

# CANNABIS/CANNABINOIDS: WHAT THE SCIENCE TELLS US



## Secretaries' Innovation Group

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NIDA | NIH



National Institute  
on Drug Abuse



# OUTLINE

- Cannabis: Patterns of Use
- Health Effects
- Therapeutic Uses
- Changing Policy Landscape

# Terminology

- Cannabis: marijuana plant
  - sativa, indica, ruderalis
- Hemp: sativa (low THC/high CBD)
- “Recreational” use: use
- “Medical” marijuana: use for (perceived) therapeutic value

# CANNABIS: PATTERNS OF USE



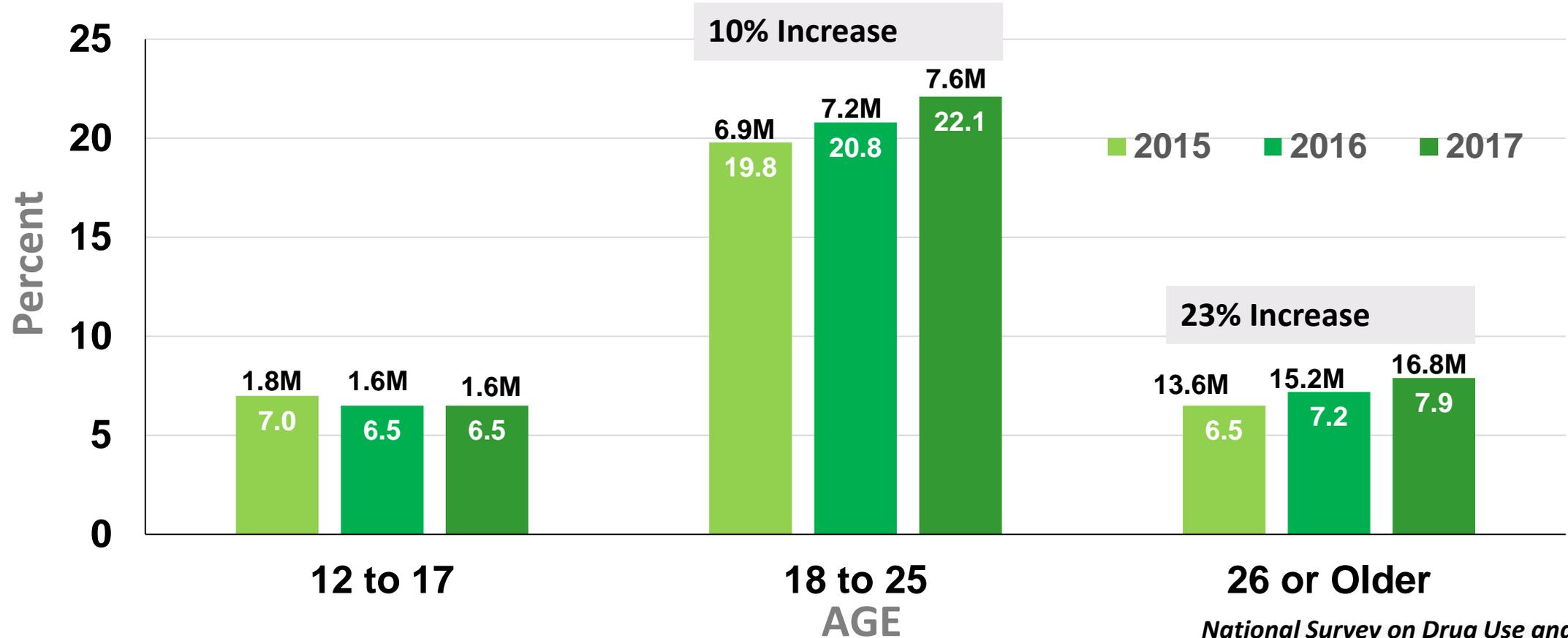
# Cannabis: Most Commonly Used Federally Illicit Drug In the U.S.

- Over 26 million Americans 12 and older report past month cannabis use.
- Approximately 4.0 million Americans met criteria for cannabis use disorders in 2017.
- An estimated 3.0 million Americans used cannabis for the first time; 1.2 million were between the ages of 12 and 17.



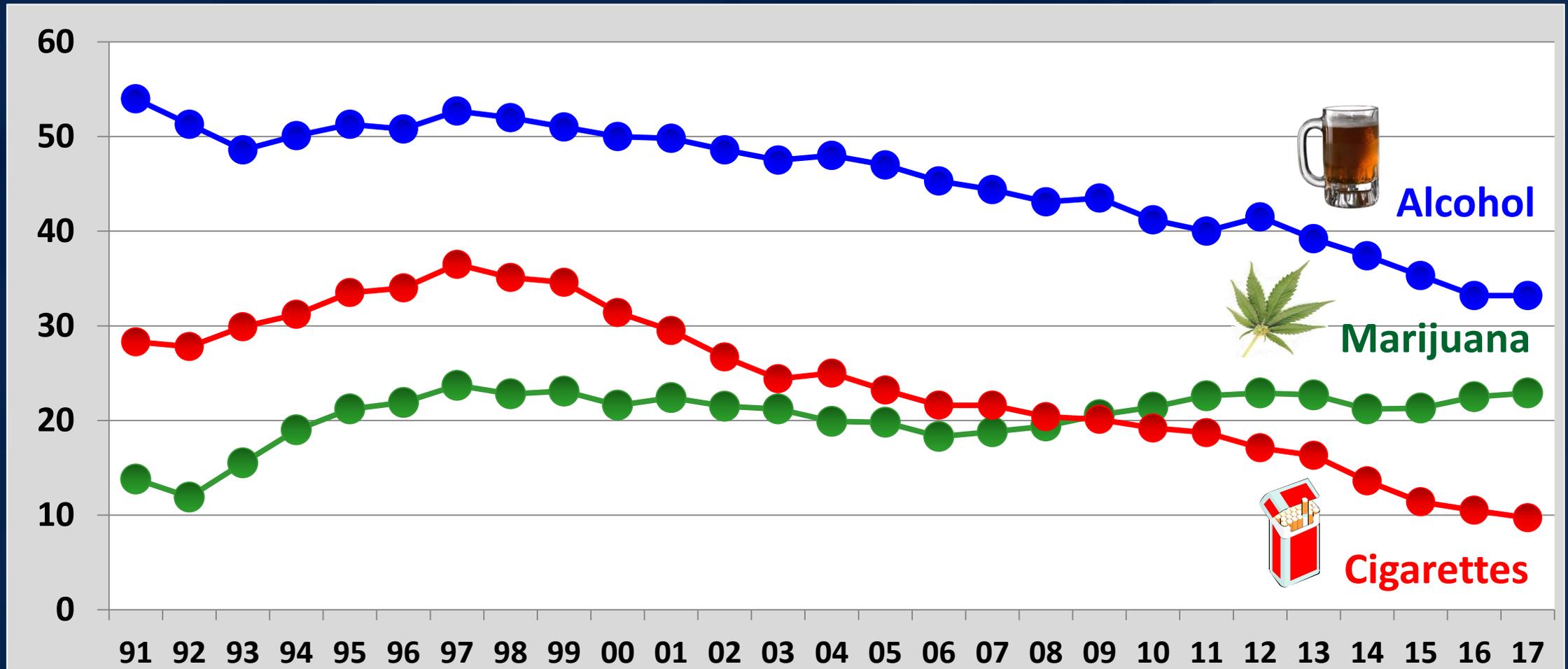
Tetrahydrocannabinol (THC)  
Psychoactive Ingredient in Marijuana

# PAST MONTH MARIJUANA USE IS INCREASING IN ADULTS



# PAST MONTH USE OF CIGARETTES, MARIJUANA, AND ALCOHOL IN 12<sup>TH</sup> GRADERS

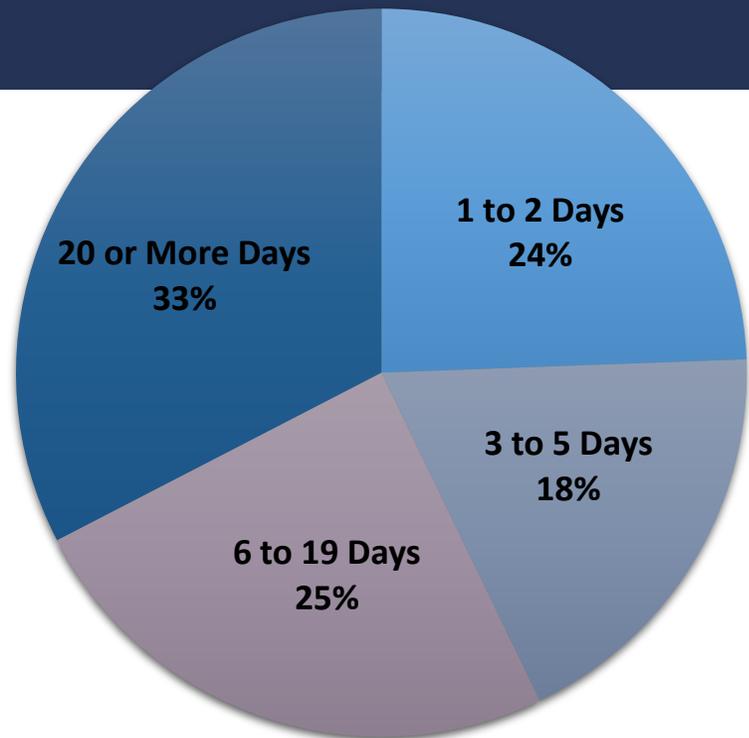
*nearly 6% report daily use of marijuana*



