2024

- 48.5 million people 12+ (17.1%) had a substance use disorder
  - AUD: 10.6% (2021) → 9.7% or 27.9 million people (2024)
  - DUD: 8.7% (2021) → 9.8% or 28.2 million people (2024)

- SUD by age group
  - 12-17: 8.5% (2021) → 7.8% (2024)
  - 18-25: 27.1% (2021) → 25.9% (2024)
  - 26+: 16.6% (2021) → 16.4% (2024)

(NSDUH, 2025)

Why psychotherapy?

Evidence-Based Treatments

- **Alcohol, Opioid, Cannabis Use Disorder**
  - MI
  - MET
  - 12-Step Facilitation
  - Cognitive Behavioral Therapy for SUDs
  - ACT for SUDs
  - DBT in conjunction with any of the above/mindfulness
  - Community Reinforcement and Family Training (CRAFT)

- **Stimulant Use Disorder, Opioid Use Disorder**
  - Contingency Management in conjunction with above modalities

Evidence Base

- **MI** (Sayegh, Huey, Zara, & Jhaveri, 2017) (Santa Ana et al., 2021)
  - Reduction in substance use at follow-up
  - Effective in group settings (attendance, lowered alcohol consumption)

- **CBT** (Magill et al., 2019)
  - Effective and durable gains in short- and long-term follow up

- **MI + CBT**
  - Combined MI and CBT for AUD + MDD decrease symptoms of both (Riper et al., 2014)

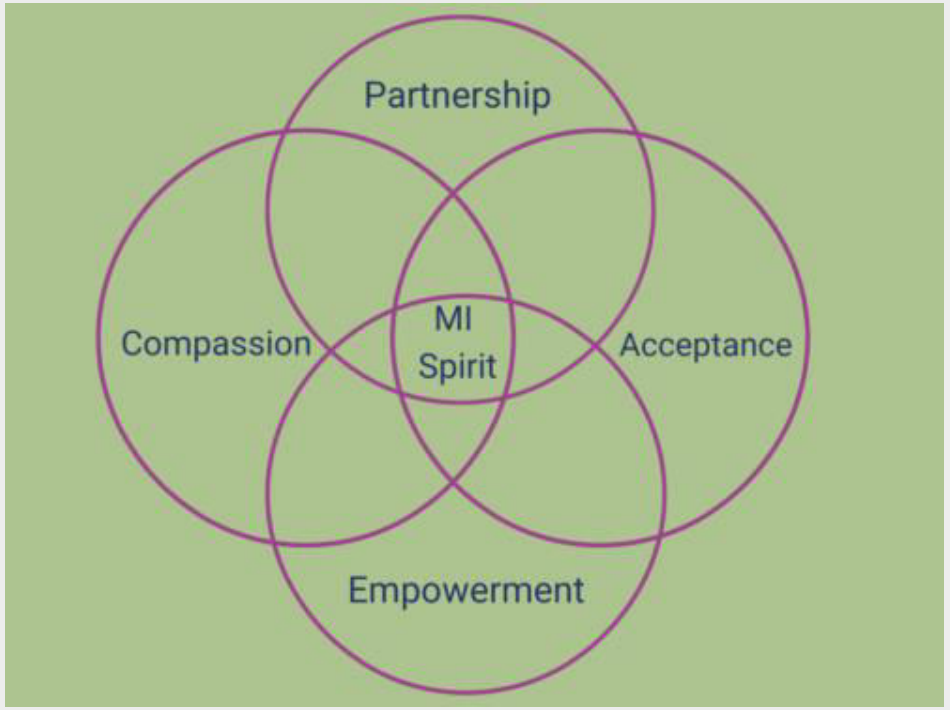
What does treatment entail?

Motivational Interviewing (MI)

From the founders: “MI is about arranging conversations so that people talk themselves into change, based on their values and interests.”

– Miller & Rollnick

- Spirit: Dancing vs. wrestling
- PACE
- Frames ambivalence as a normal reaction
- Emphasizes and encourages “change talk” (vs. “sustain talk”)

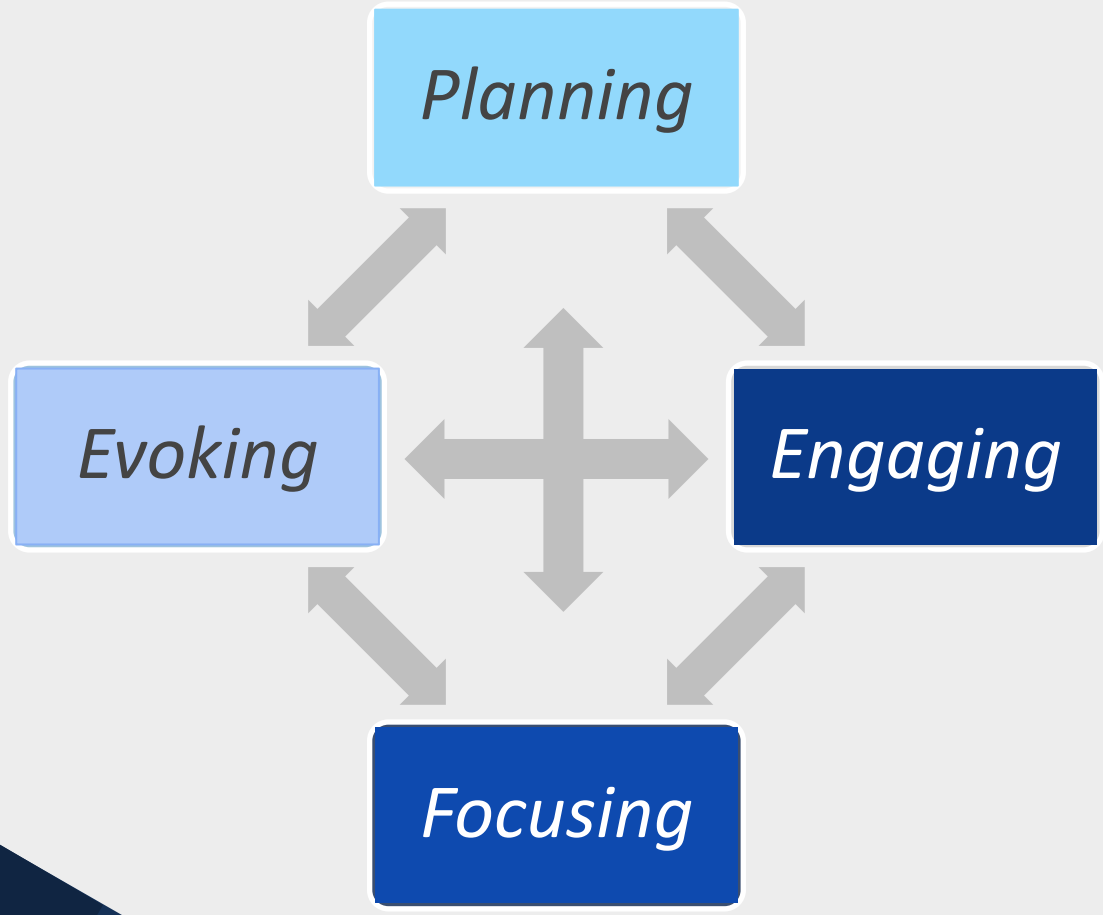


Four Fundamental Tasks

Stair-step imagery because these tasks are inherently somewhat linear…



…and also recursive



- Engaging skills (and re-engaging) continue throughout MI
- Focusing is not a one-time event; re-focusing is needed, and focus may change
- Evoking can begin very early
- “Testing the water” to see if ready for planning - may need to go back to another task

Change Talk

- DARN CAT
  - **D**esire
  - **A**bility
  - **R**easons
  - **N**eed
  - **C**ommitment
  - **A**ctivation
  - **T**aking Steps

- Generate Change Talk with:
  - **O**pen-Ended Questions
  - **A**ffirming
  - **R**eflective Listening
  - **S**ummarizing
  - Scaling questions

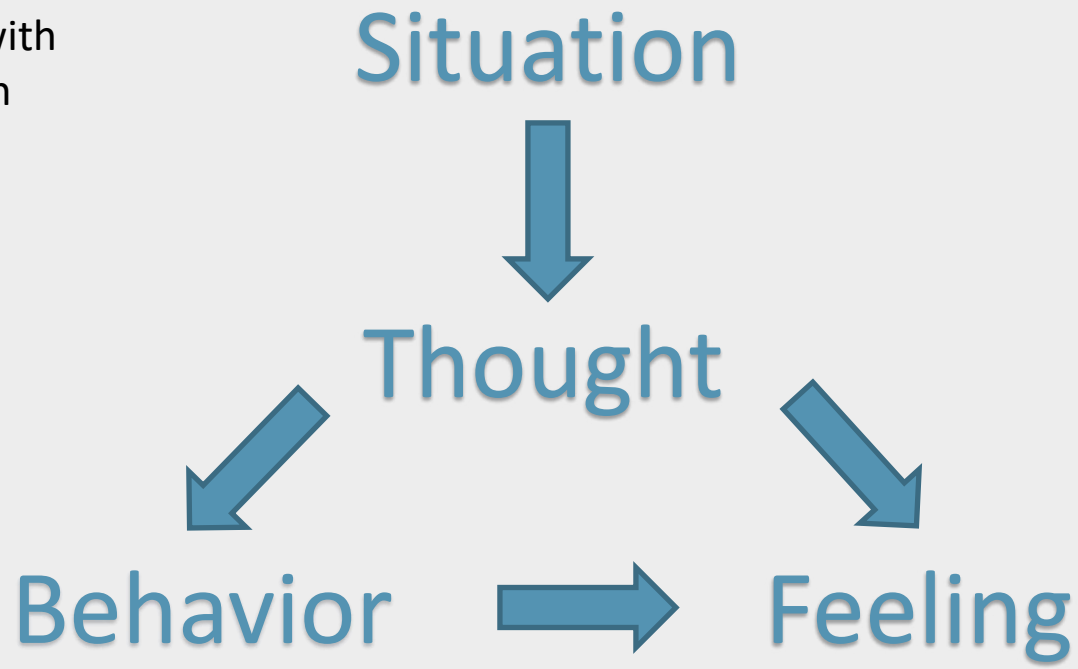


Cognitive Behavioral Therapy (CBT)

From the founder: “As applied to substance [use], the cognitive approach help individuals come to grips with the problems leading to emotional distress and to gain a broader perspective on their reliance on drugs for pleasure and/or relief from discomfort

– Aaron T. Beck

- CBT says: Substance use is inherently reinforcing, this interacts with psychological or behavioral coping deficits to produce increase in substance use
- SUD develops when this pattern is repeated over and over
- Solution: more effective coping, managing expectancies re: use
- Stages of treatment:
  - Building rapport and alliance
  - Preparing for Change
  - CBT Strategies
  - Maintaining Change/Termination



Cognitive Distortions

- Extreme or exaggerated thought patterns that lead to misery and distress
- A way to make sure we won't be surprised if things turn out badly
- Our brain's way of keeping us safe and protecting us now from the things that have hurt us in the past



Cognitive Distortions

Emotional reasoning



Assuming that because we feel a certain way what we think must be true.

