# Is Cannabis Ready as Medicine?

**Jag H. Khalsa, MS, PhD**
***Current: Special Volunteer, NIDA/NIH***
Retired 10/31/2017 after 30 years as:
Chief, Medical Consequences Branch, DTMC
National Institute on Drug Abuse, NIH

2018 ASAM CONFERENCE
San Diego, CA
April 12-15, 2018

*Thanks to many colleagues and authors for sharing/ letting me borrow material from their publications*.

# *Disclosure for Jag Khalsa*

In compliance with COI policy,
ASAM requires the following disclosures to the session audience:

| | |
|---|---|
| **Shareholder** | **No relevant conflicts of interest to declare** |
| **Grant / Research Support** | **No relevant conflicts of interest to declare** |
| **Consultant** | **No relevant conflicts of interest to declare** |
| **Employee** | **No relevant conflicts of interest to declare** |
| **Paid Instructor** | **No relevant conflicts of interest to declare** |
| **Speaker bureau** | **No relevant conflicts of interest to declare** |
| **Other** | **No relevant conflicts of interest to declare** |

Presentation includes discussion of the following off-label use of a drug or MEDICINAL device: <N/A>

# *Types of Cannabis*


Sativa generally has a higher THC to CBD ratio as compared with Indica.

# Components 2

- **104+ cannabinoids**, each with their own--often complementary—pharmacology, e.g., THC, CBD, CBN, CBC, CBG etc., **have been promoted for different medical conditions**
  - **Only THC is psychoactive**
  - **Multiple extracts can be blended to form new products**
  - **Likely research targets: cancer, epilepsy, inflammation, metabolic disorder/ diabetes, psychiatric disorders, substance abuse, etc.**

- Plus non-cannabinoid active components, e.g., terpenes, flavonoids

- Can plant extracts be adequately characterized and standardized?
  - **GW have shown that they can and have been!**

## *Active chemical constituents of Cannabis:*

**Delta-9 THC (Tetrahydrocannabinol): Active psychoactive component**

**CBD (Cannabidiol)- increases some of the effects of THC and decreases other effects of THC.**

**CBN, an oxidative product of THC; some psychoactive properties (10% of THC)**

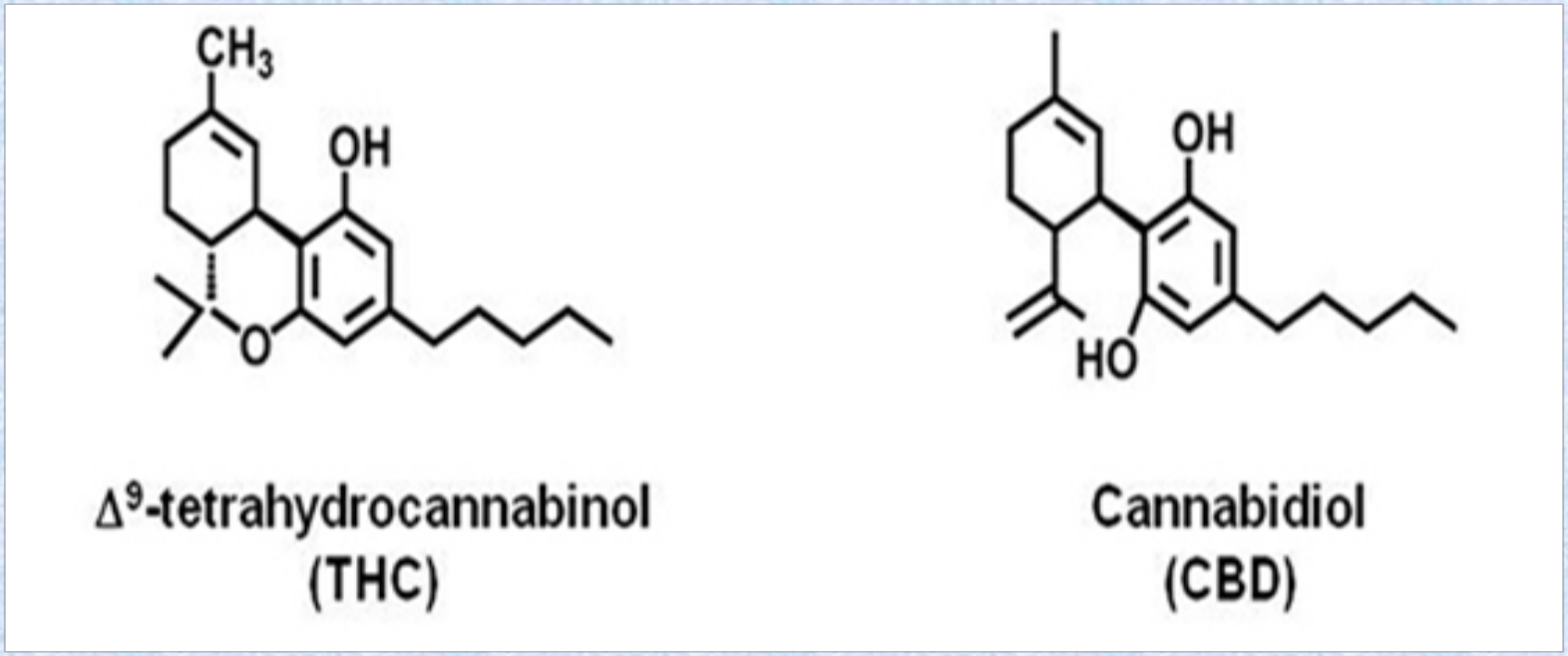
**THCV (Tetrahydrocannabivarin): found primarily in strains of African and Asian cannabis; increases the speed and intensity of THC effects, but also causes the subjective experience to end.**

**CBC (Cannabichromene), rare; is probably not psychoactive in pure form but is thought to interact with THC to enhance the subjective experience; has anti-depressive effects**

**CBL (Cannabicyclol) is a degradative product like CBN (cannabinol). Light converts CBC to CBL.**

**CBG (cannabigerol); non-psychoactive; anti-inflammatory; reduced IOP in glaucoma; antibiotic and antiplatelet clotting.**

- **Cannabinoids**



# Components of Cannabis Plant

- Cannabis plant is the unique source of cannabinoids
- Cannabis used centuries ago possessed a 1:1 CBD:THC ratio

**THC**
(tetrahydrocannabinol)

- **? analgesic, anti-spasmodic, anti-tremor, anti-inflammatory, appetite stimulant, anti-emetic**

**CBD**
(cannabidiol)

- **? anti-inflammatory, analgesic, anti-convulsant, anti-psychotic, anti-oxidant, neuroprotective**

Both compounds are in Sativex, unlike other licensed cannabinoid medicines (e.g. dronabinol, nabilone)

- **does not bind to cannabinoid receptors**
- **does bind to other receptors in the body**
- **reduces the negative effects of THC**
- **has been bred out of modern herbal cannabis!**

Single product polypharmacology

# *Approved Cannabinoid Pharmaceuticals*

- ✓ **Sativex** (GW) - Mouth spray; contains natural extract of the cannabis plant; THC+CBD (1:1 ratio);[20 countries but not US]

- ✓ **Dronabinol / Marinol (**Unimed)/Solvay; Synthetic Delta-9-THC – Approved for appetite stimulation and reducing nausea

- ✓ **Nabilone / Cesamet (**Valeant); Synthetic cannabinoid similar to THC. For Treatment of nausea and vomiting in patients undergoing cancer treatment.

# Clinical Evidence

## Anti-emetic Effects:

- **Nabilone** (*Cesamet*) approved; dose: 2-6 mg/day; approximately **15** controlled studies with ~600 patients with cancer, drug was effective (superior to other known drugs such as prochlorperazine, domperidone etc.) for treating chemotherapy-associated nausea/vomiting.
- **Dronabinol** (Marinol) (5-15 mg/m2/day) was found to be effective in **14** controlled studies involving 681 patients with cancer for treating chemotherapy-associated nausea and vomiting. However, there are significant side effects (dizziness, drowsiness, hallucinations, euphoria etc.) that have reduced their use.

## Anti-emetic Effects (contd.):

- **Smoked marijuana**: Three Canadian studies, 2 by Chang et al. 1979 and 1981; and one by Levitt et al. 1984 used smoked marijuana for anti-emetic effects.
- Was effective in 25% patients; of 20 study patients, 20% preferred smoked Mj, 30% preferred oral nabilone and 45% did not express any preference.

- The newer agents such as 5HT3 receptor antagonists are much better than cannabinoids.

## **Appetite-Stimulant Effects:**

- [741 patients; 5 controlled studies] Oral THC (**dronobinol** [***Marinol***]), 2.5-20 mg/day; --
- **As a stimulant of appetite-(FDA-for treating AIDS-anorexia); and by Canada.**
- Smoked marijuana (2.5 mg, tid) was effective in stimulating appetite in 67 HIV-infected patients without affecting viral load or immune function (CD4 counts) (Abrams et al. 2003).

- (*References for appetite stimulant effects: Iversen 2000; Beal et al. 1995 [139 pts]; Regelson et al. 1976 [54 pts]; Struwe et al. 1993 [12 pts]; Jatoi et al. 2002 [469 pts]; and Abrams et al. 2003 [67 pts]*).

## Analgesic Effects:

- 14 studies [353 pts]; oral THC, sublingual spray, or iv THC, have been tested.
- Oral THC at 10, 15 and 20 mg doses was effective, but with significant ADRs (e.g., drowsiness, confusion). The 5mg THC was ineffective as an analgesic.
- Recent data from Ware et al. (2010) in **21 patients**, a single inhalation dose of 25 mg of 9.5% THC showed positive effects on neuropathic pain. No significant effects at lower doses.
- (*References for analgesic effects: Noyes et al. 1975a, b [46 pts]; Raft et al. 1977 [10 pts]; Staquet et al. 1978a [10 pts]; 1978b [30 pts]; Jochimsen et al. 1978 [35 pts]; Jain et al. 1981 [56 pts]; Lindstrom et al. 1987 [10 pts; Holcroft et al. 1997 [1 pt]; Karst et al. 2003 [21pts]; Buggy et al. 2003 [40 women]; Neef et al. 2003 [12 pts]; Notcutt et al. 2004 [34 pts]; Berman et al. 2004 [48 pts]; Ware et al. 2010 [23 pts]*).

**Multiple Sclerosis:**

- **13 controlled studies** [total 939 pts]; smoked marijuana, hashish, oral THC in capsule, oral extracts of C. sativa in oral and sublingual spray forms containing THC, cannabidiol, or a combination of the two and oral nabilone.
- **Two clinical trials** are worthy of note: Zajicek et al. 2003 [**630 pts-15 wks**]; Wade et al. 2004; **160 pts**). Data from most studies showed **some effect on mobility and muscle spasticity compared to placebo.**

**Multiple Sclerosis (contd.):**

- **Zajicek et al**: [double blind randomized placebo controlled trial]: **206** SS on oral THC in capsule, **211** SS on oral cannabis extract [2.5 mg THC+ 1.25 mg cannabidiol, + <5% other cannabinoids/capsule], and **213** SS on placebo, for 15 wks.
- No objective effects on spasticity but **subjective improvement in spasticity was observed**; there was objective improvement in mobility and decreased hospitalizations with oral THC. ADRs were mild and tolerable. **Overall, one year f/u showed positive effects on spasticity**.

**Multiple Sclerosis (contd.):**

- **Wade et al** (2004) study [160 pts]; (**Sativex** capsules; cannabis extract [oral THC 2.5 mg + cannabidiol 2.7 mg]; total doses: 2.5-120 mg/d; 6 wks].

- **Results showed significant reduction in spasticity, sleep quality and mobility with Sativex compared to placebo.**

- ADRs were mild and well-tolerated.

## Multiple Sclerosis (contd.):

- Randomized, double-blind, parallel groups, placebo controlled study of 4 wks [n=32/group] (Rog et al. 2005) showed similar beneficial effects of Sativex [THC+CBD by oromucosal spray] on pain and sleep disturbance (spasticity).

- ADRs (dizziness, dry mouth, and somnolence] were mild]; cognitive effects were limited to long term memory storage.

## **Spinal cord injuries:**

- Only 3 studies in the literature;
- (i)-5 patients, (ii) 1 patient, (iii) 4 patients;
- oral THC or *C. sativa* extracts (THC, cannabidiol or a combination] in sublingual spray, may lead to an improvement in spasticity, muscle spasm, pain, vesicle dysfunction and sleep quality.

- (*References for Spinal cord injuries: Hanigan et al. 1986 [5 pts]; Wade et al. 2003 [4 pts]; Maurer et al. 1990 [1 pt])*.

## Gilles de la Tourette's Syndrome:

- Two randomized, double-blind, placebo controlled studies (***12 and 24 patients***), oral THC (up to 10 mg/d for 6 wks) **significantly reduced the frequency of tics.**
- ADRs –no serious ADRs (one patient dropped out due to anxiety and agitation).

- (*References for Gilles de la Tourette's syndrome: Muller-Vahl et al. 2002a [12 pts], 2003a [24 pts])*;

## **Epilepsy:**

- Several anecdotal observations suggest positive effects of cannabidiol on grand mal epilepsy.
- *One controlled RDBPC-clinical study of* ***15 patients inadequately controlled on conventional anti-epileptic meds;***
- **Group 1**: **8** patients; oral CBD at 200-300 mg/d, for 8-18 wks, in addition to their conventional meds;
- **Group 2**: **7** on placebo.
- Tx group: of the 8 pts, 4 remained convulsion-free for the duration; 3 showed clinical improvement.
- Placebo: No change
- ADRs: Drowsiness in 4 of the treated patients.
- (Cunha et al. 1980)

**Epilepsy (contd.):**

- Tzadok et al. (2016): CBD-enriched cannabis showed reduced the frequency of seizures in 89% (66/74) of the treated children with intractable epilepsy; 7% pats reported aggravation of seizures leading to CBD withdrawal.

| **% Subjects** | **Reduction in seizure activity** |
|---|---|
| 18% | 75-100% |
| 34% | 50-75% |
| 12% | 25-50% |
| 26% | <25% |

Improvement in behavior, alertness, language, communication, motor skills and sleep.

**Epilepsy (contd.):**

- Devinsky et al. (2016): Large 11 Center study (n=214)
- Open label interventional clinical trial, CBD at 2-5 mg/kg/d for 12 weeks tested in patients (1-30 yr old) with severe intractable, childhood-onset, treatment-resistant epilepsy, receiving conventional anti-epileptics.
- Median monthly frequency of seizures reduction was 36.5% over 12 wk period.

***ADRs in 79% patients***:

Somnolence, 25%; reduced appetite, 19%; diarrhea 19%;

Fatigue, 13%; convulsions, 11%; one unexpected death, status epilepticus 9%.

**Additional trials are underway**.

**Glaucoma:**

- Anecdotal reports of cannabis on intraocular pressure but only two controlled studies in the literature.
- Merritt et al. (1980), in a RDBPC study showed that one Mj cigarette containing 2% THC significantly reduced IOP.
- In another RDBPC study, Merritt et al. (1981) showed that eye drops containing 0.01, 0.05, and 0.1% THC, significantly reduced the IOP. ADRs were significant: tachycardia, palpitations, and postural hypotension.

- *(References for glaucoma: Merritt et al. 1980 [18 pts], 1981 [8 pts])*

**Parkinson Disease:**

- Only two controlled clinical trials have studied the effect of cannabinoids on Parkinson disease.
- Both clinical trials (one of 7 and another of 19 pts) did not show any beneficial effect of oral THC (nabilone) on the disease.
- (*References for Parkinson Disease: Sieradzan et al. 2001 [7 pts]; Carroll et al. 2004 [19 pts])*

**Dystonia:** Only one RDB cross-over PC- controlled study (Fox et al. 2002) of 15 patients showed no beneficial effects of oral THC (nabilone) on generalized and segmental dystonia.

- *(References for dystonia: Fox et al. 2002 [15 pts])*

## PTSD & Nabilone (Cesamet)

- Nabilone: 72% of patients experienced cessation of nightmares or reduction in nightmare intensity; subjective improvement in sleep quality & time, reduction of daytime flashbacks and night sweats. Suggesting potential benefit of nabilone in PTSD. (Fraser, GA CNS Neurosci Ther. 2009)
- Nabilone at 4.0 mg: sig improved PTSD-symptoms including insomnia, nightmares; and global assessment of function, subjective improvement in chronic pain in 104 male inmates with serious mental illness. (Cameron et al. 2014)
- A RDPC study of 15 patients: No beneficial effect on generalized segmental dystonia (Fox et al. 2002). More randomized trials are needed to confirm the efficacy of cannabis in treatment of PTSD (Wilkinson et al.)

