Hot Topics in Medicine Webinar Alcohol Use Disorder Treatment

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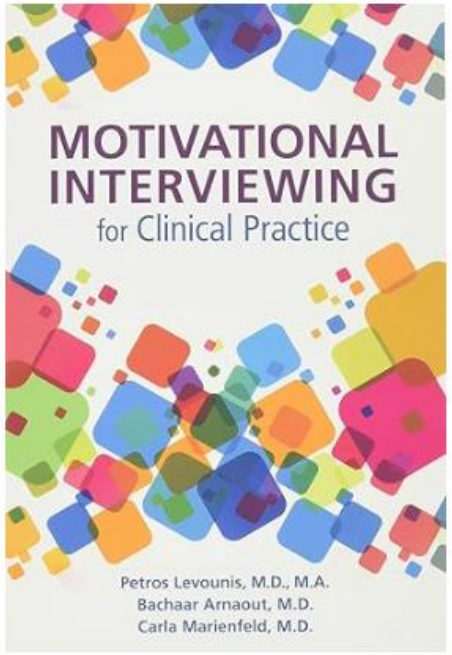
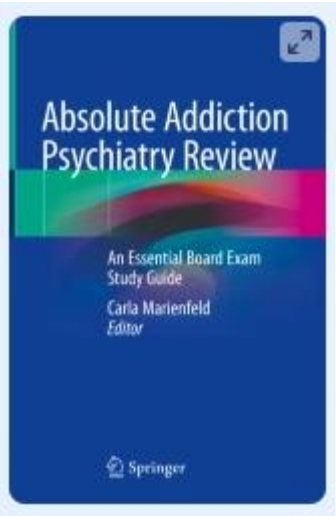
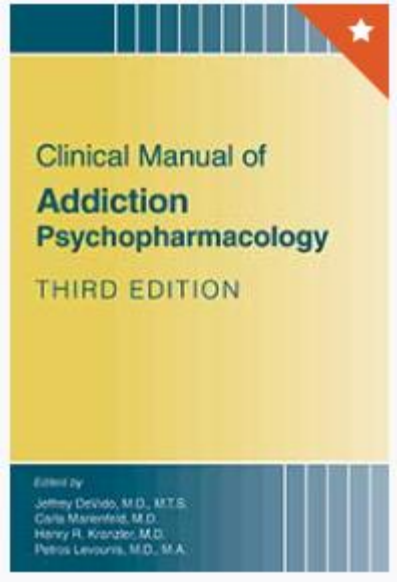
DISCLOSURES

- I am a advisory board member, paid consultant, and have stock options in the following companies:
  - CARI Health
- The content of this talk, and the opinions described therein are mine alone and do not represent those of any of my employing organizations.
- I will identify when speaking about potential off-label uses of medications
- Royalties/payments for editing books:
  - 3rd Edition of Clinical Manual of Addiction Psychopharmacology
  - The forthcoming 2nd Edition of the American Academy of Addiction Psychiatry Clinical Review of Addiction Psychiatry
  - Absolute Addiction Psychiatry Review: An Essential Board Exam Study Guide
  - Motivational Interviewing for Clinical Practice







OBJECTIVES

- Review the basic epidemiology and neurobiology of addiction to inform the understanding and approach to treating substance use disorders
- Communicate updates pharmacotherapy for a Alcohol Use Disorder (AUD)
- Provide strategies for incorporating pharmacotherapies for alcohol use disorders into clinical practice

Why do I love this work? (Personal anecdote)

The patients can be difficult when intoxicated or in withdrawal…

Community wrap around services are scarce…

But!

…patients (and lots of them!) get SO MUCH better!

…it’s rewarding to be a partner in recovery and watch people’s live improve.

What is addiction?

Part 1: A treatable, chronic medical disease involving complex interactions among brain circuits, genetics, the environment, and an individual's life experiences.

Part 2: People with addiction use substances or engage in behaviors that become compulsive and often continue despite harmful consequences.

Part 3: Prevention efforts and treatment approaches for addiction are generally as successful as those for other chronic diseases.

American Society of Addiction Medicine – 2019
https://www.asam.org/Quality-Science/definition-of-addiction

What is addiction Part 1?

A treatable, chronic medical disease involving complex interactions among brain circuits, genetics, the environment, and an individual's life experiences.

- Genetic vulnerability
- Brain structural changes with long term use
- Biochemical changes after repeated stimulation of dopamine reward pathways
  - Stimulation ↑ with substances
  - When not stimulated → severe cravings
  - Over time, receptors are less responsive → tolerance
  - Long term changes result → need drug to feel normal

American Society of Addiction Medicine – 2019
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What is addiction Part 2?

People with addiction use substances or engage in behaviors that become compulsive and often continue despite harmful consequences.

Impaired Control

- Taking the substance in **larger amounts or for longer** than you intend
- **Repeated unsuccessful efforts to quit or cut down**
- **Spending a lot of time** getting, using, or recovering from use of the substance
- **Cravings**

Social Problems

- **Problems at work, school, or home** roles because of substance use
- Interpersonal problems or causing **problems in relationships**
- Giving up **important activities** to use instead

Risky Use

- **Hazardous** use
- **Continuing use, despite** causing/worsening physical/ psychological **problems**

Physical/Pharmacological

- Tolerance
- Withdrawal

Unhealthy substance use: use of amounts that risk adverse health consequences

Substance use disorder (SUD): at least 2/11 of the DSM-5 criteria within a 12-month period; 2-3 = mild; 4-5 = moderate; 6+ = severe

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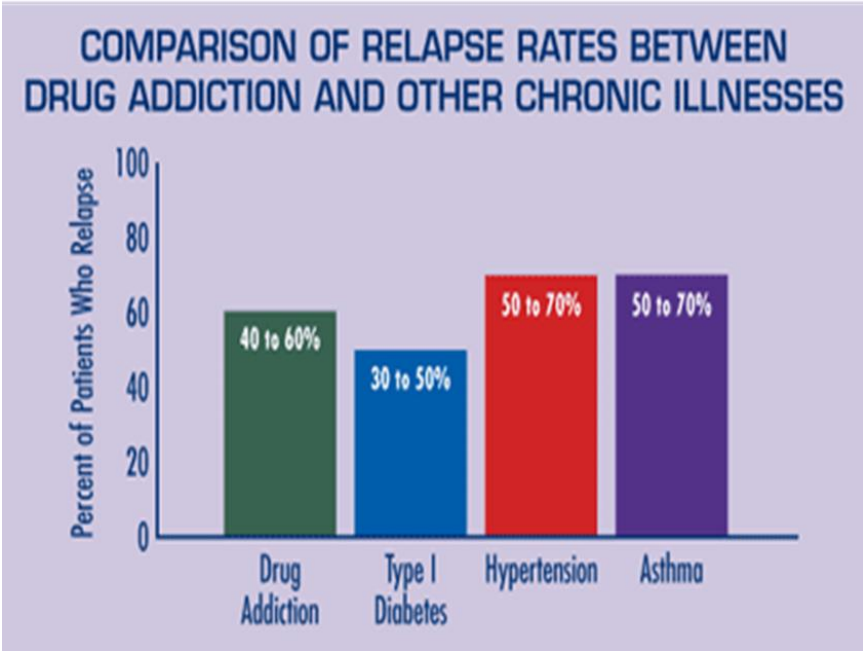
What is addiction Part 3?

Prevention efforts and treatment approaches for addiction are generally as successful as those for other chronic diseases.



Similarly to diabetes, high blood pressure, asthma…

- Biologically, psychologically, and socially mediated
- Life style changes and meds both can help
- Symptoms relapse and remit

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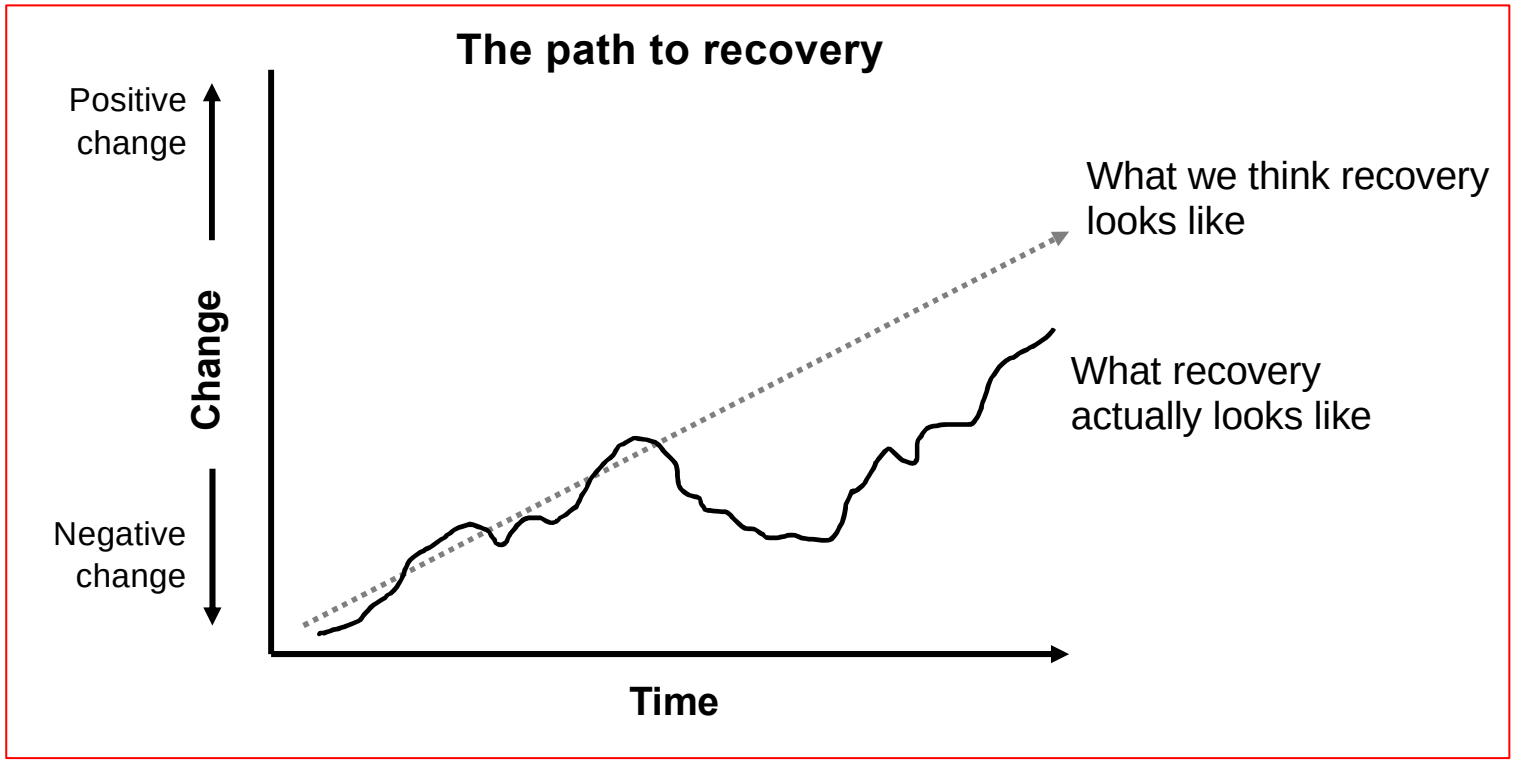
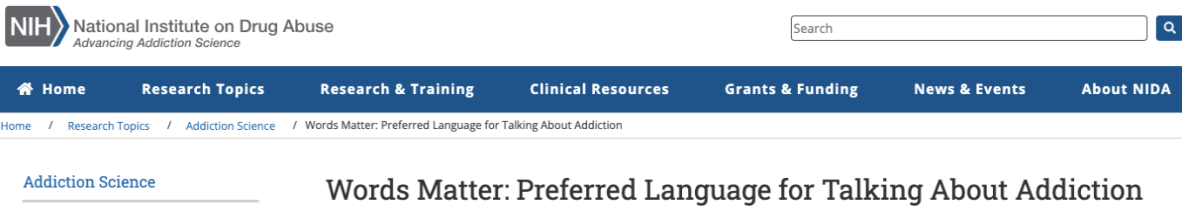
"A bend in the road is not the end of the road...unless you fail to make the turn." - Helen Keller