Source: University of Michigan, 2017 Monitoring the Future Study

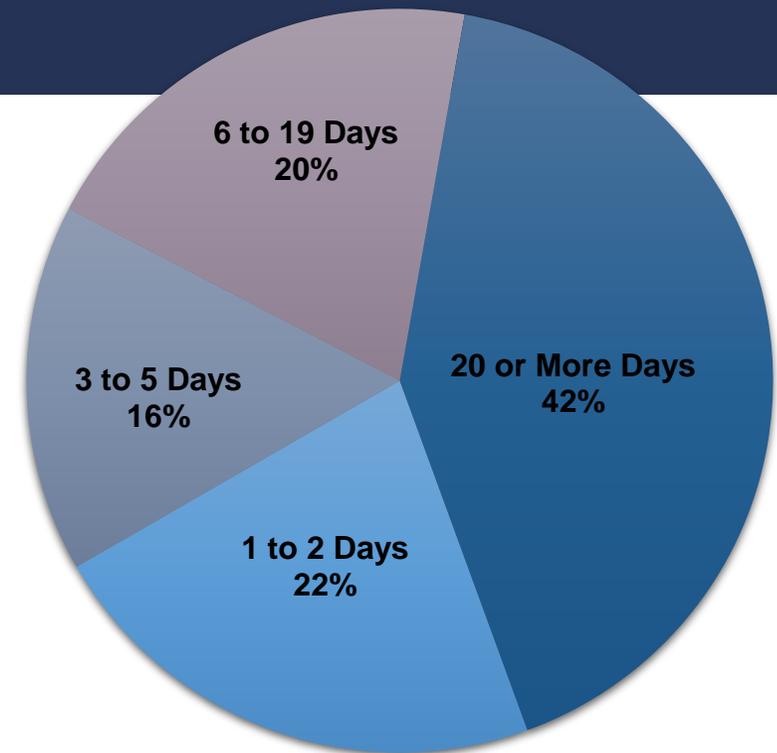
# AMONG CURRENT MARIJUANA USERS, MORE THAN TWO IN FIVE ARE *DAILY OR ALMOST DAILY* USERS

Number of Days Used Marijuana in the Past Month



2002

**14.6 Million Past Month Users of Cannabis in 2002**

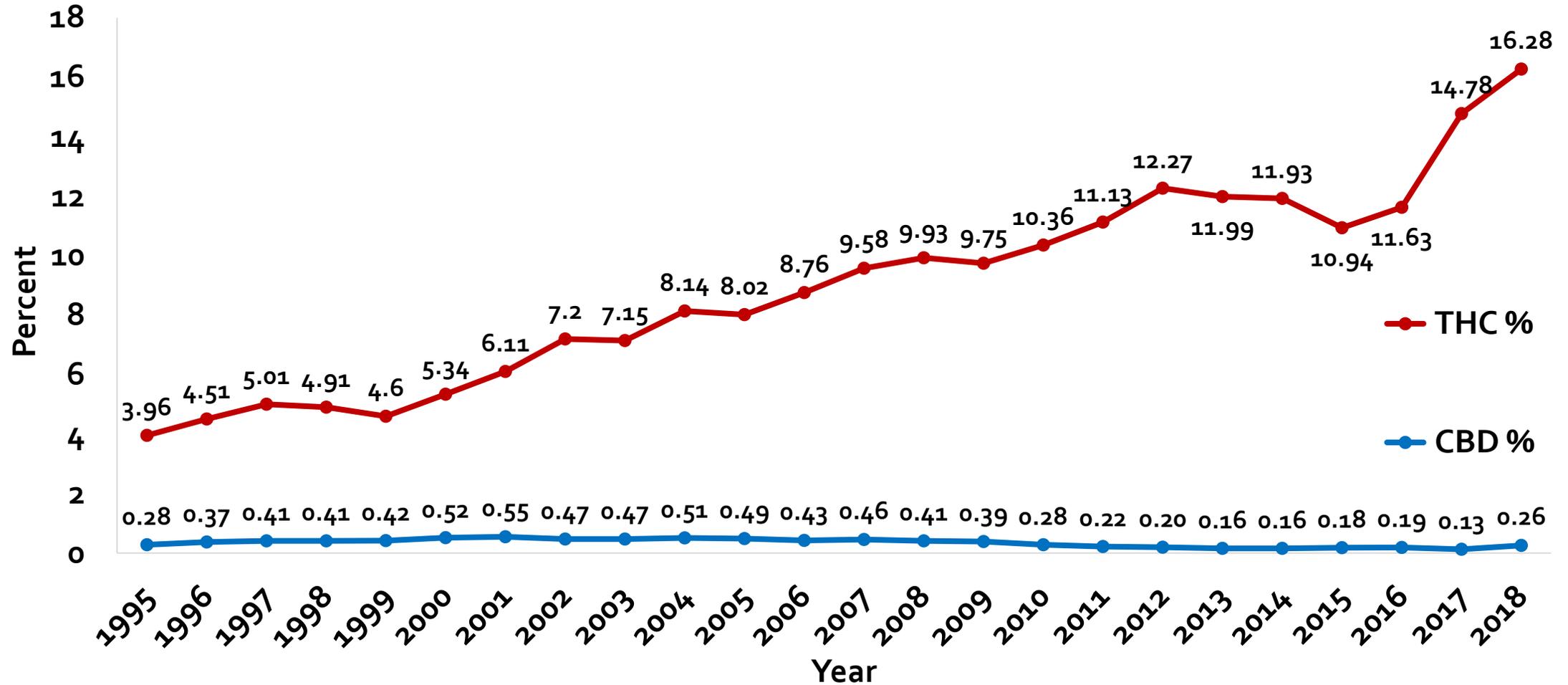


2017

**26.0 Million Past Month Users of Cannabis in 2017**

Source: SAMHSA, 2017 National Survey on Drug Use and Health (September 2018).

# MARIJUANA POTENCY (% Δ-9 THC) QUADRUPLED IN PAST 20 YEARS



THC Potency of Domestic and Non-Domestic Cannabis Samples Provided by the DEA, Percent Averages from 1995 to Present, by Year.  
Source: Potency Monitoring Program, Quarterly report Number 138, NIDA Contract Number: N01DA-15-7793

# HEALTH EFFECTS

# CANNABIS' ACUTE EFFECTS (INTOXICATION PHASE)

- Euphoria
- Calmness
- Appetite stimulation
- Altered perception of time
- Heightened sensation
- Impairs coordination and balance
- Increased heart rate: 20 - 100%
  - Some evidence for increased risk of heart attack, may be exacerbated in vulnerable individuals (e.g., baby boomers?)
- Orthostatic (postural) hypotension
- Increased risk of accidents (~2 fold), higher when combined with alcohol
- Hyperemesis (abdominal pain and vomiting)



# CANNABIS' ACUTE EFFECTS (INTOXICATION PHASE)

## ➤ Cognition

- Impaired short-term memory
  - Difficulty with complex tasks
  - Difficulty learning

## ➤ Executive Function

- Impaired decision-making
- Increased risky behavior – STDs, HIV?

## ➤ Mood (especially after high doses or edibles)

- Anxiety – panic attacks
- Psychosis – paranoia



# Long Term Outcomes:

WE KNOW LESS ABOUT THE LONG  
TERM HEALTH IMPACT FOLLOWING  
CHRONIC CANNABIS USE,  
PARTICULARLY WITH RESPECT TO  
*CAUSALITY.*

