

North Dakota Medical Association

10/4/19



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Disclaimer



- Nothing to declare, nothing to hide...



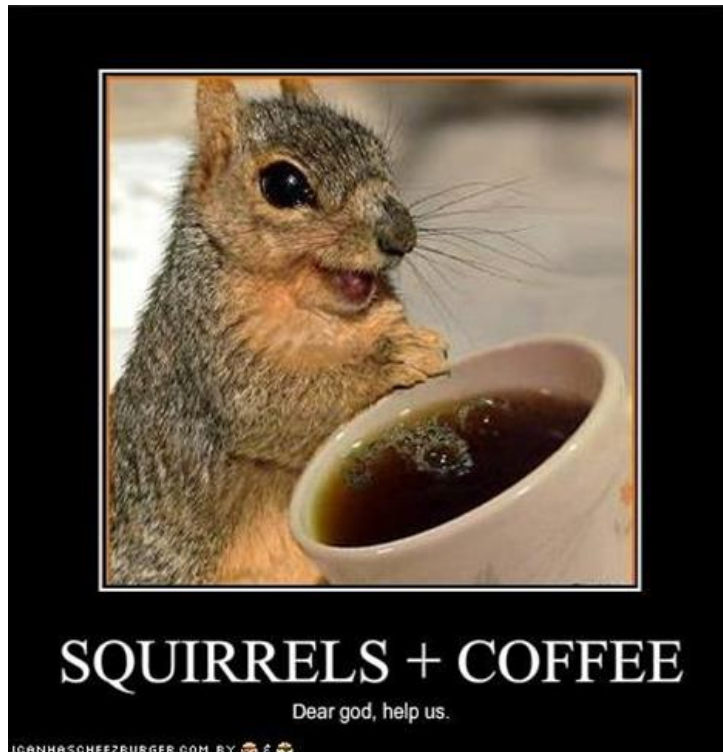
After the presentation, the participant should be able to:

- Describe general criteria used in diagnosing substance use disorders
- Understand the impact of substance misuse and substance use disorders on individual and population health
- Describe available treatments for substance use disorders.

- **Brief** overview...
- Won't be discussing: Physicians and substance use issues
- Will be emphasizing marijuana use issues

First, a question!

- What is the most widely abused substance in the world?



The Onset of “Addiction”



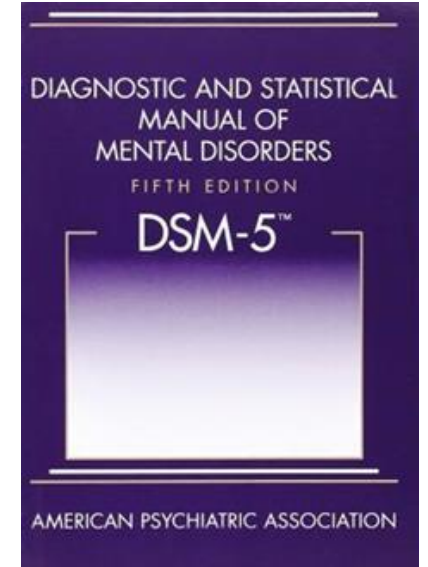
- Genetics
- Chippers vs “Addicts”



Formal Diagnosis



- Symptoms
- Time
- Impact
- Differential



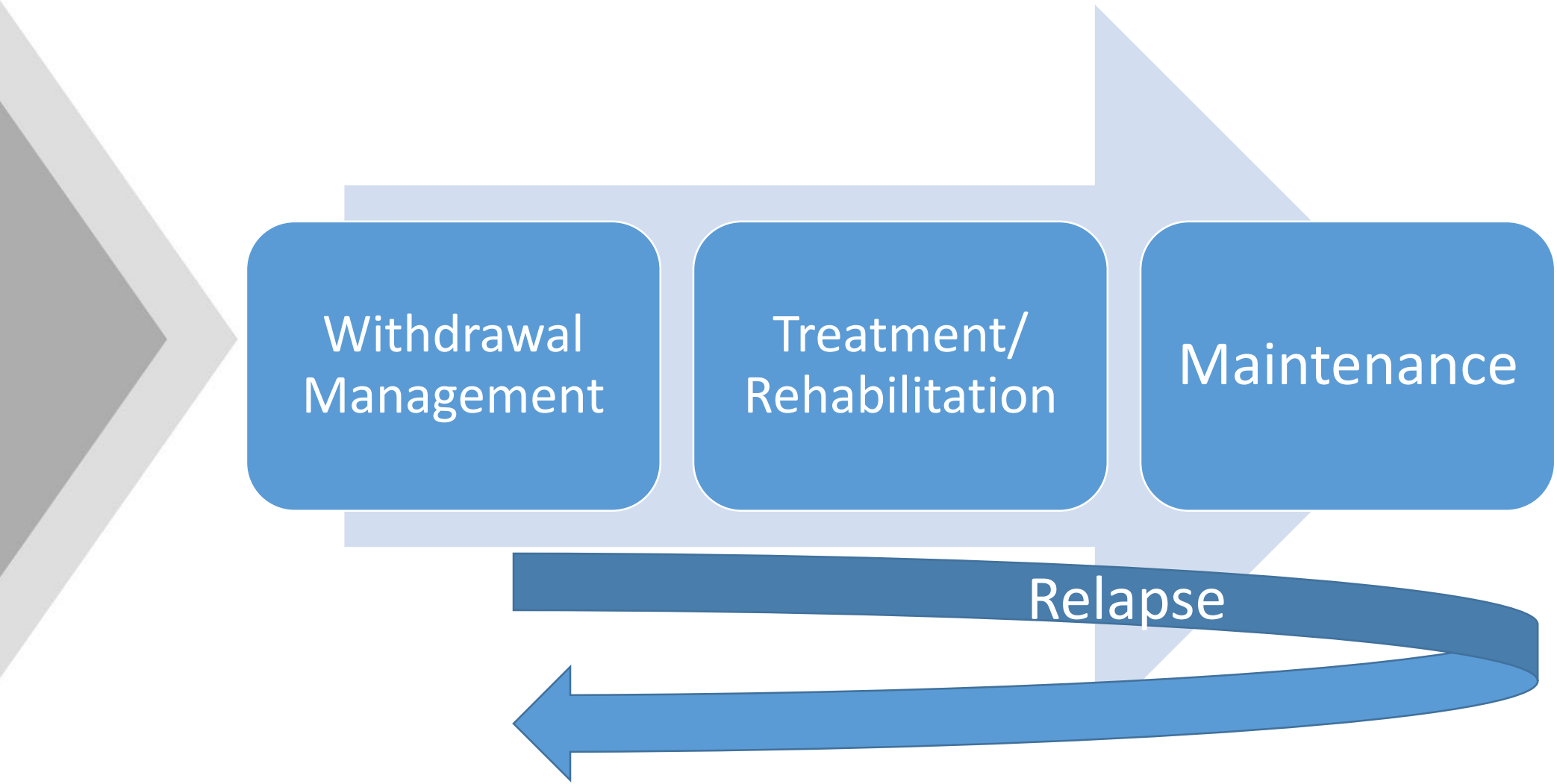
Example-Substance X

Pattern of use, number of concerns (>2), time-frame (within a 12 month period), length of remission/maintenance

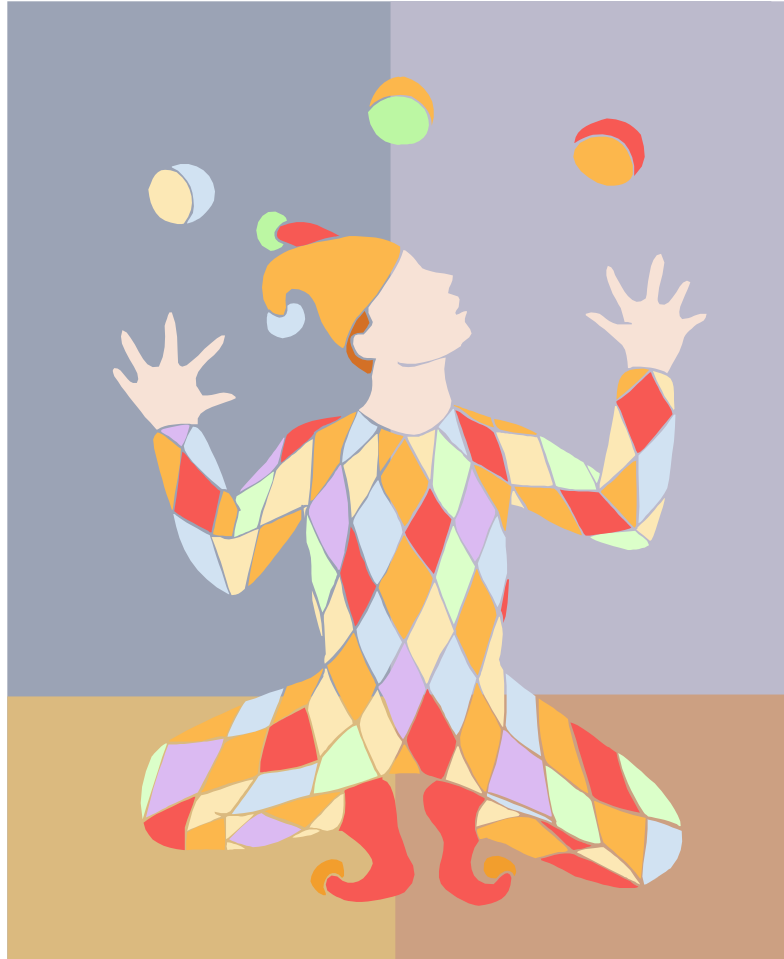


1. Larger amounts used, or for longer than intended
2. Can't cut down/control use
3. Focus/time spent on obtaining drug or recovering
4. Craving
5. Recurrent issue with fulfilling obligations/roles due to use
6. Using despite ongoing problems re: above
7. Important activities are given up/reduced (social, occupational, etc...)
8. Recurrent use despite physical hazards
9. Recurrent use despite medical/psychological impact from use
10. Tolerance
11. Withdrawal