- Obstacles and lapses are inevitable, and response to them that matters.
- >60% experience relapse within the first year after discharge from treatment[1,2]
- The increased risk of relapse persists for many years[3,4]
- Ideally, chronic care at varying levels of intensity rather than short-term treatment limited to periods of acute exacerbation[3,4]

1. McLellan A et al. JAMA. 2000; 284(13), 1689-1695.
2. Hubbard R et al. Journal of Substance Abuse Treatment. 2003. 25(3), 125- 134.
3. Hser, Y et al. Archives of General Psychiatry. 2001; 58(5), 503-508.
4. https://nida.nih.gov/publications/principles-drug-addiction-treatment-research-based-guide-third-edition/principles-effective-treatment

Language Matters!



Terms to avoid, terms to use, and why

Consider using these recommended terms to reduce stigma and negative bias when talking about addiction.

Instead of...	Use...
▪ Addict	▪ Person with substance use disorder[1]
▪ User	▪ Person with OUD or person with opioid addiction (when substance in use is opioids)
▪ Substance or drug abuser	▪ Patient

- Person-first language.
- The change shows that a person "has" a problem, rather than "is" the problem.[7]
- The terms avoid eliciting negative associations, punitive attitudes, and individual blame.[7]

Stigma results in worse behaviors by care providers and worse experience for patients

- **A patient feeling stigmatized is less willing to seek treatment[1,2]**
- **Stigmatizing language can negatively influence a provider's perceptions of a patient and impact treatment[3]**

Many reasons for stigma:

- Historically seen as moral weakness; Segregated from other medical conditions
- Co-occurrence with mental illness, criminal justice
- Limited training and education

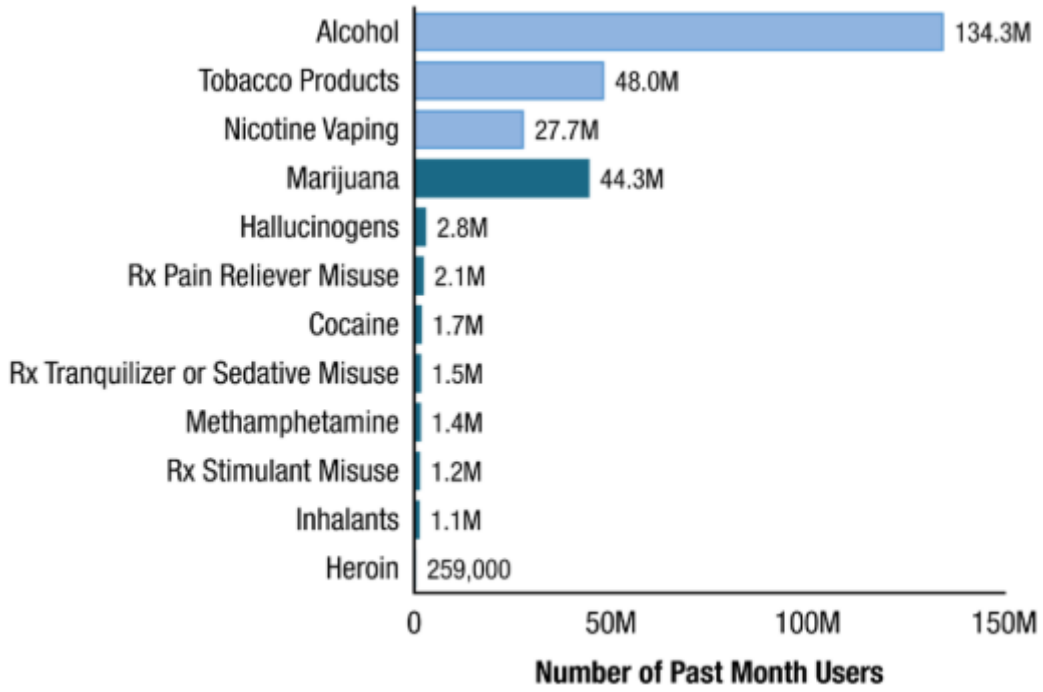
1.Hadland S et al. Addict Sci Clin Pract. 2018;13(1):15.
2.Yang L et al. Curr Opin Psychiatry. 2017; 30(5):378-388.
3.Ashford R et al. 2019. Substance Use & Misuse; 54(8):1376-1384.

Engagement is Foundational: Build a Therapeutic Alliance

- Language **matters**
  - Including body language
  - Person First language
- Open-ended questions – invite the person to explore, active listening
- Non-judgmental stance in language, approach, attitude
- Non-confrontational; come along side with common ground
- **Be aware of your own biases** (and how they may influence you)

National Survey on Drug Use and Health (NSDUH): Nationally representative data on use of tobacco, alcohol, and illicit drugs, SUD and treatment among noninstitutionalized US population 12 years or older

Figure 1. Number of Americans 12 Years or Older Reporting Past Month Use of Specific Substances, 2024



General Alcohol Use (Past Year/Month, Aged 12+)

- **Past-Year Alcohol Use: ~178.7 million people (62%)**
- **Past-Month Alcohol Use: 134.3 million people (46.6%)**

Trends: The percentage of people aged 12 or older who used alcohol in the past month showed no significant change from 2021 to 2024.

Alcohol Use Disorder (AUD)

- **Total with AUD past year: 27.9 million people (9.7%)**
- **Demographics:**
  - **Sex**
    - **Males:** 16.7 million (11.8%)
    - **Females:** 11.2 million (7.6%)
  - **Age**
    - **Youth (12-17):** 775,000 had an AUD (3.0%).
    - **Adults (18+):** 27.1 million had an AUD (10.3%).

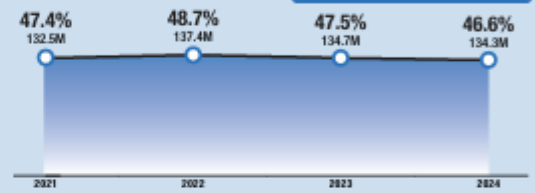
Trends: The percentage of people 12 or older with an AUD decreased from 10.6% in 2021 to 9.7% in 2024.

Alcohol Use in the Past Month

NSDUH asked respondents aged 12 or older about their alcohol use in the 30 days before the interview.

ALCOHOL USE

1 drink on at least 1 day

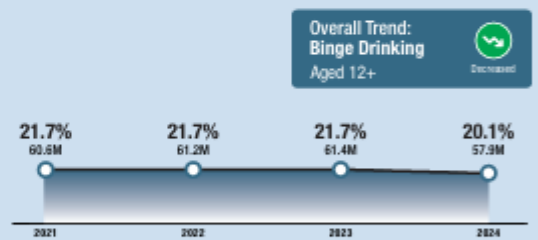


BINGE DRINKING

Number of drinks on the same occasion on at least 1 day

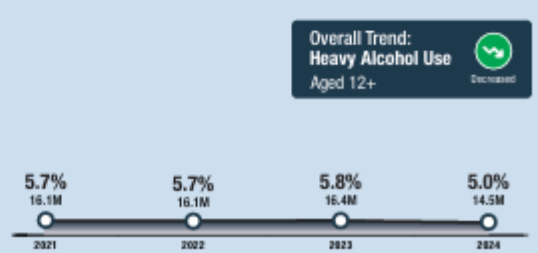
Males 5 or more

Females 4 or more



HEAVY ALCOHOL USE

Binge drinking on 5 or more days in the past 30 days

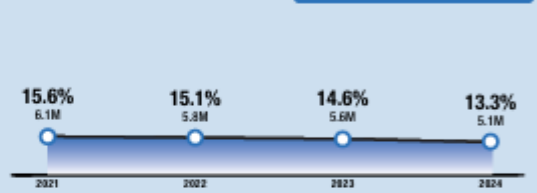


Underage Alcohol Use in the Past Month

NSDUH asked respondents aged 12 to 20 about their alcohol use in the 30 days before the interview.

