Understanding the Impact of Recreational Marijuana: Public Health Concerns and Clinical Issues

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Center for Practice Transformation
Second Friday Webinar Series
December 13, 2019

Marijuana Legalization Status

- Medical marijuana broadly legalized
- Marijuana legalized for recreational use
- No broad laws legalizing marijuana

Professional Disclosure

- I am a coalition member of Smart Approaches to Marijuana Minnesota (www.SAMMn.org).

- Mission: To educate the citizens of Minnesota on the research and science of marijuana usage with the scientific understanding of marijuana's harms and potential as medicine.

  Our public health position is that <u>current science</u> does not support the commercialization and normalization of recreational marijuana use.

A Personal Disclosure

- It's Friday the 13th but I am not superstitious!

- **Many great or interesting things have occurred on a Friday the 13th:**
  1. First heavy metal album debuted in 1970 (Black Sabbath)
  2. One of the most famous video games of all time was released, *Super Mario Bros.*
  3. In Finland, every Friday the 13th, this particular daily flight demarcation is offered: Flight 666 to HEL

Select Web-Based Resources on Cannabis

National Organization for the Reform of Marijuana Laws (NORML):
http://norml.org/

Marijuana Policy Project (MPP):
https://www.mpp.org/

NIDA:
https://www.drugabuse.gov/publications/drugfacts/marijuana

Smart Approaches to Marijuana (SAM):
www.learnaboutsam.org

National Marijuana Initiative:
https://thenmi.org/

Consider This Recent Resource from SAM (www.learnaboutsam.org)

LESSONS LEARNED FROM STATE MARIJUANA LEGALIZATION

MAY 2019

CA WA CO OR AK DC NV MA

Reviewed by researchers from:
University of Colorado at Denver
Harvard Medical School
Boston Children's Hospital
University of Connecticut
Yale University
University of Kansas
and more

SAM Smart Approaches to Marijuana
preventing another big tobacco

www.learnaboutsam.org

1. **Background**
   - research challenges
   - legalization & use

7. Summary

2. Major Reviews of Health Effects

6. Prevention & Treatment

3. Mental Health

5. Cannabis as Medicine

4. Driving Impairment

Cannabis is Complex to Study

- **Contains hundreds of chemicals**
- **Impacts numerous regions of the brain**
- **Federal regulations for access by scientists can frustrate the advancement of research (same as all Schedule 1 drugs)**
- **Difficult to administer to animals in standardized ways**
- **Difficult to measure 'intoxication' levels in humans**
- **Rapid changes in use and perceptions**

Effects of Cannabis Use on Human Behavior, Including Cognition, Motivation, and Psychosis: A Review

Nora D. Volkow, MD; James M. Swanson, PhD; A. Eden Evins, MD; Lynn E. DeLisi, MD; Madeline H. Meier, PhD;
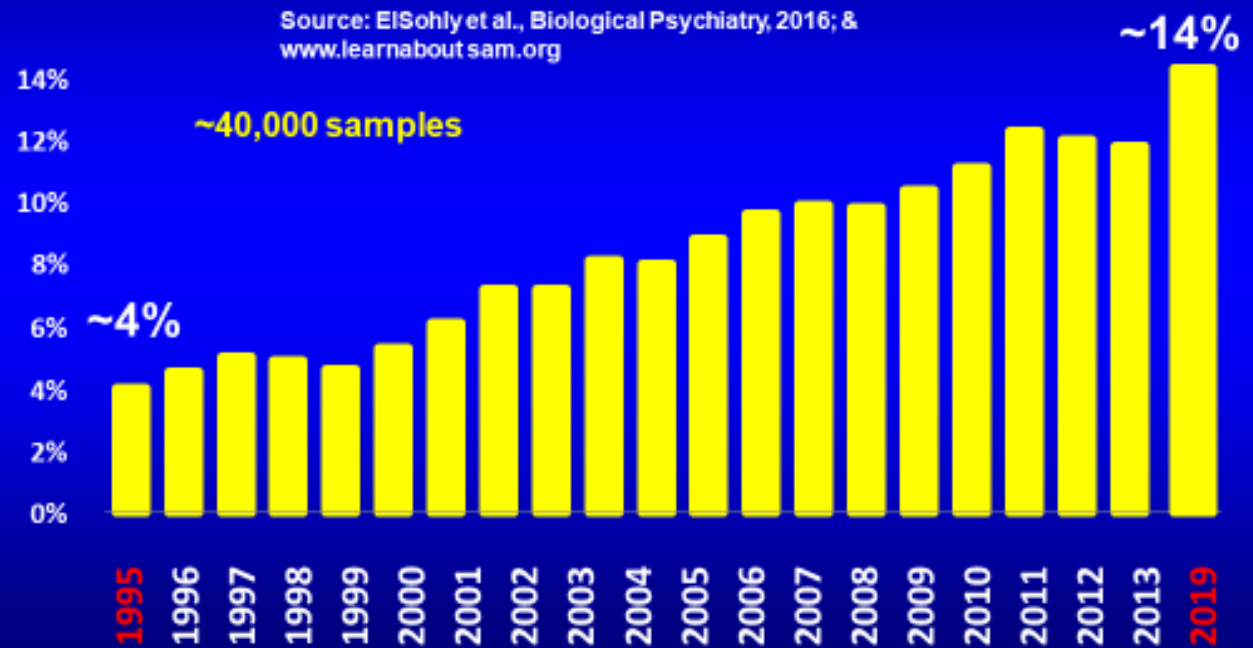Raul Gonzalez, PhD; Michael A. P. Bloomfield, MRCPsych; H. Valerie Curran, PhD; Ruben Baler, PhD

"The changing landscape of cannabis (e.g., strains with THC potency; new routes of administration; novel drug combinations), and a culture of rapidly changing norms and perceptions, raise the possibility that our current, limited knowledge may only apply to the ways the drug was used in the past."

Avg. % THC Content among Confiscated Cannabis Products in U.S. (1995-2019)

Source: ElSohly et al., Biological Psychiatry, 2016; & www.learnaboutsam.org

~40,000 samples

~4%

~14%

1995 1996 1997 1998 1999 2000 2001 2002 2003 2004 2005 2006 2007 2008 2009 2010 2011 2012 2013 2019

"Public Health" Questions are Difficult to Research

Let this magic mineral, ASBESTOS, protect the buildings on your farm!

Asbestos! The magic mineral of the Middle Ages. Today, still a "magic" mineral; fireproof, rot-proof,

JM

BUTTER

GOOD AND GOOD FOR YOU

YOUR NUTRITION TIP:
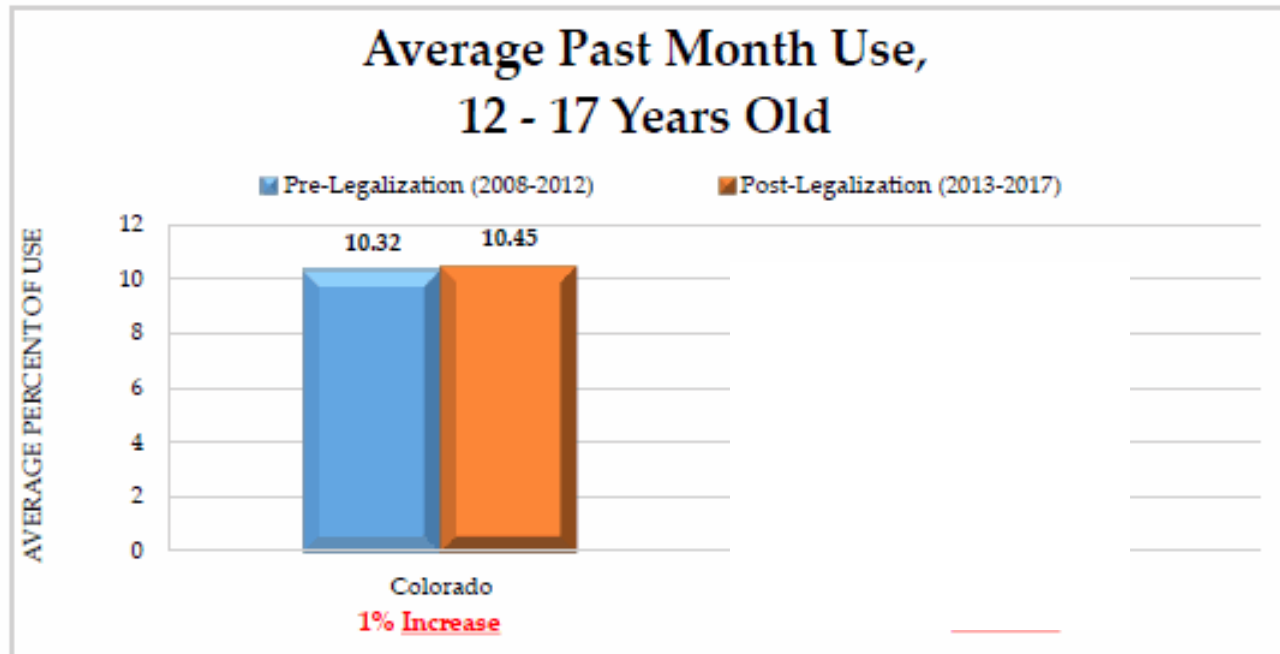BUTTER IS SLIPPERY. THAT'S WHY WE EAT AS MUCH AS POSSIBLE TO LUBRICATE OUR ARTERIES AND VEINS.

Considerations when Interpreting Public Health Data and Reports

CAUSE

EFFECT

1. **Confirmation bias**

2. Small sample sizes

3. Community-level vs. individual-level data

4. Too small a time window

Adolescent Use and Legalization

Average Past Month Use, 12 - 17 Years Old

■ Pre-Legalization (2008-2012) ■ Post-Legalization (2013-2017)

Colorado
1% Increase

SOURCE: SAMHSA.gov, National Survey on Drug Use and Health

NOTE: When comparing the three year averages, the years for pre-legalization include: 2009/2010; 2010/2011; and 2011/2012. Post-legalization years include: 2013/2014; 2014/2015; 2015/2016; and 2016/2017. The data for 2012/2013 was not include since it represents a year with and a year without legalization.

Vaping THC

December 6, 2019 issue of CDC's *Morbidity and Mortality Weekly Report* (*MMWR*)

- **2,291 vaping-related lung injury cases in all 50 states, 2 US territories; 48 deaths in 25 states**
- **THC is present in most of the samples tested by FDA.**
- **Vitamin E acetate is a chemical of concern**

From a anti-legalization organization: "While the marijuana industry insists that the THC cartridge brands making people sick are purchased exclusively from illicit, black-market dealers, several individual states report some patients have bought them from licensed dispensaries."

From a pro-cannabis organization: "The THC-vaping illnesses are due to unregulated and illegal manufactures and distributors who are diluting the product with contaminants."

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The Dunedin Study (New Zealand) (N=1,037)

13 yrs
(Pre-initiation)

18 yrs   **21 yrs**   **32 yrs**   **38 yrs**

1   2   3   4   5

Assessment ages

Marijuana and Cognitive Development

Adolescent Vulnerability
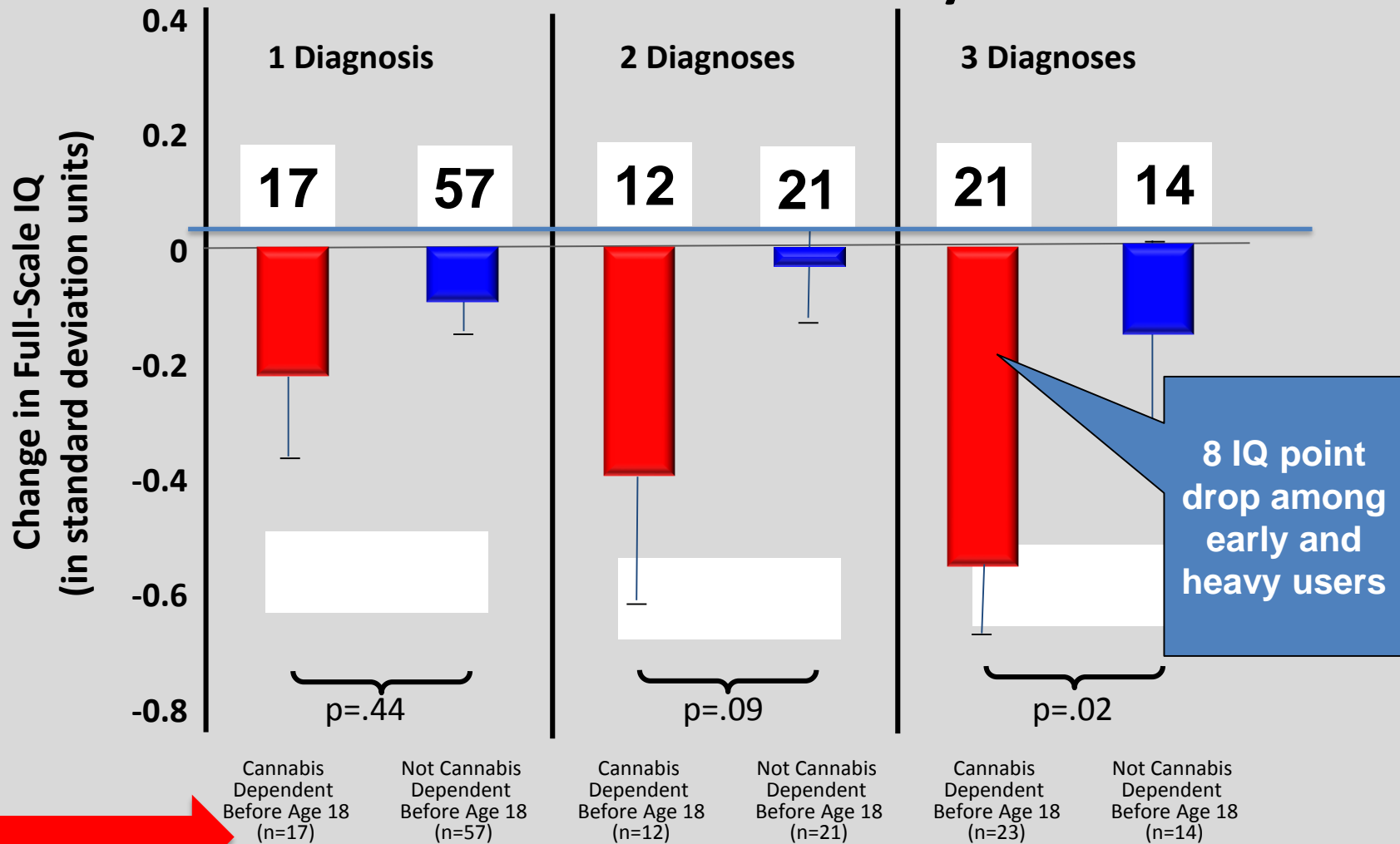
Source: Meier MH et al., PNAS Early Edition 2012

Adolescent Brain Cognitive Development (ABCD) National Longitudinal Study

Ten year longitudinal study of 13,000 children from age 10 to 20 years to assess effects of drugs on individual brain development trajectories

See the Center's webinar library for a recent talk on the ABCD study (https://practicetransformation.umn.edu/webinars/)

Slide courtesy of Maureen Boyle, PhD

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Will legalization help alleviate the opioid abuse crisis?