I feel embarrassed so I must be an idiot

Labeling



Assigning labels to ourselves or other people

I'm a loser
I'm completely useless
They're such an idiot

should

must

Using critical words like 'should', 'must', or 'ought' can make us feel guilty, or like we have already failed

If we apply 'shoulds' to other people the result is often frustration

Personalization

"this is my fault"

Blaming yourself or taking responsibility for something that wasn't completely your fault. Conversely, blaming other people for something that was your fault.

All or nothing thinking

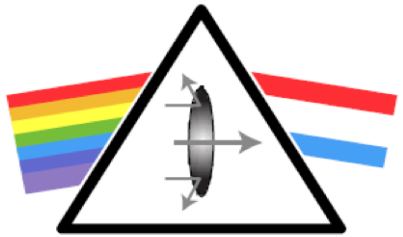


Sometimes called 'black and white thinking'

If I'm not perfect I have failed

Either I do it right or not at all

Mental filter



Only paying attention to certain types of evidence.

Noticing our failures but not seeing our successes

Over-generalizing



Seeing a pattern based upon a single event, or being overly broad in the conclusions we draw

Jumping to conclusions



There are two key types of jumping to conclusions:

- **Mind reading** (imagining we know what others are thinking)
- **Fortune telling** (predicting the future)

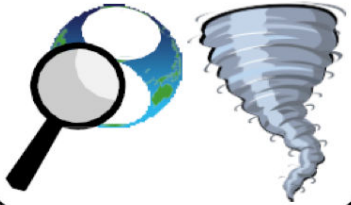
Disqualifying the positive



Discounting the good things that have happened or that you have done for some reason or another

That doesn't count

Magnification (catastrophizing) & minimization



Blowing things out of proportion (catastrophizing), or inappropriately shrinking something to make it seem less important



1 Catch It



2 Check It



3 Change It



What happened?	What were your feelings?	What was your thought?	Examine your thought. Is it helpful or harmful? Is it accurate, complete and balanced?	Replace the harmful thought with a helpful thought.
I had a fight with my partner.	*Sad, angry.*	*My partner always gets his/her way.*	*Was there a time when I got what I needed? Maybe my thought isn't complete.*	*We won't always agree. My partner gets his/her way sometimes, but I often get what I want too.*
_____	_____	_____	_____	_____
_____	_____	_____	_____	_____
_____	_____	_____	_____	_____
_____	_____	_____	_____	_____

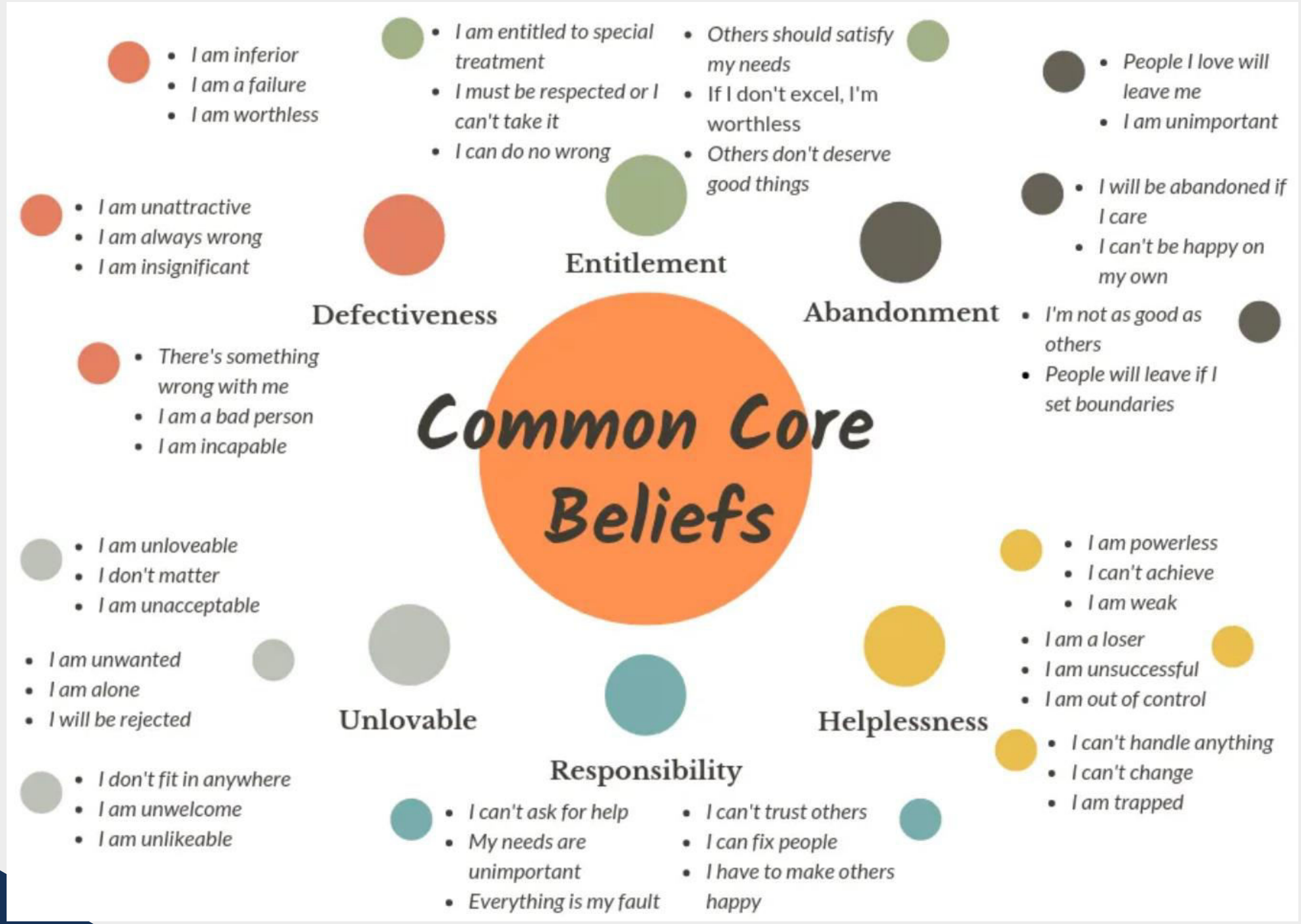
Core Beliefs

- Core beliefs: Our deeply held assumptions about ourselves, the world, and others

- Impact the way situations are interpreted (thoughts), emotional reactions (feelings), and behavior

- Trauma: Safety, Trust, Power/Control, Intimacy, Self-Esteem




Common Core Beliefs
Defectiveness
I am inferior
I am a failure
I am worthless
I am unattractive
I am always wrong
I am insignificant
There's something wrong with me
I am a bad person
I am incapable
Entitlement
I am entitled to special treatment
I must be respected or I can't take it
I can do no wrong
Others should satisfy my needs
If I don't excel, I'm worthless
Others don't deserve good things
Abandonment
People I love will leave me
I am unimportant
I will be abandoned if I care
I can't be happy on my own
I'm not as good as others
People will leave if I set boundaries
Unlovable
I am unloveable
I don't matter
I am unacceptable
I am unwanted
I am alone
I will be rejected
I don't fit in anywhere
I am unwelcome
I am unlikeable
Helplessness
I am powerless
I can't achieve
I am weak
I am a loser
I am unsuccessful
I am out of control
I can't handle anything
I can't change
I am trapped
Responsibility
I can't ask for help
My needs are unimportant
Everything is my fault
I can't trust others
I can fix people
I have to make others happy

List three pieces of evidence contrary to your negative core belief.

1. _____

2. _____

3. _____

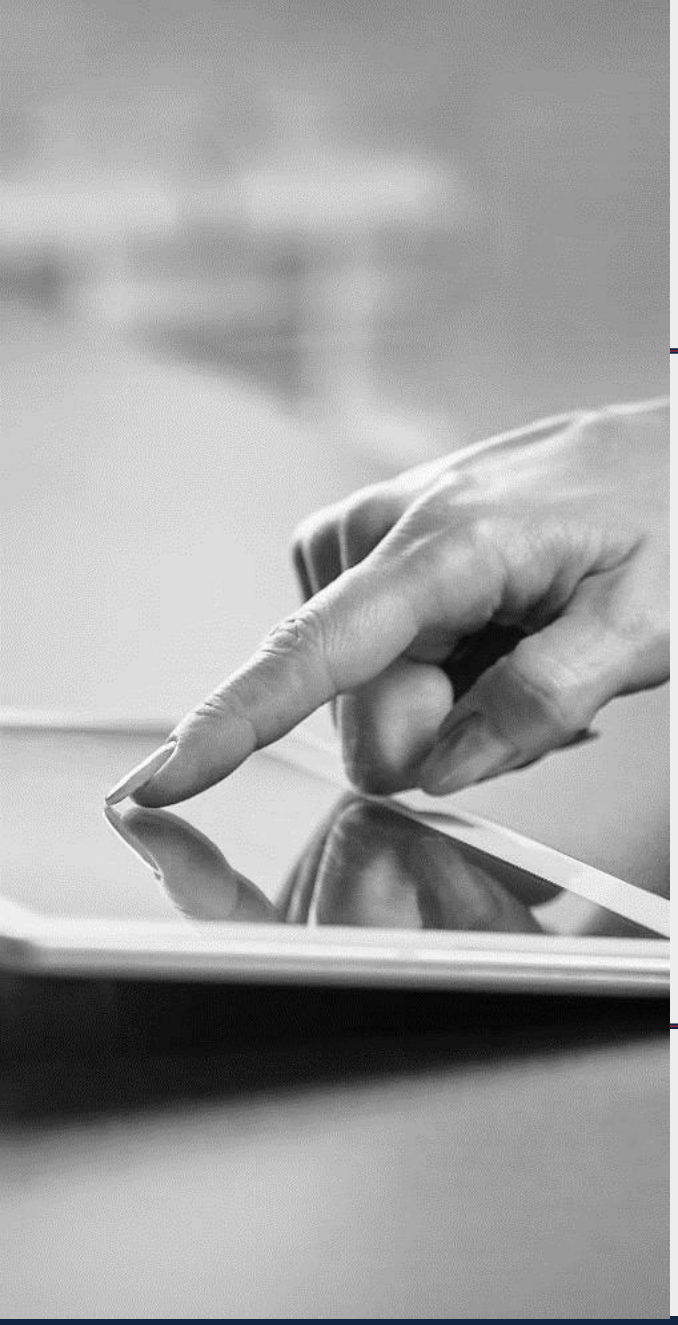
Thank you!