ALCOHOL USE

1 drink on at least 1 day



BINGE DRINKING

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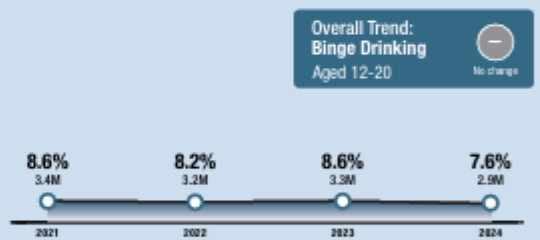
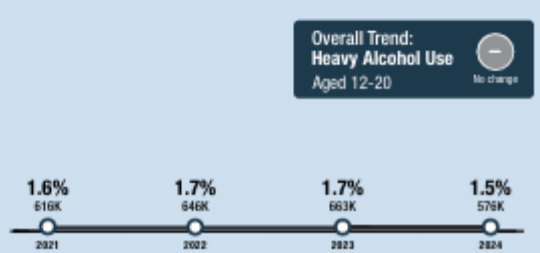


HEAVY ALCOHOL USE

Binge drinking on 5 or more days in the past 30 days



Alcohol Use Disorder

- Similar prevalence to other chronic diseases – asthma, diabetes, major depressive disorder (MDD)
- Direct or indirect cause of many other problems
  - ~6% of global deaths attributable to alcohol
  - Deaths among ages 20 to 64
    - ~ 13% were attributable to excessive alcohol consumption
      - Higher among men (15%) than women (~9%)
  - Deaths among age 20 to 49
    - ~20% were attributable to excessive alcohol consumption
- Gen X and Boomers are drinking more now; Gen Z is drinking less
- Increases in both genders (concerning for women given biology)
- Alcohol use is increasing in retiring baby boomers
  - Less resilient to it's effects

Estimated Deaths Attributable to Excessive Alcohol Use Among US Adults Aged 20 to 64 Years, 2015 to 2019

Marissa B. Esser, PhD; Gregory Leung, PhD; Adam Sherk, PhD; Michele K. Bohm, MPH; Yong Liu, MD; Hua Lu, MS; Timothy S. Naimi, MD

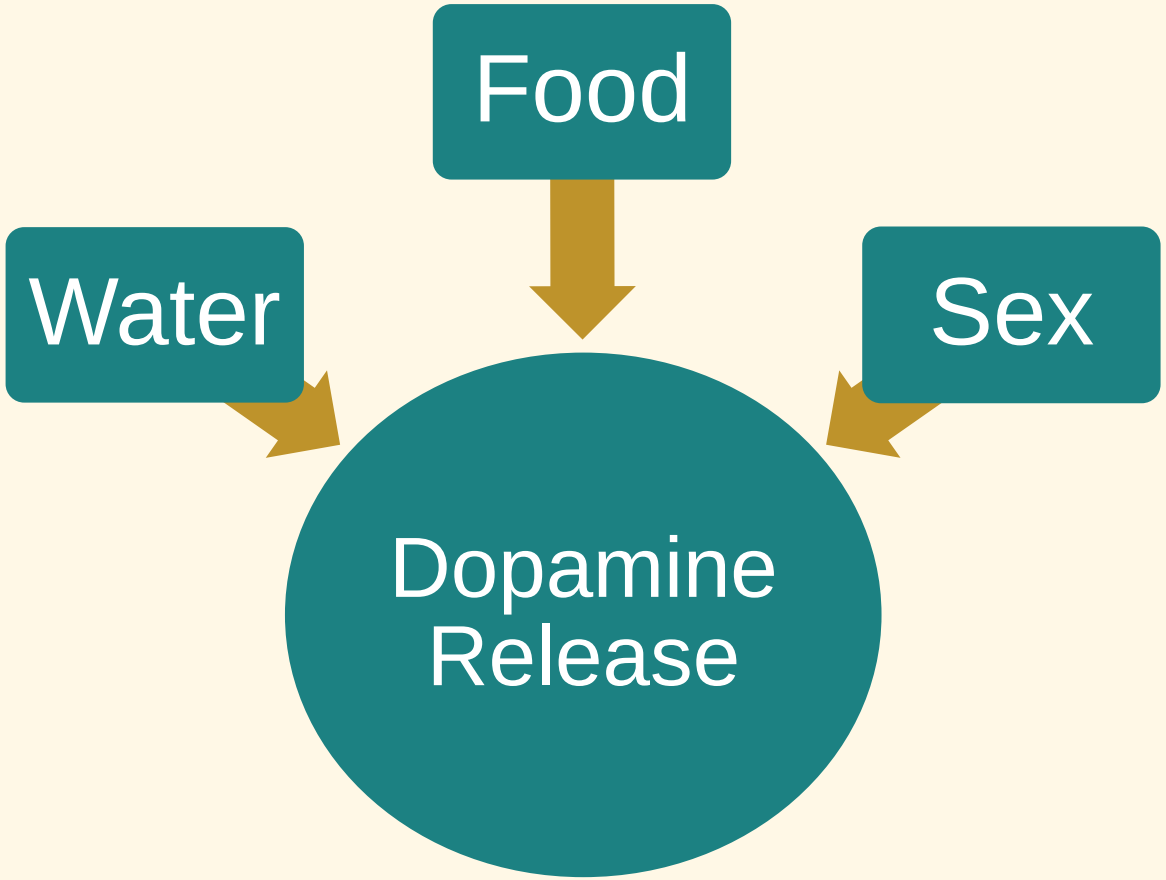
Risk factors for developing a SUD

- 1 in 7 (14.6%) Americans develop a SUD at some point in their lives[1]
  - **Majority who use substances do not develop a SUD[2]**
- **Environmental factors**: physical, emotional, and sexual abuse; neglect; parental substance use, parental conflict and mental illness; incarceration of household members[3], poverty[4], and easy access to addictive substances[2]
- Individual factors: **genetics (may account for 40-70 % of individual differences** in risk for addiction[6,7]), mental health disorders[8], **substance use during adolescence[5]**
  - Majority began using during adolescence and met criteria for SUD by age 20-25[9-11]

1. Kessler R et al. Archives of General Psychiatry. 2005;62(6), 593-602.
2. U.S. Department of Health and Human Services (HHS), Office of the Surgeon General, Facing Addiction in America: The Surgeon General's Report on Alcohol, Drugs, and Health. Washington, DC: HHS, November 2016.
3. Dube S et al. Pediatrics. 2003; 111(3), 564-572.
4. Najavits, L. M., Hyman, S. M., Ruglass, L. M., Hien, D. A., & Read, J. P. (2017). Substance use disorder and trauma. In S. Gold, J. Cook, & C. Dalenberg (Eds.), *Handbook of Trauma Psychology* (pp. 195-214): American Psychological Association.
5. Chilcoat, H. D., & Menard, C. (2003). Epidemiological investigations: Comorbidity of posttraumatic stress disorder and substance use disorder. In P. Ouimette & P. J. Brown (Eds.), Trauma and substance abuse: Causes, consequences, and treatment of comorbid disorders. (pp. 9-28). Washington, DC: American Psychological Association.
6. Prescott C et al. American Journal of Psychiatry. 1999;156, 34-40. 53.
7. Schuckit M et al. Alcoholism: Clinical and Experimental Research. 2001;25(3), 323-329.
8. Grant B et al. Archives of General Psychiatry. 2004; 61(8), 807-816.
9. Jacobsen L et al. American Journal of Psychiatry. 2001;158(8), 1184-1190.
10. Leeies M et al. Depression and Anxiety.2010; 27(8), 731-736.
11. Kumari V et al. Neuroscience and Biobehavioral Reviews. 2005; 29(6), 1021-1034.

Neuroscience of Addiction

Natural rewards release dopamine

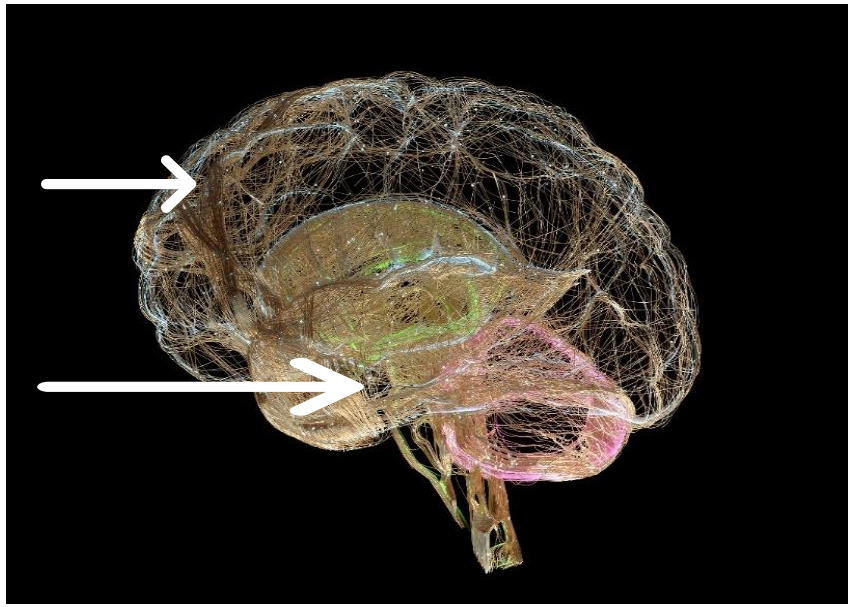


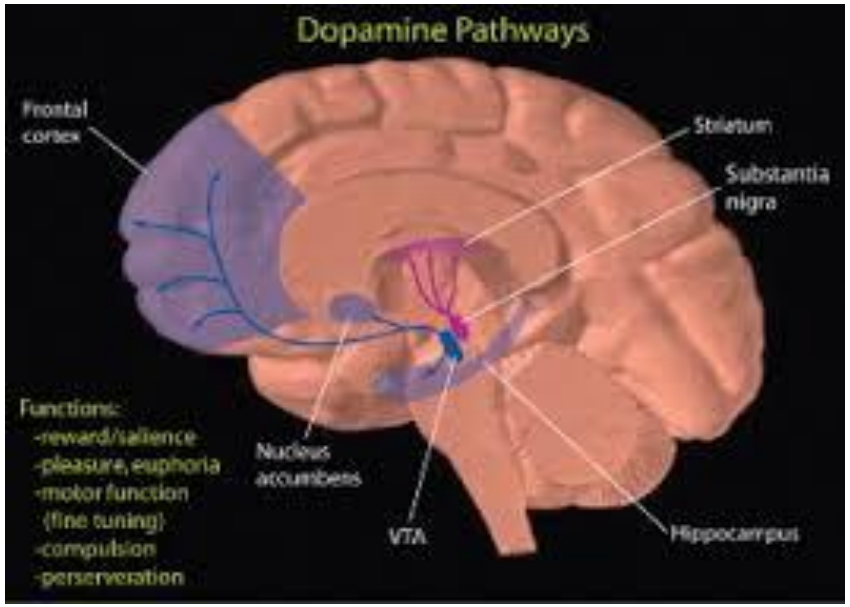
How Substances Affect the Brain

- All misused substances activate the reward pathway
  - The same pathway activated by naturally rewarding substances and events

