Is Marijuana Medicine?
What We Know and What We Don't about Cannabis, THC, and CBD, and How Treatment Courts Can Respond

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Disclaimer

The views expressed in this presentation are solely those of the presenter and do not represent those of the Veterans Health Administration or the United States government.

The presenter has no conflicts of interest to disclose.

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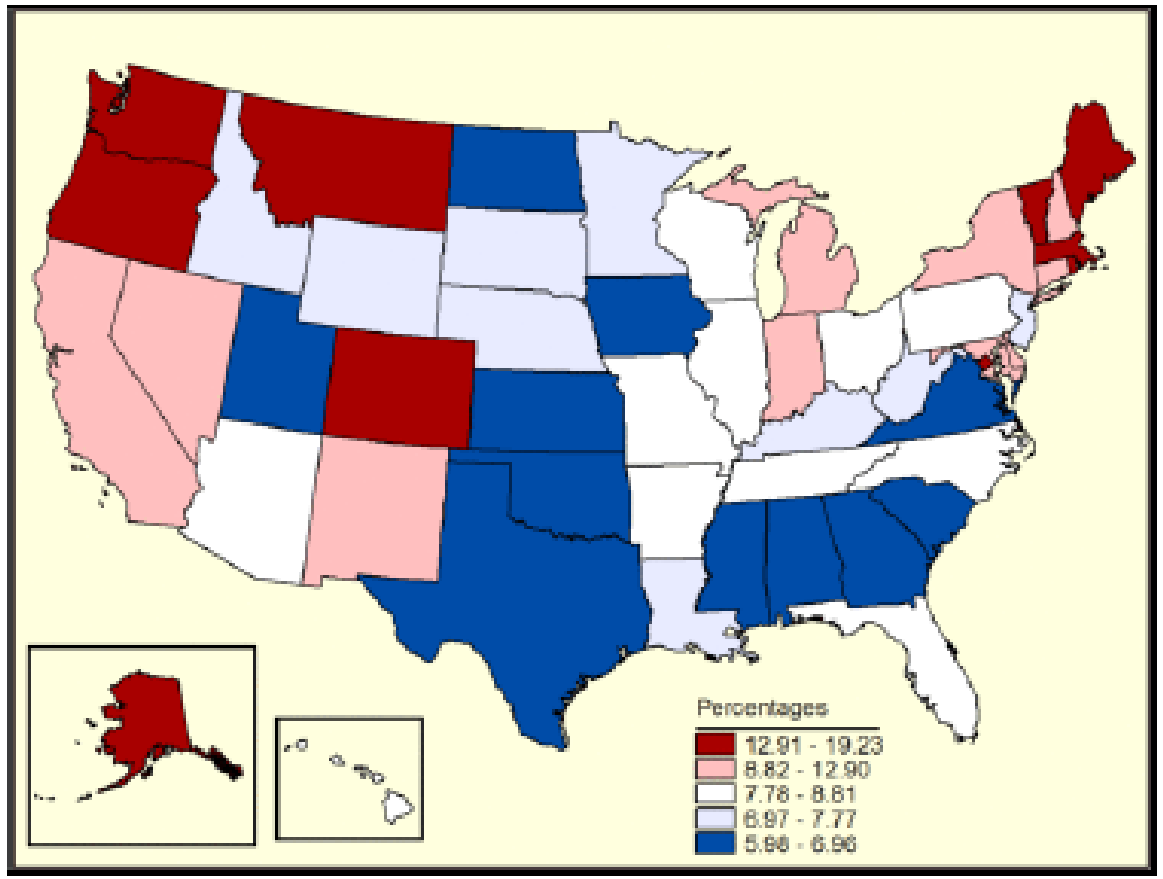
CANNABIS USE IN THE U.S.

Legality of Marijuana

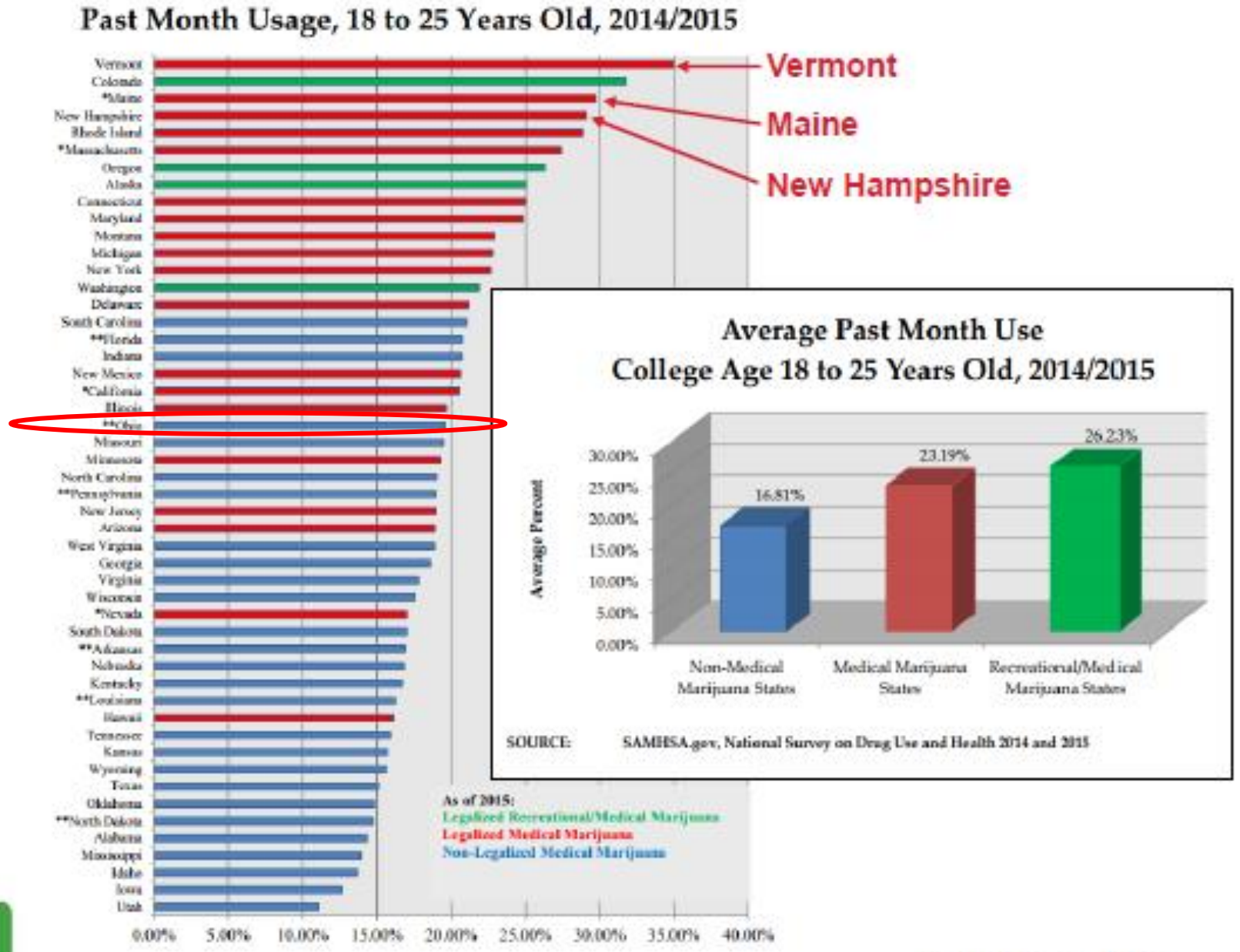
- Illegal at federal level
- 18 states plus Washington DC have legalized recreational marijuana
- 38 states have legalized medical marijuana
  - 29 include PTSD
  - 33 include pain
  - 3 include TBI

Marijuana Use in the United States

Past-Month Marijuana Use, Ages 12 and Older, 2016-2017



SAMHSA graphic based on 2016 and 2017 NSDUH responses



Northern New England Poison Center

1-800-222-1222

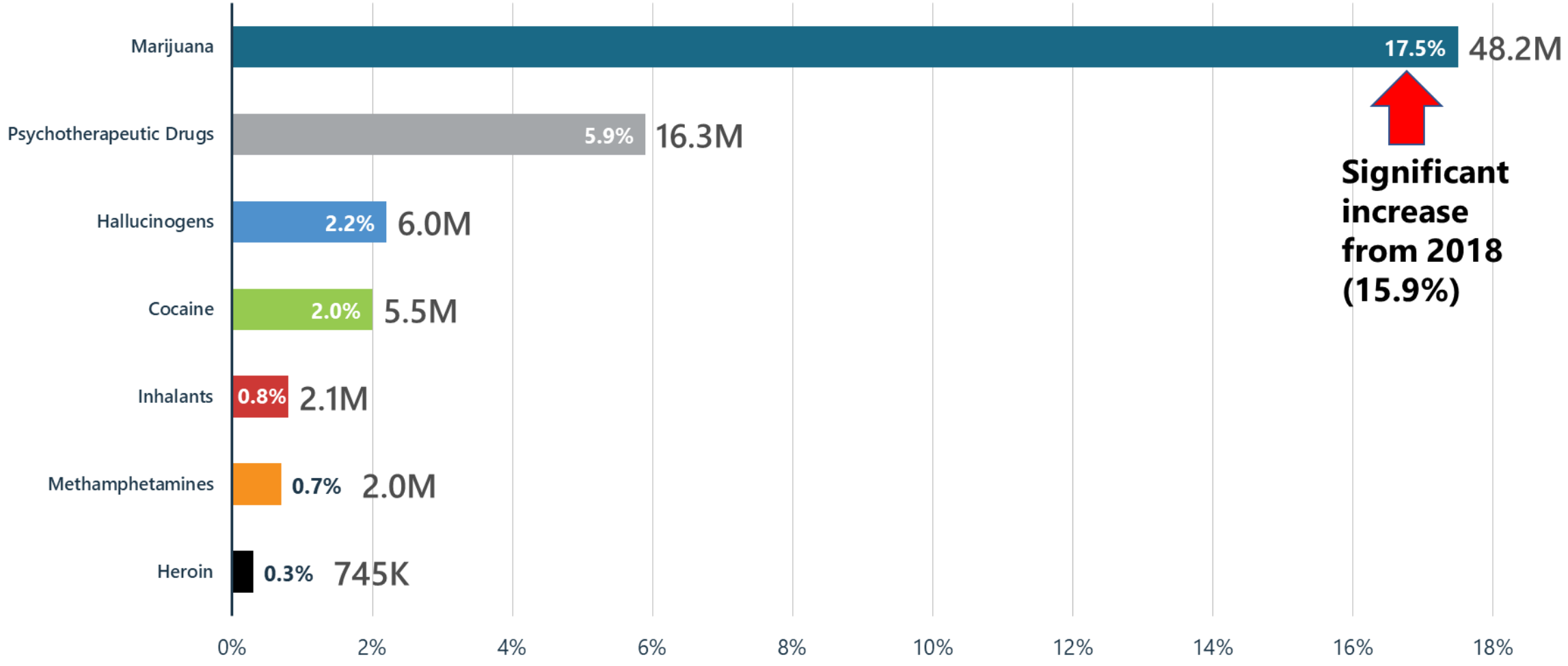
www.nnepc.org

Cannabis Use

- Cannabis is now the most widely used drug in the U.S.
  - It is used by >15% of the population (NSDUH, 2019)
  - Since 2007, past year usage has increased 37%
  - Using > 200 days/year increased 37% since 2002 (SAMHSA, 2019)
    - Nearly 1/3 marijuana users in 2016

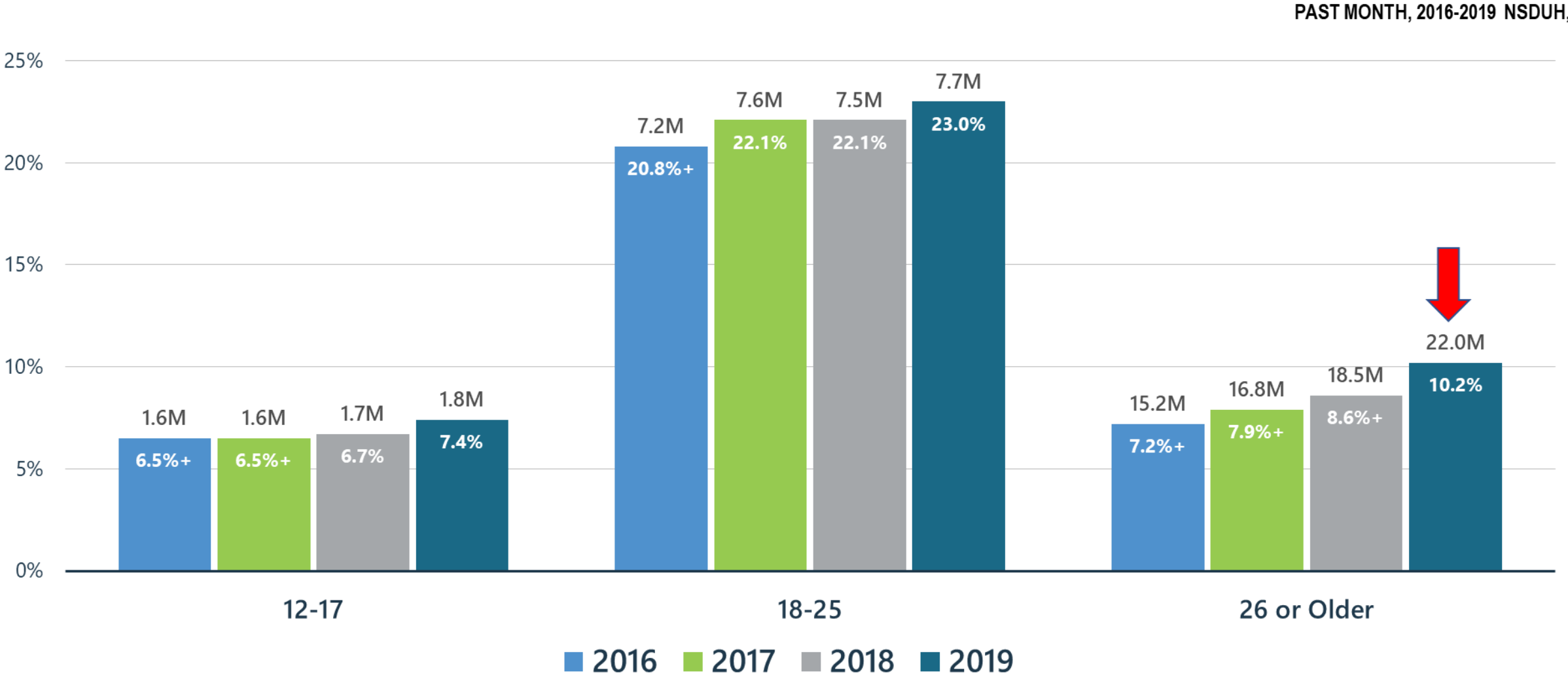
Illicit Drug Use: Major Concerns: Opioids, Marijuana, Methamphetamines