References

- American Psychiatric Association. (2013). *Diagnostic and statistical manual of mental disorders* (5th ed.). Washington, DC.
- Bischof, G., Iwen, J., Freyer-Adam, J., & Rumpf, H.-J. (2016). Efficacy of the Community Reinforcement and Family Training for concerned significant others of treatment-refusing individuals with alcohol dependence: A randomized controlled trial. *Drug and Alcohol Dependence*, *163*, 179–185. https://doi.org/10.1016/j.drugalcdep.2016.04.015
- Coughlin, L. N., Zhang, L., Frost, M. C., Khazanov, G., McKay, J. R., DePhilippis, D., & Lin, L. A. (2024). Contingency management for substance use disorders in the U.S. Veterans Health Administration: 2018-2022. *Journal of substance use and addiction treatment*, *163*, 209400. https://doi.org/10.1016/j.josat.2024.209400
- DeMarce, J. M., Gnys, M., Raffa, S. D., & Karlin, B. E. (2014). Cognitive Behavioral Therapy for Substance Use Disorders Among Veterans: Therapist Manual. Washington, DC: U.S. Department of Veterans Affairs.
- Dimeff, L. A., & Linehan, M. M. (2008). Dialectical behavior therapy for substance abusers. *Addiction science & clinical practice*, *4*(2), 39–47.
- El-Lawaty, K. S., Shaheen, S. H., ELGueneidy, M. M., & Alhelaly, A. A. A. (2024). Effect of Motivational Enhancement Therapy on Probability of Relapse among Clients with Substance Use Disorders. *Alexandria Scientific Nursing Journal*, *26*(4), 216–227. https://doi.org/10.21608/asalexu.2024.392479
- Fals-Stewart, W., O'Farrell, T. J., Birchler, G. R., & Gorman, C. (2006). *Behavioral couples therapy for drug abuse and alcoholism: A 12-session manual* (2nd ed.). Buffalo, New York: Addiction and Family Research Group.
- Kelly, J. F., Kaminer, Y., Kahler, C. W., Hoeppner, B., Yeterian, J., Cristello, J. V., & Timko, C. (2017). A Pilot Randomized Clinical Trial Testing Integrated Twelve-Step Facilitation (iTSF) Treatment for Adolescent Substance Use Disorder. *Addiction (Abingdon, England)*, *112*(12), 2155–2166. https://doi.org/10.1111/add.13920
- Lenz, A. S., Rosenbaum, L., & Sheperis, D. (2016). Meta-analysis of randomized controlled trials of motivational enhancement therapy for reducing substance use. *Journal of Addictions & Offender Counseling, 37*(2), 66–86. https://doi.org/10.1002/jaoc.12017
- Magill, M., Ray, L., Kiluk, B., Hoadley, A., Bernstein, M., Tonigan, J. S., & Carroll, K. (2019). A meta-analysis of cognitive-behavioral therapy for alcohol or other drug use disorders: Treatment efficacy by contrast condition. *Journal of Consulting and Clinical Psychology, 87*(12), 1093-1105. https://doi.org/10.1037/ccp0000447
- Management of Substance Use Disorders Workgroup (2015). VA/DoD Clinical Practice Guideline for the Management of Substance Use Disorders. Retrieved from: https://www.healthquality.va.gov/guidelines/MH/sud/VADoDSUDCPGRevised22216.pdf
- Meyers, R.J., Miller, W.R., Hill, D.E., & Tonigan, J.S. (1998). Community reinforcement and family training (CRAFT: Engaging unmotivated drug users in treatment. *Journal of Substance Abuse, 10*(3), 291-308.

References

- Merikangas, K.R., & McClair, V.L. (2012). Epidemiology of substance use disorders. *Human Genetics, 131*(6), 779-789.
- Miller, W. R., & Rollnick, S. (2023). Motivational interviewing: Helping people change and grow (4th ed.). Guilford Press.
- Project MATCH Research Group. Matching alcoholism treatments to client heterogeneity: Project MATCH three-year drinking outcomes. (1998). *Alcoholism, clinical and experimental research*, *22*(6), 1300–1311. https://doi.org/10.1111/j.1530-0277.1998.tb03912.x
- Riper, H., Andersson, G., Hunter, S. B., de Wit, J., Berking, M., & Cuijpers, P. (2014). Treatment of comorbid alcohol use disorders and depression with cognitive-behavioural therapy and motivational interviewing: a meta-analysis. *Addiction (Abingdon, England)*, *109*(3), 394–406. https://doi.org/10.1111/add.12441
- Roozen, H. G., de Waart, R., & van der Kroft, P. (2010). Community reinforcement and family training: an effective option to engage treatment-resistant substance-abusing individuals in treatment. *Addiction (Abingdon, England)*, *105*(10), 1729–1738. https://doi.org/10.1111/j.1360-0443.2010.03016.x
- Santa Ana, E. J., LaRowe, S. D., Gebregziabher, M., Morgan-Lopez, A. A., Lamb, K., Beavis, K. A., Bishu, K., & Martino, S. (2021). Randomized controlled trial of group motivational interviewing for veterans with substance use disorders. *Drug and Alcohol Dependence*, *223*, 108716–108716. https://doi.org/10.1016/j.drugalcdep.2021.108716
- Sayegh, C. S., Huey, S. J., Zara, E. J., & Jhaveri, K. (2017). Follow-Up Treatment Effects of Contingency Management and Motivational Interviewing on Substance Use: A Meta-Analysis. *Psychology of Addictive Behaviors*, *31*(4), 403–414. https://doi.org/10.1037/adb0000277
- Stavrinaki, M., Kelly, M., & Karekla, M. (2023). Acceptance and commitment therapy for substance use. In M. P. Twohig, M. E. Levin, & J. M. Petersen (Eds.), *The Oxford handbook of acceptance and commitment therapy* (pp. 483–500). Oxford University Press.
- Substance Abuse and Mental Health Services Administration. (2025). Key substance use and mental health indicators in the United States: Results from the 2024 National Survey on Drug Use and Health (HHS Publication No. PEP25-07-007, NSDUH Series H-60). Center for Behavioral Health Statistics and Quality, Substance Abuse and Mental Health Services Administration. https://www.samhsa.gov/data/data-we-collect/nsduh-national-surveydrug-use-and-health/national-releases



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ASAM REVIEW COURSE 2026

Psychosocial Interventions: Mutual Help and Social Support

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Financial Disclosure

Smita Das, MD, PhD, MPH

- No relevant disclosures

Theoretical Frameworks

Mechanisms of Action in Social Recovery Support

Main Effect Vs. Buffering Models

Main Effect Model

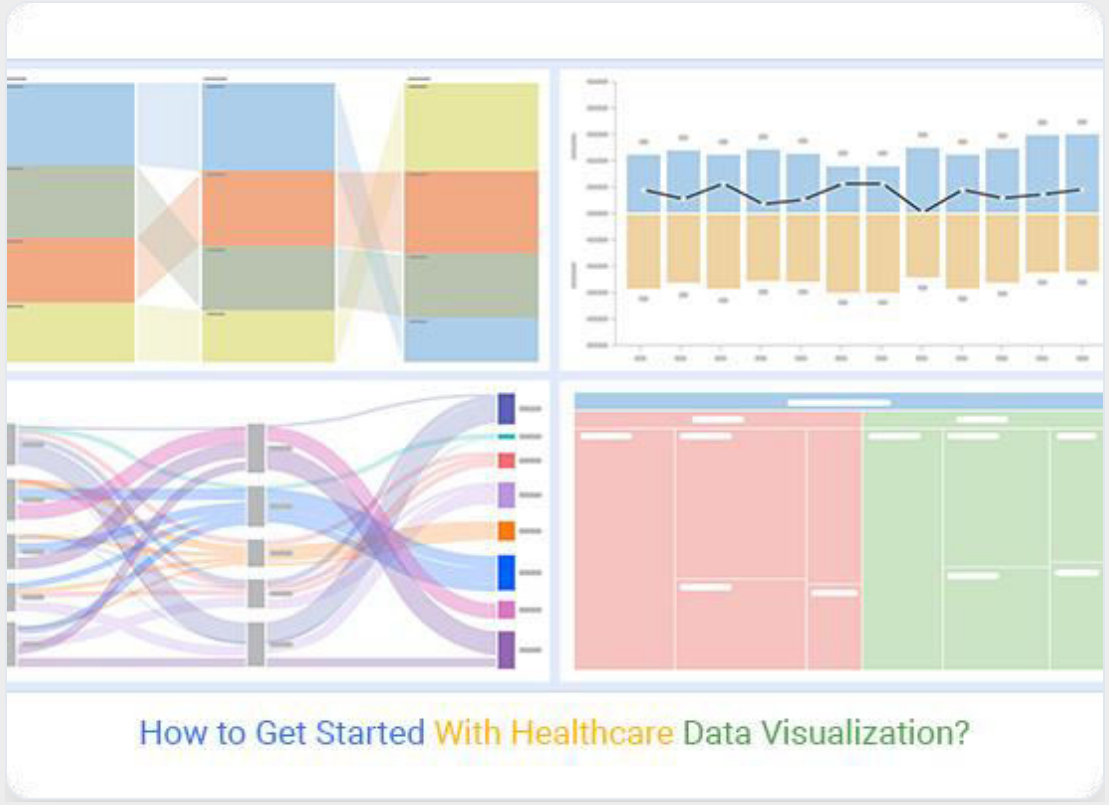
Proposes that social integration is **universally beneficial**. Participation in mutual aid provides a sense of predictability and stable social identity, regardless of stress level.(1)