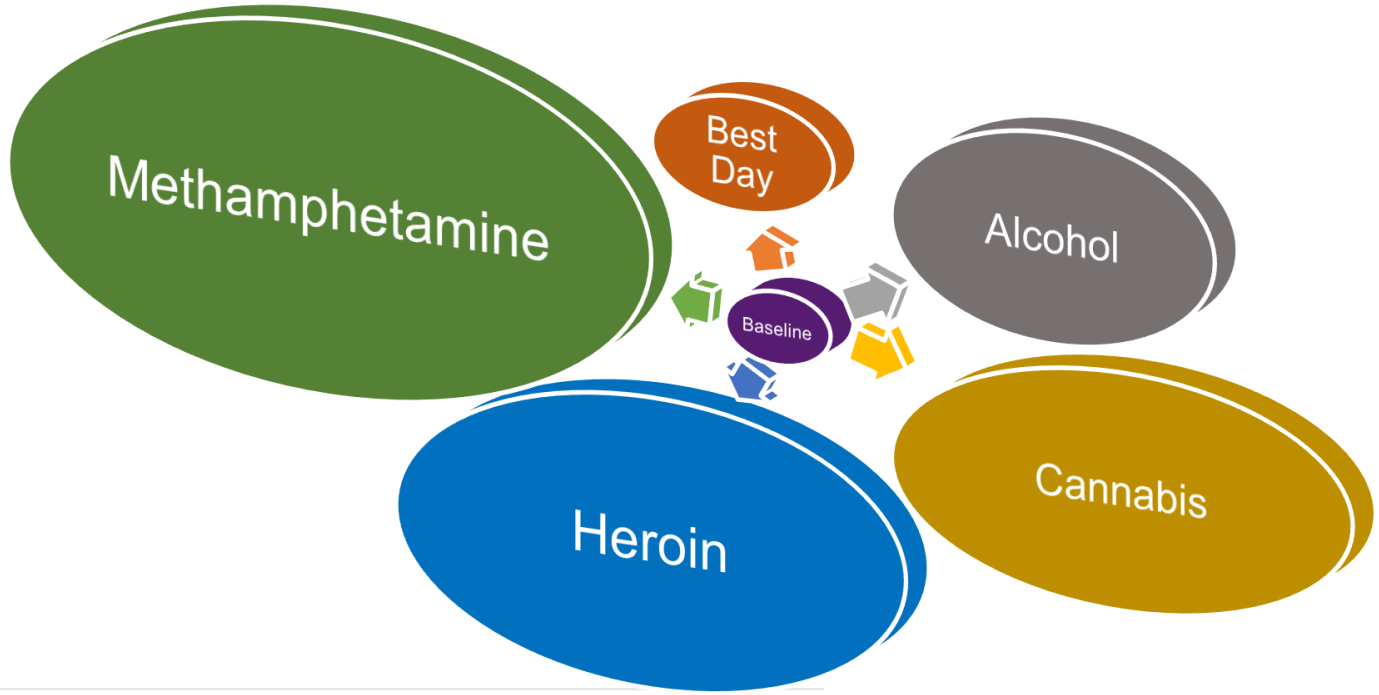
Thinking part of brain

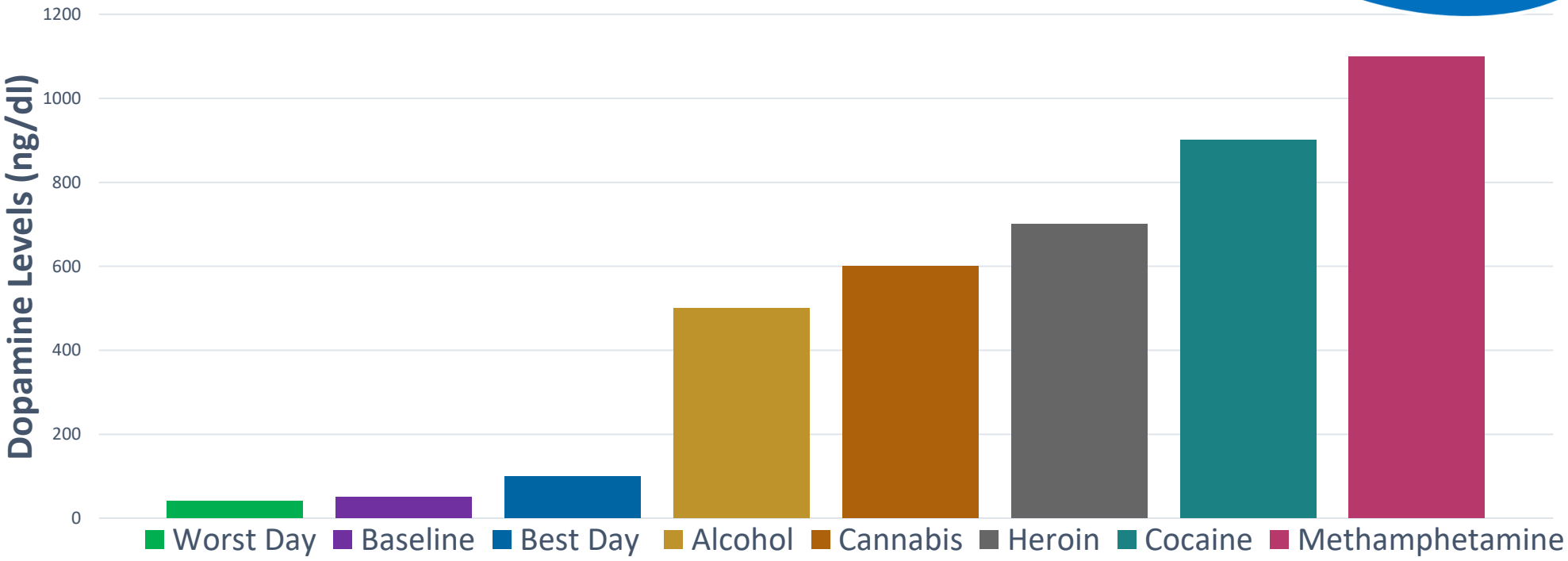
Primitive parts of brain



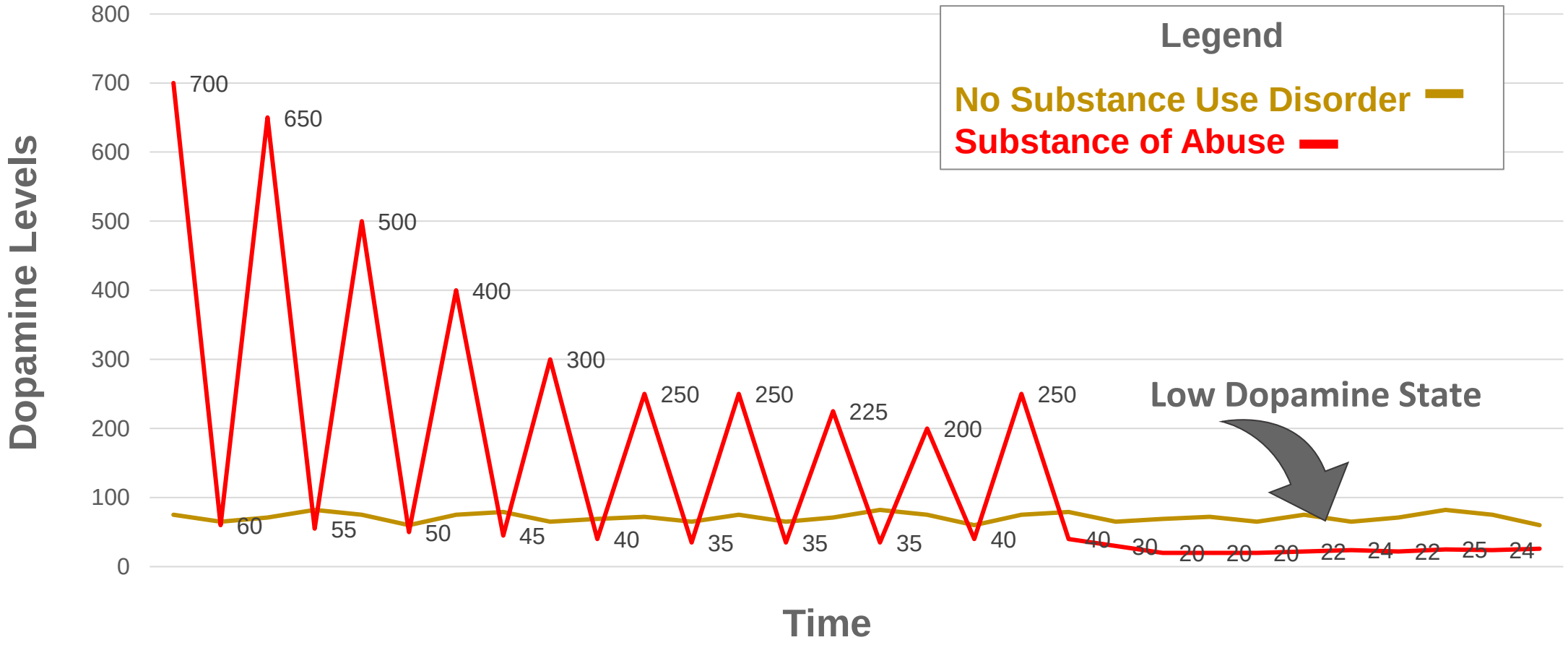


DOPAMINE RESPONSE

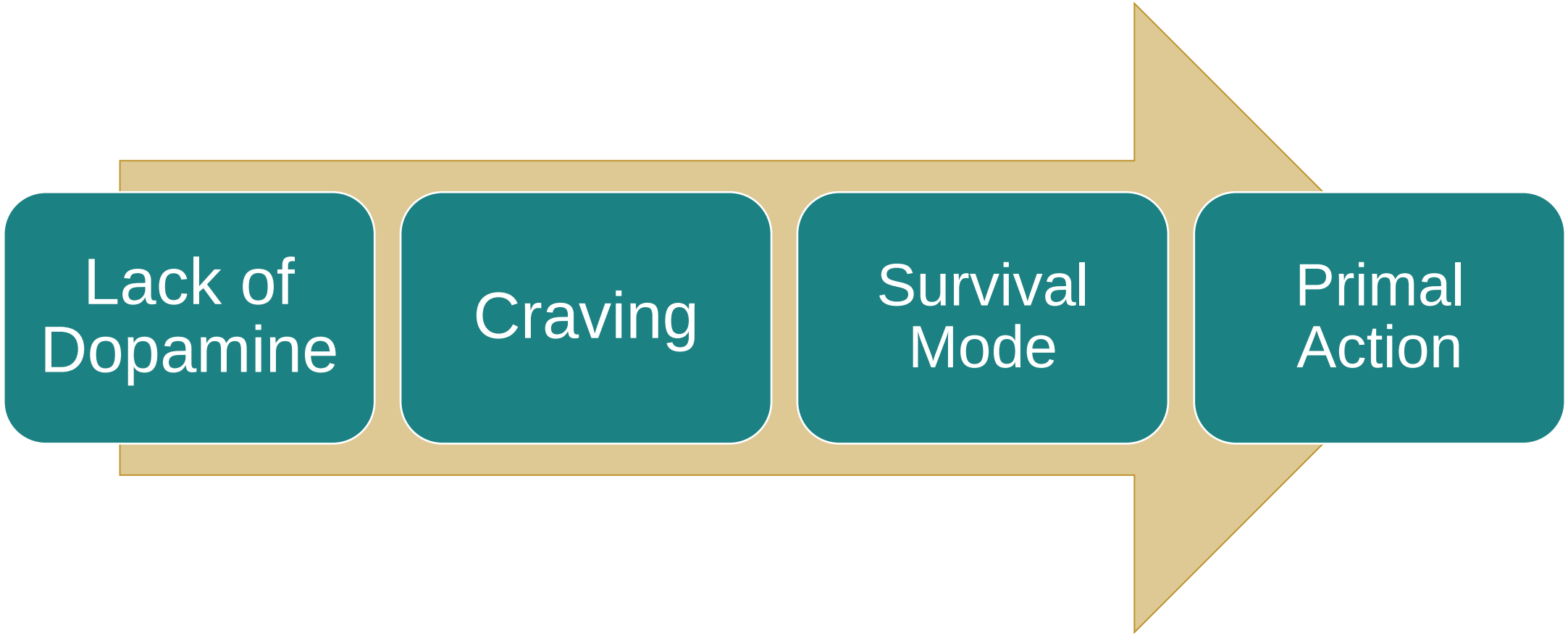




Brain changes with episodes of substance use



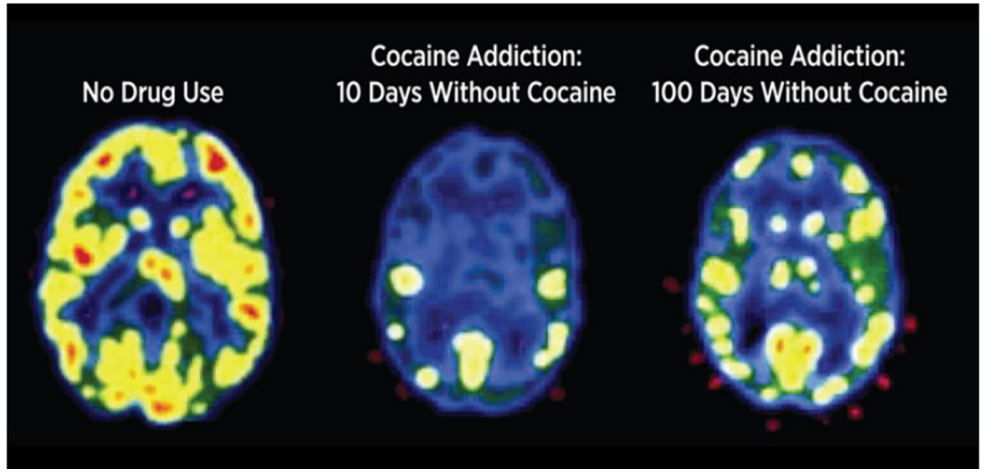
Understanding addiction to inform treatment



It takes time for your brain to recover – but it does!

- Prolonged drug use changes the brain in very long-lasting ways
- Return to the brain function you had before heavy substances of use takes months to years
- If you stop medications/treatments before a year, you may lose ground

How the Brain Changes and Recovers From Drug Use



Source: https://nida.nih.gov/publications/teaching-addiction-science/bringing-power-science-to-bear-drug-abuse-addiction

Treatment of Addiction

Why Treat Substance Use Disorders?

- SUDs common and easily identified
- Effective treatment exists
- Cost effective compared to social costs
- Similar outcomes to other chronic diseases
- Rewarding to watch patient’s lives improve

Screening for Unhealthy Substance Use

- **SISQs are as well-validated as longer questionnaires and have similar sensitivity and specificity for detection of drug use, drug use with adverse consequences, and drug use disorders used in primary care settings[1]**
- SISQ-drug has 93% sensitivity and 94% specificity for detecting past-year drug use[1]
- Limitations include that quantities and frequencies of use that risk health consequences are not well-defined across drugs outside of alcohol
- Strengths include that SISQs are short, but still, rarely implemented[2]

Single Item Screening Questions

- SISQ-alcohol

How many times in the past year have you had X or more drinks in a day?

(X=5 for men, and X=4 for women)

- SISQ-drug