Substance Use Disorders Continuum



Comorbidity is the rule



General Categories



- Depressants (alcohol, benzodiazepines, barbiturates, etc...)
- Opioids (prescription pain meds, heroin, codeine, methadone, buprenorphine...)
- Stimulants (amphetamines, cocaine, methylphenidate, as well as caffeine, nicotine, etc...)
- Cannabinols
- New Psychoactive Substances (Synthetics)
- Hallucinogens
- Inhalants

Reward System

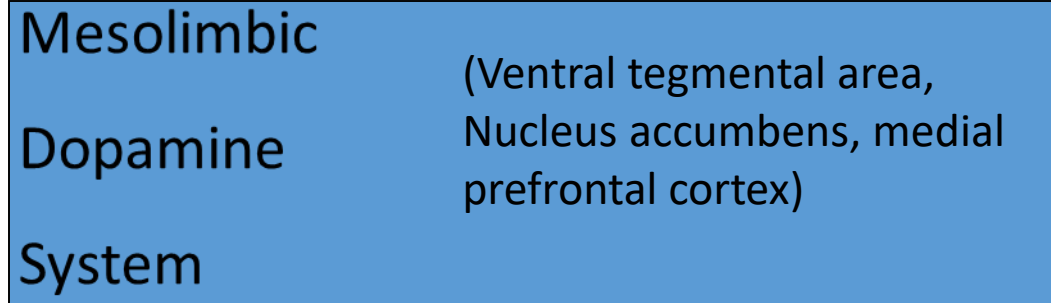


Alcohol (depressant)

GABA receptor
NMDA receptor

Cocaine (stimulant)

Monoamine
transporters



Opioid receptors

Morphine (opioid)

Depressants



(alcohol, benzodiazepines, barbiturates, etc...)

- High: Silly, laid back. Occasionally disinhibition
- Decrease in anxiety
- Decrease in blood pressure, temperature. At high doses, respiratory depression.
- Sedation, dysarthria, ataxia
- Muscle relaxation
- Overdose: Dangerous

Withdrawal

- More or less, opposite of intoxication symptoms.
- With alcohol, also risk of convulsions, delirium tremens.



Alcohol. What is “a drink?”



- Beer: 12 fluid ounces (355 milliliters)
- Wine: 5 fluid ounces (148 milliliters)
- Distilled spirits (80 proof):
1.5 fluid ounces (44 milliliters)



Drinking levels—risk?



- “Low risk,” per the National Institute on Alcohol Abuse and Alcoholism:

For women: (or men > 65) No more than 3 drinks on any single day
No more than 7 drinks per week

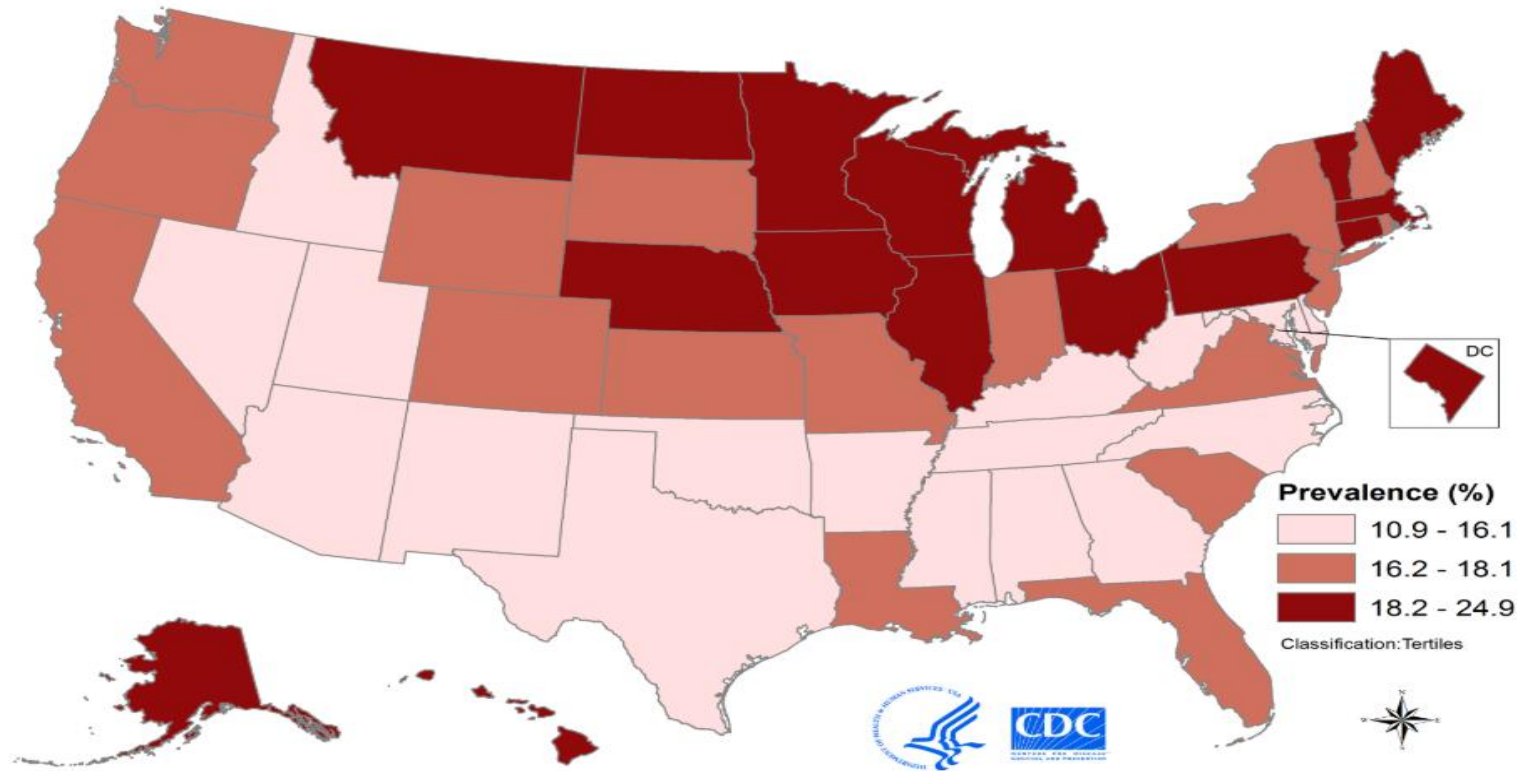
For men: No more than 4 drinks on any single day
No more than 14 drinks per week.

Risk of alcohol use disorder within this group: 2/100

Percent of Population



Prevalence of Binge Drinking Among US Adults, 2015



alcohol
use that
brings
the BAC
up to
0.08
g/dL in
about 2
hours

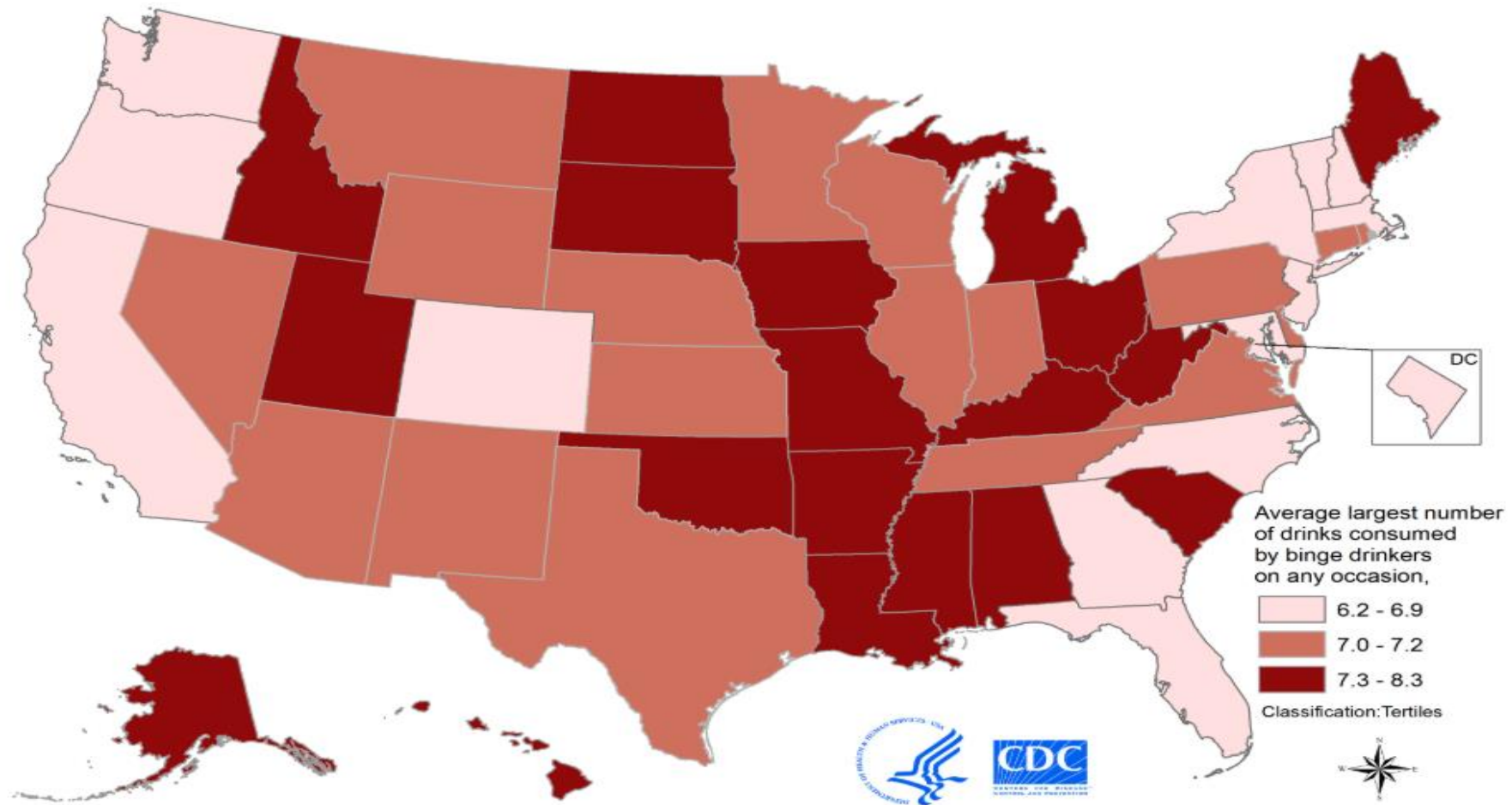
Note: Age-adjusted to the 2000 US Census standard population. Binge drinking is defined as 4 or more drinks for a woman or 5 or more drinks for a man on an occasion during the past 30 days.