# EFFICACY SUMMARY:

- Limited data from small clinical studies or trials show the following:
- **Nausea/Vomiting**: Oral THC (FDA-approved nabilone or dronabinol) for treating chemotherapy-associated **nausea/vomiting**.
- Oral THC shows some **appetite stimulant activity** in HIV-infected patients, but large clinical trials with oral THC or smoked marijuana are needed for FDA approval.
- Neuropathic pain: Sativex approved in Canada and other countries;
- For inflammation, MS, dystonia, Tourette's syndrome, Parkinson disease, or glaucoma:
- ***No good evidence from large clinical trial(s) that would support the use of either oral THC or smoked marijuana in clinical practice.***
- PTSD: Limited evidence to treat with cannabis
- **Well-designed RDB-placebo controlled trials are needed to obtain the FDA approval to use smoked marijuana or cannabinoids for the treatment of any of the above mentioned conditions.**

# *CONTACT*


- Jag H. KHALSA, MS, PhD
- Special Volunteer, NIDA/NIH
- National Institute on Drug Abuse, NIH
- E-mail: jag.khalsa@nih.gov

- Personal e-mail: jkhalsa@yahoo.com
- Address;
- 24924 McNair Place
- ALDIE, VA 20105
- Telephone: 703-475-6727

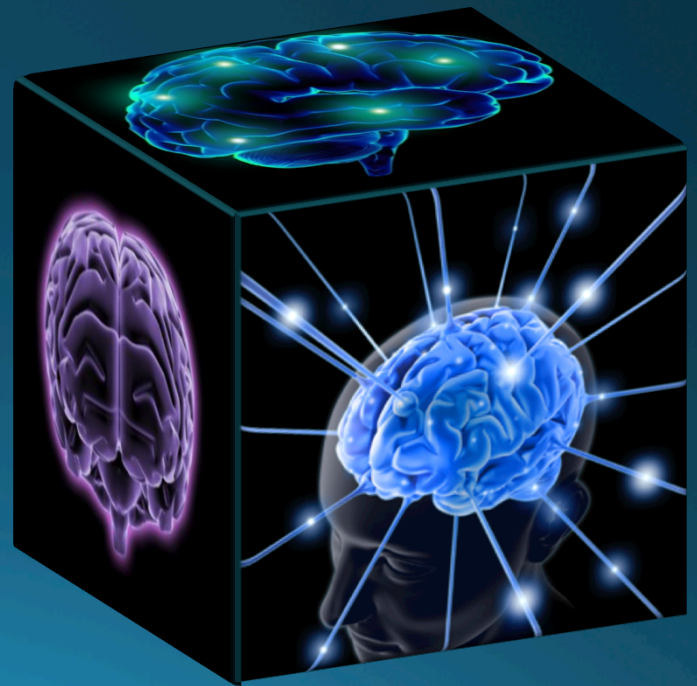
# ASAM ISAM AND CANNABIS LEGALIZATION

**GREGORY BUNT, M.D.**

Clinical Assistant Professor of Psychiatry NYU School of Medicine

Past President of the New York Society of Addiction Medicine

Immediate Past President of the International Society of Addiction Medicine



# Marijuana and Cannabinoids

Science
Myth

Legalization
Decriminalization

Possession
Sale

Medical Marijuana
Recreational Marijuana

Clinical Issues
Policy and Regulatory

Models:

Dutch
Colorado

California
New York

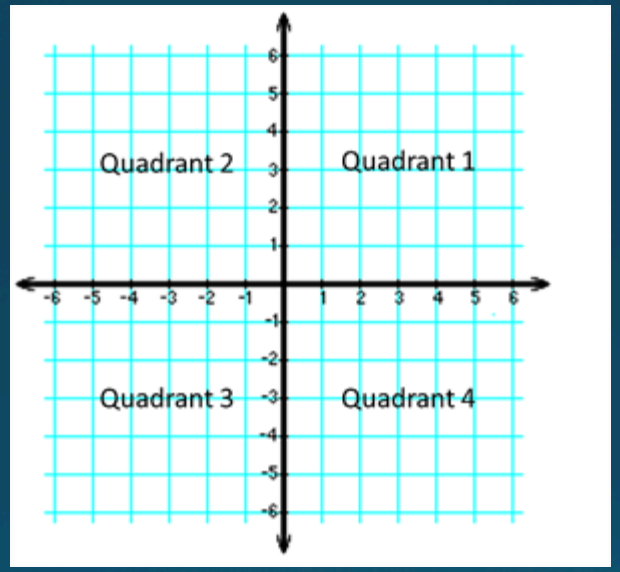
# Definitions

- **Legalization** Regulated market - supply is permitted, possession is allowed
- **Decriminalization** Supply is not permitted, possession will still be punished, but with minor penalty
- **Medicinal use** - Under supervision (?!) of doctor or similar
- **Recreational use** - No supervision

Regulated Deregulated

Recreational

Medical



# HARMFUL EFFECTS OF MARIJUANA

as an addictive substance

as a toxic substance

as  an intoxicating substance

as a gateway drug

**Addictive Potential**

Initiate after age 18-9% eventually satisfy DSM criteria of dependence

Initiate before age 18-17% become addicted within 2 years of use

With daily use-estimate 35-40% rate of cannabis dependency

**Adolescents**

impaired neural connectivity fewer fibers

in hippocampus and prefrontal cortex

increased sensitivity to drugs (more likely to develop cannabis dependency and use other drugs)

daily pot for 3 yrs in adolescence-tested in 20's after abstinent for 2 yrs- had abnormal shape to hippocampus and memory deficits

**Adverse Health Effects of Marijuana Use**

Nora D. Volkow, M.D., Ruben D. Baler, Ph.D., Wilson M. Compton, M.D., and Susan R.B. Weiss, Ph.D.

N Engl J Med 2014; 370:2219-2227June 5, 2014DOI: 10.1056/NEJMra1402309

***State of the Science of Cannabis Research: Update from the NIH Marijuana Summit*** **Susan R.B. Weiss, PhD**

**Director Division of Extramural Research May 20, 2016**

**Policy Research: The Details Matter *Different models of legalization*: advertising, involvement of big business, medical vs. recreational, pricing, taxes, dispensaries, edible products, potency restrictions** ***Why research is not definitive on the effects of MJ policy… Source: Pacula, March 2016***

***Much of the research ignores important policy heterogeneity. It also ignores how laws were implemented - how they have changed over time the lack of attention to specificity and timing***

The NEW ENGLAND JOURNAL of MEDICINE

REVIEW ARTICLE

Dan L. Longo, M.D., *Editor*

# Adverse Health Effects of Marijuana Use

Nora D. Volkow, M.D., Ruben D. Baler, Ph.D., Wilson M. Compton, M.D., and Susan R.B. Weiss, Ph.D.

IN LIGHT OF THE RAPIDLY SHIFTING LANDSCAPE REGARDING THE LEGALIZATION of marijuana for medical and recreational purposes, patients may be more likely to ask physicians about its potential adverse and beneficial effects on health. The popular notion seems to be that marijuana is a harmless pleasure, access to which should not be regulated or considered illegal. Currently, marijuana is the most commonly used "illicit" drug in the United States, with about 12% of people 12 years of age or older reporting use in the past year and particularly high rates of use among young people.[1] The most common route of administration is inhalation. The greenish-gray shredded leaves and flowers of the *Cannabis sativa* plant are smoked (along with stems and seeds) in cigarettes, cigars, pipes, water pipes, or "blunts" (marijuana rolled in the tobacco-leaf wrapper from a cigar). Hashish is a related product created from the resin of marijuana flowers and is usually smoked (by itself or in a mixture with tobacco) but can be ingested orally. Marijuana can also be used to brew tea, and its oil-based extract can be mixed into food products.

The regular use of marijuana during adolescence is of particular concern, since use by this age group is associated with an increased likelihood of deleterious consequences[2] (Table 1). Although multiple studies have reported detrimental effects, others have not, and the question of whether marijuana is harmful remains the subject of heated debate. Here we review the current state of the science related to the adverse health effects of the recreational use of marijuana, focusing on those areas for which the evidence is strongest.

From the National Institute on Drug Abuse, National Institutes of Health, Bethesda, MD. Address reprint requests to Dr. Volkow at the National Institute on Drug Abuse, 6001 Executive Blvd., Rm. 5274, Bethesda, MD 20892, or at nvolkow@nida.nih.gov.

N Engl J Med 2014;370:2219-27.
DOI: 10.1056/NEJMra1402309


## ADVERSE EFFECTS

### RISK OF ADDICTION

Despite some contentious discussions regarding the addictiveness of marijuana, the evidence clearly indicates that long-term marijuana use can lead to addiction. Indeed, approximately 9% of those who experiment with marijuana will become addicted[3] (according to the criteria for dependence in the *Diagnostic and Statistical Manual of Mental Disorders*, 4th edition [DSM-IV]). The number goes up to about 1 in 6 among those who start using marijuana as teenagers and to 25 to 50% among those who smoke marijuana daily.[4] According to the 2012 National Survey on Drug Use and Health, an estimated 2.7 million people 12 years of age and older met the DSM-IV criteria for dependence on marijuana, and 5.1 million people met the criteria for dependence on any illicit drug[1] (8.6 million met the criteria for dependence on alcohol[1]). There is also recognition of a bona fide cannabis withdrawal syndrome[5] (with symptoms that include irritability, sleeping difficulties, dysphoria, craving, and anxiety), which makes cessation difficult and contributes to relapse. Marijuana use by adolescents is particularly troublesome. Adolescents' increased vulnerability to adverse long-term outcomes from marijuana use is probably related

## EXPOSURE

Smoking cannabis during pregnancy is linked to lower birth weight in the offspring.

The relationship between smoking cannabis during pregnancy and other pregnancy and childhood outcomes is unclear.

## PROBLEM CANNABIS USE

Greater frequency of cannabis use increases the likelihood of developing problem cannabis use.

Initiating cannabis use at a younger age increases the likelihood of developing problem cannabis use.

## CANNABIS USE AND ABUSE OF OTHER SUBSTANCES

Cannabis use is likely to increase the risk for developing substance dependence (other than cannabis use disorder).

TO READ THE FULL REPORT AND VIEW RELATED RESOURCES, PLEASE VISIT

**NATIONALACADEMIES.ORG/CANNABISHEALTHEFFECTS**

A limited number of studies suggest that there are impairments in cognitive domains of learning, memory, and attention in individuals who have stopped smoking cannabis.

Cannabis use during adolescence is related to impairments in subsequent academic achievement and education, employment and income, and social relationships and social roles.

## MENTAL HEALTH

Cannabis use is likely to increase the risk of developing schizophrenia and other psychoses; the higher the use the greater the risk.

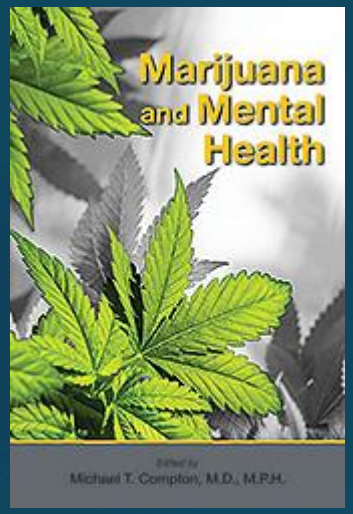
In individuals with schizophrenia and other psychoses, a history of cannabis use may be linked to better performance on learning and memory tasks.

Cannabis use does not appear to increase the likelihood of developing depression, anxiety, and posttraumatic stress disorder.

For individuals diagnosed with bipolar disorders, near daily cannabis use may be linked to greater symptoms of bipolar disorder than non-users.

Heavy cannabis users are more likely to report thoughts of suicide than non-users.

Regular cannabis use is likely to increase the risk for developing social anxiety disorder.




Edited by Michael T. Compton, M.D., M.P.H.

•2016
•272 pages
•Paperback
•Description

Even while many states have passed legislation pertaining to “medical marijuana” and others have decriminalized or even legalized recreational use, a debate continues within society as to whether marijuana is simply a harmless substance that should be fully legalized, a possibly beneficial treatment for patients with certain illnesses, or a drug with the potential to worsen addiction and cause mental health problems. It provides an academic foundation for further study while also informing clinical mental health practice as well as policy decisions by articulating the connection between marijuana and mental health, particularly in the United States.

- •The effects of marijuana on the brain and mind
- •Marijuana-related legislation
- •Medical marijuana
- •Comorbidities between marijuana misuse and mood and anxiety disorders
- •The complex link between marijuana use and psychotic disorders
- •Synthetic cannabinoids
- •Treatment and prevention of marijuana misuse

# DOHMH WARNS NEW YORKERS OF DANGERS OF "SYNTHETIC MARIJUANA" AFTER INCREASE IN EMERGENCY DEPARTMENT VISITS

**Between April 8 and April 15, more than 120 emergency** department visits related to "synthetic marijuana" were detected by DOHMH

April 17, 2015 – The Health Department today warned New Yorkers not to use synthetic cannabinoids – most commonly referred to as "synthetic marijuana" – after a significant increase in emergency department visits. Between April 8 and April 15, more than 120 emergency department visits related to synthetic cannabinoids were detected by the Health Department. During the first few months of 2015, an average of two to three synthetic-marijuana related emergency department visits occurred each day.

[cid:image004.png@01D07938.40891700]The majority of cases are in East Harlem. The median age of cases is 35 years old, and almost 90 percent of cases are male. In response to this troubling increase in emergency department visits, the Health Department will issue Commissioner's Orders to stores in East Harlem and surrounding areas to remind owners that it is illegal to sell synthetic cannabinoids in New York City.

Why are synthetic cannabinoids so dangerous?

Different brands of smoking mixtures can have very different effects, but the strength of a specific brand appears to owe more to the ratio of cannabinoids to chemically inactive plant material in the mixture, rather than the variation in the chemical structure of compounds themselves

Due to the high potency of some synthetic cannabinoids, the amount needed for each "hit" can be as little as a few tens of milligrams (about the size of a match head). The intoxicating effects of more potent brands – such as Clockwork Orange, Pandora's Box and Annihilation – can be quite overpowering

Because of the substantial risks of synthetic cannabinoids, many countries have already outlawed their production, possession and distribution.

But it is unlikely that the “war on drugs” will show any sign of relenting, given the rapidly evolving nature of the recreational drugs market and the lack of globalized drug-control legislation.

Only by working collectively can scientists, medical professionals and law makers help to stem the flow of these dangerous compounds before they pose a serious threat to health of vulnerable groups in society

Drug and Alcohol Dependence
Volume 144, 1 November 2014, Pages 12-41

Review

# Synthetic cannabinoids: Epidemiology, pharmacodynamics, and clinical implications ☆

Author links open overlay panel
Marisol S.Castaneto[ab] David A.Gorelick[c] Nathalie A.Desrosiers[ab] Rebecca L.Hartman[ab] SandrinePirard[a] Marilyn A.Huestis[a]

[a] Chemistry and Drug Metabolism, Intramural Research Program, National Institute on Drug Abuse, NIH, Baltimore, MD, United States

[b] Program in Toxicology, University of Maryland Baltimore, Baltimore, MD, United States

[c] Department of Psychiatry, University of Maryland School of Medicine, Baltimore, MD, United States

Received 6 June 2014, Revised 4 August 2014, Accepted 5 August 2014, Available online 18 August 2014

# CANNABIS RELATED MEDICATIONS


**Marinol / Dronabinol** Synthetic Delta-9 THC

**Sativex** THC (delta-9-tetrahydrocannabinol)
CBD (cannabidiol)

**Nabilone / Cesamet** Synthetic cannabinoid similar to THC

**Dexanabinol** Synthetic non-psychotropic cannabinoid that blocks NMDA receptors

**Epidiolex®** Pure plant-derived Cannabidiol (CBD)


**Rimonabant / Acomplia** Synthetic chemical that blocks endocannabinoids

•Epilepsy from Physician-Led Expanded Access Treatment Program

**GW Pharmaceuticals Announces Physician Reports of Epidiolex® Treatment Effect in Children and Young Adults with Treatment-Resistant Epilepsy from Physician-Led Expanded Access Treatment Program**

*Data show promising signals of efficacy and safety*

*Conference Call Today at 8:30 a.m. ET, 1:30 p.m. (UK)*

**GW Pharmaceuticals Announces Physician Reports of Epidiolex® Treatment Effect in Children and Young Adults with Treatment-Resistant Epilepsy from Physician-Led Expanded Access Treatment Program**

**17 June 2014**

London, UK; 17 June 2014: GW Pharmaceuticals

Sativex® is an oromucosal spray of a formulated extract of the cannabis sativa plant that contains the principal cannabinoids THC and CBD in a 50/50 ratio as well as specific minor cannabinoids and other non-cannabinoid components.

Sativex is developed to be administered as an oral spray, whereby the active ingredients are absorbed in the lining of the mouth, either under the tongue or inside the cheek.

GW's licensing partners are commercializing Sativex for MS spasticity in 16 countries outside the United States. Two additional countries have recommended approval for Sativex and regulatory filings are ongoing in 12 other countries, principally in the Middle East and Latin America where we expect approvals over the next 12 months.

# MEDICAL MARIJUANA

Nov 5, 1996: California becomes the first state to legalize medical marijuana.
1998, Nov 3: Alaska, Oregon, Washington legalize medMj

Approved Conditions: AIDS, anorexia, arthritis, cachexia, cancer, chronic pain, glaucoma, migraine, persistent muscle spasms, seizures, severe nausea, *or other chronic or persistent medical symptoms*.
Allowed Possession: 8 ounces (1oz += 28 grams)
Fee: $66, unless on Medicaid, then $33.
Note that a typical 1/8$^{th}$ ounce bag of marijuana costs about $50 on the street.
Also note that one ounce of marijuana can be used to make approximately 50 joints

Is there a currently accepted medical use?

- The drug's chemistry is known and reproducible
- There must be adequate safety studies
- There must be adequate and well-controlled studies proving efficacy
- The drug must be accepted by qualified experts
- Scientific evidence must be widely available

NEWS

The National Academies of SCIENCES • ENGINEERING • MEDICINE

# Nearly 100 Conclusions on the Health Effects of Marijuana and Cannabis-Derived Products Presented in New Report; One of the Most Comprehensive Studies of Recent Research on Health Effects of Recreational and Therapeutic Use of Cannabis and Cannabis-Derived Products

**Therapeutic Effects**

One of the therapeutic uses of cannabis and cannabinoids is to treat chronic pain in adults. The committee found evidence to support that patients who were treated with cannabis or cannabinoids were more likely to experience a significant reduction in pain symptoms. For adults with multiple sclerosis-related muscle spasms, there was substantial evidence that short-term use of certain "oral cannabinoids" – man-made, cannabinoid-based medications that are orally ingested – improved their reported symptoms. Furthermore, in adults with chemotherapy-induced nausea and vomiting, there was conclusive evidence that certain oral cannabinoids were effective in preventing and treating those ailments.

**THE NATIONAL ACADEMIES OF SCIENCES, ENGINEERING, AND MEDICINE**
Health and Medicine Division
Board on Population Health and Public Health Practice

**Committee of the Health Effects of Marijuana: An Evidence Review and Research Agenda**

Copies of ***The Health Effects of Cannabis and Cannabinoids: The Current State of Evidence and Recommendations for Research*** are available from the National Academies Press at http://www.nap.edu or by calling 1-800-624-6242

*THE NATIONAL ACADEMIES OF SCIENCES, ENGINEERING, AND MEDICINE Health and Medicine Division Board on Population Health and Public Health Practice Committee of the Health Effects of Marijuana: An Evidence Review and Research AgendaCopies of The Health Effects of Cannabis and Cannabinoids: The Current State of Evidence and Recommendations for Research are available from the National Academies Press at http://www.nap.edu or by calling 1-800-624-6242* **Nearly 100 Conclusions on the Health Effects of Marijuana and Cannabis-Derived Products Presented in New Report; One of the Most Comprehensive Studies of Recent Research on Health Effects of Recreational and Therapeutic Use of Cannabis and Cannabis-Derived Products** *One of the therapeutic uses of cannabis and cannabinoids is to treat chronic pain in adults. The committee found evidence to support that patients who were treated with cannabis or cannabinoids were more likely to experience a significant reduction in pain symptoms. For adults with multiple sclerosis-related muscle spasms, there was substantial evidence that short-term use of certain "oral cannabinoids" – man-made, cannabinoid-based medications that are orally ingested – improved their reported symptoms. Furthermore, in adults with chemotherapy-induced nausea and vomiting, there was conclusive evidence that certain oral cannabinoids were effective in preventing and treating those ailments*

***Controversial Study***

Medical cannabis laws are associated with significantly lower state-level opioid overdose mortality
Further investigation is required to determine how medical cannabis laws may interact with policies aimed preventing opioid analgesic overdose.