How many times in the past year have you used an illegal drug or used a prescription medication for non-medical reasons (for example, because of the experience or feeling it caused?

Recommendation Summary

Population	Recommendation	Grade
Adults age 18 years or older	The USPSTF recommends screening by asking questions about unhealthy drug use in adults age 18 years or older. Screening should be implemented when services for accurate diagnosis, effective treatment, and appropriate care can be offered or referred. (Screening refers to asking questions about unhealthy drug use, not testing biological specimens.)	B

1. Smith P et al. Arch Intern Med. 2010;170(13):1155-60.
2.Mertens J et al. Addict Sci Clin Pract. 2015;10:26.

Brief Counseling Interventions

- **Can be as simple as HOW you say things**
  - **Motivational Interviewing is more about the SPIRIT than any techniques**
    - **though reflective listening is powerful**
- Increase motivation to change alcohol intake, reduce alcohol consumption, and risks of associated health problems[1-3]
- Many different forms: can be unstructured or structured

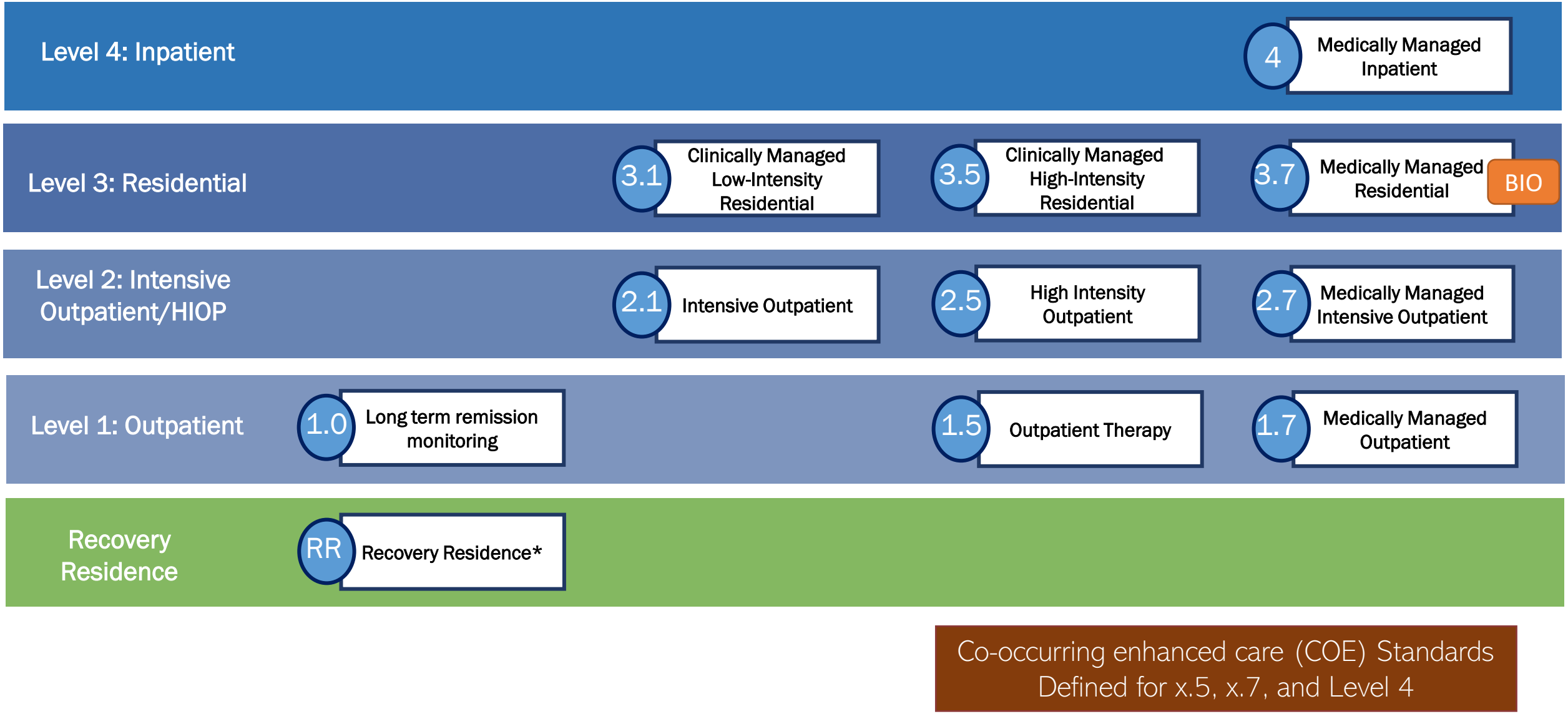
1. Orford J.et al. Behavior Research and Therapy. 1976; 14:409-418
2. Edwards G et al. Journal of Studies on Alcohol. 1977;38(5):1004–1031.
3. Bien T et al. Addiction. 1993;88:315-336
4. Drummond D et al. Lancet. 1990; 336:915-918
5. US Preventive Services Task Force, Krist AH, Davidson KW, Mangione CM, Barry MJ, Cabana M, Caughey AB, Curry SJ, Donahue K, Doubeni CA, Epling JW Jr, Kubik M, Ogedegbe G, Pbert L, Silverstein M, Simon MA, Tseng CW, Wong JB SOJAMA. 2020;323(22):2301.
6. US Preventive Services Task Force, Curry SJ, Krist AH, Owens DK, Barry MJ, Caughey AB, Davidson KW, Doubeni CA, Epling JW Jr, Kemper AR, Kubik M, Landefeld CS, Mangione CM, Silverstein M, Simon MA, Tseng CW, Wong JB SOJAMA. 2018;320(18):1899.
7. Whitlock E et al. Ann Intern Med. 2004;140(7):557.

