CANNABIS USE UPDATE

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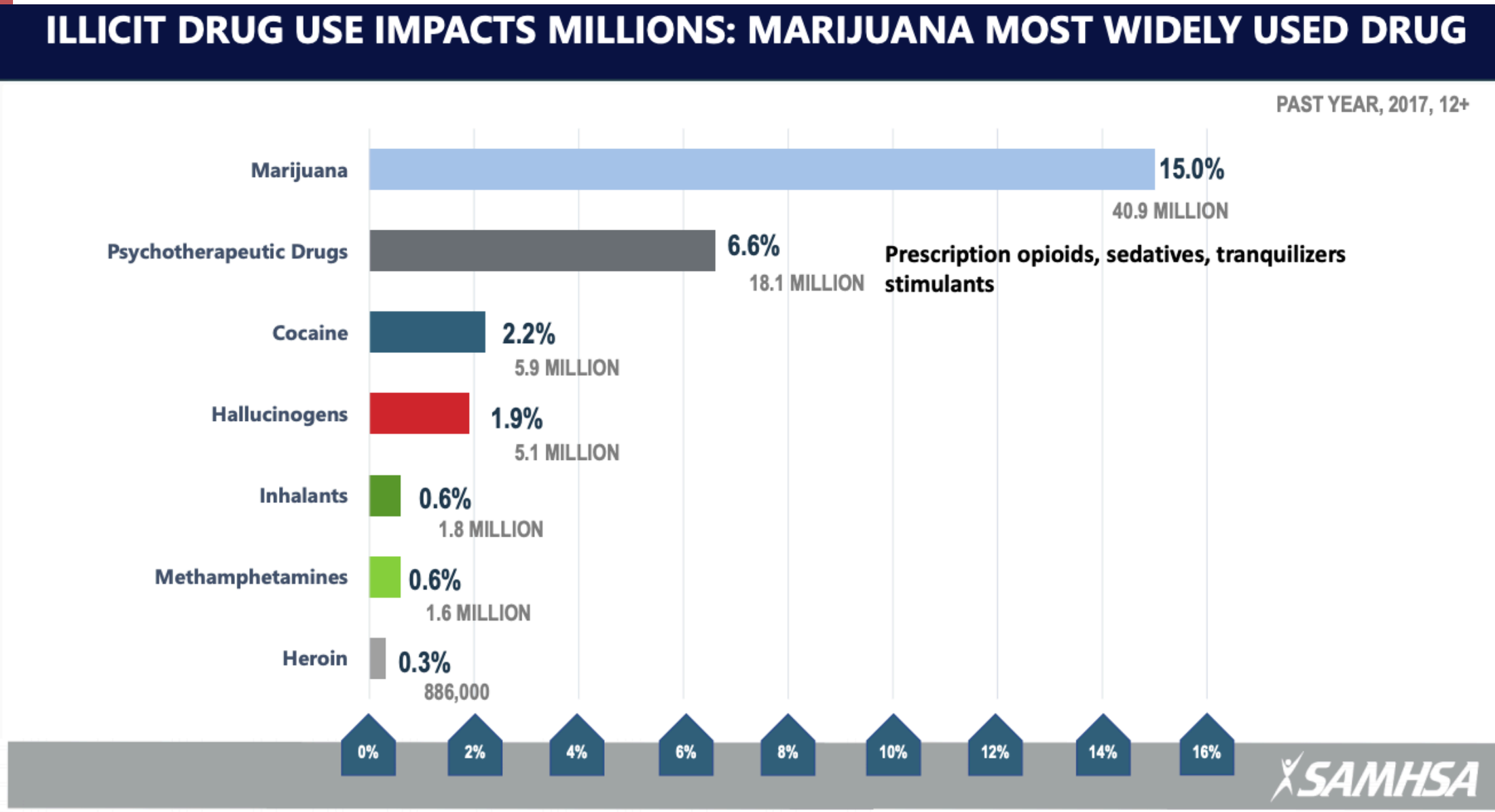
BEHAVIORAL HEALTH ECHO
OCTOBER 24, 2019

EPIDEMIOLOGY OF CANNABIS USE: NSDUH, 2017



https://www.samhsa.gov/data/sites/default/files/nsduh-ppt-09-2018.pdf

EPIDEMIOLOGY OF CANNABIS USE

- Most commonly used illegal substance in the US and world
- Lifetime prevalence in US: 42-46%
- Past year use highest in age 18-25 group
- Past year Cannabis Use Disorder (CUD) highest in ages 21-26
- CUD (old abuse/dependence):
  - 2001: 1.5%
  - 2012: 2.9%
  - Psychiatric samples: 15-50%
- Greater increases in use and CUD in US states with Medical Marijuana Laws

https://jamanetwork.com/journals/jamapsychiatry/article-abstract/2619522

TRENDS IN MARIJUANA USE PATTERNS, DISORDERS AND PERCEIVED RISK OF HARM

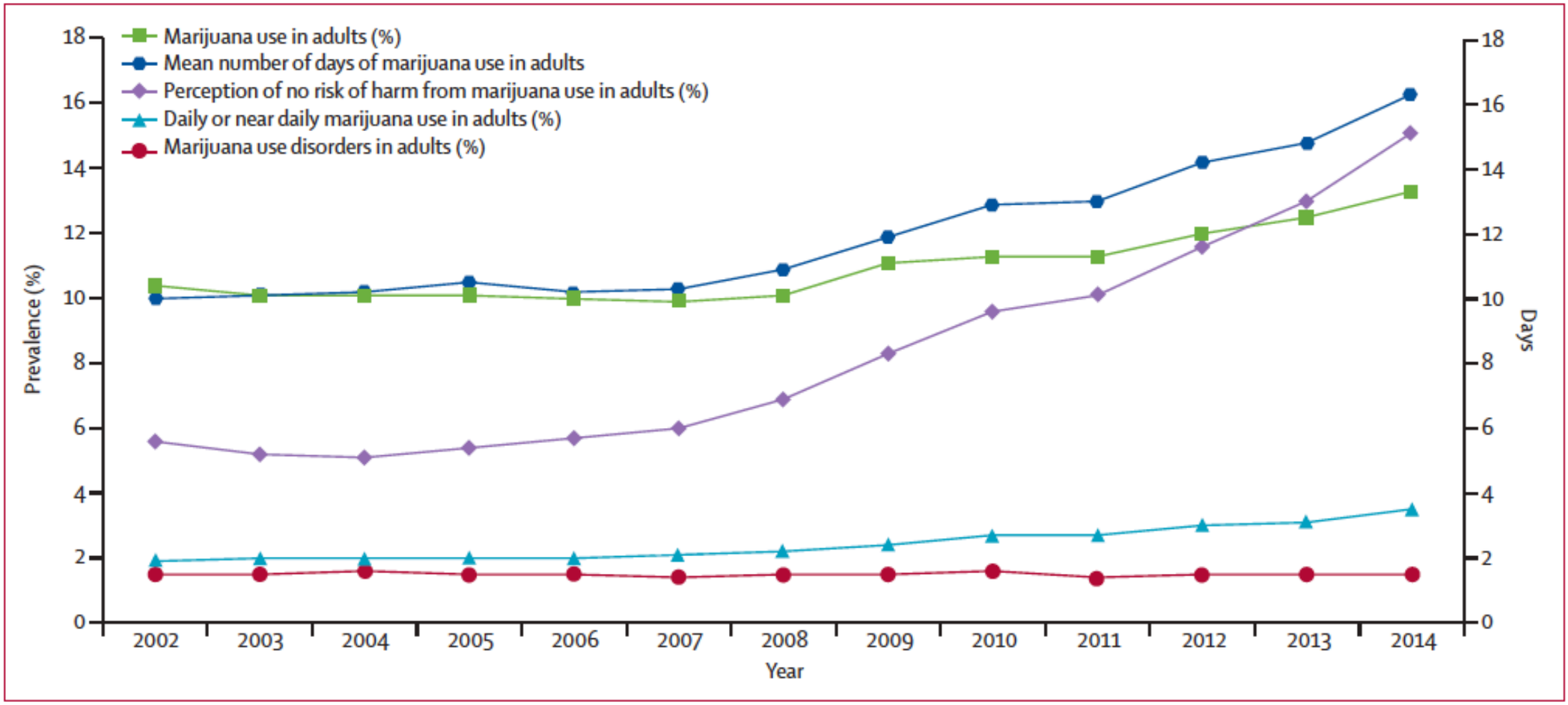
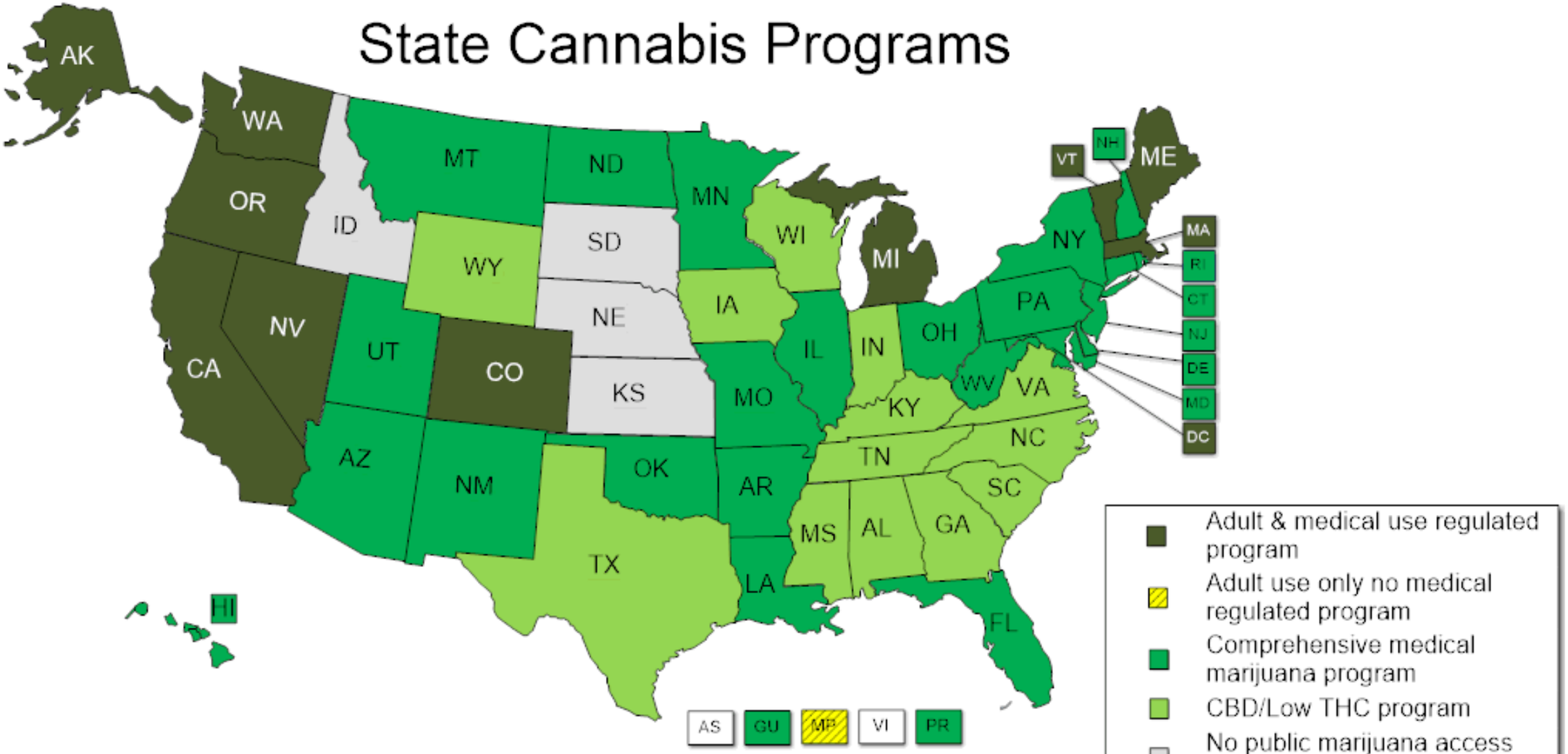