PAST YEAR, 2019 NSDUH, 12+



SAMHSA
Substance Abuse and Mental Health Services Administration

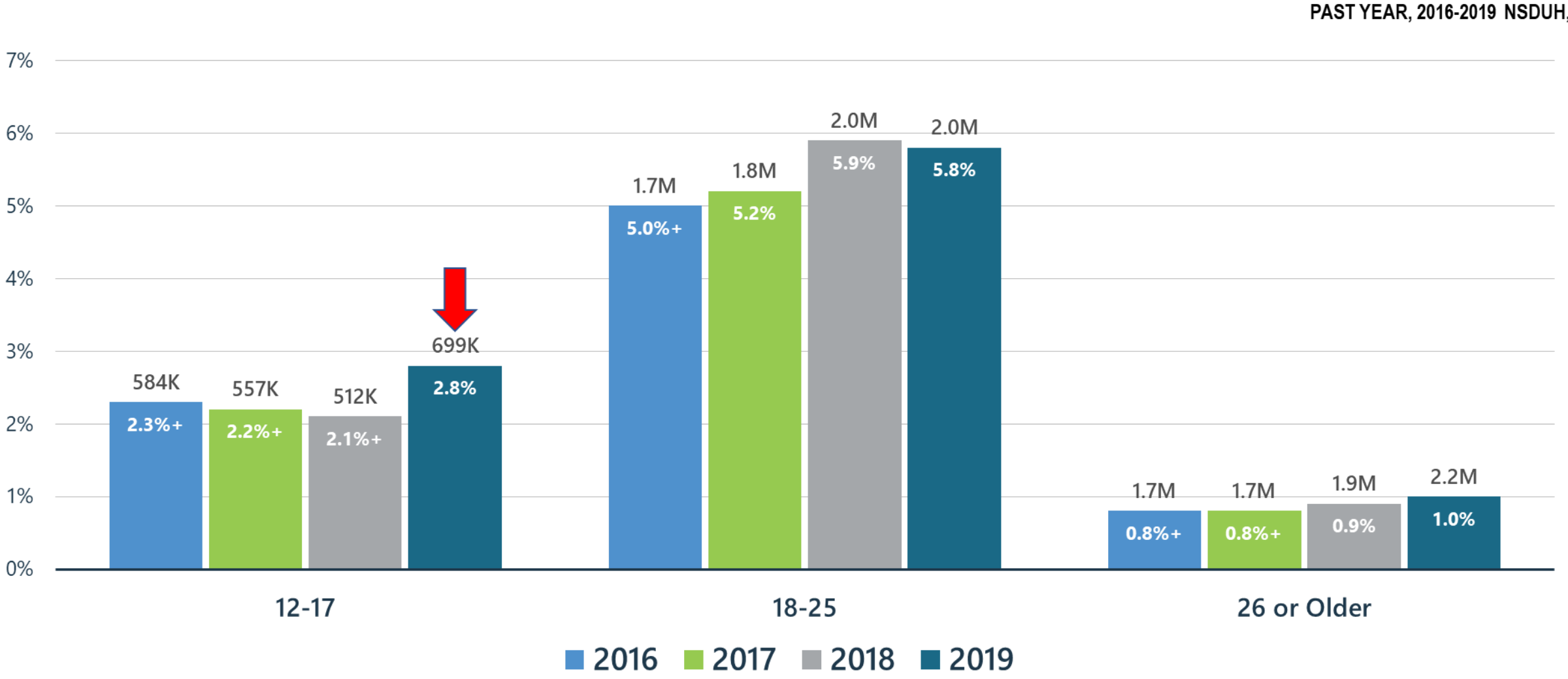
Past Month Marijuana Use for All Age Groups



+ Difference between this estimate and the 2019 estimate is statistically significant at the .05 level.

SAMHSA
Substance Abuse and Mental Health Services Administration

Marijuana Use Disorder: Significant Increase for 12-17 y.o.



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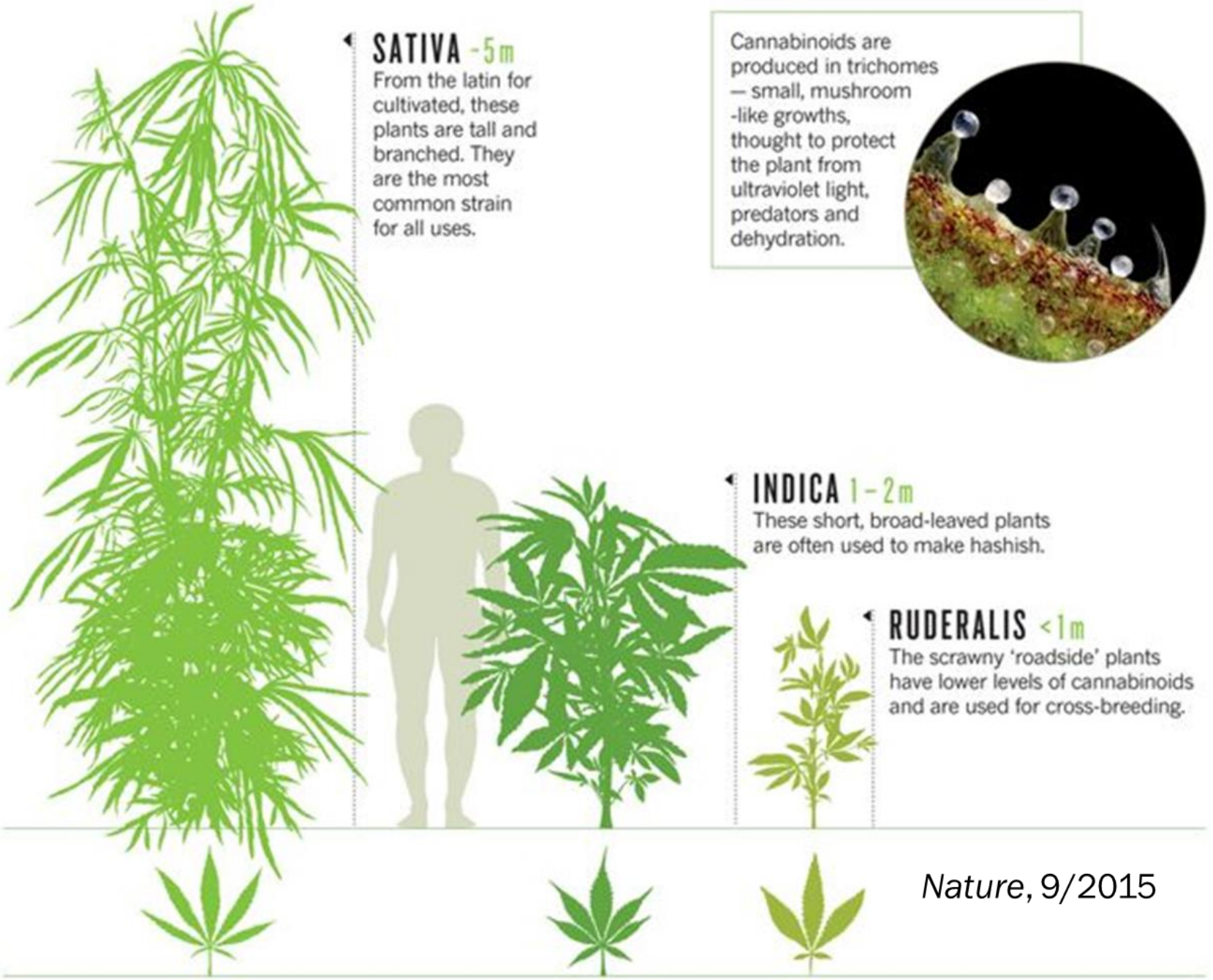
SAMHSA
Substance Abuse and Mental Health Services Administration

WHAT IS MARIJUANA?

Species of Cannabis



Despite many claims otherwise, there is little to no research indicating that ingestion of different species results in different effects.

Different Types of Marijuana?

- **Hemp** is a strain of cannabis sativa with less than 0.3% THC content
- **Sinsemilla** is a strain of cannabis sativa in which female plants are kept seedless to produce high THC content
- Potency of marijuana varies from crop to crop and even plant to plant

Beware the power of testimonials!

ARE THERE POSSIBLE MEDICAL USES OF MARIJUANA?

23 Conditions that Qualify for Medical Marijuana in Ohio

- AIDS
- Amyotrophic Lateral Sclerosis
- Cachexia (wasting disorder)
- Cancer
- Chronic traumatic encephalopathy
- Crohn's Disease
- Epilepsy or another seizure disorder
- Fibromyalgia
- Glaucoma
- Hepatitis C
- HIV+ status
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- Parkinson's Disease
- Post-traumatic Stress Disorder
- Sickle Cell Anemia
- Spinal Cord Disease or injury
- Terminal Illness
- Tourette syndrome
- Traumatic brain injury
- Ulcerative colitis

Types of Cannabinoids

Phytocannabinoids are compounds produced by the cannabis plant (e.g., THC, CBD, CBN)

Endocannabinoids are neurotransmitters produced naturally in the body

- They play roles in cognition, emotion, and memory

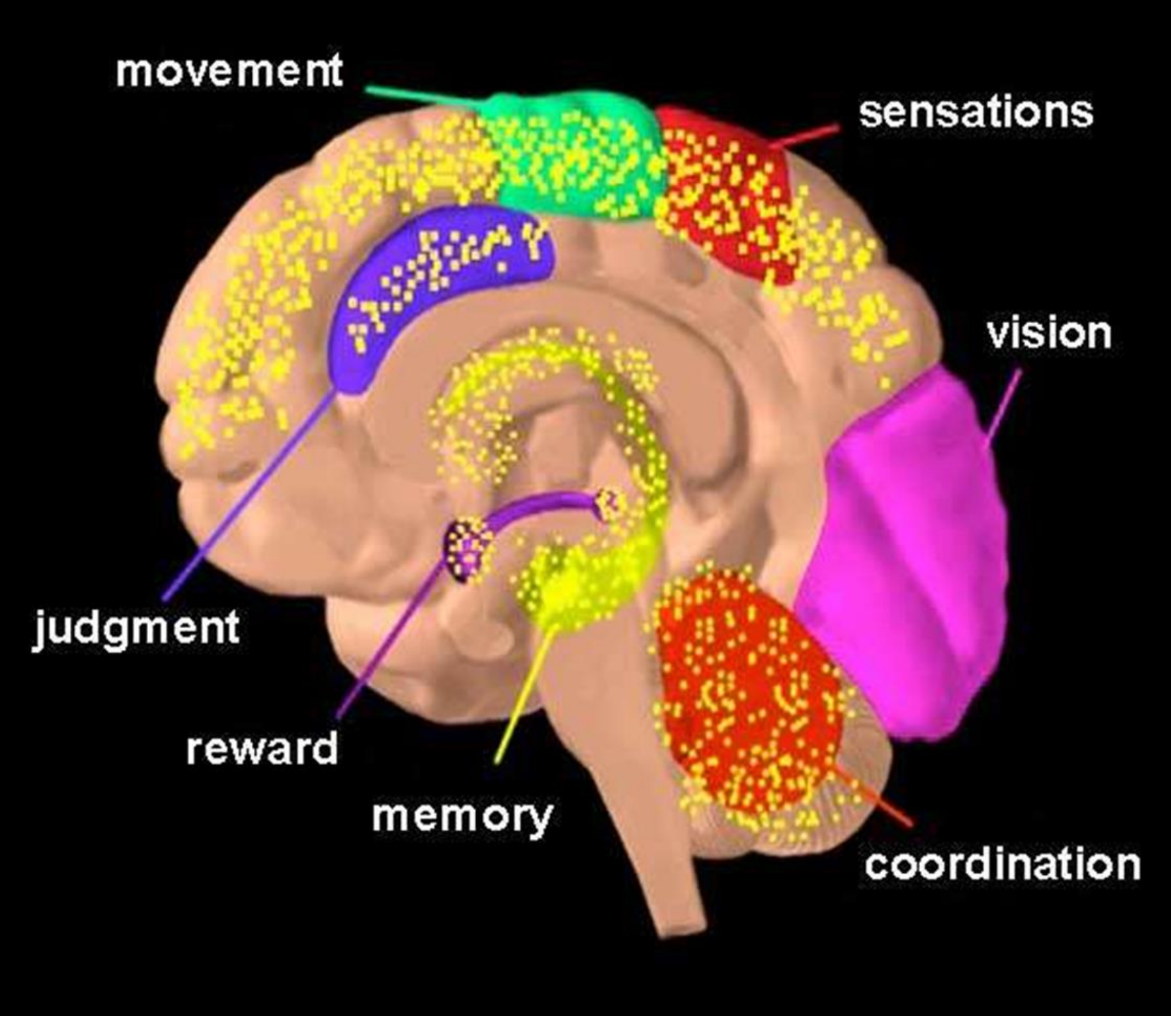
Pharmaceutical cannabinoids are synthetic analogs produced in a lab or pharmaceutically prepared as a whole plant extract