OVERDOSE DEATH RATES IN AMERICA

- Opioid Pain Relievers
- Heroin
- Cocaine
- Marijuana

All underlying causes of death*

25k
20k
15k
10k
5k
0

'99 '00 '01 '02 '03 '04 '05 '06 '07 '08 '09 '10 '11 '12 '13
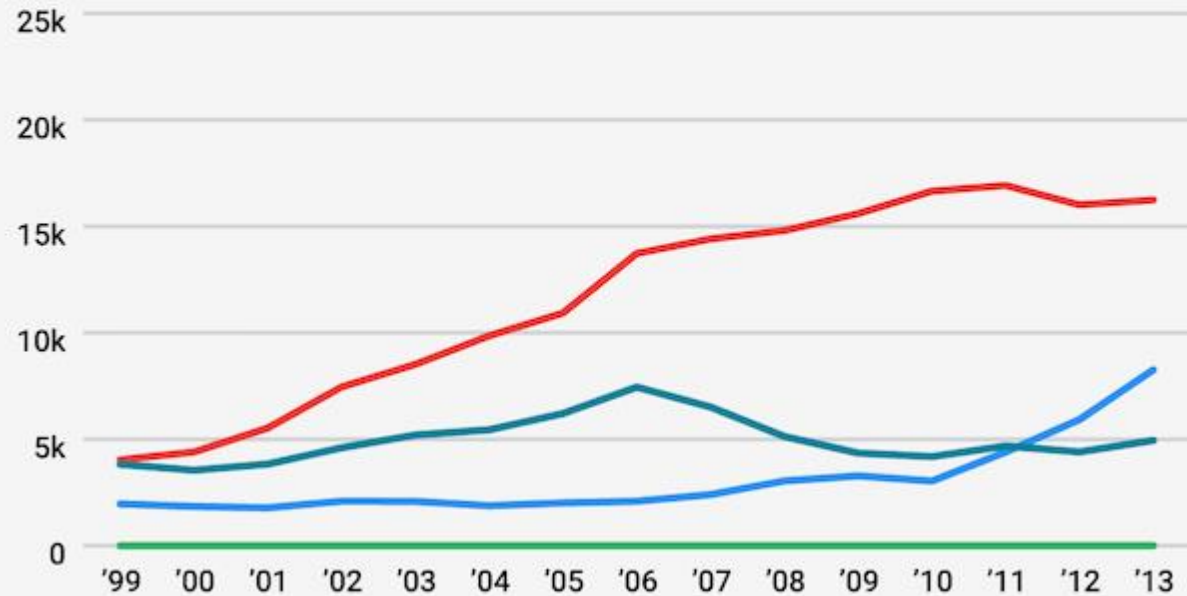
*Includes deaths from unintentional drug poisoning, suicide drug poisoning, homicide drug poisoning or drug poisoning of undetermined intent.

You may have seen this...

Early Rounds: Opioid Abuse in Medical Marijuana States

Bachhuber et al., 2014:

"Medical cannabis laws (MCLs) are associated with significantly lower state-level opioid overdose mortality rates."

- 13 states with MCLs compared to non-MCL states
- <u>MCL states had 25% lower</u> mean annual opioid overdose mortality rate compared to non-MCL states

Early Rounds: Opioid Abuse in Medical Marijuana States

Wen & Hockenberry, 2018:

"State implementation of medical marijuana laws was associated with a 5.9% lower rate of opioid prescribing. Moreover, the implementation of adult-use marijuana laws, which all occurred in states with existing medical marijuana laws, was associated with a 6.4% lower rate of opioid prescribing."

Not so Fast?

- **Epidemiological-based data is the weakest design to confer causation between two variables or domains.**

- **Several confounds not considered**
  - changes in opioid prescribing regulations and restrictions
  - changes in use of medication-assisted therapies

- **Individual-based data on actual use represent stronger data**

- **What if a longer time frame were examined?**

Later Rounds: Opioid Abuse and Cannabis: Re-Do of Bachhuber study
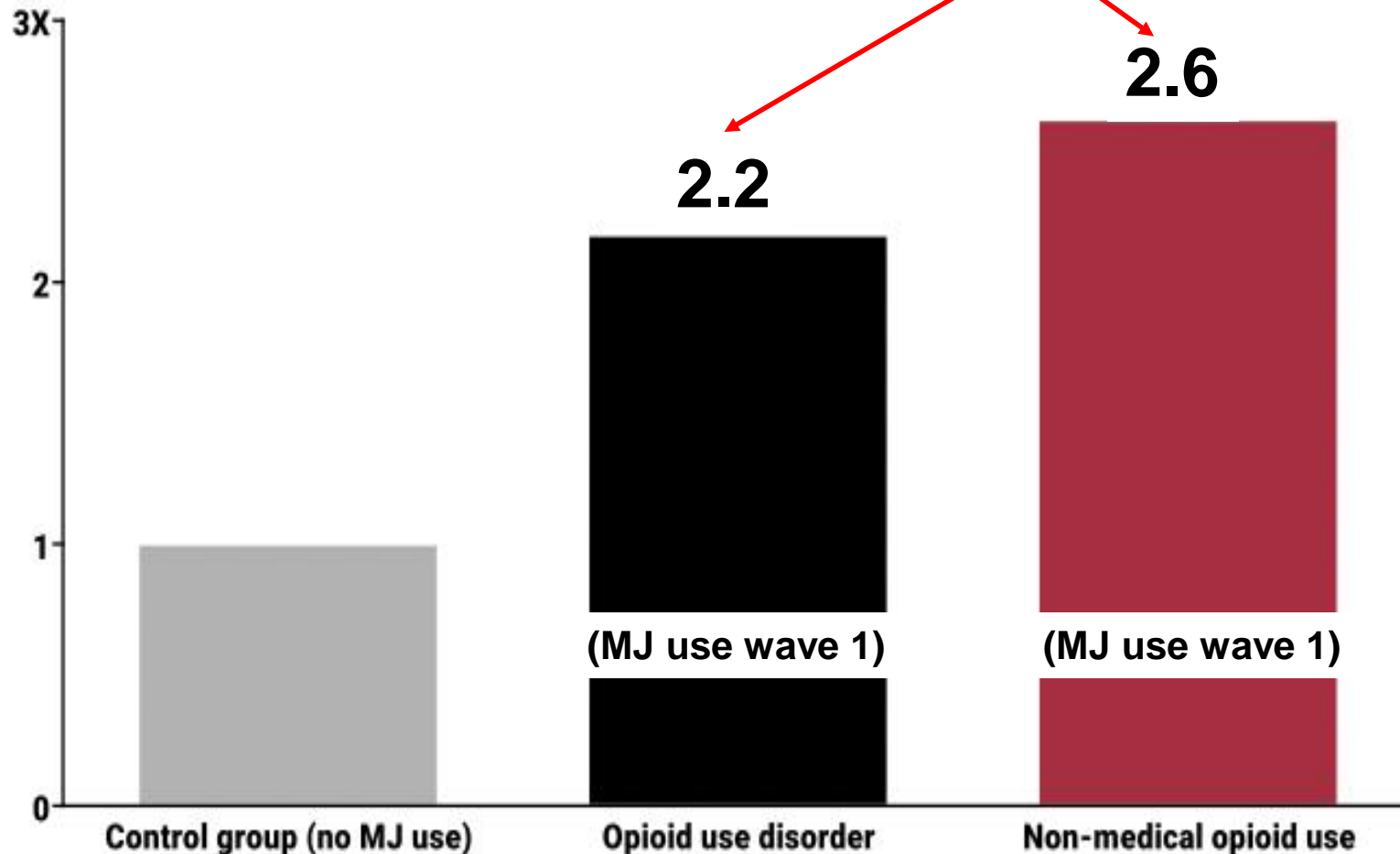**(Shover et al., 2019)**

- **This recent study used the same methods and data as the Bachhuber study but included an additional seven years of data (2011-2017) – a period in which overdose death rates rose sharply and more states legalized recreational and medical marijuana. By including the full 1999–2017 dataset, the authors found that states with medical cannabis laws experienced a <u>22.7% increase in overdose deaths</u>.**

- **"Research into therapeutic potential of cannabis should continue, but the claim that enacting medical cannabis laws will reduce opioid overdose death should be met with skepticism."**

- **Reminder: Bachhuber et al. study based on 1999-2010**

Later Rounds: Opioid Abuse and Cannabis: Individual-Level Data

(Olfson et al., 2018. Based on NESARC data, comparing 2001-2002 and 2004-2005)
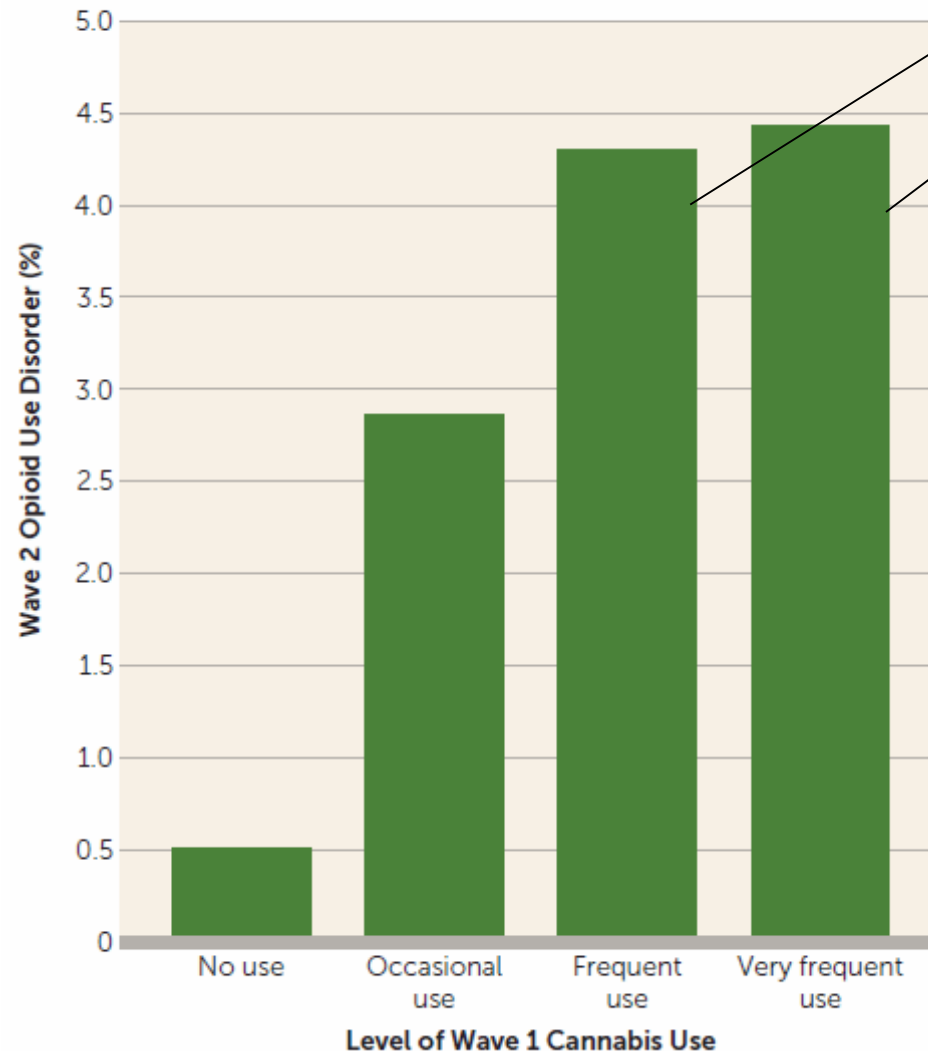
Chance of subsequent opioid abuse for marijuana users compared to control group

Odds of later opioid "abuse" among earlier cannabis users

- 3X
- 2.6
- 2.2
- 2
- 1
- 0

Control group (no MJ use) — **Opioid use disorder** (MJ use wave 1) — **Non-medical opioid use** (MJ use wave 1)

More on Olfson et al., 2018. Based on NESARC data, comparing 2001-2002 and 2004-2005)

FIGURE 1. Level of Wave 1 Cannabis Use and Incident Wave 2 Prescription Opioid Use Disorder in the NESARC[a]

Greater MJ Use at W1 was Linked to Higher % of Opioid Use Disorder

Y-axis: Wave 2 Opioid Use Disorder (%)

X-axis: Level of Wave 1 Cannabis Use (No use, Occasional use, Frequent use, Very frequent use)

Later Rounds: Opioid Abuse and Cannabis: Individual-Level Data

(Campbell et al., 2018. Australian study; comparing 2012-2014 and 2016-2018)

- Longitudinal study of 1,514 Australians with chronic non-cancer pain. Baseline and 4-year follow-up data pertaining to marijuana use, opioid use and pain were examined.

- **"Cannabis use was common in people with chronic non-cancer pain who had been prescribed opioids, but we found no evidence that cannabis use improved patient outcomes. There was no evidence that cannabis use reduced pain severity or interference, or exerted an opioid-sparing effect."**

Later Rounds: Opioid Abuse and Cannabis: Individual-Level Data

(Stockings et al., 2018. Literature Review

Cannabis and cannabinoids for the treatment of people with chronic noncancer pain conditions: a systematic review and meta-analysis of controlled and observational studies

- The researchers reviewed 104 studies from 91 publications involving a total of 9,958 participants. About half (47) were randomized controlled trials; the rest (57) were observational studies.

- The studies included numerous sources of chronic non-cancer pain (CNCP): neuropathic pain, fibromyalgia, rheumatoid arthritis, multiple sclerosis-related pain, visceral pain, and a mix of different kinds or undefined kinds of chronic non-cancer pain.

- **"Evidence for effectiveness of cannabinoids in chronic non-cancer pain (CNCP) is limited. It seems unlikely that cannabinoids are highly effective medicines for CNCP."**

(Cannabinoids included THC, CBD, THC+CBD, other MJ plant-based compounds, and synthetic THC)

NORML:
http://norml.org/

Marijuana Policy Project (MPP:
https://www.mpp.org/

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Historical Perspective

- **Popularity of cannabis in recent times**
  - **40' – 50's:** tobacco use and alcohol popularized; illicit drugs dangerous; *Reefer Madness*
  - **60's – late 70's:** Woodstock generation; push for decriminalization or legalization; Cheech & Chong
  - **80's – early 90's:** crack epidemic; downturn in use of all illicit drugs
  - **1995 – current:** resumption of push for legalization; cannabis as medicine (Compassionate Use Act in CA); despite federal law, almost two-thirds of states have pro-cannabis laws

Cannabis and Legalization, Dec. 2019
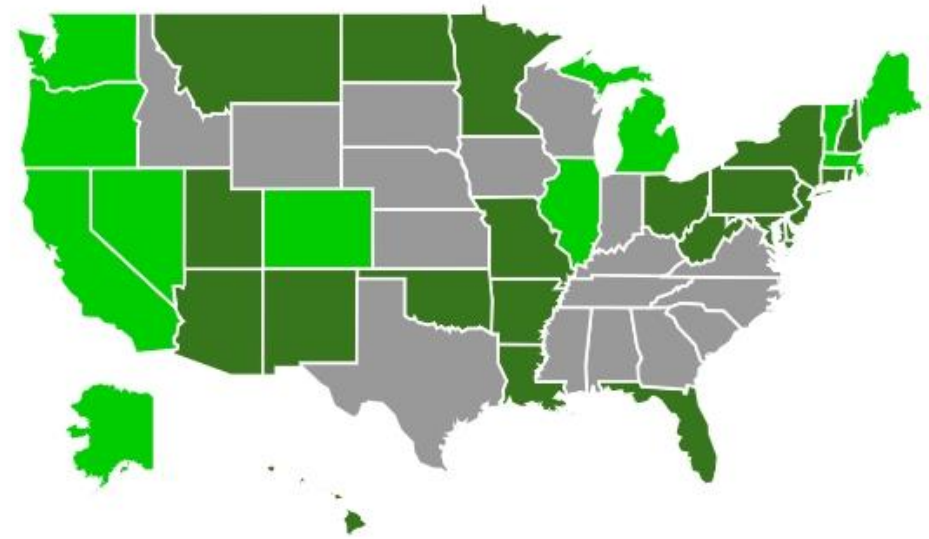
Marijuana Legalization Status
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Total # of "pro-cannabis" states: 33 & D.C.

Commercial use: 11 & D.C.