***Figure*: Trends in marijuana use patterns, marijuana use disorders, and perceived risk of harm**
Annual prevalence and trends in any marijuana use, daily or near daily marijuana use, marijuana use disorders, mean number of days of marijuana use, and perception of no risk of harm from marijuana use in adults in the USA. *Joinpoints indicate significant changes in non-linear trends.

www.thelancet.com/psychiatry Vol 3 October 2016

Compton W et al, 2016

State Cannabis Programs



Vermont adult use law signed Jan. 22, 2018. Effective July 1, 2018
Limited adult possession and growing allowed, no regulated production or sales: DC, VT

March 2019

http://www.ncsl.org/research/health/state-medical-marijuana-laws.aspx ; March 2019

HAVE YOU HEARD?

- It's natural, so it must be safe!
- It's an herb, so it must be safe!
- It's from the earth, so it must be healing!
- It's a panacea!
- The medical profession is denying people the miraculous properties of this drug!
- Etc.
- Etc.
- Etc.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Distilleries,

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FLASHBACK TO OLDER MARKETING

CANNABINOIDS

- Phytocannabinoids
  - Derived from Cannabis plants
- Endocannabinoids
  - Endogenous ligand of cannabinoid receptors
- Synthetic cannabinoids
  - compounds developed for potential medical uses (but most never tested in animals or humans)
  - Ideally should mimic the therapeutic effects of phytocannabinoids while having no psychoactivity (not the reality)

CANNABIS SATIVA

Plant originated in Central Asia, Likely Himalayan foothills, Hindu Kush mountain range

Did not appear in Western hemisphere until 16th century

Identified thus far:
>500 chemical compounds
and
>60 cannabinoids

Is it all one species?
Or four species?
[C.sativa, C.indica, C.ruderalis, C.afghanica]

Chemotypes:
THC Predominant
CBD Predominant
Mixed Types

Hemp=<0.3% THC, high CBD

COMMON CANNABIS PREPARATIONS

Table 2. Common Cannabis Preparations

Preparations	Description
Marijuana[a]	Dried plant product consisting of leaves, stems, and flowers; typically smoked or vaporized
Hashish	Concentrated resin cake that can be ingested or smoked
Tincture[a]	Cannabinoid liquid extracted from plant; consumed sublingually
Hashish oil	Oil obtained from cannabis plant by solvent extraction; usually smoked or inhaled; butane hash oil (sometimes referred to as "dabs"), for example
Infusion[a]	Plant material mixed with nonvolatile solvents such as butter or cooking oil and ingested

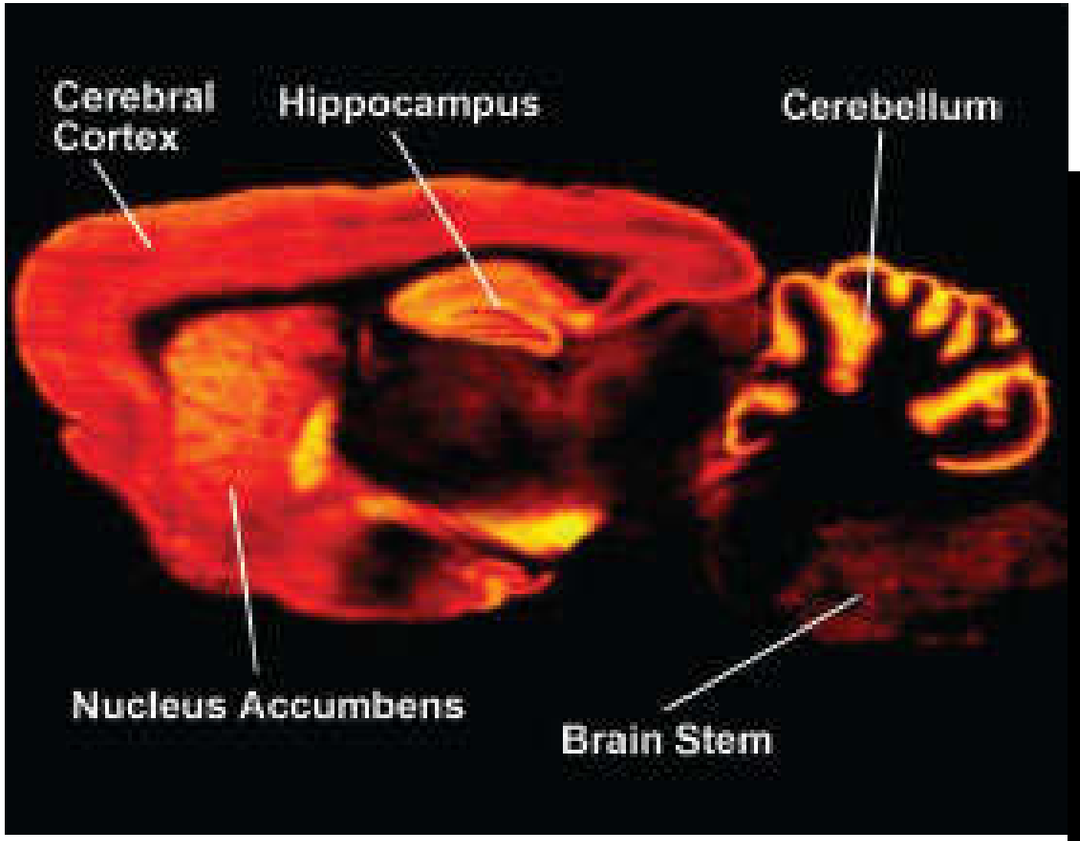
[a] These preparations are available from state-approved medical marijuana dispensaries.

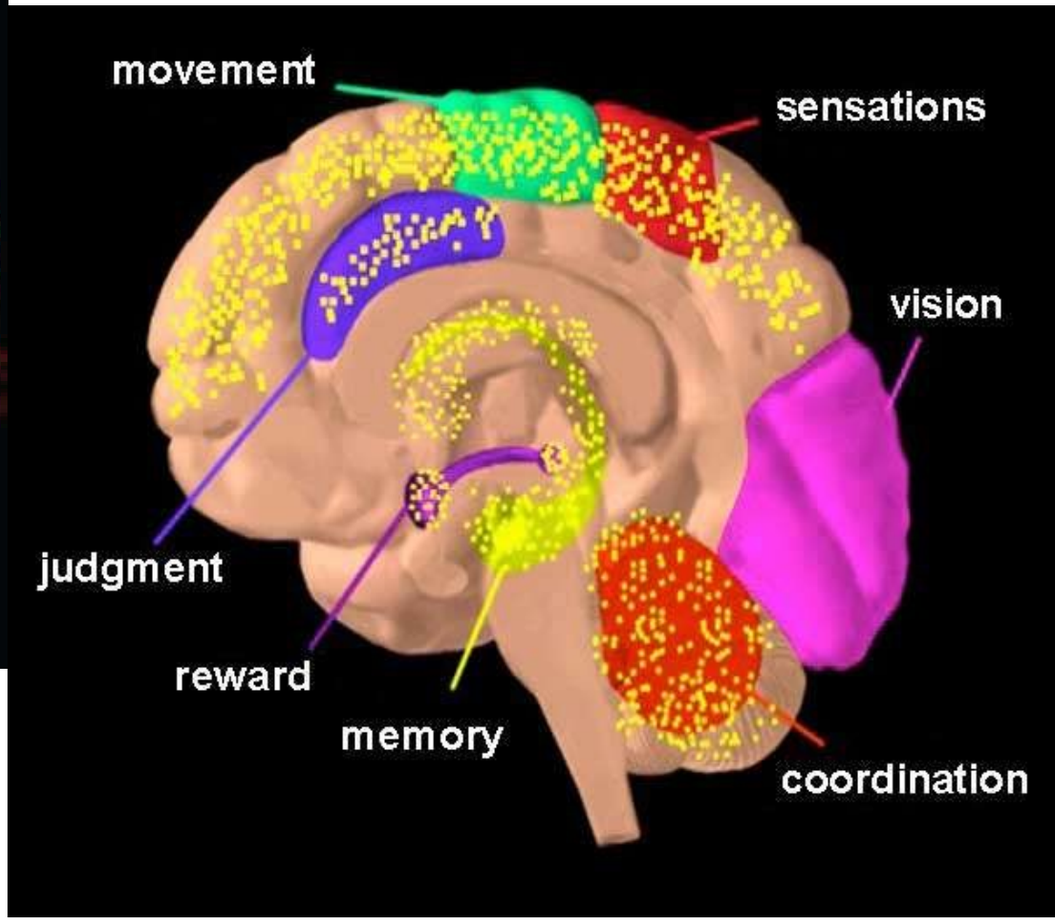
JAMA. 2015;313(24):2474-2483. doi:10.1001/jama.2015.6299