# Cannabis And Brain Development: Most Vulnerable Populations

**Prenatal**



**Adolescent**

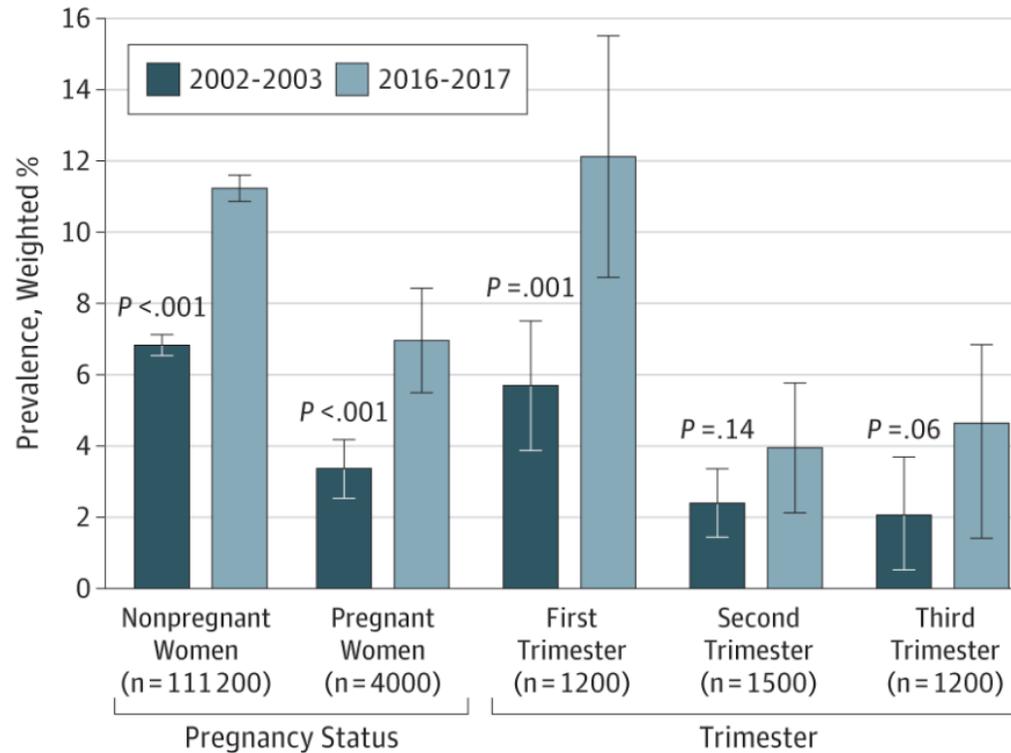


**Adolescent Brain Cognitive Development<sup>®</sup>**  
*Teen Brains. Today's Science. Brighter Future.*

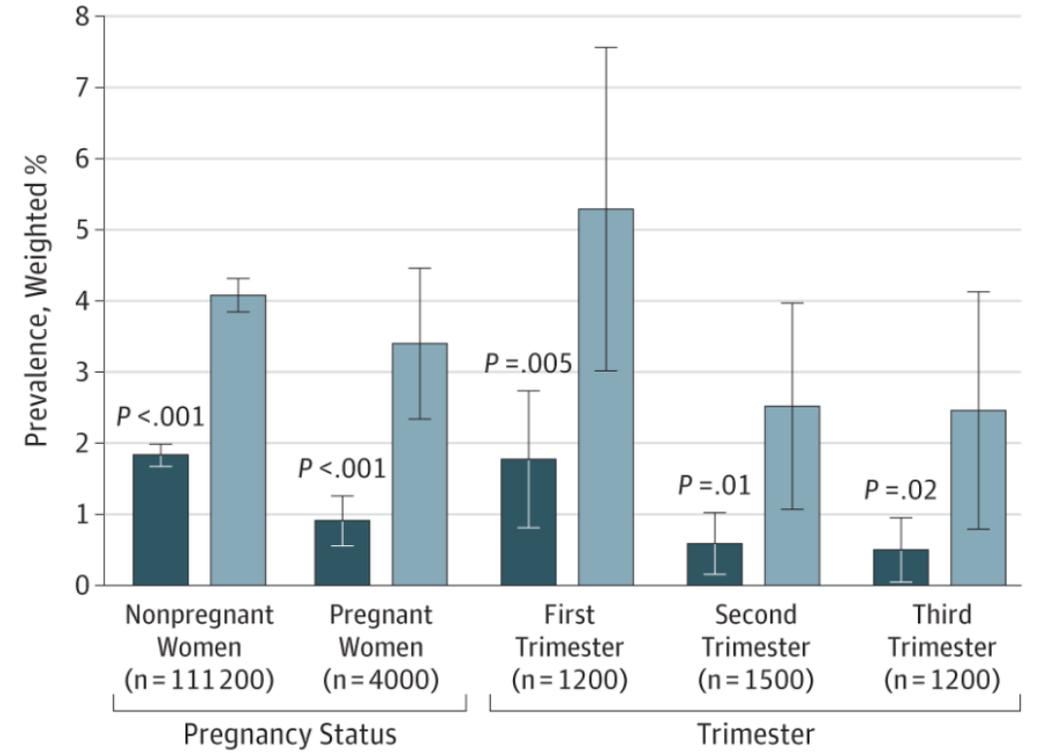
**Older Adults?**



# CANNABIS USE DURING PREGNANCY HAS DOUBLED SINCE 2002 GREATEST USE DURING FIRST TRIMESTER



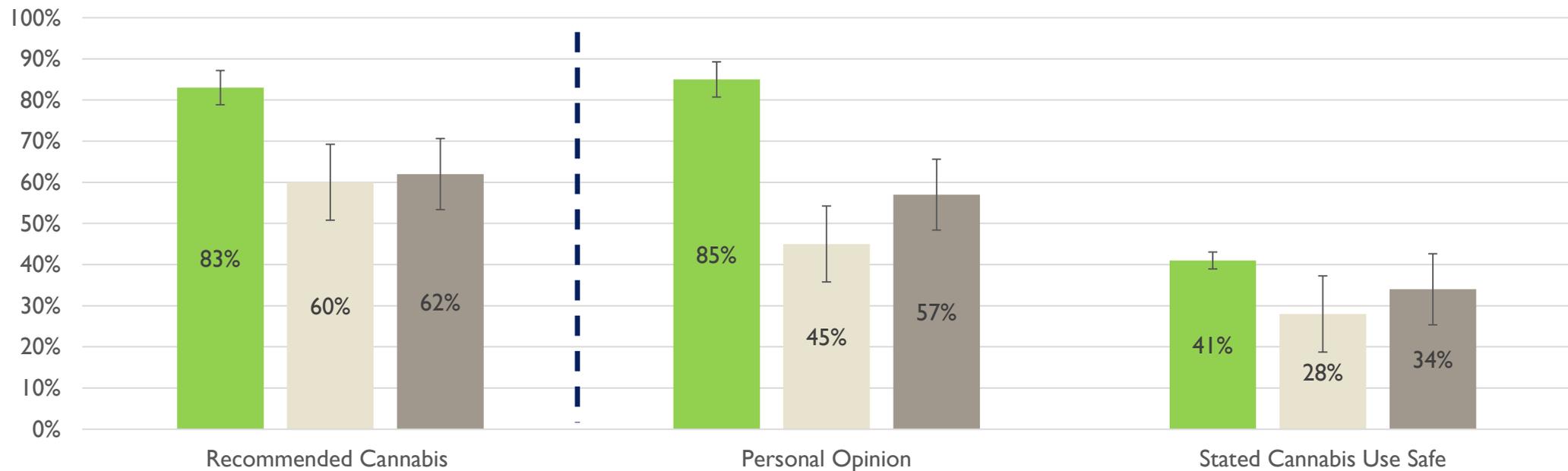
Adjusted prevalence of past-month cannabis use



Adjusted prevalence of past-month daily/near daily cannabis use

# FIRST TRIMESTER CANNABIS USE: RECOMMENDATIONS FROM CANNABIS DISPENSARIES IN COLORADO

- 277 of 400 dispensaries recommended cannabis products for “morning sickness” (71% urban; 63% rural)
- 275 of 277 recommended a specific cannabis type (26% CBD-only; 17% THC-only; 56% both CBD & THC)



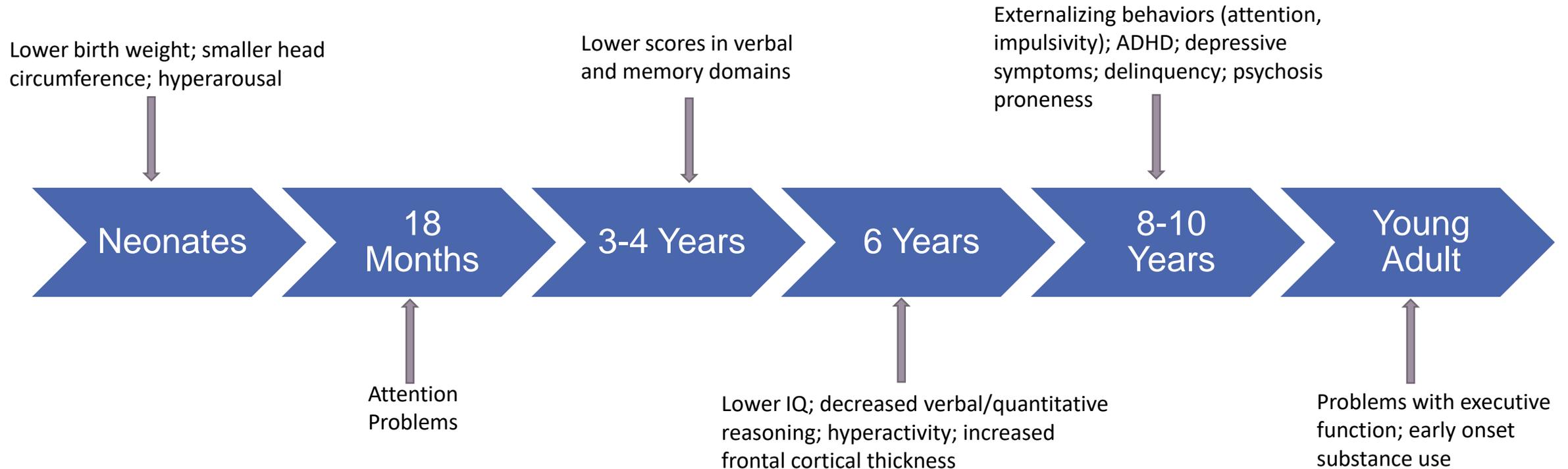
Dispensary/License Type:

■ Medical (n=148)

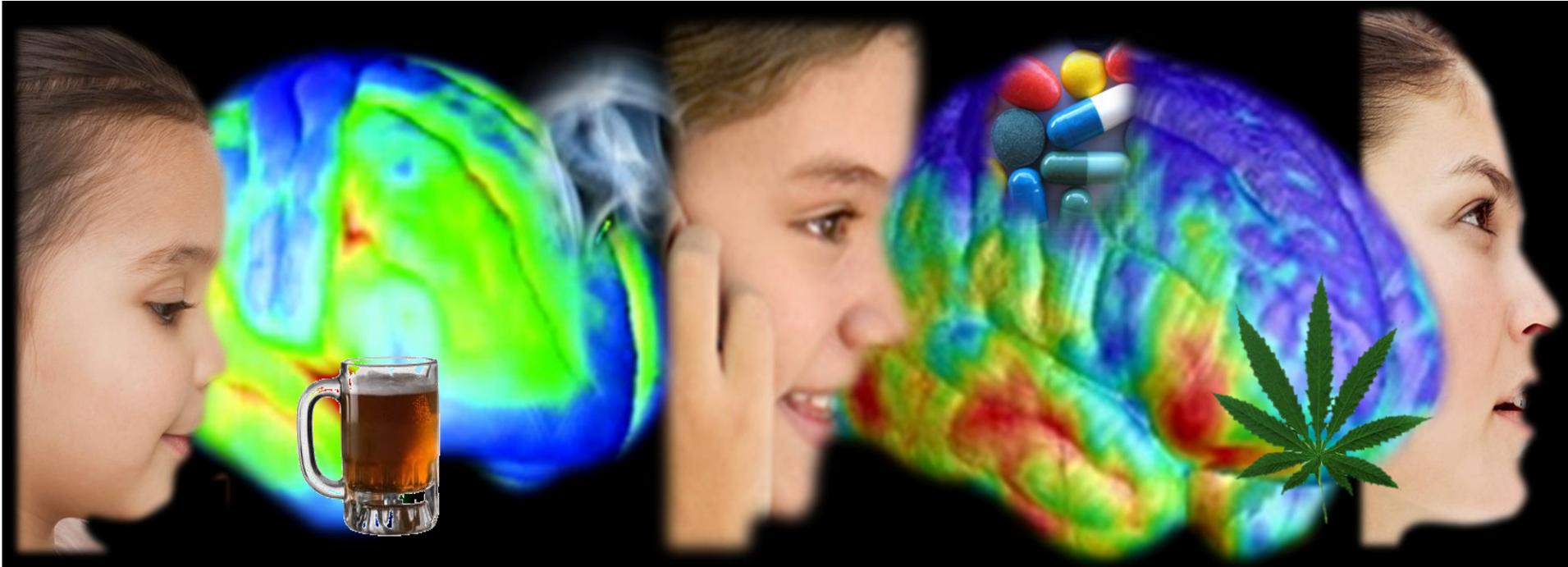
■ Medical and Recreational (n=141)

■ Recreational Only (n=111)

# Prenatal Cannabis Exposure: Overview of Effects\*



# THE BRAIN CONTINUES TO MATURE INTO EARLY ADULTHOOD

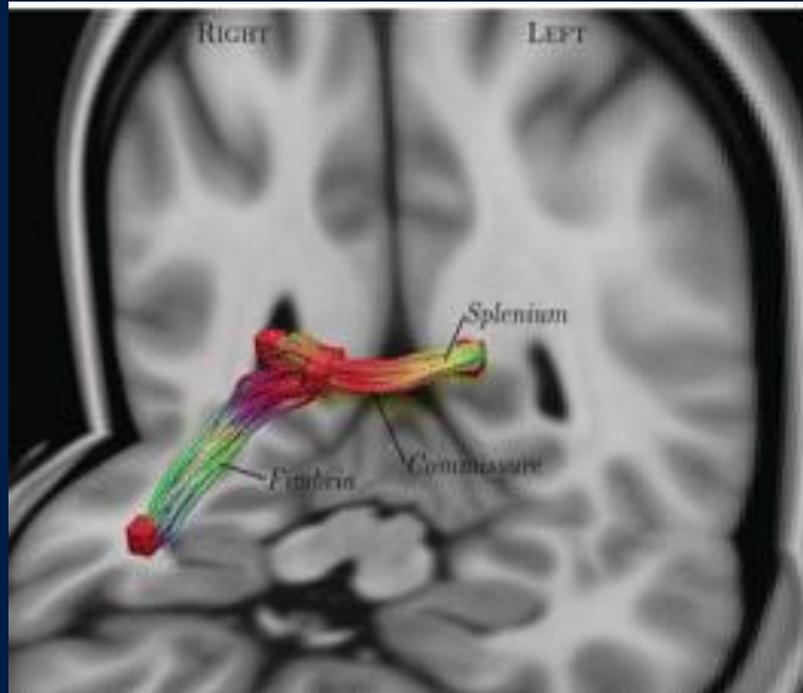


How does **cannabis** (and other substances) affect the developing brain and an individual's trajectory into adulthood?

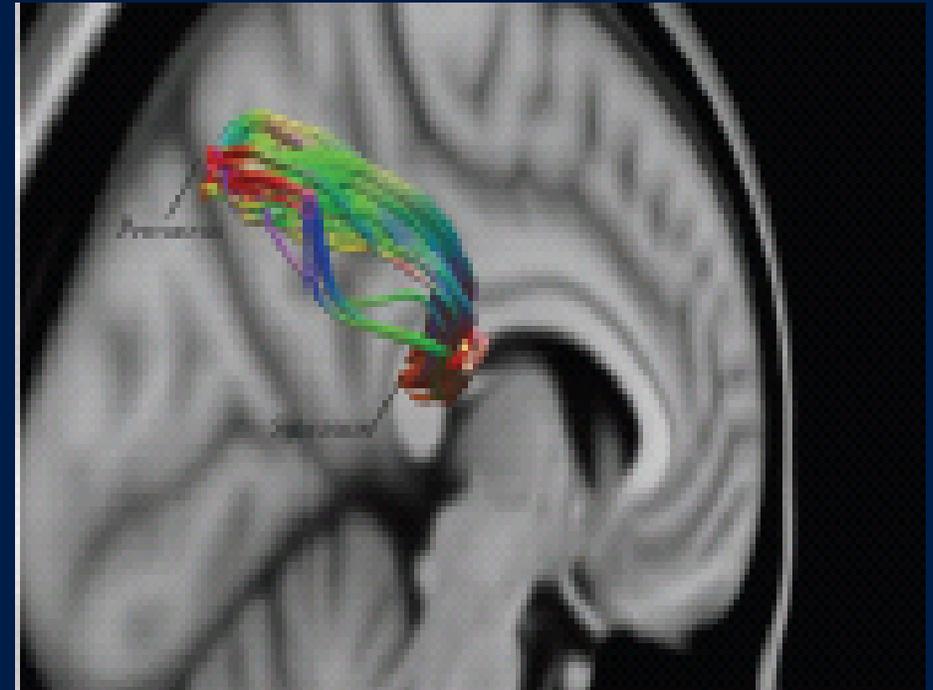
# MULTIPLE STUDIES SHOW ALTERED BRAIN STRUCTURE AND FUNCTION IN YOUTH WHO REGULARLY USE CANNABIS

