

AVOIDING POT HOLES: NAVIGATING THE CAUTIONARY TRAIL OF CANNABIS

37TH Annual Family Medicine & Sports Medicine Conference
The Family Medicine Foundation of West Virginia

jberry@hsc.wvu.edu

November 10, 2023

DISCLOSURES

- I serve on the West Virginia Medical Cannabis Advisory Board
- I serve on the WV Governor's Council of Substance Abuse Prevention and Treatment
- I have not received any financial remuneration from the multi-billion dollar cannabis industry
- I AM biased



OVERVIEW

- What is it?
- What are the risks?
- Is it a medicine?
- What can we do?



CANNABIS

- > 400 compounds (60 pharmacologically active)
- Δ^9 -THC (tetrahydrocannabinol) + 120 other cannabinoids
- Each has individual, interactive and entourage effects
- Clinical trials w/ individual cannabinoids can't be extrapolated to the "Cannabis plant"
- Composition varies among product



Cannabinoids

Endocannabinoids (brain derived)

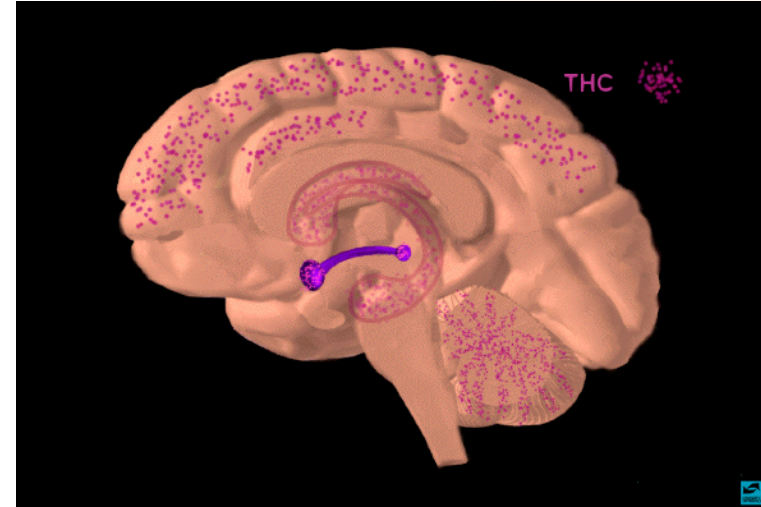
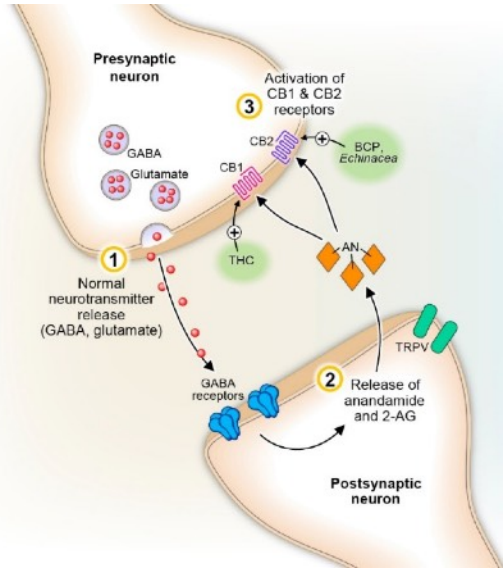
- Anandamide (AEA)
- 2-Arachidonylglycerol (2-AG)

Phytocannabinoids (plant derived)

- Cannabidiol (CBD)
- Tetrahydrocannabinol (THC)
- Cannabichromene (CBC)
- Cannabigerol (CBG)
- Many others

Synthetic cannabinoids (laboratory derived)

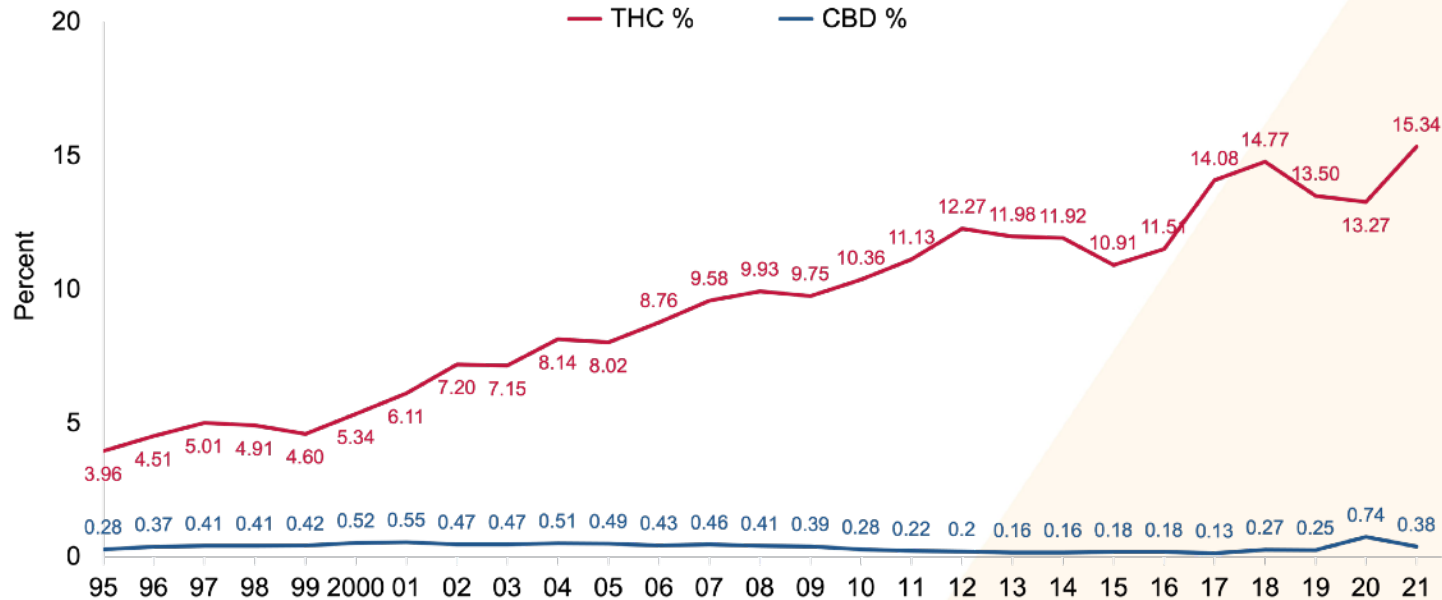
- Dronabinol
- Nabilone



NIDA

Mayo Clinic Proceedings 2019 94, 1840-1851 DOI: (10.1016/j.mayocp.2019.01.003)