Medical use only: 22

Decriminalized only: 5

11th state: Illinois in 2020

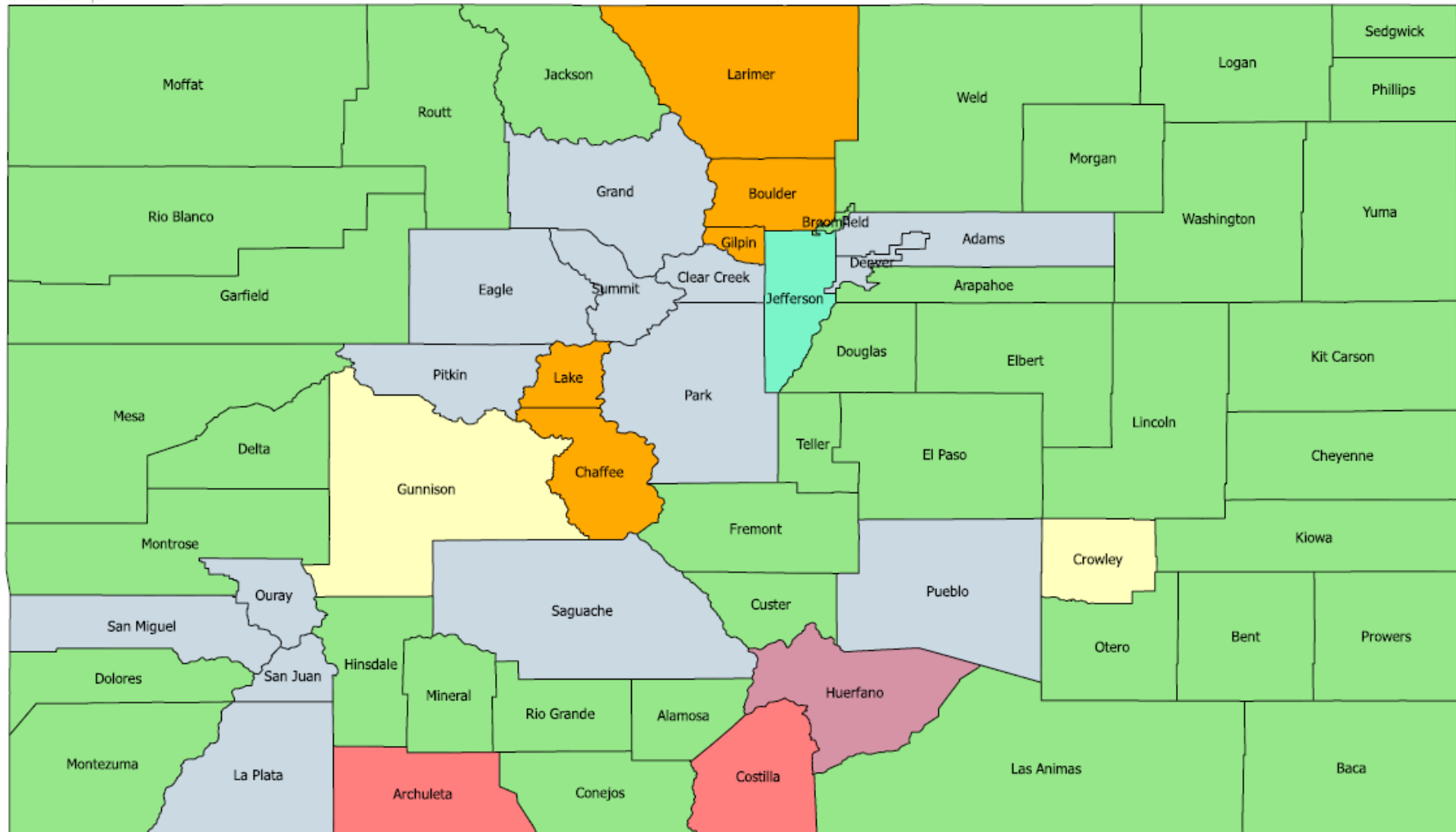# Marijuana and Legalization, June, 2019
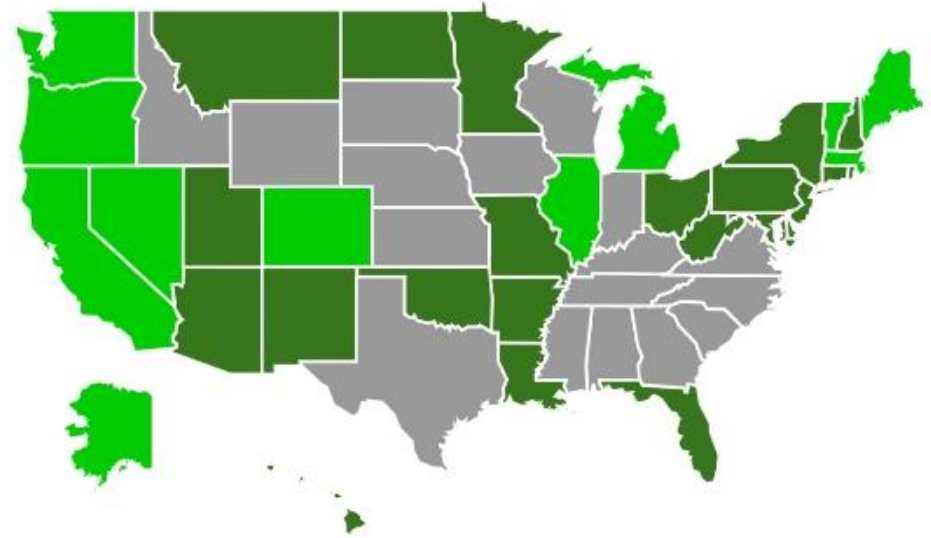
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10 states in the past two years have applied the brakes to full-legalization efforts (CT, FL, MN, ND, NH, NJ, NM, NY, WI, VT)
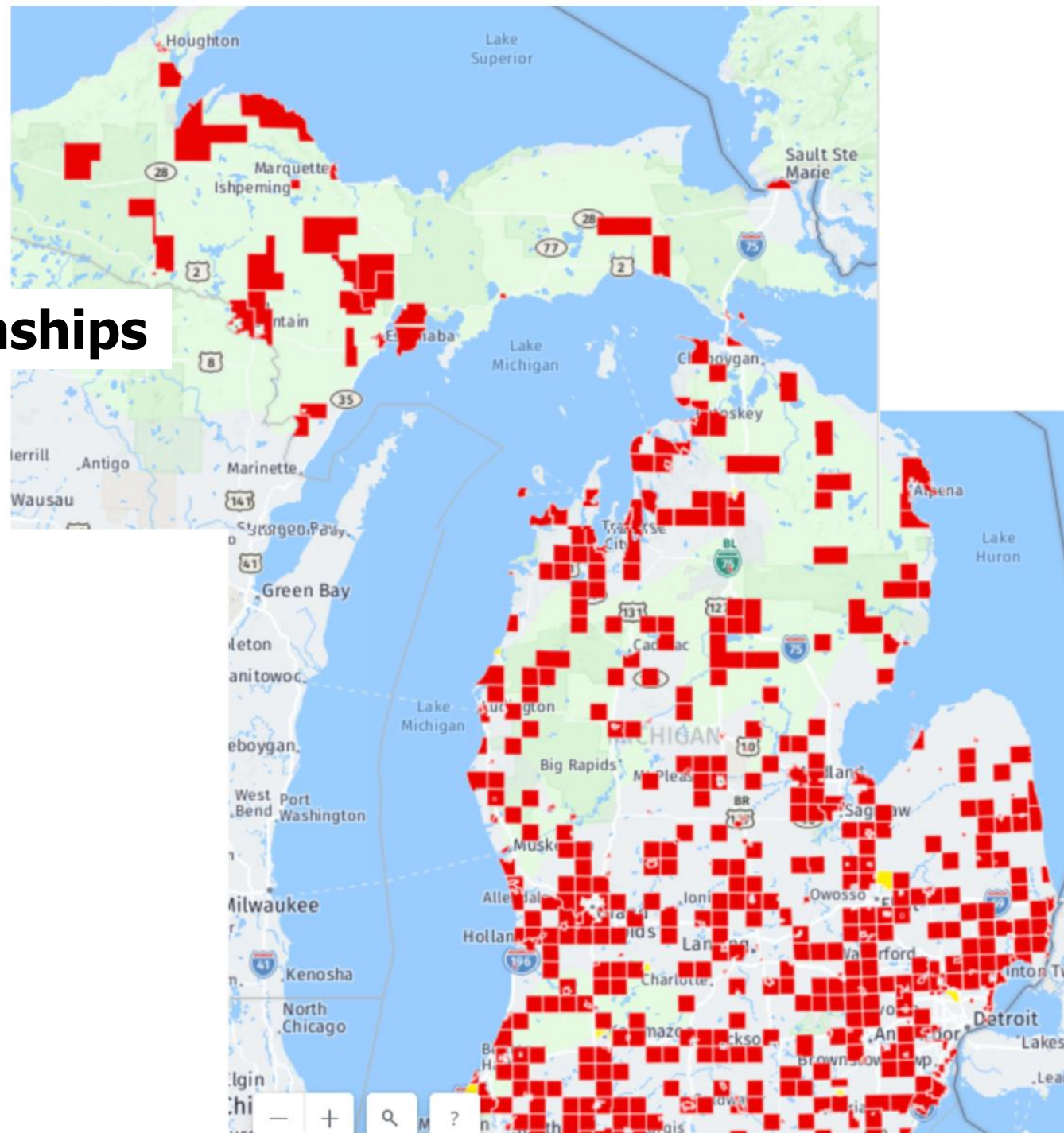
Colorado Counties and Cannabis Regulations

Legend:

- Allowing Cultivation Only
- Allowing Sales and Cultivation Only
- Allowing Testing Only
- Ban or Moratoria in Effect
- Allowing Sales, Cultivation, Product Manufacturing & Testing
- Prohibiting New Establishments, but Allowing Migration of Existing
- Allowing Cultivation, Product Manufacturing & Testing Only

For Information purposes ONLY. Please contact individual counties for specifics on their regulatory status.

Created by Trent Pingenot for CCI

Map Revision: August 4, 2017

Counties shown: Moffat, Routt, Jackson, Larimer, Weld, Logan, Sedgwick, Phillips, Rio Blanco, Grand, Boulder, Broomfield, Adams, Washington, Yuma, Gilpin, Denver, Morgan, Garfield, Eagle, Summit, Clear Creek, Jefferson, Arapahoe, Mesa, Pitkin, Lake, Park, Douglas, Elbert, Kit Carson, Delta, Teller, Lincoln, Cheyenne, Chaffee, El Paso, Gunnison, Fremont, Montrose, Kiowa, Crowley, Ouray, Saguache, Custer, Pueblo, San Miguel, Dolores, Hinsdale, Mineral, Rio Grande, Alamosa, Huerfano, Otero, Bent, Prowers, San Juan, Montezuma, La Plata, Archuleta, Conejos, Costilla, Las Animas, Baca

21

Michigan Cities\Townships

Massachusetts Towns

Counties/townships banning or moratorium commercial sales

County Regulatory Status - Recreational Marijuana

Colorado

Michigan

Massachusetts
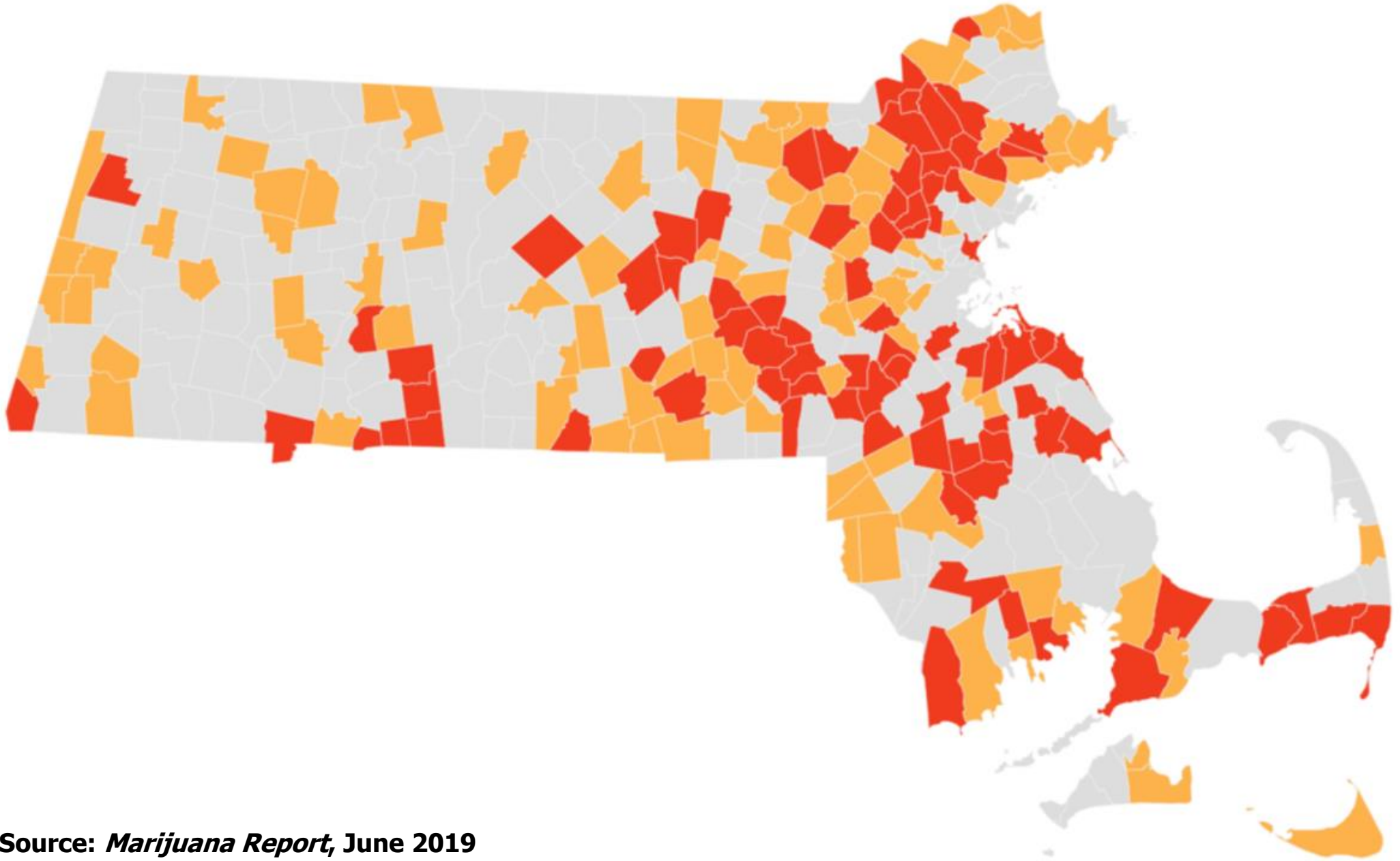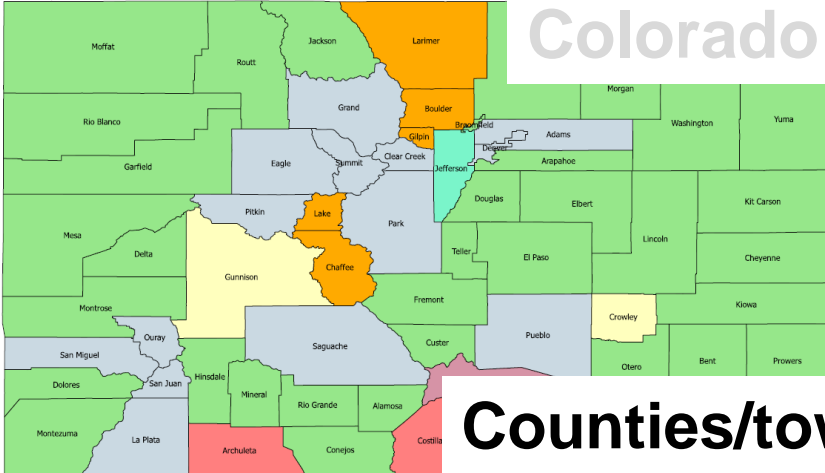
Allowing Cultivation Only
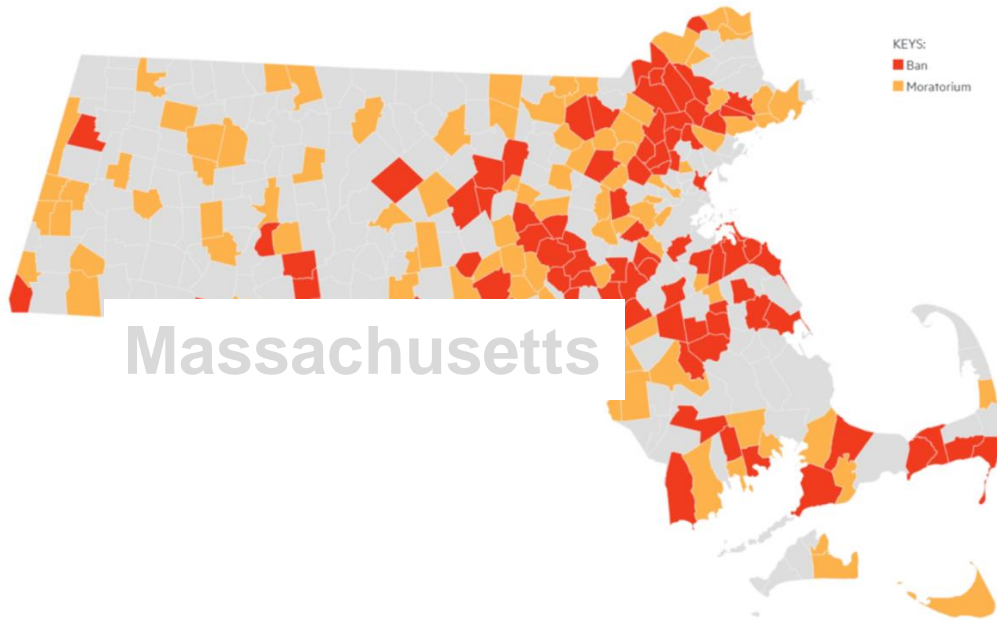Allowing Sales and Cultivation Only
Allowing Testing Only
Ban or Moratoria in Effect
Allowing Sales, Cultiva
Prohibiting New Estab
Allowing Cultivation, P

For Information purposes ONLY. Please contac

KEYS:
Ban
Moratorium

SOURCE: WBUR analysis of Massachusetts Municipal Association Data

Use of Cannabis – The Plant is Complex

- **Contains over 400 chemicals**

  - **delta-9-tetrahydrocannabinol (THC)**

  - **delta-8-tetrahydrocannabinol**

  - **cannabidiol (CBD)**

  - cannabinol

  - cannabichromene

  - cannabigerol

 - etc.