Source: Behavioral Risk Factor Surveillance System.

Average number of drinks when binge drinking...



Intensity of Binge Drinking Among US Adults, 2015



Binge Drinking, 2018



1. North Dakota

- Adults drinking excessively: 24.7%
- Alcohol-related driving deaths: 46.7% (the highest)
- Adults in fair or poor health: 13.4% (9th lowest)
- Drunkest metro area: Fargo, ND-MN

The state with the highest share of adults drinking excessively is North Dakota, with nearly 25% of adults reporting binge drinking or drinking heavily. Not surprisingly, the state with the highest drinking rate also has the highest rate of alcohol-related driving deaths. A total of 46.7% of all roadway fatalities are attributable to alcohol consumption, much higher than the national share of 30%.

“Misuse”



- Excessive drinking can increase the risk of serious health problems, including:
 - Certain cancers, including breast cancer and cancers of the mouth, throat, esophagus and liver
 - Pancreatitis
 - Sudden death if you already have cardiovascular disease
 - Heart muscle damage (alcoholic cardiomyopathy) leading to heart failure
 - Stroke
 - High blood pressure
 - Liver disease
 - Suicide
 - Accidental serious injury or death
 - Brain damage and other problems in an unborn child
 - Alcohol withdrawal syndrome

Stimulants



Stimulants

- INTAKE
- Oral
- Snorting
- Smoking
- Injection



- Intoxication: “rush”, euphoria, decreased sleep, appetite, increased stereotypic behavior. Paranoia may occur. Increased pulse, BP, temp. Risk of stroke.
- Withdrawal: opposite symptoms- Crash. Peaks in couple of days, over by day five. But lingering symptoms such as moodiness, cognitive difficulty . High relapse risk. Cues, euphoric recall.

- Telescoping/Compression
- Physical
- Mental
- Social



"It's just a simple Rorschach ink-blot test. Mr. Bromwell, so just calm down and tell me what each one suggests to you."

Methamphetamine



- In addition: Easy to make
- Scarring (crank bugs)
- Increased risk for STDs
- Dental complications
- Tweaking (Run)
- The Wall (roughly half a year)
- Cognitive difficulties might last months, sometimes indefinitely
- Psychosis....

Misuse of stimulants



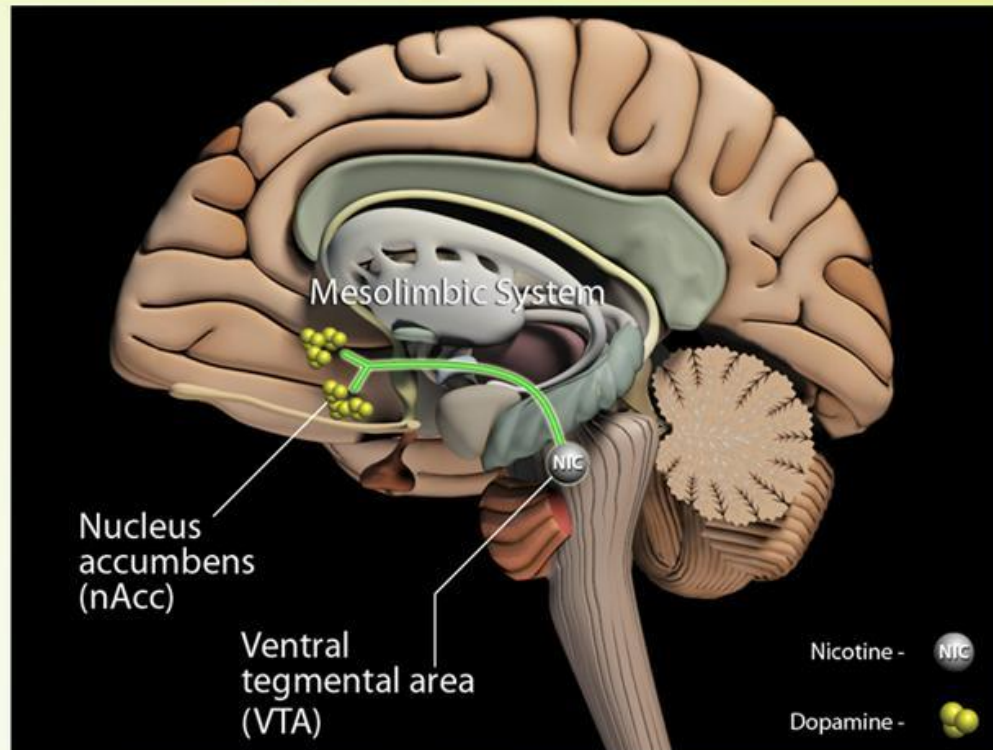
• Study of college-age students' reasons for illicit use:

- Improve concentration: 28.8%
- Increase alertness 23.4%
- Get high 6.3%
- Control appetite 4.2%
- Lose weight 3.6%
- Enhance exercise 2.6%
- Counteract other drugs 2.1%
- Experiment 1.2%

Risks (not all-inclusive)

- Tachycardia
- Hypertension
- Stroke
- Anxiety
- Agitation
- Confusion
- Paranoia

Mechanism of Action of Nicotine in the Central Nervous System



- Nicotine binds predominantly to nicotinic acetylcholine (nACh) receptors in the CNS; the primary is the $\alpha 4\beta 2$ nicotinic receptor in the Ventral Tegmental Area (VTA)
- After nicotine binds to the $\alpha 4\beta 2$ nicotinic receptor in the VTA, it results in a release of dopamine in the Nucleus Accumbens (nAcc) which is believed to be linked to reward

A highly addictive substance

Nicotine



Quitting is obviously good. However...

Know what medication or over-the-counter substances people taking when planning/starting tobacco/nicotine cessation

Nicotine (and Caffeine) stimulate 1A2 liver enzyme system:

Common substrates: *

Amitriptyline, Theophylline, Warfarin, Propranolol, Olanzapine, Clozapine

Inhibitors: fluvoxamine, grapefruit juice, quinolones

Additional inducers: omeprazole, phenobarbital, phenytoin, rifampin

Long-term and short-term benefits to quitting smoking

After quitting for:

20 minutes

An individual's heart and blood pressure decrease.

2-3 weeks

Circulation and lung functionality improve.

1 year

The risk of coronary heart disease and heart attack is reduced.

10 years

The risk of mortality from lung cancer is 50% less likely compared with a current smoker's risk. Pancreas and larynx cancer risks are also decreased.

12 hours

The body's carbon monoxide levels return to healthy levels.

1-9 months

Lungs continue to improve and heal, reducing coughing and shortness of breath.

5 years

The risk of mouth, throat, esophagus and bladder cancer are decreased by half. The risk of cervical cancer and stroke decline to that of a nonsmoker.

15 years

The risk of coronary disease equates to that of a nonsmoker's.

What about Vaping?