Percentage of THC and CBD in Cannabis Samples Seized by the DEA, 1995-2021



SOURCE: U Miss, Potency Monitoring Project

<https://nida.nih.gov/research-topics/marijuana/cannabis-marijuana-potency>

Higher Potency = Higher Risks

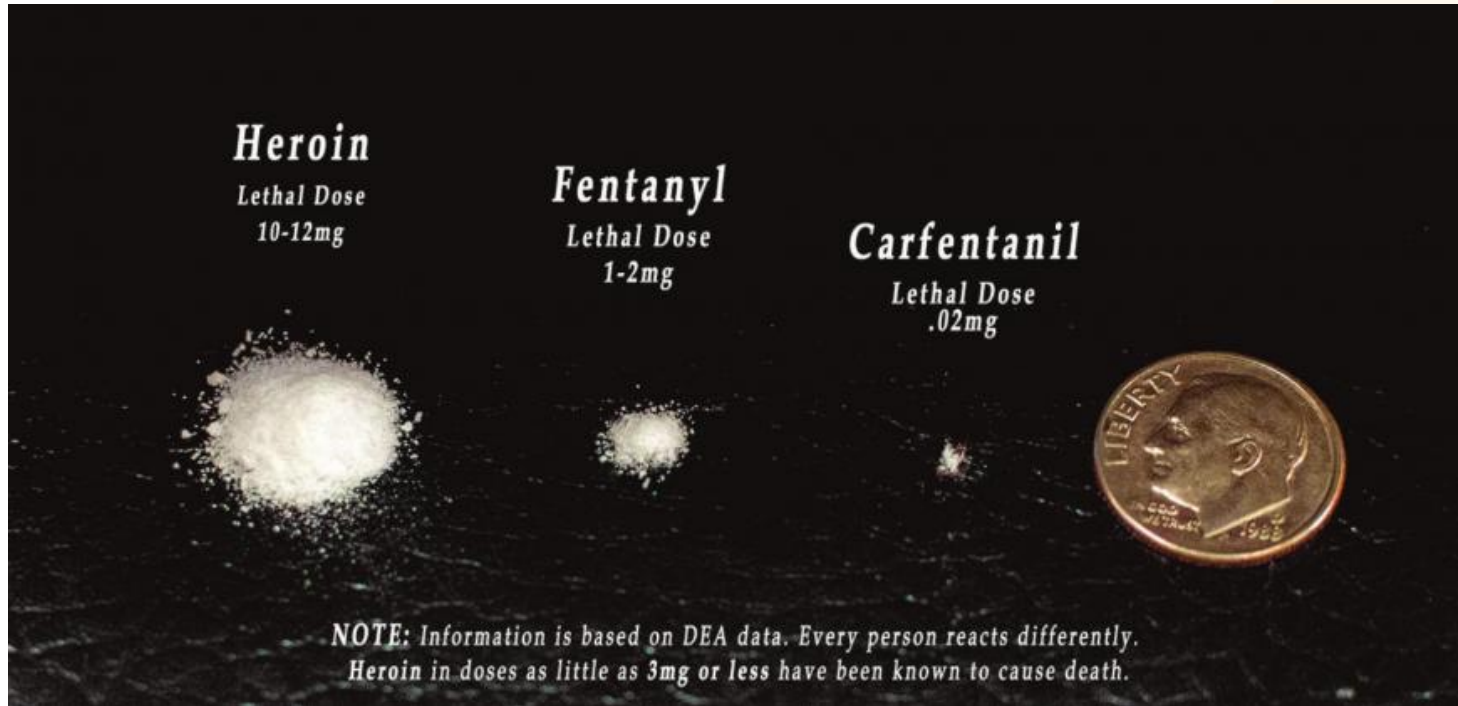
- Ave THC content is 17-28% in today's MJ plant (compared to 2% in 1960-80s)
- THC content in concentrates up to 85-90%
- FDA considering reducing nicotine concentration in tobacco
- **NO** research that THC>10% is beneficial
- Dutch concluded that >15% should be considered a hard drug



Higher Potency = Higher Risks



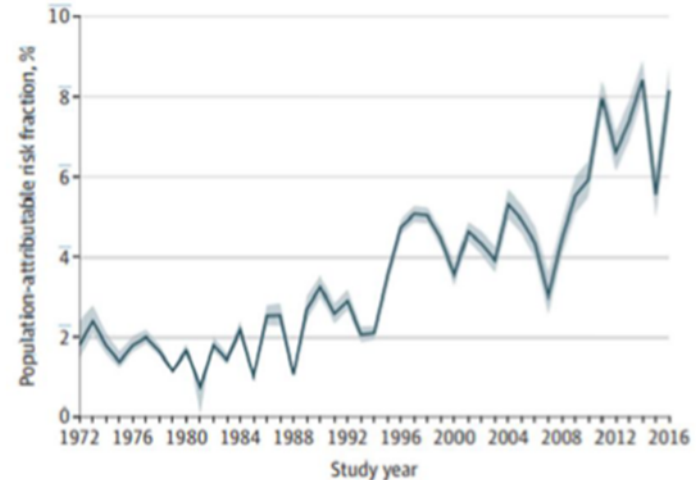
Higher Potency = Higher Risks



High Potency and Psychosis

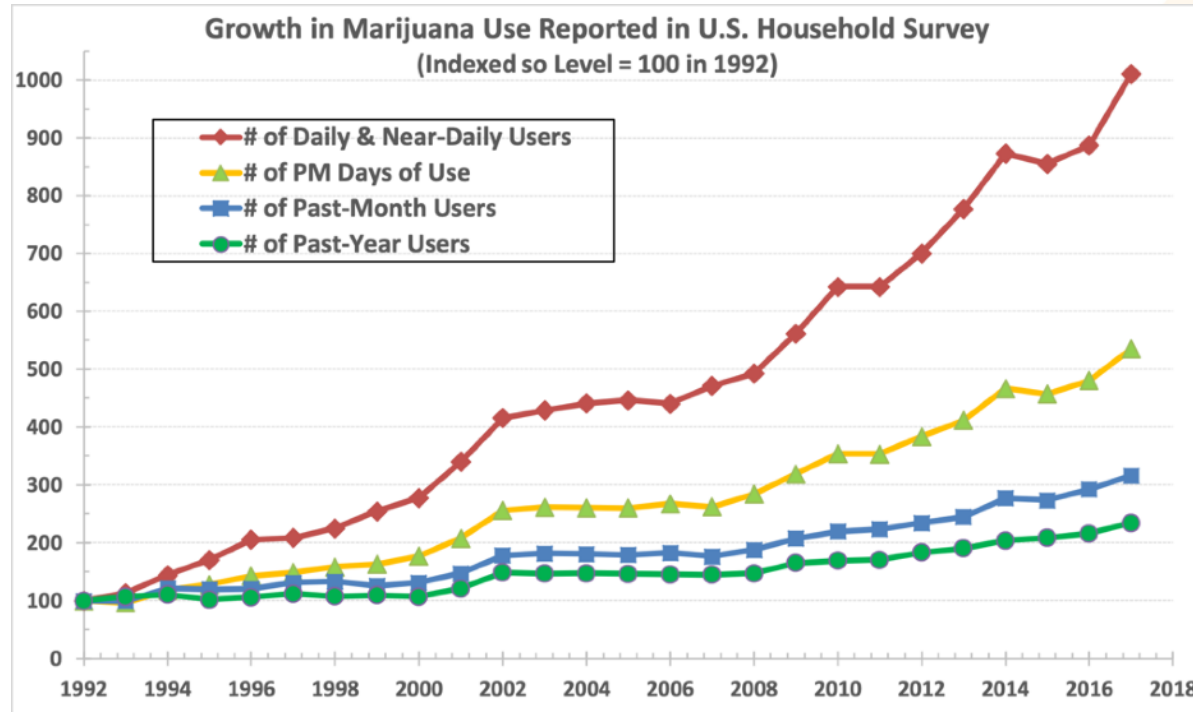
- **Potency $\geq 10\%$**
- European Study
1st Episode Psychosis
3X Risk
5X Risk with daily use
- Denmark Study
CUD and Schizophrenia
4X Risk

Figure 2. Development of the Population-Attributable Risk Fraction (PARF) of Cannabis Use Disorder in Schizophrenia in Denmark



Shaded areas indicate 95% CIs.

Daily or Near-Daily Use Has Grown Tenfold from 0.9 to 9 million



Source: National Household Survey on Drug Use and Health data analyzed by Jonathan Caulkins, Carnegie Mellon University

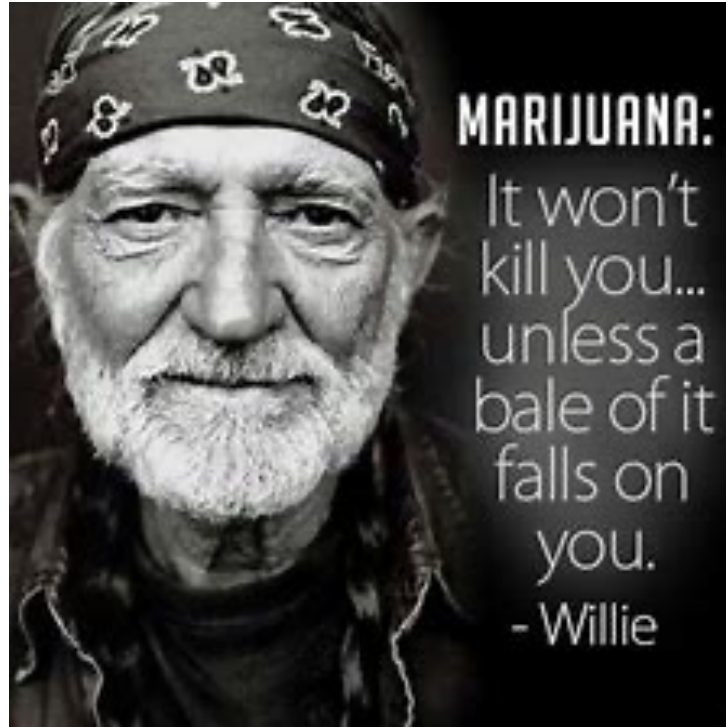
Increased Frequency and Potency

- Pre-2000 avg user: 2 nights/wk
- Today: Daily (frequency + potency = **70X THC!**)