Buffering Hypothesis

Social support acts as a **protective shield** specifically during stressful events. Peers "buffer" the physiological and psychological impact of high-craving states.(1)

1. Cohen S, Wills TA. Psychol Bull. 1985;98(2):310-357. PMID: 3901065

Self-efficacy & Social Learning



The Cognitive Bridge

The primary mechanism in mutual help is the restoration of **Self-Efficacy**—the patient's belief in their capability to execute a sober lifestyle.(2)

- **Vicarious Reinforcement:** Modeling success via peer storytelling.
- **Social Persuasion:** Affirmation from established members.
- **Recurrence Prevention:** Shared coping strategies for withdrawal stress, triggers, slips

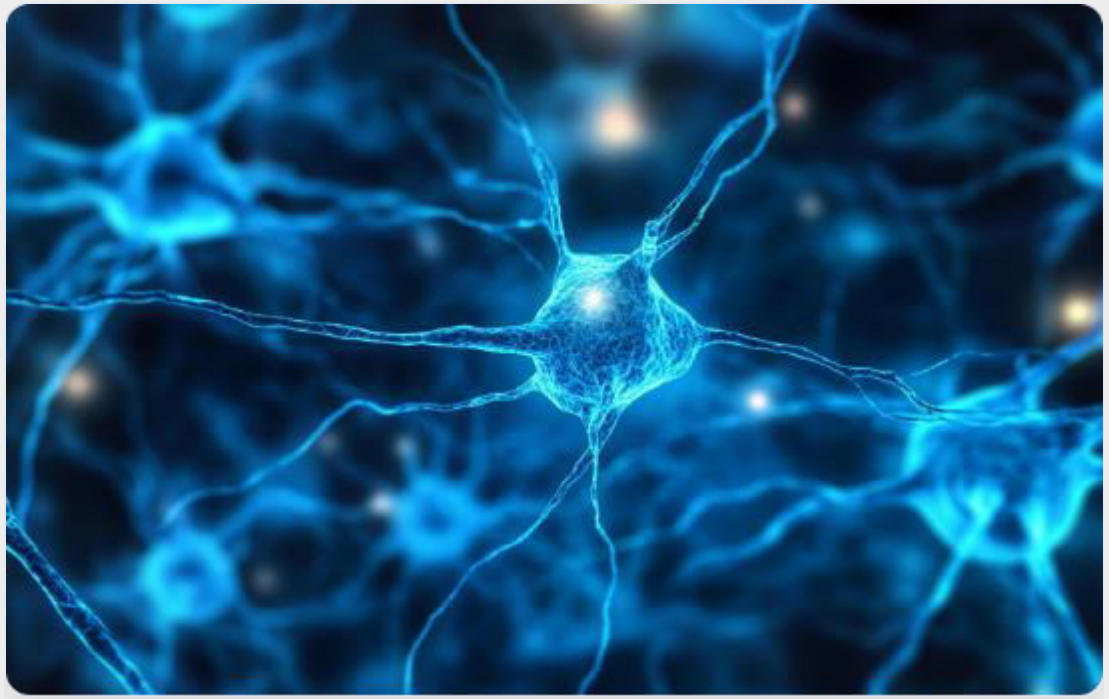
2. Bandura A. Psychol Rev. 1977;84(2):191-215. PMID: 847061

The Simor Identity Model

Identity Transition

Recovery is conceptualized as a socially negotiated transition from an identity centered on substance use to a **pro-social recovery identity**.(3)

- **Social Capital:** Access to non-financial group resources.
- **Social Influence:** Reconfiguring networks toward sober peers.
- **Stigma Neutralization:** Validation within a "spoiled identity" peer group.



3. Best D, et al. Addict Res Theory. 2016;24(2):111-123.

Clinical Evidence & Efficacy

Manualized TSF vs. Alternative Approaches

Cochrane Review: AA/TSF Efficacy



TSF interventions typically produce higher continuous abstinence rates than established treatments at 12, 24, and 36 months.(4)

4. Kelly JF, et al. Cochrane Database Syst Rev. 2020. PMID: 32159228

Non-12-Step Mutual Aid Groups

SMART Recovery

CBT-based self-empowerment. Comparable outcomes to 12-step for AUD.6

PMID: 28165272

LifeRing Secular

Focus on sober identity and personal recovery planning.7

Women for Sobriety

Gender-responsive support focusing on emotional regulation and worth.7

6. Beck AK, et al. 2017. 7. Zemore SE, et al. J Subst Abuse Treat. 2018. PMID: 29606223

Systems of Clinical Care

Integrating Peer and Digital Recovery Supports

Peer Recovery Specialists

Retention Impact

Integrated Peer Recovery Support Specialists (PSS) improve outpatient treatment retention by **2.3x**

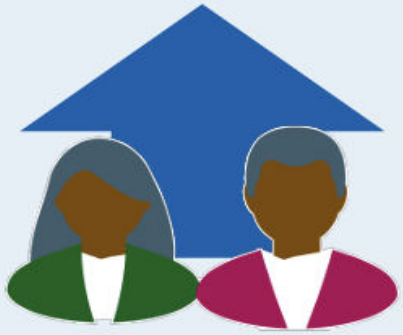
They mitigate ER utilization and inpatient readmissions by bridging the "empathy gap" between clinician and patient.



8. Eddie D, et al. Front Psychol. 2019;10:1268.

Does Peer Support Make A Difference?

Emerging research shows that peer support is effective for supporting recovery from behavioral health conditions. Benefits of peer support may include:



Increased self-esteem and confidence
(Davidson, et al., 1999; Salzer, 2002)



Increased sense of control and ability to bring about changes in their lives
(Davidson, et al., 2012)



Raised empowerment scores
(Davidson, et al., 1999; Dumont & Jones, 2002; Ochoka, Nelson, Janzen, & Trainor, 2006; Resnick & Rosenheck, 2008)



Increased sense that treatment is responsive and inclusive of needs
(Davidson, et al., 2012)

Image from SAMHSA https://www.samhsa.gov/sites/default/files/programs_campaigns/brss_tacs/value-of-peers-2017.pdf

Does Peer Support Make A Difference? cont.

Emerging research shows that peer support is effective for supporting recovery from behavioral health conditions. Benefits of peer support may include:



Increased sense of hope and inspiration
(Davidson, et al., 2006; Ratzlaff, McDiarmid, Marty, & Rapp, 2006)



Increased empathy and acceptance (camaraderie)
(Coatswortha Puspokey, Forchuk, & Warda Griffin, 2006; Davidson, et al., 1999)



Increased engagement in selfa care and wellness
(Davidson, et al., 2012)



Increased social support and social functioning
(Kurtz, 1990; Nelson, Ochocka, Janzen, & Trainor, 2006; Ochoka et al., 2006; Trainor, Shepherd, Boydell, Leff, & Crawford, 1997; Yanos, Primavera, & Knight, 2001)

Image from SAMHSA https://www.samhsa.gov/sites/default/files/programs_campaigns/brss_tacs/value-of-peers-2017.pdf

Does Peer Support Make A Difference? cont.

Emerging research shows that peer support is effective for supporting recovery from behavioral health conditions. Benefits of peer support may include:



Decreased psychotic symptoms
(Davidson, et al., 2012)



Reduced hospital admission rates and longer community tenure
(Chinman, Weingarten, Stayner, & Davidson, 2001; Davidson, et al., 2012; Forchuk, Martin, Chan, & Jenson, 2005; Min, Whitecraft, Rothbard, Salzer, 2007)



Decreased substance use and depression
(Davidson, et al., 2012)

Image from SAMHSA https://www.samhsa.gov/sites/default/files/programs_campaigns/brss_tacs/value-of-peers-2017.pdf

Family Support & Care Partners

The "Care Partner" Paradigm

Moving from "Caregiver" to **"Care Partner"** acknowledges relational reciprocity. Family involvement reduces patient relapse risk by 25%.9

- **Al-Anon:** Significant distress reduction (88%).
- **SMART F&F:** Focuses on CBT-based boundaries.



Adelman RD, Tmanova LL, Delgado D, Dion S, Lachs MS. Caregiver burden: a clinical review. JAMA. 2014;311(10):1052-1060. PMID: 24618967

Digital Recovery (D-rss)

Accessibility & Adherence

Digital Recovery Support Services (D-RSS) leverage telehealth and mobile platforms to provide 24/7 accountability.[10]

- High retention in rural/stigmatized groups.
- App engagement predicts sustained abstinence.



10. Ashford RD, et al. Hum Behav Emerg Technol. 2020;2(1):18-32. DOI: 10.1002/hbe5.143

Barriers

- “Medication Stigma” within some 12-step groups
- Concern about spirituality
- Patients feeling like groups are “other”
- Logistics

History of Mutual Help

1935

AA Foundations: Community-based mutual aid.

1990s

Manualization: Project MATCH formalizes TSF.

2013

Professionalization: PSS becomes billable.

2026+

D-RSS Hybrid: AI-integrated peer networks.