Early (<18y) Cannabis Use Decreases Axonal Fiber Connectivity

Precuneus  
to splenium



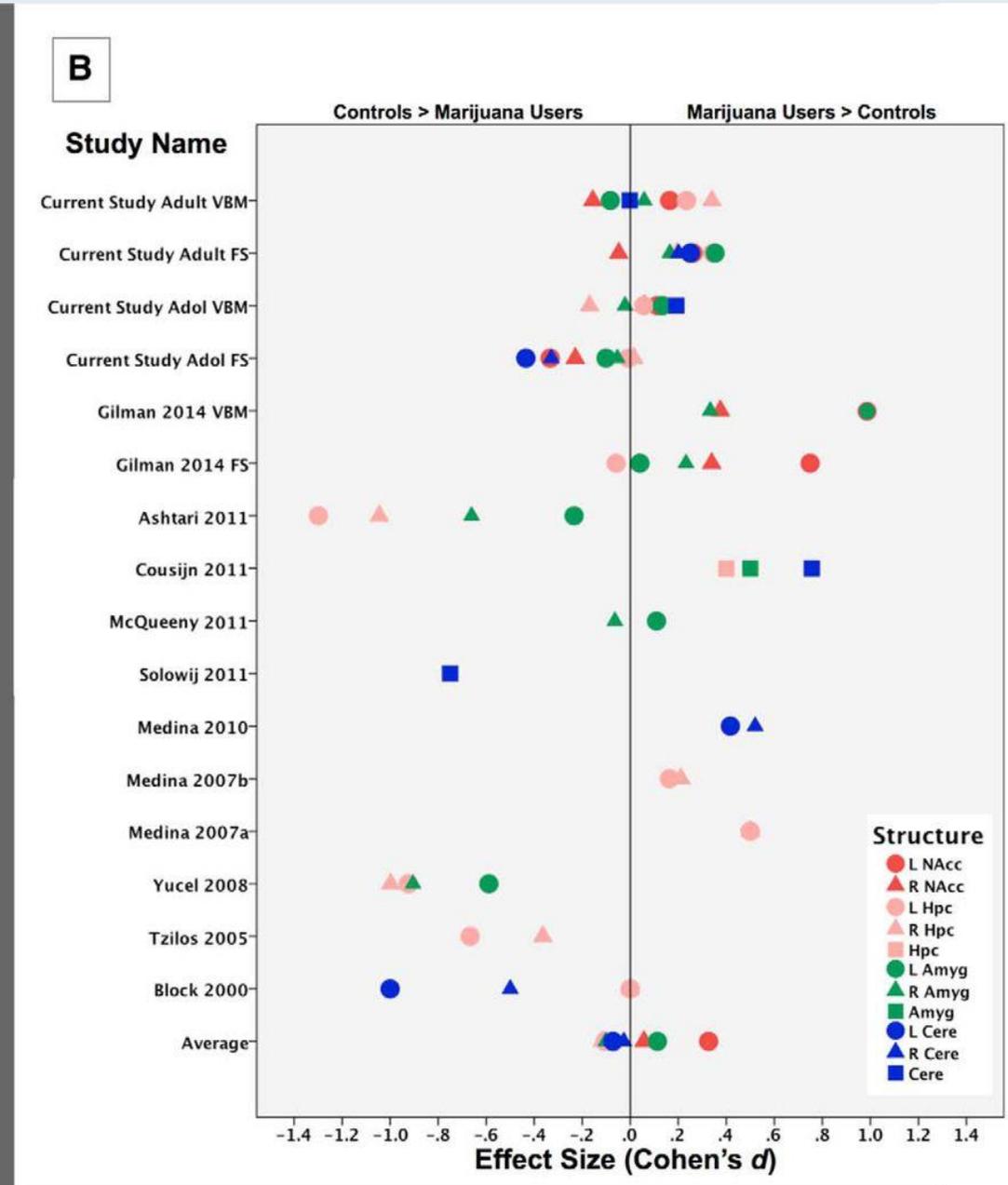
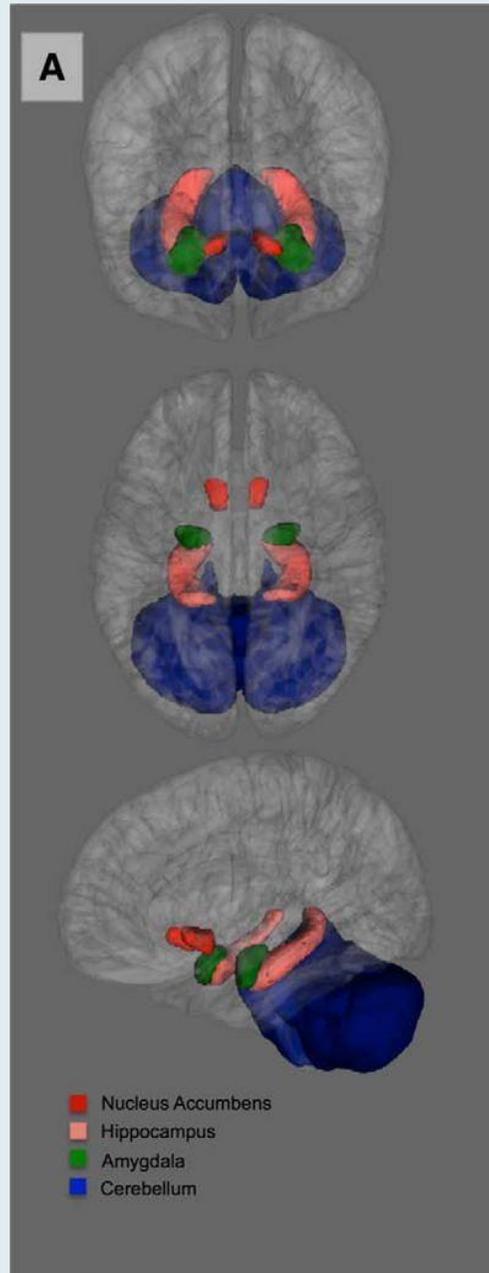
Fimbria of  
hippocampus,  
hippocampal  
Commissure,  
and  
splenium



Axonal paths with reduced connectivity (measured with diffusion-weighted MRI) in cannabis users (n=59) than in controls (N=33).

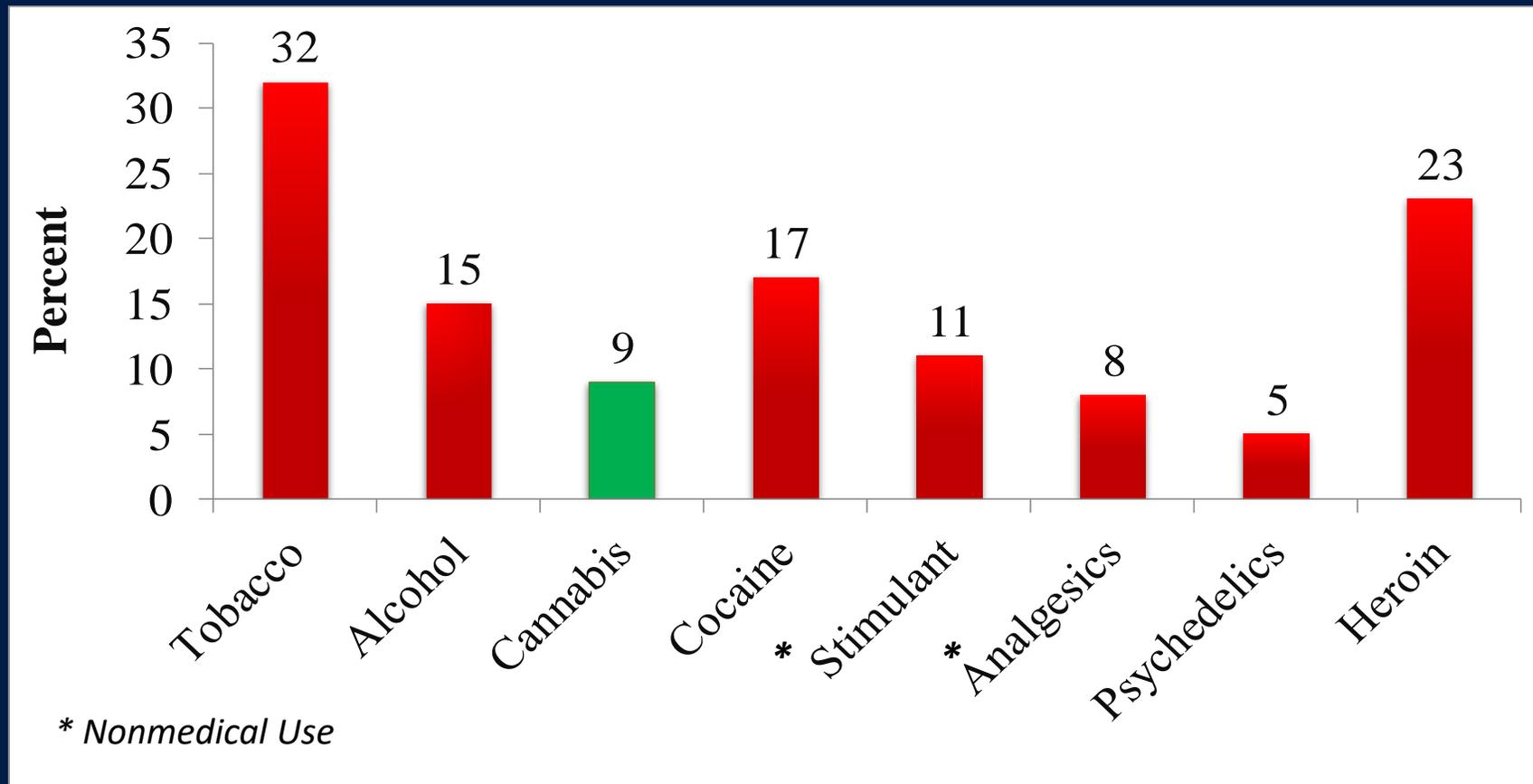
# NOT ALL STUDIES FIND DIFFERENCES: SUBCORTICAL STRUCTURES

NO DIFFERENCES BETWEEN REGULAR MARIJUANA USERS AND NONUSERS WHEN PARTICIPANTS WERE MATCHED ON ALCOHOL USE



**ADDICTION: ABOUT 9% OF USERS BECOME DEPENDENT,  
1 IN 6 WHO START USE IN ADOLESCENCE,  
25-50% OF DAILY USERS**

**Estimated Prevalence of Dependence Among Users**



# THERAPEUTIC USES

# CANNABIS/CANNABINOIDS FOR MEDICAL PURPOSES

- Difficult to develop a botanical-based product with accurate and consistent doses
- Medications which use purified chemicals derived from the cannabis plant considered most promising
- Several FDA-approved compounds show medical benefits:
  - Dronabinol (Marinol<sup>®</sup>) and nabilone (Cesamet<sup>®</sup>) (synthetic THC): treatment of nausea in patients undergoing cancer chemotherapy and to stimulate appetite in patients with wasting syndrome due to AIDS.
  - Epidiolex<sup>®</sup> (plant-based CBD): treatment of two forms of severe childhood epilepsy, Dravet syndrome and Lennox-Gastaut syndrome.
  - Nabiximols (Sativex<sup>®</sup>) (plant-based THC/CBD) - a mouth spray for treating spasticity and neuropathic pain that may accompany multiple sclerosis (not yet available in US)