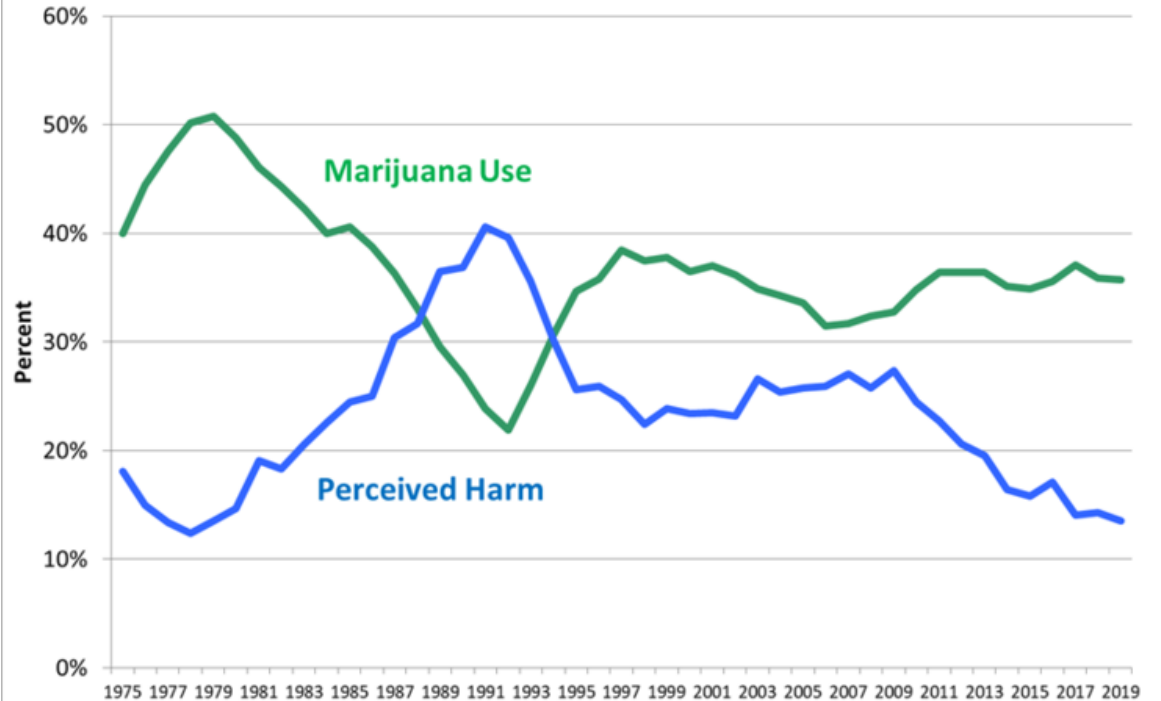


J Caulkins. Marijuana Legalization: What Everyone Needs to Know

What's the Big Deal?

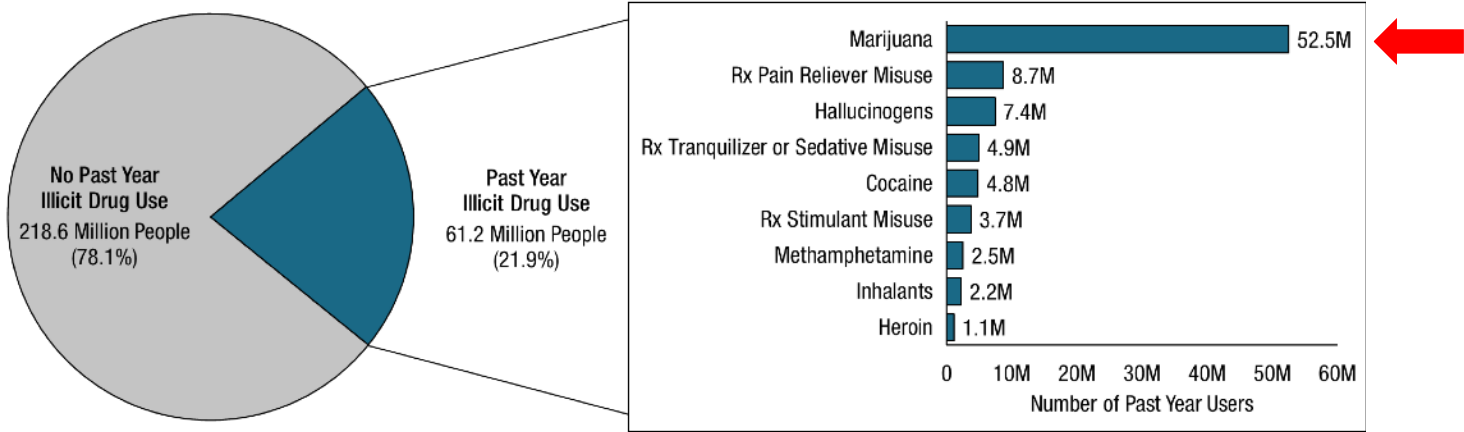


Past Year Marijuana Use and Perceived Risk of Harm of Occasional Marijuana Use Among 12th Graders, 1975-2019



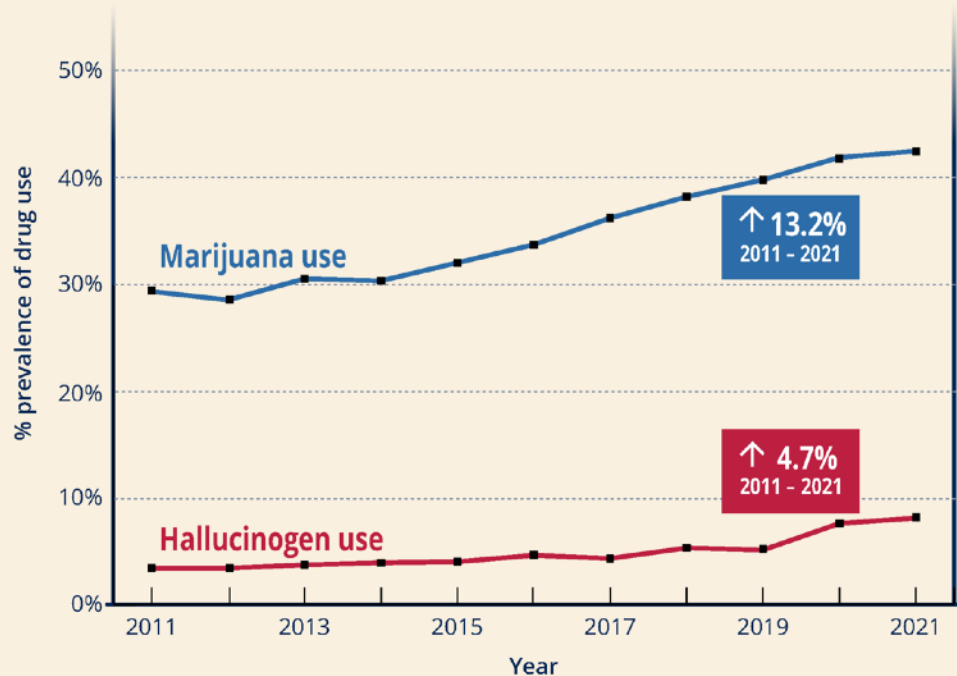
Source: Monitoring the Future

Past Year Illicit Drug Use: Among People Aged 12 or Older; 2021



Rx = prescription.
Note: The estimated numbers of past year users of different illicit drugs are not mutually exclusive because people could have used more than one type of illicit drug in the past year.