Bachhuber MA, Saloner B, Cunningham CO, Barry CL.
Medical Cannabis Laws and Opioid Analgesic Overdose Mortality in the United States, 1999-2010.
*JAMA Intern Med.* 2014;174(10):1668-1673.

## CANNABIS and the DEA

### Schedule I of the Controlled Substances Act

In August 2016 the DEA reaffirmed its position and refused to remove Schedule I classification.

However, the DEA announced that it will end restrictions on the supply of marijuana to researchers and drug companies that had previously only been available from the government's own facility at the University of Mississippi.

Cannabis for the Management of Pain: Assessment of Safety Study (COMPASS)

Ware MA, et al 2015

Prospective cohort study to describe safety issues among individuals with chronic, non cancer pain

# Role for Cannabis in Treatment for Opioid Addiction?

It is important to move with a deep sense of urgency to leverage the opportunity presented by increased legalization of medical marijuana to expedite the development of cannabidiol for therapeutic interventions for opioid use disorder, thus curbing the opioid epidemic," writes Yasmin L. Hurd, PhD, of the Friedman Brain Institute, Departments of Psychiatry and Neuroscience, Icahn School of Medicine at Mount Sinai, Center for Addictive Disorders, Mount Sinai Behavioral Health System, New York City.

"[The study] serves as an important foundation, along with accumulating evidence in animal models, to warrant expedited efforts for additional clinical studies to evaluate the potential therapeutic benefits of cannabidiol as a treatment for opioid use disorders," Dr Hurd writes.

## Opioid Addiction Being Treated With Medical Marijuana in Massachusetts

Hundreds of people in Massachusetts who are addicted to opioids are being treated with medical marijuana according to the Boston Herald

"We have a statewide epidemic of opioid deaths," said Dr. Gary Witman of Canna Care Docs, a network of facilities that qualifies patients into medical marijuana programs in Rhode Island, Massachusetts, Maine, Connecticut, Delaware and the District of Columbia. "As soon as we can get people off opioids to a nonaddicting substance — and medicinal marijuana is nonaddicting — I think it would dramatically impact the amount of opioid deaths."

Witman, who works in a Massachusetts Canna Care clinic, has treated about 80 patients who were addicted to opioids, anti-anxiety medication or muscle relaxers with cannabis through a one-month tapering program. More than three-quarters of patients stopped taking the harder drugs, he told the newspaper.

Witman said cannabis can be a safer alternative for managing the symptoms patients had been using opioids to treat, such as chronic pain or anxiety.

Another Massachusetts physician, Dr. Harold Altvater, said he has also successfully used medical marijuana as a substitute for other medications. "You are basically taking something that can be very harmful for an individual, and substituting it with another chemical, just like you would any other drug, that has a wider safety margin," he said. "So if the goal is to decrease the body count … the goal would be to get them on to a chemical that was safer."

Some doctors say cannabis substitution therapy needs extensive followup. "It might be an exit drug for some, or an entry drug for others," said Dr. Anil Kumar. "If you don't have a way of monitoring this patient who is saying 'give me marijuana and I will stop taking narcotics,' they may do both."

Cannabis does not kill patients (no case of death from marijuana overdose has ever been reported)

- Medical cannabis is has been shown to be effective for the treatment of chronic pain
- Neuropathy has the highest quality evidence
- Medical cannabis has a very well-tolerated side effect profile
- Medical cannabis works synergistically with opioids
- The medical community should be a pillar of education and support surrounding medical cannabis

# New York Governor Cuomo bill

He said he would sign a bill, but it had to include the following, or he would veto the bill:

1. Can not be smoked
2. Very limited conditions
3. Limited number of dispensaries
4. Careful controls: the marijuana is labeled and tested in a laboratory
5. No advisory committee: Department of health would make decisions
6. Doctors need a special permit to prescribe it and have to take a course.
7. It is a crime for a patient to lie to obtain it, and a crime for a doctor to misprescribe it

**Is Cannabidiol Legal?**

On December 14, 2016, the Drug Enforcement Administration (DEA) delivered a new ruling that classifies CBD oil as a Schedule 1 drug, making it illegal under federal law. With that said, the Rohrabacher-Farr amendment, limits the Justice Department (and DEA) from overriding state medical marijuana laws. This means that while the DEA considers cannabidiol illegal, if your state allows patient access to medical marijuana you are still able to possess cannabidiol oil (if it doesn't contain psychoactive THC). Therefore, if you wish to benefit from CBD, it's critical that you know your state's laws, partner with trusted marijuana doctors, possess a medical marijuana card and have a valid medical marijuana prescription.

Even though CBD is non-psychoactive, it's still illegal if it comes from a medical marijuana plant and you don't have a prescription. Generally, most high CBD strains are illegal and if a product contains more than around one percent THC, it's currently classed as a psychoactive Schedule 1 drug and therefore illegal.

## FDA Targets Country's Largest Cannabidiol Producer In Warning Over Cancer Claims

The U.S. Food and Drug Administration sent letters on Tuesday to four cannabis companies, warning them against making medical claims about cannabidiol (CBD). The agency also took issue with the businesses marketing CBD products as dietary supplements.

The FDA's warning letters targeted companies in California, Florida and Colorado: Natural Alchemist, Greenroads Health, That's Natural! and the Stanley Brothers, who produce CBD products under CW Botanicals and CW Hemp.

It's certainly not the first time the agency has gone after CBD producers. The FDA sent similar letters to more than a dozen companies in 2015 and 2016. But the latest warnings are notable in that they target one of the biggest players in the CBD market.

Source: Forbes

CBD Oil Reduced Toddler's Seizures. Still, Indiana CPS threatened to take away her child a Mother says

The parents of a 20-month-old girl say Indiana child welfare authorities threatened to take the child away from them because they chose to treat her epilepsy with legal CBD oil. Lelah Jerger, the child's mother, said personnel at Riley Hospital for Children at IU Health reported her to Indiana's Child Protective Services after she and her husband decided to use cannabidiol oil, or CBD, to treat their daughter Jaelah, rather than use the medication prescribed by a Riley doctor. Jerger said CPS dropped the case after a state legislator intervened and emphasized the legality of the treatment. "Our daughter was never taken away from us, but the fear was horrible to live with," Lelah Jerger said. "I would look outside my window just scared to death I would see a police officer and CPS here to take my kid."

The case raises more questions about what state officials consider to be the legal status of CBD oil — and whether medical professionals consider the substance to be a viable alternative to pharmaceuticals.

Source: IndyStar.com

National Institute on Drug Abuse
Advancing Addiction Science



# The Biology and Potential Therapeutic Effects of Cannabidiol

**June 24, 2015**
presented by Nora D. Volkow, Director, National Institute on Drug Abuse
Senate Caucus on International Narcotics Control

Drug Caucus Hearing on Barriers to Cannabidiol Research (United States Senate Caucus on International Narcotics Control)

**"Cannabidiol: Barriers to Research and Potential Medical Benefits"**

Mr. Chairman, Ms. Chairwoman, and Members of the Senate Drug Caucus, thank you for inviting the National Institute on Drug Abuse (NIDA), a component of the National Institutes of Health (NIH), to participate in this hearing to share what we know about the biology and the potential therapeutic effects of cannabidiol (CBD), one of the main active chemical compounds found in marijuana. In light of the rapidly evolving interest in the potential use of marijuana and its derivative compounds for medical purposes, it is important to take stock of what we know and do not know about the therapeutic potential of CBD.

## Background

To date, 23 states and the District of Columbia have passed laws allowing marijuana to be used for a variety of medical conditions. Fifteen additional states have enacted laws intended to allow access to CBD oil and/or high-CBD strains of marijuana. Interest in the potential therapeutic effects of CBD has been growing rapidly, partially in response to media attention surrounding the use of CBD oil in young children with intractable seizure disorders including Dravet syndrome and Lennox-Gastaut syndrome. While there are promising preliminary data, the scientific literature is currently insufficient to either prove or disprove the efficacy and safety of CBD in patients with epilepsy.[i] and further clinical evaluation is warranted. In addition to epilepsy, the therapeutic potential of CBD is currently being explored for a number of indications including anxiety disorders, substance use disorders, schizophrenia, cancer, pain, inflammatory diseases and others. My testimony will provide an overview of what the science tells us about the therapeutic potential of CBD and of the ongoing research supported by NIH in this area.

## CBD Biology and Therapeutic Rationale

CBD is one of more than 80 active cannabinoid chemicals in the marijuana plant.[ii] Unlike the main psychoactive cannabinoid in marijuana, tetrahydrocannabinol (THC), CBD does not produce euphoria or intoxication.[iii,iv,v] Cannabinoids have their effect mainly by interacting with specific receptors on cells in the brain and body: the CB1 receptor, found on neurons and glial cells in various parts of the brain, and the CB2 receptor, found mainly in the body's immune system. The euphoric effects of THC are caused by its activation of CB1 receptors. CBD has a very low affinity for these receptors (100 fold less than THC) and when it binds it produces little to no effect. There is also growing evidence that CBD acts on other brain signaling systems, and that these actions may be important contributors to its therapeutic effects.[ii]

## Preclinical and Clinical Evidence

Rigorous clinical studies are still needed to evaluate the clinical potential of CBD for specific conditions.[i] However, pre-clinical research (including both cell culture and animal models) has shown CBD to have a range of effects that may be therapeutically useful, including anti-seizure, antioxidant, neuroprotective, anti-inflammatory, analgesic, anti-tumor, anti-psychotic, and anti-anxiety properties.


According to WHO, CBD is not addictive or toxic.

**Important Findings from the WHO's CBD Report**

WHO Cannabidiol (CBD) Pre-Review Report from November 2017 says:
"To date, there is no evidence of recreational use of CBD or any public health related problems associated with the use of pure CBD."

In the report, WHO says that CBD offers medical benefits without the potential risk of addiction. The report notes: "In an animal drug discrimination model, CBD failed to substitute for THC. In humans, CBD exhibits no effects indicative of any abuse or dependence potential."

The WHO report says CBD has "been demonstrated as an effective treatment for epilepsy" in adults, children, and animals. In addition, the report indicates that there is preliminary evidence showing that CBD could be beneficial in treating many diseases including alzheimer's disease, cancer, psychosis, parkinson's disease, and other conditions.

# ASAM White Paper on State-Level Proposals to Legalize Marijuana July 25, 2012

Committee to Develop a Response to State-Level Proposals to Legalize Marijuana: Robert L. DuPont, M.D., Co-Chair Andrea G. Barthwell, M.D., Co-Chair
Mark Kraus, M.D. Kevin Sabet, Ph.D. Richard Soper, M.D.
Scott Teitelbaum, M.D.

Marijuana is not a safe and harmless substance and its use is not health-promoting (though as acknowledged by ASAM, the use of some cannabinoids prepared in a standardized manner in well-tested pharmaceutical products can alleviate specific diseases and distress in specific patients and is supportable[113]).

ASAM policy on marijuana is based on the scientific fact that marijuana is a drug with distinct effects on the brain and behavior and the fact that addiction to cannabinoids and to marijuana is a significant health problem.

In reviewing the significant role the criminal justice system plays in reducing marijuana use, ASAM recognizes that an improved link is needed between the systems of criminal justice and health care with the additional goals of reducing criminal recidivism and reducing incarceration.

ASAM opposes proposals to legalize marijuana anywhere in the United States

In summary, ASAM recommends against the approval of state initiatives to legalize marijuana. . Further, specifically focusing on state proposals to legalize marijuana, ASAM recommends:

That physicians lead efforts to oppose legislative or ballot initiatives that would result in the legalization of marijuana production, distribution, marketing, possession and use by the general public.  That public education campaigns

**ASAM Public Policy Statement**
**Marijuana, Cannabinoids and Legalization**
Adoption Date: September 21, 2015

ASAM supports the decriminalization of marijuana, which would reduce penalties for marijuana possession for personal use to civil offenses linked to contingencies, such as mandated referral to clinical assessment, educational activities, and, when indicated, formal treatment for addiction or other substance-related disorders

ASAM does not support the legalization of marijuana and recommends that jurisdictions that have not acted to legalize marijuana be most cautious and not adopt a policy of legalization until more can be learned from the natural experiments now underway in jurisdictions that have legalized marijuana.

**VULNERABLE POPULATIONS**
Adolescents
Psychiatric Disorders
Predisposition to Addictions

# ASAM Clinical Recommendations

1. **ASAM recommends that addiction medicine physicians and other clinicians educate their patients about the known medical risks of marijuana use,**
2. **ASAM recommends a significant expansion of opportunities for youth with cannabis use disorder to receive medically necessary treatment as well as for youth to receive appropriate clinical preventive services related to cannabis use, and that private and public insurance coverage be available for youth to be able to access such services.**
3. **ASAM supports the consensus of most addiction professionals that clinicians should counsel persons suffering from addiction about the need for abstinence from marijuana and synthetic cannabinoids and the role of cannabis and cannabinoid use in precipitating relapse,** even if the original drug involved in their addiction is a substance other than marijuana
4. **ASAM supports the expanded establishment of clinical entities such as Student Assistance Programs in middle schools, high schools, and post-secondary schools, including professional schools,**

## SURVEY AREAS AND DATA

1. Potential Adverse Effects

2. Cannabis and Cannabinoids – Medicinal Effects

3. Vulnerable Populations

4. Legal Sanctions

5. Public Policy – Models of Legalized “Medical” and Recreational Cannabis

6. Marijuana, Addiction Physicians and Public Policy

## Vulnerable Populations

**Do you believe smoking marijuana is harmful to adolescents?**

**Do you believe smoking marijuana is harmful for those with chronic mental illness?**

**Do you believe smoking marijuana is harmful those with a predisposition to addictions?**

**Do you believe smoking marijuana is harmful for opiate addicts in recovery?**

# MARIJUANA ISSUES IN 2018

Kevin A. Sabet, Ph.D.
President, SAM

ASAM American Society of Addiction Medicine

Kevin A. Sabet, Ph.D.
No disclosures

# SAM promotes an evidence-based approach to marijuana policy that prioritizes public health

- SAM takes an evidence-based, scientific approach to marijuana policy that **rejects the false dichotomy that we must either lock up marijuana users OR legalize pot**

- **We are non-partisan,** and work with Democrats, Republicans, and independents

- **Groups we have collaborated with** include:
  - American Society of Addiction Medicine
  - American Academy of Pediatrics
  - American Academy of Child and Adolescent Psychiatry
  - Over 30 state affiliates

SAM Smart Approaches to Marijuana
preventing another big tobacco

ASAM American Society of Addiction Medicine

# Two Organizations, One Mission

SAM Smart Approaches to Marijuana
ACTION
preventing another big tobacco

- SAM Action is dedicated to promoting healthy marijuana policies that do not legalize drugs.
- Active at all levels of national, state, and local policy-making
- Invests in and starts organizations to promote smart marijuana policies

SAM Smart Approaches to Marijuana
preventing another big tobacco

- SAM's mission is to educate citizens on the science of marijuana and to promote health-first, smart policies and attitudes that decrease marijuana use and its consequences.
- Brings light to and conducts research into marijuana's negative effects

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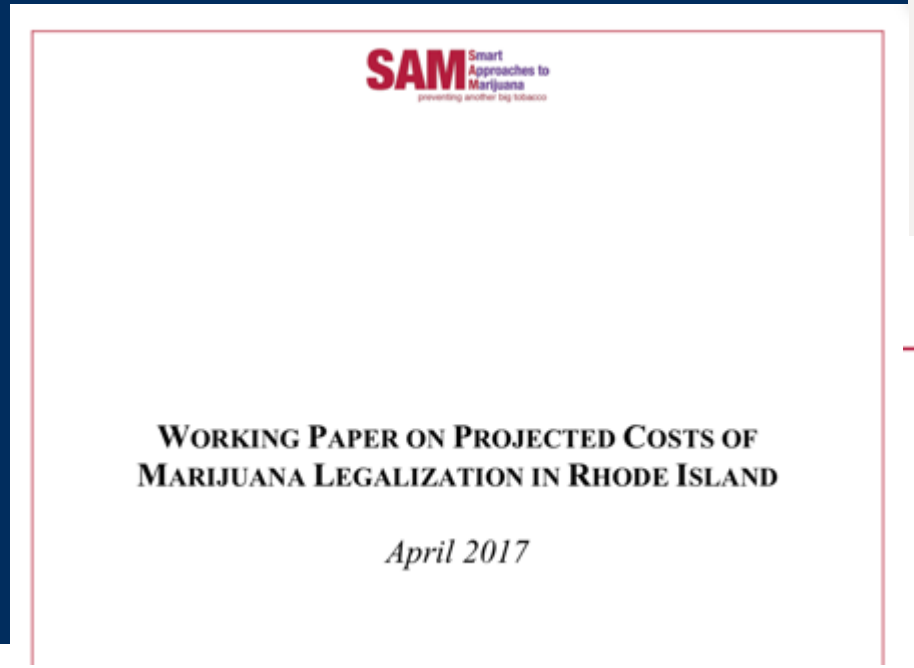
# SAM Activities

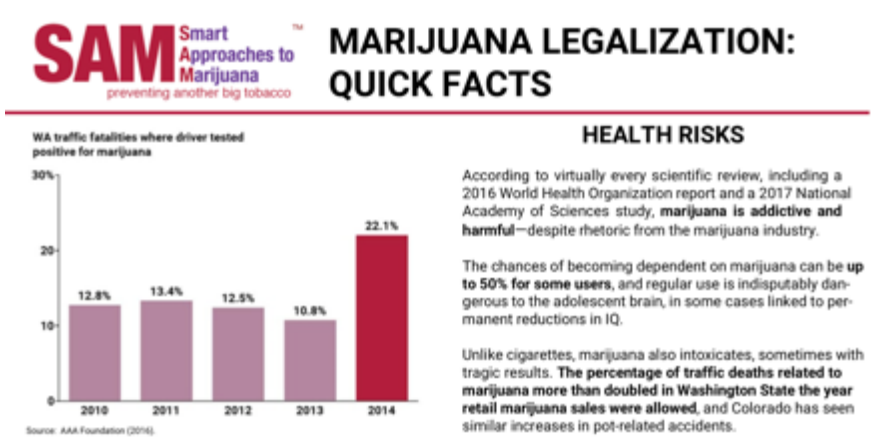
SAM Smart Approaches to Marijuana
preventing another big tobacco

**SAM Summit at NCAD Aug 19-22**
**Anaheim, CA**


SAM Smart Approaches to Marijuana
preventing another big tobacco

WORKING PAPER ON PROJECTED COSTS OF MARIJUANA LEGALIZATION IN RHODE ISLAND

*April 2017*



SAM Smart Approaches to Marijuana
preventing another big tobacco

MARIJUANA LEGALIZATION: QUICK FACTS

WA traffic fatalities where driver tested positive for marijuana



Source: AAA Foundation (2016).