- Marinol (dronabinol), Nabilone
- Nabiximols, Epidiolex

Synthetic cannabinoids are man-made chemicals sprayed on dried plants or sold as liquids (e.g., k2, spice)

Herkenhamet al., 1990; Mechoulam& Parker, 2013; Moreira & Lutz, 2008; WHO, 2016

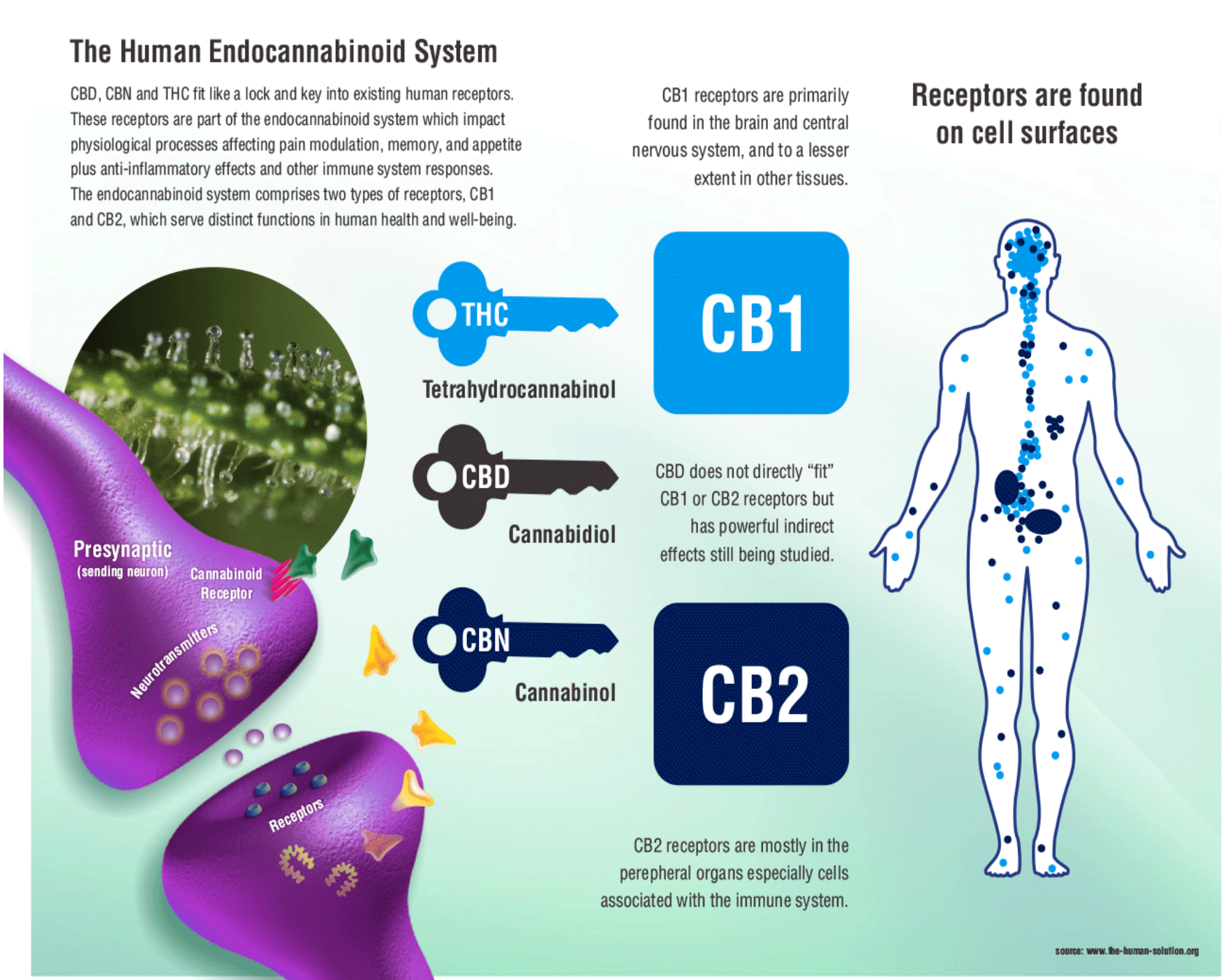
THE EFFECTS OF MARIJUANA



THC Receptors in the Brain

Volkow, NIDA 2014

There are at least 113 identified cannabinoids in a cannabis plant. We know very little about most of them, and less about how they affect the human brain and body.



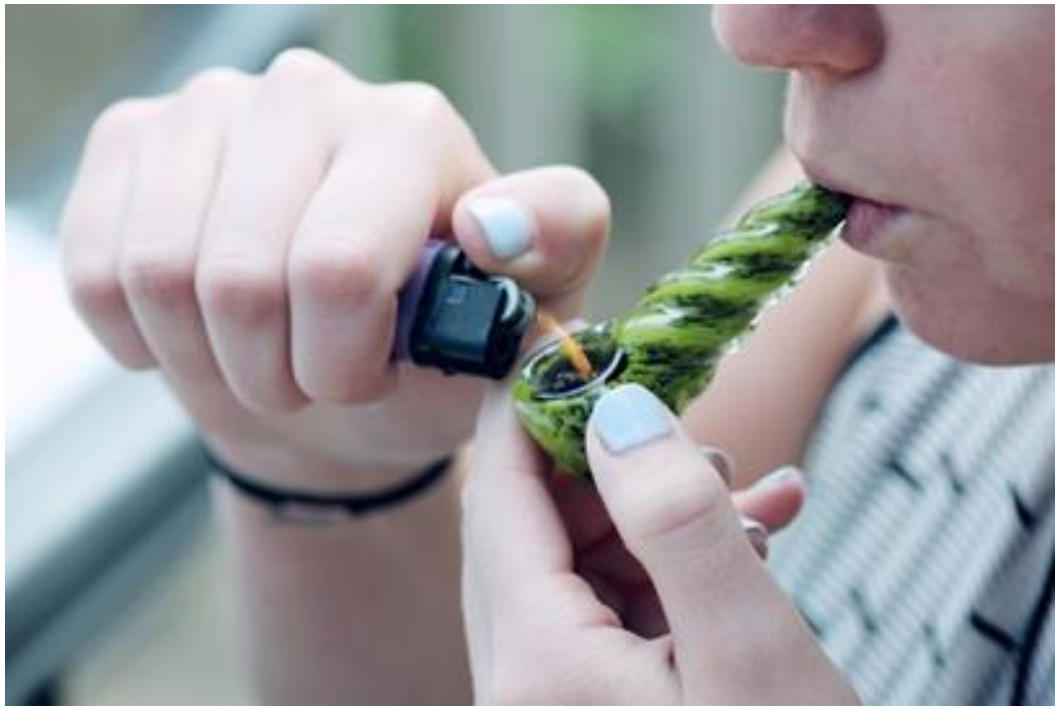
Short-Term Effects of Marijuana

- Mild euphoria, “High”, “buzz”
- Appetite stimulation, “munchies”
- Altered senses (for example, seeing brighter colors)
- Altered sense of time
- Changes in mood from euphoria to anxiety and panic
- Impaired body movement
- Difficulty with thinking and problem-solving
- Impaired memory
- Hallucinations (when taken in high doses)
- Delusions (when taken in high doses)
- Psychosis (risk is highest with regular use of high potency marijuana)

NIDA, 2019

Short-Term Effects of Marijuana Vary Depending on:

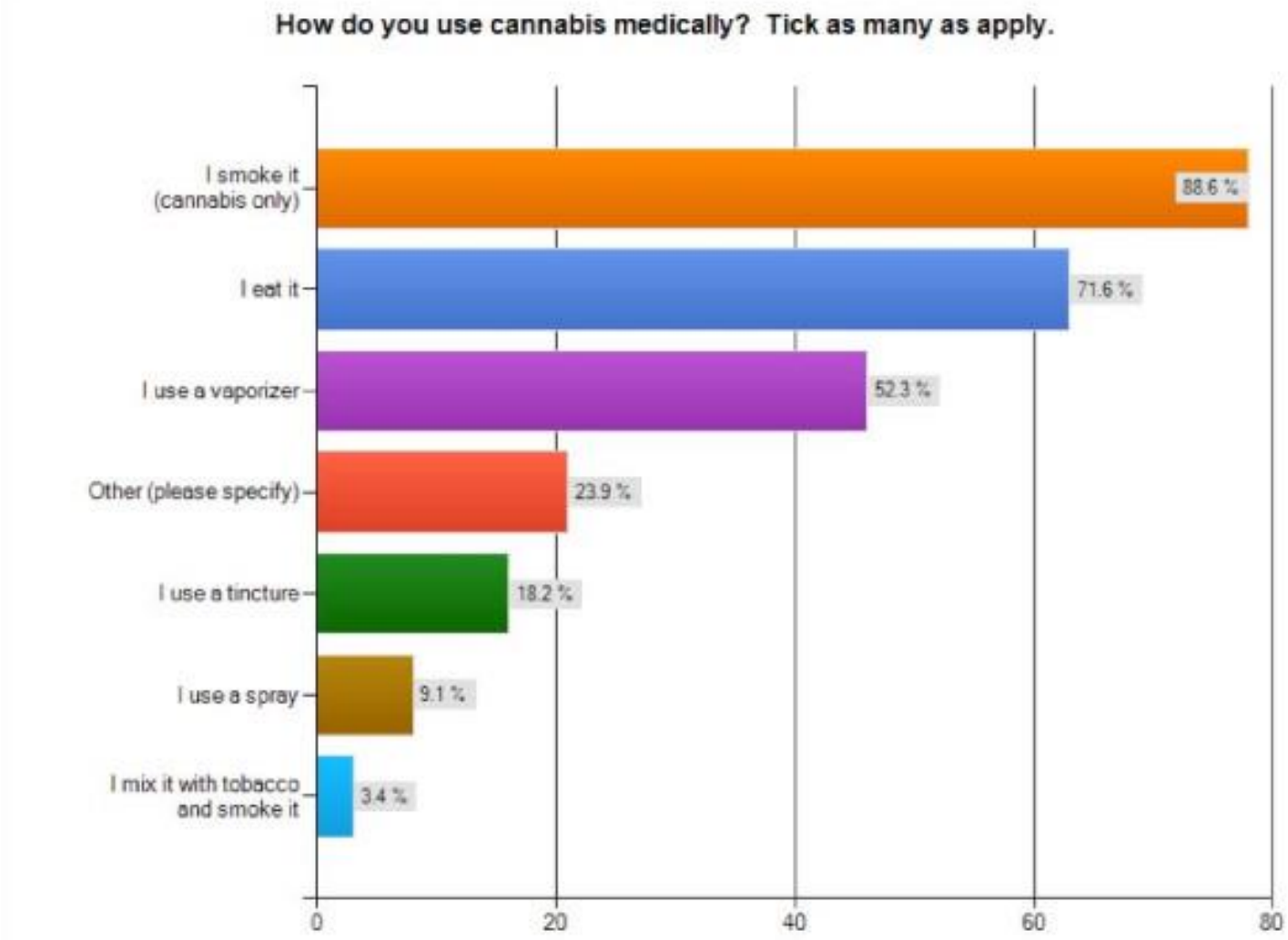
- Proportions and concentration of cannabinoids
- Route of administration
- Dose and quantity consumed
- Frequency of use
- Gender
- Genetic vulnerability
- History of use/prior experience
- Mood state
- Environment/context of use
- Concurrent drug use



Crippaet al., 2009; WHO, 2016

slide information by Browne, 2019

Routes of Cannabis Administration



Lucas, 2012

Some Proposed Medical Uses of Marijuana

- May help with inflammation such as in inflammatory bowel disease (Nagarkatti et al., 2009)
- Decreases nausea
- Stimulates appetite
- Anticonvulsant effect
- May help movement disorders
- Decreases eye pressure in glaucoma
- Analgesic effects

The use of medical marijuana for a wide range of disorders is inconsistent with the science supporting its effectiveness.

Andrew Monte, Richard Zane, & Kennon Heard, 2015

ARE THERE POSSIBLE MEDICAL USES OF MARIJUANA?

There is no current scientific evidence that marijuana is in any way beneficial for the treatment of any psychiatric disorder. In contrast, current evidence supports, at minimum, a strong association of cannabis use with the onset of psychiatric disorders. Adolescents are particularly vulnerable to harm, given the effects of cannabis on neurological development.

American Psychiatric Association, 2013

The Relationship between Marijuana and Anxiety Is Complex

- Cannabis causes acute anxiety in 20-30% of users after smoking it (Thomas, 1996)
  - This is especially true at high doses and in drug-naïve people Manzanare et al., 2004)
- Frequent users have higher anxiety levels than non-users (Crippa et al., 1998)
- The probability of mood or anxiety disorders in users with dependence doubles (Agosti, Nunes, & Levin, 2002)
- Cannabis dependence is also related to panic attacks (Zvolensky et al., 2006)
- Long-term users report a reduction in anxiety (Hathaway, 2003)

Does Marijuana Treat PTSD?