Discussion & Bibliography

- Kelly JF, et al. *Cochrane Database Syst Rev.* 2020;3(3). PMID: 32159228.
- Cohen S, Wills TA. *Psychol Bull*. 1985;98(2). PMID: 3901065.
- Best D, et al. *Addict Res Theory*. 2016;24(2). doi:10.3109/16066359.2015.1075980.
- Bandura A. *Psychol Rev*. 1977;84(2). PMID: 847061.
- Ashford RD, et al. *Hum Behav Emerg Technol*. 2020;2(1):18-32. DOI: 10.1002/hbe5.143
- Zemore SE, et al. *J Subst Abuse Treat*. 2018;88. PMID: 29606223.
- Beck AK, et al. *Psychol Addict Behav*. 2017. PMID: 28165272.
- Adelman RD, et al. JAMA. 2014;311(10):1052-1060. PMID: 24618967
- Eddie D, et al. *Front Psychol*. 2019;10. PMID: 31275210.
- NASEM. *Cannabis Policy Impacts*. NAP; 2024.

Image Sources



https://static.vecteezy.com/system/resources/previews/057/274/608/large_2x/abstract-neuron-network-visualization-with-glowing-connections-in-electric-blue-hues-against-a-dark-background-representing-the-human-brain-free-photo.jpg

Source: www.vecteezy.com



https://chartexpo.com/blog/wp-content/uploads/2022/06/healthcare-data-visualization.jpg

Source: chartexpo.com



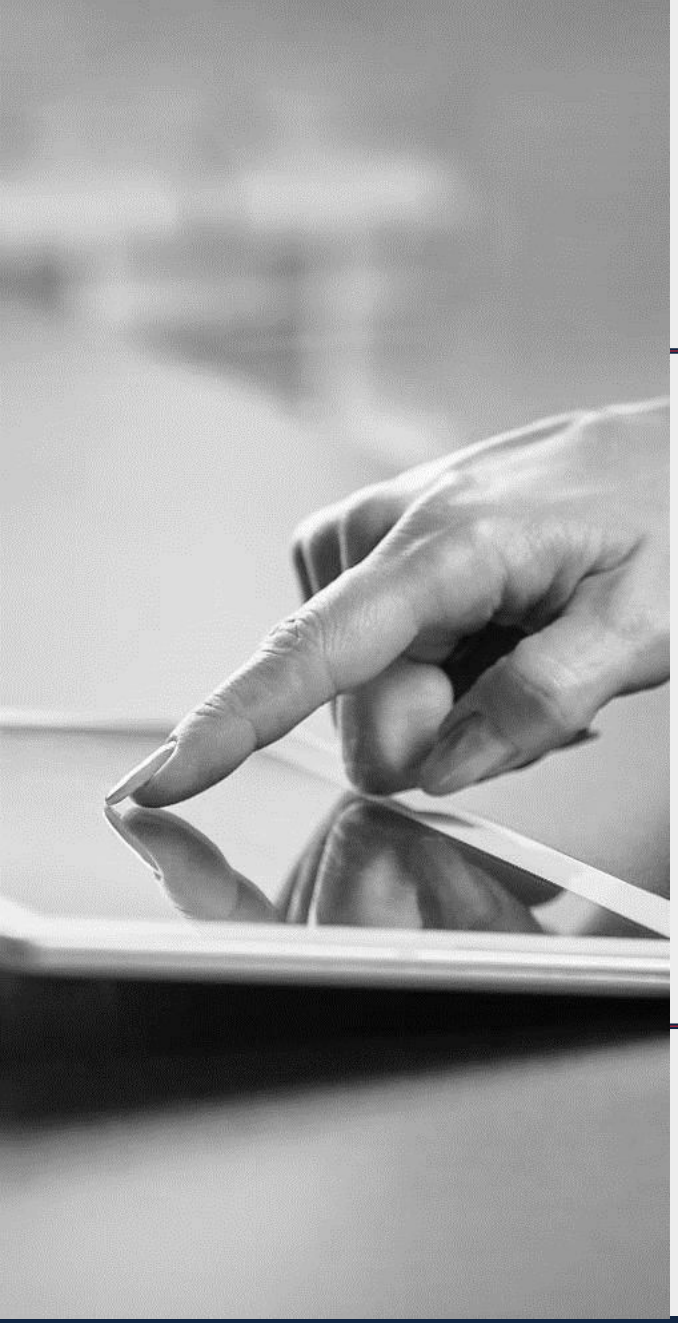
https://www.helpguide.org/wp-content/uploads/2023/02/Support-Groups.jpeg

Source: www.helpguide.org



https://www.behavioralhealthtech.com/insights/new-roi-research-on-evidence-based-answer-to-mental-health-provider-shortages-via-digital-peer-support

Source: Behavioral Health Tech



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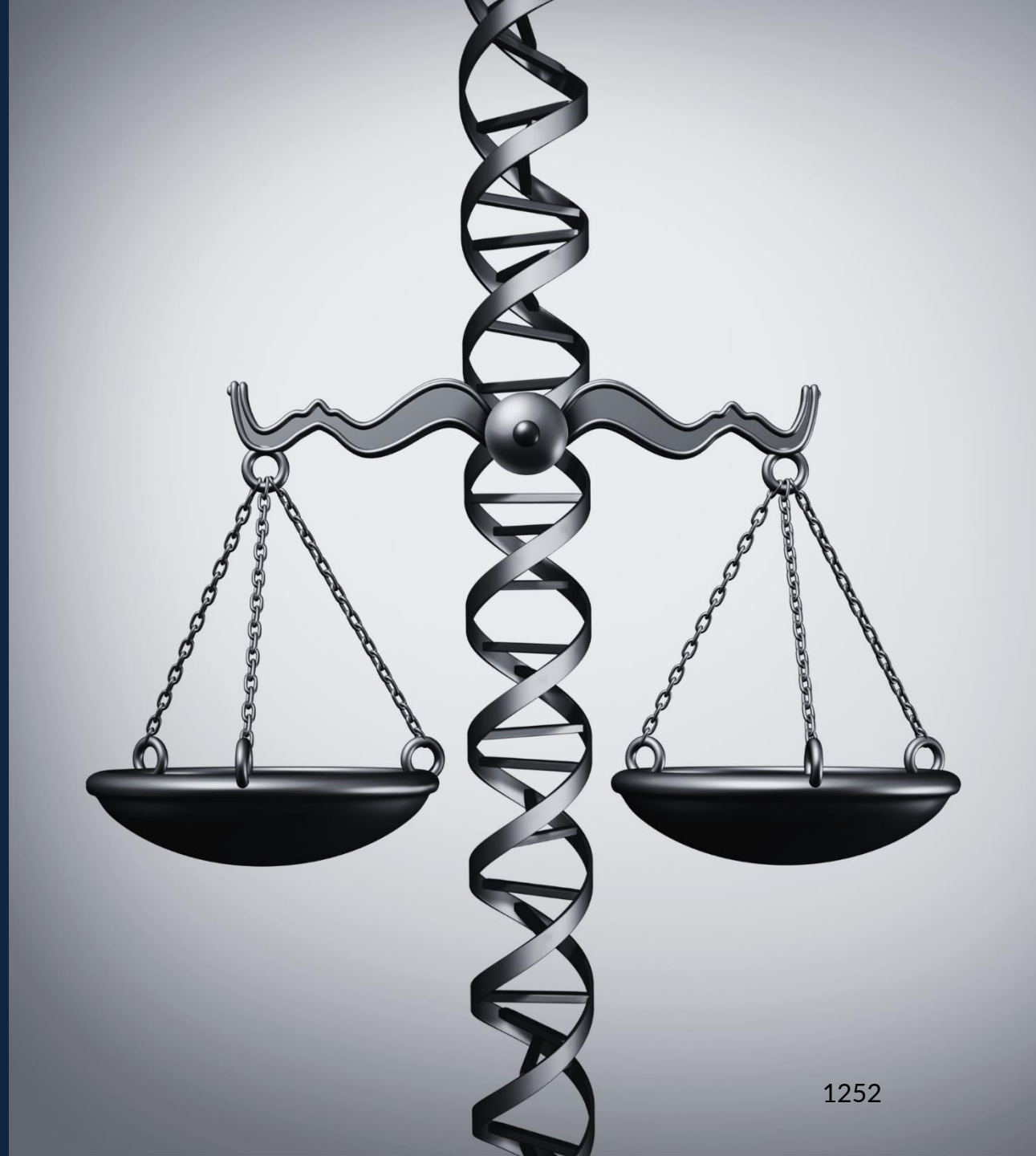
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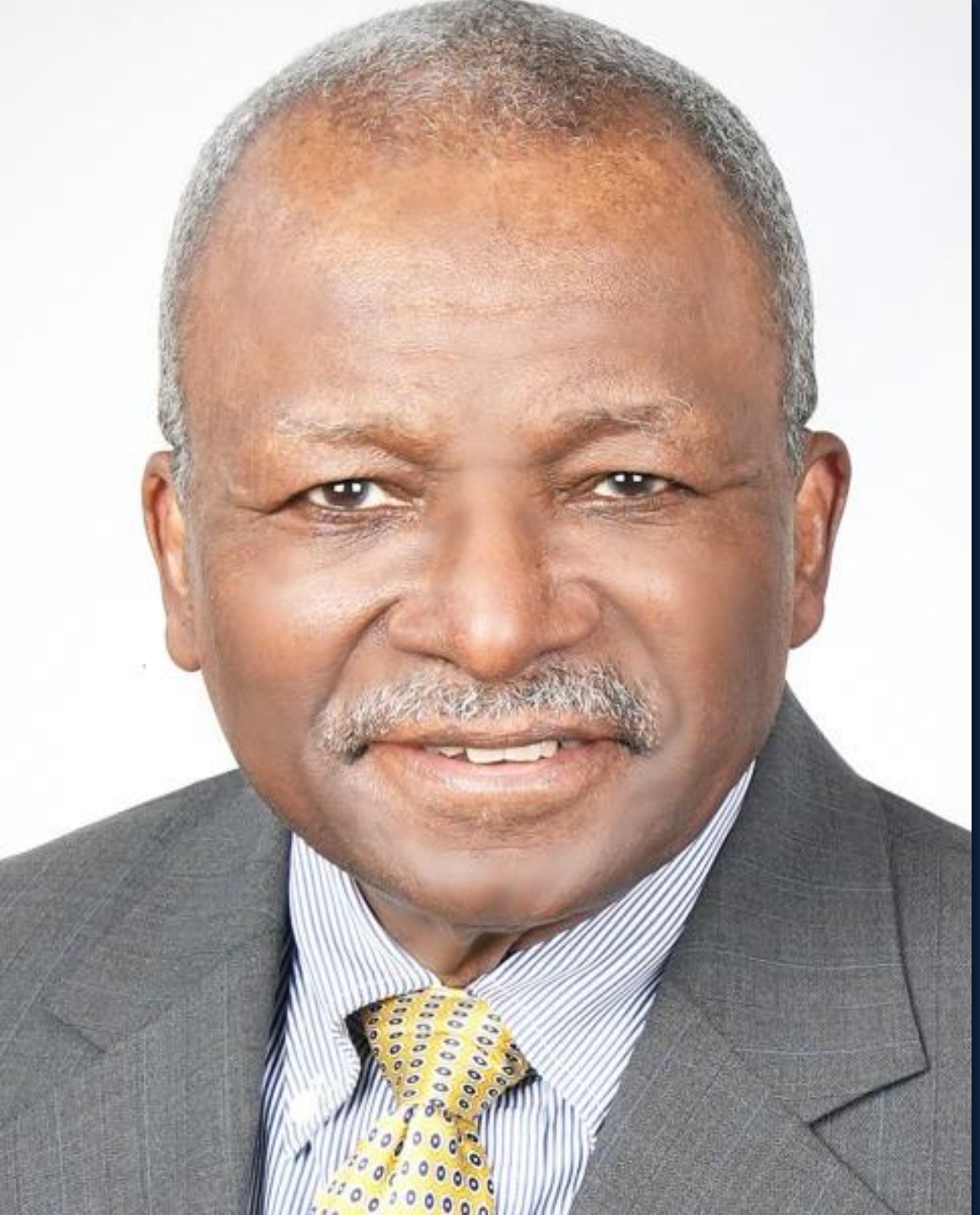
ASAM REVIEW COURSE 2026