ENDOGENOUS CANNABINOID SYSTEM

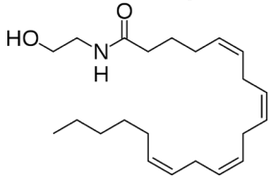
- Endogenous cannabinoids
  - Anandamide (arachidonoehanolamide)
  - 2-AG (2-arachidonoglycerol)
  - Noladin ether, Virodhamin
  - N-arachidonoyldopamine
- Receptors
  - CB1
  - CB2
  - Others
- Enzymes that synthesize and break down endocannabinoids

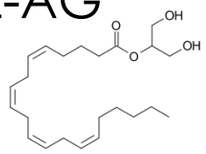
CANNABINOID RECEPTOR 1 (CB1) WIDE DISTRIBUTION IN THE BRAIN





Endogenous cannabinoids:

- Normally produced by the brain
- Anandamide 

- 2-AG 

https://www.nimh.nih.gov/labs-at-nimh/research-areas/clinics-and-labs/lcmr/sfn/past-research.shtml
https://www.drugabuse.gov/publications/drugfacts/marijuana

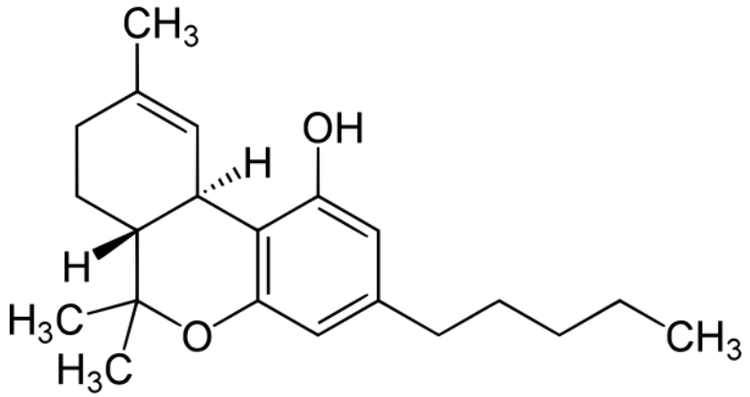
CANNABINOID RECEPTOR 1 (CB1R)

CB1 receptor location	Clinical manifestations of THC activity
Cerebral cortex	Altered consciousness, perceptual distortions, memory impairment, hallucinations
Hypothalamus	Increased appetite
Brain stem	Antiemetic, tachycardia, reduced BP, drowsiness, pain reduction, reduced spasticity, reduced tremor
Basal ganglia	Slowed reaction time
Cerebellum	Reduced spasticity, impaired coordination
Hippocampus	Memory impairment
Nucleus accumbens	Motivation and reward
Amygdala	Increased or decreased anxiety; Increased or decreased panic
Spinal cord	Altered pain sensitivity

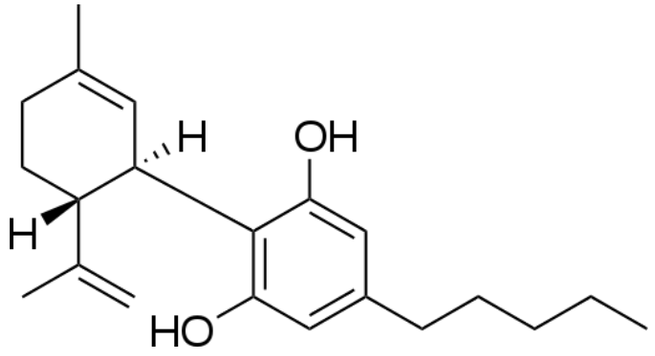
Levounis et al: Pocket Guide to Addiction Assessment and Treatment, 2016

CANNABINOIDS WE WILL DISCUSS

- Tetrahydrocannabinol (THC)(Delta-9 THC)
  - Primary compound to produce intoxicating effects or the "high"
  - Acts on CB1 receptor
  - Can cause anxiety



- Cannabidiol (CBD)
  - Not intoxicating
  - Effects:
    - Antianxiety
    - Antipsychotic
    - Antidepressant
    - Antiseizure
    - Analgesic



  - But can breakdown into Delta-9 and Delta-8 THC

Risk/Benefit Profile of Cannabis Use

HEALTH
UNIVERSITY OF UTAH

THE HEALTH EFFECTS OF CANNABIS AND CANNABINOIDS

January 2017

In the report *The Health Effects of Cannabis and Cannabinoids: The Current State of Evidence and Recommendations for Research*, an expert, ad hoc committee of the National Academies of Sciences, Engineering, and Medicine presents nearly 100 conclusions related to the health effects of cannabis and cannabinoid use and makes recommendations for an agenda to help expand and improve cannabis research efforts and better inform future public health decisions.

The Chapter Highlights below provide broad overview statements of the report's chapters regarding certain prioritized health conditions. To read the committee's conclusions in detail, as well as the definitions of weights of evidence, please see the "Committee's Conclusions" document at nationalacademies.org/CannabisHealthEffects.

Each blue header below links to the corresponding chapter in the report, providing much more detail. To read the full report, please visit **nationalacademies.org/CannabisHealthEffects.**

tting cannabis smoking is likely to reduce chronic cough and phlegm production.

It is unclear whether cannabis use is associated with COPD, asthma, or worsened lung function.

IMMUNITY

There exists a paucity of data on the effects of cannabis or cannabinoid-based therapeutics on the human immune system.

There is insufficient data to draw overarching conclusions concerning the effects of cannabis smoke or cannabinoids on immune competence.

There is limited evidence to suggest that regular exposure to cannabis smoke may have anti-inflammatory activity.

There is insufficient evidence to support or refute a statistical association between cannabis or cannabinoid use and adverse effects on immune status in individuals with HIV.

PRENATAL, PERINATAL, AND NEONATAL 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

INJURY AND DEATH

Cannabis use prior to driving increases the risk of being involved in a motor vehicle accident.

In states where cannabis use is legal, there is increased risk of unintentional cannabis overdose injuries among children.

It is unclear whether and how cannabis use is associated with all-cause mortality or with occupational injury.

PSYCHOSOCIAL

Recent cannabis use impairs the performance in cognitive domains of learning, memory, and attention. Recent use may be defined as cannabis use within 24 hours of evaluation.

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.

The National Academies of
SCIENCES • ENGINEERING • MEDICINE

http://nationalacademies.org/hmd/reports/2017/health-effects-of-cannabis-and-cannabinoids.aspx

Therapeutic Benefits

Conclusive or Substantial Evidence

- Reduce Chronic pain
- Antiemetics for chemo-induced nausea or vomiting
- Reduce MS spasticity symptoms

Moderate Evidence

- ↑ short-term sleep in obstructive sleep apnea syndrome
- fibromyalgia
- chronic pain
- MS

Limited Evidence

- ↑ appetite and ↓ weight loss associated w/ HIV/AIDS
- ↓ symptoms of Tourette syndrome
- ↓ anxiety in social anxiety disorders
- ↓ PTSD symptoms
- Improve outcomes (i.e. disability) after traumatic brain injury

No or Insufficient Evidence

- Treatments for Cancers, including glioma
- Cancer-associated anorexia cachexia syndrome and anorexia nervosa
- Symptoms of irritable bowel syndrome
- Epilepsy
- ALS symptoms
- Dystonia
- Chorea and certain symptoms associated w/ Huntington's
- Motor system symptoms associated w/ Parkinson's disease
- Spasticity in patients w/ paralysis due to spinal cord injury
- Abstinence in the use of addictive substances
- Outcomes in individuals w/ schizophrenia

Parhami I, Andres-Kim M, Hurley B, Presented at 2019 American Society Of Addiction Medicine's Annual Meeting (Adapted from: National Academies of Sciences, Engineering, and Medicine. 2017. The health effects of cannabis and cannabinoids: Current state of evidence and recommendations for research. Washington, DC: The National Academies Press.)

LOS ANGELES COUNTY DEPARTMENT OF MENTAL HEALTH
hope. recovery. wellbeing.

Associated Risks

	MEDICAL RISKS	MENTAL HEALTH RISKS
Conclusive or Substantial Evidence	▪ ↑ respiratory symptoms and chronic bronchitis episodes ▪ ↑ motor vehicle crashes ▪ ↑ lower birth weight of offspring	↑ schizophrenia or other psychoses, w/ highest risk among most frequent users
Moderate Evidence	▪ ↑ overdose injuries, including respiratory distress, among pediatric populations ▪ CESSATION of cannabis use associated w/ improvements in respiratory symptoms ▪ NO association w/ lung, head and neck cancers	▪ ↑ Impairment in learning, memory, and attention ▪ ↑ Bipolar and Depression symptoms ▪ ↑ suicidality w/ higher incidence among heavier users ▪ ↑ social anxiety disorder ▪ ↑ negative symptoms of schizophrenia
Limited Evidence	▪ ↑ prediabetes, ↑ acute MI or stroke ▪ ↑ COPD ▪ ↑ pregnancy complications, ↑ admission of infant to neonatal ICU ▪ ↑ non-seminoma-type testicular tumors ▪ ↓ production of several inflammatory cytokines ▪ ↓ metabolic syndrome and diabetes	▪ ↓ academic achievement ▪ ↑ unemployment/low income rates ▪ ↓ social functioning and developmentally appropriate social roles ▪ sustained abstinence continues to be associated ↓ cognitive domains of learning ▪ ↑ positive symptoms of schizophrenia (e.g., hallucinations) ▪ ↑ anxiety symptoms ▪ ↑ PTSD severity ▪ ↑ development of bipolar or any anxiety disorder, except social anxiety disorder
No or Insufficient Evidence	▪ Esophageal, bladder, prostate, cervical, penile, and anal cancer; malignant gliomas, non-Hodgkin lymphoma, Kaposi's sarcoma, leukemia, rhabdomyosarcoma, astrocytoma, or neuroblastoma in offspring ▪ Asthma development or asthma exacerbation ▪ Hospital admissions for COPD ▪ All-cause mortality	▪ Occupational accidents or injuries ▪ Death due to cannabis overdose ▪ Later outcomes in offspring (e.g., sudden infant death syndrome, cognition/academic achievement, and later substance use) ▪ Development of PTSD ▪ Changes in course of depressive disorders

Parhami I, Andres-Kim M, Hurley B, Presented @ 2019 American Society Of Addiction Medicine's Annual Meeting (Adapted from: National Academies of Sciences, Engineering, and Medicine. 2017. The health effects of cannabis and cannabinoids: Current state of evidence and recommendations for research. Washington, DC: The National Academies Press.)