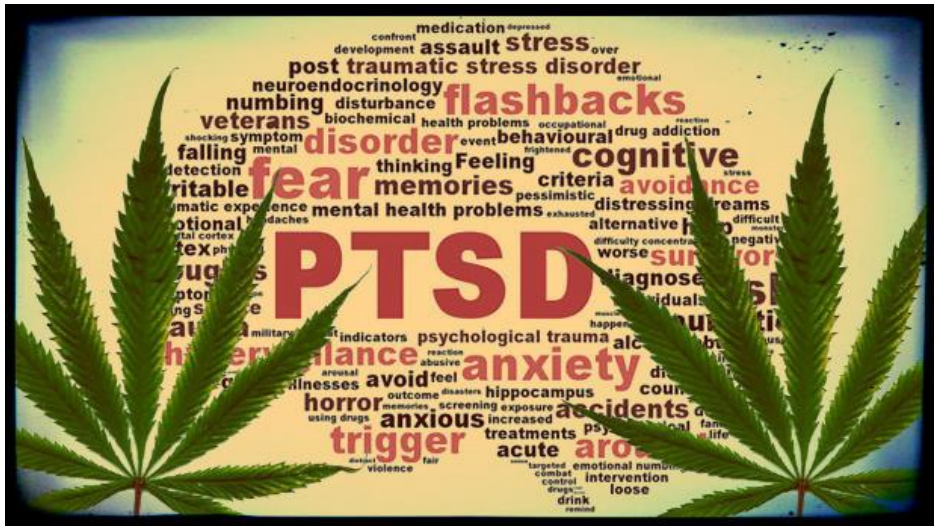
There is no current scientific evidence that *the cannabis plant* is an effective treatment for PTSD. What we have:

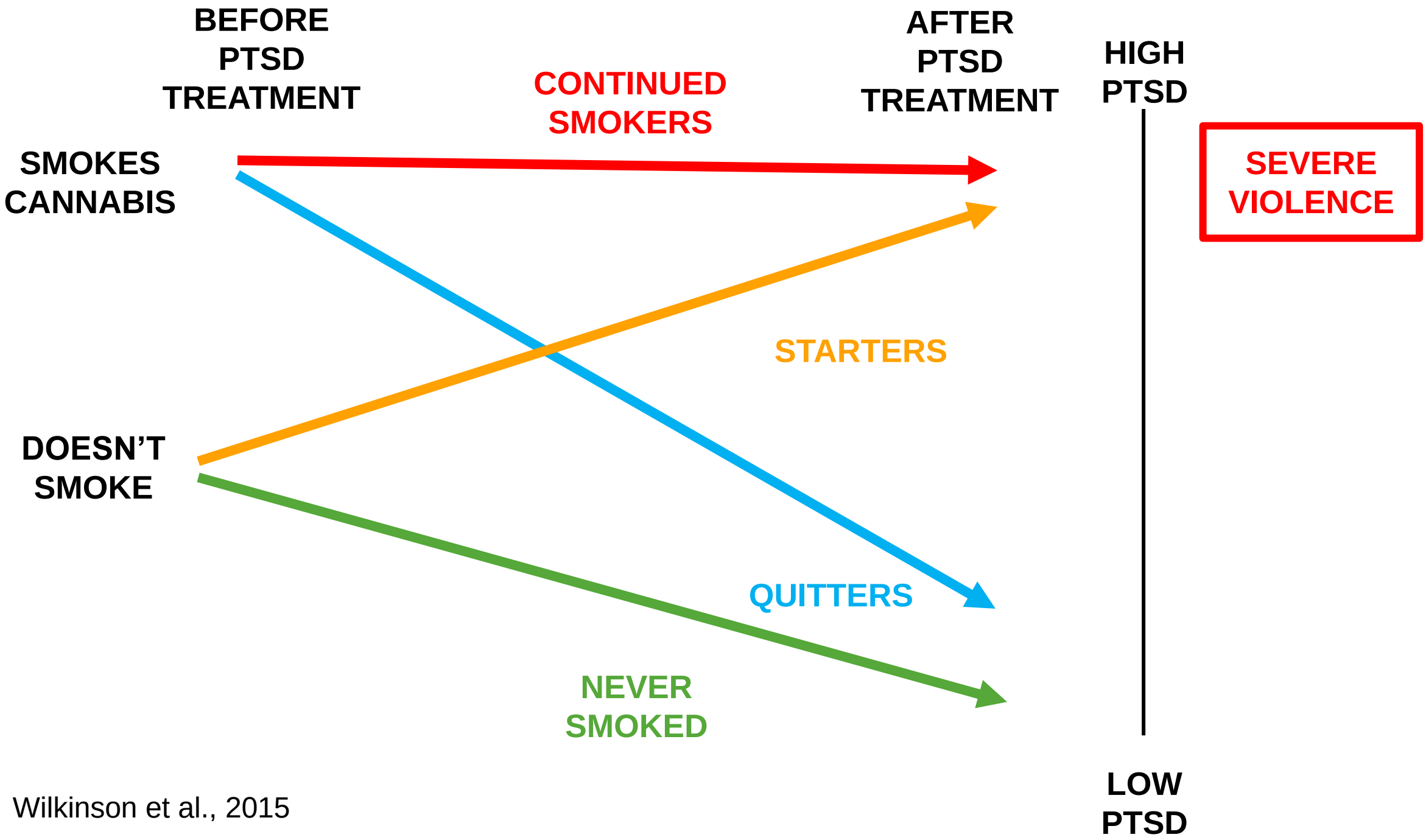
- Anecdotal evidence from cannabis users that drug helps with PTSD
- Preclinical studies testing a specific pharmaceutical cannabinoid
- Few studies of pharmaceutical cannabinoids in humans
- Case studies
- No randomized controlled trials studying the cannabis plant
- Long term effects are largely unknown

Browne, 2019

Does Marijuana Treat PTSD?

- Many people with PTSD claim that marijuana is the only thing that helps their PTSD
  - Some Veterans are lobbying Congress to allow the VA to prescribe medical marijuana
- There is no research evidence for this claim
  - The first two studies shows that marijuana makes PTSD *worse*
  - One found that cannabis use <u>prolonged</u> PTSD symptoms (Bonn-Miller et al., 2011)





Wilkinson et al., 2015

Does Marijuana Reduce the Incidence of Opioid Use Disorder?

- This hypothesis is based on the idea that marijuana may substitute as a treatment for pain, thus reducing the need for opioids
- The effects of cannabis and cannabinoids on chronic noncancer pain are small to none, and the likelihood of harm is moderate to high (Hauser et al., 2019; Stockings et al., 2018)
- Sativex, a pharmaceutical mix of THC and CBD not available in the U.S., has failed Phase III clinical trials in reducing cancer pain (Fallon et al., 2015)

Does Marijuana Reduce the Incidence of Opioid Use Disorder?

- Cannabis use is associated with opioid misuse (Reisfield et al., 2009)
- Cannabis use increases the risk of developing nonmedical prescription opioid use and Opioid Use Disorder (Olfson et al., 2018)

Meta-analyses…do not strongly support the use of cannabinoids for chronic pain nor do prospective studies demonstrate significant cannabinoid-mediated opioid sparing effects.

Babalonis & Walsh, 2019

Does Marijuana Decrease Opioid Deaths?

- Some people have argued that marijuana can be used to decrease opioid deaths
- A 2014 study (Bachhuber et al., 2014) of the years 1999-2010 found that there were 25% fewer opioid overdose deaths in states with medical marijuana laws compared to those without
  - This was trumpeted by the marijuana industry
- However, a 2019 follow-up study (Shover et al., 2019) found that this was true only for the years 1999-2010
  - It found that, when the analysis was extended to 2017, there were 23% *more* opioid overdose deaths in states with medical marijuana laws

To Be Fair, There Are Problems in Marijuana Research

- The federal government has limited research on marijuana
- All marijuana used for federally-approved research comes from one 12 acre farm at the University of Mississippi
  - It is one strain
  - It is less potent than most marijuana available today
  - Often there are more approved studies than marijuana available
- Many studies have been done with pharmaceutical THC or CBD, not the cannabis plant

Therefore, most research that has been conducted is not generalizable

IS MARIJUANA MEDICINE?

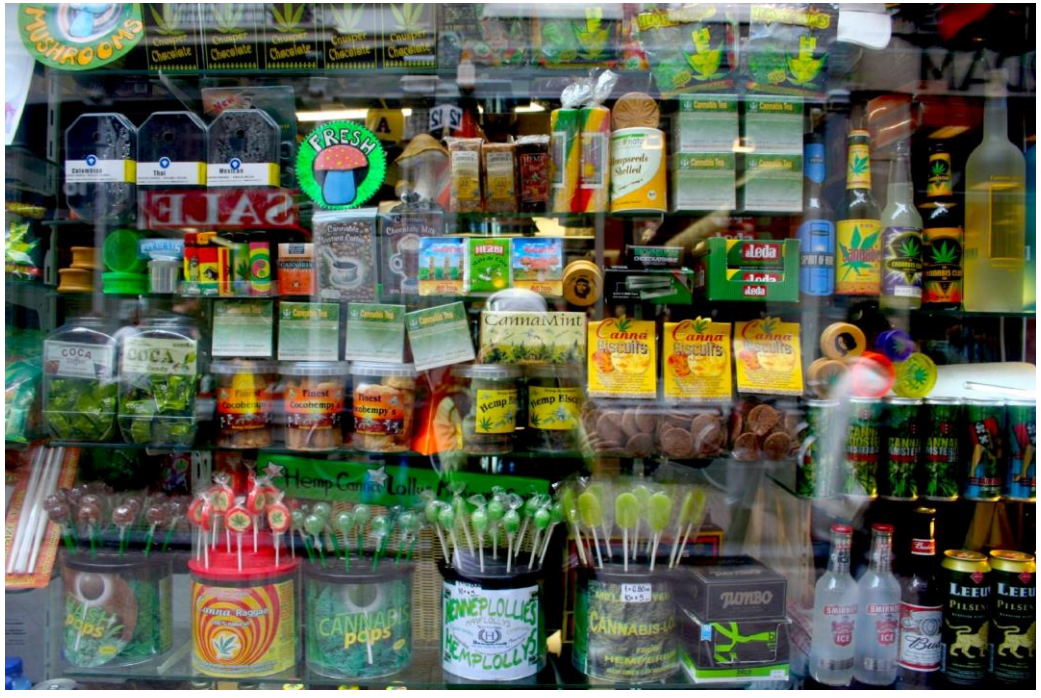
What Do You Get When You Buy Marijuana Products?

We don't know

- A study of 84 CBD products made by 31 companies sold online (Bonn-Miller et al., 2013) found:
  - Only 26 were accurately labeled
    36 underestimated the amount of CBD
    22 overestimated the amount of CBD
  - THC was detected in 18 samples
  - Cannabidiolic acid was found in 13 samples
  - Cannabigerol was found in 2 samples

What Do You Get When You Buy Edible Marijuana?

16-26% of patients using medical marijuana consume edibles (Grella et al., 2014; Walsh et al., 2013)