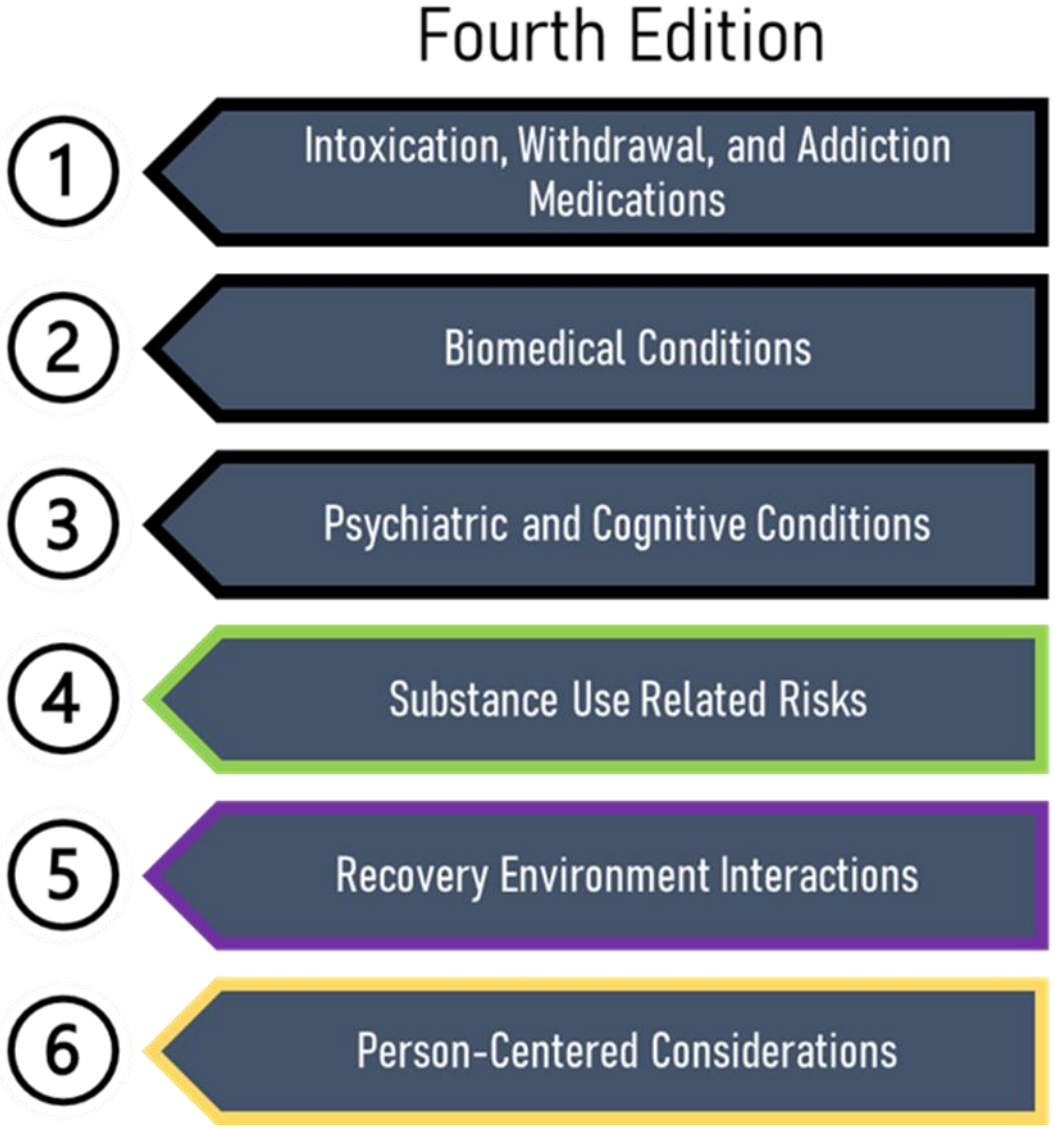
FOUNDATIONAL PRINCIPLES OF HARM REDUCTION

Harm reduction incorporates a **spectrum of strategies** that includes safer use, managed use, abstinence, meeting people who use drugs "where they are," and **addressing conditions of use along with the use itself**. Because harm reduction demands that interventions and policies designed to serve people who use drugs reflect specific individual and community needs, there is **no universal definition or formula for implementing harm reduction**.

- National Harm Reduction Coalition

The ASAM Criteria Continuum of Care – Adult





ASAM Criteria: Assessment Dimensions

Hazelden and the Minnesota Model

- Centralized system
- Focus on detoxification
- Broadly, used principles of AA
- Ideology
  - Alcoholism = involuntary, primary, chronic, progressive
    - Biopsychosocial spiritual disease
  - Recovery is the goal; not just abstinence
  - Initial motivation not needed
  - Motivation = responsibility of patient and milieu
- Treatment of a disease process
  - Abandoned psychoanalytic and moral models of addiction
- Treatment milieu – dignity and respect

Behavioral Therapies: *Groups*

- Modal format for much SUD therapy:
  - Cost effective
  - Increase access
  - Peers powerful agent of change
  - Better fidelity to model
- Advantages:
  - Modeling, varied coping skills
  - Public affirmations, confession, support
  - Networks of support

Treatment Modalities

- Motivational interviewing
    - Style of treatment interaction/conversation to ↑ motivation to change
- Counseling and psychotherapy
    - Cognitive behavioral therapy
        - Restructuring thoughts to change behavior / feelings
        - Relapse Prevention
    - Group based therapy
        - Psychotherapy provided with peer input / support as part of therapy
    - Acceptance and Commitment Therapy (ACT)
    - Community Reinforcement Approach (CRA) with Family Therapy (CRAFT)
        - Make not using more rewarding than using; Concerned Significant Others (CSO)
- Mutual Help Groups
    - Grew out of Alcoholics Anonymous; free, available
- Medications

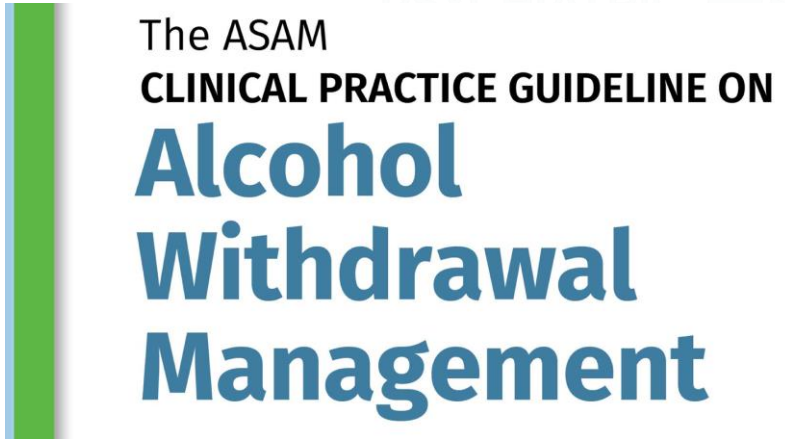
Alcoholics Anonymous (AA)

- Emancipated spirituality from religious institutions
  - Varieties of spiritual experiences in recovery
- Alternatives to religious guilt
  - Self-inventory, Confession
  - Acts of Restitution, Acts of Service
- Encouraged service work, working with others
- Established a chronic care system for a chronic disease
- Peer-led, decentralized, social movement
- Explicit instructions

Clinically Effective Addiction Medications

Opioid Use Disorder	Alcohol Use Disorder	Tobacco Use Disorder	Sedative Withdrawal Management	Stimulant Use Disorder	Cannabis Use Disorder
Methadone	**Naltrexone**	**Nicotine Replacement**	Benzodiazepines	Naltrexone	N-acetyl cysteine
Buprenorphine	**Acamprosate**	**Varenicline**	Barbiturates	Bupropion	Naltrexone
Naltrexone	**Disulfiram**	**Bupropion**	Anticonvulsants	Mirtazapine	Gabapentin
	Topiramate			Topiramate	Topiramate
	Gabapentin			Methylphenidate	
	Baclofen			Dextroamphetamine/ Amphetamine	
	Ondansetron			Modafinil	

ALCOHOL WITHDRAWAL FUNDAMENTALS



- Kindling
  - Repeated episodes worsen course
  - Positive relationship of withdrawal seizures to repeated detox

- Goals
  - Alleviate symptoms
  - Prevent progression to more severe symptoms
    - Autonomic hyperactivity, hallucinations, neuronal excitation → seizures, delirium tremens (DT's)
  - Entry point to treatment, NOT TREATMENT for AUD

- Medications: Benzodiazepines! – Act on GABA A Receptor
  - Fixed dosing vs. symptom triggered
  - Phenobarbitol, a barbiturate, also popular in EDs (avoid with OUD/fentanyl)
  - Can use alcohol, anti-convulsants ("benzo sparing protocols")
  - Supplement with thiamine, folic acid, multivitamin

- CIWA-Ar – Clinical Institute Withdrawal Assessment – Alcohol, revised
  - Takes 2 mins, predicts severity of withdrawal
  - Dose benzodiazepines based on score instead of standing doses

https://downloads.asam.org/sitefinity-production-blobs/docs/default-source/quality-science/the_asam_clinical_practice_guideline_on_alcohol-1.pdf?sfvrsn=ba255c2_0

BENZODIAZEPINES FOR ALCOHOL WITHDRAWAL

- For some more severe individuals, fixed dosing may be more effective

  (Bahji 2022, meta-analysis 149 controlled trials)

  - Medications that were superior to placebo in reducing incident alcohol withdrawal seizures were fixed-schedule chlormethiazole; fixed-schedule diazepam, lorazepam, or chlordiazepoxide; and divalproex

- Supporting use of benzos over anticonvulsant monotherapy

  (Lai 2022—systematic review and meta-analysis)…BUT confusing

  - There was no evidence of significant differences on any of the efficacy outcomes (number of patients experiencing alcohol withdrawal-related seizures or delirium, CIWA-Ar score, or the need for rescue medications) when comparing anticonvulsants with benzodiazepines.
  - HOWEVER… Anticonvulsants showed significantly greater odds of requiring rescue medications than benzodiazepines and significantly more dropouts due to adverse events than placebo

PAWSS

Prediction of Alcohol Withdrawal Severity Scale (PAWSS)

Maldonado et al, 2015

Part A: Threshold Criteria: ("Y" or "N", no point)

Have you consumed any amount of alcohol (i.e., been drinking) within the last 30 days? OR did the patient have a "+" BAL on admission? _____

IF the answer to either is YES, proceed with test:

Part B: Based on patient interview: (1 point each)

1. Have you been recently intoxicated/drunk, within the last 30 days? _____
2. Have you ever undergone alcohol use disorder rehabilitation treatment or treatment for alcoholism? (i.e., in-patient or out-patient treatment programs or AA attendance) _____
3. Have you ever experienced any previous episodes of alcohol withdrawal, regardless of severity? _____
4. Have you ever experienced blackouts? _____
5. Have you ever experienced alcohol withdrawal seizures? _____
6. Have you ever experienced delirium tremens or DT's? _____
7. Have you combined alcohol with other "downers" like benzodiazepines or barbiturates, during the last 90 days? _____
8. Have you combined alcohol with any other substance of abuse, during the last 90 days? _____

Part C: Based on clinical evidence: (1 point each)

9. Was the patient's blood alcohol level (BAL) on presentation ≥ 200? _____
10. Is there evidence of increased autonomic activity? (e.g., HR > 120 bpm, tremor, sweating, agitation, nausea) _____

Total Score: _____

Notes: Maximum score = 10. This instrument is intended as a SCREENING TOOL. The greater the number of positive findings, the higher the risk for the development of AWS.
A score of ≥ 4 suggests HIGH RISK for moderate to severe (complicated) AWS; prophylaxis and/or treatment may be indicated.