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Therapeutic Evidence for Cannabis Use

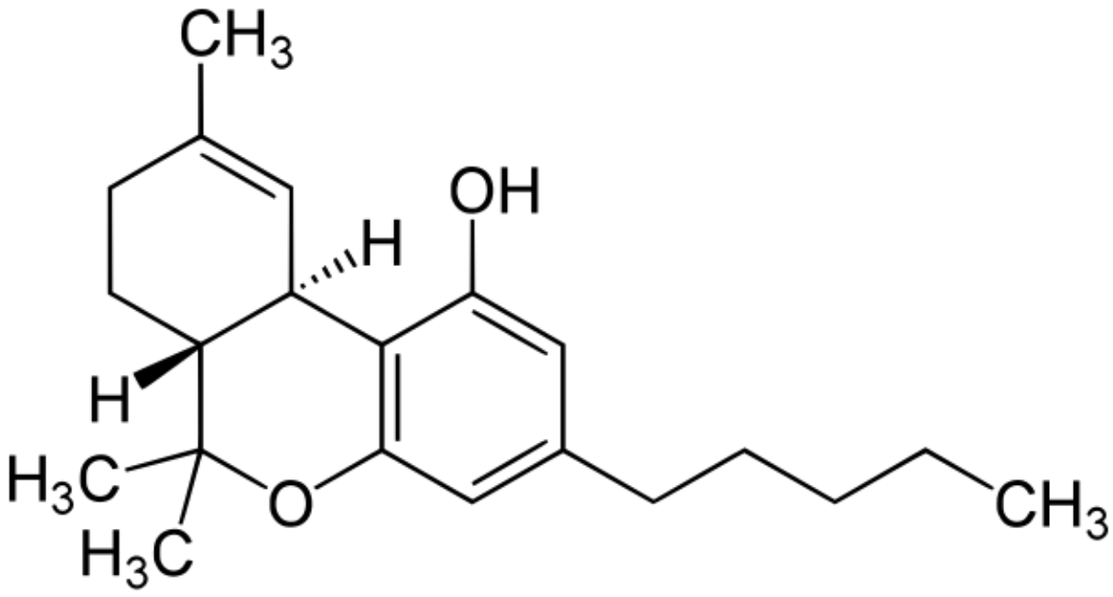
	Medical Disorders	Psychiatric Disorders
Rating 3: Strong Evidence	Spasticity in Multiple Sclerosis Neuropathic Pain	**NONE**
Rating 2: Equivocal or Modest Evidence	Chemotherapy-Induced Nausea/Vomiting HIV Wasting Syndrome	Depressive Disorders Panic Disorders Generalized Anxiety Disorder PTSD SUDs
Rating 1: Minimal or No Evidence	Glaucoma	NONE
CLEAR HARMS	--	**Schizophrenia** **Bipolar Disorders**

George, T.P. et al., 2017, under review

Not your parents' or grandparents' marijuana?

CANNABINOIDS

- Tetrahydrocannabinol (THC)(Delta-9 THC)
  - Primary compound to produce intoxicating effects or the "high"
  - Acts on CB1 receptor
  - Can cause anxiety



THC CONTENT OF CANNABIS PRODUCTS

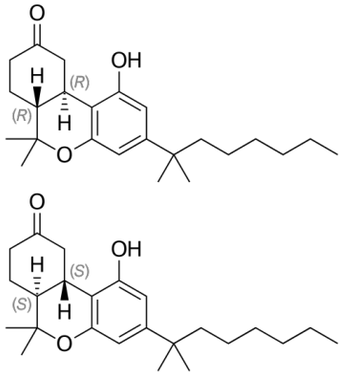
- THC content of cannabis products
  - Whole plant: 1-5% THC
    - However, many hybrid strains with names like Girl Scout Cookies, King Tut, Blissful Wizard have THC concentrations up to 35% THC; others up to 50+%
  - Unfertilized flowers: 7-15% THC
  - Hashish or resin: 10-20% THC
  - Hash oil: 20-60% THC
  - Dab, shatter: 80-90% THC
- Route of Use
  - Smoking, vaporizing: onset 1 min, high lasts 4 hrs
  - Ingesting: onset 30 mins, high lasts 12 hrs
  - Topical (oils): variable onset and effects

EXAMPLES OF DOSING FROM DIFFERENT FORMS OF THC

- Dose obtained from smoking cannabis= 2 mg
- Dose in 1 "serving" of retail edible=10 mg
- Total amount in medical edible=100 mg
- Medical capsule/suppositories=up to 100 mg
- Concentrate or tincture:
  - 1000 mg/container retail
  - 4000 mg/container medical

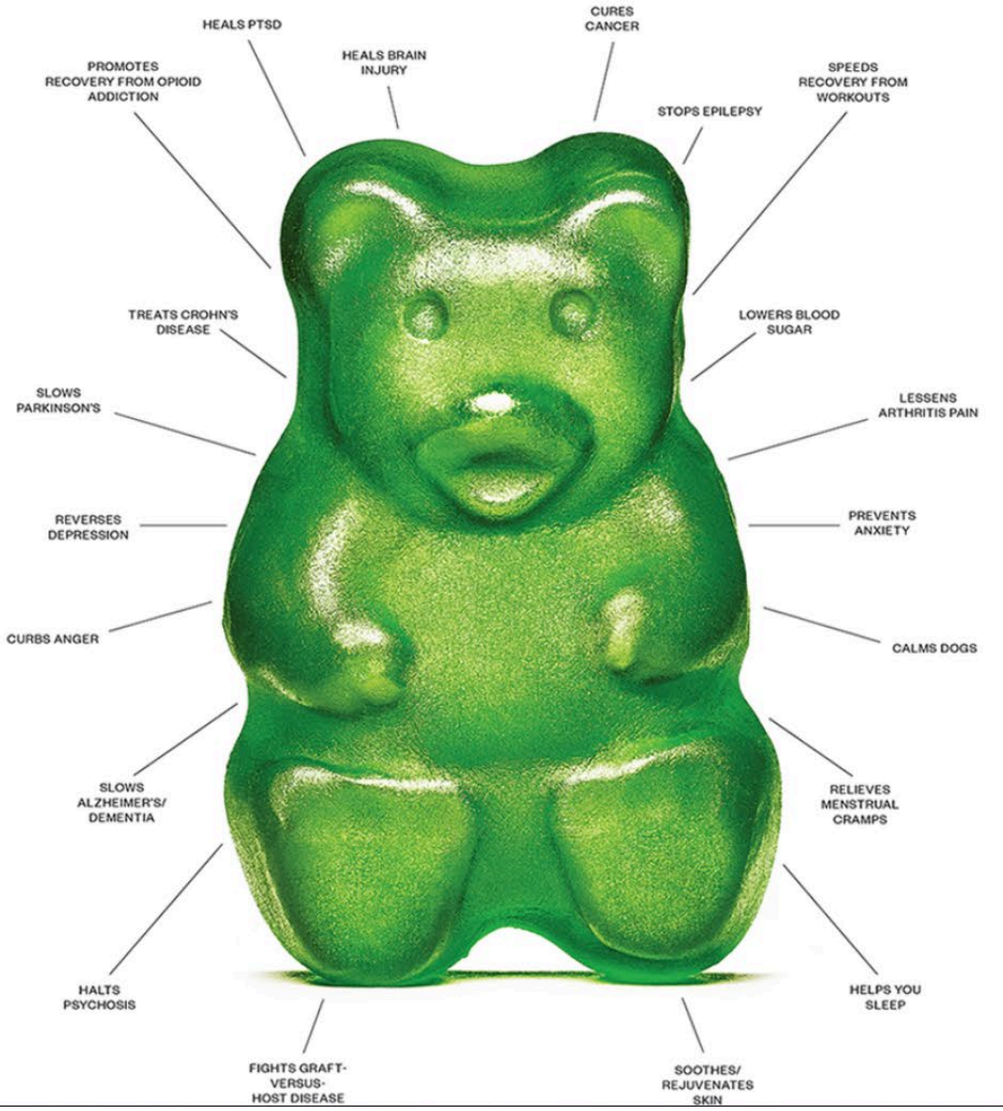
PHARMACEUTICAL GRADE CANNABINOIDS

- US FDA-approved cannabinoids
  - Dronabinol (Marinol ®, THC) oral C-III; 2.5 mg, 5 mg, 10 mg caps
    - Anorexia in people with HIV/AIDS
    - Refractory nausea and vomiting in people undergoing chemotherapy (CINV)
  - Nabilone (Cesamet ®) C-III; 1 mg caps
    - For severe nausea and vomiting caused by cancer chemotherapy (CINV)
  - Cannabidiol (Epidiolex®) oral (CBD) C-V
    - Treatment resistant seizures
    - Available in U.S. 2018
    - oral solution 100mg/ml; dosing 5-20 mg/kg BID
- **Approved in UK and other countries, not US**
  - Nabiximols (Sativex®) oral mucosal spray (100 ml)
    - ~50/50 mixture THC (2.7 mg) and CBD (2.5 mg) in each dose
    - Spasticity in MS



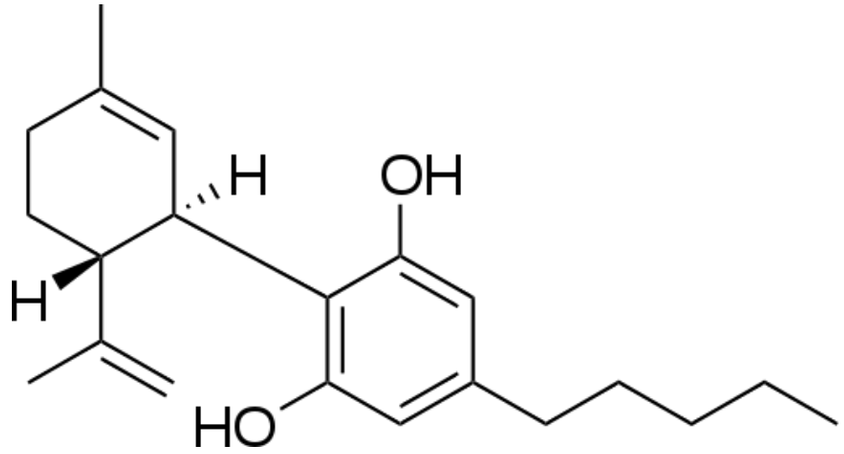
THE MIRACLE OF CBD?