- A moving target...
- NEJM published British study showed:
 - **Tobacco free after 1 year using e-cigarettes: (Not FDA approved)**
 - People who try to quit on own- 3% successful
 - People using nicotine patches, gum, etc... 10% successful
 - People using e-cigarettes... 18% successful

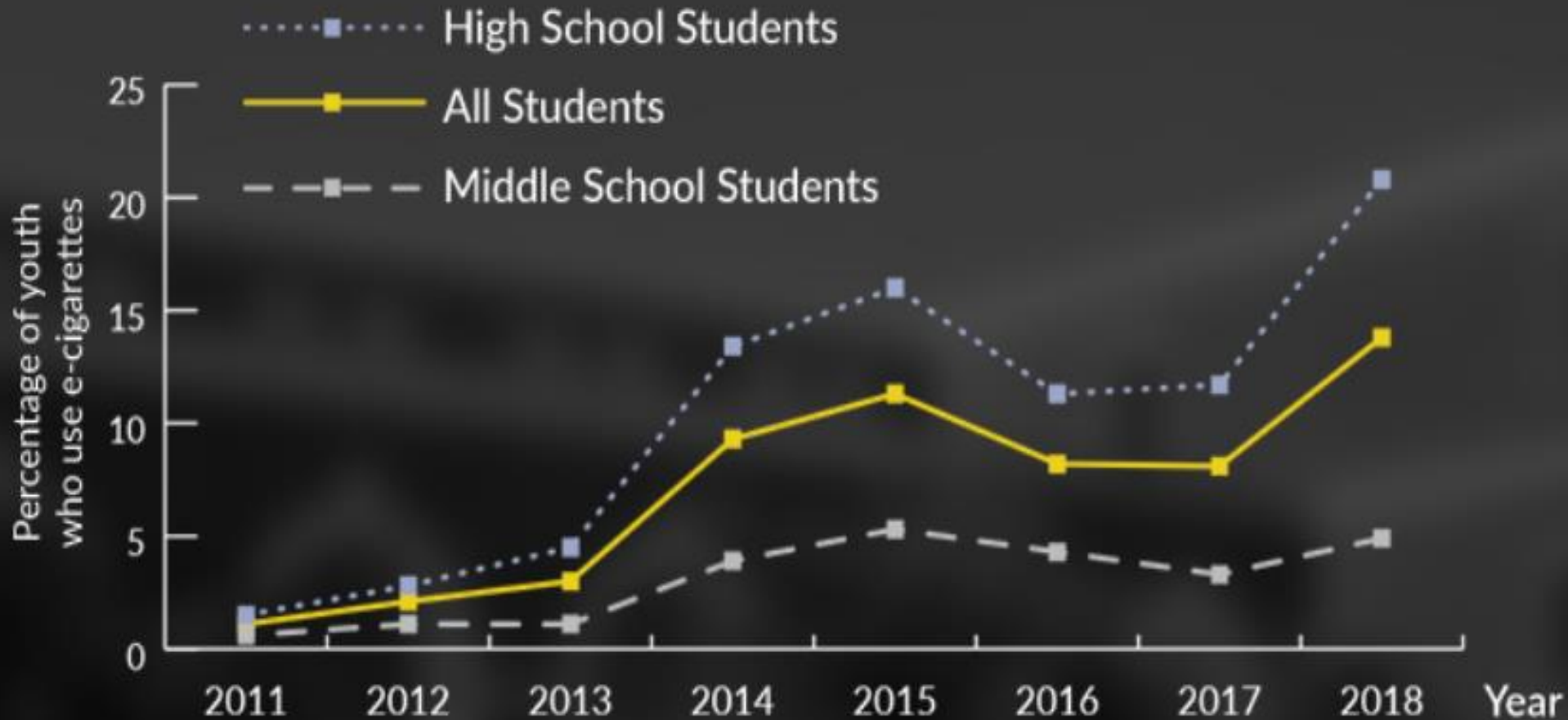
Risks:

- Nicotine is toxic: with e-cigs you can increase nicotine concentration by cartridges or voltage
- Cardiovascular concerns
- Vape burns can occur
- Addiction

Vaping and youth



Growth in E-Cigarette Use



Estimated at least 40% never smoked cigarettes prior to vaping

Source: National Youth Tobacco Survey 2011-2018

However...



- Well publicized recent lung problems associated with vaping.
 - “No common thread” (FDA Director for Tobacco Products-9/26/19)
 - Many involve THC use, but not all (some CBD, some nicotine).
 - Many, but not all, involve illicit cartridges.
 - While damage originally was thought to be similar to lipoid pneumonia, with vitamin E acetate a potential contributor; Mayo autopsy study indicates chemical injury, not oil, may be cause.

Caffeine-DSM 5 research diagnosis...

Caffeine: A socially acceptable psychoactive drug...

➤ Avg. US consumption 300mg per day (2-4 cups)

- Over 400mg per day linked with insomnia, irritability, tachycardia, migraine headache, restlessness, frequent urination, G.I. upset, tremors. (Mayo Clinic)
- Arrhythmias can occur
- Rare--seizures

Caffeine Comparisons



8.4 FL OZ

FILTER COFFEE

90 mg

RANGE: 69–127 MG

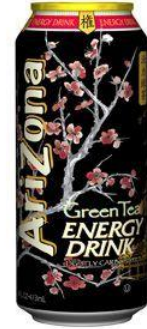


8.4 FL OZ

BLACK TEA

63 mg

RANGE: 26–116 MG



16 FL. OZ

Green Tea Energy

200 mg

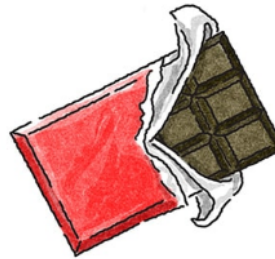


8.4 FL OZ

INSTANT COFFEE

79 mg

RANGE: 63–90 MG



40G

DARK CHOCOLATE

28 mg

RANGE: 7-49MG



16 FL. OZ

Cold Brew Coffee

200 mg



8.4 FL OZ

COCOA BEVERAGE

6 mg

RANGE: 3–34 MG



12 FL OZ

COLA DRINK

40 mg

RANGE: 30–60 MG



12 FL. OZ

113 mg

What are opioids?



- Opiates- drugs derived from opium.
- Opioids- term previously used to describe synthetic opiates.
- Now it is common to refer to all as “opioids.”



Opioids



Rush of euphoria, tranquility, then drowsiness, mood changes, mental clouding, motor slowing.

Constipation

Overdose: respiratory collapse

Coma

(potent effects on brainstem and spinal cord)



How is opioid misuse a different type of problem than misuses of other substances?



- The good news- withdrawal is usually not potentially life-threatening, as opposed to withdrawal from alcohol, some CNS depressants
- Depending on supply and demand, some individuals cycle from prescription misuse to street use.
- Bad news- for unknown quantities (particularly with heroin, “counterfeit” pills, and synthetic analogues/fentanyl) one time use can result in death. In other words, a person might not even have time to become “addicted...”

Cannabis

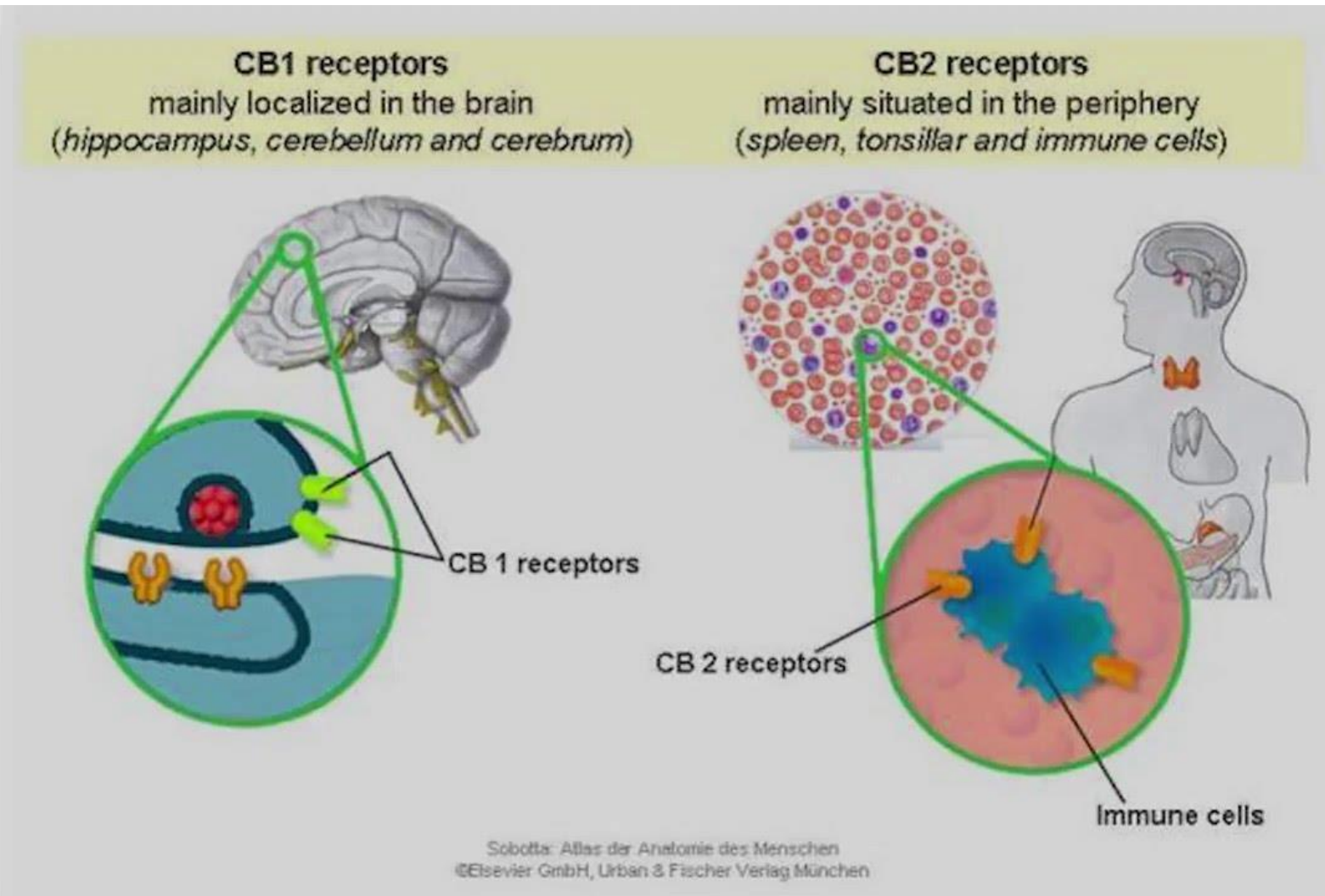


Marijuana refers to the dried leaves, flowers, stems, and seeds from the *Cannabis sativa* or *Cannabis indica* plant.