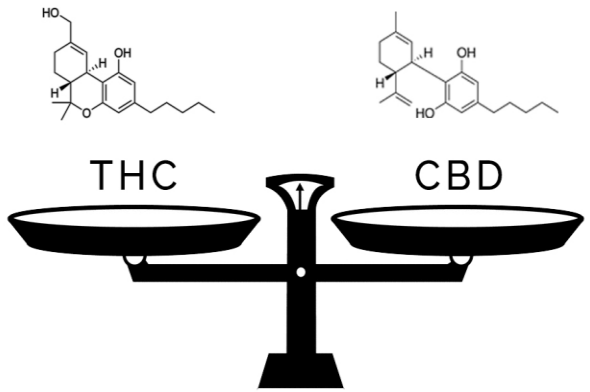


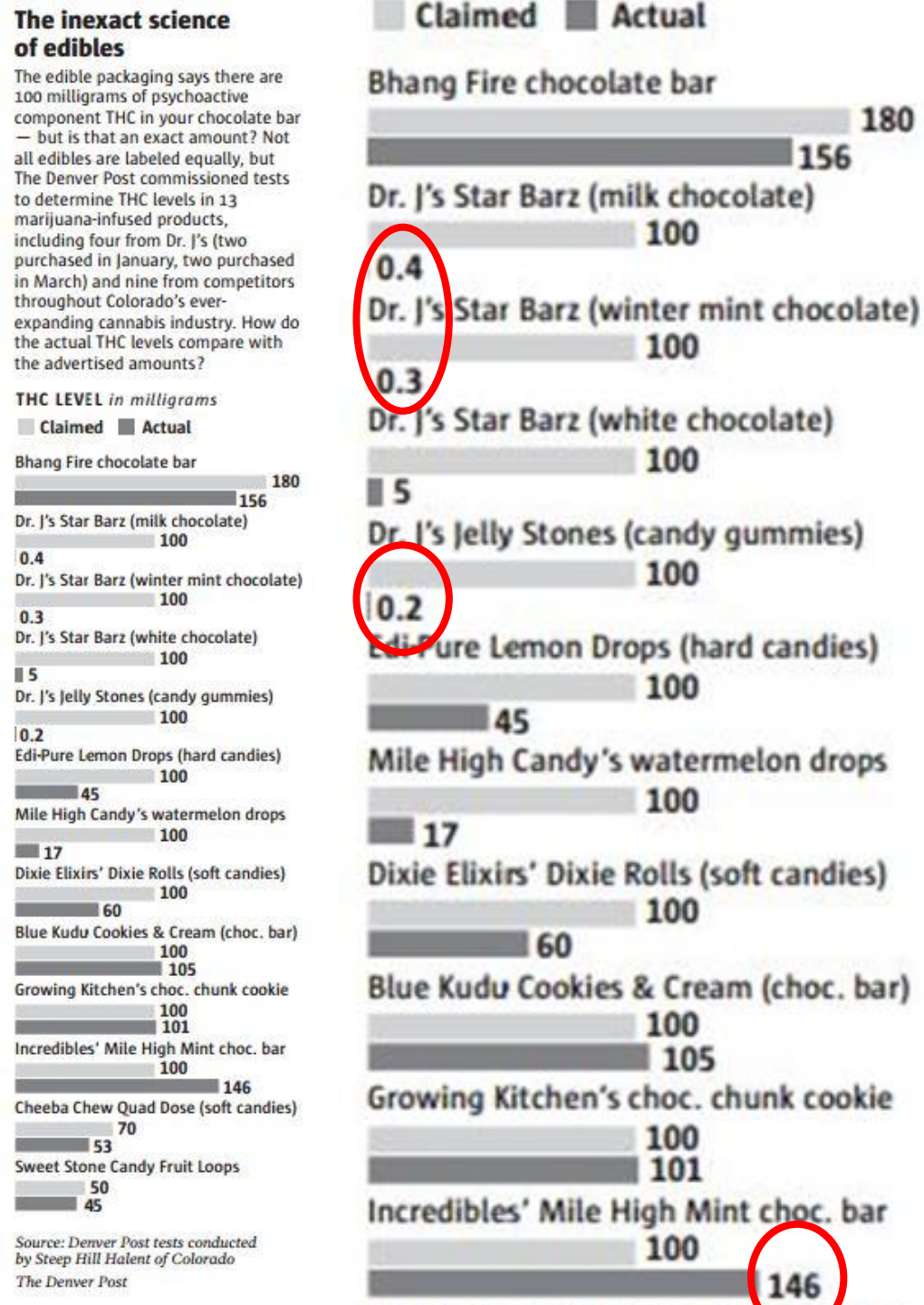
We don't know

- A study of 75 edible products from 47 brands sold in California and Washington (Vandrey et al., 2015) found that:
  - 13 were accurately labeled for THC
    17 were underlabeled for THC
    40 were overlabeled for THC
  - 44 had detectable levels of CBD
    Only 13 had CBD labeled
    4 were underlabeled for CBD
    9 were overlabeled for CBD
  - Other cannabinoids were found

The Ratio of CBD:THC May Matter

- THC and CBD have inverse quantities in a cannabis plant
  - The more THC there is, the less CBD there is
- There is more CBD in stems and more THC in leaves and flowers
- CBD can inhibit some of the psychoactive effects of THC (Russo & McPartland, 2003)
- One study suggests a ratio of 1:1 may be optimal (Vermersch, 2011)
  - This is the ratio in Sativex





Effects of Edibles

- Inconsistent dosing: An examination in the Denver Post (3/9/14) of 10 edibles claiming to contain 100 mg. of THC found that the actual amounts varied from <1mg. To 146 mg.
- The delayed effects of ingestion may cause some people to ingest more of the product

Problems in Determining What People Get When They Use Cannabis

- Different subtypes of cannabis
- Unknown concentrations of THC, CBD, and other cannabinoids in individual plants
- Differing ratios of THC:CBD
- Differing methods of ingestion can increase percentage of THC ingested
- Inaccurate labeling
- Lack of information about dosages
- Lack of research

Is Marijuana Medicine?

- According to the federal Food and Drug Administration (FDA), a drug is defined as:
  - A substance recognized by an official pharmacopoeia or formulary.
  - A substance intended for use in the diagnosis, cure, mitigation, treatment, or prevention of disease.
  - A substance (other than food) intended to affect the structure or any function of the body.
  - A substance intended for use as a component of a medicine but not a device or a component, part or accessory of a device.
- FDA considers drug products to be pharmaceutical equivalents if they meet these three criteria:
  - They contain the same active ingredient(s)
  - They are of the same dosage form and route of administration
  - They are identical in strength or concentration

FDA, 2019

Is Marijuana Medicine?

- All FDA-approved medicines have clearly-defined and measurable ingredients that are consistent from one dose to the next
- Cannabis plants contain hundreds of chemical compounds that vary from plant to plant
- Medicine from a pharmacy provides information on:
  - Brand/manufacturer
  - Drug strength
  - Directions for administration
  - Indications for use (that have been proven by research)
  - Reactions/side effects
- Marijuana is not a single entity

Is There Medical Use for Marijuana?

- Evidence for some medical value of some components
  - CBD and seizure disorder (Dravet's syndrome and Lennox-Gastaut syndrome)
  - THC products for wasting illnesses and appetite production

- Medications must have undergone substantial research to answer critical questions before getting to market and widespread use in humans:
    - Isolation of single components; manufacture processes
    - Delivery mechanism
    - Pharmacokinetics/pharmacodynamics
    - Dose-response relationships (e.g.: doubling a dose may or may not double the effect)
    - Therapeutic range
    - Adverse events: what are they and how best to avoid/address should they occur?
  - These types of studies would be difficult for marijuana because there are so many components

Summary of Recent Meta-analysis of Cannabinoid Effects on Mental Health Problems

- 83 studies from 40 randomized controlled trials
- N=3,067

There is scarce evidence to suggest that cannabinoids improve depressive disorders and symptoms, anxiety disorders, attention-deficit hyperactivity disorder, Tourette syndrome, post-traumatic stress disorder, or psychosis. There is very low quality evidence that pharmaceutical THC (with or without CBD) leads to a small improvement in symptoms of anxiety among individuals with other medical conditions. There remains insufficient evidence to provide guidance on the uses of cannabinoids for treating mental disorders within a regulatory framework.

Black et al., *The Lancet,* 10/28/19

23 Conditions that Qualify for Medical Marijuana in Ohio

- AIDS
- Amyotrophic Lateral Sclerosis
- Cachexia (wasting disorder)
- Cancer
- Chronic traumatic encephalopathy
- Crohn's Disease
- Epilepsy or another seizure disorder
- Fibromyalgia
- Glaucoma
- Hepatitis C
- HIV+ status
- Huntington's Disease
- Inflammatory Bowel Disease
- Multiple Sclerosis
- Pain that is either chronic and severe or intractable
- Parkinson's Disease
- Post-traumatic Stress Disorder
- Sickle Cell Anemia
- Spinal Cord Disease or injury
- Terminal Illness
- Tourette syndrome
- Traumatic brain injury
- Ulcerative colitis

Which Conditions Are Proven to Respond to Some Part of Cannabis among Those That are Legal in Ohio?

- AIDS
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- Traumatic brain injury
- Ulcerative colitis

Which Conditions Are Proven to Respond to Some Part of Cannabis among Those That are Legal in Ohio?

- Multiple Sclerosis

- Cachexia (wasting disorder)
- Cancer (only for nausea)

- Two rare childhood seizure disorders: Dravet's Syndrome and Lennox-Gastaut Syndrom

IF MARIJUANA IS MEDICAL, DOES IT HAVE SIDE EFFECTS?

Effects on Major Organ Systems

Respiratory

- Many of the same mutagens and carcinogens in nicotine are found in marijuana smoke
- Impact on lung function and respiratory cancer is being studied

Immunologic

- Evidence of immunosuppression due to impact on CB2 receptor
- Observed increase in mortality of HIV positive patients with cannabinoid abuse
- Increased incidence of viral infections

Cardiovascular

- Increases heart rate and produces orthostatic hypotension
- May impact platelet function and play a role in atherogenesis

Information from Ilene Robeck

Effects on Major Organ Systems

Liver

- **Daily** cannabinoid use is associated with liver steatosis that can lead to fibrosis

Endocrine

- Inhibition of Pituitary Luteinizing hormone, Prolactin, and Growth Hormone
- Induction of ACTH and Corticosterone Secretion

Information from Ilene Robeck

Cannabis and Fertility

- Cannabis decreases sperm count, seminal fluid, and causes abnormal sperm behavior (Burkman et al., 2019)
- It decreases sperm motility
- Cannabis causes changes in DNA of sperm (Kollins et al., 2018)
- Marijuana may delay or prevent ovulation
- Marijuana use during pregnancy may lead to low birth weight, developmental delays, and behavioral problems

Neonatal Effects of Exposure to Cannabis In Utero

Laboratory exposure to THC and other cannabinoids leads to the formation of functionally impaired neurons. (Miranda et al., 2020)

- Vasoconstriction, which reduces blood supply and oxygenation, which can lead to hypoxia and possible ischemic injury (Thompson et al., 2009)
- Low birth weight babies
- Mild withdrawal symptoms at birth
- Increased newborn morbidity, especially susceptibility to illness (Metz et al., 2017)
- Increased NICU admissions (Warshak et al., 2015)

Recent Research on Prenatal Exposure to Cannabis In Children

- Longitudinal Adolescent Brain and Cognitive Development Study of 11,489 9-11 year-olds (Paul et al., 2020)
- Fetal exposure to cannabis after knowledge of pregnancy related to lower birth weight, total intracranial volume, and white matter volume
- Exposure both before and after knowledge of pregnancy related to lower cognition, lower grey matter, BMI, and sleep problems
  - They were also related to psychopathology, including psychotic-like experiences, depression, anxiety, thought problems, social problems, and problems in attention, impulsivity, internalizing behaviors, and externalizing behaviors
- A 20 year study of birth outcomes (Hines et al, 2021) found that both maternal and paternal use of cannabis increased the likelihood of pre-term birth 6 X

Effects of Prenatal Exposure to Cannabis

In Children

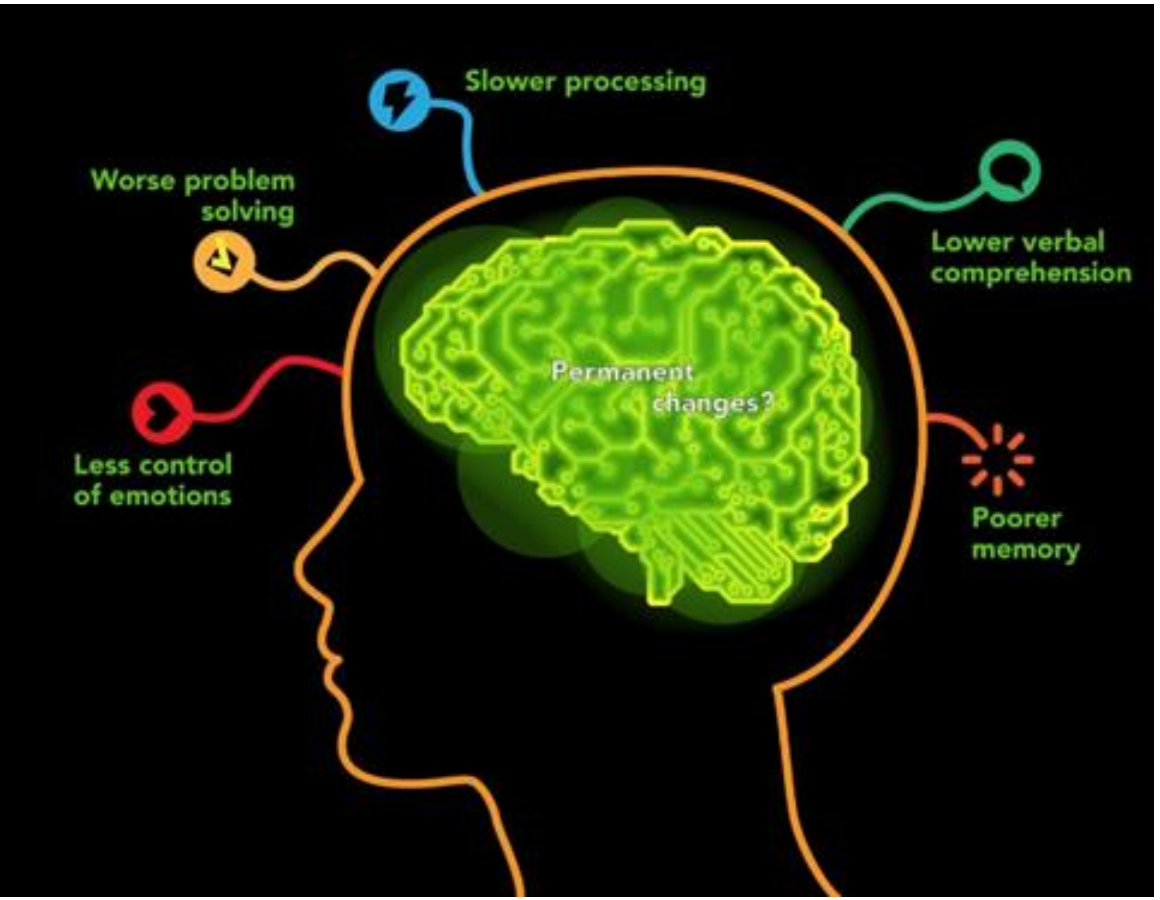
- Poorer school achievement, especially in reading and spelling
- Poorer problem-solving
- Impaired attention
- Deficit in memory
- Learning disabilities
- Impaired planning
- Increased impulsivity
- Hyperactivity
- Depressive symptoms

In Adolescents

- Decreased working memory
- Impaired executive function
- 2X risk of tobacco and marijuana use, starting earlier
- Delinquent behaviors
- Increased risk for psychiatric disorders

Goldschmidt et al., 2004;
Minnes et al., 2011;
Smith et al., 2004

Acute Cognitive Effects



- Decline in verbal fluency
- Decline in memory recall
- Changes in sensory perception
- Slower reaction time, including driving
- Decreased attention span
- Decreased accuracy in assessing time and distance
- Slower ability to shift sets
- Decreased psychomotor coordination
- Decreased problem solving
- Declines in academic performance