Even a bed of roses has thorns….



https://www.nytimes.com/interactive/2019/05/14/magazine/cbd-cannabis-cure.html?searchResultPosition=5

CANNABINOIDS



- Cannabidiol (CBD)
  - Addictive properties?
    - Many commercially available "CBD" preparations contain THC; Buyer Beware
    - CBD can breakdown into Delta-9 and Delta-8 THC
      - Not significant on drug screens, according to ARUP
  - Adverse effects with pharmaceutical grade CBD:
    - somnolence; decreased appetite; diarrhea; transaminase elevations; fatigue, malaise, and asthenia; rash; insomnia, sleep disorder and poor-quality sleep; infections; hematologic abnormalities; suicidal ideation. [listed in FDA-approved information]
  - Organ damage?
    - Risk of liver damage even with pharmaceutical grade CBD (Epidiolex®)

CBD AND LIVER DAMAGE: CONFLICTING RESULTS

- Wang Y et al, 2017:
  - CBD improved chronic-plus-binge-alcohol-induced hepatocellular liver injury in **mice**
  - CBD attenuates alcohol-induced liver steatosis and dysregulation of numerous key genes and pathways implicated in development of alcohol-induced steatohepatitis.
- Ewing LE et al, 2019:
  - In **mice**, CBD exhibited clear signs of hepatotoxicity, possibly of a cholestatic nature.

CANNABIDIOL (EPIDIOLEX®) WARNINGS AND PRECAUTIONS

- **Hepatocellular Injury:**
  - Can cause dose-related transaminase elevations.
  - Concomitant use of valproate and elevated transaminase levels at baseline increase this risk.
  - Transaminase and bilirubin levels should be obtained prior to starting treatment, at one, three, and six months after initiation of treatment, and periodically thereafter, or as clinically indicated.
  - Resolution of transaminase elevations occurred with discontinuation, reduction of cannabidiol and/or concomitant valproate, or without dose reduction.
  - Dose adjustment and slower dose titration is recommended in patients with moderate or severe hepatic impairment. Consider not initiating in patients with evidence of significant liver injury.
  - Transaminase elevations are dose-related. Overall, **ALT elevations greater than 3 times the ULN were reported in 17% of patients taking 20 mg/kg/day compared with 1% in patients taking 10 mg/kg/day.**
- **Somnolence and Sedation:**
  - Can cause somnolence and sedation that generally occurs early in treatment and may diminish over time; these effects occur more commonly in patients using clobazam and may be potentiated by other CNS depressants.

https://www.epidiolexhcp.com/; FDA-approved

CANNABIDIOL (EPIDIOLEX®) WARNINGS AND PRECAUTIONS

- **Suicidal Behavior and Ideation:** Antiepileptic drugs (AEDs), including cannabidiol, increase the risk of suicidal thoughts or behavior. Inform patients, caregivers, and families of the risk and advise to monitor and report any signs of depression, suicidal thoughts or behavior, or unusual changes in mood or behavior. If these symptoms occur, consider if they are related to the AED or the underlying illness.
- **Adverse Reactions:** The most common adverse reactions in patients receiving cannabidiol (≥10% and greater than placebo) include somnolence; decreased appetite; diarrhea; transaminase elevations; fatigue, malaise, and asthenia; rash; insomnia, sleep disorder and poor-quality sleep; and infections. Hematologic abnormalities were also observed.

https://www.epidiolexhcp.com/; FDA-approved

ADDICTIVE POTENTIAL OF CANNABIS

- All users → 9% addicted/CUD
- Adolescent users → 17% addicted/CUD
- Daily users → 25-50% addicted/CUD

NIDA Drug Facts: Lopez-Quintero C et al, 2011;

DSM-5 DISORDERS

- Cannabis Use Disorder (CUD) criteria consistent with other Use DO's
- Cannabis Intoxication
- Cannabis Withdrawal

Intoxication:

- Clinically significant problematic behavioral or psychological changes: impaired motor coordination, euphoria, anxiety, sensation of slowed time, impaired judgment, social withdrawal
- Two (or more) within 2 hours of use:
  - Conjunctival injection.
  - Increased appetite.
  - Dry mouth.
  - Tachycardia.

Withdrawal:

- Cessation of cannabis use that has been heavy and prolonged
- (Three (or more) of the following develop within approximately 1 week:
  - Irritability, anger, or aggression.
  - Nervousness or anxiety.
  - Sleep difficulty (e.g., insomnia, disturbing dreams).
  - Decreased appetite or weight loss.
  - Restlessness.
  - Depressed mood.
  - At least one of the following physical symptoms causing significant discomfort: abdominal pain, shakiness/tremors, sweating, fever, chills, or headache.

SCREENING FOR CANNABIS USE DISORDERS

- CUDIT-R
- Cannabis Use Disorders Identification Test—Revised
- 8 questions, scored 0-4 points each
- Cutoffs:
  - Score ≥ 8 = hazardous Cannabis Use
  - Score ≥ 12 = Possible CUD, see an expert

The Cannabis Use Disorder Identification Test – Revised (CUDIT-R)

Have you used any cannabis over the past six months? YES / NO

If YES, please answer the following questions about your cannabis use. Circle the response that is most correct for you in relation to your cannabis use *over the past six months*

1. How often do you use cannabis?

Never	Monthly or less	2-4 times a month	2-3 times a week	4 or more times a week
0	1	2	3	4

2. **How many hours were you "stoned" on a typical day when you had been using cannabis?**

Less than 1	**1 or 2**	**3 or 4**	**5 or 6**	**7 or more**
0	**1**	**2**	**3**	**4**

3. How often during the past 6 months did you find that you were not able to stop using cannabis once you had started?

Never	Less than monthly	Monthly	Weekly	Daily or almost daily
0	1	2	3	4

4. **How often during the past 6 months did you fail to do what was normally expected from you because of using cannabis?**

Never	**Less than monthly**	**Monthly**	**Weekly**	**Daily or almost daily**
0	**1**	**2**	**3**	**4**

5. How often in the past 6 months have you devoted a great deal of your time to getting, using, or recovering from cannabis?

Never	Less than monthly	Monthly	Weekly	Daily or almost daily
0	1	2	3	4

6. **How often in the past 6 months have you had a problem with your memory or concentration after using cannabis?**

Never	**Less than monthly**	**Monthly**	**Weekly**	**Daily or almost daily**
0	**1**	**2**	**3**	**4**

7. How often do you use cannabis in situations that could be physically hazardous, such as driving, operating machinery, or caring for children:

Never	Less than monthly	Monthly	Weekly	Daily or almost daily
0	1	2	3	4

8. **Have you ever thought about cutting down, or stopping, your use of cannabis?**

Never	**Yes, but not in the past 6 months**	**Yes, during the past 6 months**
0	**2**	**4**

This scale is in the public domain and is free to use with appropriate citation:

Adamson SJ, Kay-Lambkin FJ, Baker AL, Lewin TJ, Thornton L, Kelly BJ, and Sellman JD. (2010). An Improved Brief Measure of Cannabis Misuse: The Cannabis Use Disorders Identification Test – Revised (CUDIT-R). *Drug and Alcohol Dependence* 110:137-143.

https://alcol
https://www

This questionnaire was designed for self administration and is scored by adding each of the 8 items:
- Question 1-7 are scored on a 0-4 scale
- Question 8 is scored 0, 2 or 4.

Scores of 8 or more indicate hazardous cannabis use, while scores of 12 or more indicate a possible cannabis use disorder for which further intervention may be required.