HEALTH RISKS

According to virtually every scientific review, including a 2016 World Health Organization report and a 2017 National Academy of Sciences study, **marijuana is addictive and harmful**—despite rhetoric from the marijuana industry.

The chances of becoming dependent on marijuana can be **up to 50% for some users**, and regular use is indisputably dangerous to the adolescent brain, in some cases linked to permanent reductions in IQ.

Unlike cigarettes, marijuana also intoxicates, sometimes with tragic results. **The percentage of traffic deaths related to marijuana more than doubled in Washington State the year retail marijuana sales were allowed**, and Colorado has seen similar increases in pot-related accidents.

ASAM American Society of Addiction Medicine

# Our Educational Work

- SAM partnered with Communities for Alcohol- and Drug-free Youth (CADY) to create a comprehensive resource for marijuana-targeted media campaigns. **Copies available for purchase by contacting SAM.**
- SAM Website www.learnaboutsam.org also provides many resources for marijuana prevention and education.



ASAM American Society of Addiction Medicine

# High Means DUI

- High Means DUI seeks to bring light to the victims of marijuana-related traffic fatalities
- The effort also educates the public on the effects of marijuana impairment while driving



ASAM American Society of Addiction Medicine

# SAM Action Activities

SAM Smart Approaches to Marijuana
ACTION
preventing another big tobacco

**NEW FDU POLL SHOWS MAJORITY OF NEW JERSEYANS OPPOSE LEGALIZING RECREATIONAL MARIJUANA**

*"Anyone who expected legalization to happen quickly and easily might reconsider given these findings," said Krista Jenkins to the Star-Ledger, professor of political science and director of the FDU Poll.*

THE HILL

## Half of Americans support alternatives to full marijuana legalization: poll

BY JOSH DELK - 01/17/18 04:20 PM EST

## Legal weed isn't living up to all of its promises. We need to shut it down

- Legalizing marijuana not only harms public health and safety, it places a significant strain on local economies and weakens the ability of the American workforce to compete in an increasingly global marketplace.

COMMENTARY

Kevin Sabet, president of Smart Approaches to Marijuana

Published 9:17 AM ET Thu, 27 July 2017 | Updated 10:58 AM ET Mon, 31 July 2017

CNBC

## Newark Bishop Jethro James Announces Opposition to Legalization of Recreational Marijuana

January 12, 2018, 4:15 pm | in

www.nj-ramp.org

**Newark Bishop Jethro James Announces Opposition to Legalization of Recreational Marijuana**

***On MLK Day, Bishop James to Issue a Call-to-Action for Religious Leaders to Speak out Against Social Injustice of Marijuana Legalization***

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# 5 Priority States

SAM Smart Approaches to Marijuana
preventing another big tobacco

NJ Responsible Approaches to Marijuana Policy

SAM Vermont
Smart Approaches to Marijuana

Healthy & Productive Illinois
In Partnership with SAM Action


SAM Rhode Island

HEALTHY AND PRODUCTIVE michigan

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# SAM Action at the Federal Level

- Working strategically to block bills and amendments
  - Rohrabacher/Leahy amendment (medical marijuana)
  - McClintock/Polis amendment (recreational marijuana)
  - Gaetz amendment (banking)

- Educating Congress about the Cole Memo
  - 3 briefings this year already, more to come
  - New national poll shows support for DOJ action

- Advancing proactive legislation
  - High Means DUI
  - Responsible research instead of legalization

# Key Bills to Follow

- Deschedule/Reschedule Bills (H.R.1227)
- Exempt states from CSA (H.R. 975)
- Tax and regulate (H.R. 1841)
- Banking and tax breaks (H.R. 2215, H.R.1810/S.777)

- These bills will not advance through the House Judiciary Committee, but have been gaining cosponsors following the new DOJ guidance

- Most Action will occur as amendments to unrelated bills (ex: attempted Gardner Amendment to Tax Reform)

# Does the Public Support Marijuana Legalization?


ASAM American Society of Addiction Medicine

# How You Ask the Question Is Key

- Most polls pose a binary question: legalization or criminalization
- The public equates decrim and legalization
- But there is a difference
- When you introduce additional options, the polling changes significantly

# Example: Support for Legalization Dips Below 50% When Given Other Choices

**National Poll, 1000 Registered Voters, Mason Dixon, Jan 10-13, 2018**

Question: Currently, possessing and using marijuana is against federal law. Which one of the following best describes your preference on national marijuana policy?

For full legalization: 49%
Prefer some other option: 50%

| Option | Percentage |
|---|---|
| Keep the current policy: | 16% |
| Keep the current policy, but legalize the use of marijuana for physician supervised medical use: | 29% |
| Decriminalize marijuana use by removing the possibility of jail time for possession and also allowing for medical marijuana, but keep the sale of marijuana illegal: | 5% |
| Legalize the commercial production, use and sale of marijuana for recreational use, as they have done recently in several states: | 49% |

# Example: Marijuana Replacement Guidance

**National Poll, 1000 Registered Voters, Mason Dixon, Jan 10-13, 2018**

Question: Would you support or oppose enforcement of federal marijuana laws if it did not involve penalties for possession and use of small amounts of marijuana?

**Support: 50%** **Oppose: 42%** **Undecided: 8%**

# Example: Support for Legalization Drops 20 Points

**NY state poll, 600 voted in 2016 election, Emerson College (Nov 30-Dec 2, 2017)**

Question: Do you think the use of marijuana should be made legal for adults aged 21 and older?

**Yes: 60%** No: 29% Unsure: 11%

Question: Knowing that personal marijuana possession is already decriminalized and medicalized in New York, which one of the following marijuana policies do you prefer?

Keep current policy: 26%
Keep medical, repeal decriminalization: 22%
**Legalize marijuana: 40%**
Repeal both, make marijuana completely illegal: 11%

# More Polls Coming…

- Recent polls in Michigan, New Jersey and Illinois have similar results
- Polls are critical for rebutting the industry's media narrative about inevitability
- Also critical for politicians to let them know there is support

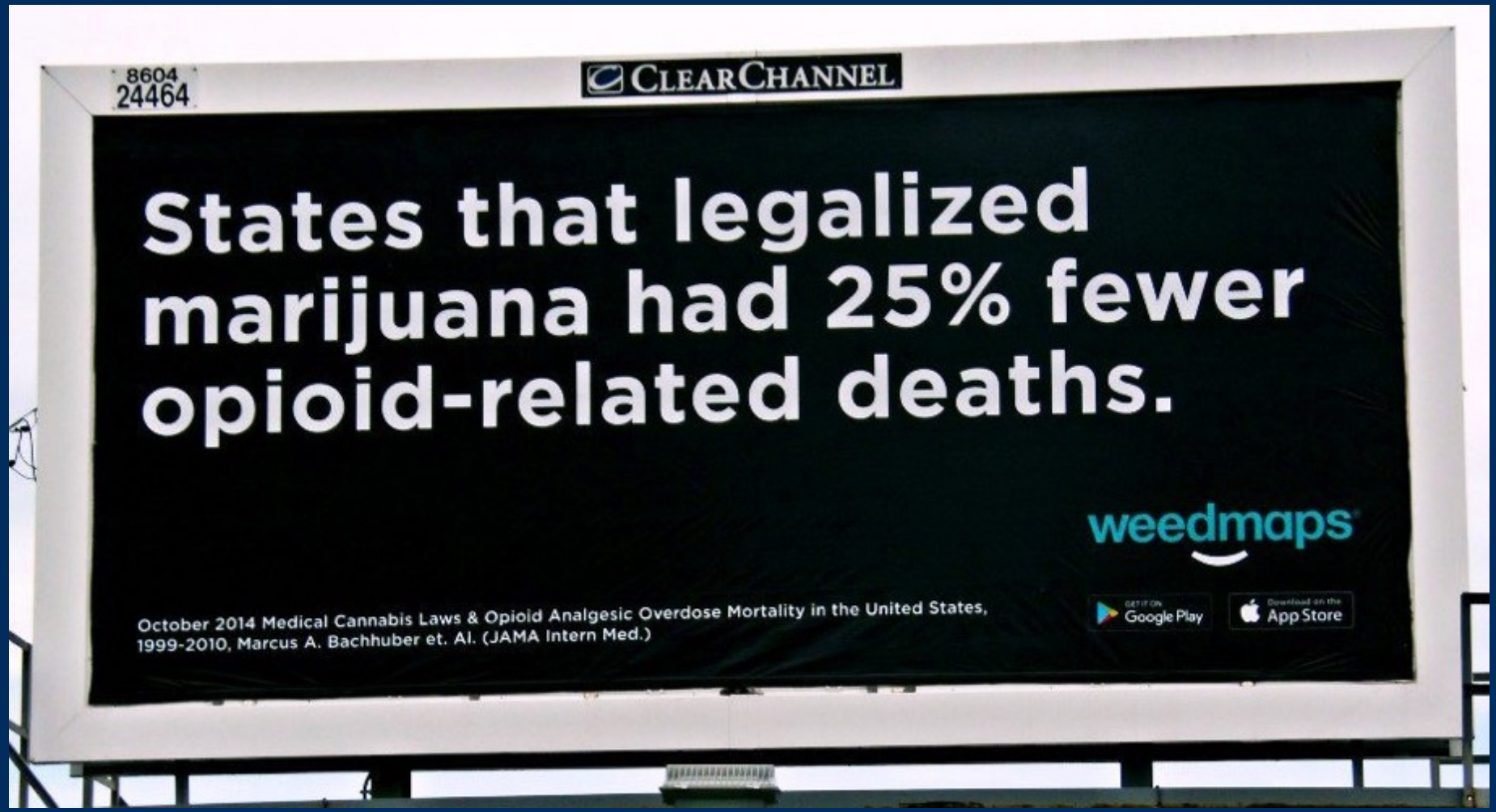
# Hot issues

# Why talk POT

# During an opiate epidemic ?

ASAM Addiction Medicine

# The Marijuana Industry Sees a Business Opportunity



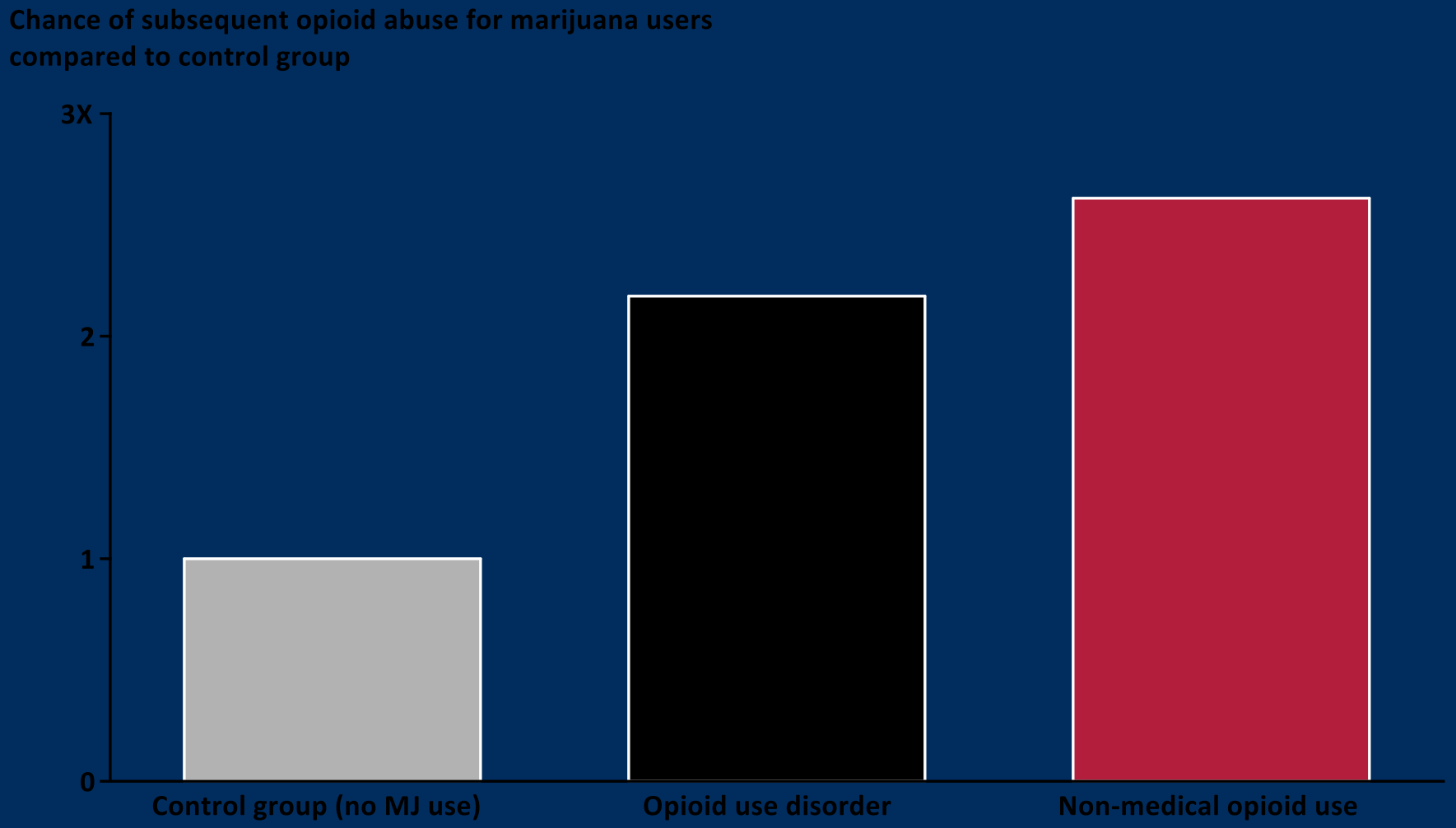

https://media.jamanetwork.com/news-item/lower-opioid-overdose-death-rates-associated-with-state-medical-marijuana-laws/

# Something doesn't add up…

*In the 2014 JAMA Study:*

- The raw data showed that medical marijuana states had **higher** rates of opioid deaths until the authors introduced four possible reasons.
- The study lumped together highly restricted states with highly permissive states.
- The study left out critical alternative explanations, like **expanded Medication Assisted Treatment programs or expanded Naltrexone use**.

# Marijuana use goes hand-in-hand with increased prescription opioid abuse



# RAND study showing < opioid deaths

**Top-Line Understanding:**

- A recent study found that before 2009, the existence of legally protected pot dispensaries in a state *correlates* with a lower number of opiate deaths in that state.
- This correlation disappears after 2009. Authors interpret this as the "post-Ogden memo era" and surmise that pot dispensaries were more strictly controlled after 2009.
- The study does not control for naloxone distribution as a reason for a reduction in opiate mortality, and it is highly dubious to assume pot shops became less widespread and more controlled after 2009. Indeed, after 2009, pot shop regulations remained extremely lax, and the number of pot shops exploded in response to the industry protections in the Ogden memo.
- Multiple studies have shown no substitution between opiates and marijuana and no reduction in opiate use by those who also use marijuana. Studies also show a higher dosing of opiates/greater likelihood of opiate abuse in patients who also use cannabis.

# How was the Cole Memo Used?

Waved at institutional investor conferences to raise capital

# The Marijuana Industry Has Exploded as a Result

JAN 3, 2017 @ 09:00 AM 56,721

Forbes

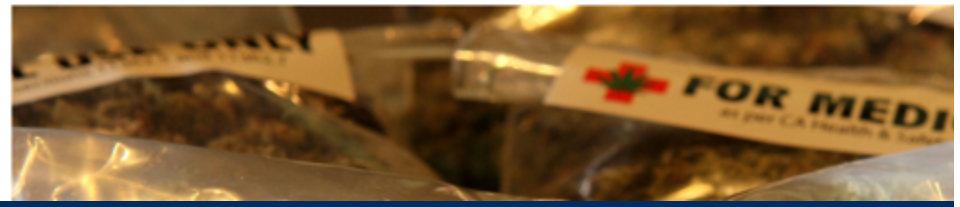
## Marijuana Sales Totaled $6.7 Billion In 2016

STAT Sections Topics Multimedia Popular STAT Plus Job Board About Us

BUSINESS

## Big-name tech investors pour millions into marijuana — both medicinal and not

By CHARLES PILLER @cpiller / AUGUST 28, 2017

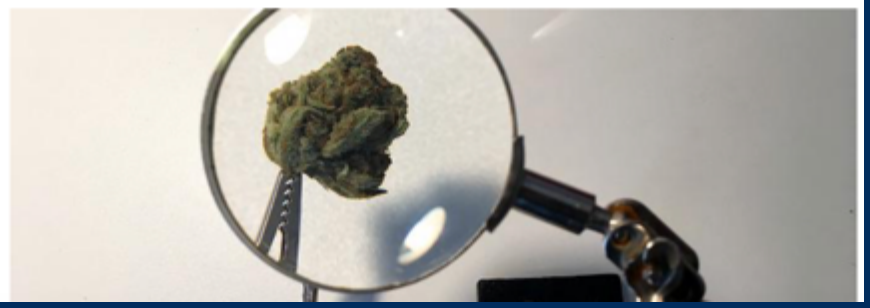



## Investing In Marijuana: Cannabis Industry Raises Hit $1.8 Billion, Up 150% Year Over Year

Javier Hasse , Benzinga Staff Writer | FOLLOW

October 16, 2017 8:41am | Comments

benzinga



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# What is the New Replacement Guidance?

Office of the Attorney General
Washington, D. C. 20530

January 4, 2018

MEMORANDUM FOR ALL UNITED STATES ATTORNEYS

FROM: Jefferson B. Sessions, III
Attorney General

SUBJECT: Marijuana Enforcement

# Does the Replacement Guidance Mean Arresting Marijuana Users?

"We have never historically seen the federal government prosecute people for small possession of marijuana. I think it's highly unlikely the federal government will be using their scarce federal resources to hone in on marijuana users."