Ethics and the Law: Principles and Implications

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Financial Disclosure

David Kan, MD, DFASAM

- No relevant disclosures

LEARNING OBJECTIVE

Describe the ethical and legal considerations that impact treatment of patients with addiction.



Presentation Outline

Ethical Principles

Informed Consent

Privacy and Confidentiality

Ethical Prescribing

Special Topics

Ethical Principles

- Autonomy: self-determination, self-governance, moral independence
  - Example: Patient with alcohol use disorder, experiencing a recurrent upper GI bleed refusing voluntary inpatient addiction psychiatry admission



Ethical Principles

- Beneficence: actions should promote patient well-being
  - Example: A patient with a severe heroin use disorder sees PCP who offers him buprenorphine, referral to methadone treatment or inpatient withdrawal management and community recovery resources



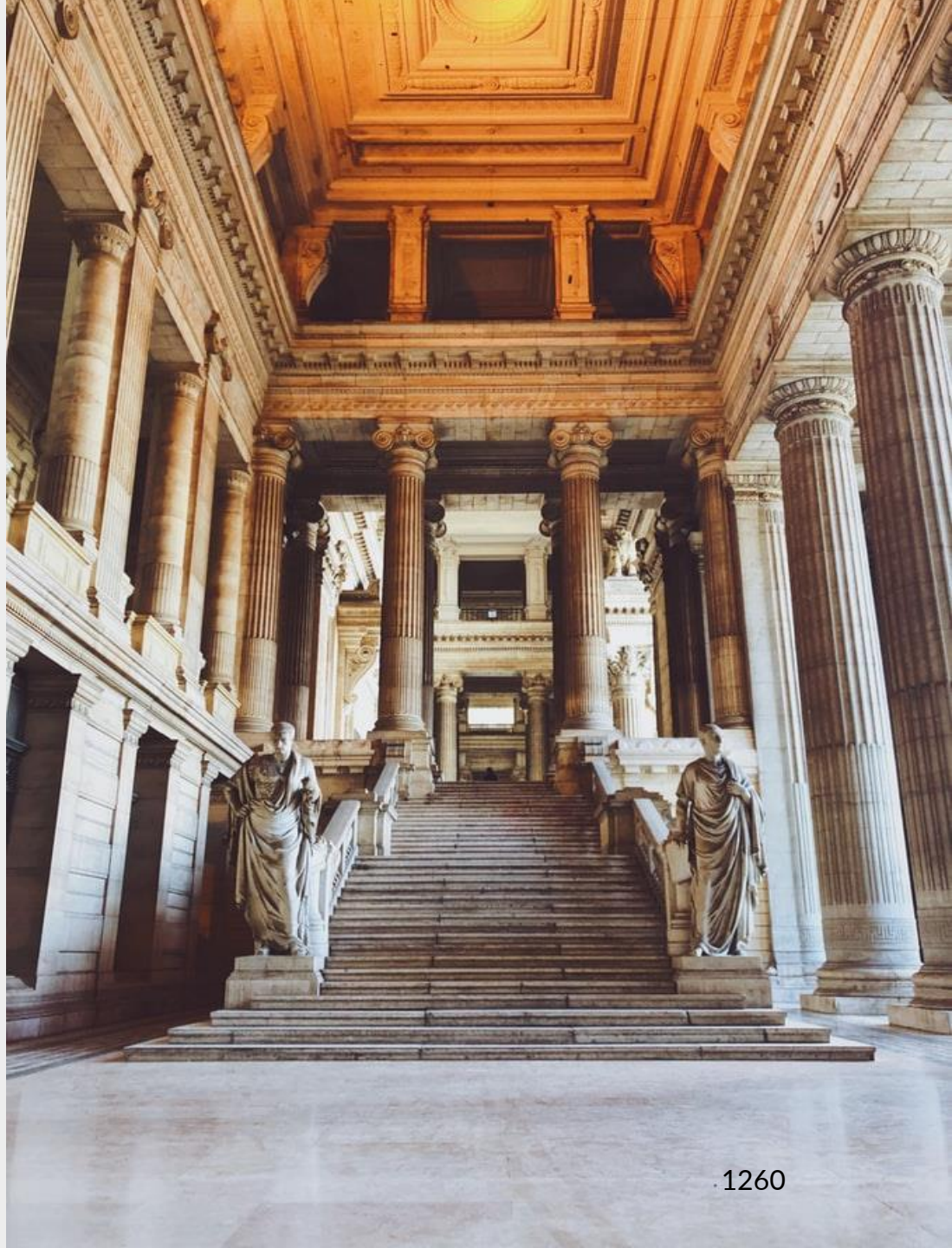
Ethical Principles

- Non-maleficence: do no harm (or as little as necessary)
  - Examples of harm: (1) Providing benzodiazepines for patients on high dose opioids or (2) prescribing buprenorphine without an exam for cash



Ethical Principles

- Justice:
  - Fairness in decisions
  - Equal distribution of resources and new treatments
  - Medical practitioners uphold laws
  - Examples: (1) Advocating for a patient rejected from inpatient substance use disorder treatment when the insurance provider deems it “not clinically indicated” or (2) Accepting cash only for the use of buprenorphine or naltrexone, limiting access to treatment .



Ethical Principles

- Respect for people: treating people in a manner that acknowledges their intrinsic dignity
- Truth-telling: honesty, sharing information



Complex Ethical Scenario

- 40-year-old female anesthesiologist
- Taking opioid medications meant for patients, replacing with saline
- Has used oral opioids on the job but denies problems
- Asks you to notify nobody



Which of the following is NOT true regarding informed consent?

A. It must be given voluntarily.
B. An individual must possess decisional capacity.
C. Patients with psychosis cannot give informed consent.
D. It involves the disclosure of information between the clinician and the patient.

Informed Consent

- Voluntariness
- Information disclosure
- Decisional capacity



Voluntariness

- Freely given
- Coercion: punishment or excessive rewards
- Persuasion
- Influence
- Context-dependent
- Risk of infringing
  - SUDs treatment in custody
  - Drug court
  - Inpatient treatment



Information Disclosure

- Nature of illness and proposed treatment
- Risks/benefits
- Alternatives
- Consequences of foregoing treatment
- “Reasonable person” standard
- High standard of disclosure
  - Dependency producing medications (opioids)
  - Medications with known adverse events (disulfiram)
  - Medication combinations that should be avoided with MAOIs (methadone, bupropion, tramadol, etc.)



Decisional Capacity

- Communicate a choice
- Understand the relevant information
- Appreciate the situation and its consequences
- Reason about treatment options
- “Sliding scale” approach
- Potentially impaired
  - Intoxication
  - Substance-related neurocognitive problems
  - Dual diagnosis



For Those Lacking Capacity

- Durable power of attorney for healthcare decisions (DPOAHC): form identifying surrogate decision-maker if one becomes incapacitated
- Advanced directive/living will: written statement expressing specific wishes, does not designate healthcare POA
- Guardian/conservator of the person: person appointed to make care decisions when patient is incapacitated



Pearls

- There are various ethical principles underlying medicine and addictions treatment that may come into conflict
- The process of informed consent requires voluntariness, information disclosure, and decisional capacity
- Certain treatment settings have the potential to infringe on voluntariness

Privacy and Confidentiality

- Privacy: patient's right to protection of sensitive information
- Confidentiality: clinician's obligation to protect sensitive information
- 42 CFR Part 2: Confidentiality of Alcohol and Drug Abuse Patient Records
- HIPAA



42 CFR Part 2 – Covered Programs

- Individual, entity, or identified unit within a general medical facility that provides SUDs diagnosis, treatment, or referral for treatment

- Medical personnel/staff in a general medical facility whose primary function is provision of SUDs diagnosis, treatment, or referral for treatment and who are identified as such providers.