Historic Highs in Past-Year Marijuana and Hallucinogen Use Among Young Adults (Ages 19-30) in 2021

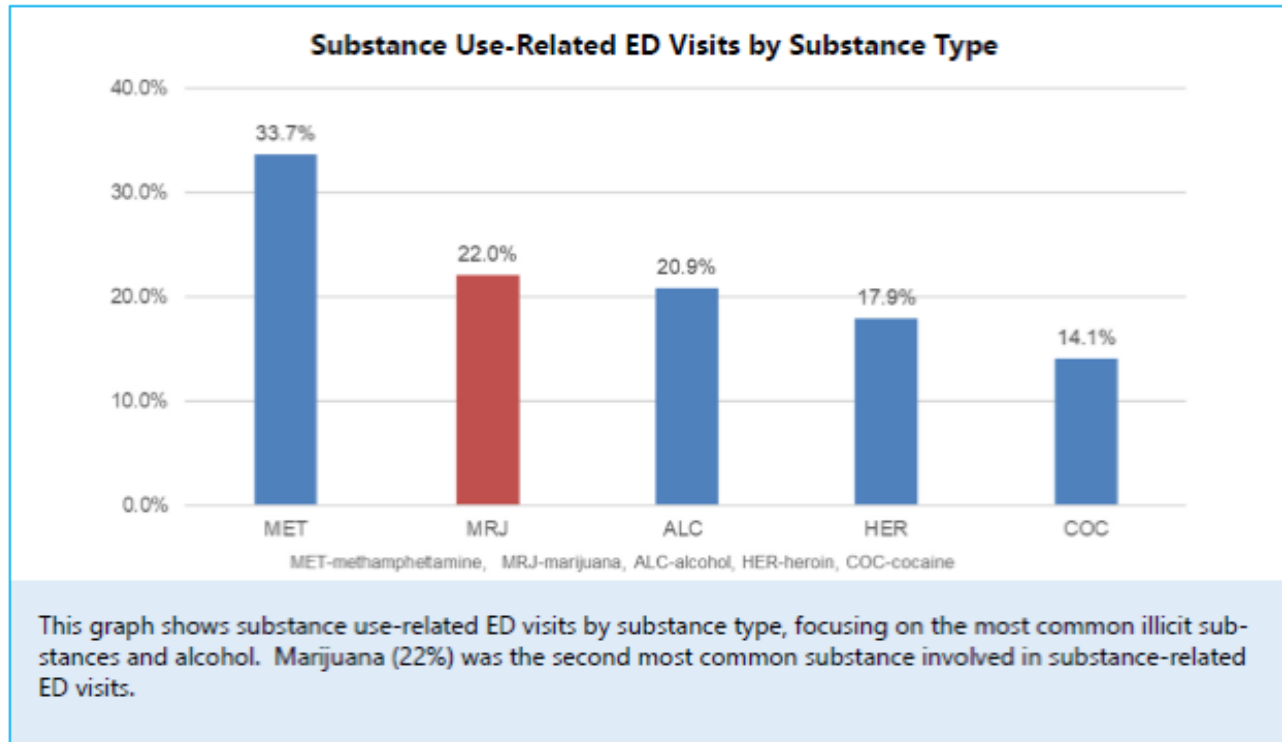


Source: 2021 Monitoring the Future Panel Survey

Record levels of year/month/daily use:


- **43%** Past Year
- **29%** Past Month
- **11%** Daily

DAWN December 2020



BRIEF REPORT |  Full Access

Trends in emergency department visits associated with cannabis use among older adults in California, 2005–2019

Benjamin H. Han MD , Jesse J. Brennan MA, Mirella A. Orozco BA, Alison A. Moore MD, Edward M. Castillo PhD, MPH

First published: 09 January 2023 | <https://doi.org/10.1111/jgs.18180>

1,808% INCREASE IN ELDERLY ED VISITS

Trends in Cannabis Involvement and Risk of Alcohol Involvement in Motor Vehicle Crash Fatalities in the United States, 2000–2018

Marlene C. Lira MPH, Timothy C. Heeren PhD, Magdalena Buczek MS, Jason G. Blanchette JD, MPH, Rosanna Smart PhD, Rosalie Liccardo Pacula PhD, and Timothy S. Naimi MD, MPH

[+] Author affiliations, information, and correspondence details

Accepted: June 18, 2021 Published Online: November 17, 2021

- **Cannabis related fatalities increased 9% ➡ 21%**

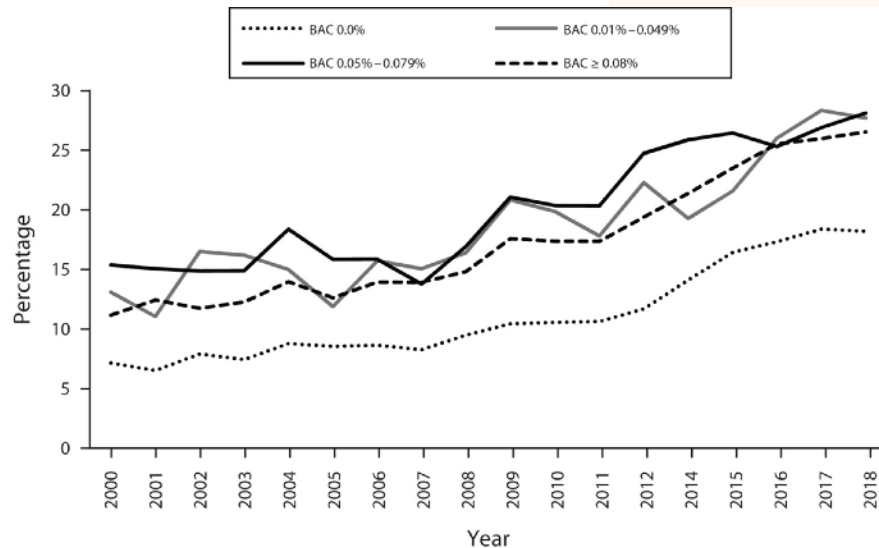
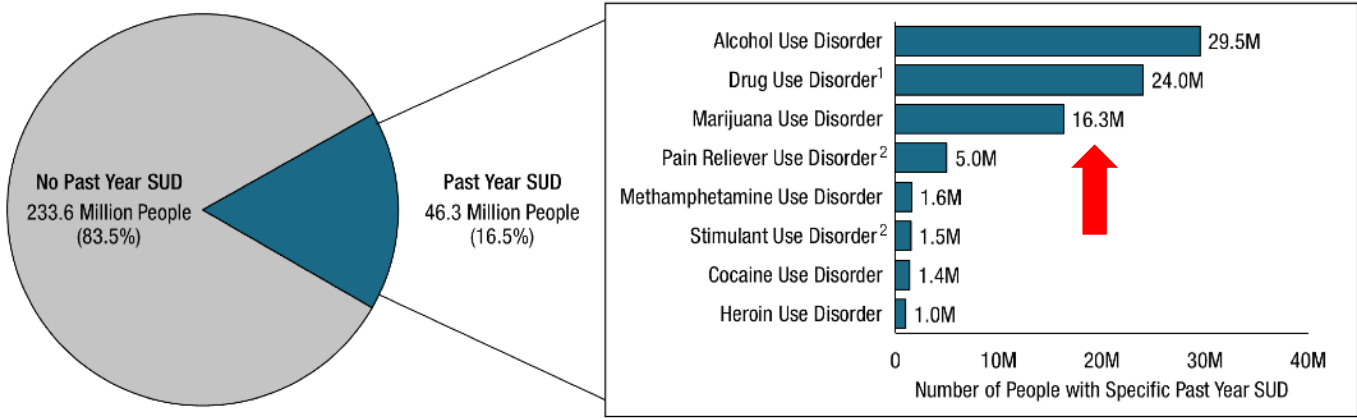


FIGURE 2— Percentage of Motor Vehicle Crash Fatalities Involving Cannabis by Blood Alcohol Concentration (BAC) Level: Fatality Analysis Reporting System, United States, 2000–2018