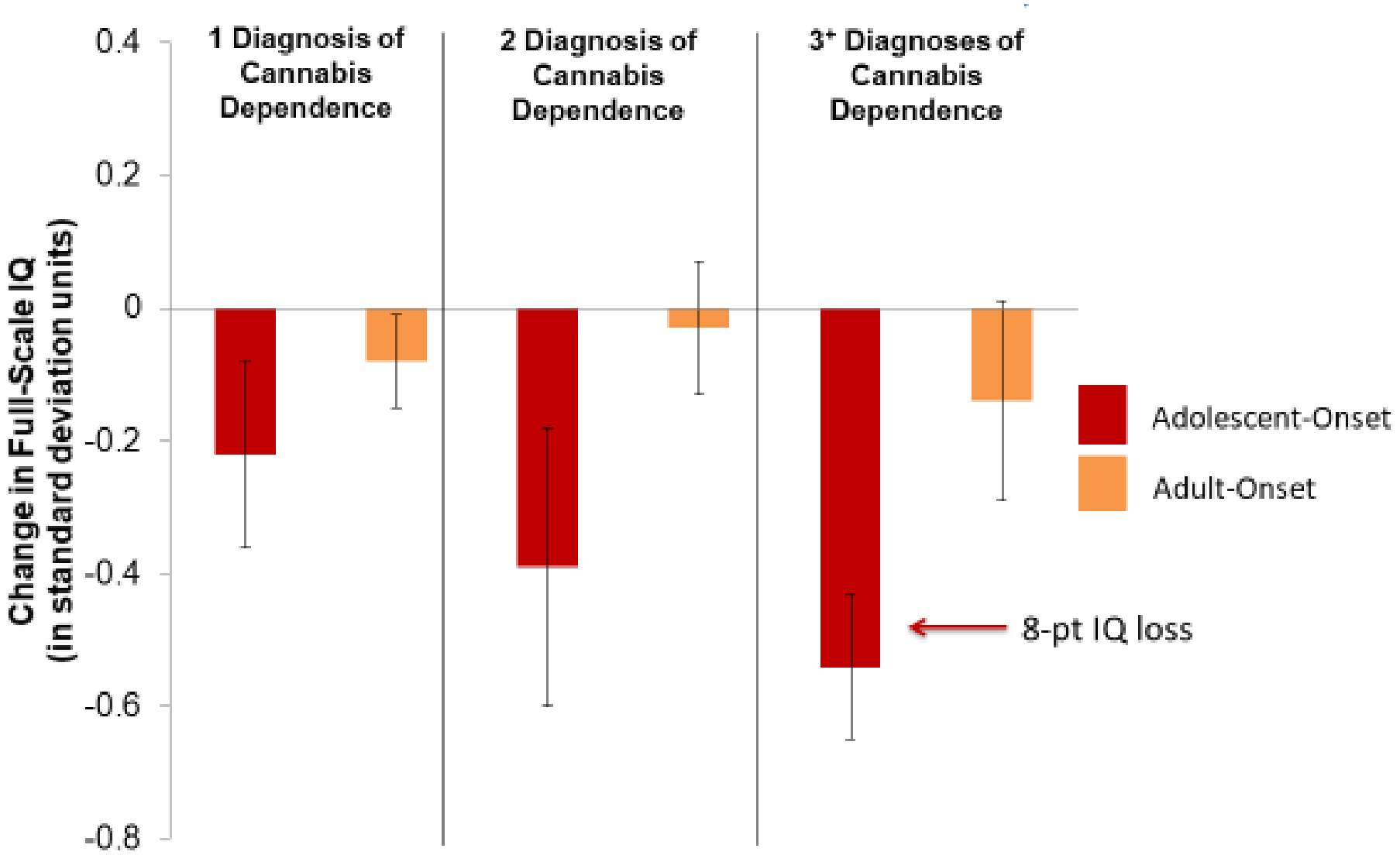
Even Small Amounts of Cannabis Can Change the Teenage Brain

- 14 year-olds with 1-2 instances of cannabis use (Orr et al., 2019)
- Several regions of the brain had increased grey matter volume compared to matched controls
- Perceptual reasoning was worse
- Use was associated with future generalized anxiety symptoms

Adolescent Onset of Cannabis Use Results in IQ Decline

Longer persistence of use led to greater impairment.

IQ did not rebound after cannabis use stopped.



Adolescent cannabis exposure is associated with greater decrease In IQ

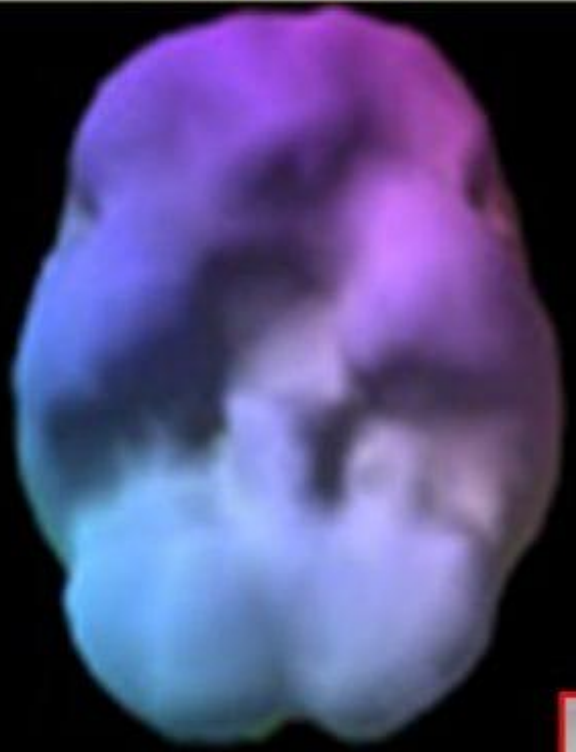
Mohini Ranganathan

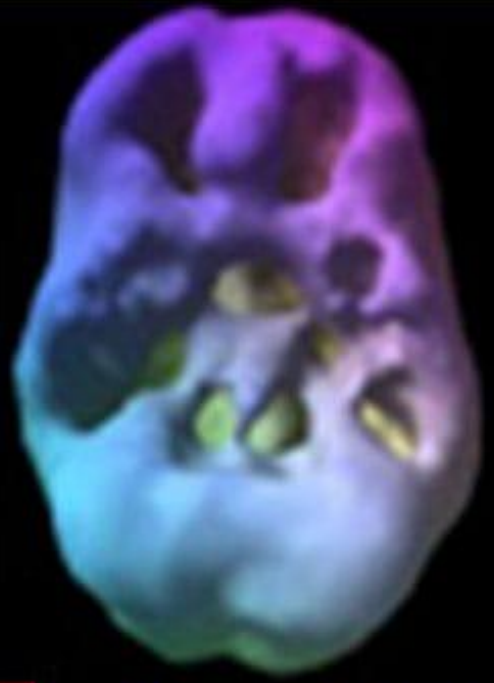
Meier et al., 2012

OPTIMAL?

Healthy Brain

Marijuana Brain

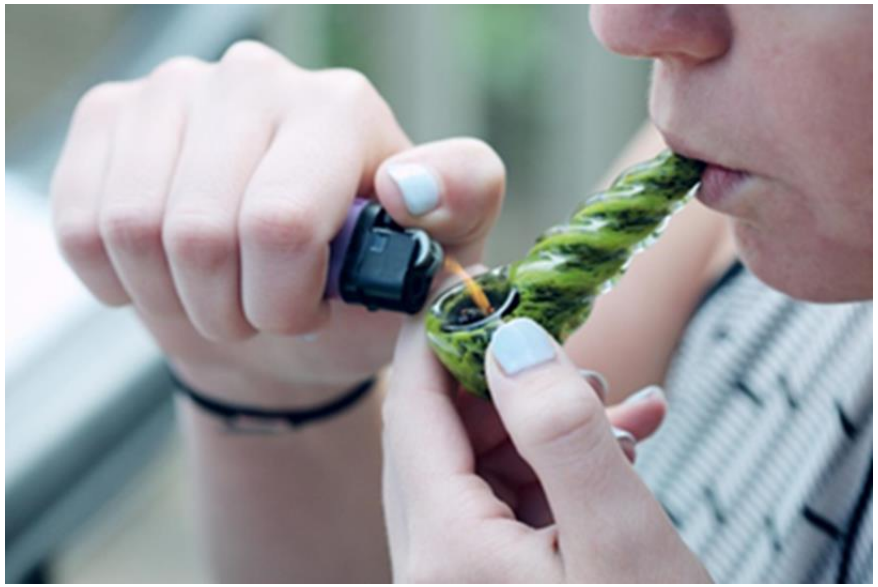




16 yr. old daily user

Amen Clinics

Early Initiators Have Worse Outcomes

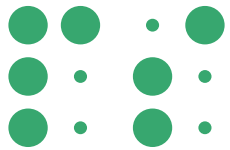


- Study of the NSDUH results from 2015-2018 (Volkow et al., 2021) indicates:
  - 15.4% of adolescents had used cannabis and 51.5% of 18-25 y.o. had used cannabis
  - Adolescent initiators were more likely to develop Cannabis Use Disorder than young adult initiators
- A longitudinal 20 year Australian study of adolescent vs. young adult initiators (Chan et al., 2021) found that early initiators of cannabis use were more likely to use illicit drugs, to become high-risk alcohol drinkers, to smoke daily, and less likely to be in a relationship

Long-Term Effects

Impaired memory

Decreased attention



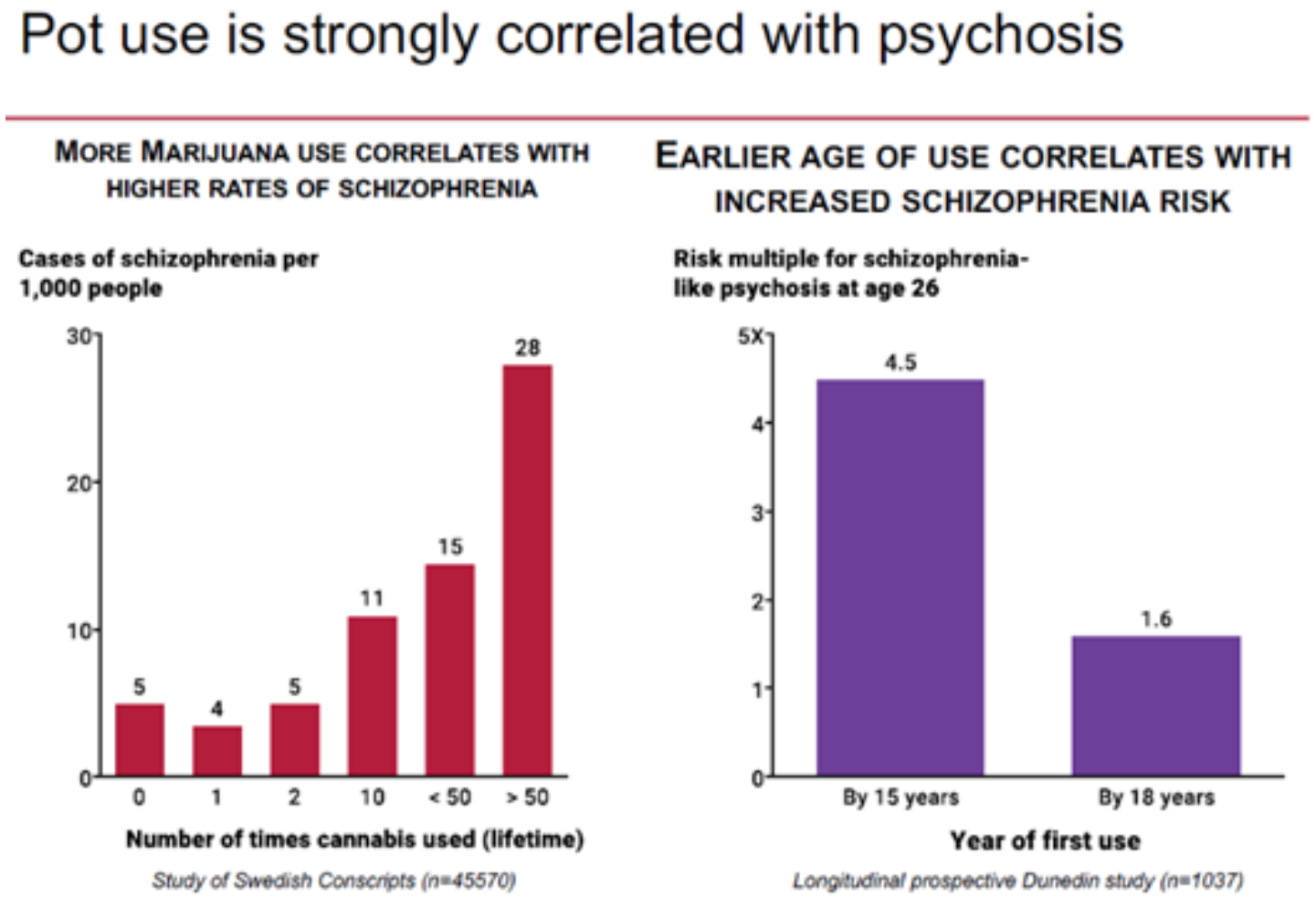
Impaired learning ability

Slowed information processing

Decreased motivation

- These all worsen with increasing usage
- These all worsen when usage begins in childhood or adolescence

Mental Health Effects of THC



- Increased paranoia
- Can trigger psychosis, including schizophrenia (Andreasson et al., 1987; Arseneault, 2002)
- Paranoid psychotic disorder in adulthood (D'Souza et al., 2016)
- Increased panic
- Increased anxiety disorders
- Increase depressive disorders