Use of Cannabis – The Plant is Complex

- **All the cannabinoids in the cannabis plant remain a Schedule I substance under federal law and are thus illegal**

- **The one exception is pharmaceutical-grade CBD products that have been approved by FDA, which currently includes one drug: GW Pharmaceutical's Epidiolex**

- **Can THC or CBD products be sold as dietary supplements? FDA: no**

- **Can CBD products be sold as cosmetics and creams? FDA: not their jurisdiction so "yes" (buyer beware)**

- **Hemp is no longer an illegal substance. Hemp is any part or derivative of the cannabis plant containing less than 0.3 percent THC by weight.**

THC Binds to Cannabinoid Receptors Located Throughout the Brain
(source NIDA)

- Brain Development
- Memory & Cognition
- Motivational Systems & Reward
- Appetite
- Immunological Function
- Reproduction
- Movement Coordination
- Pain Regulation & Analgesia

movement

sensations

vision

judgement

reward

memory

coordination
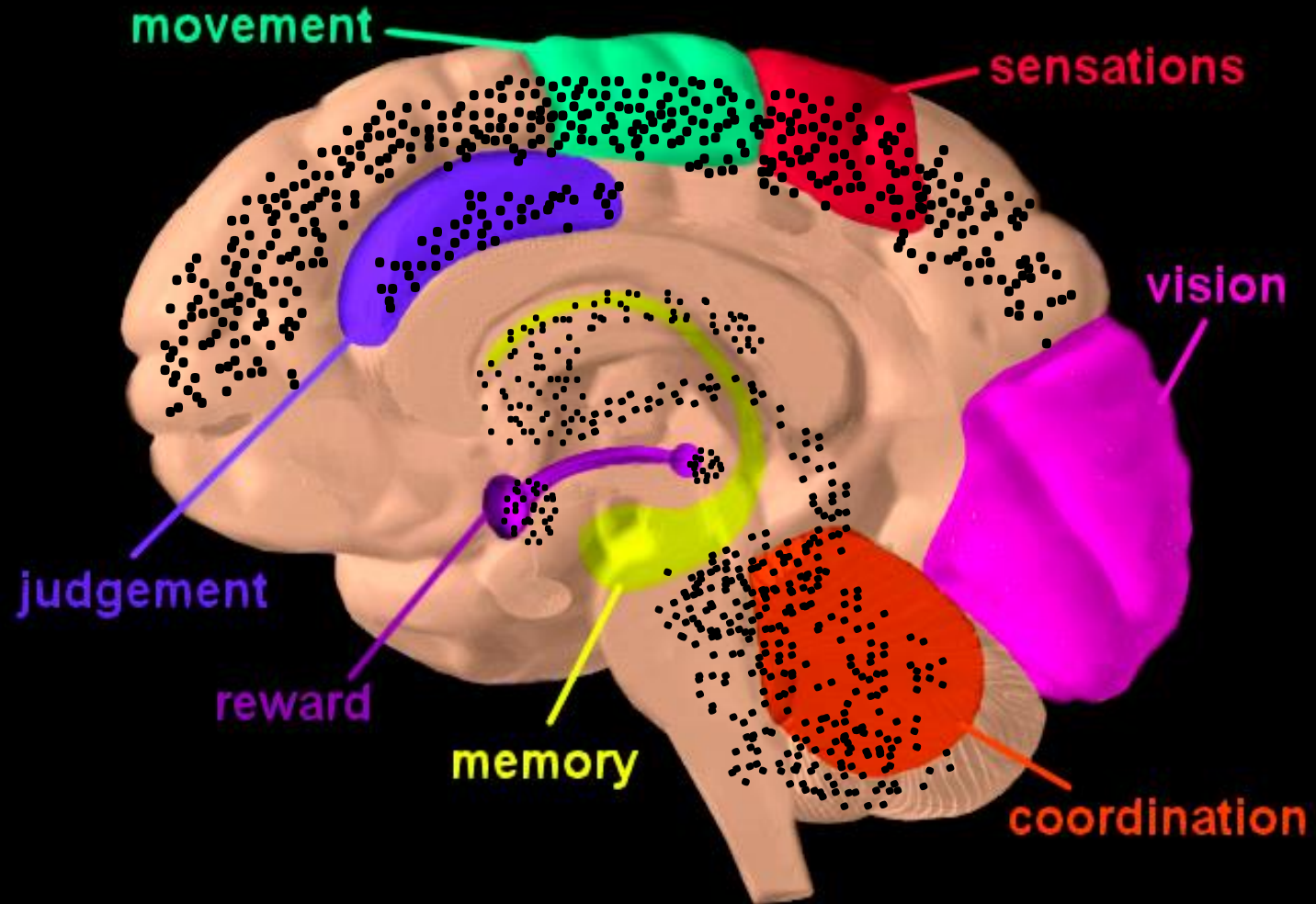
Slide courtesy of Maureen Boyle, PhD
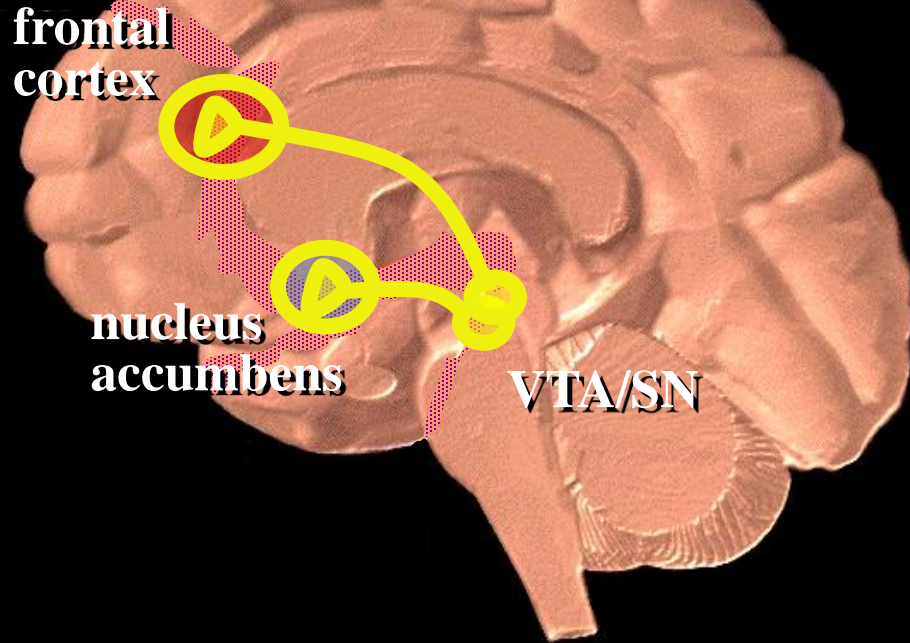
Cannabinoid receptors in our brains - why?

- **These receptors are the main "volume" controls for neurotransmitters that affect pleasure, mood, pain, appetite, motivation, memory**

- **Animal studies show that without these receptors…**
  - **Experience more pain**
  - **Can't control appetite**
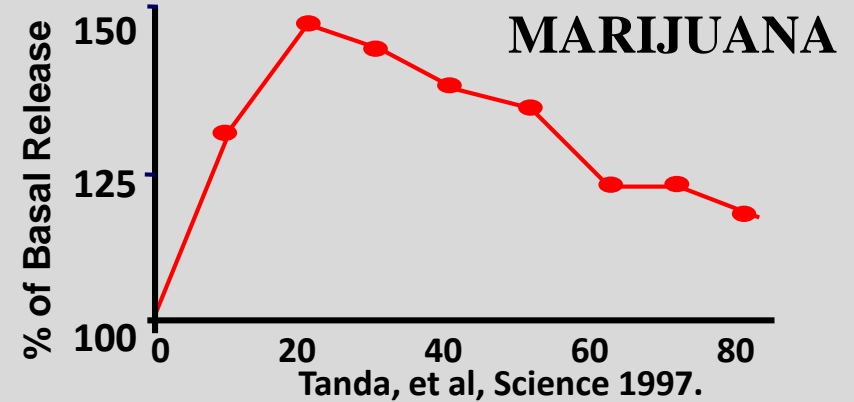 - **More anxious**
  - **Less able to cope with stress**

Addictive Risk

Reward Pathway

frontal cortex

nucleus accumbens

VTA/SN

Drugs of abuse increase dopamine in the reward pathway region

AMPHETAMINE

% of Basal Release

1100 1000 900 800 700 600 500 400 300 200 100 0

0   1   2   3   4   5 hr

MARIJUANA

% of Basal Release

150

125

100

0   20   40   60   80

Tanda, et al, Science 1997.
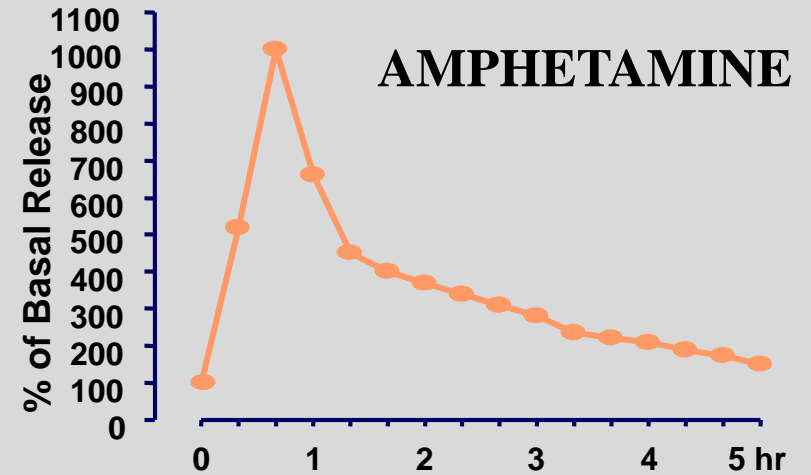
Slide courtesy of Maureen Boyle, PhD

"Addictive" Potential of Psychoactive Substances

Estimated Prevalence <u>in 1994</u> of Dependence Among Users (lifetime; age 15-54)

More current est:
9-30%
4-7 times > risk if teen onset
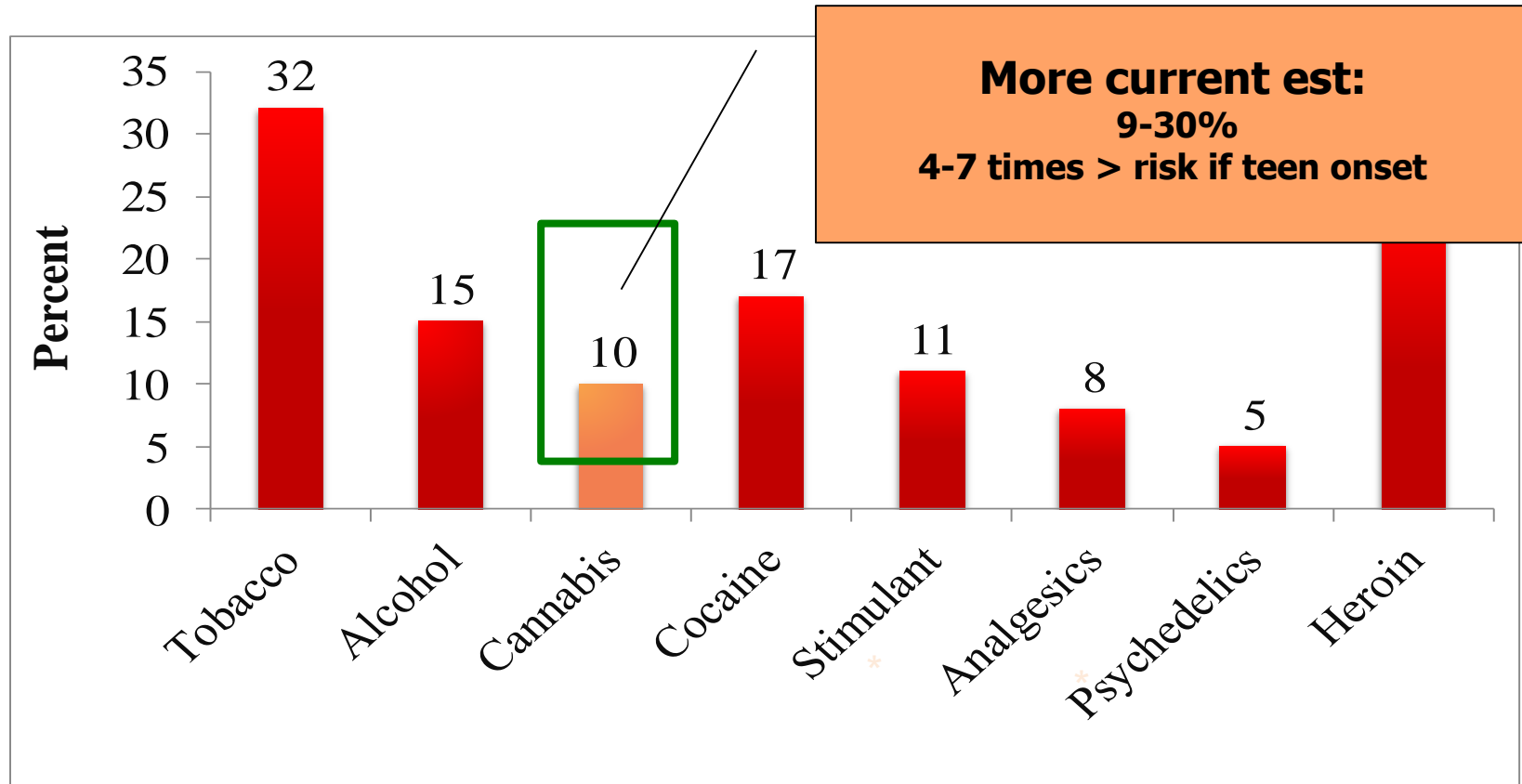
Source: Anthony JC et al., 1994

How Popular is Cannabis Use?