Past Year Substance Use Disorder (SUD): Among People Aged 12 or Older; 2021



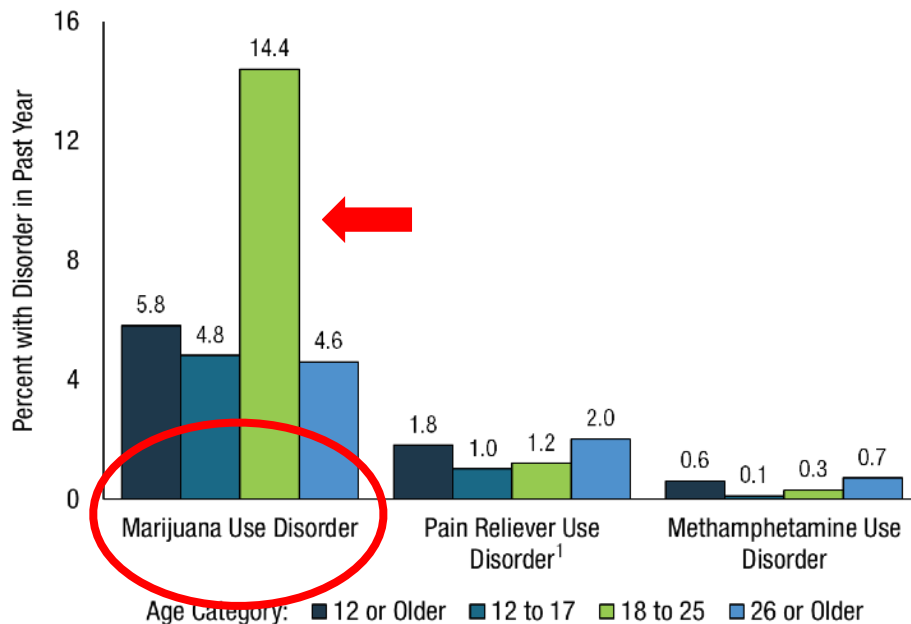
Note: The estimated numbers of people with substance use disorders are not mutually exclusive because people could have use disorders for more than one substance.
¹ Includes data from all past year users of marijuana, cocaine, heroin, hallucinogens, inhalants, methamphetamine, and prescription psychotherapeutic drugs (i.e., pain relievers, tranquilizers, stimulants, or sedatives).

ADDICTION

- 1 in 5 risk of CUD in all users
- Risk increase if initiated early and used frequently: **22-44% (avg 33%)**

Janni Leung, Gary C.K. Chan, Leanne Hides, Wayne D. Hall,
What is the prevalence and risk of cannabis use disorders among people
who use cannabis? a systematic review and meta-analysis, Addictive
Behaviors, Volume 109, 2020, 106479, ISSN 0306-4603,

Marijuana Use Disorder, Pain Reliever Use Disorder, and Methamphetamine Use Disorder in the Past Year: Among People Aged 12 or Older; 2021



¹ Includes data from all past year users of prescription pain relievers.

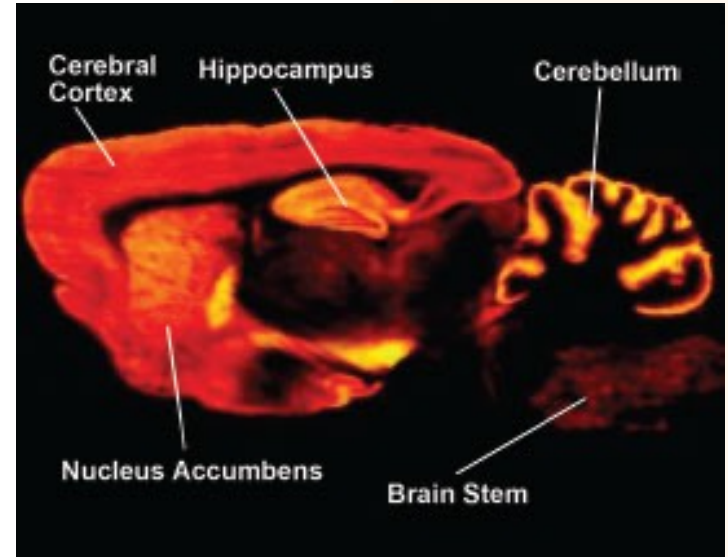
Effect of Medical Marijuana Card Ownership on Pain, Insomnia, and Affective Disorder Symptoms in Adults A Randomized Clinical Trial

Jodi M. Gilman, PhD; Randi M. Schuster, PhD; Kevin W. Potter, PhD; William Schmitt, BA; Grace Wheeler, BA; Gladys N. Pachas, MD; Sarah Hickey, BSN; Megan E. Cooke, PhD; Alyson Dechert, BA; Rachel Plummer, BA; Brenden Tervo-Clemmens, PhD; David A. Schoenfeld, PhD; A. Eden Evins, MD, MPH

- What are the risks/benefits of obtaining a MM card?
- Increased incidence of CUD = **2.9X**
- **No** improvement in pain, anxiety or depression
- Improved self-reported sleep

RAT BRAIN

- Exposure to THC around birth or adolescence demonstrates impaired learning and memory later in life
- Hippocampus changes
- Altered reward system



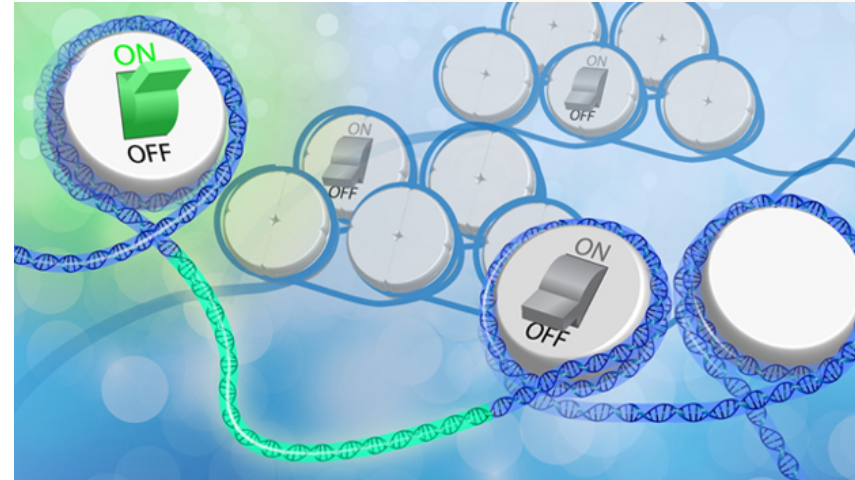


Sperm DNA methylation alterations from cannabis extract exposure are evident in offspring

Rose Schrott^{1,2}, Jennifer L. Modliszewski³, Andrew B. Hawkey⁴, Carole Grenier², Zade Holloway⁴, Janequia Evans⁴, Erica Pippen⁴, David L. Corcoran⁵, Edward D. Levin⁴ and Susan K. Murphy^{1,2*}

- Changes were heritable in sperm and brain areas involved in development
- Gene in hippocampus and NA
- Cardiomegaly
- *As cannabis legalization expands and consumption increases, it is imperative that we improve understanding of how exposure in one generation can shape health and disease of future generations.”*

EPIGENETICS



GATEWAY?

- **NSDUH** 2004 to 2014 survey of 12-21 y/o (n=275,559)
- Self reported **first** use: Marijuana, Tobacco, ETOH
 - **MJ** as 1st : doubled from 4.8% to 8.8%
 - **Cigarettes** as 1st : dropped from 21.4% to 8.9%
 - **ETOH** as 1st : constant around 30%
- Using MJ as first:
 - increased odds of CUD and heavy current MJ use
 - equal to tobacco for developing TUD
- As youth aged, they were more likely to start with MJ
- Compared to tobacco, using MJ or ETOH as 1st were more likely to use other drugs

Association of Cannabis Use in Adolescence and Risk of Depression, Anxiety, and Suicidality in Young Adulthood

A Systematic Review and Meta-analysis

Gabriella Gobbi, MD, PhD; Tobias Atkin, BA; Tomasz Zytynski, MD; Shouao Wang, MSc; Sorayya Askari, PhD; Jill Boruff, MLIS; Mark Ware, MD, MSc; Naomi Marmorstein, PhD; Andrea Cipriani, MD, PhD; Nandini Dendukuri, PhD; Nancy Mayo, PhD

- Meta-analysis of 11 studies (n=23,317)
- Adolescent consumption associated with **increased risk of developing depression and suicidal behavior** later in life, even in the absence of a premorbid condition.
- There was no association with anxiety.

TEEN SUICIDE

...the high prevalence of adolescents consuming cannabis generates a large number of young people who could develop depression and suicidality attributable to cannabis. This is an important public health problem and concern, which should be properly addressed by health care policy.