42 CFR Part 2 – Federal Assistance

- Conducted in a federal department or agency
- Supported by federal funds
- Carried out under a license or registration from federal government
  - Medicare providers
  - Authorization to conduct maintenance treatment or withdrawal management
  - Registration under Controlled Substances Act to dispense a substance used in treatment of SUDs





Disclosure

- Part 2 programs may only release patient information with the patient's consent
- Exceptions include:
  - Medical emergency
  - Error in manufacture, labeling, or sale of a product under FDA jurisdiction
  - Research
  - Valid court order with subpoena
  - Crimes committed on part 2 program premises
  - Reporting suspected child abuse or neglect
- Failure can result in criminal penalty (a fine)

HIPAA (‘96), Privacy Rule (‘00)

- All PHI protected
- Exceptions related to medical operations and public interest/benefit

Alignment 42 CFR Part 2/HIPAA/HITECH 2024 Amendments

- Single Consent for Part 2
  - One consent is enduring
- Re-disclosure
  - Permitted within HIPAA Privacy Rule
- SUD Counseling Notes
  - Additional protections – maintained separately from Part 2 record
- Accounting of Disclosure/Restriction
  - Must track disclosures for 3 years
  - Can limit disclosure
- Prohibition on Use and Disclosure without consent or court order
  - Legal proceedings
  - Law enforcement
  - Warrant
- Penalties and breach reporting
  - Civil penalties in addition to criminal
  - Breach reporting required within 60 days
- HIPAA Privacy Practices
  - Now aligned
- More changes in reference

https://www.hhs.gov/hipaa/for-professionals/special-topics/hipaa-part-2/index.html

Controlled Substance Act (1970)

- Classification and regulation
- Manufacturing
- Distribution
- Exportation and sale

CSA Regulation/Classification

- DEA licensure requirement
- Schedule I: illegal, no medical use (MDMA, methaqualone, gamma-hydroxybutyric acid (GHB), peyote)
- Schedules II-V: addictive potential
  - II: cocaine, methamphetamine, methadone, phencyclidine, oxycodone, fentanyl
  - III: ketamine, testosterone, buprenorphine, sodium oxybate
  - IV: benzos, zolpidem, tramadol,
  - V: diphenoxylate, pregabalin, *

** As of April 2023, gabapentin is not controlled under the CSA, but a number of states have made it a Schedule V drug. The DEA has been requested to reschedule gabapentin schedule V.*



Ethical Prescribing

- Patient risks
  - SUDs
  - Diversion
  - Exacerbation of comorbid medical or psychiatric illness
- Practices to address
  - Urine drug testing
  - Medication contract
  - PDMPs

Universal Precautions

1. Make a diagnosis with appropriate differential, including a physical exam
2. Psychological assessment (risk of substance use disorders)
3. Obtain informed consent
4. Treatment agreement
5. Pre- and post-intervention assessment of pain level and function
6. Appropriate trial of opioid therapy +/- adjunctive medication
7. Reassess pain score and level of functioning
8. Regularly assess 4 A's: analgesia, activity, adverse effects, aberrant behavior
9. Periodically review diagnosis and comorbid conditions
10. Documentation

Which of the following is NOT an example of misprescribing?

A. Providing a patient opioids at a dangerously high dose.
B. Providing a prescription for three months of opioids following an uncomplicated outpatient surgical procedure.
C. Providing a friend a prescription for Ativan for no medical purpose.
D. Providing a patient a prescription for Ativan for short-term treatment of anxiety after checking with the PDMP, without knowing she had multiple prescriptions from different providers.

Legal Consequences

- Misprescribe: inappropriate rationale, dose, quantity, lack of physical examination
- CSA: “unlawful for any person to knowingly or intentionally… manufacture, distribute, or dispense, or possess with intent… a controlled substance”
- Knowingly or Intentionally
- Without legitimate medical purpose
- Outside the usual course of professional practice

  - State medical board sanctions
  - Civil: malpractice
  - Criminal: CSA, murder



Recent Case

- Oscar Lightner, MD.
- From March 2016 through August 2018
- Unlawfully prescribing over 600,000 pills of hydrocodone and prescriptions of carisoprodol and alprazolam
- People paid cash $250 to $500 for each visit to the clinic deemed by the DEA as a pill mill.
- Physician convicted by a jury



Prescription Drug Monitoring Programs

- 50 states, D.C., Guam
- Mitigate abuse/diversion
- Models
  - Non-mandated use
  - Proactive reporting
  - Mandated use
- Criticisms
  - Inadequate information collection
  - Ineffective utilization in clinical settings
  - Limited interstate sharing
- Mixed data on effectiveness, differs by state

Pearls

- Confidentiality of substance abuse treatment is governed by 42 CFR Part 2, and HIPAA's Privacy Rule
- The Controlled Substances Act of 1970 established the DEA regulation and classification of addictive drugs and criminal penalties for distribution of drugs
- There are various models of ethical prescribing that generally involve informed consent, regular assessment and dose planning, and appropriate clinical documentation
- PDMPs, though potentially helpful, differ in their implementation and effectiveness

Addiction & the Law: Special Topics

- Adolescents
- Pregnant patients
- Justice-involved populations
- Civil commitment & substance use
- Americans with Disabilities Act (ADA)
- Impaired Clinician

Adolescents, Addiction, & the Law

A 15-year-old patient comes to you requesting treatment for alcohol use disorder. Which of the following scenarios most likely requires guardian informed consent before initiating treatment?

A. She is a mature minor
B. She is married
C. She is serving in the military
D. She has run away from home
E. She is experiencing severe withdrawal



Legal Standards: Minor Informed Consent

- Age of majority
- Minor's ability to consent
- General medical care
- Mental health
- Substance use disorders
- Emancipation
- Legal
- Marriage, military
- Other forms
- Mature minors
- Have children
- High school graduate



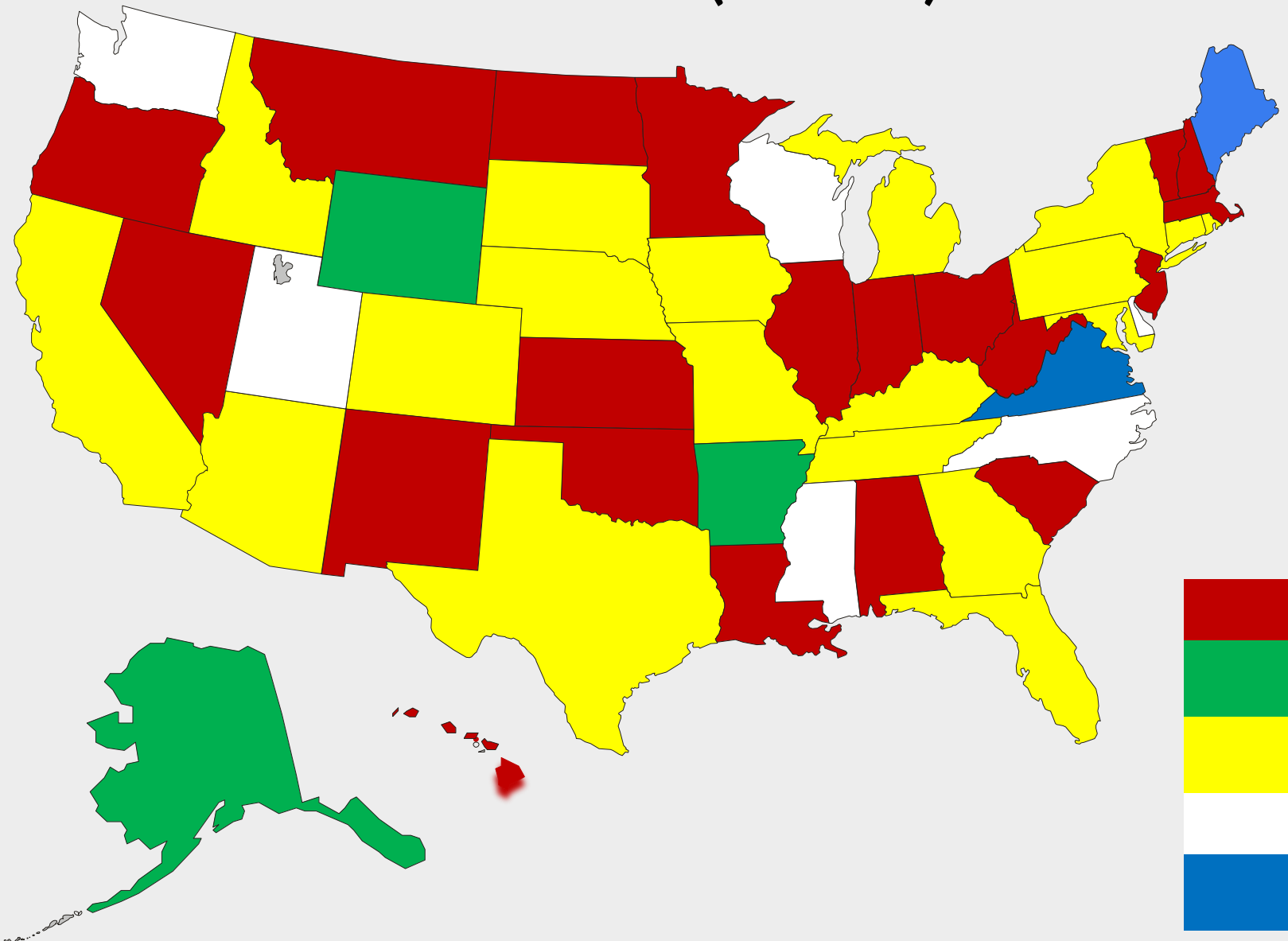
Mature Minor Doctrine

- Definition
- Assessment of maturity:
- Age & maturity
- Emotional capacity
- Intelligence
- Risk of procedure/treatment
- Benefit to minor
- Informed consent assessment:
- Risks of forgoing treatment
- Long term consequences
- Brain development, impulsivity & “charged” environments

Minor Consent for SUD Treatment

- Laws vary by state
- Minimum age of consent can range from age 12-16
- May be able to consent to some services but not others
  - Withdrawal Management
  - Outpatient
    - Buprenorphine for those 16 -18
  - Inpatient
- Parental notification may still be required

Consent for Inpatient Substance Treatment
Kerwin et al. (2015)



Adolescent Autonomy, Privacy & Confidentiality

- Parental involvement
- Confidentiality can be preserved
- Insurance & privacy



Pearls

- State laws vary regarding minor consent requirements and may allow for a mature minor to consent
- Adolescents usually have the greatest autonomy to consent for substance use disorder treatment compared to other medical treatments
- When treating an adolescent patient, involve parents if possible while preserving the adolescent's confidentiality