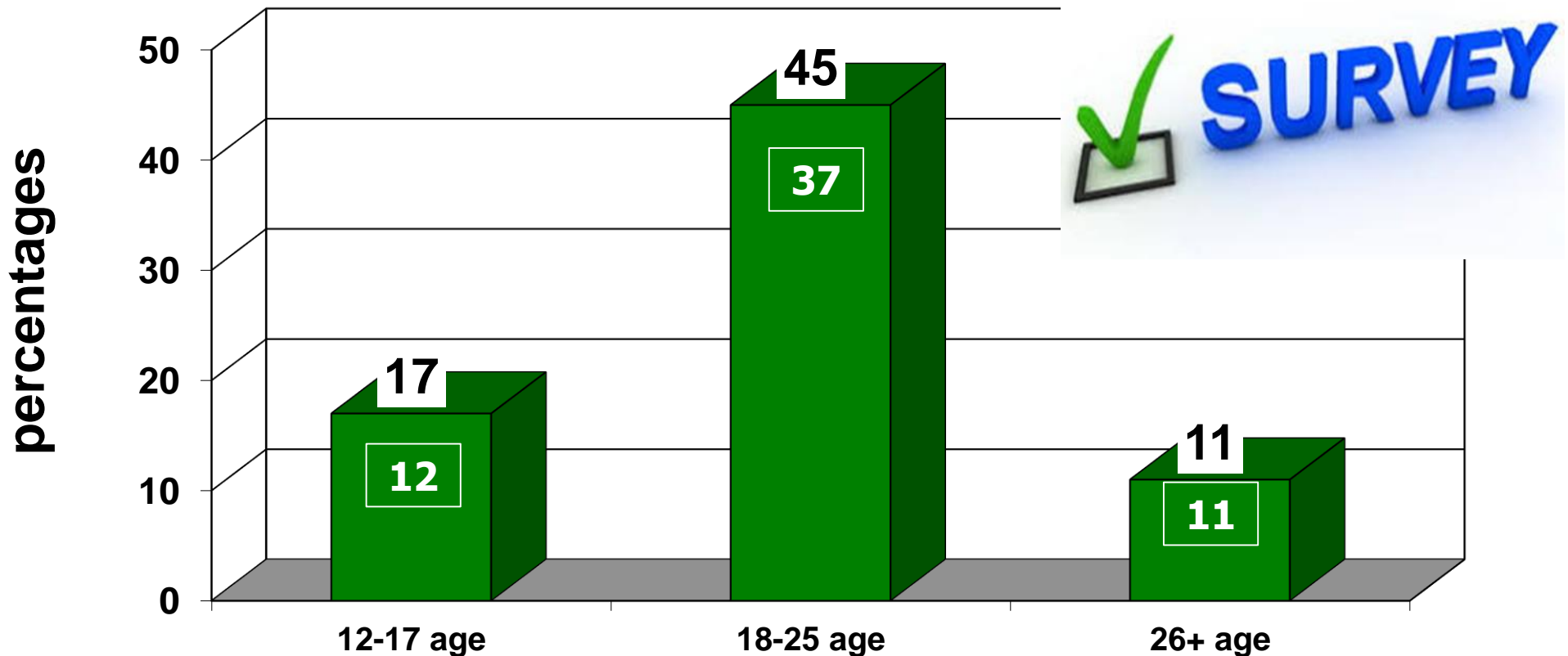## Prevalence of Past Year Cannabis Use: Among 40 U.S. States <u>Not</u> <u>Legalizing</u> Recreational Cannabis Use
(NSDUH, 2016-2017)
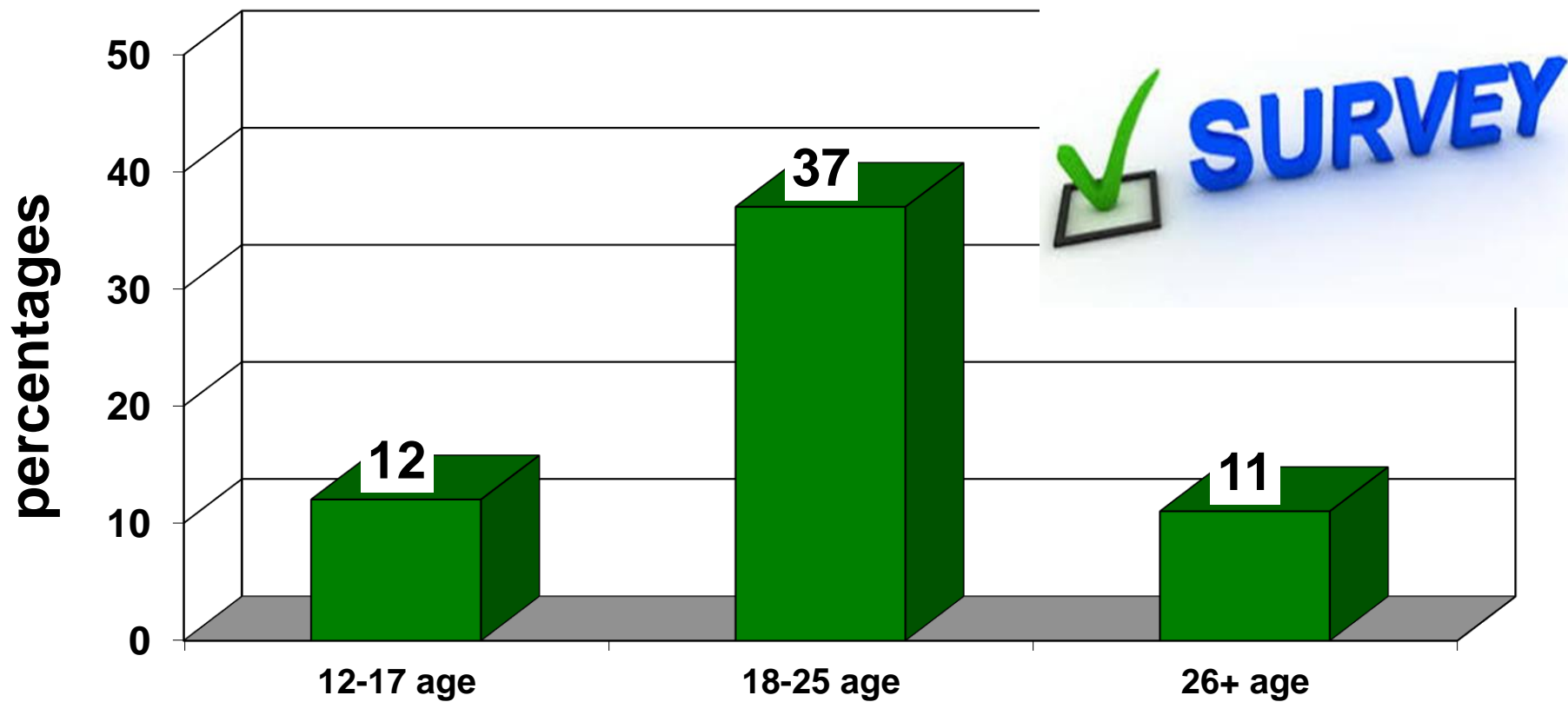
Minnesota rates are in-line with national trends

How Popular is Cannabis Use?

Prevalence of Past Year Cannabis Use: Among 4 U.S. States <u>with Substantial Years of Legalized</u> Recreational Cannabis Use
(NSDUH, 2016-2017)

The insert numbers = non-legalization states

Prevalence of Past Year **Alcohol** and Cannabis Use
(NSDUH, 2016-2017)
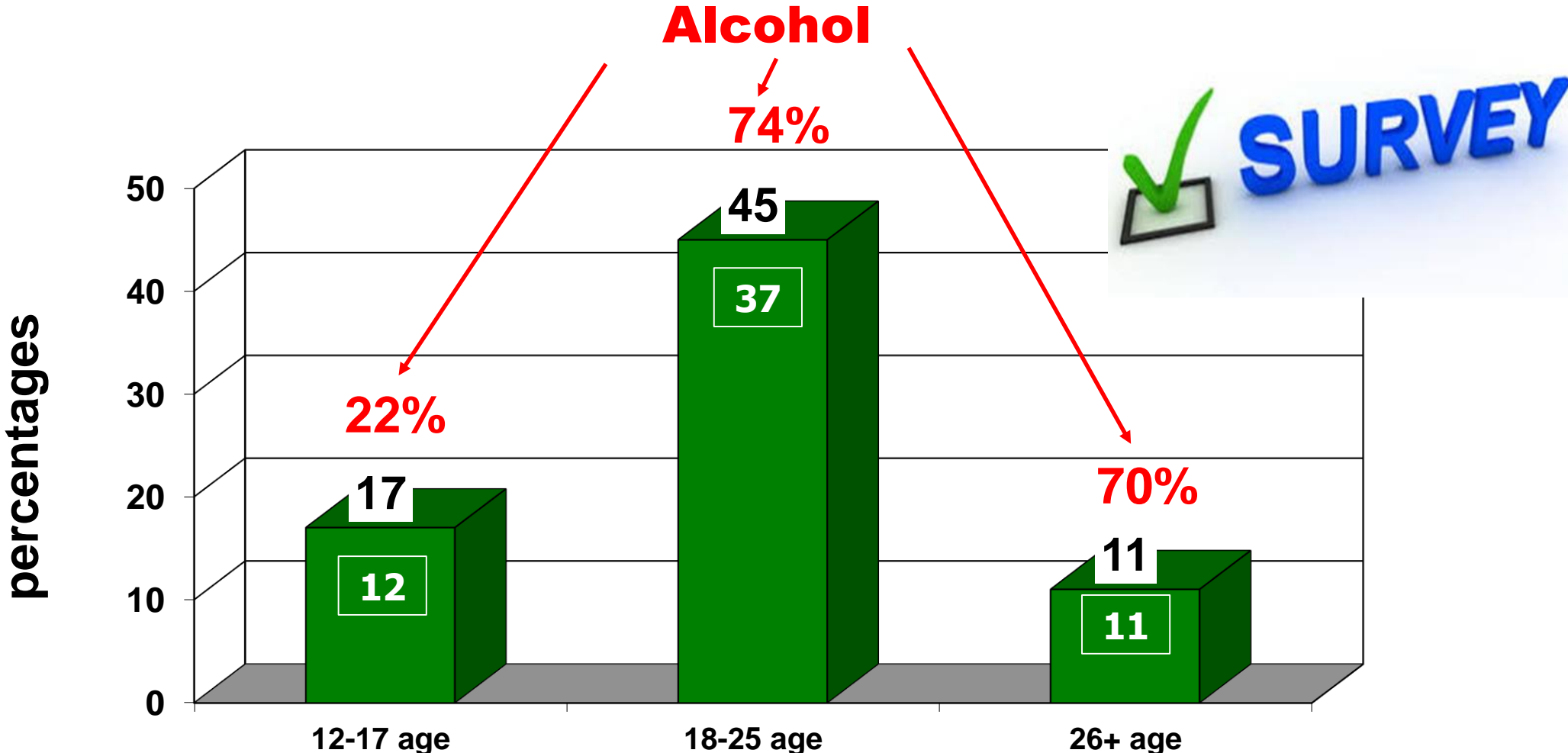
The insert numbers = non-legalization states

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Eight Adverse Health Effects of Chronic Marijuana Use (Volkow et al., 2014)

"Low Level of Confidence"

- Lung cancer

"Medium Level of Confidence"

- Altered brain development
- Progression to the use of other drugs
- Increased risk of chronic psychosis disorders (including schizophrenia) and depression and anxiety in persons with a predisposition to such disorders

"High Level of Confidence"

- Addiction
- Motor vehicle accidents
- Diminished life achievement (including cognitive impairment and poor educational outcome)
- Symptoms of chronic bronchitis

The Health Effects "Strongly Associated with Initial Marijuana Use Early in Adolescence"
(Volkow et al., 2014)

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- Symptoms of chronic bronchitis
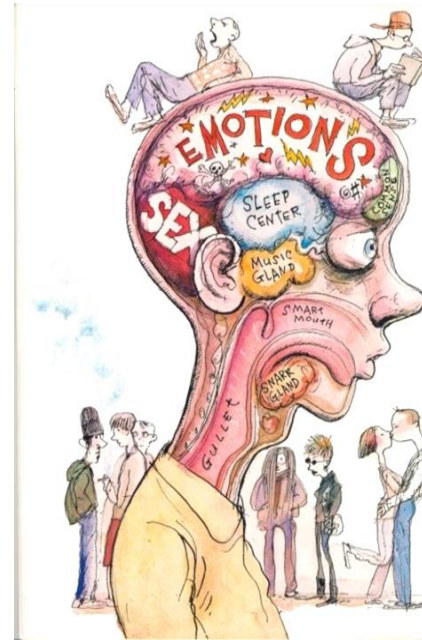
Source: US News & World Report, 2005

THC Binds to Cannabinoid Receptors Located Throughout the Brain
(source NIDA)

Exposure to cannabis during adolescence …

…can affect neurobehavioral functions, especially cognition, emotional functioning, the risk of psychosis, and addiction.

…is thought to interfere with the normal trajectories and mechanisms underlying brain maturation.

Sources: Rubino and Parolaro, 2014; Bossong and Niesink, 2010; Renard et al., 2016).
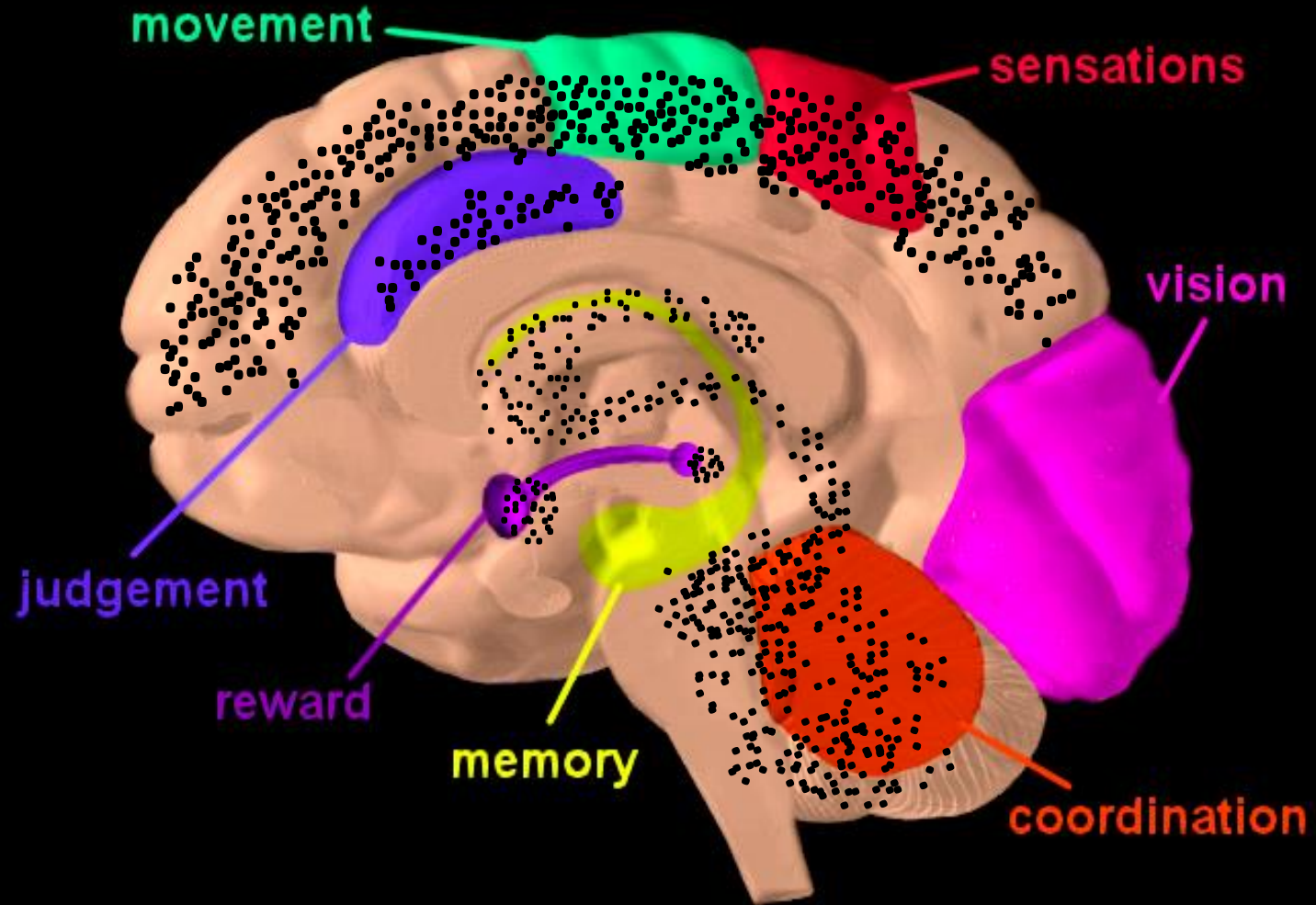
movement

sensations

vision

judgement

reward

memory

coordination

Slide courtesy of Maureen Boyle, PhD

Score Box for Negative Health Effects

Nature of Evidence	# of Health Domains
Conclusive	0
Substantial	5
Moderate	6
Limited	7
No/Insufficient	7

Substantial/moderate evidence that cannabis is associated with these adverse health effects:

- increased risk of motor vehicle crashes

- increased risk for lung cancer

- lower birth weight of the offspring (maternal cannabis smoking)

- cognitive impairments (acute effects)

- development of schizophrenia or other psychoses; highest risk among heavy users

- development of problem cannabis use when early onset of use

Heavy cannabis use, dependence and the brain: a clinical perspective

Emese Kroon[1,2], Lauren Kuhns[1,2], Eva Hoch[3,4] & Janna Cousijn[1,2] (iD)

Neuroscience of Addiction Lab, Department of Psychology, University of Amsterdam, Amsterdam, the Netherlands,[1] The Amsterdam Brain and Cognition Center (ABC), University of Amsterdam, Amsterdam, the Netherlands,[2] Cannabinoid Research and Treatment Group, Department of Psychiatry and Psychotherapy, University Hospital, Ludwig Maximilan University, Munich, Germany[3] and Division of Clinical Psychology and Psychological Treatment, Department of Psychology, Ludwig Maximilian University Munich, Munich, Germany[4]

- **Although causality is unclear, heavy and dependent cannabis use is consistently associated with a high prevalence of comorbid psychiatric disorders, and learning and memory impairments that seem to recover after a period of abstinence.**

- **Potential moderators: age of onset, heaviness of use, the ratio of 9-tetrahydrocannabinol to cannabidiol and severity of comorbid disorders.**

- **Conclusions: use is associated with <u>psychiatric morbidity</u> and with <u>cognitive impairments</u> (that may recover after a period of abstinence).**

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MJ / Mental Health

Miller's Review of the Cannabis and Mental Health Connection

Disorder	Cross-Sectional Data	Longitudinal Data
Schizophrenia	++	++
Bipolar	+	
Anxiety Disorders	+	+
Depressive Disorders	+	+
Risk of Suicide	+	

Key: ++ = several studies; +a few studies
Yellow box = risk greater when cannabis use onset during youth.