JAMA: *Preadolescents and adolescents should avoid using cannabis as use is associated with a significant increased risk of developing depression or suicidality in young adulthood*

PREGNANCY

- US Surgeon General issued advisory
- CDC: 16% of pregnant women use illicit drugs, cannabis most common
- Use doubled 2009 - 2016
- Linked with increased anxiety, aggression, hyperactivity and decreased immune response
- Linked with low birthweight, gestational weight, stillbirth
- THC is excreted in breast milk
- ~70% of dispensaries recommended



Dickson B1, Mansfield C, Guaihi M, et al. Recommendations From Cannabis Dispensaries About First-Trimester Cannabis Use. *Obstet Gynecol.* 2018;131:1031-1038.

Azofeifa A, Mattson ME, Schauer G, et al. National Estimates of Marijuana Use and Related Indicators - National Survey on Drug Use and Health, United States, 2002-2014. *MMWR Surveill Summ.* 2016;65:1-28. www.cdc.gov/mmwr/volumes/65/ss/ss6511a1.htm

Rompala G. Maternal cannabis use is associated with suppression of immune gene networks in placenta and increased anxiety phenotypes in offspring. *Proceedings of the National Academy of Sciences.* Nov 2021, 118 (47)

PREGNANCY

- Adolescent Brain Cognitive Development Study (ABCD)
 - ~11,000 children 9-11y and follow into adulthood
 - MJ exposure after maternal knowledge had greater **psychopathology** during middle childhood, even after controlling for confounders
- Canadian Birth Registry
 - ~500,000 births
 - Greater risk of **Autism Spectrum Disorder**
 - Hazard ratio: 1.51 (controlled for confounders)
 - Relied on self-report, likely risk is under-estimated

September 12, 2022

Association of Mental Health Burden With Prenatal Cannabis Exposure From Childhood to Early Adolescence

Longitudinal Findings From the Adolescent Brain Cognitive Development (ABCD) Study

David A. A. Baranger, PhD¹; Sarah E. Paul, MA¹; Sarah M. C. Colbert, BA²; [et al](#)

[» Author Affiliations](#) | [Article Information](#)

JAMA Pediatr. Published online September 12, 2022. doi:10.1001/jamapediatrics.2022.3191

- Adds longitudinal data to the baseline 2021 report
- Persisting vulnerability as children progress through early adolescence
- Increased psychopathology may lead to greater risk of psych d/o and substance use

“Evidence that the impact of PCE on psychopathology does not ameliorate as children enter adolescence further cautions against cannabis use during pregnancy.”

HEART AND LUNGS

- **Cardiac**

- THC is proinflammatory
- HTN, Platelet activation, endothelial dysfunction
- Increase risk for CVD, cardiomyopathy, tachy, arrhythmia, mortality

- **Pulmonary**

- >CO and tar than cigs
- COPD
- Decline in pulmonary function
- Bronchitis, infections
- Cancer?

Cannabinoid Hyperemesis Syndrome

- Intense and persistent (e.g. 5/hour) episodes of nausea, vomiting, dehydration and abdominal pain
- Often take hot showers for relief for hours
- 1/3 of regular MJ smokers use hot shower/bath to relieve nausea and/or vomiting
- ~2.1 – 3.3 million in US annually
- Up to 6% of ED visits for recurrent vomiting
 - In CO, visits to ED for cyclic vomiting doubled after legalization
- Discontinuing is only cure

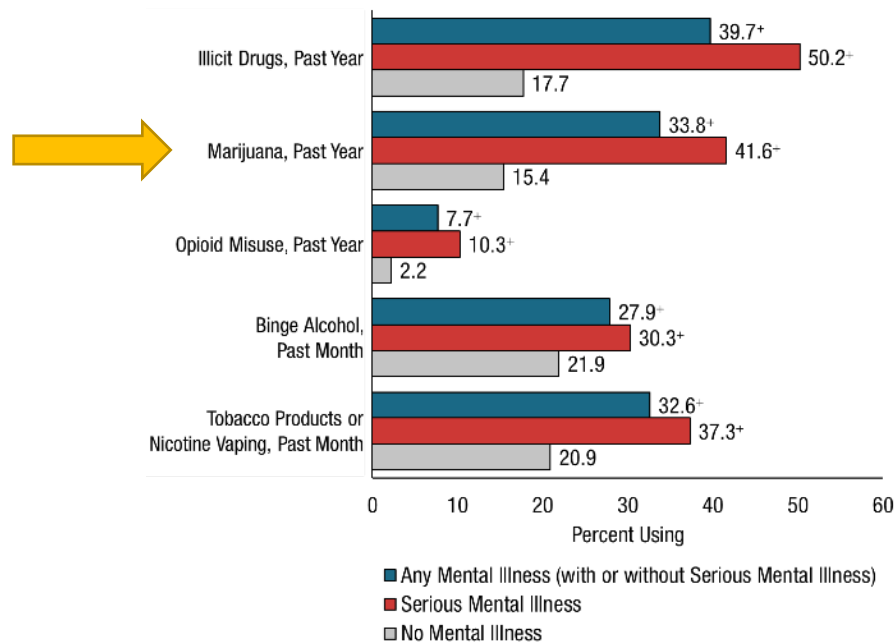
Chocron Y, Zuber J, Vaucher J. Cannabinoid hyperemesis syndrome *BMJ* 2019; 366 :l4336

CANNABIS WITHDRAWAL

- **Cessation of use that has been heavy and prolonged** (i.e. daily or almost daily over a few months)
- **3 of following s/s develop w/i ~ 1wk of stop:**
 - Irritability, anger, or aggression
 - Nervousness or anxiety
 - Sleep difficulty (e.g. insomnia, disturbing dreams)
 - Decreased appetite or weight loss
 - Restlessness
 - Depressed mood
 - At least 1 of the following physical symptoms causing significant discomfort:
 - Abdominal pain, shakiness/tremors, sweating, fever, chills, or headache
- **Cause clinically significant distress or impairment in social occupational, or other important areas of functioning**



Substance Use: Among Adults Aged 18 or Older; by Mental Illness Status, 2021



+ Difference between this estimate and the estimate for adults aged 18 or older without mental illness is statistically significant at the .05 level.

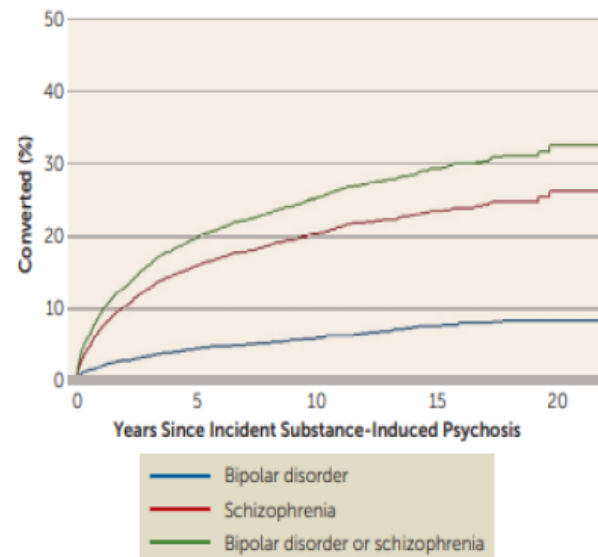
Rates and Predictors of Conversion to Schizophrenia or Bipolar Disorder Following Substance-Induced Psychosis

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

Published Online: 28 Nov 2017 | <https://doi.org/10.1176/appi.ajp.2017.17020223>

- 32.2% converted to BPD or schizophrenia
- Cannabis = 47.4%
- Risk highest for 16-25 y/o

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



MJ LEGALIZATION AND OPIOID DEATHS

Journal of Health Economics

Volume 88, March 2023, 102728



Neil K. Mathur & Christopher J. Ruhm

**Medical cannabis
dispensaries raise opioid
deaths by 28%**

“...legal medical marijuana, particularly when available through retail dispensaries, is associated with *higher* opioid mortality. The results for recreational marijuana, while less reliable, also suggest that retail sales through dispensaries are associated with greater death rates relative to the counterfactual of no legal cannabis.”

“...we provide evidence that cannabis legalization leads to relatively large increases in deaths involving synthetic opioids, particularly during the current era of widespread illicit fentanyl.”