- There are hundreds of compounds in marijuana

CB1/CB2

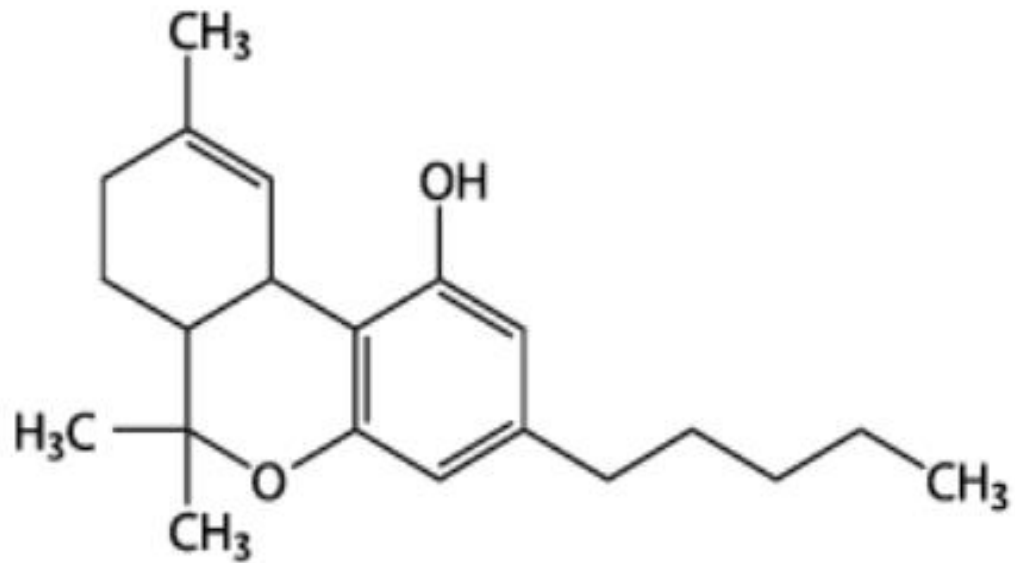


Marijuana

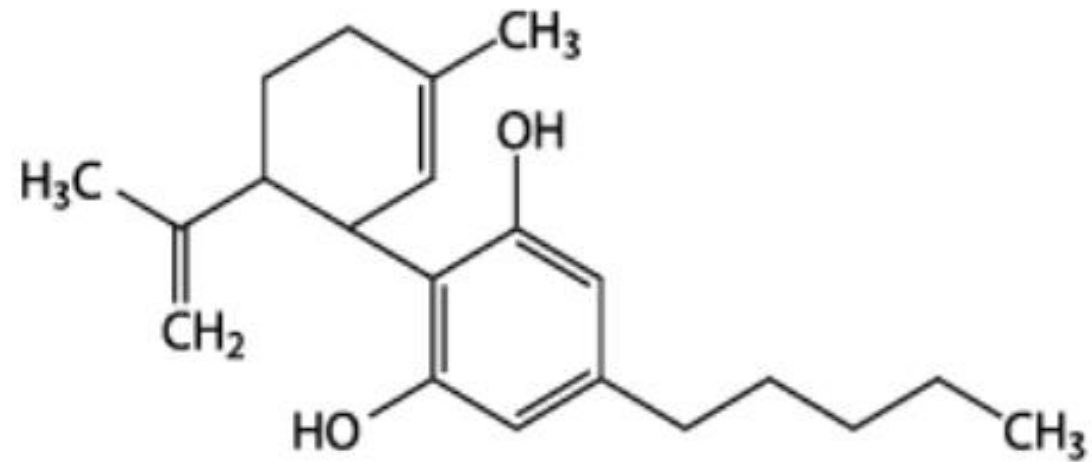


- Can have both stimulant and sedative properties.
- Antiemetic properties*
- Anticonvulsant effects
- Muscle-relaxing effects
- Reduction of intraocular pressure

THC vs CBD



Tetrahydrocannabinol



Cannabidiol

THC vs. Cannabidiol (CBD)



• THC

- Dronabinol as Marinol
- Approved for AIDS associated anorexia or treatment-resistant nausea/vomiting secondary to cancer chemotherapy

Synthetic THC analogue

Nabilone as Cesamet

“last resort” chemotherapy anti-emetic

• CBD

- FDA Approved as Epidiolex for:
- Lennox-Gastaut Syndrome and
- Dravet Syndrome

THERAPEUTIC EFFECTS

In adults with chemotherapy-induced nausea and vomiting, oral cannabinoids are effective antiemetics.

In adults with chronic pain, patients who were treated with cannabis or cannabinoids are more likely to experience a clinically significant reduction in pain symptoms.

In adults with multiple sclerosis (MS)-related spasticity, short-term use of oral cannabinoids improves patient-reported spasticity symptoms.

For these conditions, the effects of cannabinoids are modest; for all other conditions evaluated, there is inadequate information to assess their effects.

2017

CANCER

The evidence suggests that smoking cannabis does not increase the risk for certain cancers (i.e., lung, head, and neck) in adults.

There is modest evidence that cannabis use is associated with one subtype of testicular cancer.

There is minimal evidence that parental cannabis use during pregnancy is associated with greater cancer risk in offspring.

CARDIOMETABOLIC RISK

The evidence is unclear as to whether and how cannabis use is associated with heart attack, stroke, and diabetes.

RESPIRATORY DISEASE

Smoking cannabis on a regular basis is associated with chronic cough and phlegm production.

Quitting cannabis smoking is likely to reduce chronic cough and phlegm production.

It is unclear whether cannabis use is associated with COPD, asthma, or worsened lung function.

- See Surgeon General's report
- <https://www.hhs.gov/surgeongeneral/reports-and-publications/addiction-and-substance-misuse/advisory-on-marijuana-use-and-developing-brain/index.html>
- Article on adolescent use: threshold age 17...
- Renard et al...Front. Neurosci., 10 November 2014

Absorption and bio-availability



- **Smoking or vaporizing** allows for pulmonary first-pass metabolism with direct systemic blood stream absorption across lung lining. THC bio-availability ~ 30%
- Similarly, **sublingual** (i.e., use of oils, etc...) absorption also avoids first-pass metabolism, with slightly less rapid absorption than above. Bio-availability~20%?
- **Edible** use-absorbed via intestinal mucosa and transported to the liver and metabolized prior to reaching other organs, such as the brain. THC bio-availability ~10%
- Only about 1% of administered TCH dose reaches the brain.
- **However**-THC variability in marijuana plants can range from 0.3-30% or higher

Some Psychoactive effects of THC



Acute effects:

Usually temporary and reversible, and do not present a risk of harm (outside of risk of activities when intoxicated).

Pleasant: Euphoria and relaxation.

Sleepiness

Unpleasant:

Anxiety

Paranoia/Psychotic symptoms, depending on genetic and vulnerability characteristics

Study of Canadian medical marijuana users



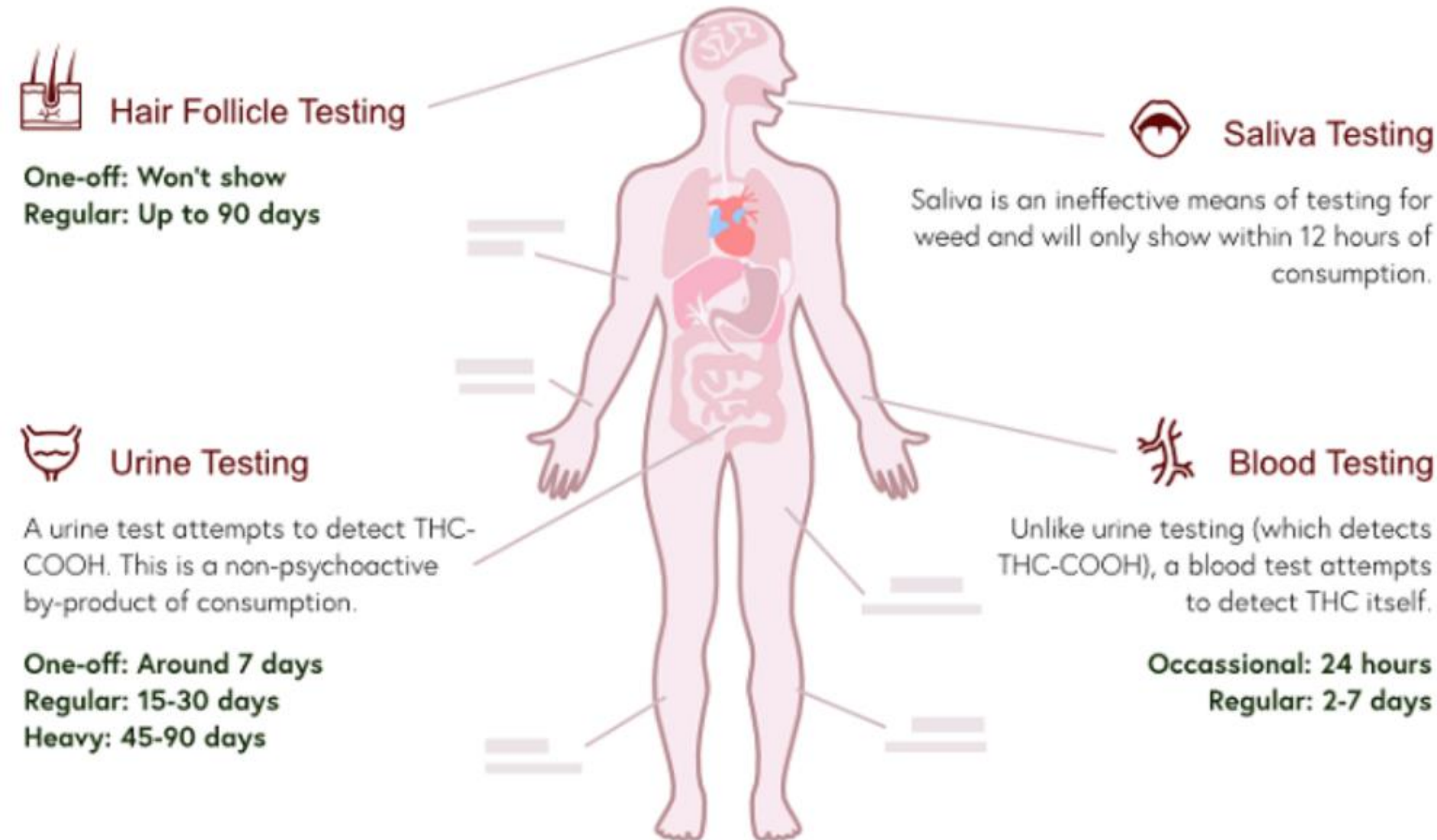
- Subjective acute reduction in anxiety, depression and stress
- Subjective increase in depression over time