Miller, C. L. (2018). The impact of marijuana on mental health. In K. Sabet & K.C. Winters, *Contemporary health issues on marijuana.* NY: Oxford University Press.

# Rates and Predictors of Conversion to Schizophrenia or Bipolar Disorder Following Substance-Induced Psychosis

Marie Stefanie Kejser Starzer, M.D., Merete Nordentoft, Dr.Med.Sc., Carsten Hjorthøj, Ph.D., M.Sc.

- **Danish registry: 6,788 patients who received ICD-10 diagnosis of "substance induced psychosis" from 1994-2014**

- **Overall, 32% converted to bipolar or schizophrenia over up to a 20 yr. period**

- **Cannabis-induced psychosis was associated with a 47% conversion rate, the highest drug-specific rate**

- **Young age was associated with higher risk of converting to schizophrenia**

FIGURE 1. Rates of Conversion to Schizophrenia and Bipolar Disorder Following Incident Substance-Induced Psychosis in a Registry Study (N=6,788)

Legend:
- Bipolar disorder
- Schizophrenia
- Bipolar disorder or schizophrenia

(X-axis: Years Since Incident Substance-Induced Psychosis; Y-axis: Converted (%))
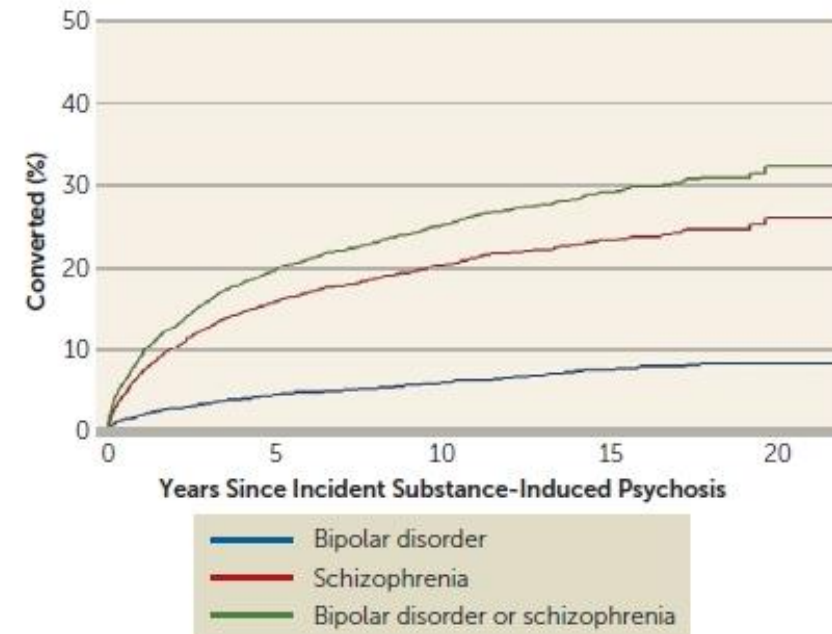
The contribution of cannabis use to variation in the incidence of psychotic disorder across Europe (EU-GEI): a multicentre case-control study

Marta Di Forti, PhD • Diego Quattrone, MD • Tom P Freeman, PhD • Giada Tripoli, MSc •
Charlotte Gayer-Anderson, PhD • Harriet Quigley, MD • et al. Show all authors •

Source: *Lancet Psychiatry*, 2019

- **901 patients with first episode psychosis across 11 clinic sites in Europe**

- **Compared 1237 population controls from those same sites**

- **Cannabis use was associated with increased odds of psychotic disorder compared with never users**
  - **Daily use of low potency cannabis = adjusted odds ratio, 3.2 (95% CI 2.2 – 4.1)**
  - **Daily use of high potency cannabis = adjusted odds ratio, 4.8 (95% CI 2.5 – 6.3)**
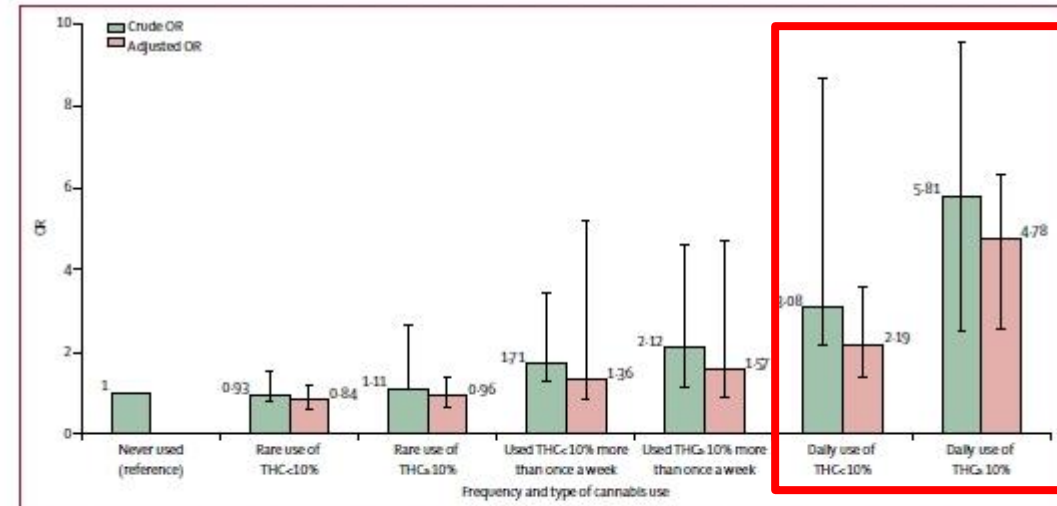

Figure 1: Crude and fully adjusted ORs of psychotic disorders for the combined measure of frequency plus type of cannabis use in the whole sample
Crude ORs are adjusted only for age, gender and ethnicity and fully adjusted ORs are additionally adjusted for level of education, employment status, and use of tobacco, stimulants, ketamine, legal highs, and hallucinogenics. Error bars represent 95% CIs. OR=odds ratio.

Stopping cannabis use benefits outcome in psychosis: findings from 10-year follow-up study in the PAFIP-cohort.

Setién-Suero E[1,2,3], Neergaard K[4], Ortiz-García de la Foz V[2,3], Suárez-Pinilla P[1,2,3], Martínez-García O[1], Crespo-Facorro B[3,5,6], Ayesa-Arriola R[1,2,3].

Cannabis use was described in 209 psychotic patients. Patients were divided into three groups according to cannabis use: persistent users, ex-users, and never-users. Groups were longitudinally (baseline and 10-year follow-up) compared on clinical, functional, and cognitive variables.

RESULTS:
Clinical differences at 10-year follow-up were observed between persistent cannabis users and the other two groups (ex-users and never-users), showing persistent users more severe symptoms and poorer functionality. Patients who stopped cannabis use prior to the reassessment showed a similar pattern to those who had never consumed.

CONCLUSION:
The use of cannabis could negatively affect the evolution of the psychotic disorder. Perhaps the negative effects caused by cannabis use could be reversed with the cessation of consumption.

Role of Drug Use and Early Onset Psychosis
(Large et al., 2011)

Legend: ■ years earlier psychosis onset

- Alcohol*: 0.28
- Cannabis: 2.7
- Any Drug: 1.7
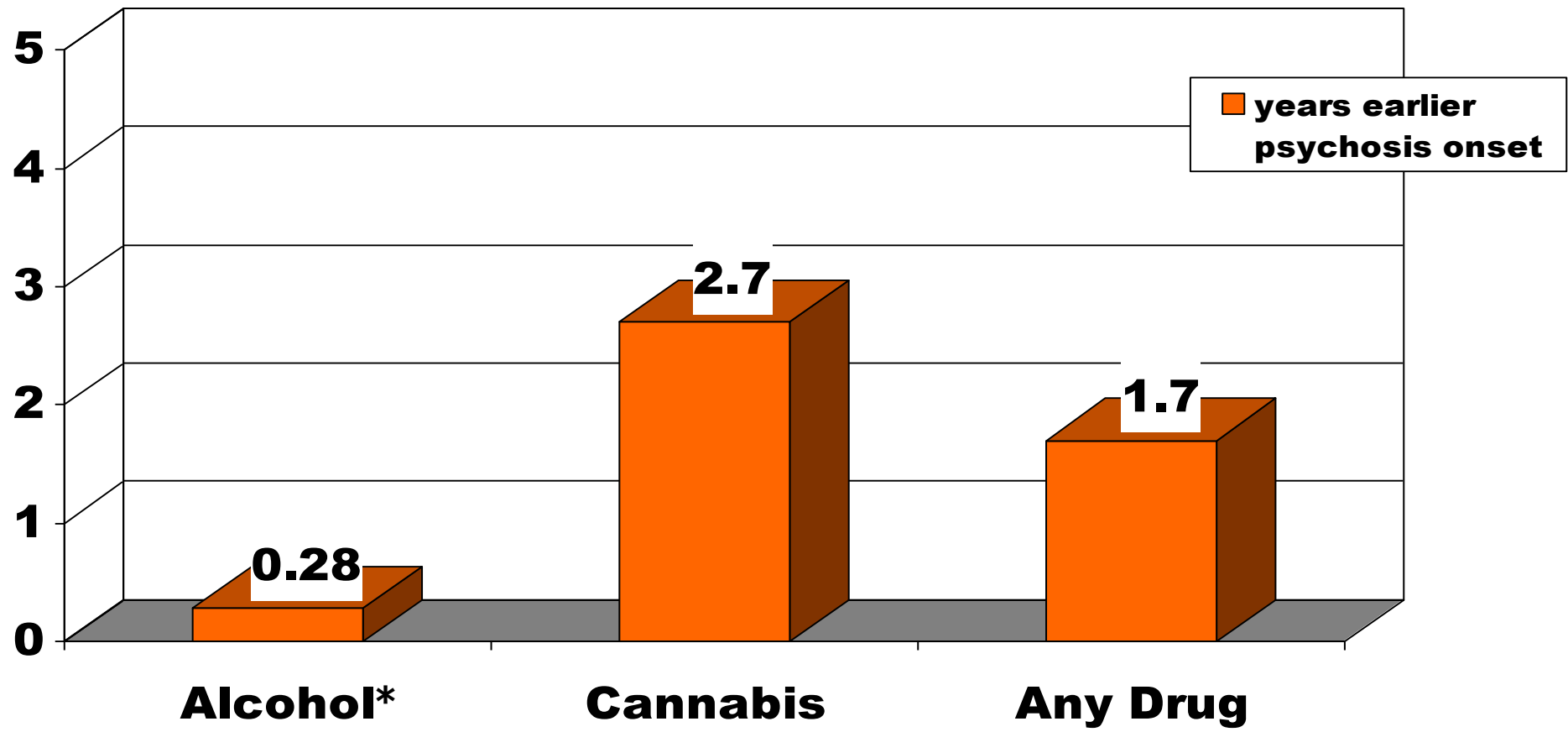
mean years earlier of age at onset of psychosis compared to non-drug using controls

* = nonsig. with controls

THC Binds to Numerous Cannabinoid Receptors

Slide courtesy of Maureen Boyle, PhD
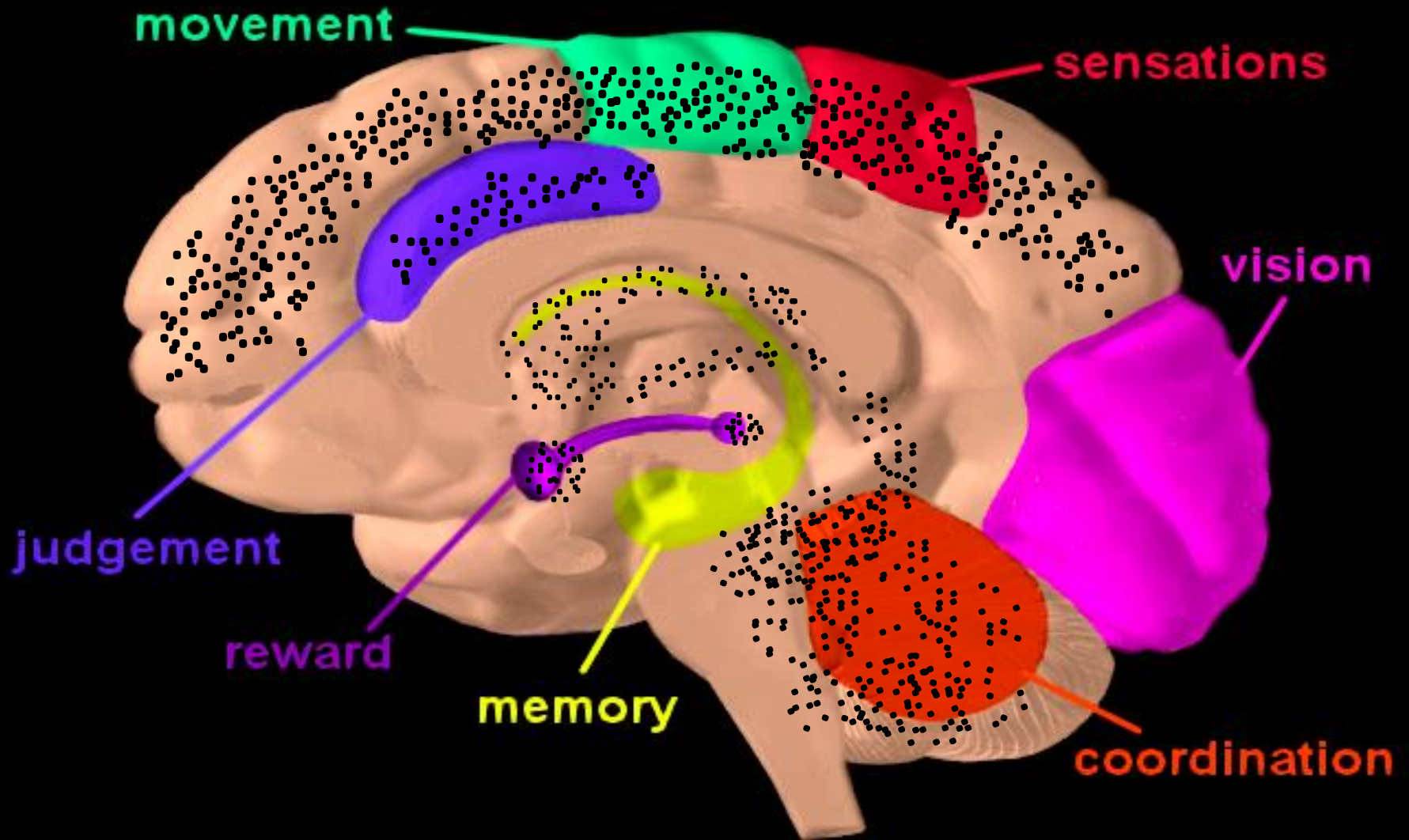
Review of Performance and THC (adapted from Berghaus et al., 1998; cited in Ramaekers et al., 1994)

- **Synthesis from 87 experimental studies**

- **Frequency of performance decrements (%) observed in the total number of psychomotor tests (several measures: tracking, reaction time performance, eye-hand coordination, distractibility) as a function of THC concentration in plasma after eating (---) and smoking (—) cannabis**

THC Concentration – Effect Relation

eating

smoking

significantly impaired test-results (%)

