

# RECREATIONAL AND MEDICAL MARIJUANA: POTENTIAL IMPLICATIONS FOR ADOLESCENT AND PSYCHIATRIC POPULATIONS

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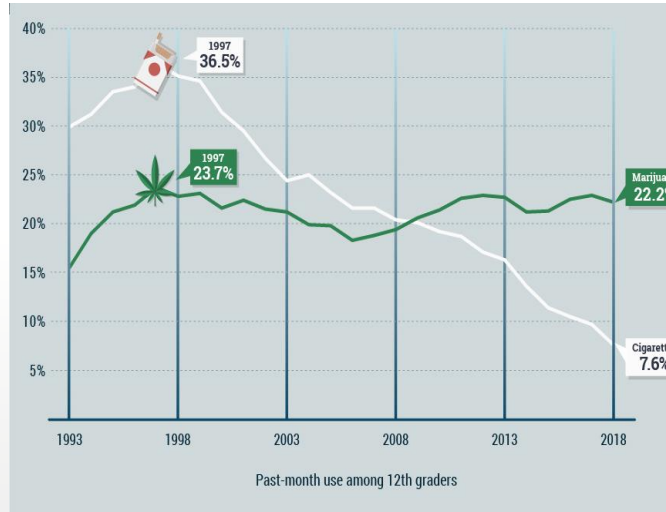
**Teen cannabis use is common.**



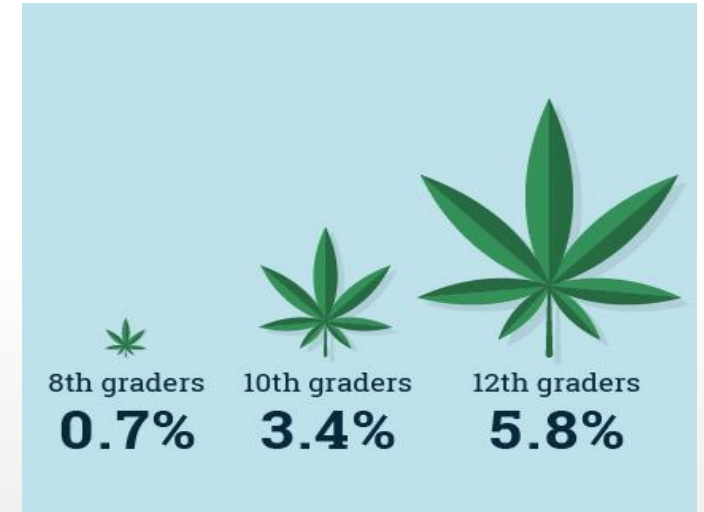
## Past Year Use



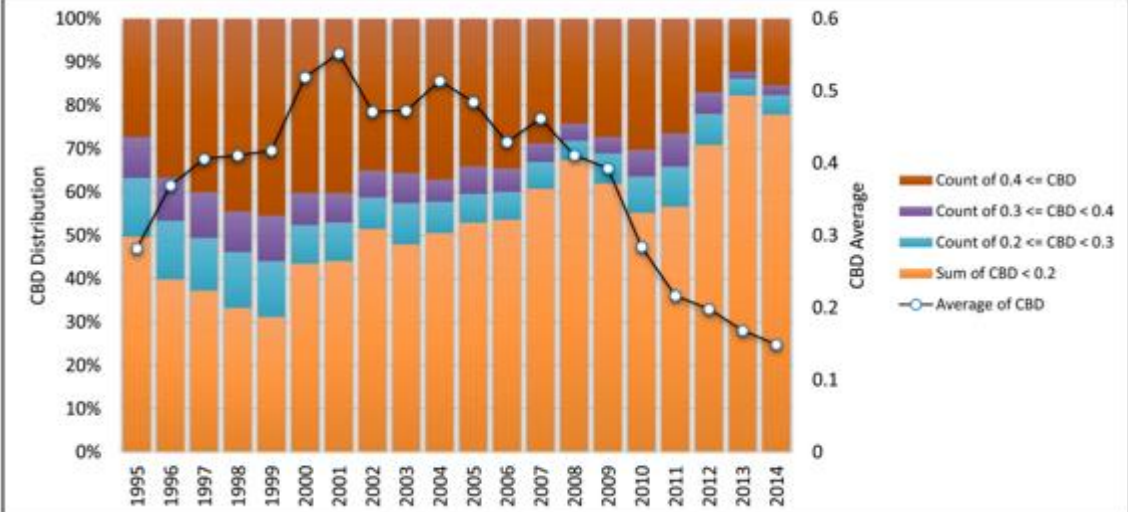
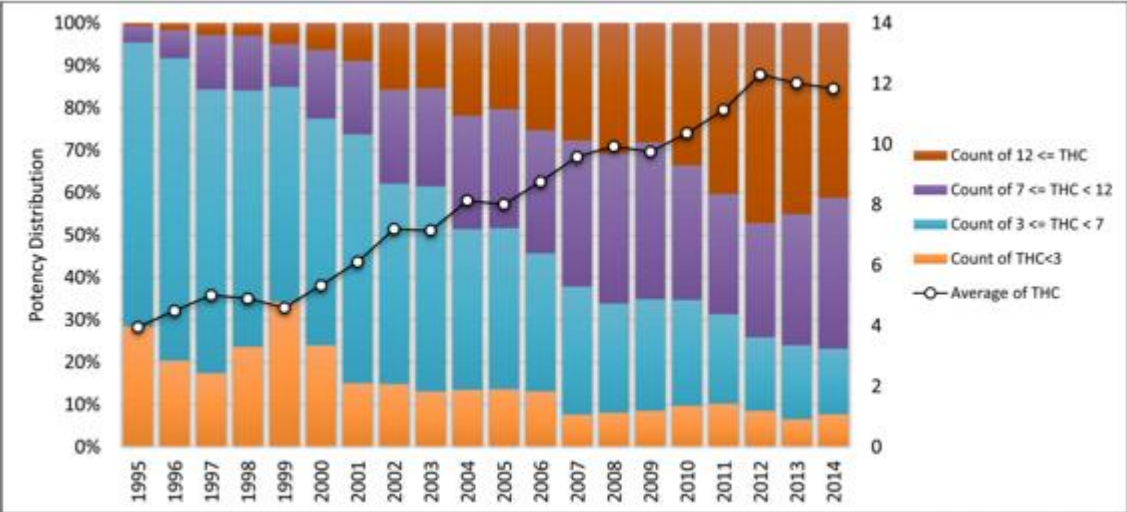
## Past Month Use