Edible vs. inhaled and ER visits



- Colorado study-approx. 10,000 patients
- While cannabinoid hyperemesis syndrome was twice as likely with inhaled vs. ingested cannabis, the opposite was true for acute psychiatric symptoms, intoxication and cardiovascular symptoms.
- Cannabis-attributed presentations involving edible use-10%
- Edible Products as percent representation of state total cannabis sales:
 - 0.32%

Testing & Detection Methods

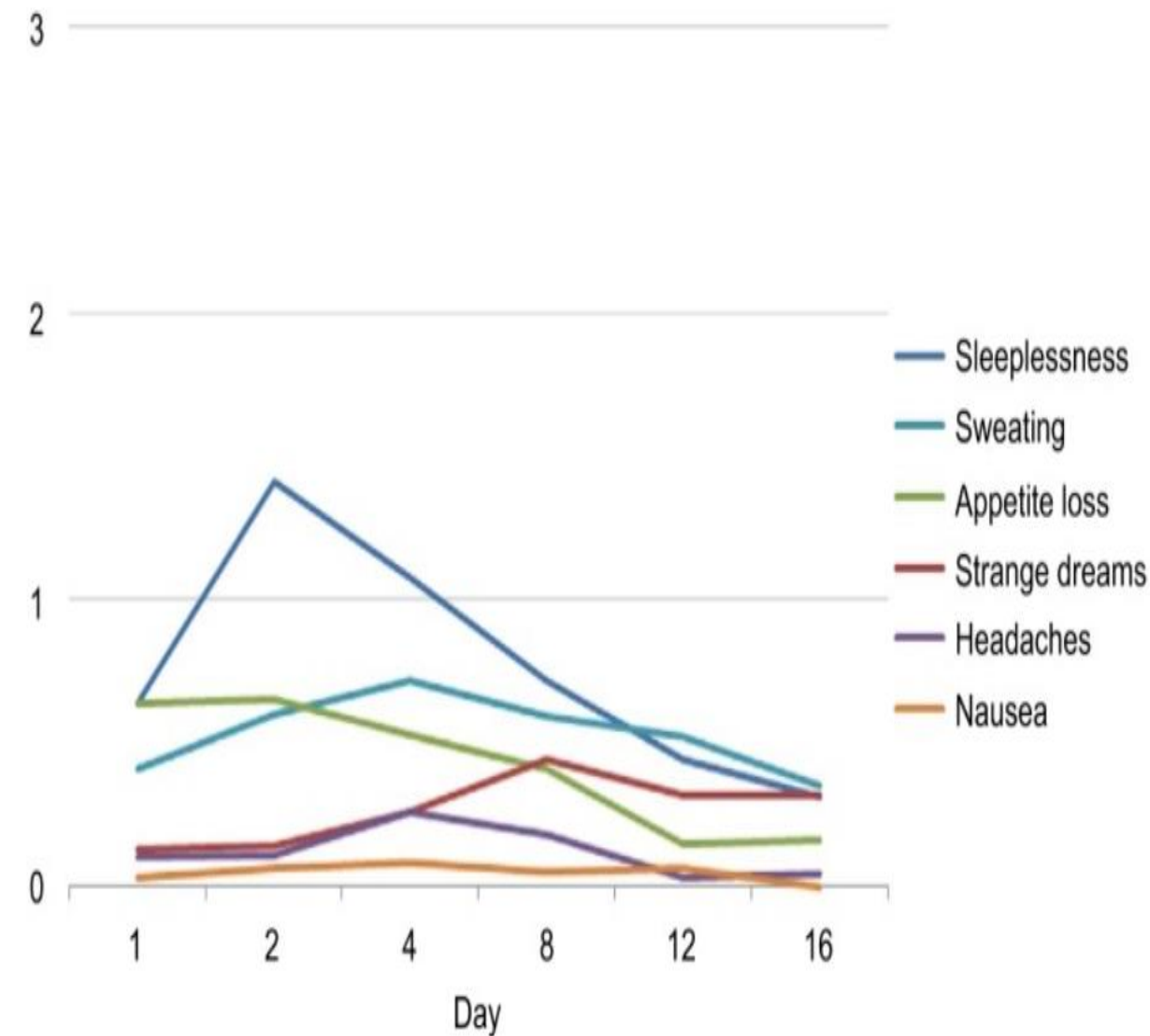
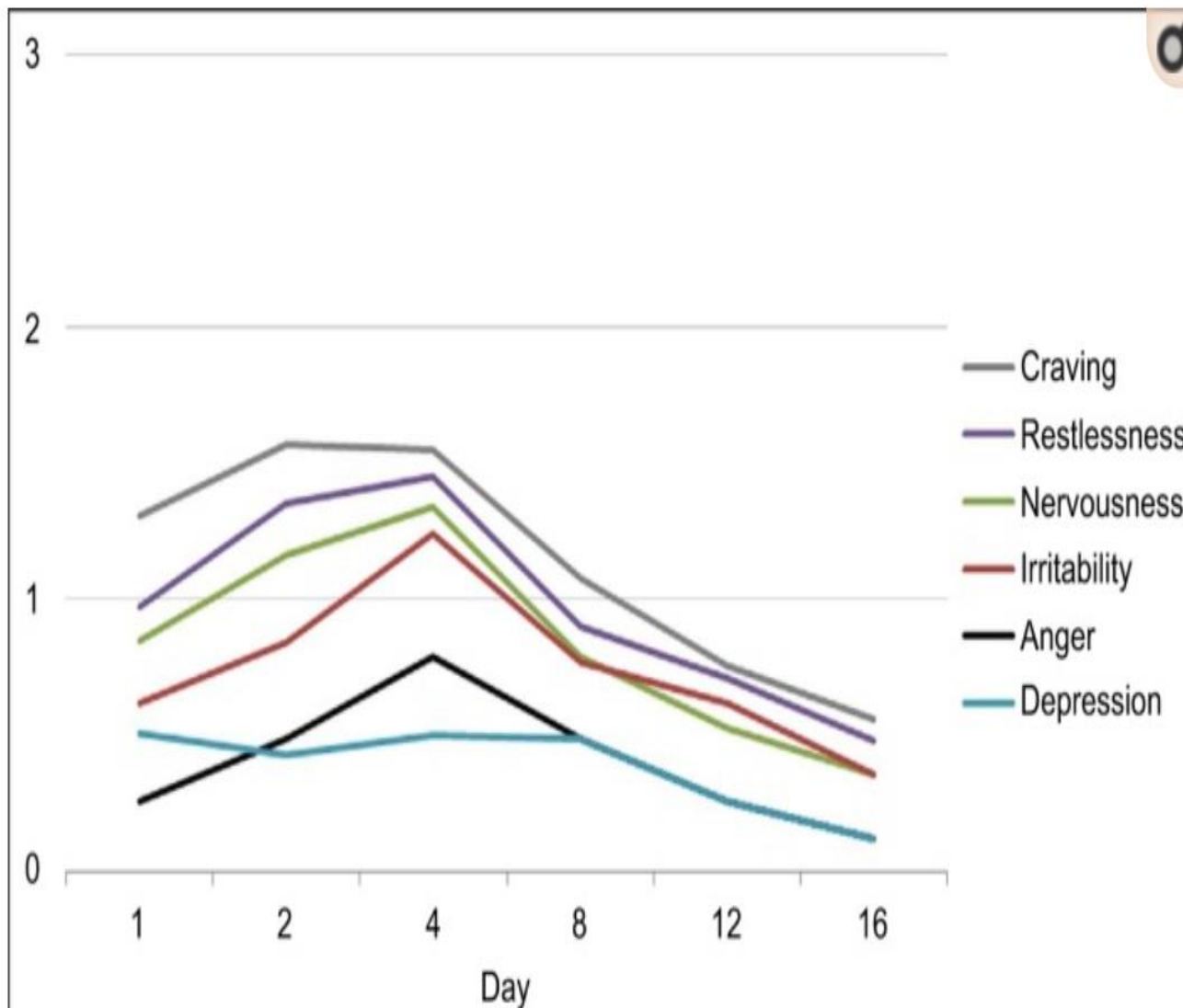