CIWA

NAUSEA AND VOMITING — Ask "Do you feel sick to your stomach? Have you vomited?" Observation.
0 no nausea and no vomiting
1 mild nausea with no vomiting
2
3
4 intermittent nausea with dry heaves
5
6
7 constant nausea, frequent dry heaves and vomiting

TREMOR — Arms extended and fingers spread apart. Observation.
0 no tremor
1 not visible, but can be felt fingertip to fingertip
2
3
4 moderate, with patient's arms extended
5
6
7 severe, even with arms not extended

PAROXYSMAL SWEATS — Observation.
0 no sweat visible
1 barely perceptible sweating, palms moist
2
3
4 beads of sweat obvious on forehead
5
6
7 drenching sweats

ANXIETY — Ask "Do you feel nervous?" Observation.
0 no anxiety, at ease
1 mild anxious
2
3
4 moderately anxious, or guarded, so anxiety is inferred
5
6
7 equivalent to acute panic states as seen in severe delirium or acute schizophrenic reactions

AGITATION — Observation.
0 normal activity
1 somewhat more than normal activity
2
3
4 moderately fidgety and restless
5
6
7 paces back and forth during most of the interview, or constantly thrashes about

TACTILE DISTURBANCES — Ask "Have you any itching, pins and needles sensations, any burning, any numbness, or do you feel bugs crawling on or under your skin?" Observation.
0 none
1 very mild itching, pins and needles, burning or numbness
2 mild itching, pins and needles, burning or numbness
3 moderate itching, pins and needles, burning ornumbness
4 moderately severe hallucinations
5 severe hallucinations
6 extremely severe hallucinations
7 continuous hallucinations

AUDITORY DISTURBANCES — Ask "Are you more aware of sounds around you? Are they harsh? Do they frighten you? Are you hearing anything that is disturbing to you? Are you hearing things you know are not there?" Observation.
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

VISUAL DISTURBANCES — Ask "Does the light appear to be too bright? Is its color different? Does it hurt your eyes? Are you seeing anything that is disturbing to you? Are you seeing things you know are not there?" Observation.
0 not present
1 very mild sensitivity
2 mild sensitivity
3 moderate sensitivity
4 moderately severe hallucinations
5 severe hallucinations
6 extremely severe hallucinations
7 continuous hallucinations

HEADACHE, FULLNESS IN HEAD — Ask "Does your head feel different? Does it feel like there is a band around your head?" Do not rate for dizziness or lightheadedness. Otherwise, rate severity.
0 no present
1 very mild
2 mild
3 moderate
4 moderately severe
5 severe
6 very severe
7 extremely severe

ORIENTATION AND CLOUDING OF SENSORIUM — Ask "What day is this? Where are you? Who am I?"
0 oriented and can do serial additions
1 cannot do serial additions or is uncertain about date
2 disoriented for date by no more than 2 calendar days
3 disoriented for date by more than 2 calendar days
4 disoriented for place/or person

Case Vignette: Alcohol Withdrawal Management

A 68-year-old man with alcoholic cirrhosis is admitted to the hospital. He has a long history of heavy daily drinking, and his last drink was on the morning of admission. Twelve hours later, he develops tremors, anxiety, and tachycardia.

Question: What is the most appropriate class of medication for his alcohol withdrawal, and which specific agent would be preferred given his age and liver disease?

Answer: Benzodiazepines are the preferred medication class. Given his age and cirrhosis, **lorazepam** or **oxazepam** are the preferred agents.

Explanation: Benzodiazepines are the standard of care for managing alcohol withdrawal. In patients who are elderly or have significant hepatic impairment, intermediate-acting benzodiazepines like lorazepam and oxazepam are favored because they are metabolized through a simpler pathway (Phase 2 glucuronidation; skipping the Phase 1 oxidative metabolism and the p450 enzymes) and do not have active metabolites that can accumulate and cause prolonged sedation.

Medication for Alcohol Use Disorder

FDA approved meds

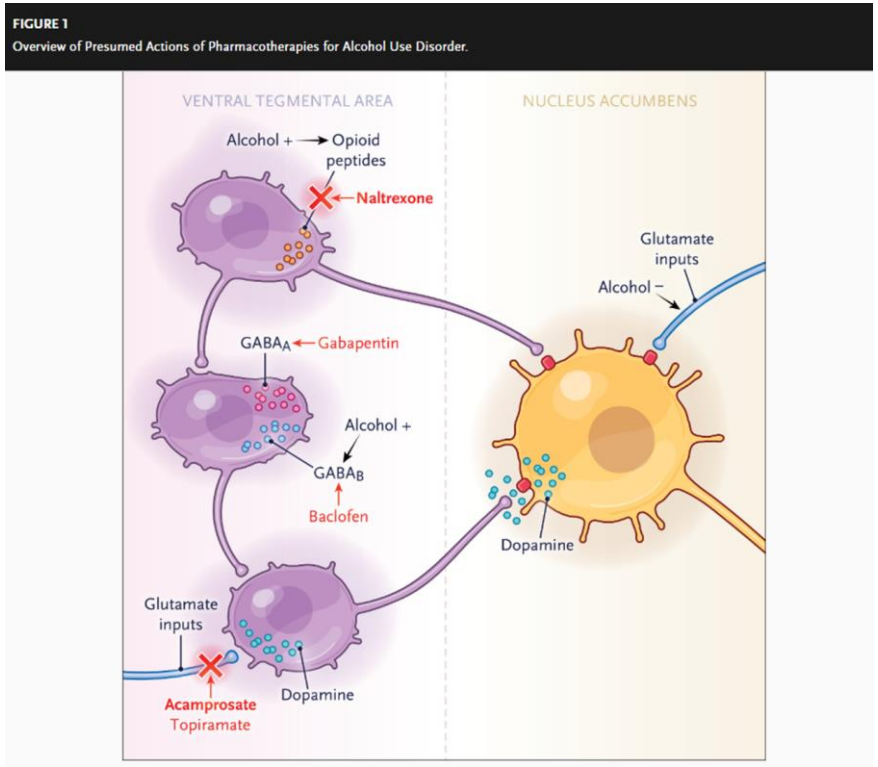
- Naltrexone (Revia) 1994
- Long Acting Naltrexone IM (Vivitrol) 2006
- Acamprosate (Campral) 2004
- Disulfiram (Antabuse) 1949

Non FDA approved; decent data

- Topiramate (similar to naltrexone in head to head trial)

Other meds; poor/limited data

- Gabapentin (higher doses; slightly more abstinence, decreased heavy drinking)
- SSRI's in subpopulations with depression and AUD
  - Sertraline maybe in "type A" low risk/severity/late onset alcohol drinkers
- Baclofen (small trials; pts with liver disease)
- Ondansetron (maybe for "early onset" AUD, before age 25)



Naltrexone (Revia, Vivitrol)

- Competitive opioid antagonist
  - Blocks rewarding aspects of drinking by occupying opioid receptors
    - Prevents alcohol from stimulating dopamine release
  - Another hypothesis – precipitates sedation with alcohol, so patients avoid
- Reduces frequency and intensity of drinking
- Reduces risk of relapse to HEAVY drinking
- Increases % of days abstinent
- Decreases cravings
- Lack of compliance associated with relapse
- Limited effects of opioids (if needed)
- Typical dose is 50 mg po daily or 380 mg IM once monthly

Acamprosate (Campral)

- Resembles GABA and glutamate, but affects many neurotransmitters
  - Acts on GABAergic receptors, but primarily modulates glutamate receptors
  - Glutamate modulator and/or weak partial NMDA antagonist
- More effective given initially after detox (<4 days)
- Data is mixed
  - COMBINE trial (big, multi-site) showed no benefit above placebo
  - European studies show benefit for those already abstinent who maintained abstinence
  - US trials included patients still drinking, Euro studies already detox'd
- Best candidates for treatment
  - Higher baseline motivation; more severe dependence
  - Post detox or in early protracted withdrawal phase
- Well tolerated; diarrhea main side effect
- Adherence a concern – two big 333 mg caps three times daily
- Renally cleared – consider for patients with severe liver impairment

Acamprosate vs Naltrexone

Addiction
MONOGRAPH
doi:10.1111/j.1360-0443.2012.04054.x

Meta-analysis of naltrexone and acamprosate for treating alcohol use disorders: when are these medications most helpful?

Natalya C. Maisel[1], Janet C. Blodgett[1], Paula L. Wilbourne[1], Keith Humphreys[1,2] & John W. Finney[1,2]

- Maintenance of abstinence?
  - Acamprosate had a significantly larger effect size
- Reduction of heavy drinking and craving?
  - Naltrexone had a larger effect size
- Detox or abstinence before starting?
  - Both are better
  - For naltrexone, larger effect sizes for abstinence maintenance and reduced heavy drinking
  - For acamprosate, better abstinence outcomes
- Men vs Women?
  - Acamprosate effective for abstinence and no heavy drinking in both
  - Naltrexone maybe less effective in women

Alcohol Clin Exp Res. 2017 March ; 41(3): 466–472. doi:10.1111/acer.13313.