## Daily Use



# Cannabis is far more potent than in prior decades.



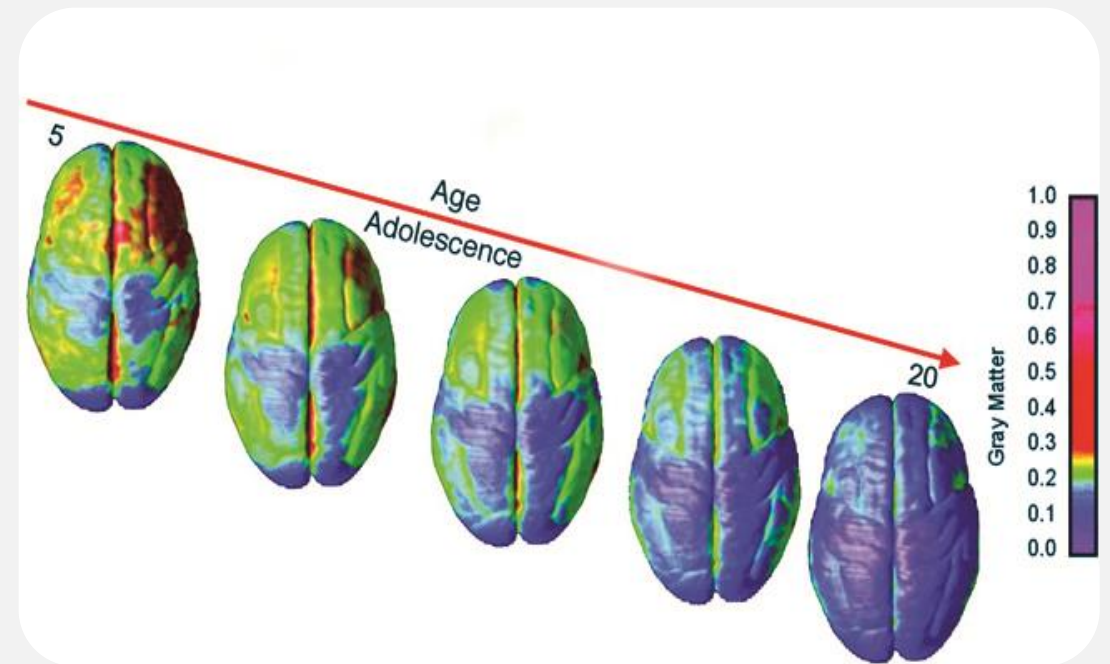


**Novel forms of THC delivery are the new norm, yet use is difficult to detect and we have very little information on long-term effects.**

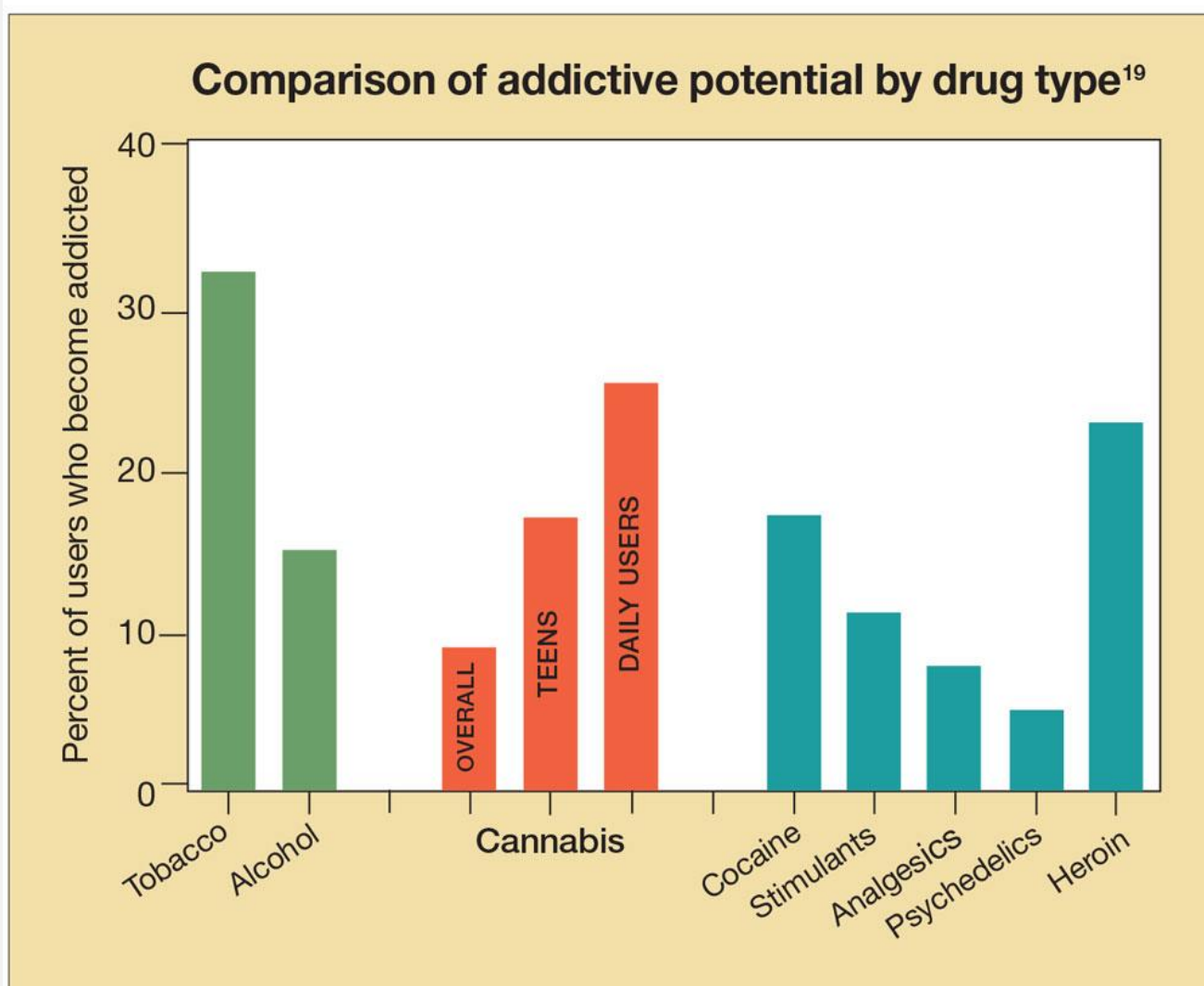


# ONGOING BRAIN DEVELOPMENT MAY MAGNIFY CANNABIS' EFFECTS

- Developmental changes in brain into 3<sup>rd</sup> decade of life
  - Connectivity
  - Chemistry
  - Morphology
- Prefrontal regions last to develop
  - Densely populated with cannabinoid receptors
  - Critically underlie higher order cognitive



# ADDICTION LIABILITY



- 4M people aged 12+ have a past year CUD
- ~23% of people who received addiction treatment received treatment for CUDs
- Average adult entering tx for CUD has used daily for 10 years, tried to quit 6 times