MANY individual factors will impact how long THC/metabolites will stay in the system

Cannabis Withdrawal Syndrome

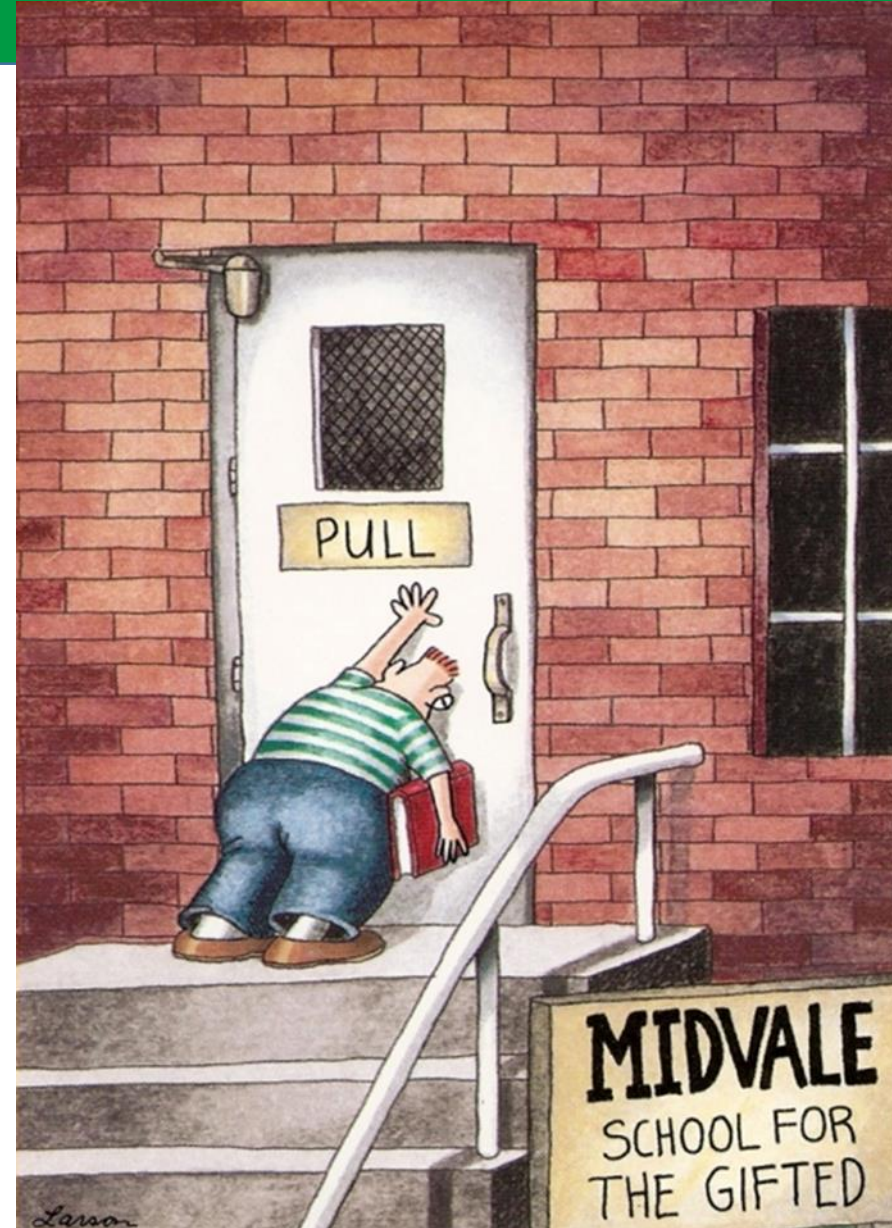
Bonnet and Preuss, [Subst Abuse Rehabil.](#) 2017; 8: 9–37

O= none, 1=mild, 2=moderate, 3=heavy



Formulations

- We have so much yet to learn...
- Are effects related to:
- THC/CBD ratio?
- THC/CBD strength?
- Sativa vs. Indica genomics?
- Terpenes?
- Other?



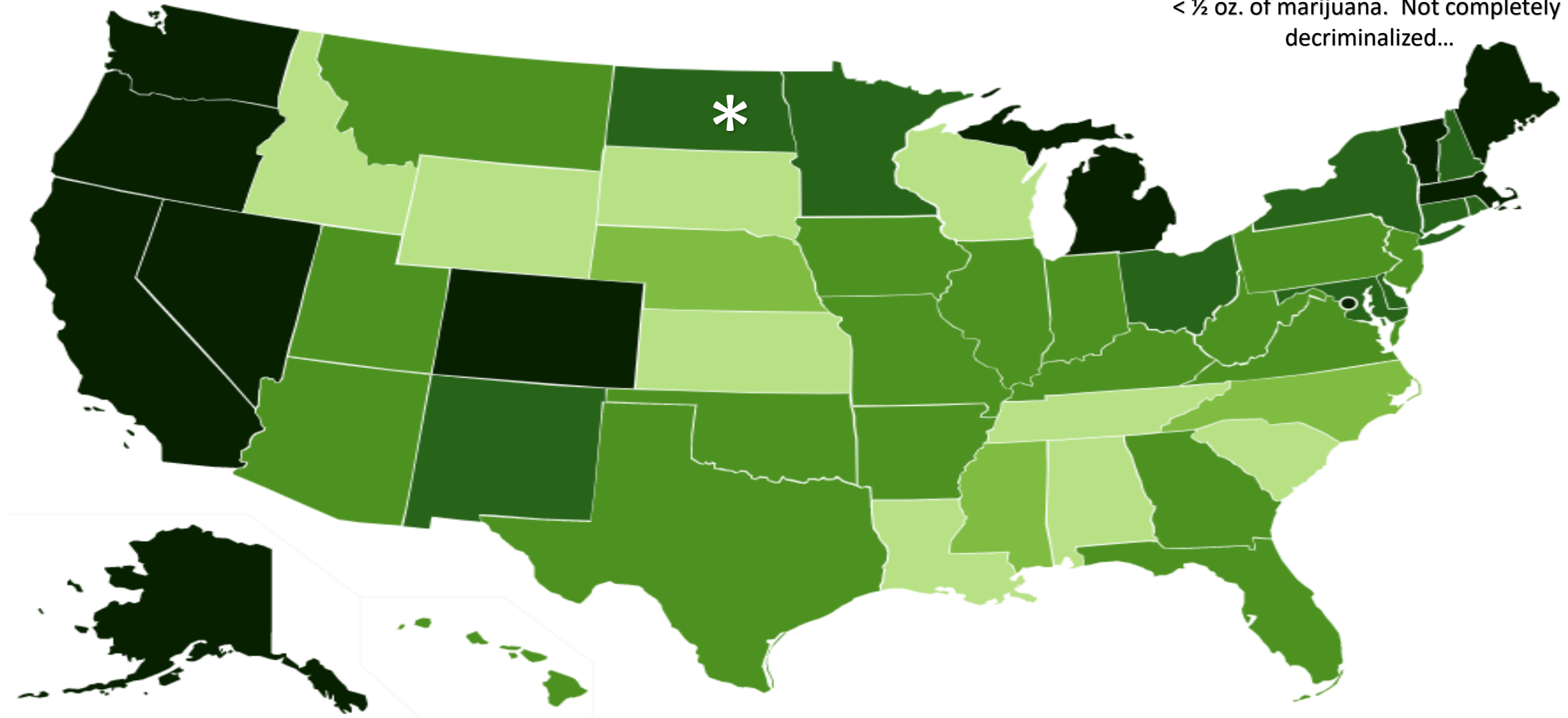
Marijuana Laws



Legalized Medical and decriminalized Medical Decriminalized Fully illegal



ND, infraction and fine for
< ½ oz. of marijuana. Not completely
decriminalized...



North Dakota Dispensaries



These are the qualifying condition under Measure 5 to get a North Dakota Medical Marijuana Card.

Qualifying conditions include:

- Cancer
- HIV/AIDS
- Hepatitis C
- ALS
- PTSD under certain circumstances
- Agitation of Alzheimer's disease
- Dementia
- Crohn's disease
- Fibromyalgia
- Spinal stenosis
- Chronic back pain (including neuropathy or damage to the nervous tissues of the spinal cord with objective neurological indication of intractable spasticity)
- Glaucoma
- Epilepsy
- A medical condition that produces cachexia or wasting, severe and debilitating pain that has not responded to previously prescribed medication or surgical measures for more than three months or for which other treatment options produced serious side effects
- Intractable nausea
- Seizures
- Severe and persistent muscle spasms

New Psychoactive Substances (NPS)

- Synthetic Cannabinoids (“K2,” “Spice”). Binds to CB1 receptors at five times the affinity of THC.
- JW Huffman, chemist and research developer: Likened using it to playing “Russian Roulette,” and that those who try it “must be idiots...”
- Synthetic Cathinones (“bath salts”) such as MDPV--synthetic derivative of khat. Excited delirium not uncommon.