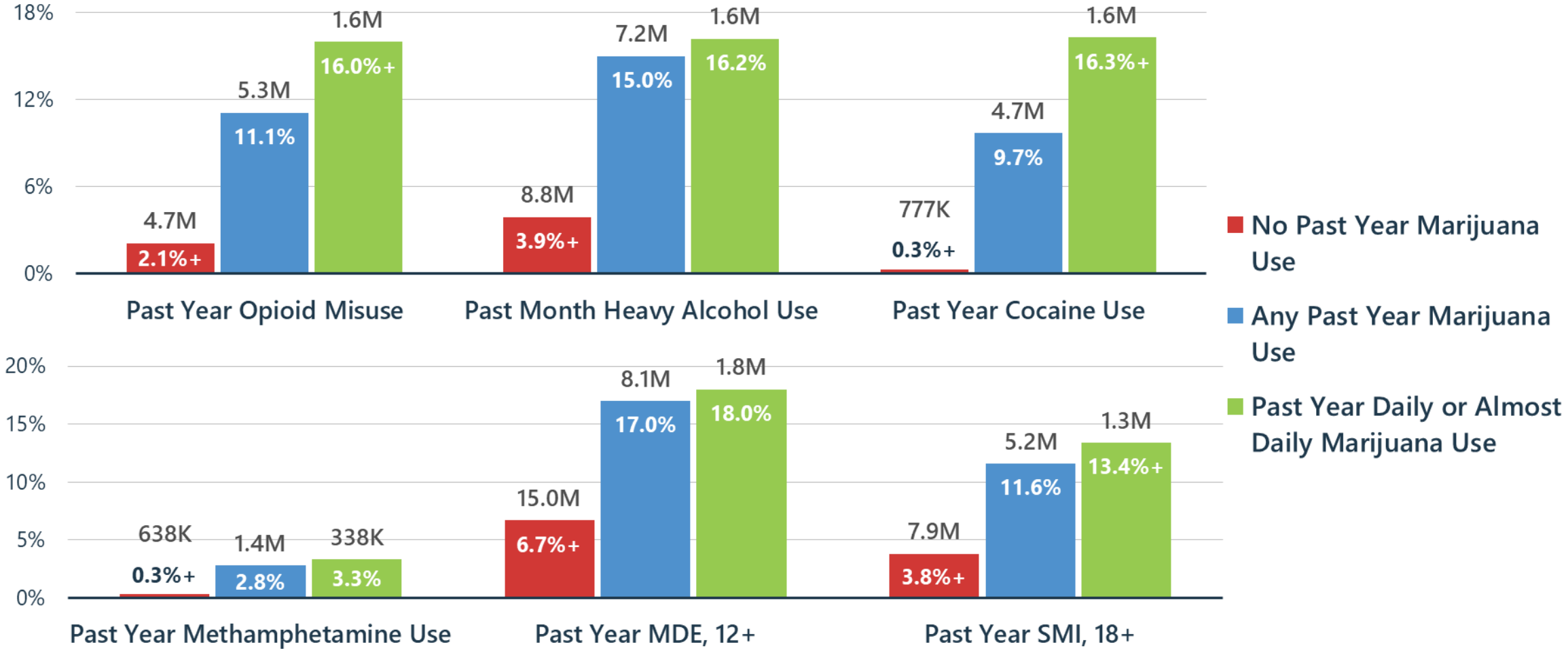
We know almost nothing about marijuana with > 16% THC content

Cannabis Use Continues to be Associated with Mental Health Problems

- Adults with depression have twice the likelihood of using cannabis compared to those without depression (Gorfinkel, Stohl, & Hasin, 2020)
  - The likelihood increased over the previous decade
- Cannabis Use Disorder (CUD) is associated with increased risks for self-harm, overall mortality, and death by unintentional overdose and homicide (Fontanella et al., 2021)
- Among Veterans, CUD is associated with increased risks for a history of suicide attempts, self-harm, and current suicidal ideation (Kimbrel et al., 2018)
- The proportion of schizophrenia cases associated with CUD has increased 3-4 X over two decades (Hjorthoj et al., 2021)

Marijuana Use Related to Other Substance Use, MDE and SMI

PAST YEAR/MONTH, 2019 NSDUH, 12+



+ Difference between this estimate and the estimate for people with past year marijuana use is statistically significant at the .05 level.

SAMHSA
Substance Abuse and Mental Health Services Administration

Other Problems Associated with Marijuana

- Anxiety
- Agitation
- Impaired judgment
- Apathy (Cannabis Amotivational Syndrome)
- Cannabis Hyperemesis Syndrome
- Impaired balance and coordination
- Unemployment
- Legal problems
- Motor vehicle accidents (Washington Post, June, 2017)

Drug Interactions

CNS Depressants

- Alcohol
- Benzodiazepines
  - Alprazolam
  - Clonazepam
  - Lorazepam
- Benzodiazepine-like
  - Zolpidem
  - Eszopiclone
- Muscle relaxants
- Opioids

Stimulants

- Amphetamines
- Cocaine

Anticholinergics

- Antihistamines

Some Antidepressants

- Tricyclic
  - Amitriptyline
- Serotoninergic
  - Fluoxetine

Northern New England Poison Center

1-800-222-1222
www.nnepc.org

Cannabis Can Be Addictive

- Regular cannabis users can develop tolerance, cravings, and withdrawal symptoms
- 10-20% become dependent on cannabis (Volkow et al., 2016)
  - 9% dependence for adult starters
  - 17% dependence for teenage starters
  - 25-50% for daily users
- Psychological dependence is also possible

Brain Aging

- The largest known study of brain aging (Amen et al., 2018)
  - 62,454 SPECT tomography scans of 30,000 brains from individuals 9 months-105 years
  - Studied 128 different brain regions
- It examined disorders that aged the brain
  - Schizophrenia was #1
  - Cannabis abuse was #2, aging the brain an average of 2.8 years
  - This was more than Bipolar Disorder, ADHD, or Alcohol Abuse
  - Cannabis aged the brain almost 5 times more than Alcohol Abuse

The cannabis abuse finding was especially important, as our culture is starting to see marijuana as an innocuous substance. This study should give us pause about it.

Daniel Amen

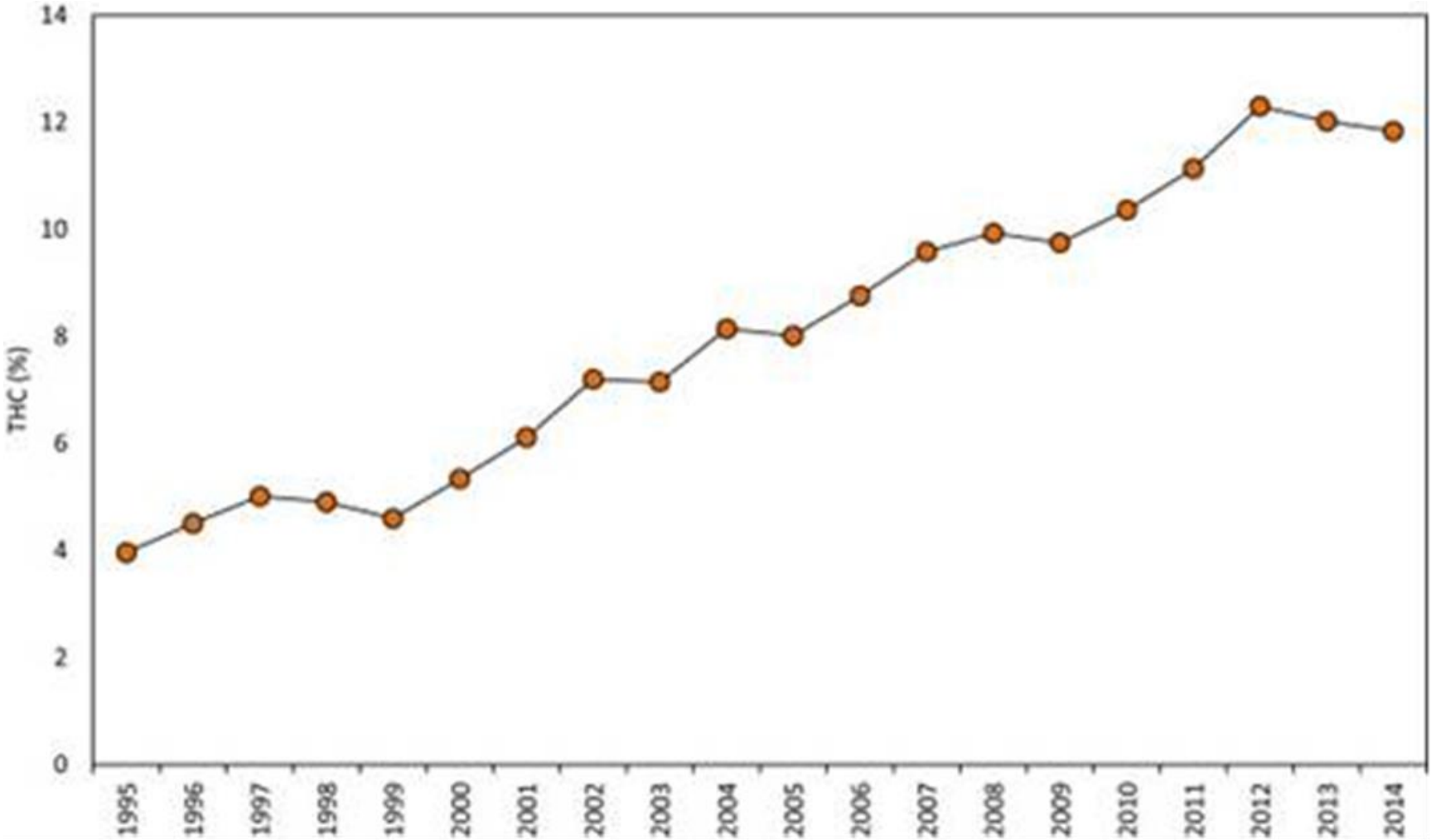
What Happened in Colorado after Medical Legalization

- An increase in ED visits for marijuana-associated illnesses
- An increases of marijuana-related burns, including some over 70% of the body and requiring as many as 21 skin grafts
- A doubling of Cannabis emesis syndrome, which involves cyclic vomiting, severe abdominal pain, and sweating
- Unintentional marijuana ingestion by children, sometimes requiring admission to pediatric intensive care
  - This is increased by edibles that are appealing to children
  - Childproof packaging is no longer childproof after opening
- Dosages that bring on delirium in adults can cause respiratory arrest in children
- Marijuana's involvement in fatal crashes doubled from 10% to 20% from 2013-2016 (Denver Post, 8/25/17)

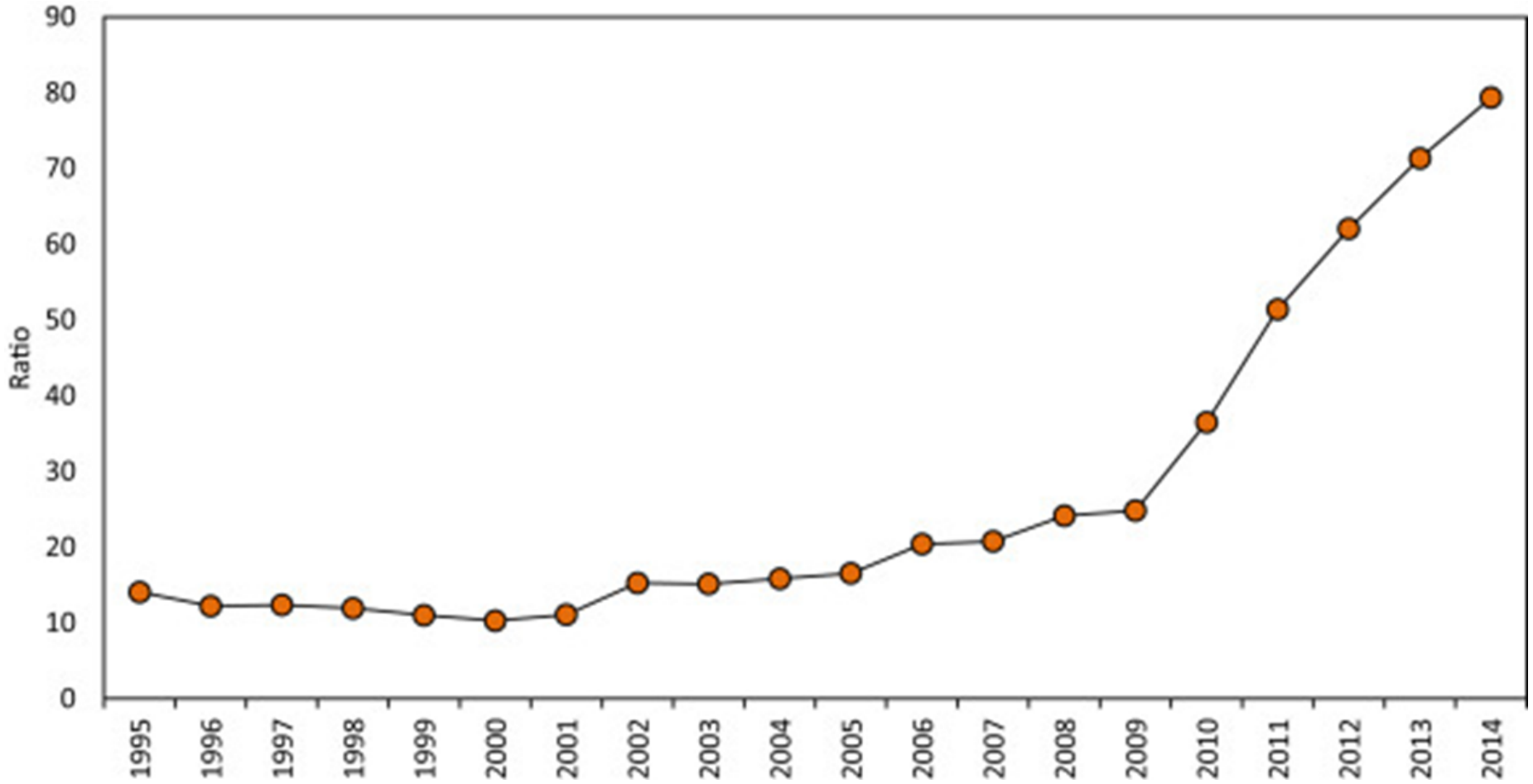
Monte et al., 2014

CANNABINOIDS

Tripling of THC Percentage in Cannabis 1995-2014



The Ratio of THC:CBD Has Increased in Cannabis 1995-2014



ElSohly et al., 2016

This Is Not Your Father's Cannabis

- A study of 38,681 samples of cannabis from 1995-2014 (Elsohly et al., 2016)
- The THC potency rose from an average of 4% in 1995 to 12% in 2014
- CBD content fell from an average of 0.28% to <0.15%
- The ratio of THC to CBD changed from 14:1 to 80:1
- Some extracts are above 50% THC