# RESIDUAL COGNITIVE EFFECTS OF CANNABIS

IQ decline

Memory

Learning & retaining new information

Attention and concentration

Response speed & variability

Executive functioning

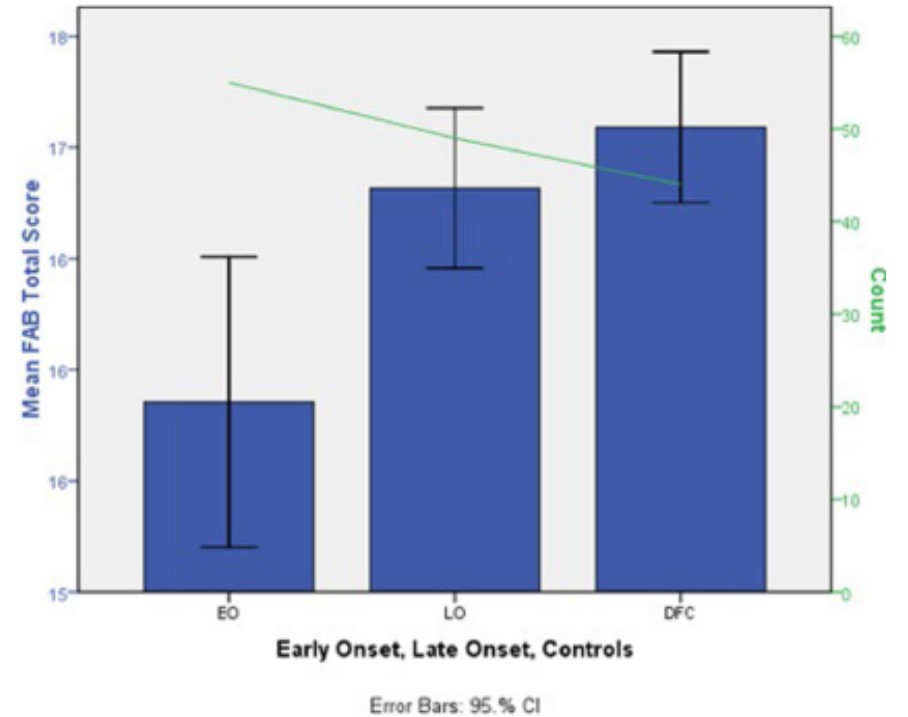
Working memory

Verbal fluency

Decision-making, risk-taking & inhibition

Abnormalities in brain structure and function

↓ Age of initiation → worse cognition



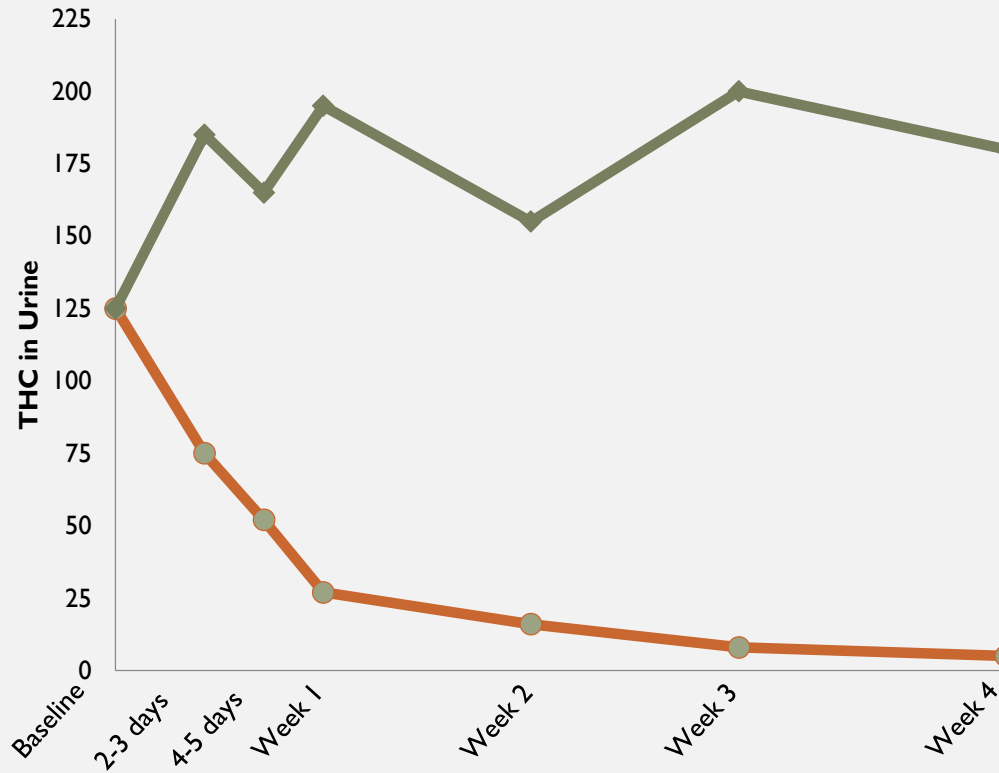
# ARE COGNITIVE DEFICITS REVERSIBLE?

- Biological markers normalize after ~4 weeks
- Cannabinoid receptor density in brain
- Cortical blood volumes
- Especially in areas important for cognition

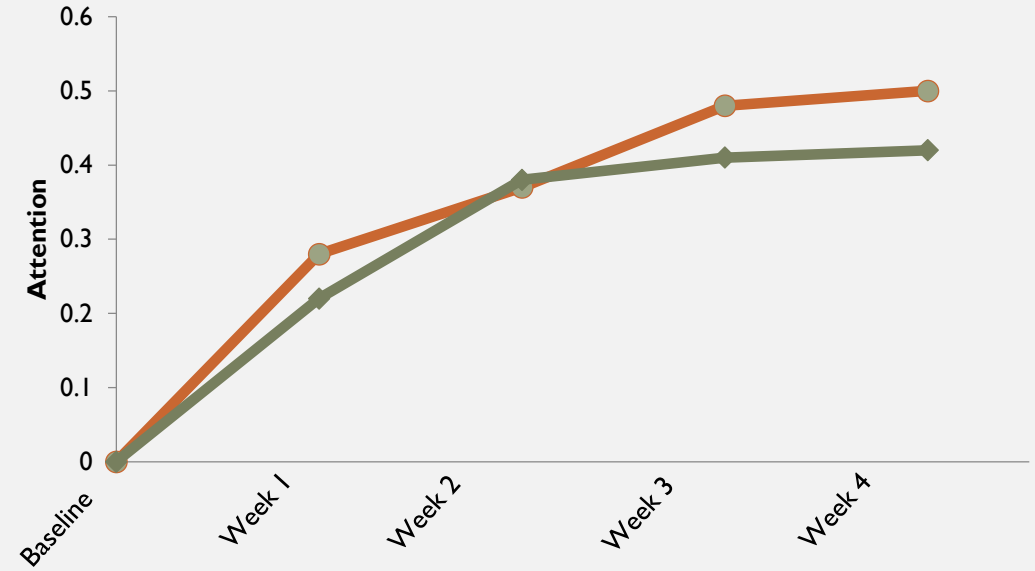
# Ongoing Study on Neurocognitive Recovery with Cannabis Abstinence in High School Students