Hallucinogens



Classic:

- 1) Serotonin-like
(indole alkylamines)
LSD, psilocybin, etc...
- 2) Resemble
norepinephrine/dopamine
(phenylalkylamines)
Mescaline

- Ecstasy “Molly,”
methylenedioxymethamphetamine
(MDMA) somewhat similar.
Unfortunately often adulterated

Dissociative:

Phencyclidine (PCP)

Ketamine

Dextromethorphan

Salvia

Hallucinogens-short term effects:



- Visual illusions, “trails” or “tracers”
- Expansive, “religious” sense
- “Trading senses” (synesthesia)
- Change in sense of time
- Depersonalization/derealization/
- Increased pulse, BP, temp
- Can approach delirium/seizures if high doses

Hallucinogens-Rare Long-term effects:



Classic types:

- 1) Persistent psychosis
- 2) Hallucinogen Persisting Perception Disorder (hallucinations, visual disturbances such as “tracers/trails”)

Dissociative drugs:

- speech problems
- memory loss
- weight loss
- anxiety
- depression and suicidal thoughts

Suspicion re: Prescription Drug misuse?



• SCREENING TOOLS

RxSearch > Patient Request



Support: 1-855-563-4767

Patient Request

[? Patient Rx Request Tutorial](#)

Can't view the file? [Get Adobe Acrobat Reader](#)

* Indicates Required Field

Patient Info

First Name*

☐ Partial Spelling

Last Name*

☐ Partial Spelling

Date of Birth*

Phone Number

Prescription Fill Dates

No earlier than 3 years from today

What is SBIRT?



- **Screening**
 - Universal, quick assessment for use/severity
 - Occurs in a variety of settings (e.g., public health, primary care settings, social service)
- **Brief Intervention**
 - Brief motivation and awareness-raising
 - 1-5 sessions lasting 5 minutes to an hour
- **Referral to Treatment**
 - Specialty care
 - 5-12 sessions

Stages of Change

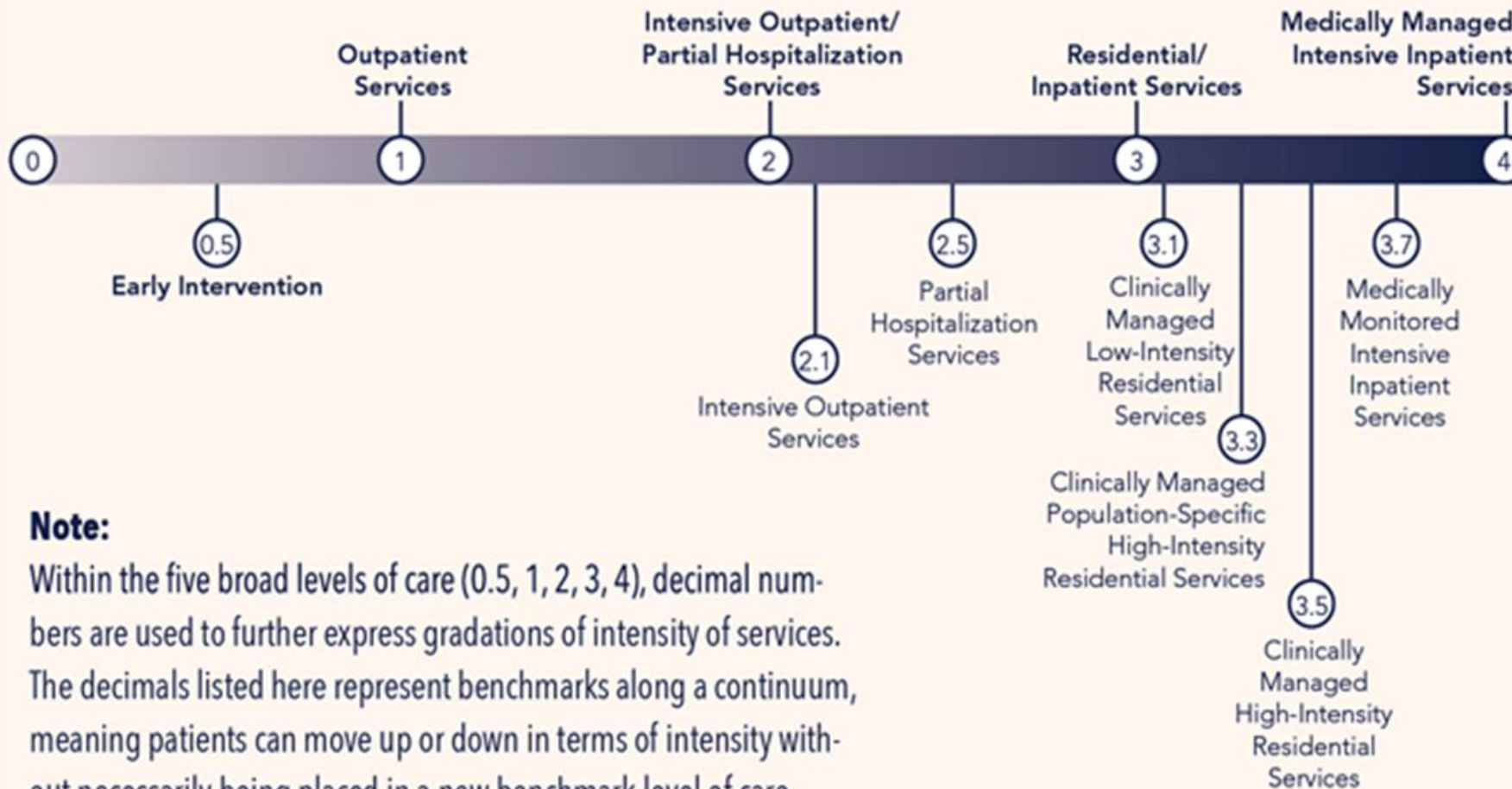


Stage	Characteristic	Strategy (MI)	Processes (MI)
Pre-contemplation	Need for change is either not on the radar or the individual is not interested in change	Education (risks/benefits)	Engaging/Eliciting
Contemplation	Ambivalence	Identify discrepancies, misconceptions as well as potential supports.	Focusing
Preparation	Planning to experiment with small changes	Develop realistic goals Positive reinforcement	Processing/planning
Action	Taking definitive action	Positive reinforcement	
Maintenance/Relapse Prevention	One day at a time, yet long-term approach	Encouragement/Support	

American Society of Addiction Medicine (ASAM)

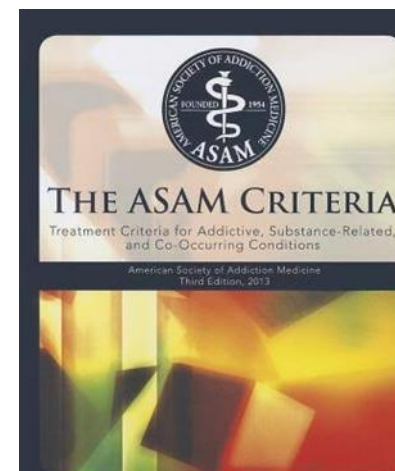


REFLECTING A CONTINUUM OF CARE



Note:

Within the five broad levels of care (0.5, 1, 2, 3, 4), decimal numbers are used to further express gradations of intensity of services. The decimals listed here represent benchmarks along a continuum, meaning patients can move up or down in terms of intensity without necessarily being placed in a new benchmark level of care.



Treatments and Supports



- Addiction Counseling*
- Cognitive/Behavioral Therapies
- Peer Supports
- Support Programs (12-step, other)
- MAT
- Other

Team Players



- Patient
- Addiction counselor(s)
- Care/Case Managers
- Nurses
- Lab staff
- Receptionists
- Prescribers
- Pharmacists



Medication Assisted Treatment:



We have MAT

- Tobacco
- Alcohol
- Opioids

We don't have MAT

- Marijuana
- Cocaine
- Methamphetamine
- Synthetics
- Inhalants

MAT for Tobacco Use Disorder



Most successful with a smoking cessation program.

- Nicotine replacement
- **Gum, nasal spray, patch, lozenge, etc...**
- Bupropion (Zyban/Wellbutrin)
- Varenicline (Chantix)
- Many other non-pharmacologic treatments including acupuncture, hypnosis, etc...
- Vaping –not FDA approved;

- **Disulfiram** (Antabuse) Aversive therapy.
- 1500mg/week
- **Naltrexone** (Revia) 50mg/day
- (Vivitrol)- monthly injection 380mg – issue of pain meds*
- **Acamprosate** (Campral) (2) 333mg tabs T.I.D
- Others-

Opioids (Heroin, Prescription Drugs, etc...)



- **Replacement Therapies:**
- **Methadone:** Special outpatient treatment center
- **Buprenorphine:** (partial agonist)/naloxone (antagonist) =
- Indicated for maintenance treatment in opioid use disorder. Office-based
- 1) Induction 2) Stabilization 3) Maintenance
- **Opiate blockade:**
- Naltrexone (Revia/Depade) and monthly injection Vivitrol

What about for withdrawal?



No longer use the term “Detox”

Use “Withdrawal Management.” We have “social,” we have “ambulatory,” we have “medically monitored,” we have “medically managed,” etc...

- Alcohol

- Benzodiazepines

- Anti-convulsants

- ▶ Opiates

- ▶ Buprenorphine / other*

- ▶ α -2 agonist (clonidine / lofexidine)

What did we just talk about again?



- Definition of substance use disorders
- Burden of illness as well as misuse.
- Potential treatments



Hope



Questions/Comments?