Pregnancy, Substance Use, & the Law

Legal Consequences Of Substance Use In Pregnancy

- Criminal
  - Feticide laws (38 states)
  - Chemical endangerment of a child (Amnesty)
  - Direct criminalization of use during pregnancy
- Civil
  - Substance Use = Child Abuse (24 States +DC)
  - Reporting to Child welfare (25 states + DC)
  - Civil commitment (3 states)



Reporting Requirements to Child Welfare (Jarlenski, Guttmacher. Org)

- Mandated reporting of child abuse/neglect
  - Standard: Reasonable belief or suspicion for abuse
  - Prenatal drug use & Substance Exposed Newborns
- Clinical & ethical problems
- Guidelines
  - Inform of any mandated reporting requirements & limits of confidentiality
  - Obtain informed consent before drug testing (ACOG)

Pearls

- A person who uses substances during pregnancy can be subjected to civil or criminal penalties in many states
- Mandated reporting requirements of perinatal substance use vary across states
- Obtain informed consent before drug testing, including notification of reporting requirements

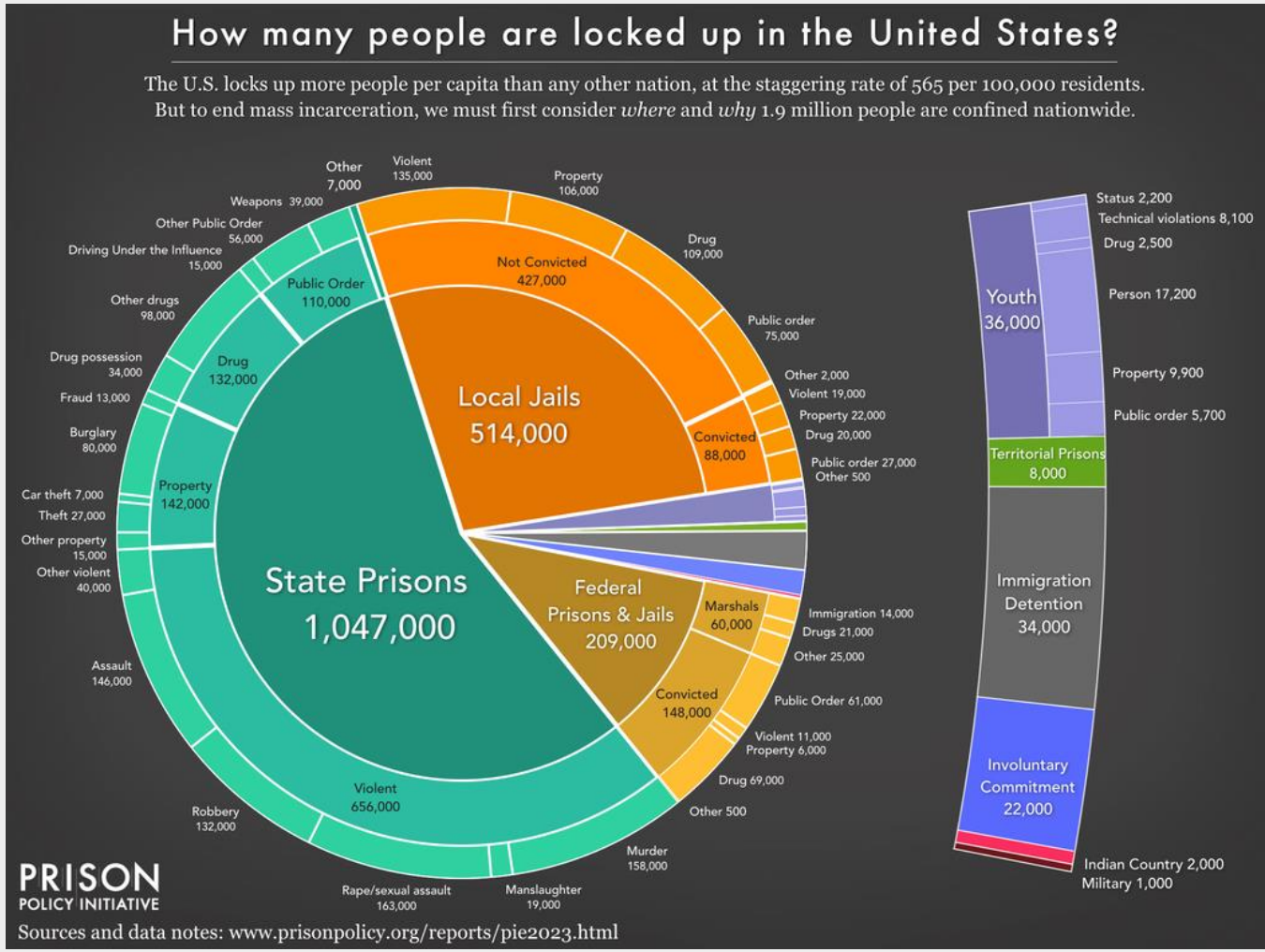
Justice-Involved Populations

Approximately what percentage of women who are incarcerated in jail have a substance use disorder?

A. 25%
B. 33%
C. 50%
D. 75%
E. 90%

Statistics

- In 2020, 5.5 million people under correctional **supervision** in the U.S.
- History of incarceration in the U.S.
- SUDs & incarceration
  - Over 65% with active SUD
    - >75% of women have SUD
  - ~10- 15% receive treatment



MAT in Corrections

- The Need
  - 75% will relapse within 3 months of release (SAMHSA)
  - 100x more likely to die of overdose within 2 weeks of release (BJS, Binswanger)
- Barriers
  - Lack of education
    - Substituting “one drug for another”/abstinence mentality
  - Diversion concerns
  - Cost
  - Lack of community providers to start or continue MAT
- BUT, more pilots across the US

Problem Solving (Treatment) Courts

- Drug, mental health, DUI, veteran's courts
- Therapeutic Jurisprudence
- Judge plays critical role
- Entry & Eligibility
- Structure & sanctions
- Efficacy (Logan)
  - Recidivism decreases
  - Future drug use reduced
- Treatment provider can be in dual role
- Some do not allow MAT (Matusow)



FINAL TOPICS

- Civil commitment
- The Americans with Disabilities Act (ADA)
- Impaired Physicians



Civil Commitment

- **Standards**
  - Mentally ill (or substance disorder, below) AND
  - Dangerous to self/others OR
  - Gravely disabled
- **Substance use disorders**
  - 37 states + DC (NAMSDL)
- **Legal process**
  - Due process required
  - Hearing occurs in timely manner
  - Committed for specified time by the judge



The Americans With Disabilities Act (ADA)

- **Disability: Physical or Mental impairment which:**
  - Limits in one or more major life activities
  - History of impairment
  - Regarded as having an impairment
- **Substance use**
  - Alcohol use disorder
  - Other substance use disorders
    - Protected: Not using now but is or has been in treatment for addiction or regarded by others as using drugs
    - Not protected: “Currently using drugs” or casual user
- **Exceptions**

Physician Regulation & Impaired Physicians

- Medical practice acts & state medical boards
- Physician health programs & impaired physicians
  - Exist in nearly every state
  - Goals
  - Voluntary vs. mandated treatment
  - High success rates
- Duty to report impaired physicians:
  - Impairment: physical, mental or substance-related disorder that interferes with abilities to safely and competently perform professional duties
  - Legal standards (have knowledge of or reason to believe) & options
  - Ethical and professional duties

Questions?

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References

1. Geppert CMA, Bogenschutz MP. (2009). Ethics in substance use disorder treatment. Psychiatric Clinics of North America 32:283-297.
2. Appelbaum PS. (2002). Privacy in psychiatric treatment: Threats and responses. American Journal of Psychiatry 159(11):1809-1818.
3. Dennis M, Rieckmann T, Baker R, McConnell KJ. (2017). 42 CFR part 2 and perceived impacts on coordination and integration of care: A qualitative analysis. Psychiatric Services 68(3):245-249.
4. Schwartz HI, Mack DM. (2003). Informed consent and competency. In "Principles and practice of forensic psychiatry, 2nd edition." Edited by Rosner R. Boca Raton: CRC Press.
5. Preuss CV, Kalava A, King KC. (2019). Prescription of controlled substances: Benefits and risks. StatPearls.
6. D'Souza RS, Eldrige JS. (2019). Prescription drug monitoring program. StatPearls.
7. Gourlay DL, Heit HA, Almahrezi A. (2005). Universal precautions in pain medicine: A rational approach to the treatment of chronic pain. Pain Medicine 6(2):107-112

References

8. Jarlenski M. et al. Characterization of U.S. state laws requiring health care provider reporting of perinatal substance use. Womens Health Issues. May-June 2017, 27(3): 264-70.
9. Guttmacher Institute. Substance use during pregnancy. February 202. Accessed at: https://www.guttmacher.org/state-policy/explore/substance-use-during-pregnancy.
10. Parental Drug Use as Child Abuse. Child Welfare Information Gateway. Access at: https://www.childwelfare.gov/pubPDFs/drugexposed.pdf.
11. Matusow, H., Dickman, S., Rich, J., Fong, C., Dumont, D., et al. (2013). Medication assisted treatment in US drug courts: Results form a nationwide survey of availability, barriers, and attitudes. Journal of Substance Abuse Treatment, 44, 473-480.
12. National Alliance for Model State Laws. Involuntary commitment of individuals with a substance use disorder or alcoholism. (2016). Accessed at: https://www.mass.gov/files/documents/2018/11/15/Involuntary%20Commitment%20for%20Individuals%20with%20a%20Substance%20Use%20Disorder%20or%20Alcoholism%20%28August%202016%29.pdf

References

13. Medication-assisted treatment (MAT) in the criminal justice system: brief guidance to the states. SAMHSA. https://store.samhsa.gov/sites/default/files/d7/priv/pep19-matbriefcjs_0.pdf
14. Drug Use, Dependence and Abuse Among State Prisoners and Jail Inmates, 2007-2009. BJS (2017). https://www.bjs.gov/index.cfm?ty=pbdetail&iid=5966.
15. APA Resource Document on recommended best practices for physician programs. (2017).
16. Fact Sheet: Drug Addiction & Federal Disability Rights Laws. At: https://www.hhs.gov/sites/default/files/drug-addiction-aand-federal-disability-rights-laws-fact-sheet.pdf



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