**Brian Vicente**

**One of the primary authors of Colorado Amendment 64, legalizing pot, and co-director of the successful 'Yes on 64' campaign**

ASAM American Society of Addiction Medicine

# Many US Attorneys Have Weighed In: Priorities Will Not Change

FOR IMMEDIATE RELEASE Thursday, January 4, 2018

## U.S. Attorney Bob Troyer Issues Statement Regarding Marijuana Prosecutions in Colorado

DENVER – U.S. Attorney Bob Troyer of the District of Colorado has issued the following statement regarding marijuana prosecutions:

"Today the Attorney General rescinded the Cole Memo on marijuana prosecutions, and directed that federal marijuana prosecution decisions be governed by the same principles that have long governed all of our prosecution decisions. The United States Attorney's Office in Colorado has already been guided by these principles in marijuana prosecutions -- focusing in particular on identifying and prosecuting those who create the greatest safety threats to our communities around the state. We will, consistent with the Attorney General's latest guidance, continue to take this approach in all of our work with our law enforcement partners throughout Colorado."

U.S. Attorney Bob Troyer, District of Colorado

## U.S. Attorney Statement on Marijuana Enforcement in the District of Oregon

PORTLAND, Ore., - Billy J. Williams, United States Attorney for the District of Oregon, provided the below statement on marijuana enforcement in the District of Oregon.

"As noted by Attorney General Sessions, today's memo on marijuana enforcement directs all U.S. Attorneys to use the reasoned exercise of discretion when pursuing prosecutions related to marijuana crimes. We will continue working with our federal, state, local and tribal law enforcement partners to pursue shared public safety objectives, with an emphasis on stemming the overproduction of marijuana and the diversion of marijuana out of state, dismantling criminal organizations and thwarting violent crime in our communities."

# So What Will The New Guidance Do?

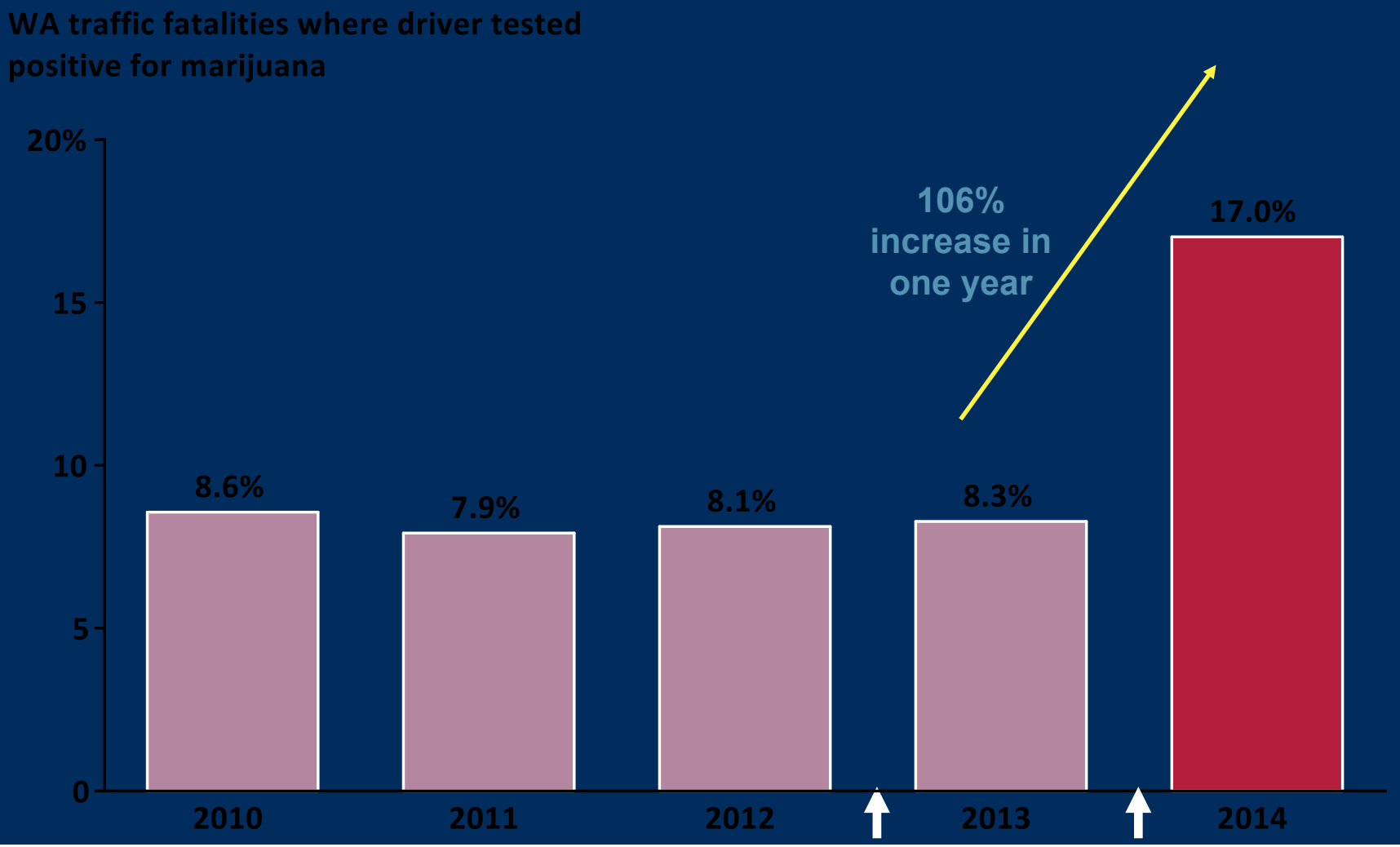
# This isn't your Woodstock Weed!


# The Industry Today


1. **Kid-friendly:** comes in shapes & colors attractive to children, like **candy and soda**
2. **Potent:** often made w/ concentrates of up to **95% pure THC** (joints are ~ 15% THC)
3. **Aggressive marketing:** free samples, billboard advertising, and other **Big Tobacco tactics**
4. **Contaminants:** In 2015, CO recalled 100s of thousands of edibles containing **banned pesticides**
5. **Fighting regulation:** The pot industry has lobbied hard against regulation (*e.g.*, warning labels, dosing rules, and bans on ads targeting kids)

- S… …siness Journal; other media…icons;

# Marijuana-related traffic fatalities in Washington State doubled after legalization

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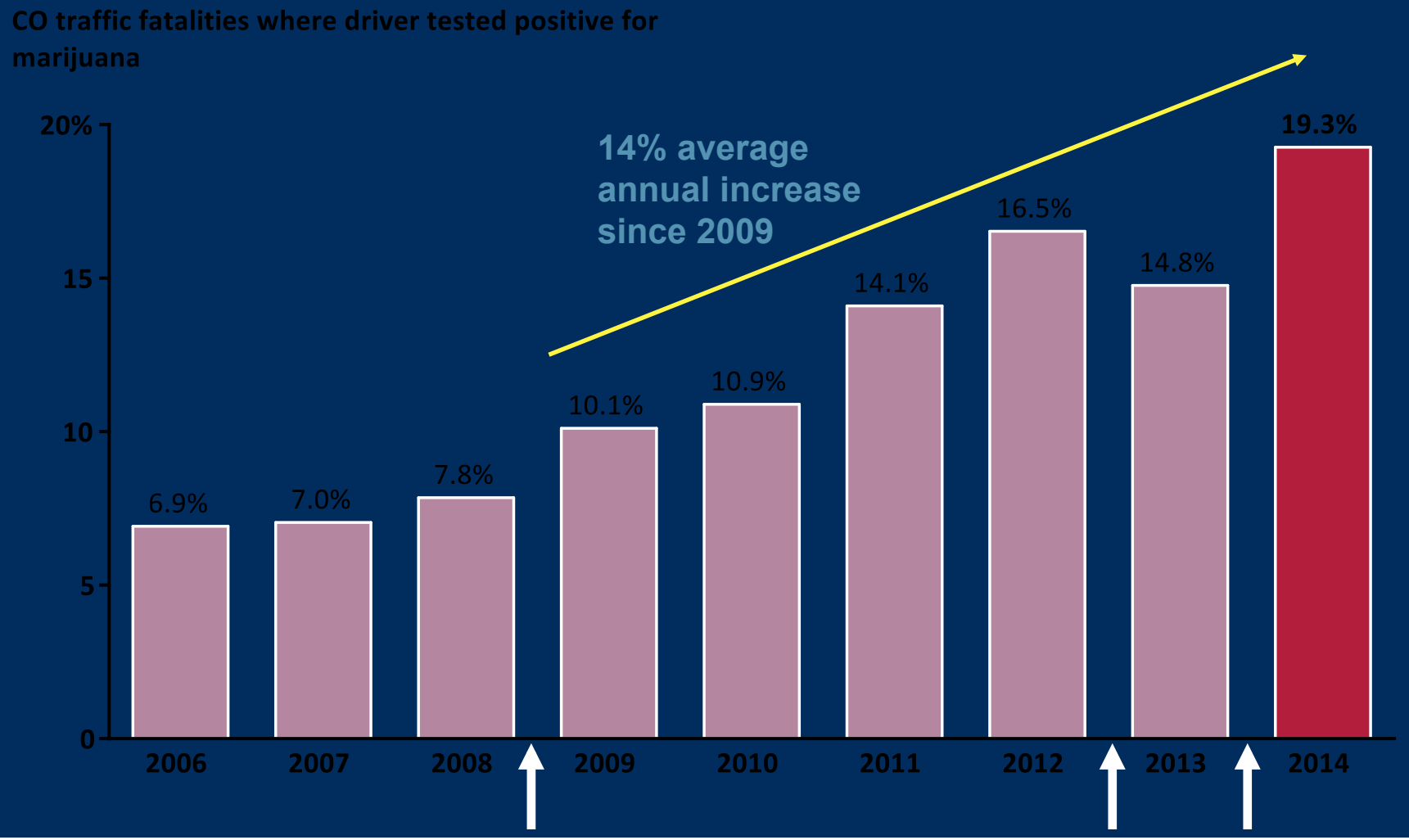
# In almost one of every five traffic fatalities in CO, the driver has been using marijuana

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# NAS: Marijuana use is also associated with other physical and mental health issues

- **Respiratory problems**, including chronic bronchitis
- Injuries & deaths from **car accidents**
- **Overdose injuries** in children
- **Low birth weight** (where pregnant mother uses)
- Impaired learning, memory, and attention (including **permanent loss of IQ** in younger heavy users)
- **Suicide**

# A final word from Volkow et al in the NEJM:

"Repeated marijuana use during adolescence may result in long-lasting changes in brain function that can jeopardize educational, professional, and social achievements.

"However, the effects of a drug (legal or illegal) on individual health are determined not only by its pharmacologic properties **but also by its availability and social acceptability.**

"In this respect, legal drugs (alcohol and tobacco) offer a sobering perspective, accounting for the greatest burden of disease associated with drugs ***not because they are more dangerous than illegal drugs*** but because their legal status allows for more widespread exposure."

# Get Involved!

Sign up for **alerts** and **news**, also **donate** to the cause at learnaboutsam.org

Grassroots organizing through SAM Action App
(text **SAM** to **797-979 or find in App Store**)

Connect with us via email at info@learnaboutsam.org
&
Follow us:
@learnaboutsam
Facebook.com/learnaboutsam

*"We were gaining momentum. But now that's flipped and we're more on the defensive." – Rep. Dina Titus (D-NV), one of the biggest marijuana supporters in Congress.*



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# SAM Action App: Available Now!


- Available free in the Apple App Store and Google Play Store
- Or text **SAM** to **797-979** right now to get a link to download

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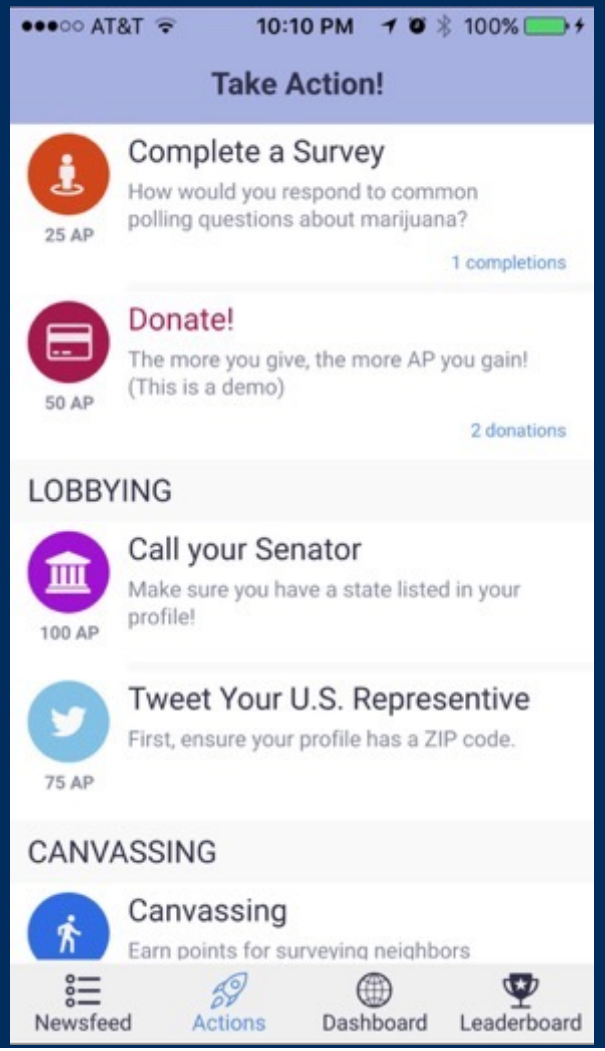
# SAM Action App




- A Powerful Tool for Organizing
- Involve Friends and Family
- Remind them to Call their Legislators within the App

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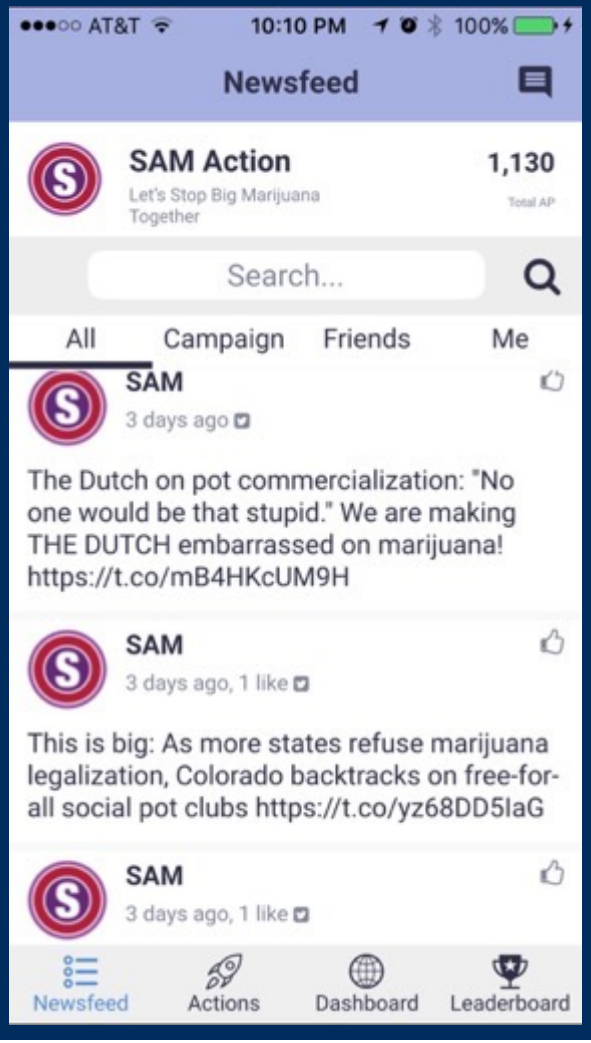
# SAM Action App: Hone Your Message




- Keep up on the latest news
- Learn field-tested messages
- Coordinate with friends to attend a town hall or council meeting

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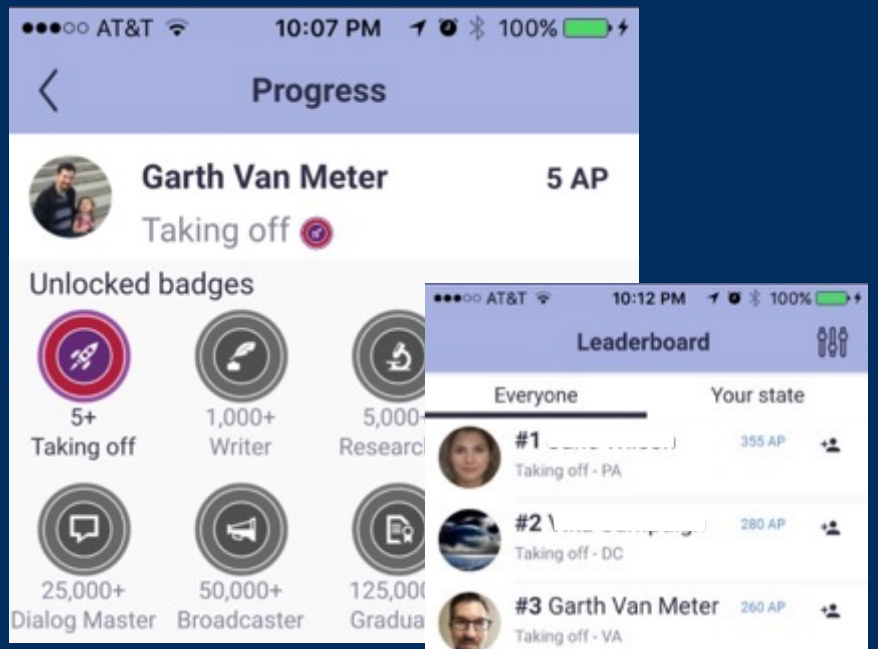
# SAM Action App: Badges




- Earn points for phone calls or adding friends in the app
- Unlock achievements
- Compete with friends on a leaderboard

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SAM Smart Approaches to Marijuana

preventing another big tobacco

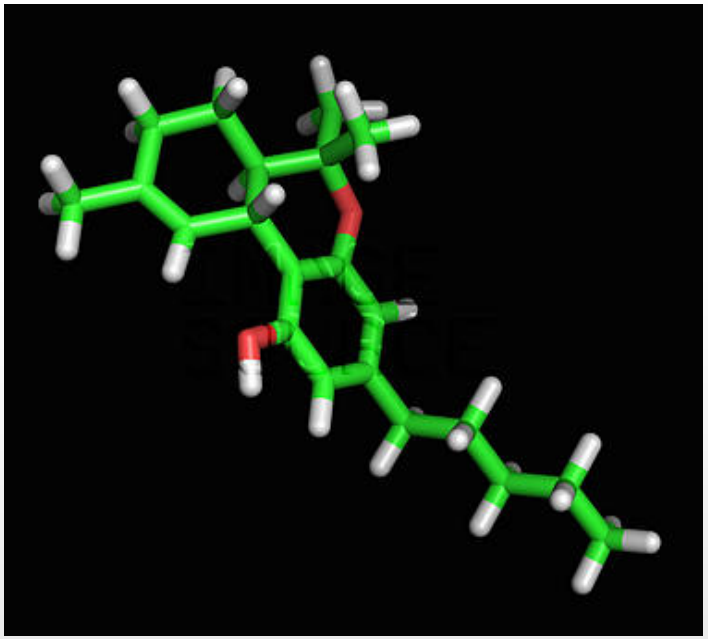
# CHANGING CANNABIS POLICY: WHAT CAN WE LEARN?