# MEDICAL APPLICATIONS: STRENGTH OF THE RESEARCH

## Strongest Evidence

- Nausea (cancer chemotherapy)
- Spasticity and pain (MS)
- Appetite stimulant (AIDS wasting)
- Neuropathic pain
- Glaucoma
- Seizures

## Moderate Evidence

- Anti-convulsant
- Anti-inflammatory
- Anti-tumor

## Weakest Evidence

- PTSD
- ADHD
- Alzheimer's
- Anxiety

# CHANGING POLICY LANDSCAPE

# WHERE ARE WE NOW: FEDERAL POLICY

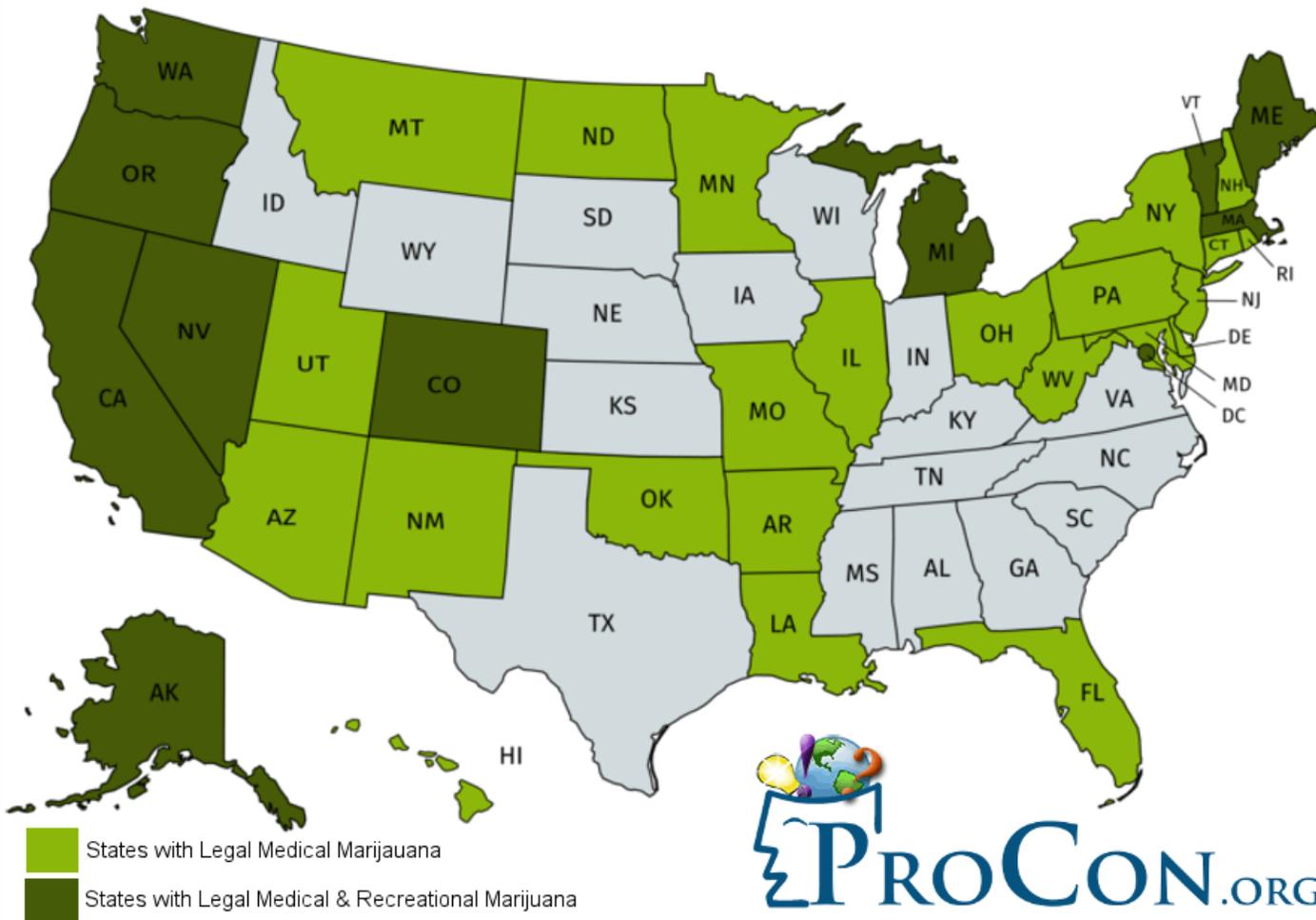
- Cannabis: Schedule I Substance → Controlled Substances Act (1970): high risk for abuse/dependence; no accepted medical use.
- *Aligns with:* Single Convention on Narcotics (1961, 1972 update) –International treaty covering opium (poppy plants), coca leaves, and cannabis
  - Cannabis is illegal to grow, possess, or distribute
  - Each nation can designate a single source of marijuana for research purposes
  - The DEA has designated *NIDA* to be that source using a contract with the University of Mississippi

## NIDA's Marijuana Farm



# U.S. STATE CANNABIS LAWS

33 Legal Medical Marijuana States & DC  
10 Legal Recreational Marijuana States & DC



## *States with MML vary on:*

- Allowable conditions and routes of administration.
- Dispensaries/home growth, registries.
- Testing, regulatory requirements.

## *States with Adult Use Laws vary on:*

- Marketing, product labeling, distribution (home growth, delivery).
- Taxation.
- Public Consumption.
- Expungement.



# NEW TERRITORY: AGRICULTURE IMPROVEMENT ACT 2018 (FARM BILL)

- Removed Industrial Hemp (defined as cannabis sativa plant containing less than 0.3% THC) from Controlled Substances Act
- Re-affirms the regulatory role of the FDA for hemp – derived products
  - Medications (to treat illnesses or symptoms)
  - Dietary Supplements (wellness)
  - Food Additives

Public Hearing: May 31; >120 speakers provided input as FDA considers how to go about regulating CBD

- *Expected to be a \$2B industry by 2020*
- Concerns re: current market: Unregulated Products; Unverified Claims; Uninformed Users (e.g., side effects, drug interactions).

The implications for research with CBD are not yet clear.



 **STRESS OR ANXIETY**  
Studies have shown that CBD oil use can help reduce anxiety and/or stress for people who may suffer from conditions like PTSD, social anxiety, and many others.

**RELIEVING PAIN**  
People suffering with chronic pain issues like Fibromyalgia and others, are finding relief when using CBD oil on a regular basis.



 **SEIZURES & EPILEPSY**  
CBD has shown to be very promising in helping control and reduce seizures in children and some adults.

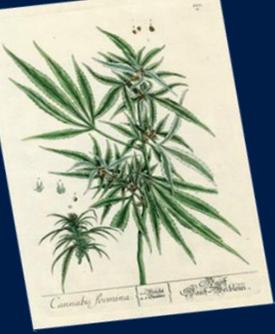
**SLEEP**  
Studies have shown that with certain doses of CBD Oil, people had reported that their sleep improved greatly.



 **CANCER**  
Numerous studies have been done and are continuing to be done showing that CBD oil may be helping with the adverse effects of some certain types of cancer and may hinder the migration of cancer cells.