THC- concentration (ng/ml serum)
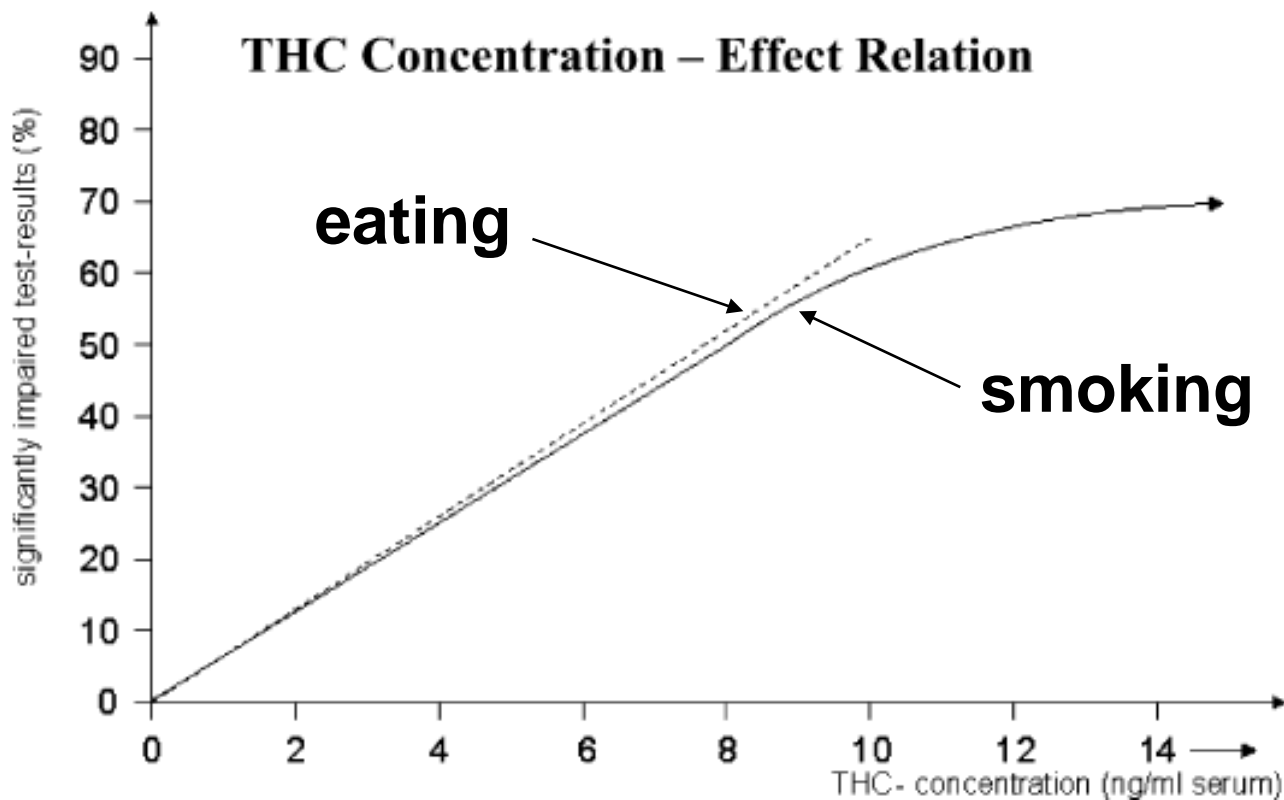
Driving and THC

- **Some indications in legalized states that the presence of THC-impaired driving is somewhat or very common (see _Lessons Learned_ report)**
  - **CO: large increase in the % of fatalities positive for THC since commercialization (12% in 2013 to 18% in 2018)**

- **Drinking alcohol and smoking marijuana can have an additive effect**

- **How long is somebody affected after ingesting THC? How to measure it?**

Percent of All Traffic Deaths That Were Marijuana-Related when a Driver Tested Positive for Marijuana

PERCENT OF DEATHS

Medical

Commercial

- 2006: 6.17%
- 2007: 5.78%
- 2008: 6.57%
- 2009: 8.82%
- 2010: 10.22%
- 2011: 12.98%
- 2012: 13.77%
- 2013: 11.43%
- 2014: 15.37%
- 2015: 17.92%
- 2016: 20.56%
- 2017: 21.30%
- 2018: 18.20%
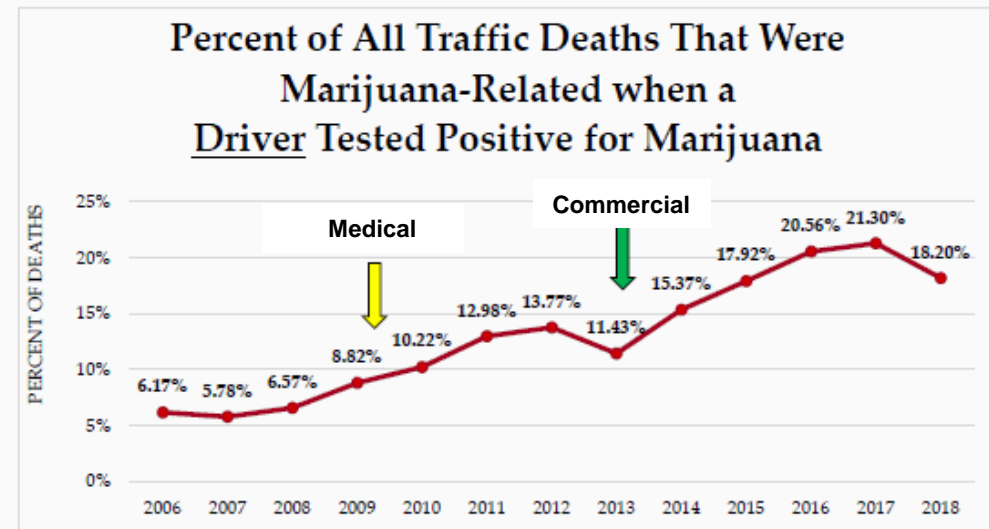
SOURCE: National Highway Traffic Safety Administration, Fatality Analysis Reporting System (FARS), 2006-2011 and Colorado Department of Transportation 2012-2018

Measuring THC – Report From Canada

MARIJUANA USE AMONG DRIVERS IN CANADA, 2000-2016

Traffic Injury Research Foundation, November 2019

By: Steve Brown, Ward G.M. Vanlaar, and Robyn D. Robertson

Figure 5: Percentage of fatally injured drivers testing positive for marijuana or alcohol, Canada, 2000-2016
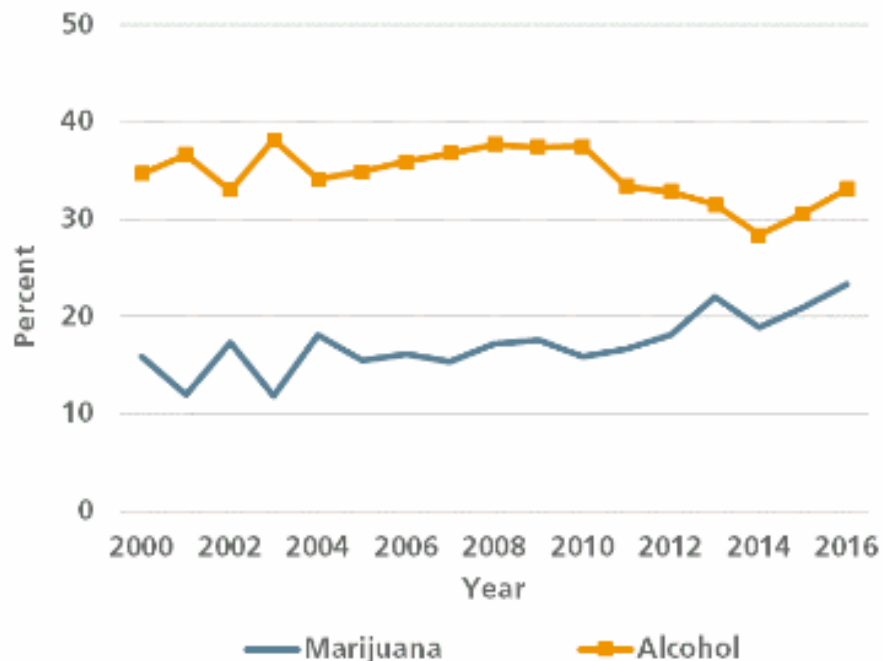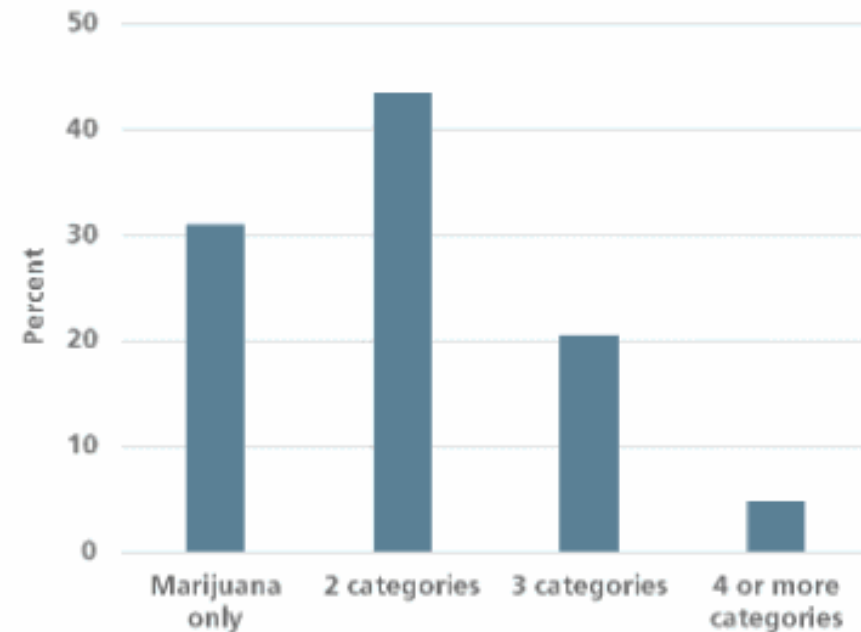
Figure 7: Percentage of fatally injured drivers testing positive for marijuana who were also positive for other types of drugs, Canada, 2012-2016

Measuring THC

- **The messy metabolite measurement problem**
  - active THC metabolite vs inactive metabolite (THC-COOH) cannot be distinguished with <u>urine test</u>; need <u>blood test</u>
  - THC-COOH metabolite can become stored in fat tissue and then be released weeks or months later (stress may be a trigger)
  - not clear what level of active THC level is associated with driving impairment

Measuring THC

- The messy metabolite measurement

"There are different methods and devices for [on-site oral] testing for cannabis use, but it is unclear if these devices meet the necessary criteria to be implemented at the roadside." (Dobri et al., 2019)

not clear what level of active THC level is associated with driving impairment
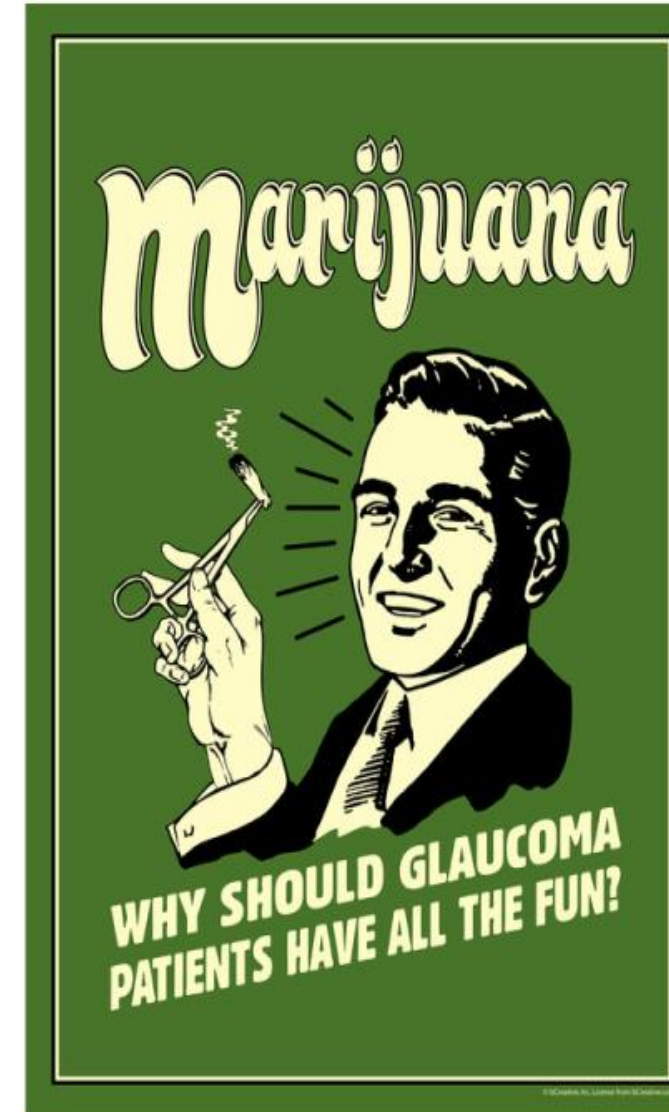
Medicinal Marijuana

Two main questions:

1. Is smoked cannabis medicine?

2. What evidence exists on the health benefits of cannabis?

Do We Need to Smoke it?

Challenges:

1. When raw marijuana is smoked, it is difficult to standardize the dosage for the patient. No physician could legally take responsibility for "prescribing" raw marijuana.

2. The smoking of almost any plant material is associated with mouth, throat and lung cancer.

3. Cannabis plant consists of only two compounds (THC and CBD) among the 400 that are believed to have medicinal properties.

4. Easy to manufacture own supply with home cultivation and avoid regulations.

Is Marijuana Medicine?

National Academies of Sciences, Engineering, and Medicine, 2017

- **Credible reports by individuals and growing body of evidence-based research that cannabis or cannabinoids may be uniquely beneficial for some conditions.**

Score Box of "Therapeutic Value"

Strengths of Evidence	# of Conditions/Ailments
Conclusive/Substantial	3
Moderate	4
Limited	5

1. Chronic pain
2. Nausea (chemotherapy meds)
3. MS

Cannabis-Based Medicines

- **Marinol and Nabilone: synthetic THC**

  - **Anti-nausea**

Cannabis-Based Medicines

- **Epidiolex® (oil) is pure cannabidiol (CBD), a non-psychoactive compound in cannabis**

- **Now FDA approved for two forms of childhood <u>epilepsy</u>**

Cannabis-Based Medicines

- **Sativex® is currently in use in Canada and across Europe to treat <u>neuropathic pain</u> and spasticity and other symptoms of <u>MS</u>.**

- **FDA-level trials in almost 60 U.S. research sites in advanced cancer patients with significant pain.**
  - **unfortunately, Sativex did not out-perform placebo at Phase 3 testing**
  - **not approved in U.S.**

Cannabis to Treat Mental Disorders?

Nicola Black, PhD [†] • Emily Stockings, PhD [†] • Gabrielle Campbell, PhD • Lucy T Tran, BPsychSci(Hons) •
Dino Zagic, BPsychSci(Hons) • Prof Wayne D Hall, PhD • et al. Show all authors • Show footnotes

- **There is <u>scarce evidence</u> 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 <u>very low quality evidence that pharmaceutical THC</u> (with or without CBD) leads to a small improvement in symptoms of anxiety among individuals with other medical conditions.**

CBD to Treat Schizophrenia?

Cannabidiol (CBD) as an Adjunctive Therapy in Schizophrenia: A Multicenter Randomized Controlled Trial

Philip McGuire, F.R.C.Psych., F.Med.Sci., Philip Robson, M.R.C.P., F.R.C.Psych., Wieslaw Jerzy Cubala, M.D., Ph.D., Daniel Vasile, M.D., Ph.D., Paul Dugald Morrison, Ph.D., M.R.C.Psych., Rachel Barron, B.Vet.Med., M.R.C.V.S., Adam Taylor, Ph.D., Stephen Wright, F.R.C.P.(Edin), F.F.P.M.