Users who Abstain for 30 Days      Users who continue to use cannabis

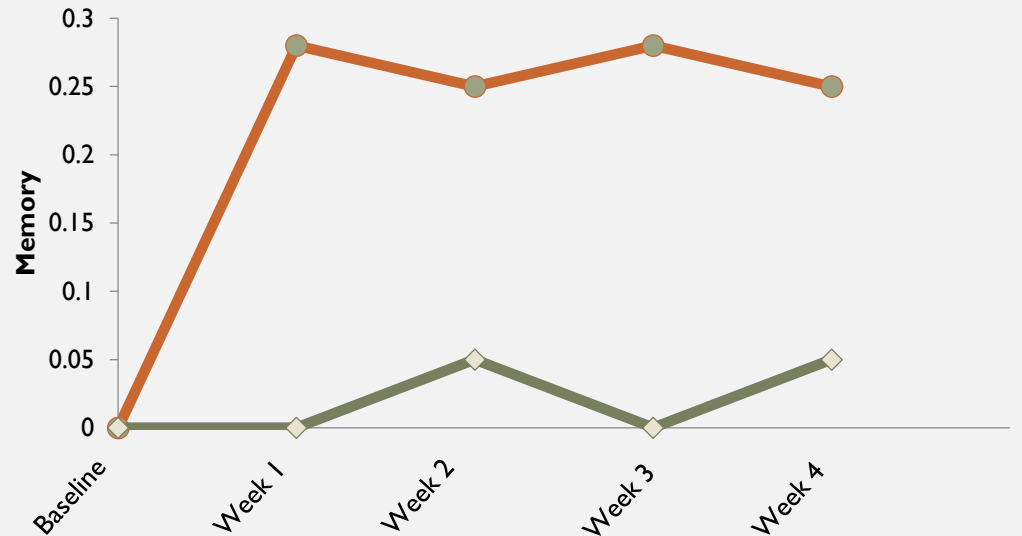
### THC Concentrations in Urine



### Attention



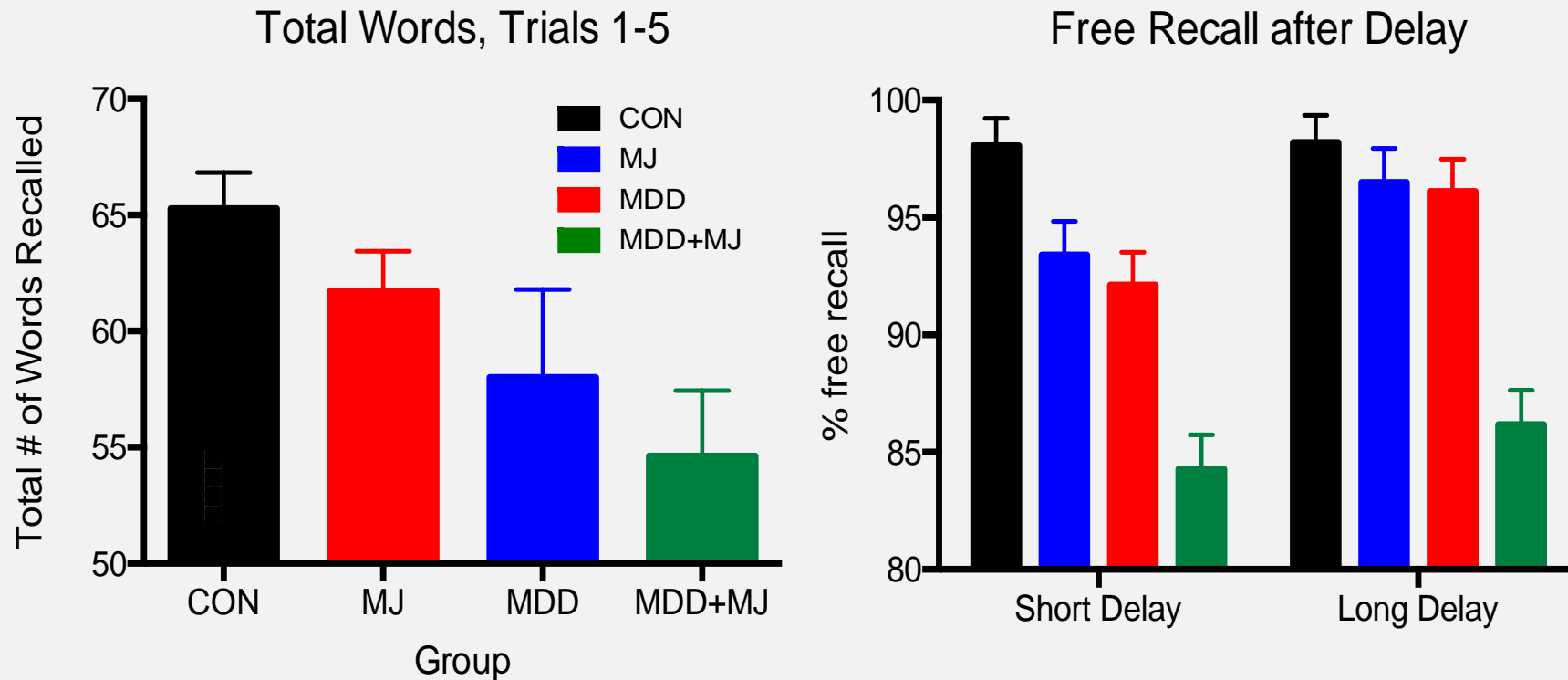
### Memory



# SO WHY THE CONTROVERSY?



# GREATER VULNERABILITY WITH PSYCHIATRIC DIAGNOSES?



**IT'S  
CLEARLY  
NOT  
SIMPLE...**

**Is MJ harmful? Yes for some:**

- For kids, there are lasting detrimental cognitive effects of heavy use
- For some, high potency MJ exposure increases risk of psychotic illness
- On roadways and workplaces, MJ intoxication is a public safety risk

**Is MJ medicine? Yes, components of MJ are medicine for some:**

- CBD for children with some forms of epilepsy now FDA approved
- For some with spasticity due to MS, for some THC for severe weight loss.
- For ALL other indications, there are too few, poor quality data to know.
- Our group is poised to study Epidiolex for chronic back pain in a clinical trial with PET imaging

**Effective regulation using a public health framework is key to mitigating risk**

**Permitting cannabis use is one thing, Promoting it is another...**

**THOSE WITH  
ADOLESCENT  
CANNABIS USE  
HAVE  
GREATER  
SEVERITY OF  
ILLNESS  
SCHIZOPHRENIA**

**Males with schizophrenia with v. without cannabis use before age 18-20 followed for 21 years had:**

- Higher median duration of first hospital stay (59 vs. 30 days)
- Greater median number of hospitalizations (10 vs. 4)
- Greater total hospital days (547 vs. 184)
- Greater odds of having >20 hospitalizations OR=3.1 (1.3–7.3)
- Greater odds of hospital stay >2 years OR=2.4 (1.1–7.4)

**Controlling for personality disorder, family SES, IQ, marital status, urban residence, risky use of alcohol, and other drug use**

Manrique-Garcia, et al., *Psychol Med* 2014

# MARIJUANA RELATED PSYCHOTIC SYMPTOMS AMONG PRIMARY CARE PATIENTS

Routine pediatric visits, mean age 16.6



- Hallucinations (27%)
- Paranoia/Anxiety (33.6%)
- Any psychotic symptom (42.9%)

Significantly higher rates among youth with depressive sx, CUD

**Source:** Levy S, Weitzman, ER. Acute mental health symptoms in adolescent marijuana users. *JAMA Pediatrics*. 2018 Dec 17;doi 10.1001/jamapediatrics.2018



# INSTITUTE OF MEDICINE

## THE HEALTH EFFECTS OF CANNABIS AND CANNABINOIDS

### COMMITTEE'S CONCLUSIONS **JANUARY 2017**

- committee considered more than **10,000** scientific abstracts
- arrived at nearly **100** different research conclusions related to cannabis and health, organizing these into 5 categories:
  - **conclusive,**
  - **substantial,**
  - **moderate,**
  - **limited,**
  - **no/insufficient evidence**

# ARE THERE THERAPEUTIC EFFECTS OF CANNABIS?

There is **NO or insufficient evidence** to support or refute the conclusion that cannabis or cannabinoids are an effective treatment for:

- Cancers, including glioma (cannabinoids)
- Anorexia nervosa (cannabinoids)
- Irritable bowel syndrome (dronabinol)
- Epilepsy (cannabinoids)
- Spasticity in patients with paralysis due to spinal cord injury (cannabinoids)
- Amyotrophic lateral sclerosis (cannabinoids)
- Chorea and neuropsychiatric symptoms associated with Huntington's disease (oral cannabinoids)
- Parkinson's disease (cannabinoids)
- Dystonia (nabilone and dronabinol)
- Achieving abstinence in the use of addictive substances (cannabinoids)
- Mental health outcomes in individuals with schizophrenia or psychosis (cannabidiol)

There is **conclusive or substantial evidence** that cannabis or cannabinoids are effective:

- For the treatment for chronic pain in adults (cannabis)\*
- Antiemetics in the treatment of chemotherapy-induced nausea and vomiting (oral cannabinoids)
- For improving patient-reported multiple sclerosis spasticity symptoms (oral cannabinoids)

# WHAT ABOUT RISK OF HARM?

## CONCLUSIONS FOR: CARDIOMETABOLIC RISK

There is **limited evidence** of a statistical association between cannabis use and:

- The triggering of **acute myocardial infarction** (cannabis smoking)
- Ischemic **stroke** or subarachnoid **hemorrhage**
- Decreased risk of **metabolic syndrome** and **diabetes**
- Increased risk of **prediabetes**

## CONCLUSIONS FOR: RESPIRATORY DISEASE

There is **substantial evidence** of a statistical association between cannabis smoking and:

- Worse respiratory symptoms and more frequent chronic bronchitis episodes (long-term cannabis smoking)

## CONCLUSIONS FOR: INJURY AND DEATH

There is **substantial evidence** of a statistical association between cannabis use and:

- Increased risk of motor vehicle crashes

There is **moderate evidence** of a statistical association between cannabis use and:

- Increased risk of overdose injuries, including respiratory distress, among pediatric populations in U.S. states where cannabis is legal

# WHAT ABOUT RISK OF HARM?

## CONCLUSIONS FOR: PSYCHOSOCIAL

There is **moderate evidence** of a statistical association between cannabis use and:

- Impairment in cognitive domains of learning, memory, and attention (acute cannabis use)

There is **limited evidence** of a statistical association between cannabis use and:

- Impaired academic achievement and education outcomes
- Increased rates of unemployment and/or low income
- Impaired social functioning or engagement in developmentally appropriate social roles

## CONCLUSIONS FOR: ABUSE OF OTHER SUBSTANCES

There is **moderate evidence** of a statistical association between cannabis use and:

- The development of substance dependence and/or substance abuse disorder for substances including alcohol, tobacco, and other illicit drugs

There is **limited evidence** of a statistical association between cannabis use and:

- The initiation of tobacco use

# WHAT ABOUT RISK OF HARM?

## CONCLUSIONS FOR: MENTAL HEALTH

There is **substantial evidence** of a statistical association between cannabis use and:

- The development of schizophrenia or other psychoses, with the highest risk among the most frequent users

There is **moderate evidence** of a statistical association between cannabis use and:

- Better cognitive performance among individuals with psychotic disorders and a history of cannabis use
- Increased symptoms of mania and hypomania in individuals diagnosed with bipolar disorders (regular cannabis use)
- Increased risk for the development of depressive disorders
- Increased incidence of suicidal ideation and suicide attempts with a higher incidence among heavier users
- Increased incidence of suicide completion
- Increased incidence of social anxiety disorder (regular cannabis use)

# WHAT ABOUT RISK OF HARM?

## CONCLUSIONS FOR: PROBLEM CANNABIS USE (CUD)

There is **substantial evidence** that:

- Stimulant treatment of ADHD during adolescence is *not* a risk factor for the development of CUD
- Being male and smoking cigarettes are risk factors for CUD
- Initiating cannabis use at an earlier age is a risk factor for CUD

There is **substantial evidence** of a statistical association between:

- Increases in cannabis use frequency and the progression to developing CUD
- Being male and the severity of CUD, but recurrence does not differ between males and females

• There is **moderate evidence** that:

- Anxiety, personality disorders, and bipolar disorders are *not* risk factors for CUD
- Major depressive disorder is a risk factor for CUD
- Adolescent ADHD is *not* a risk factor for CUD
- Exposure to the combined use of abused drugs is a risk factor for CUD
- Neither alcohol nor nicotine dependence are risk factors for CUD
- During adolescence the frequency of cannabis use, oppositional behaviors, a younger age of first alcohol use, nicotine use, parental substance use, poor school performance, antisocial behaviors, and childhood sexual abuse are risk factors for CUD

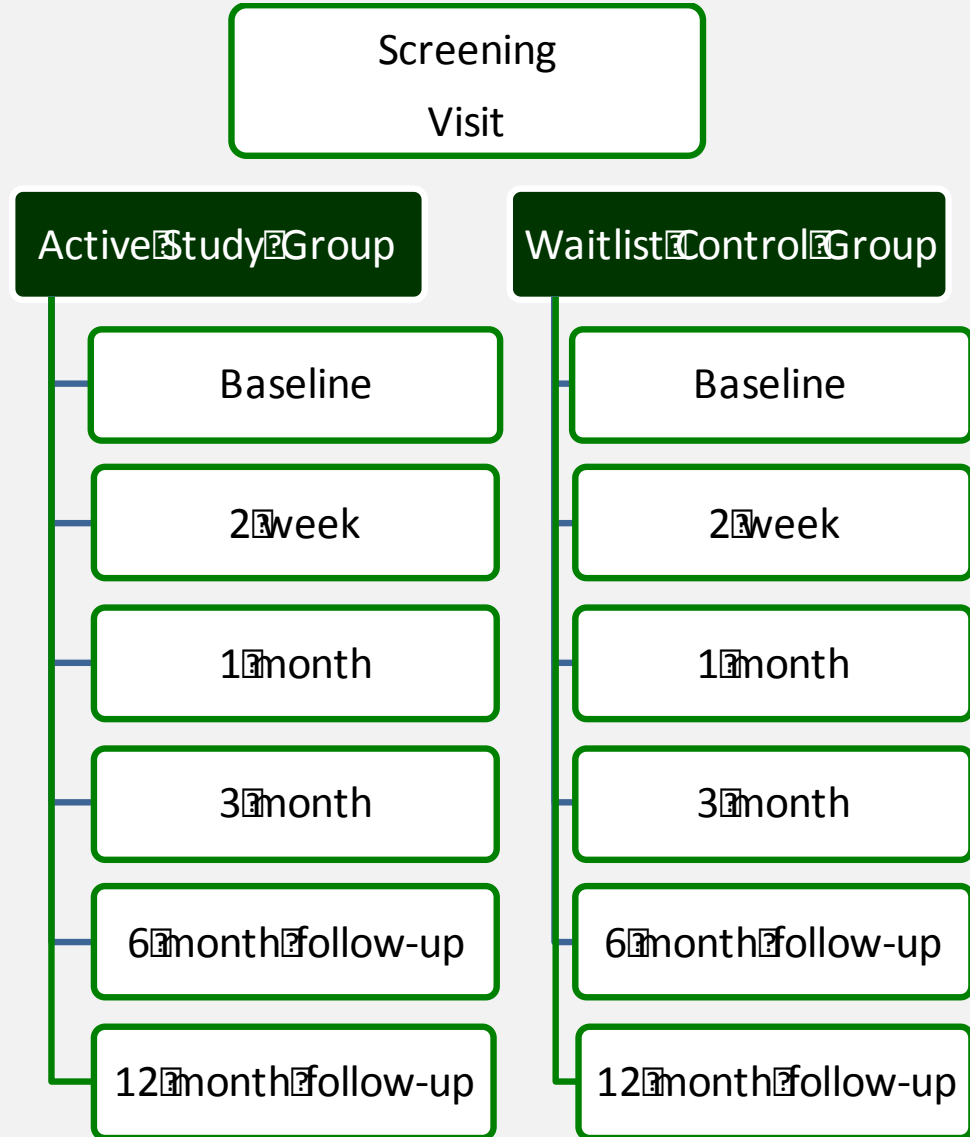
# RANDOMIZED TRIAL OF MEDICAL MARIJUANA CARDS VS. WAITLIST

Assessing adults, aged 18-55, seeking medical marijuana cards for:

- Pain,
- Insomnia,
- Depression, or
- Anxiety

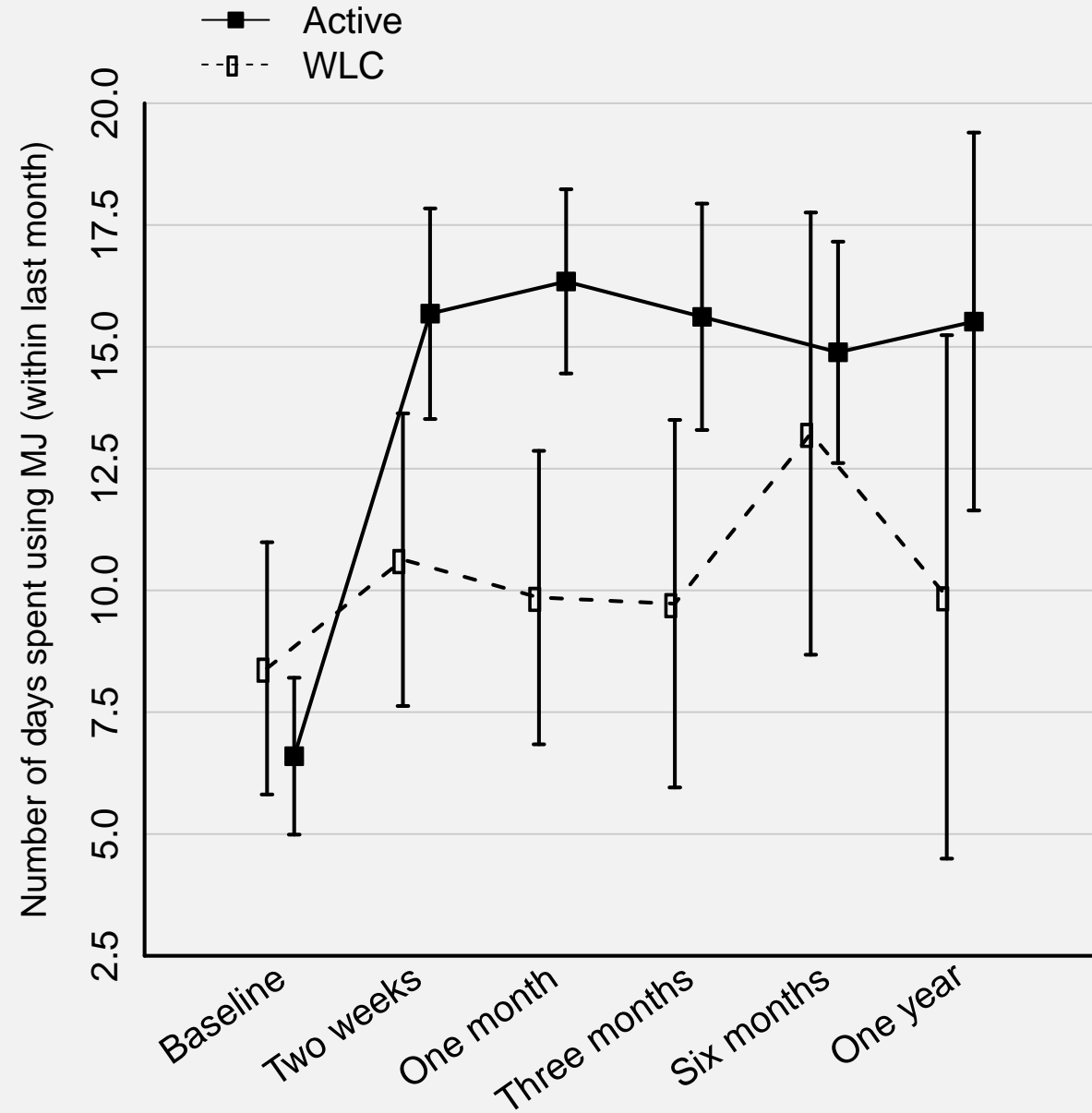
Funded by

- MGH ECOR
- ROIDA042043



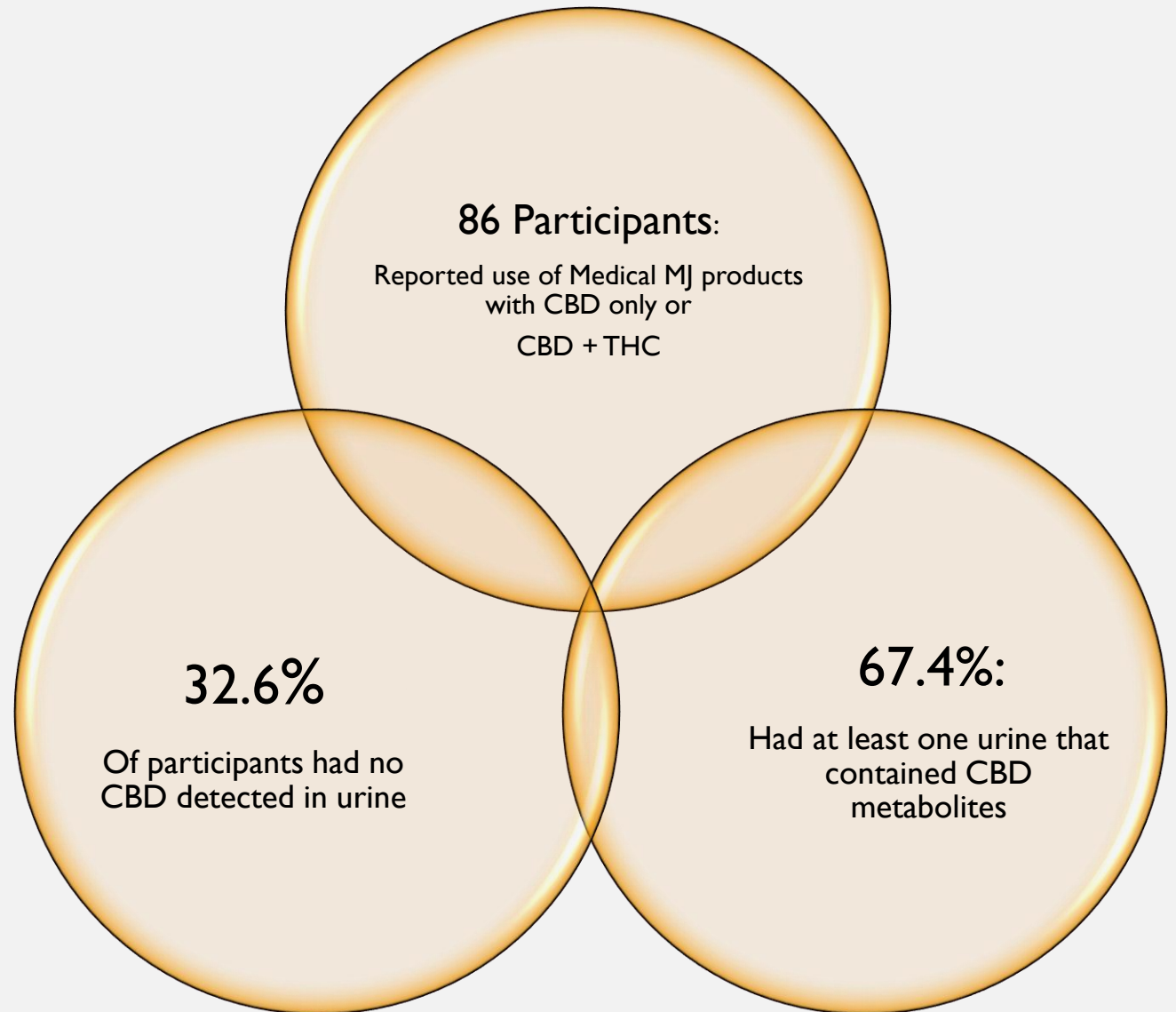
MM CARDHOLDERS  
DOUBLE THEIR USE AFTER  
GETTING THEIR MM  
CARDS, BEGIN TO OBTAIN  
CANNABIS PRODUCTS AT  
DISPENSARIES

- **Preliminary results**
- **for an ongoing trial.**
- **n = 52 MM**
- **n = 31 WLC**