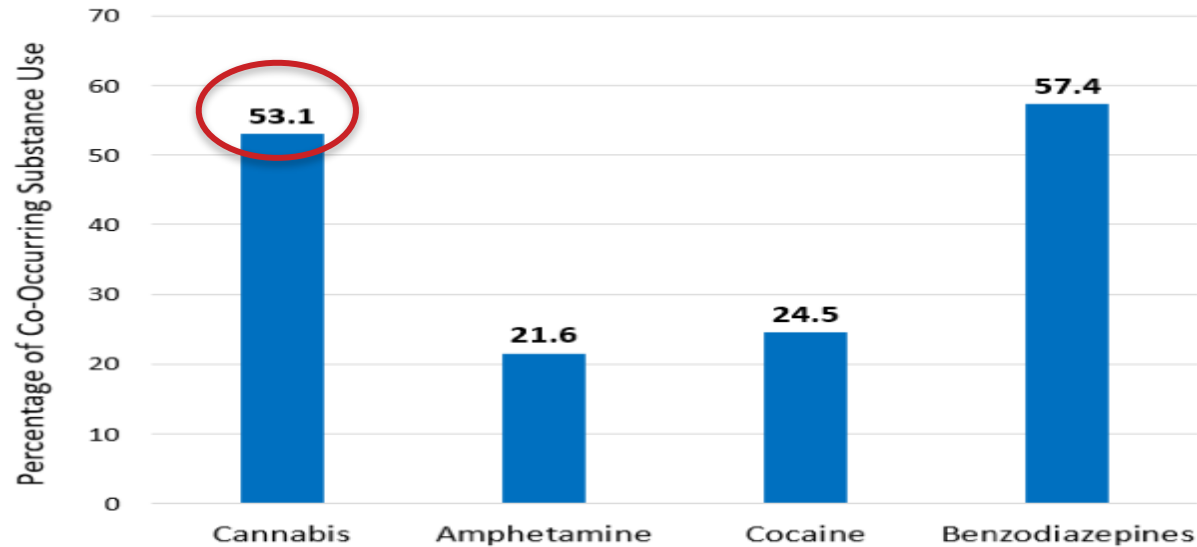
“There are many reasons why it may be desirable to legalize the use and sale of medical and recreational marijuana. Decreasing opioid mortality is not one of them.”

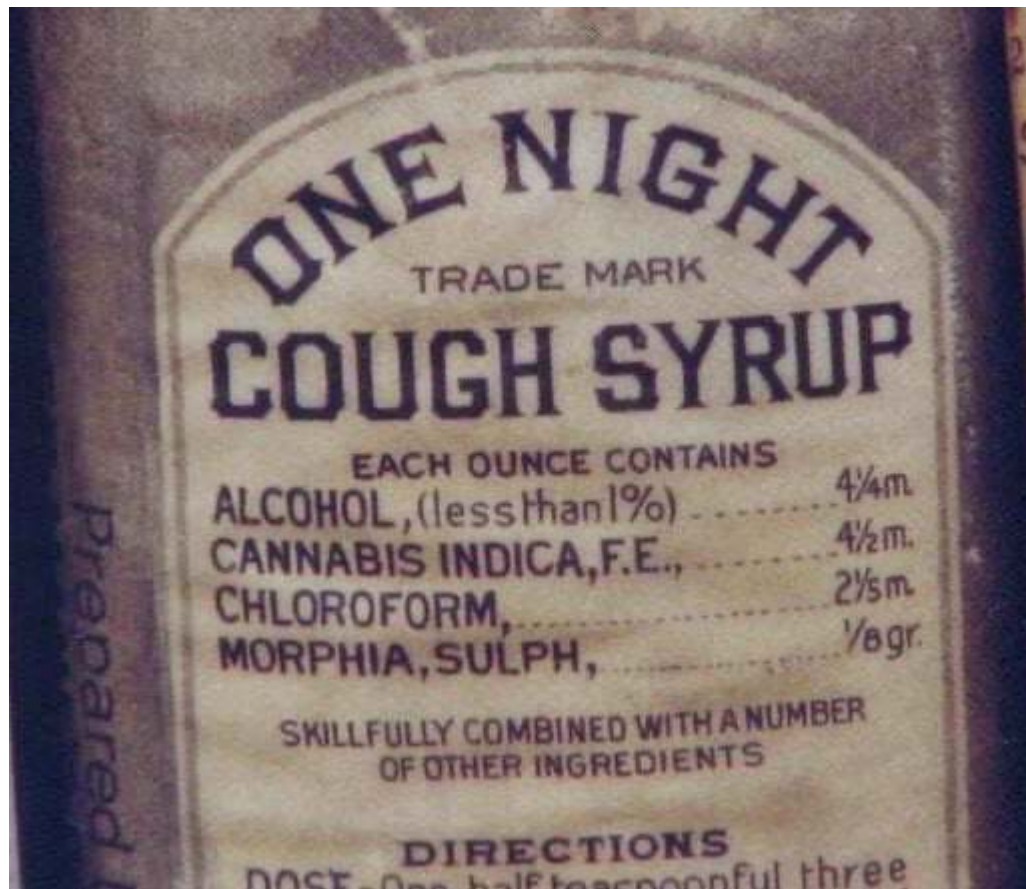
High prevalence of co-occurring substance use in individuals with opioid use disorder



James J. Mahoney III ^{a,b,*}, Erin L. Winstanley ^{a,b}, Laura R. Lander ^{a,b}, James H. Berry ^{a,b},
Patrick J. Marshalek ^{a,b}, Marc W. Haut ^{a,b,c}, Jennifer L. Marton ^{a,b}, Wesley D. Kimble ^{a,c},
Matthew Armistead ^{a,c}, Sijin Wen ^{d,e}, Yilin Cai ^d, Sally L. Hodder ^{a,c}

Specific Co-Occurring Substances Present on Urine Toxicology in Addition to Opioids (n = 2,275)







American Psychiatric Association
American Academy of Child and Adolescent Psychiatry
American Academy of Pediatrics
American Society of Addiction Medicine
American Academy of Addiction Psychiatry
American Academy of Neurology
American Academy of Ophthalmology
American College of Medical Toxicology
American College of Obstetricians and Gynecologists



cannabis for medicinal use should not be legalized through the state legislative, ballot initiative, or referendum process

MEDICINE?

- The Cannabis Plant is **NOT** an FDA approved drug
- The Cannabis Plant is a Schedule I substance
- Synthetic cannabinoids: **Dronabinol** and **Nabilone** are FDA approved
 - Nausea/vomiting due to chemo
 - Appetite and weight loss in HIV/AIDS and Cancer
- **Epidiolex**
 - CBD-based liquid
 - Lennox Gastaut & Dravet Syndromes
 - Tuberous Sclerosis Complex
- Doctors **can't** write a Rx for cannabis
 - Prescription, supply or sale is illegal by federal law



MEDICINE?

A compound or preparation used for the treatment or prevention of disease.

A substance (such as a drug or potion) used to treat something other than disease.

A spell, charm, or fetish believed to have healing, protective, or other power.

A label given to a substance used recreationally to decrease stigma and increase sales of the substance.

A compound or preparation used for the treatment or prevention of disease

- Rigorously tested for safety, efficacy, dosing, purity
- Need more than subjective experience
- Side effects more impairing than condition being treated?
- Long-term use lead to worse problems than original condition?
- Do alternative treatments exist that are superior, even if subjectively less desirable?
- Can a component be isolated or synthesized so to provide a “clean” product?
- Risk to population vs benefit to individual

Slide adapted from Stu Gitlow



OPIOIDS

- Popular and unsubstantiated claims of benefit
- Minimization of harm
- Failure to understand addiction, chronic pain, mental illness
- Driven by strong financial motives
 - BIG **PHARMA**
- Physician's duty is to do no harm



CANNABIS

- Popular and unsubstantiated claims of benefit
- Minimization of harm
- Failure to understand addiction, chronic pain, mental illness
- Driven by strong financial motives
 - BIG **FARMA**
- Physician's duty is to do no harm
- Recreational Advocacy

Recreational

- What if Anheuser-Busch sold medical beer?
- What if Philip Morris sold medical tobacco?