DRUG TESTING ISSUES

- THC is detectable in urine drug screens (UDS) for up to 4 weeks in regular or heavy users
  - Long half-life metabolites, fat storage, enterohepatic recirculation
- Threshold of 50 ng/ml for initial screening
  - Passive inhalation studies not above 20 ng/ml
- False positives:
  - Marinol (because it is THC)
  - Efavirenz
  - Unlikely NSAIDs, Hemp foods

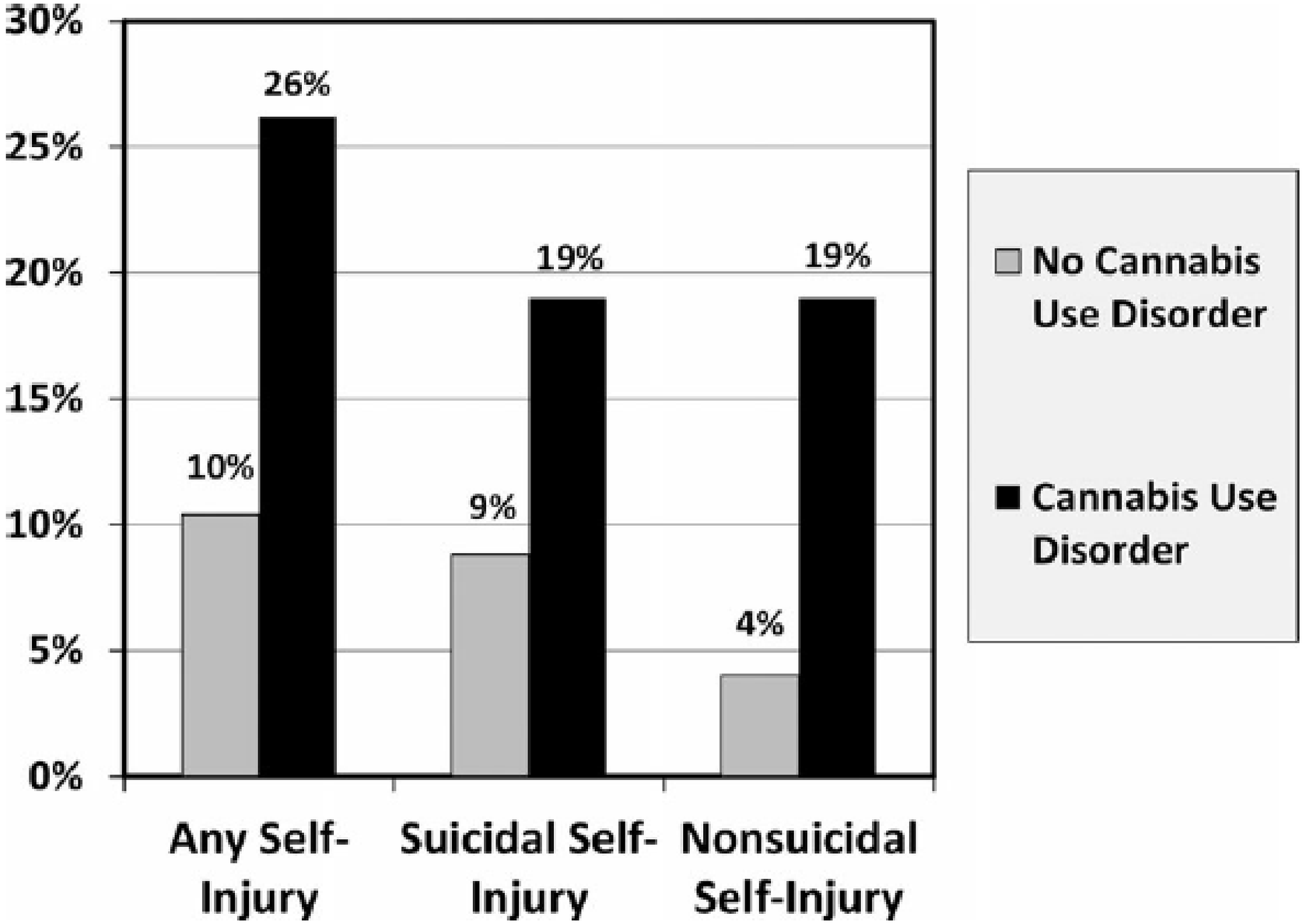
Adverse Health Effects of Cannabis

HEALTH
UNIVERSITY OF UTAH

ASSOCIATED HEALTH EFFECTS OF CANNABIS

- Suicide
- Self-harm
- Psychosis
- PTSD
- Opioid overdose
- Cardiovascular health
- Cannabis hyperemesis syndrome
- Motor vehicle accidents
- ED visits

CANNABIS USE DISORDER/SELF-INJURY

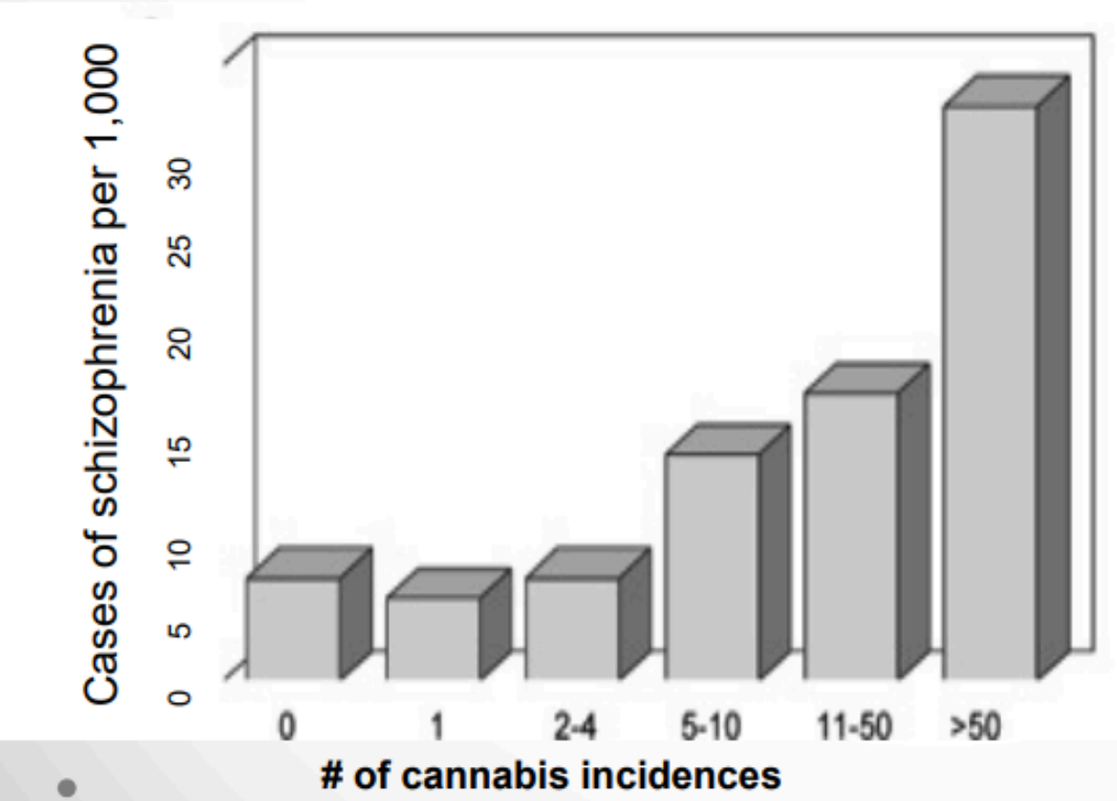


Kimbrel, N. A., Meyer, E. C., DeBeer, B. B., Gulliver, S. B. and Morissette, S. B. (2017), The Impact of Cannabis Use Disorder on Suicidal and Nonsuicidal Self-Injury in Iraq/Afghanistan-Era Veterans with and without Mental Health Disorders. Suicide and Life-Threat Behaviors.

Schizophrenia & Cannabis: Dose Effects

- Specificity to schizophrenia
- Dose-response relationship

Swedish Conscript Sample (N=50,053)



Cannabis use is associated with an increased risk of developing schizophrenia in a dose dependent fashion

Andreassen et al. Acta Psych Scand 1989

The contribution of cannabis use to variation in the incidence of psychotic disorder across Europe (EU-GEI): a multicentre case-control study

*Marta Di Forti, Diego Quattrone, Tom P Freeman, Giada Tripoli, Charlotte Gayer-Anderson, Harriet Quigley, Victoria Rodriguez, Hannah E Jongsma, Laura Ferraro, Caterina La Cascia, Daniele La Barbera, Ilaria Tarricone, Domenico Berardi, Andrei Szöke, Celso Arango, Andrea Tortelli, Eva Velthorst, Miguel Bernardo, Cristina Marta Del-Ben, Paulo Rossi Menezes, Jean-Paul Selten, Peter B Jones, James B Kirkbride, Bart PF Rutten, Lieuwe de Haan, Pak C Sham, Jim van Os, Cathryn M Lewis, Michael Lynskey, Craig Morgan, Robin M Murray, and the EU-GEI WP2 Group**

Summary

Background Cannabis use is associated with increased risk of later psychotic disorder but whether it affects incidence of the disorder remains unclear. We aimed to identify patterns of cannabis use with the strongest effect on odds of psychotic disorder across Europe and explore whether differences in such patterns contribute to variations in the incidence rates of psychotic disorder.

Methods We included patients aged 18–64 years who presented to psychiatric services in 11 sites across Europe and Brazil with first-episode psychosis and recruited controls representative of the local populations. We applied adjusted logistic regression models to the data to estimate which patterns of cannabis use carried the highest odds for psychotic disorder. Using Europe-wide and national data on the expected concentration of Δ^9-tetrahydrocannabinol (THC) in the different types of cannabis available across the sites, we divided the types of cannabis used by participants into two categories: low potency (THC <10%) and high potency (THC ≥10%). Assuming causality, we calculated the population attributable fractions (PAFs) for the patterns of cannabis use associated with the highest odds of psychosis and the correlation between such patterns and the incidence rates for psychotic disorder across the study sites.

Findings Between May 1, 2010, and April 1, 2015, we obtained data from 901 patients with first-episode psychosis across 11 sites and 1237 population controls from those same sites. Daily cannabis use was associated with increased odds of psychotic disorder compared with never users (adjusted odds ratio [OR] 3·2, 95% CI 2·2–4·1), increasing to nearly five-times increased odds for daily use of high-potency types of cannabis (4·8, 2·5–6·3). The PAFs calculated indicated that if high-potency cannabis were no longer available, 12·2% (95% CI 3·0–16·1) of cases of first-episode psychosis could be prevented across the 11 sites, rising to 30·3% (15·2–40·0) in London and 50·3% (27·4–66·0) in Amsterdam. The adjusted incident rates for psychotic disorder were positively correlated with the prevalence in controls across the 11 sites of use of high-potency cannabis ($r=0·7$; p=0·0286) and daily use ($r=0·8$; p=0·0109).

Interpretation Differences in frequency of daily cannabis use and in use of high-potency cannabis contributed to the striking variation in the incidence of psychotic disorder across the 11 studied sites. Given the increasing availability of high-potency cannabis, this has important implications for public health.