Source: *American Journal of Psychiatry, 2018*

- **Small samples in an exploratory double-blind parallel-group trial**

- **After 6 weeks of treatment, compared with the placebo group, the CBD group had significantly lower levels of positive psychotic symptoms**

- **No CBD-effect on negative symptoms**

- **CBD well tolerated**

Sidebar-1: Medical Cannabis Qualifying Conditions in Minnesota

- Cancer associated with severe/chronic pain, nausea or severe vomiting, or cachexia or severe wasting
- Glaucoma.
- HIV/AIDS
- Tourette Syndrome
- Amyotrophic Lateral Sclerosis (ALS)
- Seizures, including those characteristic of Epilepsy
- Severe and persistent muscle spasms, including those characteristic of Multiple Sclerosis.
- Inflammatory bowel disease, including Crohn's disease
- Terminal illness, with a probable life expectancy of less than one year
- Post-Traumatic Stress Disorder
- Autism
- Obstructive Sleep Apnea
- Alzheimer's Disease
- **Chronic pain**
- **Macular degeneration**

Sidebar-2: Cannabis-Based Medicines is an Active Area of Research

- **NIH is funding numerous studies**
  - **THC, CBD and other cannabinoids**
  - **several conditions and ailments**

Sidebar-3: The CBD Hype

Ben & Jerry's Announces Plans To Help Everyone Chill Out With CBD-Infused Ice Cream

JENNA MILLINER-WADDELL
JUNE 1, 2019, 2:45 PM

Testimony from Robert DuPont, MD (ex-Director of NIDA and Drug Czar)

"Commercial interests are putting CBD into more products than anyone could have imagined. Most consumers touting the benefits of CBD based on anecdotal claims are experiencing a placebo response in the midst of a financially driven mass delusion. This is not the random placebo effect; people are taking these products with magical expectations. This delusion is contagious."

1. Be Wary of 'Big Tobacco' Tactics Used to Persuade Public Sentiment

- **Heavy marketing/advertising**

- **Campaigns that minimize/ignore potential harm**

- **Campaigns that promote economic and social benefits**

- **Minimal regulations to optimize access**

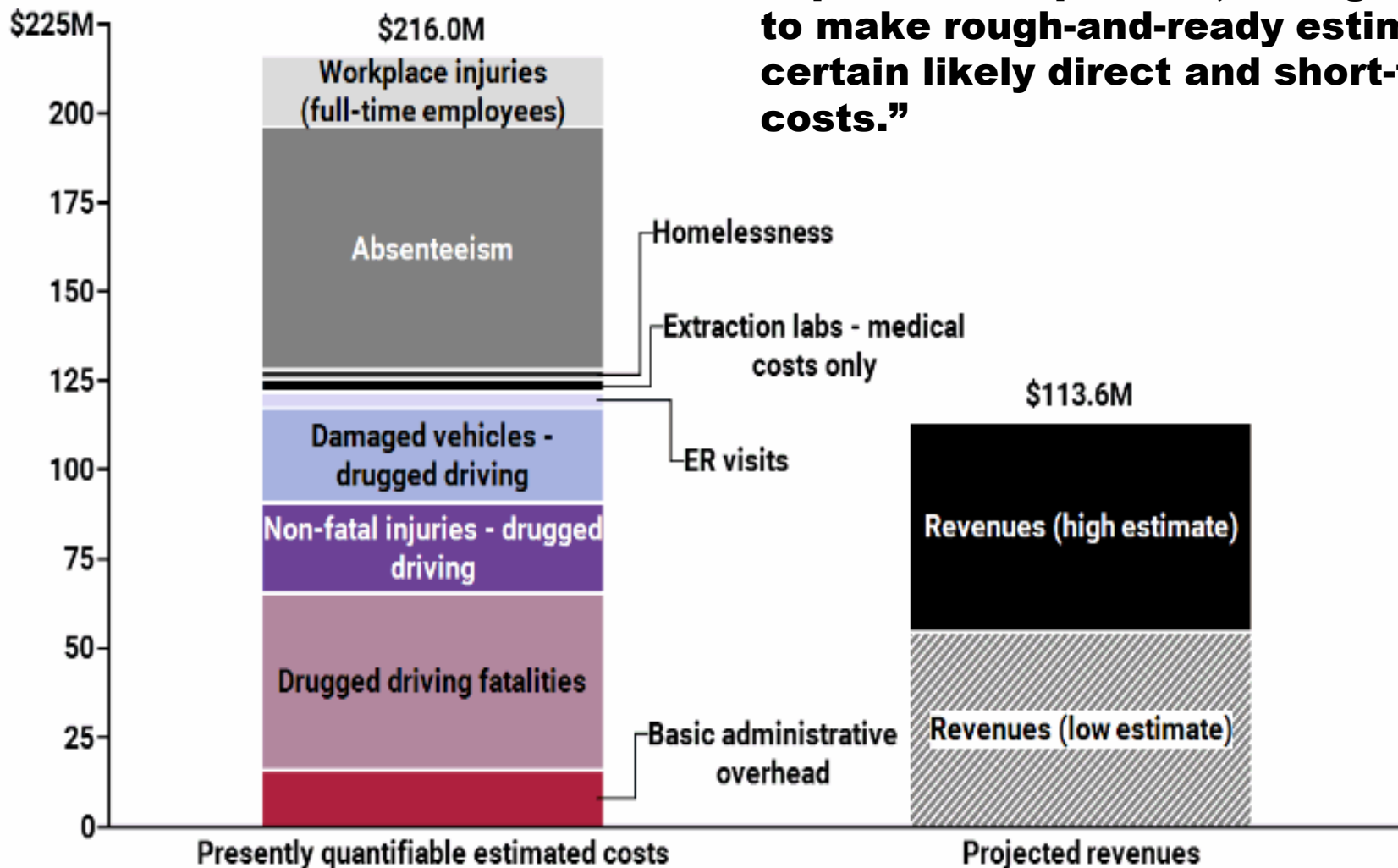# 2. Employ a Strong Regulation System

- **Governance and compliance checks regarding access and distribution**

- **Epidemiological research (hopefully prospective) on trend changes in use patterns and health effects**

- **Compare extra tax revenue vs. social and health costs**

Source: www.learnaboutsam.org

The "Estimated" Costs and Benefits if Marijuana Were Legalized in Connecticut (see learnaboutsam.org)

Estimated value for 2020
(in millions of 2016 dollars)

"Although a full cost accounting of marijuana legalization would be impossible at present, enough data exists to make rough-and-ready estimates of certain likely direct and short-term costs."

Presently quantifiable estimated costs — $216.0M:
- Workplace injuries (full-time employees)
- Absenteeism
- Homelessness
- Extraction labs - medical costs only
- Damaged vehicles - drugged driving
- ER visits
- Non-fatal injuries - drugged driving
- Drugged driving fatalities
- Basic administrative overhead

Projected revenues — $113.6M:
- Revenues (high estimate)
- Revenues (low estimate)

Challenges to Rigorous Regulations and Enforcement: Personal Production and Black Market

3. Regulate Marijuana Edibles
(Gourde et al., 2017)

- **State laws governing recreational marijuana edibles have evolved since the first recreational edible products were available for sale**

- **Four states (AK, CO, OR, WA) now require edible product labels to disclose a variety of product information, including risk factors associated with consumption**
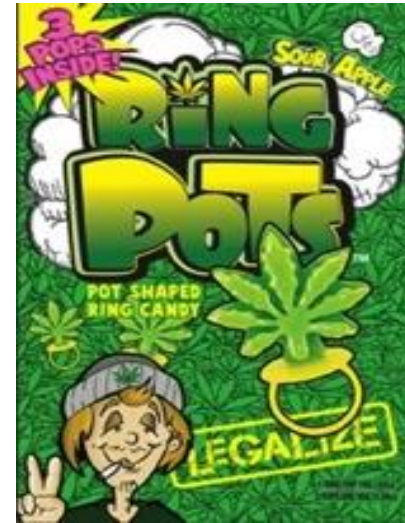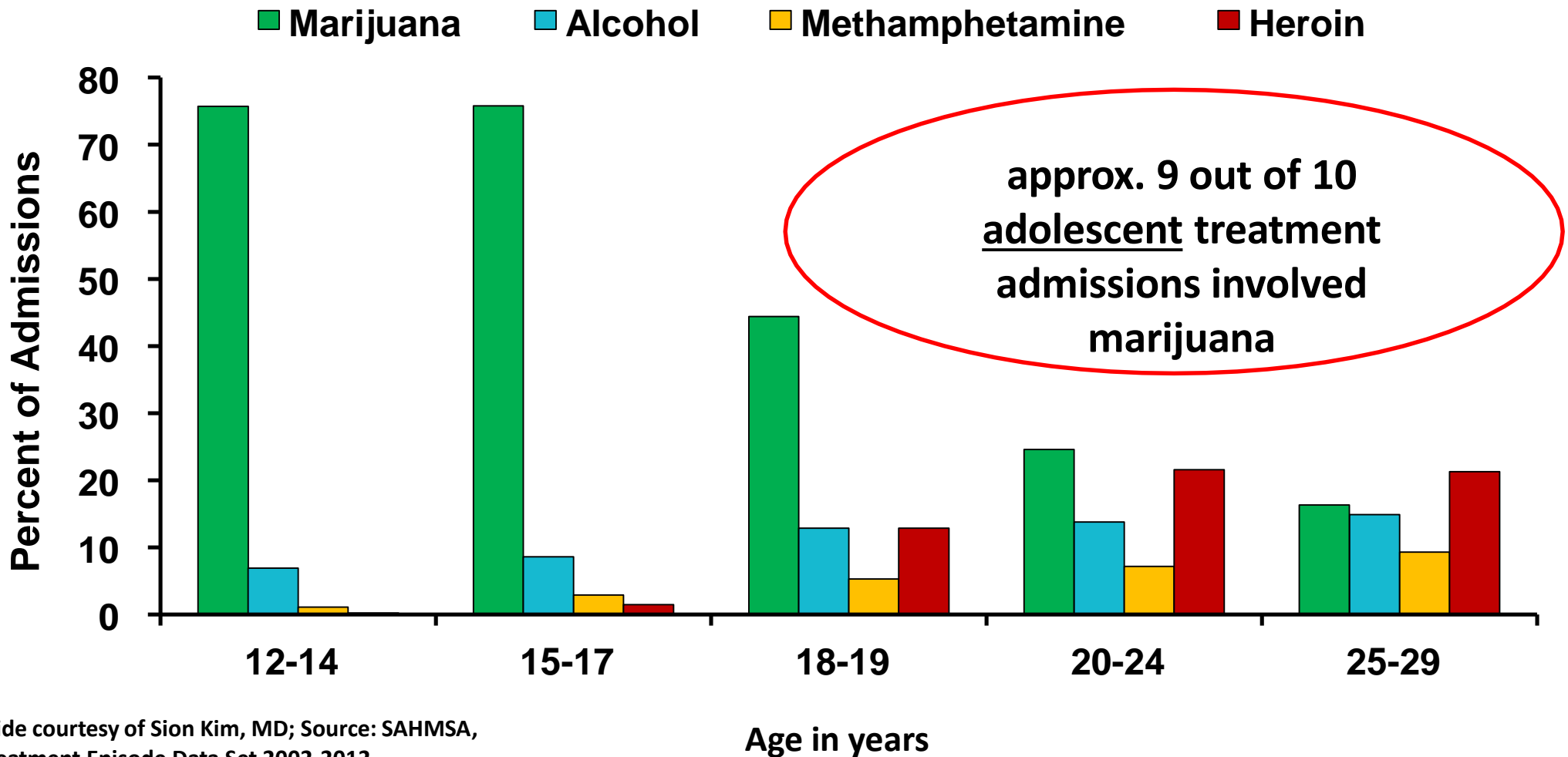
4. Policy Making

- **How is the debate progressing if commercialization bills are advanced and discussed?**

    - public health protections?

    - health updates?

    - "costs including in the updates?

    - will public health services be strengthened?

ILLINOIS LAWMAKERS PASS MARIJUANA LEGALIZATION

5a. Cannabis Use Disorder is a Very Common Primary Drug Among those in Treatment
2002-2012

■ Marijuana ■ Alcohol ■ Methamphetamine ■ Heroin

approx. 9 out of 10 adolescent treatment admissions involved marijuana

Percent of Admissions

Age in years

Slide courtesy of Sion Kim, MD; Source: SAHMSA, Treatment Episode Data Set 2002-2012

5b. Address Misperceptions and Myths

- **THC can be addictive**

- **THC may not be medicine**

- **Still not legal for "adult, open use" in Minnesota**

5c. Taking Medical Marijuana?

- **For patients taking medical marijuana: abuse potential may exist with many THC-based medicines**

Assessing Harm of Psychoactive Substances
(Nutt et al., 2007)

- **Harm ratings:**
  Physical
  Social
  Dependence

- **Class = U.K. Misuse Classification**
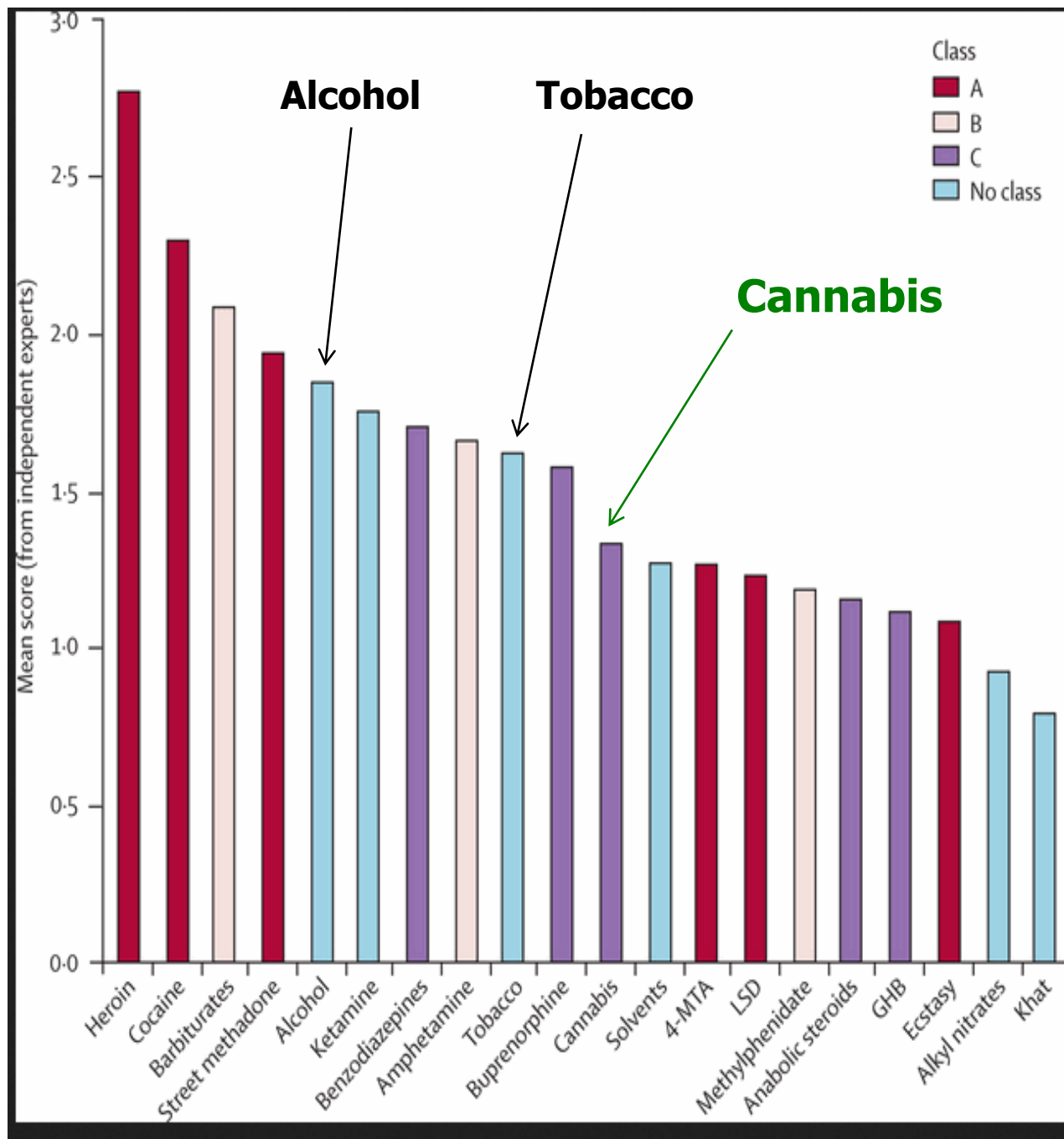
My Humble Summary: "Substantial Association" of Regular/Heavy Cannabis Use and Negative Health Effects
(greater risk to health if adolescent onset of use)

Health Issue	Sources
Mental Health	Miller et al., 2018; National Academies, 2017; Volkow et al., 2014
Cognitive Functioning	Kroon et al., 2019; National Academies, 2017; Winters & Whelan, in press
Cannabis Use Disorder	National Academies, 2017; Volkow et al., 2014
Brain Development	Mashoon et al., 2019; Volkow et al., 2014

THANK YOU

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Questions and Discussion