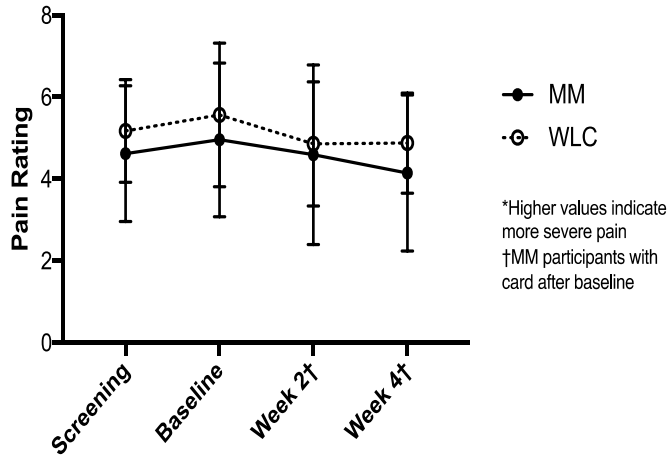


**NO  
DETECTABLE  
CBD IN 1/3 OF  
MED MJ  
PATIENTS  
PURCHASING  
CBD PRODUCTS  
AT  
DISPENSARIES**

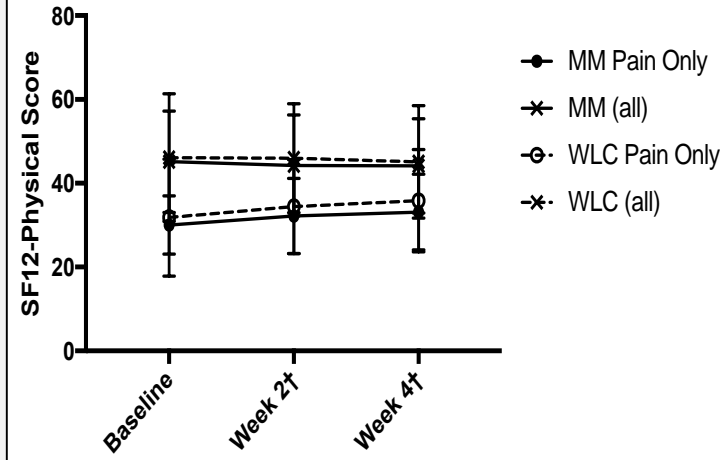


# TO DATE, MM USERS REPORT MINIMAL TO NO EFFECT ON PAIN...

How much pain (1-10) did you feel today?

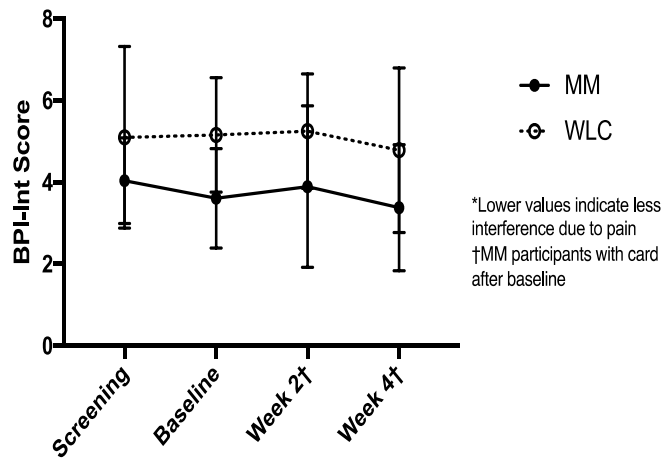


SF-12 Physical Health

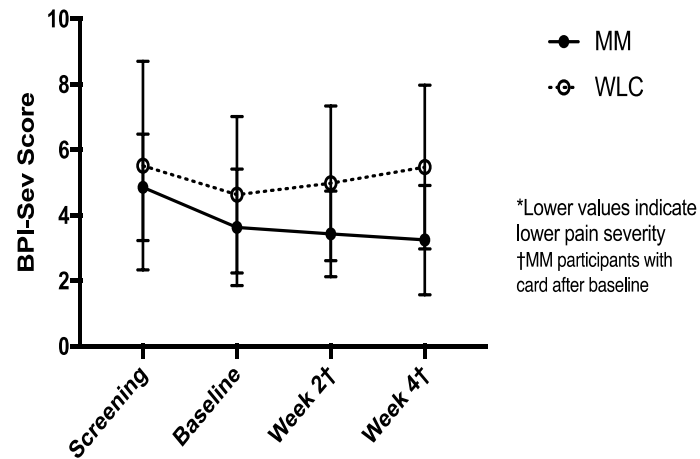


**Preliminary results  
for an ongoing trial**  
**n = 52 MM**  
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Brief Pain Inventory: Interference for Pain Patients

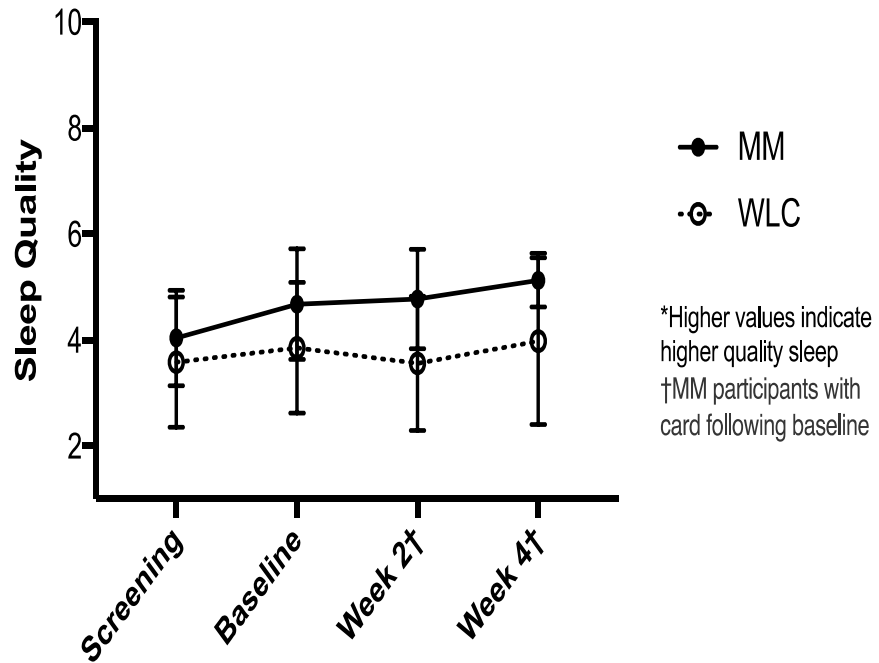


Brief Pain Inventory: Severity for Pain Patients

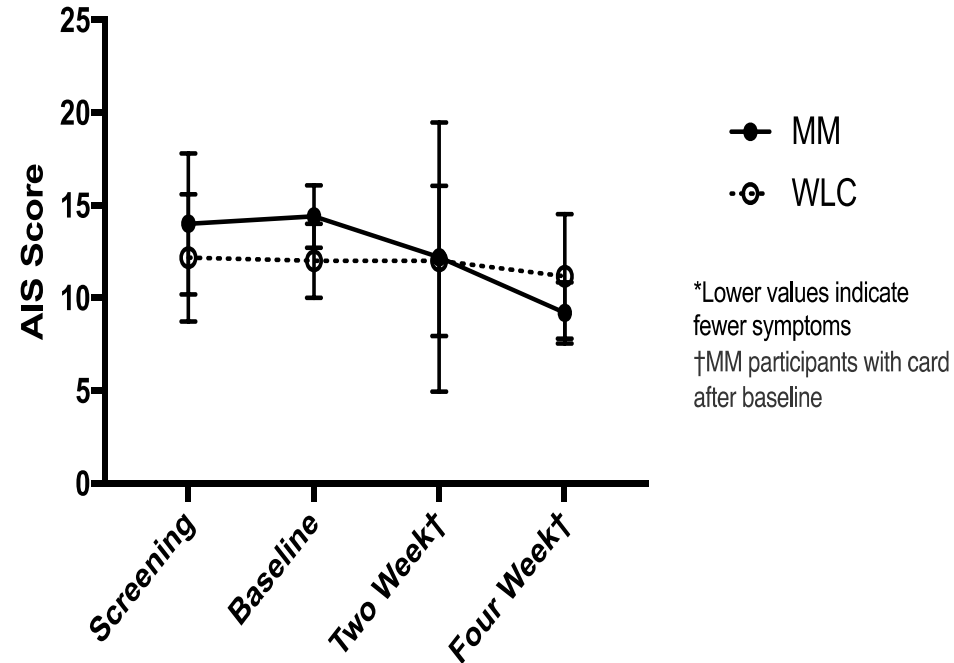


# LITTLE EFFECT ON SLEEP...

How was your sleep quality (1-10) last night?