Funding source Medical Research Council, the European Community's Seventh Framework Program grant, São Paulo Research Foundation, National Institute for Health Research (NIHR) Biomedical Research Centre (BRC) at South London and Maudsley NHS Foundation Trust and King's College London and the NIHR BRC at University College London, Wellcome Trust.

Lancet Psychiatry 2019

Published Online
March 19, 2019
http://dx.doi.org/10.1016/S2215-0366(19)30048-3

See Online/Comment
http://dx.doi.org/10.1016/S2215-0366(19)30086-0

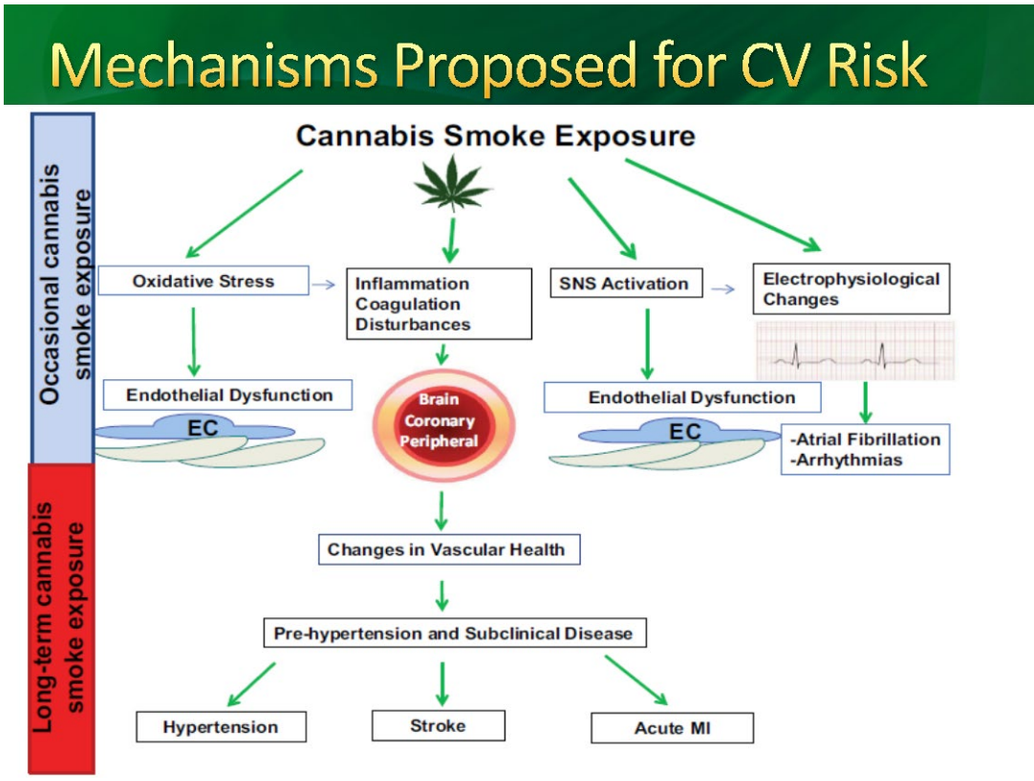
*Collaborators listed in the appendix

Social, Genetic and Developmental Psychiatry Centre (M Di Forti PhD, D Quattrone MD, Prof P C Sham PhD, Prof C M Lewis PhD) **and Department of Addiction** (Prof M Lynskey PhD), **Institute of Psychiatry, Psychology and Neuroscience and Department of Psychosis Studies** (G Tripoli MSc, H Quigley MD, V Rodriguez MD, Prof J van Os PhD, Prof R M Murray FRS) **and Department of Health Service and Population Research** (C Gayer-Anderson PhD, Prof C Morgan PhD), **Institute of Psychiatry, King's College London, London, UK; National Institute for Health Research (NIHR) Mental Health Biomedical Research Centre at South London and Maudsley NHS Foundation Trust and King's College London, UK** (M Di Forti, D Quattrone, Prof C M Lewis); **South London and Maudsley NHS Mental**

Increased odds for developing first episode psychotic disorder

CARDIAC COMPLICATIONS OF CANNABIS USE

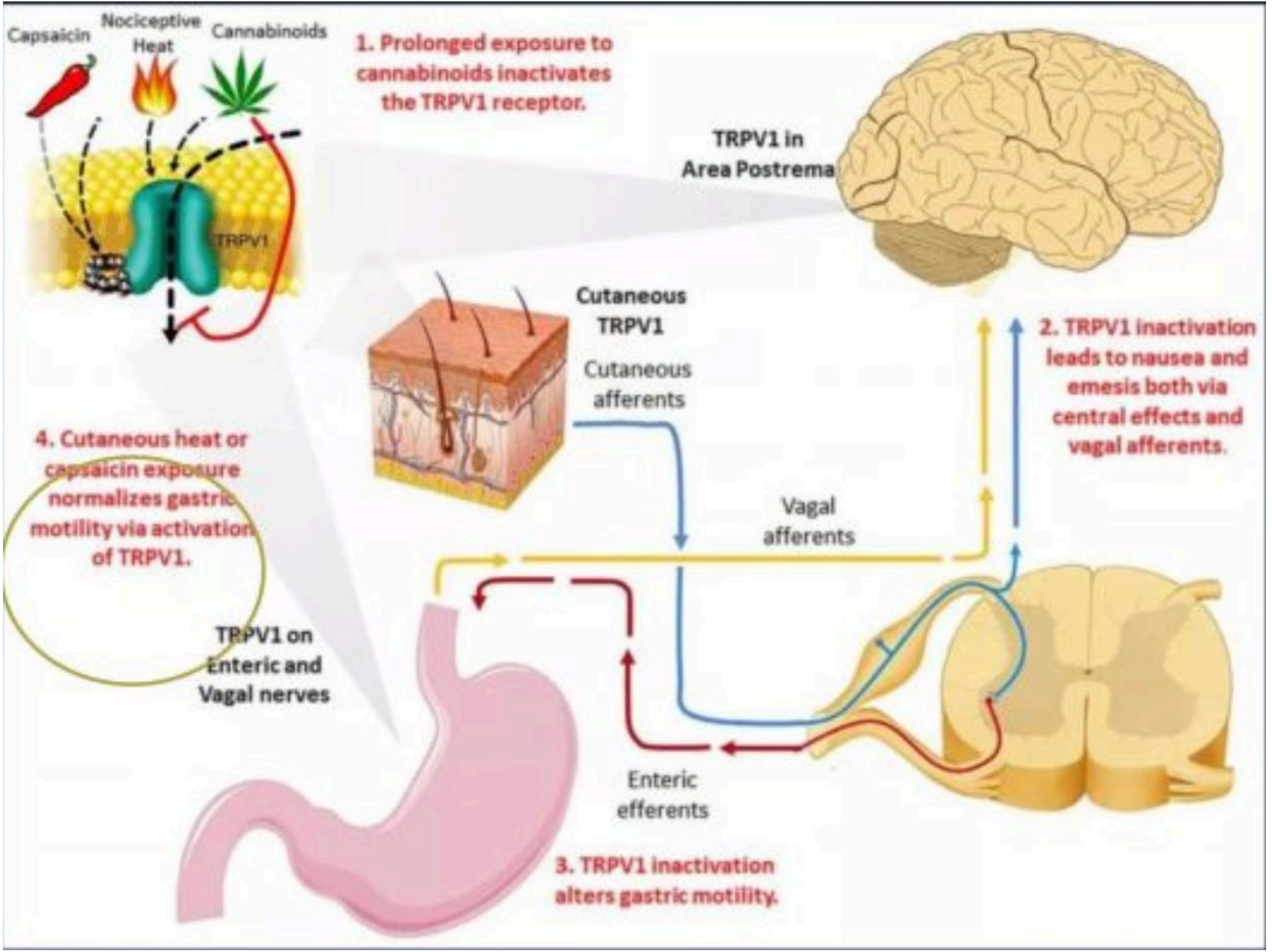
- Cannabis can cause significant cardiac effects:
  - Ischemia vs QTc prolongation
  - Ventricular tachycardia
  - Myocardial infarction
  - Asystole



CANNABIS HYPEREMESIS SYNDROME

- Cannabis hyperemesis syndrome:
  - Cyclic vomiting for hours->days
  - Abdominal pain, nausea
  - Compulsive bathing/showering with hot water
  - Excessive thirst
  - Gastric pain, esophagitis, gastritis
  - In extreme cases, death from complications of chronic vomiting
- Treatment
  - Stop cannabis use (permanently)
  - Fluids, electrolyte repletion
  - Capsaicin topical cream

Nourbakhsh M et al. J Forensic Sci. 2019 Jan;64(1):270-274.



Capsaicin binds TRPV1 (transient receptor potential vanilloid 1) with high specificity, impairing substance P signaling in the area postrema and nucleus tractus solitarius via overstimulation of TRPV1.

IS CANNABIS THE SOLUTION TO THE OPIOID CRISIS? 2014

Research

Original Investigation

Medical Cannabis Laws and Opioid Analgesic Overdose Mortality in the United States, 1999-2010

Marcus A. Bachhuber, MD; Brendan Saloner, PhD; Chinazo O. Cunningham, MD, MS; Colleen L. Barry, PhD, MPP

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

JAMA Intern Med. 2014;174(10):1668-1673

Annals of Internal Medicine

REVIEW

The Effects of Cannabis Among Adults With Chronic Pain and an Overview of General Harms

A Systematic Review

Ann Intern Med. 2017 Sep 5;167(5):319-33

Shannon M. Nugent, PhD; Benjamin J. Morasco, PhD; Maya E. O'Neil, PhD; Michele Freeman, MPH; Allison Low, BA; Karli Kondo, PhD; Camille Elven, MD; Bernadette Zakher, MBBS; Makalapua Motu'apuaka, BA; Robin Paynter, MLIS; and Devan Kansagara, MD, MCR

Background: Cannabis is increasingly available for the treatment of chronic pain, yet its efficacy remains uncertain.

Purpose: To review the benefits of plant-based cannabis preparations for treating chronic pain in adults and the harms of cannabis use in chronic pain and general adult populations.