Susan R.B. Weiss, Ph.D.

April, 2018

# CANNABIS: MOST COMMONLY USED "ILLICIT" DRUG IN THE U.S.

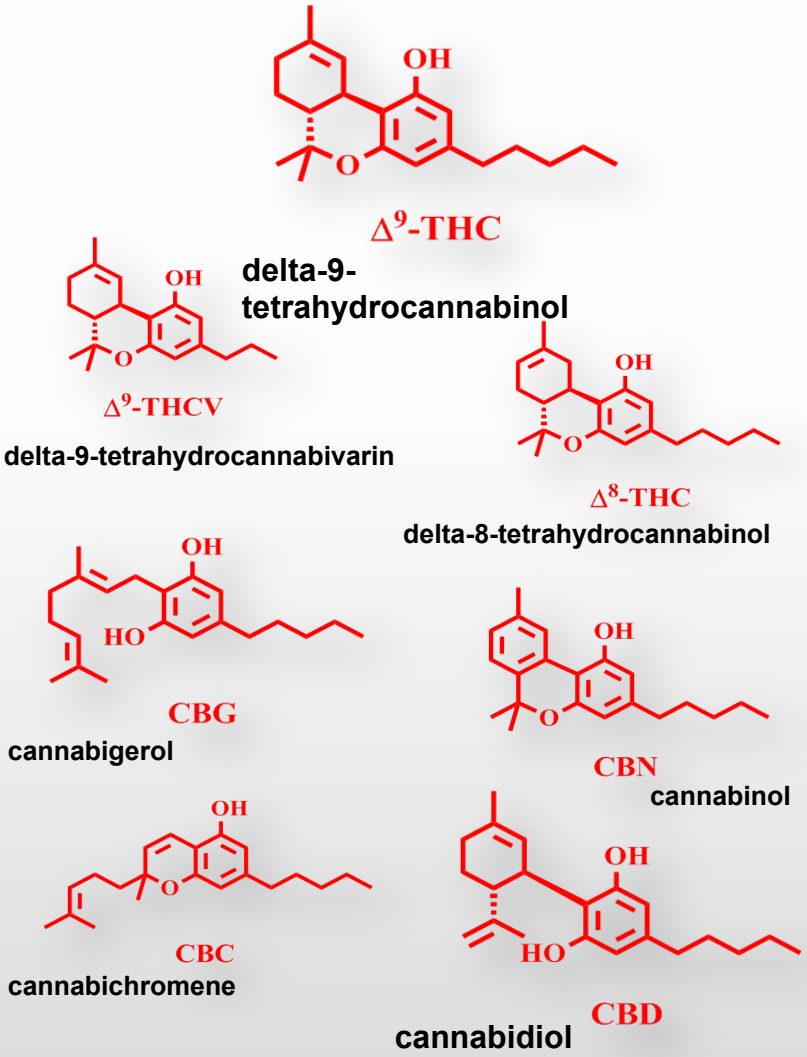
- Over 24 million Americans 12 and older were past month marijuana users.
- Approximately 4.0 million Americans met criteria for cannabis use disorders in 2015.
- An estimated 2.6 million Americans used it for the first time; 1.2 million were between the ages of 12 and 17.



**Tetrahydrocannabinol (THC)**
**Psychoactive Ingredient in Marijuana**

Source: 2017 National Survey on Drug Use and Health, SAMHSA

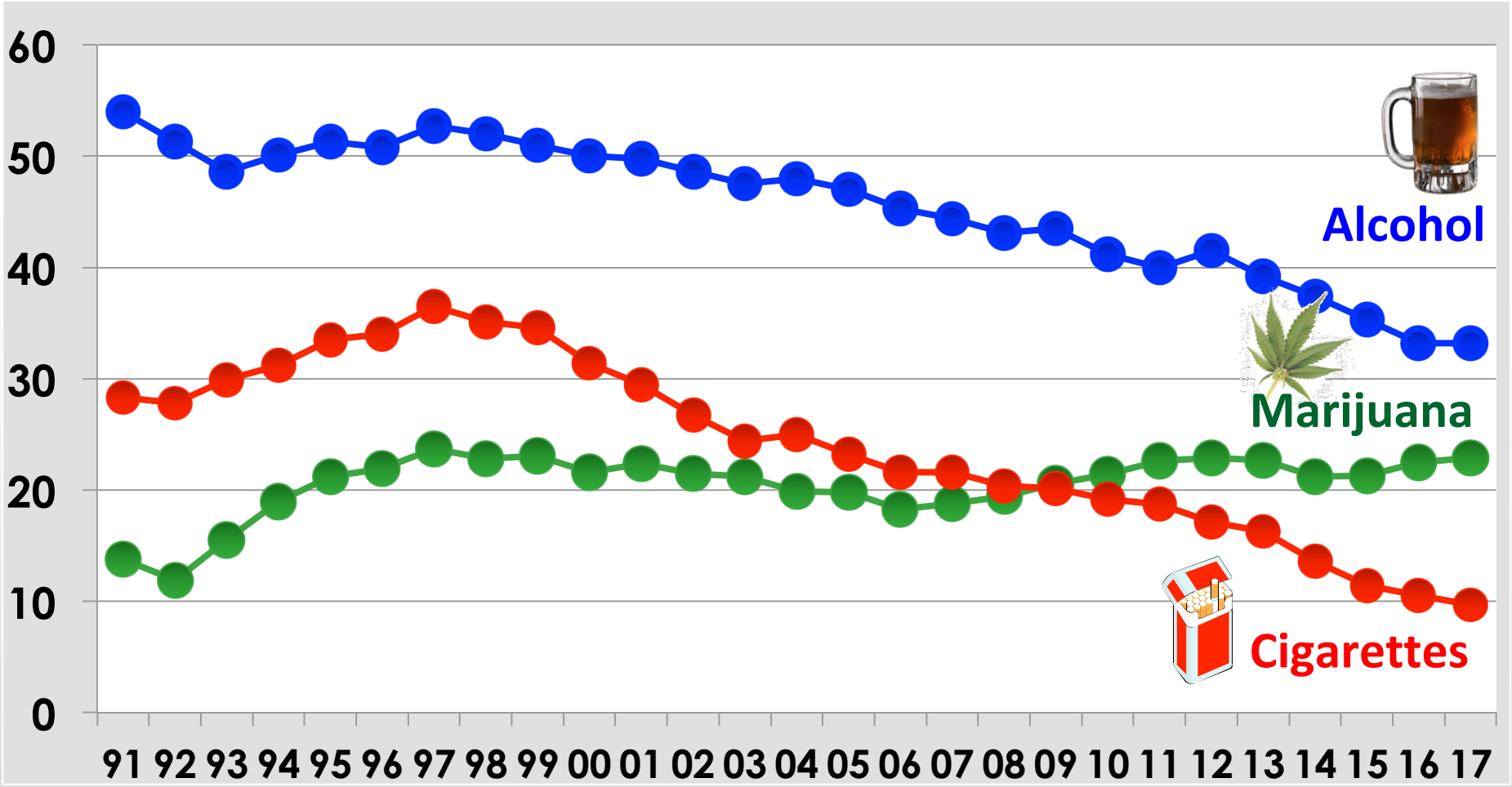
# MARIJUANA CONTAINS ~100 CANNABINOIDS PLUS OTHER CHEMICALS IN VARYING CONCENTRATIONS




- Plant with long history of use worldwide
- Illegal under Federal law (Schedule I substance—not FDA approved)
- Legal for medical use in 29 States + D.C.
- High CBD variety (or extracts) legal in 16 states for medical use
- Versions of active ingredients approved *(or in clinical trials)* for medical indications in U.S. and other countries
  - Synthetic - Marinol, Syndros, Cesamet
  - Plant Derived- Sativex (THC/CBD)
  - *Plant Derived-Epidiolex (CBD: Phase III trials)*

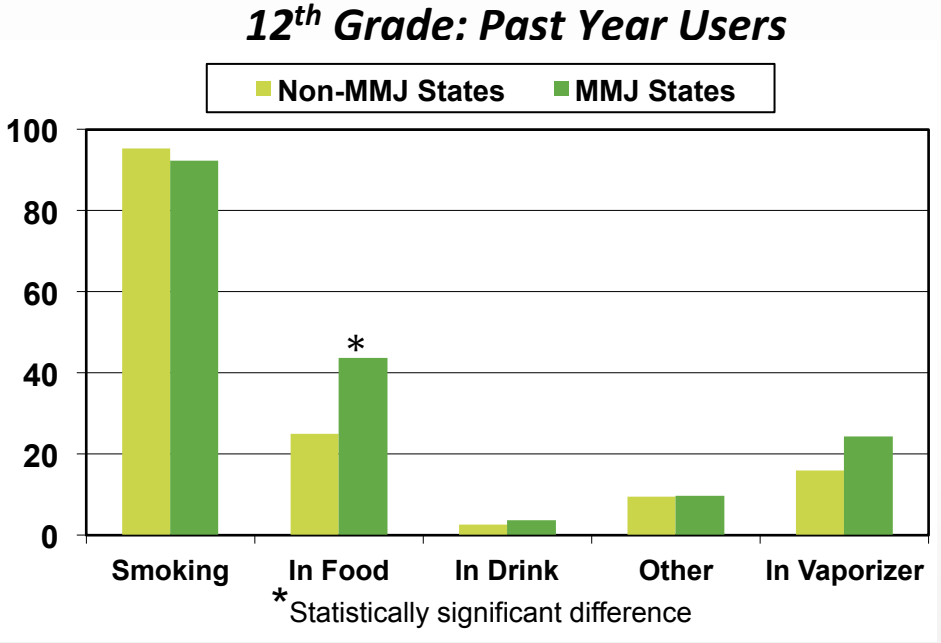
# PAST MONTH USE OF CIGARETTES, MARIJUANA, AND ALCOHOL IN 12TH GRADERS

***nearly 6% report daily use of marijuana***

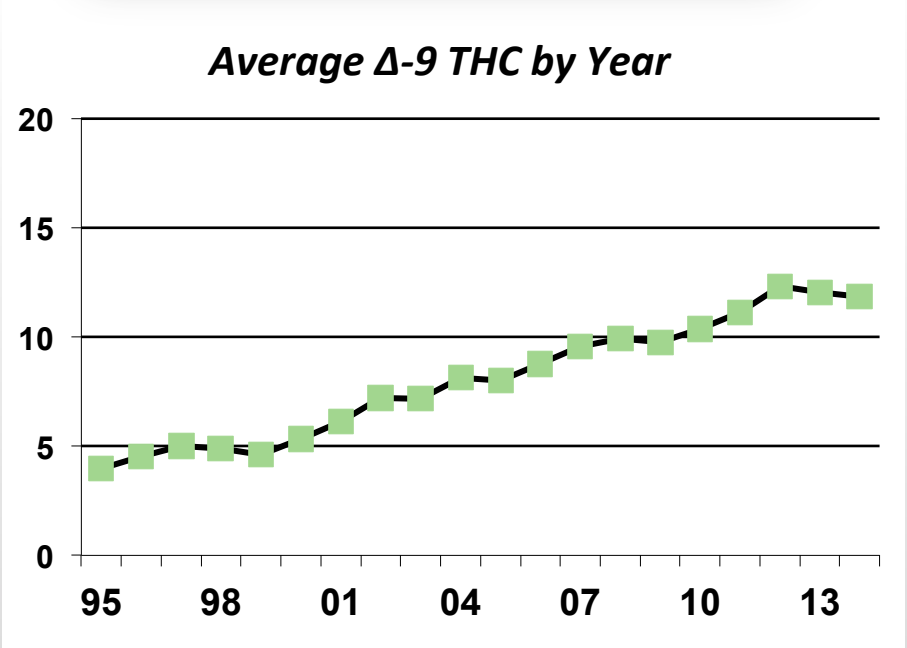



Source: University of Michigan, 2017 Monitoring the Future Study

# CHANGING LANDSCAPE: INCREASING POTENCY & NEW METHODS OF USE




SOURCE: University of Michigan, 2017
Monitoring the Future Study




SOURCE: ElSohly et al 2016; Biological Psychiatry

# CANNABIS PATTERNS AND TRENDS


**What We Know:**

- Use among youth (12-17) has not increased in recent years despite decreased perception of risk
- Use has increased in older teens and adults
- Current users use more often (daily, nearly daily) than in 2002
- Potency is increasing; plant components are changing
- Cannabis is being administered through different routes

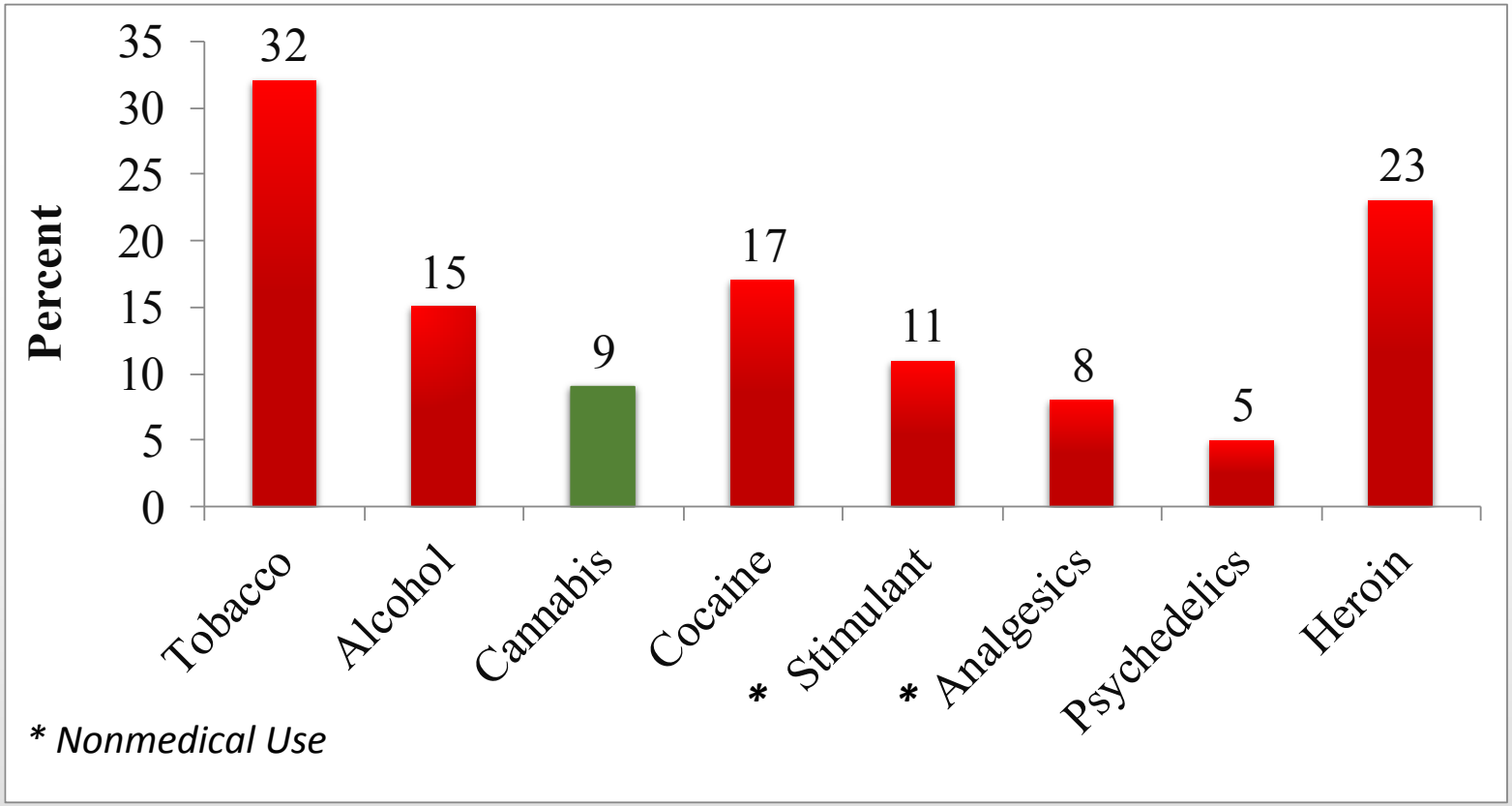
**What We Need to Know:**

- Need improved measures of frequency, dosage, patterns of use
- Persuasive Messaging (especially for youth) to counter the trend of decreasing harm perception
- Greater knowledge of the impact of changing potency, constituents, and alternative routes of administration
- Regional differences based on changing laws, policies, and social norms
- Use of other substances: complementarity vs. substitution