For more detailed information and links to the studies and information included here, please visit [www.FindingHappyinHealthy.com](http://www.FindingHappyinHealthy.com)



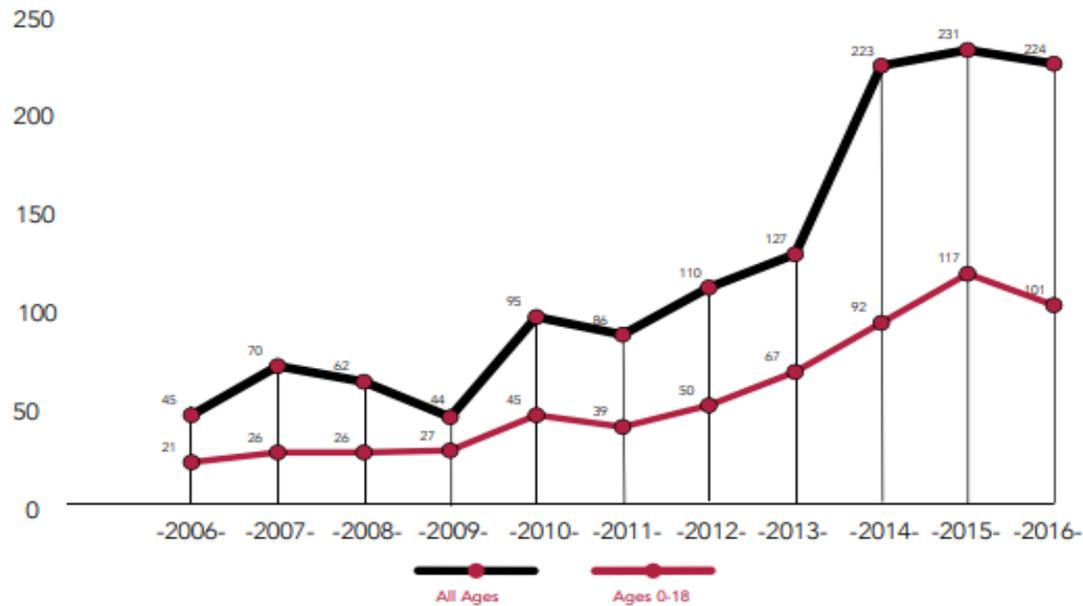


# CONSEQUENCES OF CONFLICTING FEDERAL AND STATE POLICIES

- UNCERTAINTY around what the DOJ will do in way of ENFORCEMENT
- STATES are developing DIFFERENT APPROACHES to TESTING and LABELING of PRODUCTS
  - What are ALLOWABLE products?
- UNEVEN QUALITY CONTROL, including for home grown Cannabis
- No NATIONAL Guidance, Oversight, or Monitoring of what States are dispensing to patients/recreational users
- BANKING Problems
- “Big Marijuana” industry presence
- BARRIERS to RESEARCH
  - SCHEDULE I STATUS
  - SINGLE SOURCE FOR MARIJUANA

# CANNABIS RELATED POISON CONTROL CALLS INCREASED IN COLORADO AND WASHINGTON, INCLUDING IN CHILDREN, INFANTS

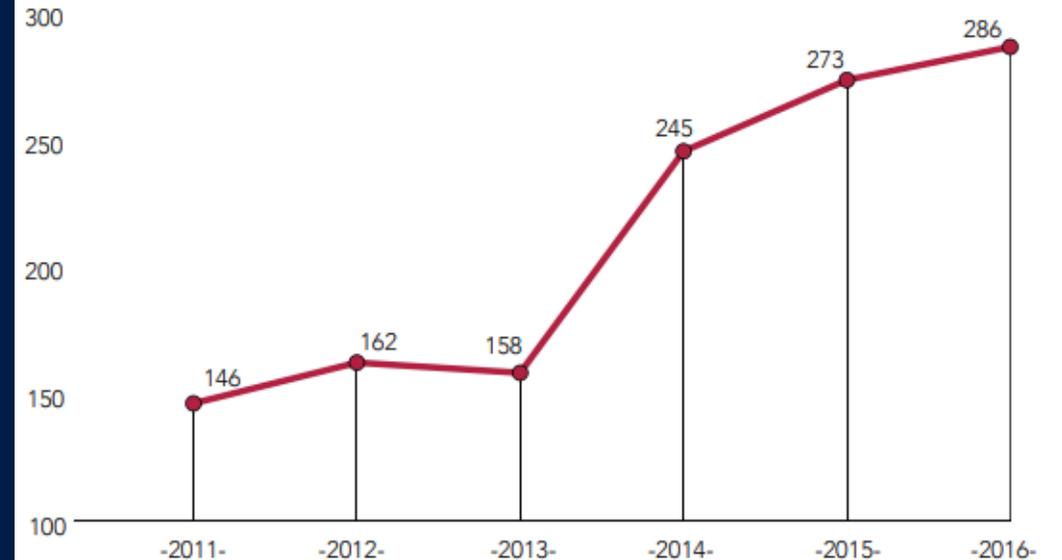
## Emergency Marijuana-Related Poison Control Calls in CO



Source: Rocky Mountain Poison and Drug Center Report, Colorado Marijuana Statistics for 2016, as reported by HIDTA

Colorado: RMPDC, 2017

## Emergency Marijuana-Related Poison Control Calls in WA



Source: Source: Washington Poison Control Center, Washington Poison Center Toxic Trends Report: 2016 Annual Cannabis Report

Washington: WSOFM, 2017

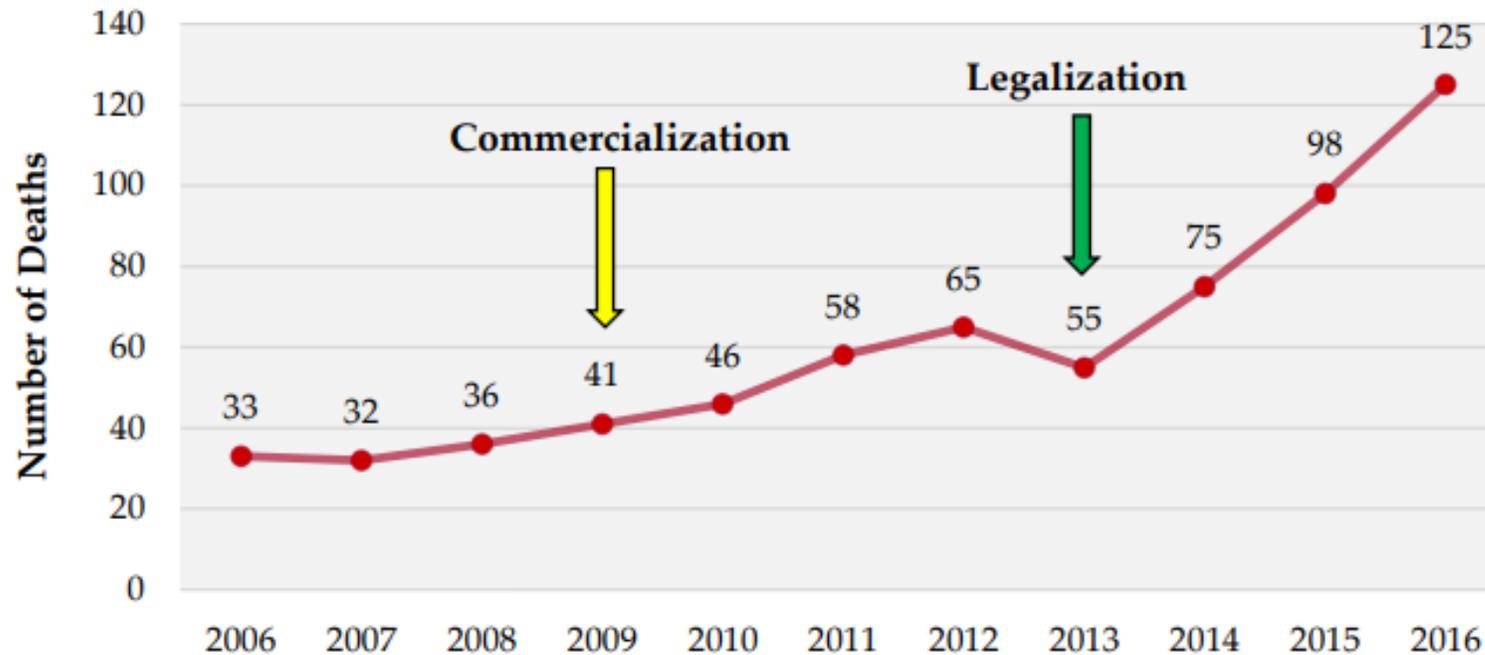
# EMERGENCY DEPARTMENT VISITS WITH CANNABIS RELATED DIAGNOSES IN SAN DIEGO COUNTY



*The Center for Community Research prepared this analysis for the San Diego County Marijuana Prevention Initiative with data from the California Department of Public Health, March 2016.*