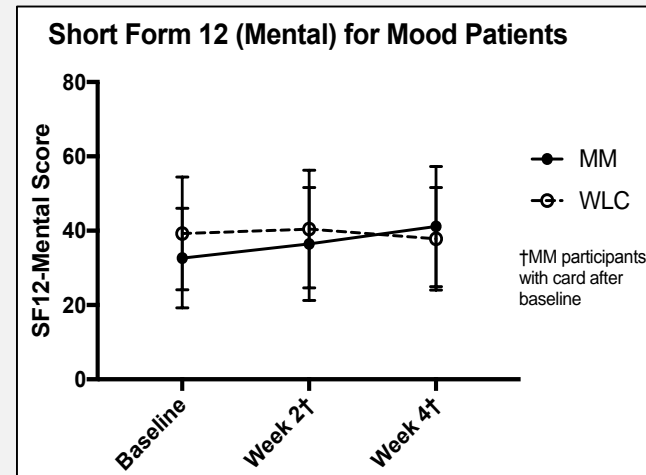
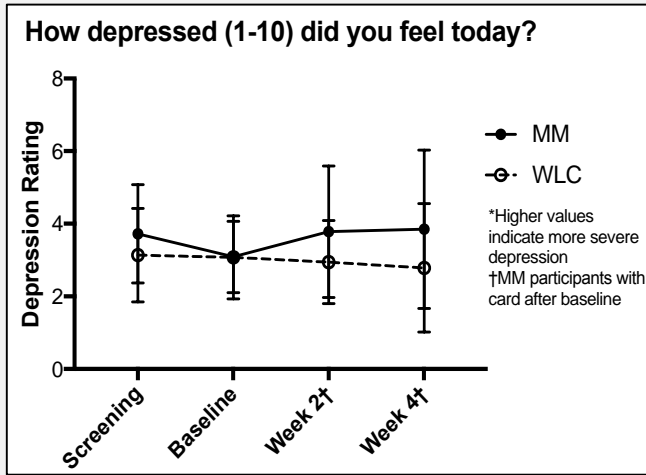


Athens Insomnia Scale for Insomnia Patients

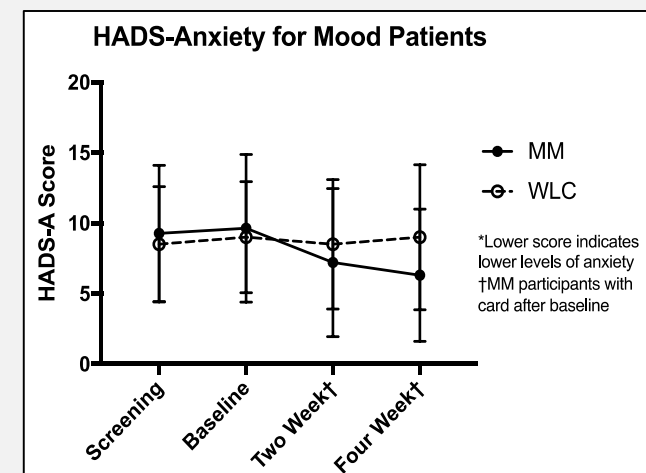
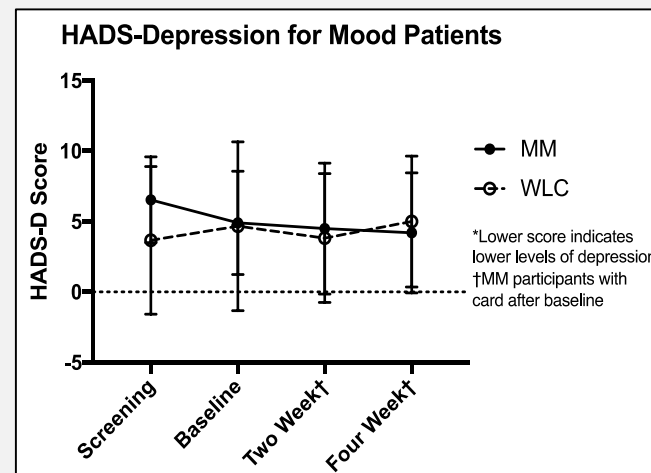
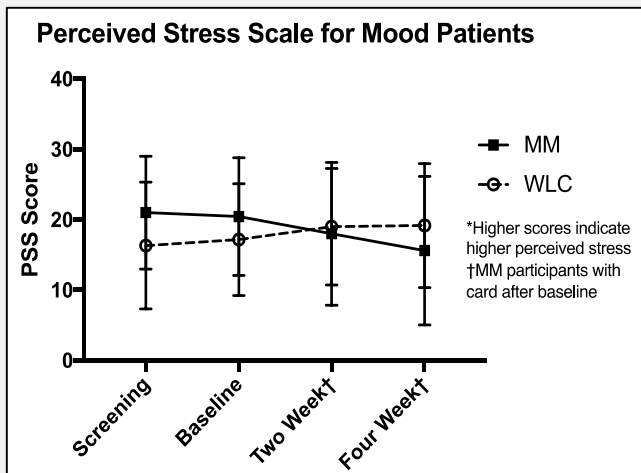


**Preliminary  
results  
for an ongoing  
trial**  
**n = 52 MM**  
**n = 31 WLC**

# AND LITTLE TO NO BENEFIT FOR ANXIETY AND DEPRESSION...



**Preliminary results  
for an ongoing trial**  
**n = 52 MM**  
**n = 31 WLC**



**WHILE MEDICAL MJ  
PURCHASED AT MA  
DISPENSARIES HAD  
NO CBD FOR 1/3 OF  
PATIENTS AND  
LITTLE EFFICACY,  
THERE WERE SIDE  
EFFECTS  
CONSISTENT WITH  
HIGH THC  
PRODUCTS...**

## 45 Psychiatric AEs

- 18 Psychotic
- 20 Worsening of Depression
- 7 Anxiety

## 27 Gastrointestinal

- 20 Nausea/vomiting/abdominal pain

## 17 Other CNS

- Headache, migraines or cluster headache


**'I was taking what I thought was CBD oil, and apparently it wasn't what I thought it was. I started feeling the effects when I was driving, which was really scary. I got home as quickly as I could. I felt so high I didn't know where I was and couldn't focus, and the only way I got home was the noises from GPS. I was paranoid that I might have hit someone or something, but I checked my car and there was no damage.'**

## **IN SUMMARY**

- MJ use in adolescence is associated with mental health disorders, cannabis use disorder, and cognitive decline that is potentially reversible.
- Substantial epidemiologic evidence suggests some of these relationships are causal.
- New high potency THC oils, dabs, vapes, and edibles are driving up THC exposure and changing the clinical picture, probably increasing the risk for psychosis.
- American Acad Peds recommends counseling all adolescents: ‘Non-use is best for health.’ First Episode Psychosis programs advising sibs not to use.
- ‘Medical’ marijuana in MA is not reliably tested or labeled
- Aside from pediatric epilepsy and MS, there is little rigorous data to support ANY medical claims

# Dozens of doctors, scientists warn Mass. marijuana is ripe for 'regulatory failure'

By Naomi Martin Globe Staff, May 30, 2019, 2:08 p.m.

- 
- Physicians and scientists, from every major medical school and hospital in Massachusetts, are signing onto a call for MA to regulate marijuana using a public health framework, putting public health ahead of commercial interests.
  - **Permitting cannabis use is one thing, Promoting it is another...**