# ADVERSE HEALTH AND SOCIAL CONSEQUENCES OF CANNABIS USE

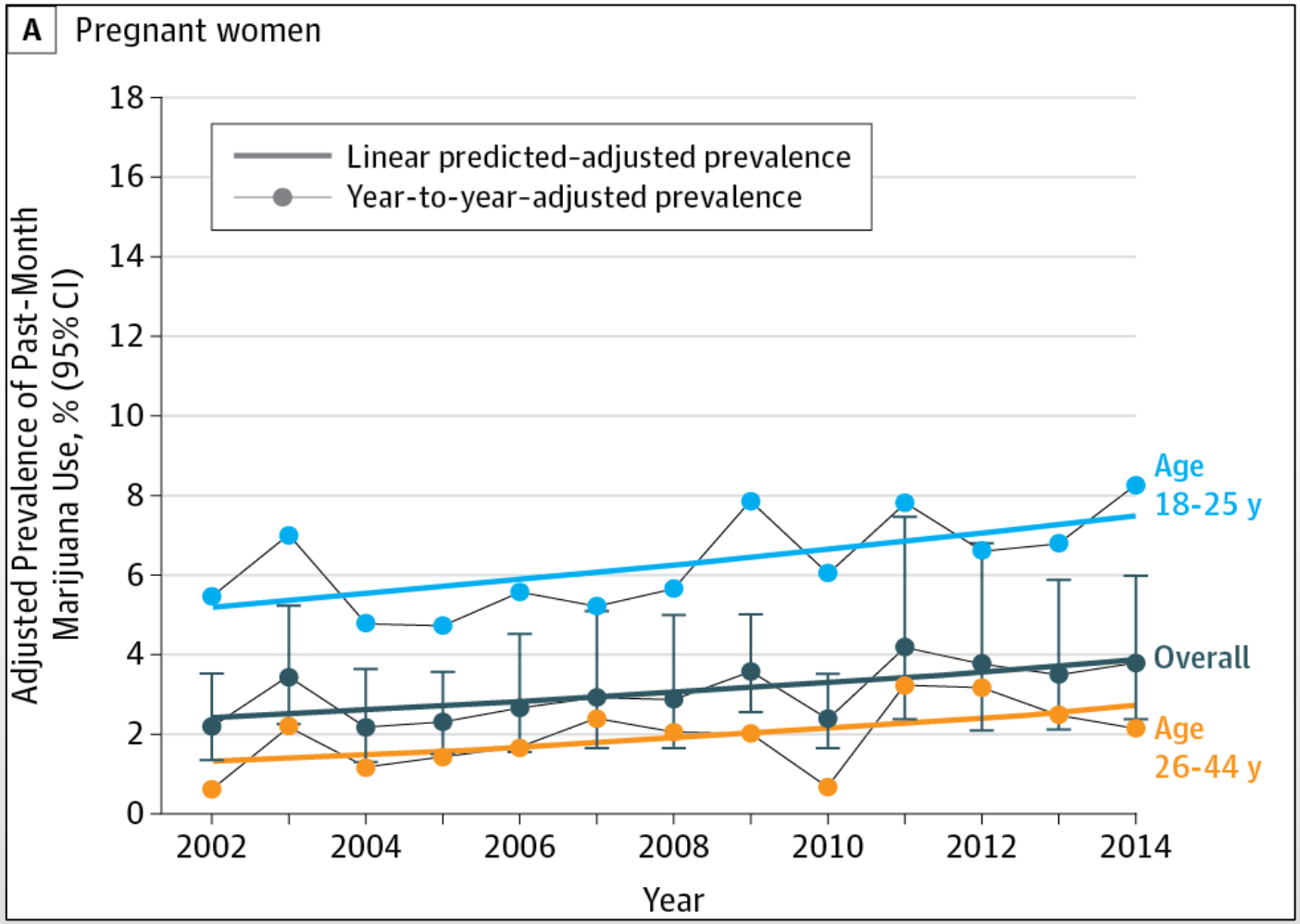
# **ADDICTION**: ABOUT 9% OF USERS BECOME DEPENDENT, 1 IN 6 WHO START USE IN ADOLESCENCE, 25-50% OF DAILY USERS

Estimated Prevalence of Dependence Among Users




Source: Anthony JC et al., 1994

# CANNABIS USE DURING PREGNANCY IS INCREASING

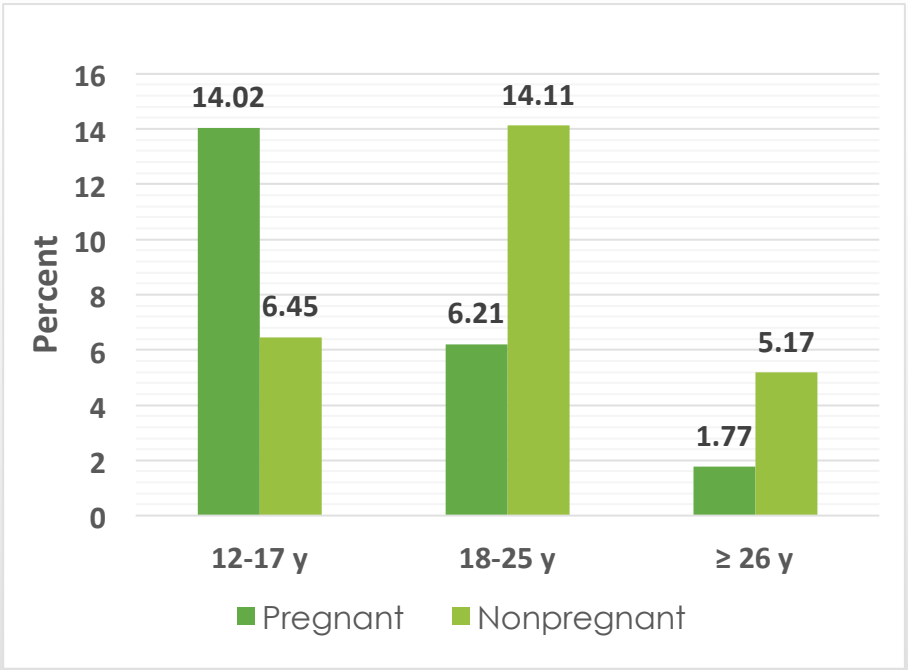



Source: Brown et al., 2017

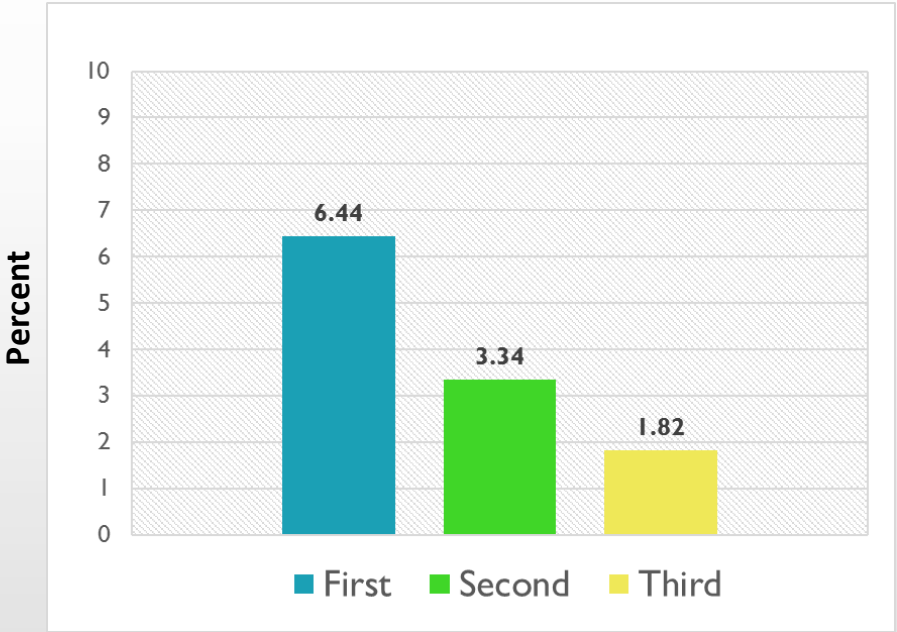
# PREGNANT TEENS REPORT HIGH PAST MONTH USE OF MARIJUANA HIGHEST RATES OF USE IN FIRST TRIMESTER

2002 to 2015 National Survey on Drug Use and Health (NSDUH)

**By Age**

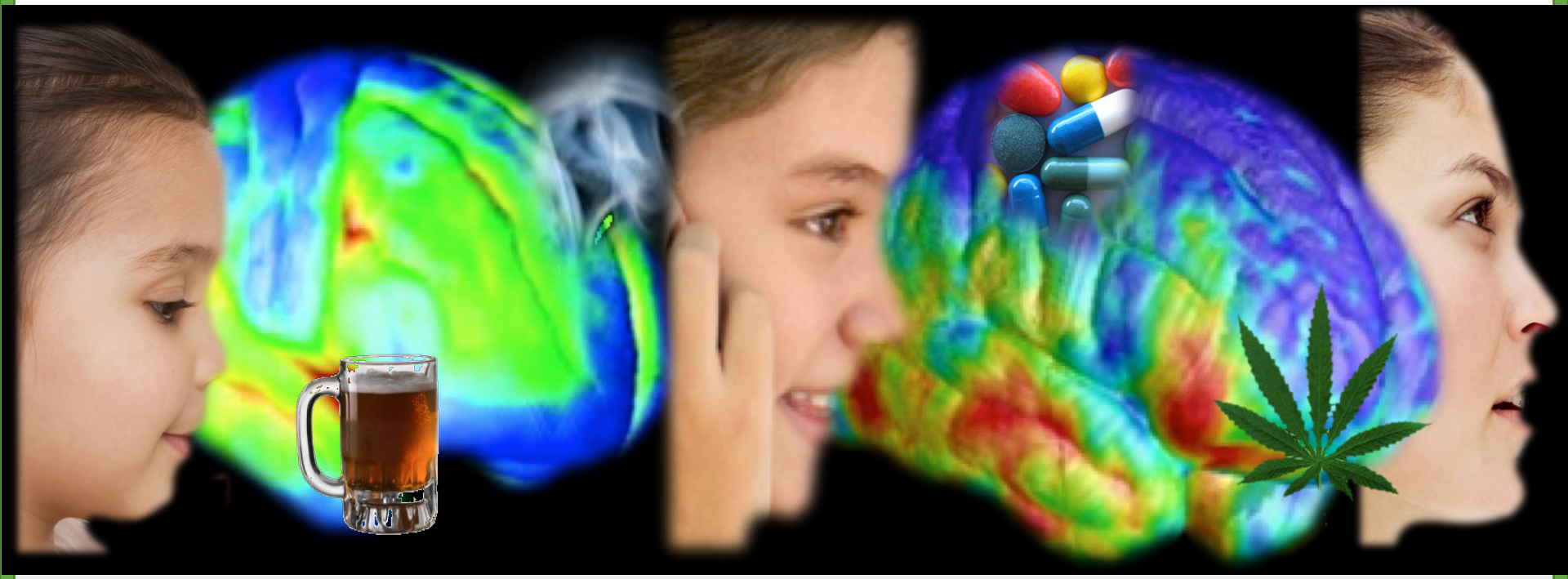



**By Trimester**




Volkow et al., Ann Intern Med. 2017; 166(10):763-764.

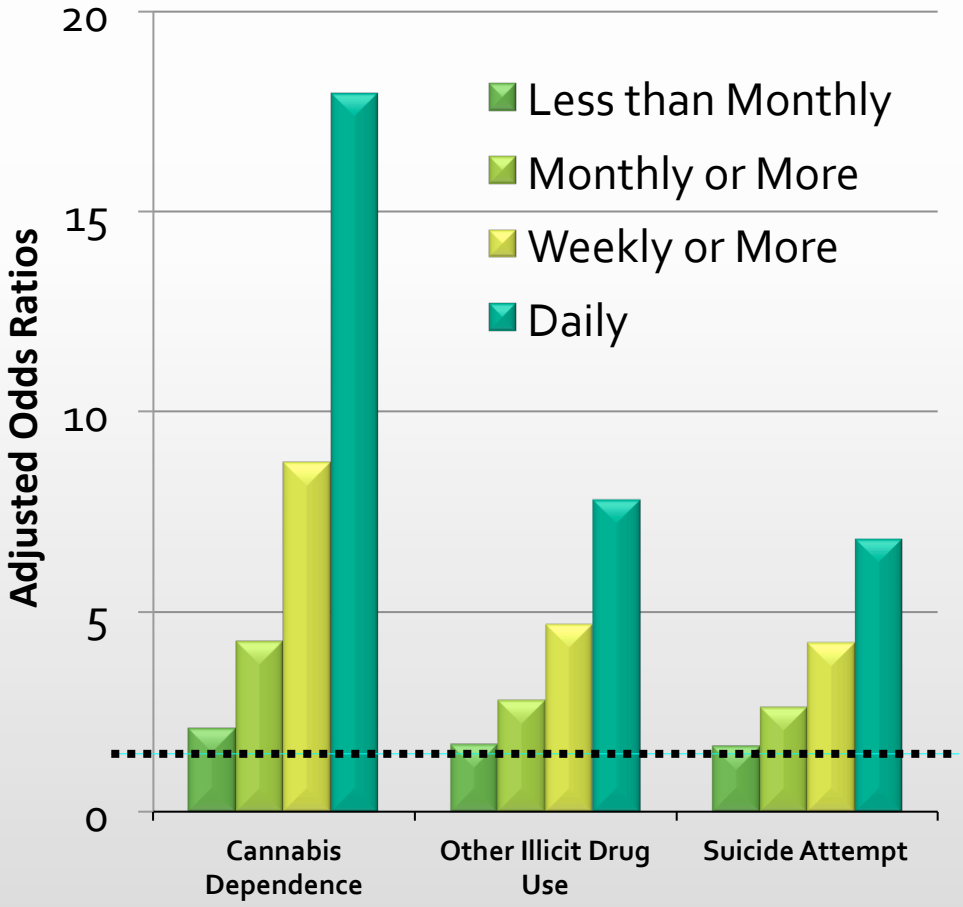
# The Brain Continues to Mature into Early Adulthood.

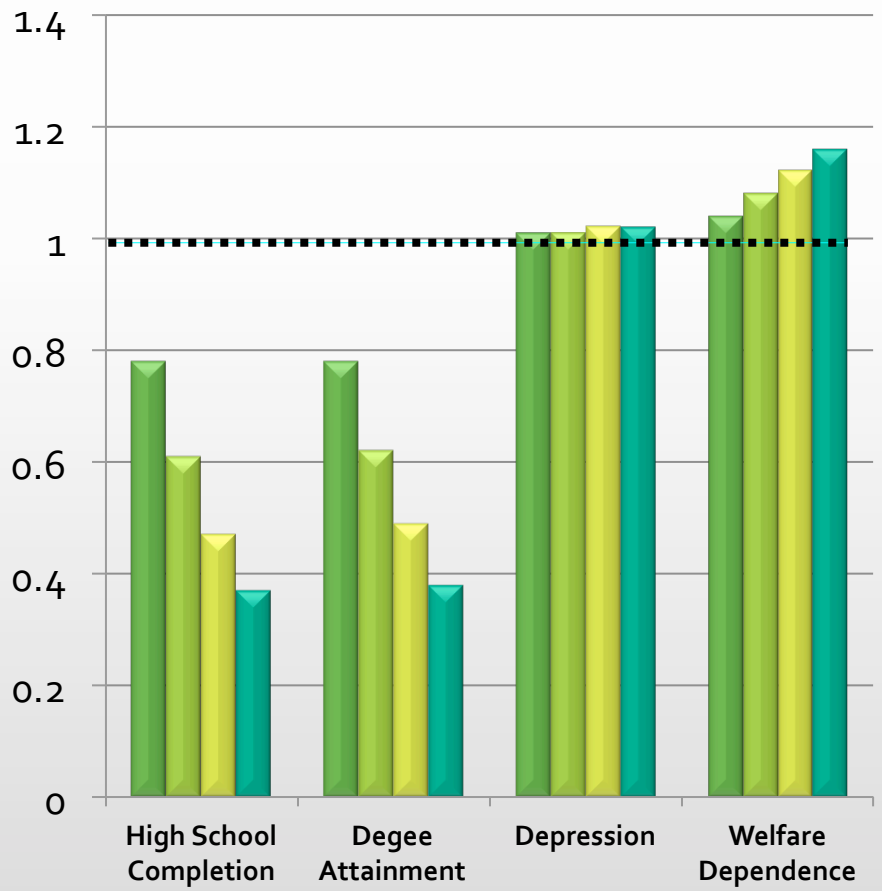


Does **Cannabis** (or other substance) exposure affect the developing brain and an individual's trajectory into adulthood?

# FREQUENCY OF CANNABIS USE BEFORE AGE 17 YEARS AND *ADVERSE OUTCOMES* (30 YEARS AGE) (N=2500-3700)

***Causation is unclear; may relate to common underlying risk factors (e.g. poverty, genetics, social environment, etc.)***



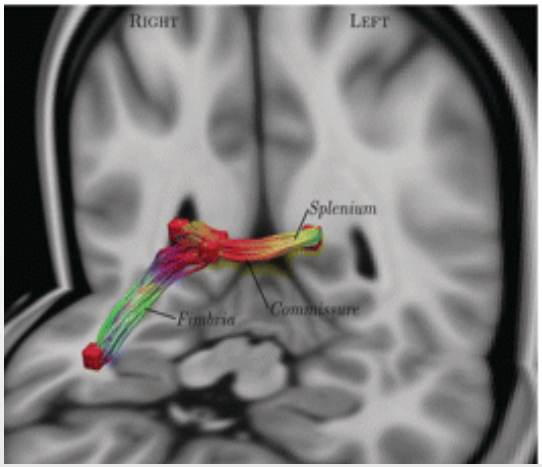




Source: Silins E et al., The Lancet September 2014

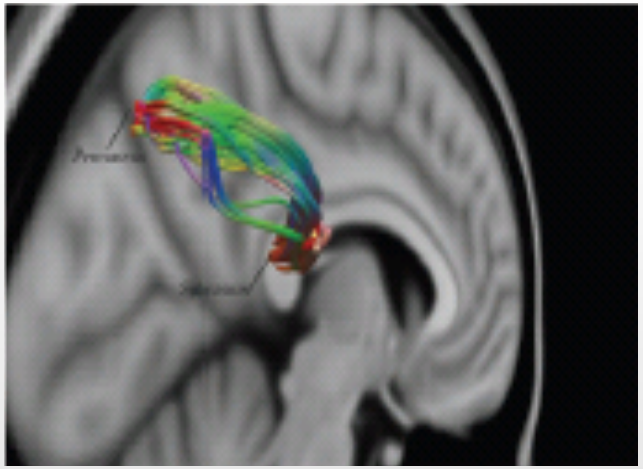
# MULTIPLE STUDIES SHOW ALTERED BRAIN STRUCTURE AND FUNCTION IN YOUTH WHO REGULARLY USE **CANNABIS**

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

Precuneus to splenium




Fimbria of hippocampus, hippocampal Commissure, and splenium

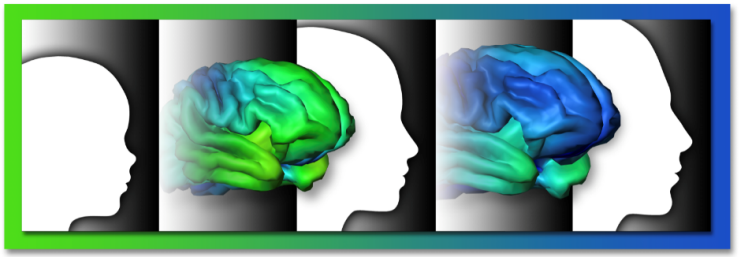


Axonal paths with reduced connectivity (measured with diffusion-weighted MRI) in cannabis users (n=59) than in controls (N=33).