A Systematic Review of Naltrexone for Attenuating Alcohol Consumption in Women with Alcohol Use Disorders (AUD)

Shantrel S. Canidate, BS, MPH[1], Giselle D. Carnaby, PhD, MPH, CCC-SLP[1,4], Christa L. Cook, PhD, MSN, RN, APHN-BC[2], and Robert L. Cook, MD, MPH[1,3]

Alcoholism: Clinical and Experimental Research
Vol. 36, No. 3
March 2012

Acamprosate for Alcohol Dependence: A Sex-Specific Meta-Analysis Based on Individual Patient Data

Barbara J. Mason and Philippe Lehert

Disulfiram (Antabuse)

- Inhibits aldehyde dehydrogenase (not alcohol dehydrogenase)
  - Acetaldehyde builds up →sweating, nausea/vomiting (N/V), flushing, tachycardia, shortness of breath (SOB), hypotension, hyperventilation, headache
  - In severe reactions, arrhythmias, MI, seizure, and death can occur
  - At high doses (above typical for AUD), concern for psychosis
- Rare liver failure
- Considered an aversive medication
  - Takes the medication and avoids alcohol to avoid the symptoms above
- Typically 125-500 mg per day – considered safe and well tolerated
- Approved 1949, first trial – 1986!!
  - Trials show mixed results
  - Adherence is a significant barrier; supervised administration works better
  - Best in older men with severe drinking, socially stable, attending AA

Topiramate (Topamax)

- Used for epilepsy, migraines
- Augments GABA function; inhibits glutamatergic pathways
  - This combo decreases dopaminergic activity; possibly decreases alcohol reward
- Started without initial period of abstinence
- In two major trials, reduced heavy drinking/drinks per drinking day, increased percent days abstinent
- Similar efficacy to naltrexone in head to head trials
- Side effects include mild cognitive impairment (“Dopamax”), kidney stones, headache, depression, paresthesias, dizziness
- Must start at a low dose and titrate upwards over a few weeks
  - Usually start 50 mg/day, increase to 150 mg twice daily

Other Meds for AUD

Gabapentin (Neurontin)

- Small trials support use for AUD
- Increased rates of abstinence, decreased heavy drinking
- Typically 900-1800 mg/day, but can go higher
- Well tolerated; some dizziness and sedation

Baclofen

- 30 mg/day, but higher dose of 60 mg/day may be more effective
- Higher rates of abstinence in some trials; others no difference
- Well tolerated; some nausea, vertigo, sleepiness

Case Vignette: Alcohol Use Disorder

A 45-year-old man presents to your clinic stating he wants to cut back on his drinking. He currently drinks 8-10 beers every evening and has found it difficult to stop despite problems it's causing with his spouse. He has strong cravings for alcohol, especially in the evening. His goal is to reduce his heavy drinking days, but he is not confident he can maintain complete abstinence at this time. He has no other medical or psychiatric conditions.

Question: Which FDA-approved medication would be most appropriate to help this patient reduce the frequency and intensity of his drinking?

Answer: Naltrexone.

Explanation: Naltrexone is an opioid antagonist that reduces the rewarding effects of alcohol. It is highly effective in **reducing the risk of relapse to heavy drinking** and decreasing cravings, which aligns perfectly with this patient's goals. Acamprosate is generally more effective for individuals who are already abstinent and are seeking to maintain that abstinence. Disulfiram is an aversive medication that requires complete abstinence and is best for highly motivated, socially stable individuals.

The Future of AUD Treatment???

- Ketamine?
- “Psychedelics”?
  - Psilocybin
  - MDMA
  - LSD
- Neuromodulation?

Ketamine

Of interest because of its possible mechanism of action

- As an NMDA receptor antagonist → increase in glutamate
  - Then further receptor activation that modulate signaling pathways that influence the limbic system and prefrontal cortex
- Hypotheses:
  - Impact the dopaminergic pathways of the mesolimbic reward pathway, possibly through the opioid system
  - Produce synaptic improvements with synaptogenesis and spine formation in the prefrontal cortex

- KARE Trial (Grabski et al., 2022)
  - The ketamine groups had a significantly higher percentage of days abstinent (**86-87%**) compared to the placebo groups at a 6-month follow-up.

Just say No

What are we asking of them?

To exert an athletic level of discipline and sustained determination

without much training or experience

in behavioral self-control

that is fully counter to their neurobiological drives

often supported only by fear incentives (loss of work, relationships, health)

Fear incentives may be effective in the short term in times of crisis, but…

Positive incentives such as

purpose financial security meaningful work relationships

Avoid the natural fatigue of sustaining long-term recovery from substance use disorders

McKay JR: Making the hard work of recovery more attractive for those with substance use disorders. **Addiction** 2017; 112:751–757

Q & A Session

Thank You!

The End

Please let me know directly anything I can do to improve this lecture or your knowledge of SUD's: cmarienfeld@health.ucsd.edu

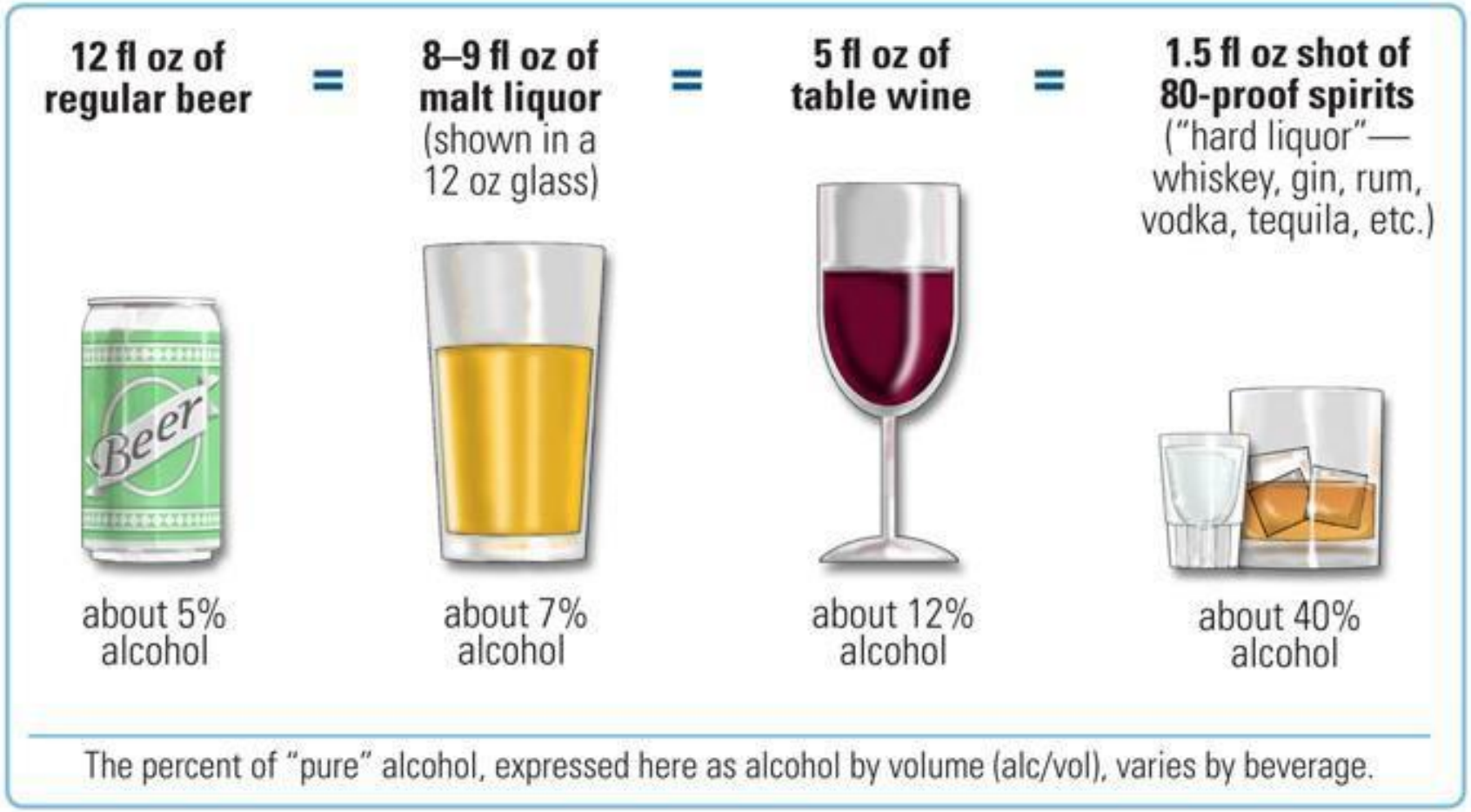
Also… please do a quick evaluation

-less than 1 minute

-VERY helpful for promotion

https://ucsd.co1.qualtrics.com/jfe/form/SV_3vDsB11w86WXazX

One Standard Drink



National Institute on Alcohol Abuse and Alcoholism (NIAAA). What Is A Standard Drink? | National Institute on Alcohol Abuse and Alcoholism (NIAAA) (nih.gov). Accessed 10/28/24.

Recommendations for Use

	ASSIGNED **FEMALE** AT BIRTH	ASSIGNED **MALE** AT BIRTH
DAILY *NO MORE THAN*		
WEEKLY *NO MORE THAN*		

- **Avoid** alcohol if:
  - Taking medications that can interact with alcohol
  - Have medical conditions that can be exacerbated by drinking
  - Recovering from AUD or unable to control the amount consumed
  - Plan to drive or participate in activities requiring mental alertness
  - Pregnant or might be pregnant
  - Younger than 21 years old

U.S. Department of Agriculture and U.S. Department of Health and Human Services. Dietary Guidelines for Americans, 2020-2025. 9th Edition, Washington, DC; 2020. Accessed 10/28/24.

Alcohol Use Disorder Screens

- NIAAA Single Alcohol Screening Question (SASQ)
  - How many times in the past year have you had ≥ 4-5 drinks in a day?
    Scores > 0 are positive
- Alcohol Use Disorders Identification Test- Consumption (AUDIT-C)

1. How often do you have a drink containing alcohol?					SCORE
Never (0)	Monthly or less (1)	Two to four times per month (2)	two or three times per week (3)	Four or more times per week (4)	
2. How many drinks containing alcohol do you have on a typical day when you are drinking?					
0-2 drinks (0)	3 or 4 drinks (1)	5 or 6 drinks (2)	7 to 9 drinks (3)	10 or more drinks (4)	
3. How often do you have six or more drinks on one occasion?					
Never (0)	Less than monthly (1)	Monthly (2)	Weekly (3)	Daily or almost daily (4)	
TOTAL SCORE *Add the number for each question to get your score.*					

Scores > 3 (women) or > 4 (men) are positive