Home > Industries > Food/Beverages/Tobacco > Cannabis Watch

GET EMAIL ALERTS

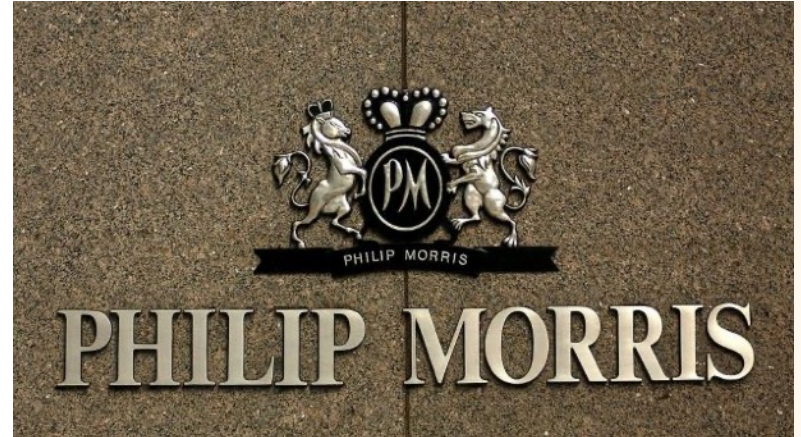
Cronos CEO: \$1.8 billion from Big Tobacco is just a beginning for cannabis industry

Published: Dec 10, 2018 7:48 a.m. ET



Aa

Altria can help Cronos standardize its approach to marijuana, CEO says after announcing investment




Anheuser-Busch InBev Lands Its Marijuana Partner

Bottoms up in the cannabis space as another infused beverage deal is announced.



 **Sean Williams** (TMFUltraLong)

 Dec 22, 2018 at 8:21AM

 [Author Bio](#)



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Space Age Cake IN
Purple Wookie IN
Mandarin Dream IN



Product and variety vary by location.



Muse

Everybody has a muse and for many, it's cannabis. Muse awakens creativity, giving you permission to let go.

[Learn More >](#)



Sweet Talk

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[Learn More >](#)



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“Consult a certified physician to find out what dose works best for your condition.”

OLD HIPPIE STASH

“Having strains of medical marijuana has been something we wanted to do for a long time; it was just a matter of finding the right situation,” David Bellamy said. “I think it was a little experimental for everybody, for us and for Trulieve.”

You may also be surprised to learn that The Bellamy Brothers are not the first country stars to create their own line of marijuana products. Jimmy Buffet launched his line of medical marijuana in 2019 called “Coral Reefer”, and Willie Nelson founded his own marijuana company called “Willie’s Reserve” in 2015.



Howard Bellamy (left) and his brother David (right) in front of the Sabraton Plaza Trulieve.
(WBOY image) September 14, 2022



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MEDICAL MARIJUANA DOCTOR

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MARCH 17TH

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Thanks to Ellen Snelling for the photos

CLEARING THE SMOKE



- More research is needed!!!
- If it is “medical”, docs need to be driving the discussion
- First Do No Harm
- Medicalizing a recreational substance has unintended consequences
- Don't use if have a psych d/o
- Don't use if a child/young adult
- Don't use if pregnant or breastfeeding

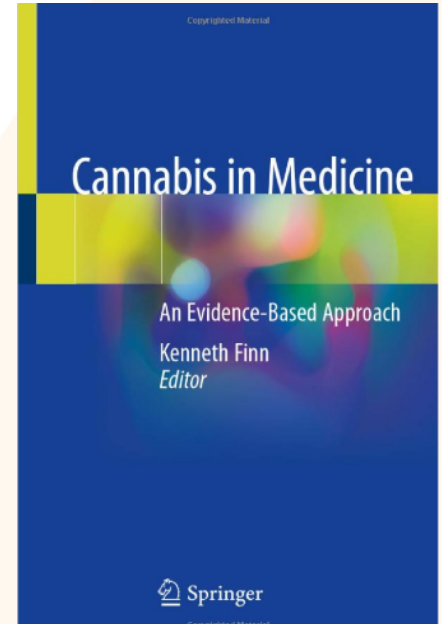
WHAT CAN WE DO?



- **Compassion – Why is someone using?**
- **Educate**
 - Peers, friends, legislators, media
- **Advocate for stricter regulations**
 - Potency caps, PDMP, Commercialization, pregnancy, youth
- **Study**
 - Efficacy/Harms, OD data, Suicide, ED, Hospitalizations, MVA
- **Screen**
 - Ask and document: product/route/frequency/potency/age of onset

Resources/Thanks

- International Academy on the Science and Impact of Cannabis (IASIC): <https://iasic1.org/>
- Elizabeth Stuyt, MD
- Keith Humphreys, PhD
- Stu Gitlow, MD




[Back to table of contents](#)


[Previous Article](#)

[Next Article](#)

Reviews and Overviews

 [Full Access](#)

Risks and Benefits of Cannabis and Cannabinoids in Psychiatry



Kevin P. Hill , M.D., M.H.S., Mark S. Gold, M.D., Charles B. Nemeroff, M.D., Ph.D., William McDonald, M.D., Adrienne Grzenda, M.D., Ph.D., Alik S. Widge, M.D., Ph.D., Carolyn Rodriguez, M.D., Ph.D., Nina V. Kraguljac, M.D., John H. Krystal, M.D., Linda L. Carpenter, M.D.


Published Online: 8 Dec 2021 | <https://doi.org/10.1176/appi.ajp.2021.21030320>

As cannabinoids become more available, the need for an evidence base adequately evaluating their safety and efficacy is increasingly important. There is considerable evidence that cannabinoids have a potential for harm in vulnerable populations such as adolescents and those with psychotic disorders. The current evidence base is insufficient to support the prescription of cannabinoids for the treatment of psychiatric disorders.

REVIEW | [ONLINE FIRST](#)

Association of cannabis potency with mental ill health and addiction: a systematic review

Kat Petrilli, MRes   • Shelan Ofori, MRes • Lindsey Hines, PhD • Gemma Taylor, PhD • Sally Adams, PhD •
Tom P Freeman, PhD

Published: July 25, 2022 • DOI: [https://doi.org/10.1016/S2215-0366\(22\)00161-4](https://doi.org/10.1016/S2215-0366(22)00161-4) •  Check for updates

In conclusion, the findings from this systematic review highlight the potential for an increased risk of negative mental health outcomes and addiction with higher potency cannabis use. The findings support recommendations to discourage the use of higher potency cannabis products for low risk use. This recommendation should be incorporated into education tools and in the management of cannabis use in clinical settings. Policy makers should carefully consider cannabis potency when regulating cannabis in legal markets, such as through limits or taxes based on THC concentration.

Medical Use of Cannabis in 2019

Kevin P. Hill, MD, MHS

It seems unlikely that cannabinoids are highly effective medicines for CNCP. There is moderate- to high-grade evidence supporting use of nabiximols to achieve modest reductions in pain as adjunctive therapy in MS-related pain. However, NNTBs were high and NNTHs low, with high rates of dropout for AEs, and long-term efficacy and safety is unknown. We also found minimal evidence that cannabinoids are effective in improving other important domains in people with CNCP such as emotional and physical functioning. Cannabinoids are unlikely to be a monotherapy for CNCP. People living with CNCP often have complex comorbidities, and multidisciplinary treatment that includes physical and psychological therapy rather than reliance on medicines alone is likely to be most effective.

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

Pain. 2018;159(10)

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47 RCTs, 57 observational studies (N=9,958)

Neuropathic Pain, Fibromyalgia, RA, Other CNCP (MS, Visceral Pain, Mixed or Undefined)

NN to **BENEFIT** = **24** (Benefit defined as 30% reduction in pain: 29%CB vs 26% placebo)

For 50% reduction in pain: No significant difference from placebo

NN to **HARM** = **4** (81%CB vs 66.2% placebo)

NO benefit on physical or emotional functioning

NEWS

How Weed Became the New OxyContin

Big Pharma and Big Tobacco are helping market high-potency, psychosis-inducing THC products as your mother's 'medical marijuana'

BY **LEIGHTON WOODHOUSE**

AUGUST 30, 2022

FOR 30 YEARS, DR. LIBBY Stuyt, a recently retired addiction psychiatrist in Pueblo, Colorado, treated patients with severe drug dependency. Typically, that meant alcohol, heroin, and methamphetamines. But about five years ago, she began to see something new.

“I started seeing people with the worst psychosis symptoms that I have ever seen,” she told me. “And the worst delusions I have ever seen.”