Source: Zalesky et al Brain 2012

# WHAT WE NEED TO KNOW ABOUT CANNABIS AND NEURODEVELOPMENT

The precise nature of the association between cannabis use and neurodevelopment, including who is at risk.



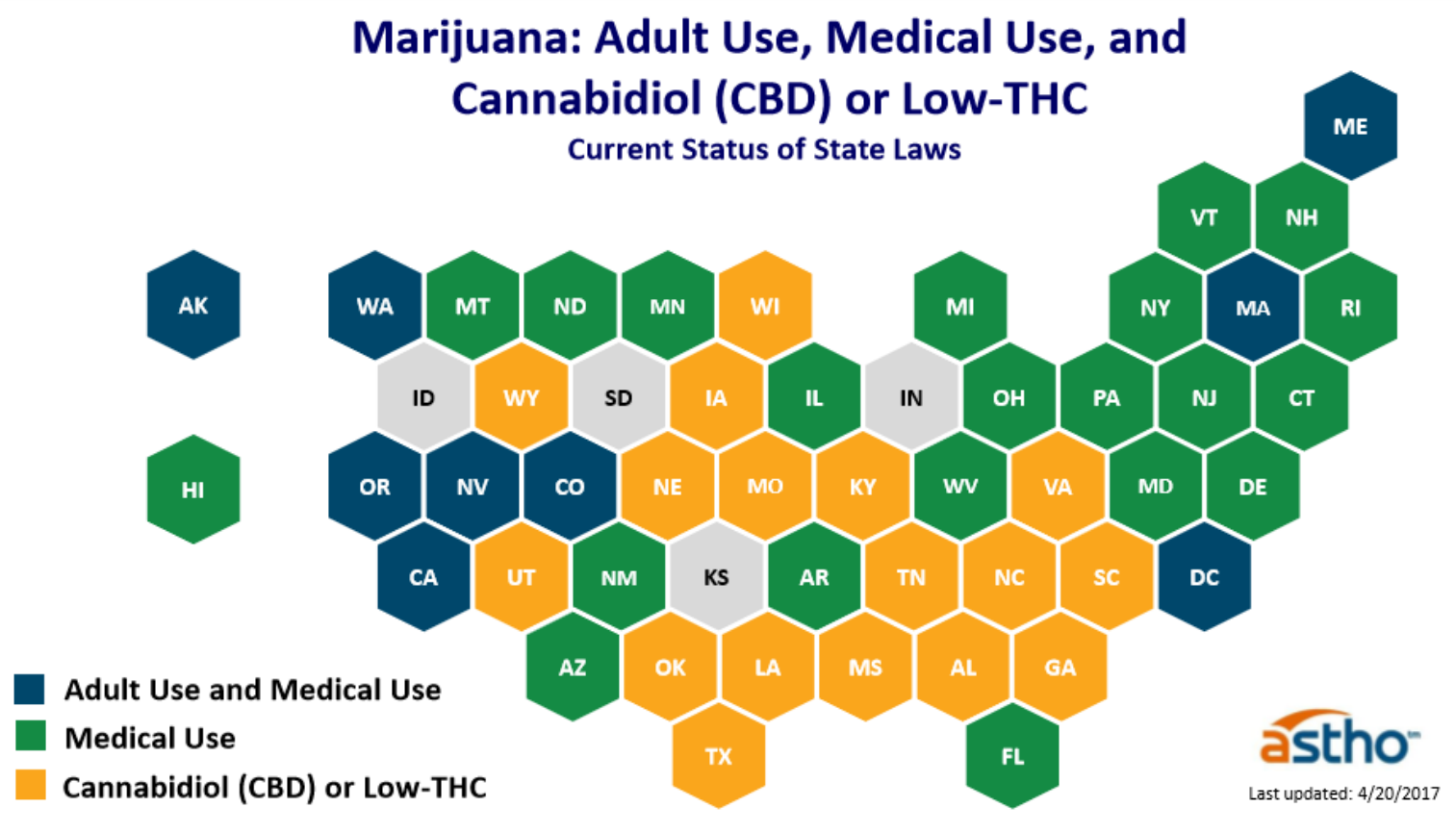

- Who is most at risk, and what are the factors that moderate the impact of cannabis exposure?
- Are the effects permanent; are there compensatory developmental responses?
- How much do other variables contribute to cannabis effects (stress and trauma, alcohol, tobacco, prenatal care, BMI, physical activity…)?

**RESEARCH GAP AREA:** What are the effects on young adults (i.e. beyond adolescence) and older adults (i.e. with cognitive decline)? What are the effects of second- or third-hand smoke exposure from cannabis?

# CANNABIS POLICY: DOMESTIC AND ABROAD

## *WHAT IS THE PUBLIC HEALTH IMPACT?*

# CANNABIS LAWS IN THE U.S.




***States with MML vary on***:

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

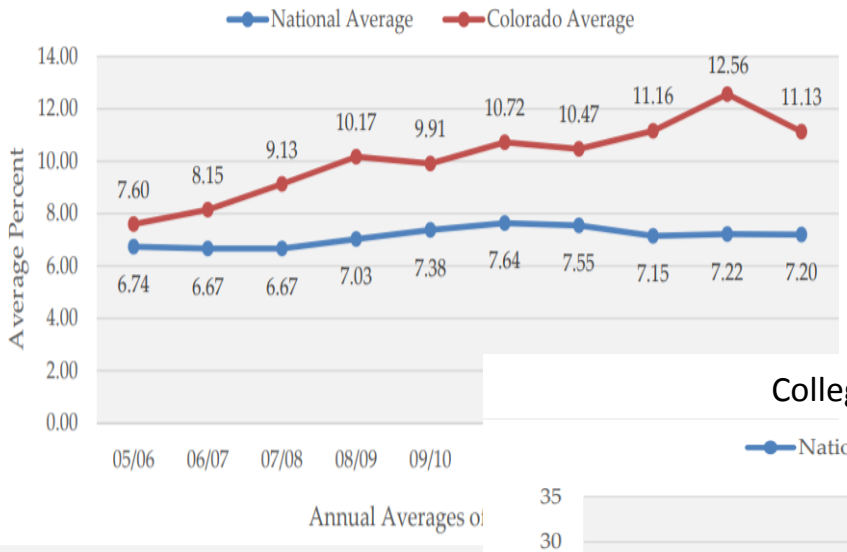
***States with Adult Use Laws vary on:***

- Marketing, product labeling, distribution (home growth).
- Taxation.

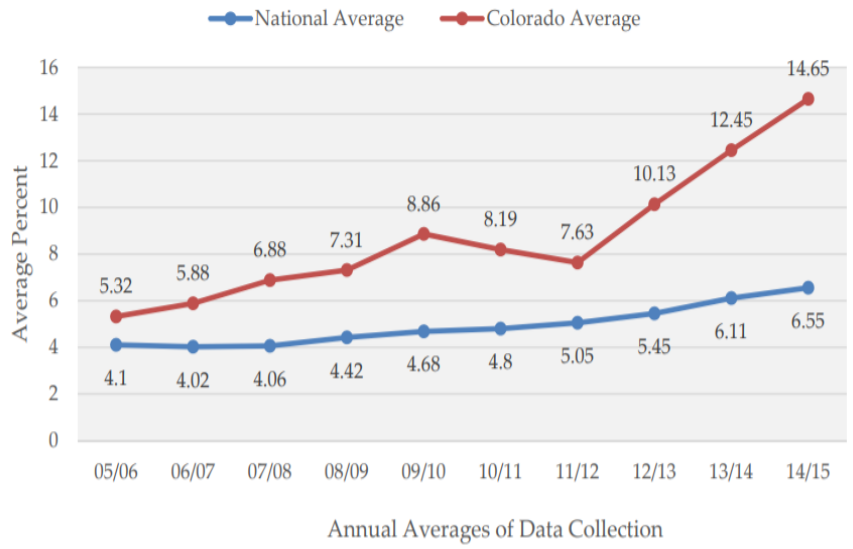
**Source:** http://www.astho.org/Public-Policy/State-Health-Policy/Marijuana-Overview/

# PAST MONTH MARIJUANA USE: Colorado vs. National Averaqe

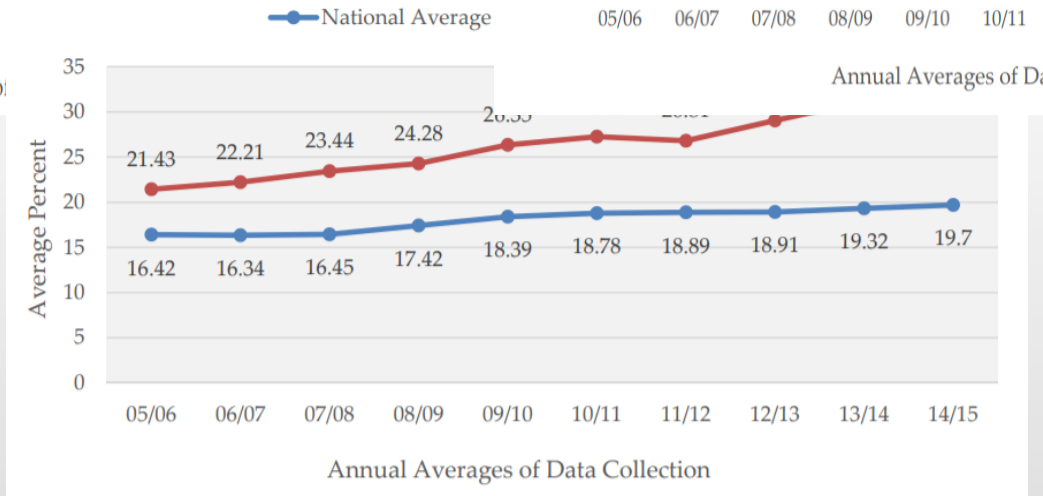
Youth Ages 12 to 17 Years Old




Adults Age ≥ 26 Years Old




College Age 1



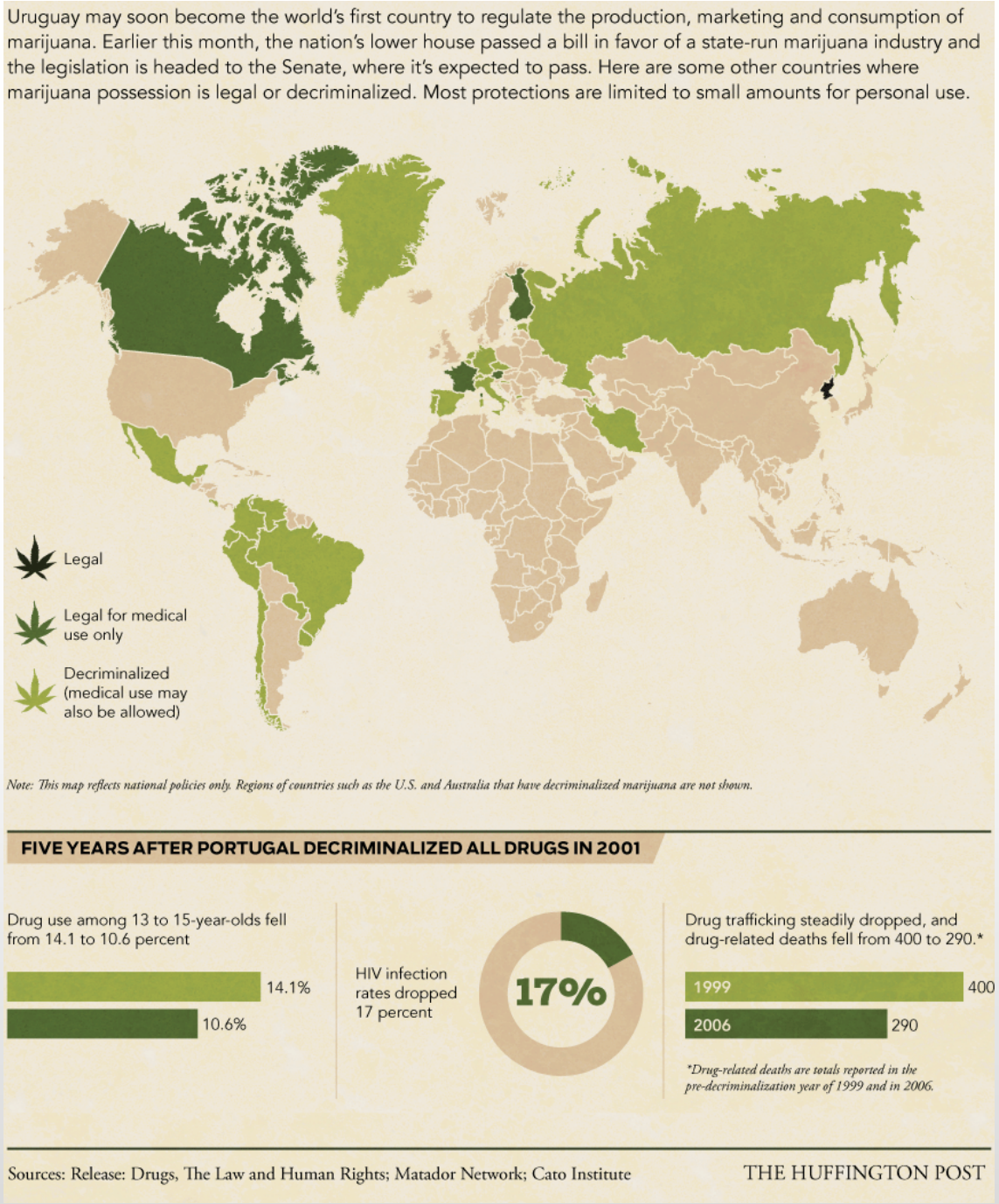

Rocky Mountain HIDTA Report www.rmhidta.org
Supplement: The Legalization of Marijuana in Colorado:
The Impact, Volume 4 (March 2017)

SOURCE: SAMHSA.gov, National Survey on Drug Use and Health 2014 and 2015

# CANNABIS POLICIES GLOBALLY

- SOURCE: Huffington Post 2013,

Updated 2017



# OVERVIEW OF CANNABIS POLICIES: U.S. & OTHER SELECTED COUNTRIES (NON-MEDICAL)

| | U.S. | Netherlands | Spain | Canada (Pending) | Uruguay |
|---|---|---|---|---|---|
| Level of Legislation | State constitution, laws and regulations (federal conflict) | Not technically legal | Personal consumption | National | National law and regulations |
| Edibles | Permitted | Available | Permitted | Permitted after 1 year | Prohibited |
| Public consumption | Not permitted | Tolerated | Not permitted | Permitted | Tolerated |
| Monthly Quota | Unlimited | Not specified | Not specified | 150 G | 40 G (Registration) |
| Drug Tourism (sales to out of state visitors) | Permitted | Permitted | Prohibited | Permitted | Prohibited |

# BEYOND CANNABIS: EVOLVING DRUG POLICIES


Other countries are experimenting with regulated cannabis markets:

- Including: Uruguay, Spain, Canada, Peru, and Jamaica.

Source: healthpovertyaction.org

# CANNABIS POLICY: CHALLENGES AND OPPORTUNITIES

## *HOW TO ALIGN PUBLIC HEALTH NEEDS*

# IMPLEMENTATION ALTERNATIVES

## Twelve Supply Alternatives to Status Quo Prohibition

- Prohibit and increase sanctions
- Allow adults to grow their own
- Retail sales only (Dutch model)
- Public authority (near monopoly)
- For-benefit companies
- Standard commercial model
- Prohibit and decrease sanctions
- Communal own-grow and distribution
- Government operates the supply chain
- Nonprofit organizations
- Very few monitored for-profit licensees
- Repeal-only of state prohibition

Extreme options | Commonly discussed options | Middle-ground options

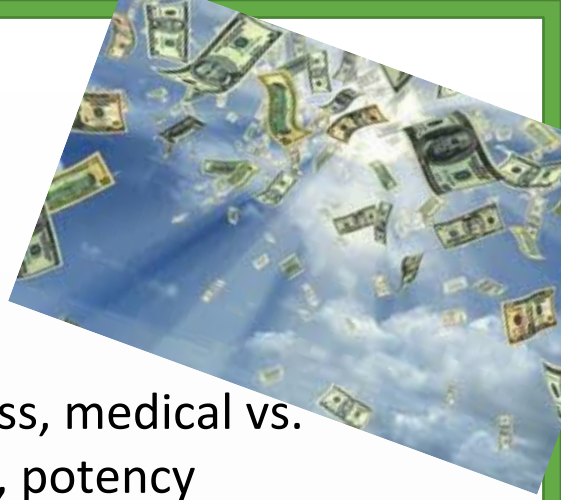
Source: Caulkins et al, 2015

# LESSONS LEARNED FROM TOBACCO CONTROL


- **R**obust demand reduction should be launched **concurrently** with legalization
- **I**ndependent oversight committees should contain public health officials, treatment providers, and researchers **exclusively**
- **C**omprehensive marijuana prevention should be modeled on the best **evidence-based tobacco control programs**
- **M**arijuana should be included in existing smokefree laws **without exemptions**
- **M**arijuana tax revenue should be dedicated to fund ongoing marijuana-disease research programs
- **M**arijuana marketing and advertising should be restricted to inside licensed retail stores to minimize young adult and vulnerable population exposure

Source: Glantz and Barry, 2016

# POLICY RESEARCH NEEDS



- ***Different Models***: advertising, involvement of big business, medical vs. recreational, pricing, taxes, dispensaries, edible products, potency restrictions

- ***Economic Impact***: revenue generated; illegal markets; costs to public (Alcohol generates ~15B in tax revenue/per year; costs to society are estimated at $235 B)

- ***Public Health Impact:***
  - Other drug use, especially alcohol, tobacco, and opiates
  - New routes of administration; potency/constituents
  - Accidents/ER visits
  - Education outcomes, workforce productivity, prenatal exposure

***How to minimize harm in a new "non-prohibition" environment***