THC vs. CBD

THC

- Psychoactive
- Get high/euphoric
- Illegal
- Proven to help:
  - Decrease nausea
- Alleged to help many problems
- Relaxing/drowsy
- Can trigger paranoid psychosis
- Can increase anxiety
- Damages memory
- Apathy

CBD

- Not psychoactive
- No high
- Legal
- Proven to help:
  - Decrease childhood epileptic seizures
- Alleged to help many problems, including pain and anxiety
- Minimal side effects

The Potential Promise of CBD

Anti-Anxiety

- Studies of laboratory animals and of people suggest that CBD may have anxiolytic properties (Fusar-Poli et al., 2009)

Anti-Pain

- Some small studies show that CBD may have analgesic properties
- This is true at low doses
- Higher doses do not bring more pain relief (Wilsey et al., 2013)
- Two studies show that CBD may be helpful in decreasing spasticity and its pain in people with Multiple Sclerosis

Proven Medical Uses of Cannabinoids

THC

- To decrease nausea and vomiting
  - Wasting Syndrome
  - Cancer patients receiving chemotherapy
- Possibly for spasticity in Multiple Sclerosis

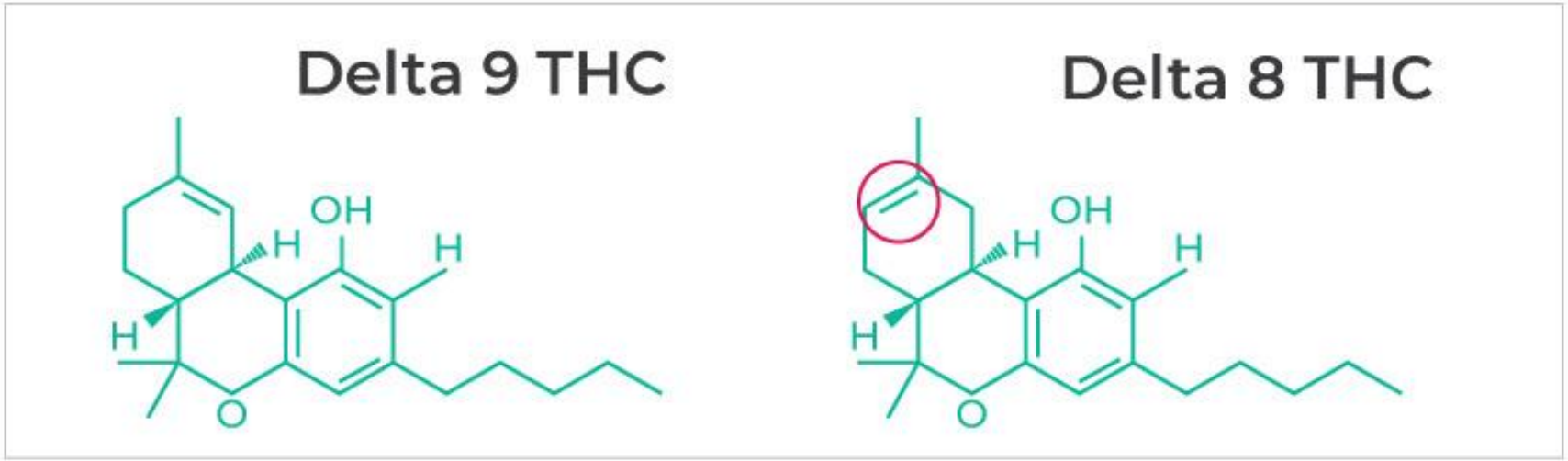
CBD

- For rare childhood forms of epilepsy
  - Dravet syndrome
  - Lennox-Gastaut syndrome
- Possibly for anxiety
- Possibly for some forms of pain

That's all

A New Cannabinoid: Delta-8 THC

- THC usually refers to the Delta-9 THC isomer
- Delta-8 THC is one of 113 cannabinoids in the cannabis plant
  - It is less potent than Delta-9 THC: marketed as “diet weed” or “weed light”
  - It is not currently illegal under federal law, and can be transported over state lines
  - It can be sold by businesses that sell hemp, not just regulated dispensaries
- Made by mixing CBD with acid (battery acid, pool chemicals, vinegar, etc.)
- Sold in smoke shops and gas stations



WHAT ABOUT PHARMACEUTICAL CANNABINOIDS?

Nabilone

- Nabilone is synthetic THC
- It is FDA-approved for treating nausea and vomiting associated with chemotherapy
- It contains flavonoids that may be therapeutic

Nabilone for nightmares?

- One study of 47 people (Fraser, 2009)
  - 72% had decreased nightmares
  - 28% quit due to side effects
- A RCT with placebo of 10 Canadian servicemen (Jetly et al., 2015)
  - Significant decrease in nightmares
  - No effects on sleep quantity or quality

Dronabinol/Marinol

- Dronabinol/Marinol is a liquid capsule used to treat nausea and vomiting caused by chemotherapy
- It has also been used to treat appetite loss in people with HIV
- It is a synthetic form of THC
- It has been used with mixed results to reduce cannabis dependence (Levin, 2011)
- It showed modest results in decreasing central neuropathic pain in patients with Multiple Sclerosis (Svendsen et al., 2004)

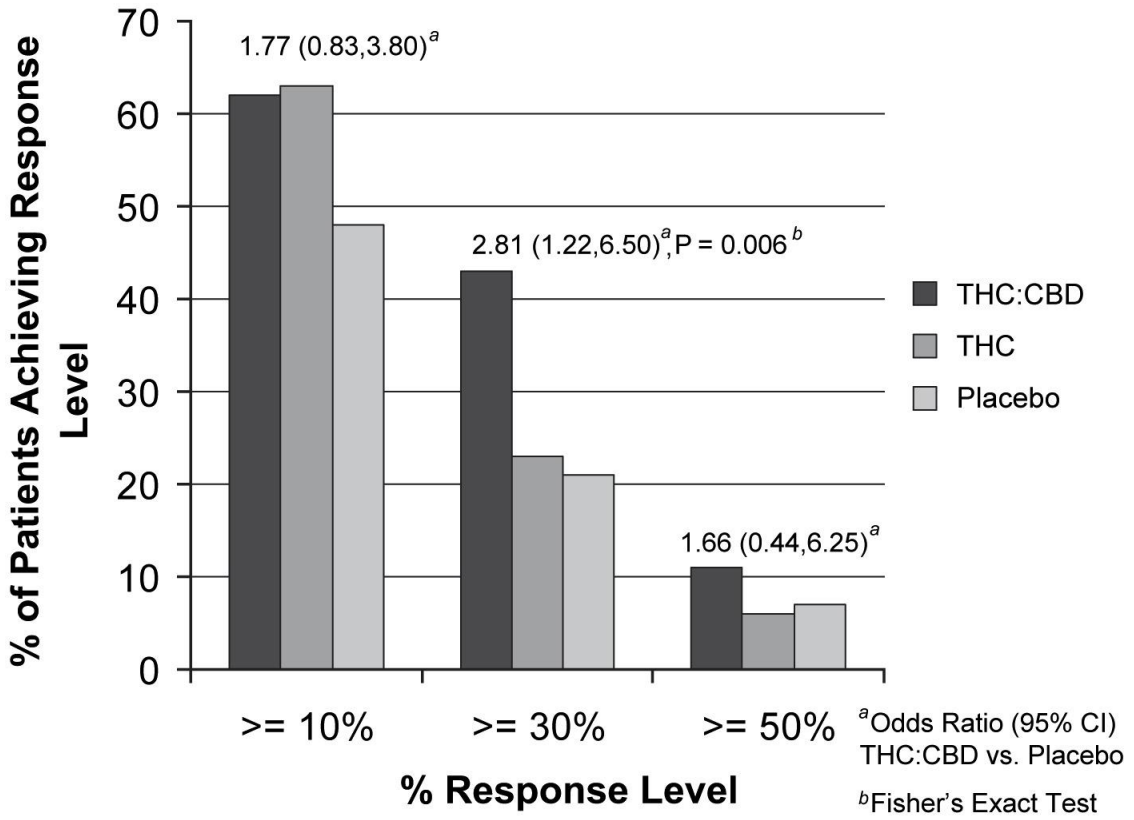
Nabiximols/Sativex

- A pharmaceutical cannabinoid
- Mix of botanical extract of cannabis sativa with chemical dronabinol in a nasal spray
- Used for central pain in Multiple Sclerosis
- Standardized dose of 2.7mg. THC and 2.5mg. CBD per spray
- 1-2 sprays up to 6x/day

- It has been used with mixed results to reduce cannabis dependence (Lintzeris et al., , 2019)

Nabiximols/Sativex for Pain

- Mixed results regarding Sativex for pain
- Pain types studied include cancer, MS, and neuropathic pain
- Some studies show pain decreases, but not increased functionality
- Metanalysis wipes out most gains



Johnson et al., 2010

Epidiolex

- Epidiolex is the first FDA-approved drug that contains a purified substance derived from marijuana
- It is an oral solution of synthetic CBD

- Epidiolex has been approved for the treatment of seizures in two rare and severe forms of epilepsy, Dravet syndrome and Lennox-Gastaut syndrome
- It is the first drug approved for treatment of Dravet syndrome
- Both of these forms of epilepsy appear in early childhood

A Small Study of the Effect of THC on PTSD

- 10 adult outpatients with chronic PTSD from MH clinics in Jerusalem
- Given adjunctive oral THC in 3-week, open-label, adjustable dose trial (starting dose 2.5 mg.)
- Statistically significant changes in PTSD hyperarousal symptoms, sleep quality, and nightmare frequency
- No significant changes in PTSD avoidance symptoms
- No significant changes in the Clinician Administered PTSD Scale (CAPS) total scores
  - The CAPS is considered to be the gold standard in PTSD measurement

Roitmanet al., 2014, summarized by Browne, 2019

Pharmaceutical Cannabinoids for Pain

- Mixed results: Only 6 of 11 studies of pharmaceutical cannabinoids (dronabinol, nabilone, and nabiximols) show that they provide more analgesic pain relief than placebo for neuropathic pain (Meng et al., 2017)
  - These are statistically significant but clinically small, measuring an average of 0.65 points on a scale of 0-10
  - Nabilone provided no relief

Summary

- Synthetic THC has been shown to decrease appetite and increase nausea
- Synthetic CBD has been shown to decrease seizures
- Mixed results of THC/CBD combination
- Some small N studies and animal model studies show possibility of that CBD may help chronic pain and/or anxiety
- Few blinded RCTs, the gold standard of research
- No studies show that cannabis leaves, oils, waxes, creams, edibles, or other forms of ingestion result in effective treatment of any problem
- Much more research needs to be done

WHAT CAN TREATMENT COURTS DO?

Treatment Courts Must:

- Be familiar with the laws of your state
- Be aware of the rapidly-changing nature of the science of cannabis and cannabinoids
- Take into account how marijuana can impact treatment (e.g., for PTSD)
  - This includes interactions with medications taken

Cannabis Interferes with Treatment

- Cannabis interferes with new learning and with the formation of memories
  - This makes it more difficult to learn new behaviors
- Cannabis interferes with treatment for PTSD
- Cannabis worsens Opioid Use Disorders
- Cannabis is associated with increased severity of Drug Use Disorders

If cannabis interferes with treatment, and you are working in a treatment court, how can you provide treatment that works?

What Can You Tell Participants?

- Those that claim it is legal: “So is alcohol, and we don’t allow alcohol consumption in Treatment Court.”
- Those who claim it is their right: “You do not have a legal right to participate in treatment court.”
- Those who claim it is medicine: “There are many medicines that we do not allow in treatment courts: opioids, benzodiazepines, stimulants, and others. All have the potential for abuse and addiction, which cannabis also does.”
- You may have to change your acceptance criteria when you screen potential participants.

Treatment Court Options

Always follow state law!

- Hold to the principle of total abstinence
- Allow the use of already-approved synthetic medicines like Marinol, Nabilone, Sativex, and Epidiolex, but only for on-label uses
- Decline to allow the use of any unproven substance or formulation (leaves, vaping, waxes, oils, creams, etc.)
- Decline to allow any alternative method of ingestion other than taking a pill composed of a synthetic cannabinoid
- Hold participants responsible for any THC showing up in their urine or blood
- Allow participants to use CBD products, holding them responsible if any THC shows up in their urine or blood

WHAT WILL YOUR COURT DECIDE TO DO?

BASE IT ON THE LAW AND THE SCIENCE.

QUESTIONS?

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