# TRAFFIC FATALITIES IN COLORADO

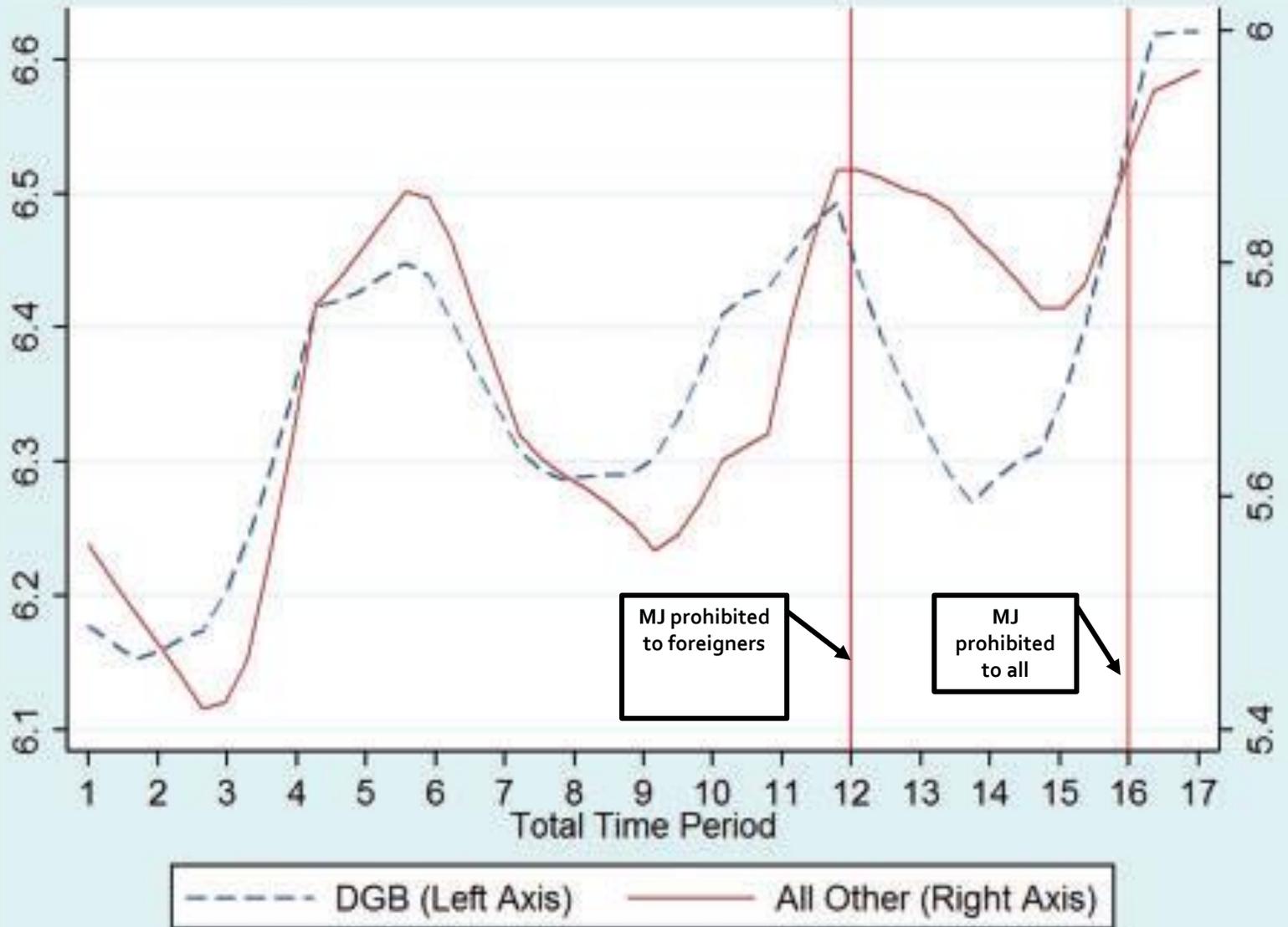
## Traffic Deaths Related to Marijuana when a Driver Tested Positive for Marijuana



SOURCE:

National Highway Traffic Safety Administration, Fatality Analysis Reporting System (FARS), 2006-2011 and Colorado Department of Transportation 2012-2016

WHEN CANNABIS  
SALES WERE  
RESTRICTED IN THE  
NETHERLANDS  
(MAASTRICHT),  
UNIVERSITY  
GRADES  
IMPROVED



# CHALLENGES INTERPRETING POLICY RESEARCH

- Lack of accurate baseline data prior to policy enactment
- Much of the research ignores important policy heterogeneity
- It also ignores how laws were implemented; how they have changed over time
- Lack of attention to specificity and timing generates mixed and inconclusive findings
- Many of the measures being collected (prevalence of use) do not necessarily relate to outcomes of interest (e.g., hospitalizations, treatment needs, school outcomes).
- Findings are observational, associative, and cannot account for all confounding factors (esp. pertinent for opioid findings).
- Few/any assess potential benefits: treatment of pain, stress relief, criminal justice, others.

# HOW CAN SCIENCE INFORM POLICY?

- Acknowledge the polarized nature of the issue.
- Need to be explicit and clear about what we know, what we think we know, and what we don't know.
- Try to answer real world questions:
  - Does cannabis legalization impact the opioid epidemic?
  - Is there a potency limit that should be imposed?
  - Should certain products be prohibited.
  - How dangerous is prenatal exposure to cannabis?
- Be precise in use of terminology
- Help ensure that the public health interests are front and

# Adolescent Brain Cognitive Development (ABCD) Study

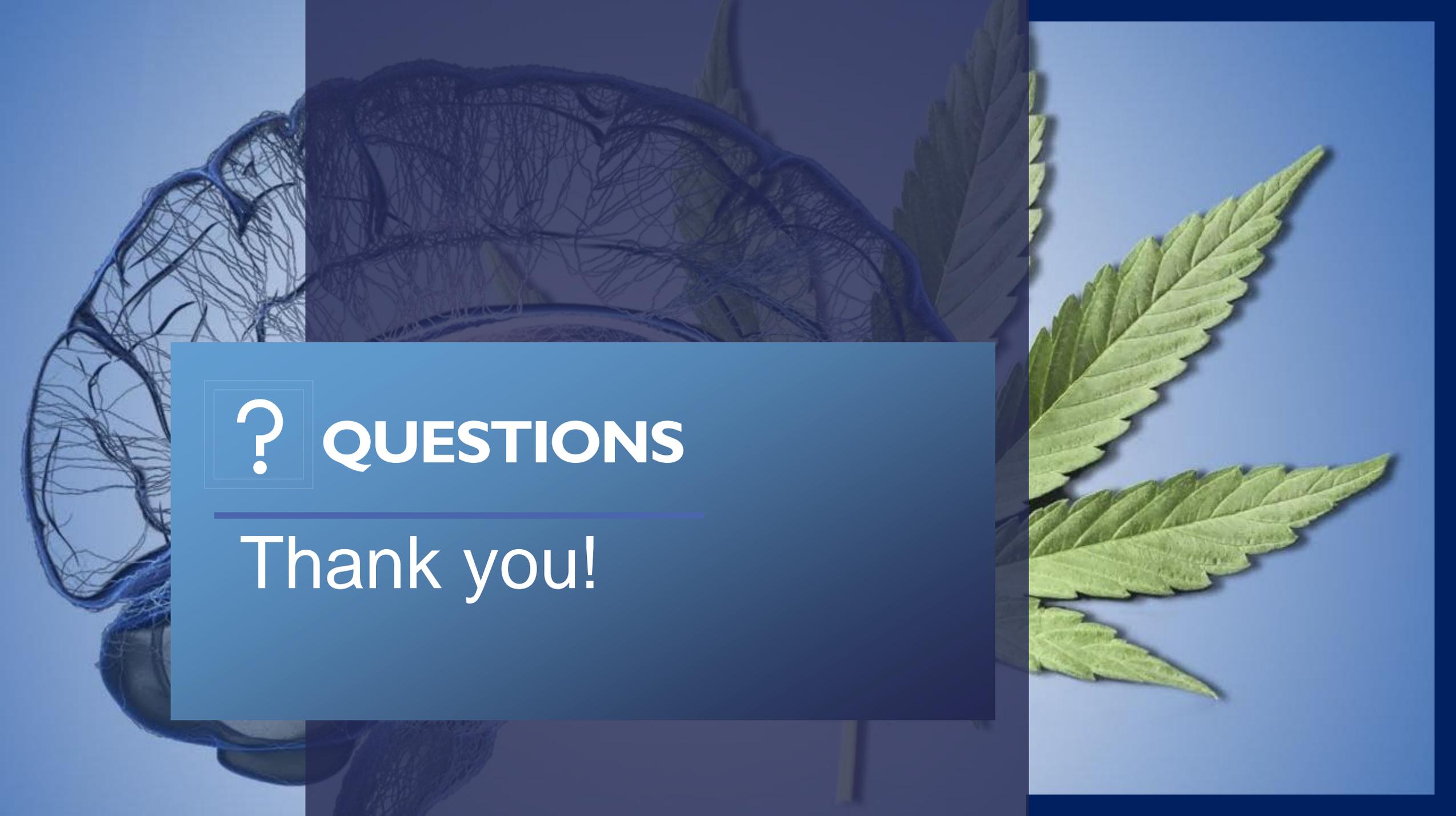
*A Federal Collaboration: NIDA, NIAAA, NCI, NIMH, NIMHD, NICHD, NINDS, OBSSR, ORWH, CDC-DASH, CDC-DVP, DOJ, NEA*

Ten year longitudinal study of ~10,000 children from age 10 to 20 years to assess effects of childhood experiences, including use of *cannabis* and other substances on individual brain development trajectories



**Adolescent Brain Cognitive Development**®

*Teen Brains. Today's Science. Brighter Future.*



? QUESTIONS

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Thank you!