Data Sources: MEDLINE, Cochrane Database of Systematic Reviews, and several other sources from database inception to March 2017.

Study Selection: Intervention trials and observational studies, published in English, involving adults using plant-based cannabis preparations that reported pain, quality of life, or adverse effect outcomes.

Data Extraction: Two investigators independently abstracted study characteristics and assessed study quality, and the investigator group graded the overall strength of evidence using standard criteria.

Data Synthesis: From 27 chronic pain trials, there is low-strength evidence that cannabis alleviates neuropathic pain but insufficient evidence in other pain populations. According to 11 systematic reviews and 32 primary studies, harms in general population studies include increased risk for motor vehicle accidents, psychotic symptoms, and short-term cognitive impairment. Although adverse pulmonary effects were not seen in younger populations, evidence on most other long-term physical harms, in heavy or long-term cannabis users, or in older populations is insufficient.

Limitation: Few methodologically rigorous trials; the cannabis formulations studied may not reflect commercially available products; and limited applicability to older, chronically ill populations and patients who use cannabis heavily.

Conclusion: Limited evidence suggests that cannabis may alleviate neuropathic pain in some patients, but insufficient evidence exists for other types of chronic pain. Among general populations, limited evidence suggests that cannabis is associated with an increased risk for adverse mental health effects.

Primary Funding Source: U.S. Department of Veterans Affairs. (PROSPERO: CRD42016033623)

Ann Intern Med. 2017;167:319-331. doi:10.7326/M17-0155 **Annals.org**

For author affiliations, see end of text.

This article was published at Annals.org on 15 August 2017.

CANNABIS AND THE OPIOID CRISIS

- Epidemiological studies of large samples of chronic pain patients:
  - Cannabis users do not use lower opioid doses than opioid users who do not use cannabis
- Analysis of NESARC data:
  - People who reported cannabis use at baseline were more (not less) likely to have an opioid use disorder 3 years later.
  - This was also true among cannabis users who reported moderate to severe pain and opioid use at baseline.
- More recent studies:
  - Increased opioid OD death rates by 52% in states that legalized cannabis

https://onlinelibrary.wiley.com/doi/full/10.1111/add.14139 ;
Bleyer et al, JAMA Int Med 2018. Olafson M et al: Am J Psychiatry 2018; 175:47–53

2019

Association between medical cannabis laws and opioid overdose mortality has reversed over time

Chelsea L. Shover[a,1], Corey S. Davis[b], Sanford C. Gordon[c], and Keith Humphreys[a,d]

[a]Department of Psychiatry and Behavioral Sciences, Stanford University, Stanford, CA 94305; [b]The Network for Public Health Law, Carrboro, NC 27516; [c]Wilf Family Department of Politics, New York University, New York, NY 10012; and [d]Center for Innovation to Implementation, Veterans Affairs Health Care System, Palo Alto, CA 94304

Edited by Kenneth W. Wachter, University of California, Berkeley, CA, and approved May 16, 2019 (received for review February 27, 2019)

Medical cannabis has been touted as a solution to the US opioid overdose crisis since Bachhuber et al. [M. A. Bachhuber, B. Saloner, C. O. Cunningham, C. L. Barry, *JAMA Intern. Med.* 174, 1668–1673] found that from 1999 to 2010 states with medical cannabis laws experienced slower increases in opioid analgesic overdose mortality. That research received substantial attention in the scientific literature and popular press and served as a talking point for the cannabis industry and its advocates, despite caveats from the authors and others to exercise caution when using ecological correlations to draw causal, individual-level conclusions. In this study, we used the same methods to extend Bachhuber et al.'s analysis through 2017. Not only did findings from the original analysis not hold over the longer period, but the association between state medical cannabis laws and opioid overdose mortality reversed direction from −21% to +23% and remained positive after accounting for recreational cannabis laws. We also uncovered no evidence that either broader (recreational) or more restrictive (low-tetrahydrocannabinol) cannabis laws were associated with changes in opioid overdose mortality. We find it unlikely that medical cannabis—used by about 2.5% of the US population—has exerted large conflicting effects on opioid overdose mortality. A more plausible interpretation is that this association is spurious. Moreover, if such relationships do exist, they cannot be rigorously discerned with aggregate data. Research into therapeutic potential of cannabis should continue, but the claim that enacting medical cannabis laws will reduce opioid overdose death should be met with skepticism.

medical cannabis | opioid overdose | public policy

also increased dramatically over that time period (8). Using the same methods as Bachhuber et al. (1), we revisited the question with seven more years of data. To investigate how newer cannabis laws may be associated with changes in the association between cannabis laws and opioid overdose mortality, we also created a model with additional terms to account for presence of a recreational cannabis law or a low-THC restriction. Because none of the states with low-THC laws operate medical dispensaries and many limit access to a small number of indications, the levels of access can be approximated as highest for recreational, then "comprehensive" medical with dispensaries, and lowest for states with low-THC only. If broader access to cannabis writ large, rather than medical cannabis specifically, is the latent factor associated with lower opioid overdose mortality, we would expect to see the most negative association in states with recreational laws and the least negative association (or even positive) association in states with low-THC-only laws.

Results

For the original 1999–2010 time period, we obtained estimates similar to Bachhuber et al. (1), with slight differences likely due to missing values for 30 state/year combinations. Whereas Bachhuber et al. (1) estimated a 24.8% reduction in deaths per 100,000 population associated with a medical cannabis law's introduction, we estimated a statistically indistinguishable 21.1% decrease. As in the original model, none of the four time-varying covariates (annual state unemployment rate and presence of the following: prescription drug monitoring program, pain management clinic oversight laws, and law requiring or allowing pharmacists to request patient identification) were significantly associated with opioid overdose mortality (Table 1). Using the

Stover CL et al. PNAS June 25, 2019 116 (26) 12624-12626; first published June 10, 2019 https://doi.org/10.1073/pnas.1903434116

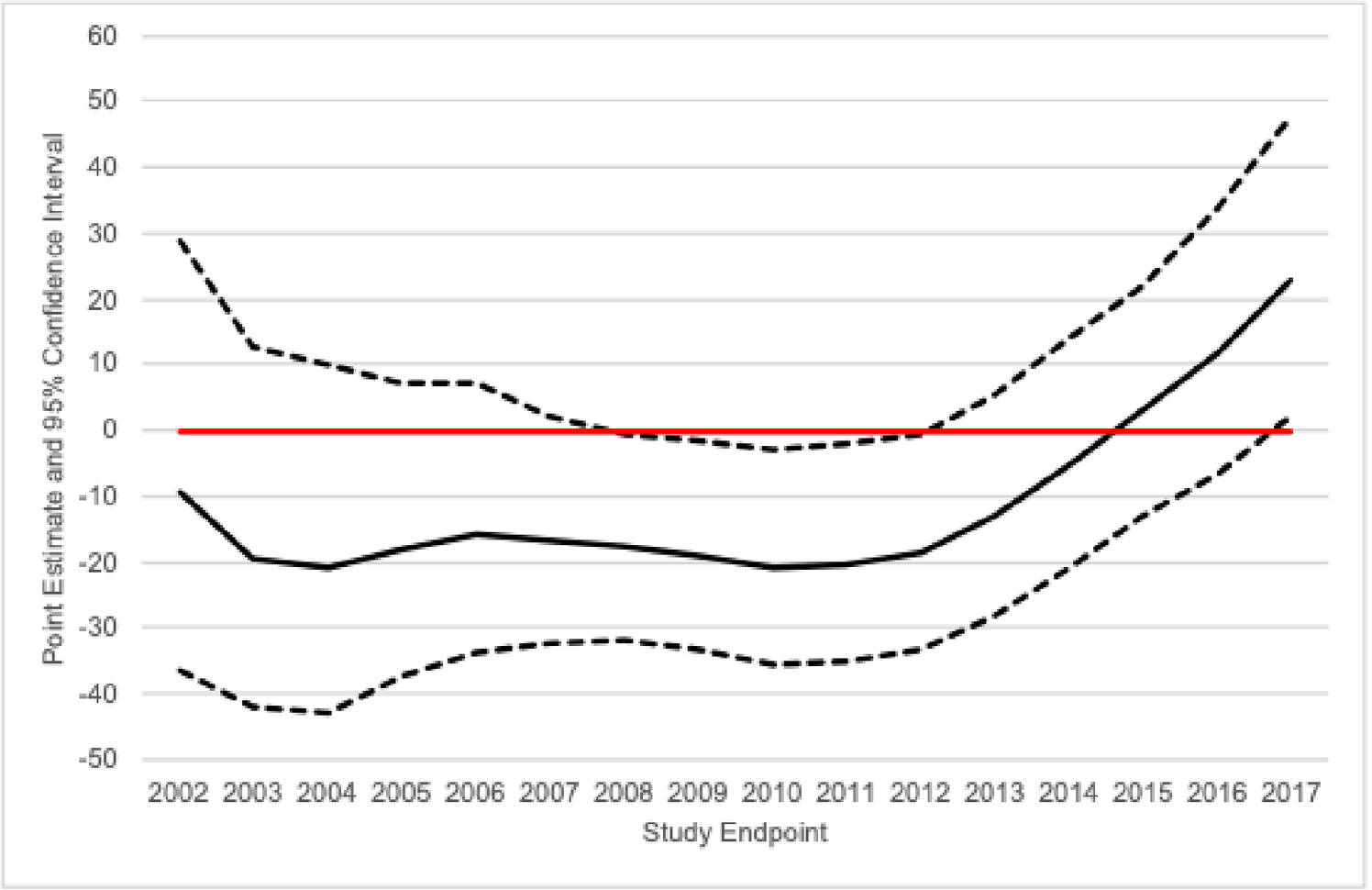


Fig. 1. Changes in point estimate and 95% CI of association between medical cannabis law and age-adjusted opioid overdose death rate by the last year included in the analysis since 1999. Fixed (year and state) and time-varying effects (prescription drug monitoring program, state unemployment, pain management clinic oversight laws, and prescription drug identification laws) were also adjusted for.

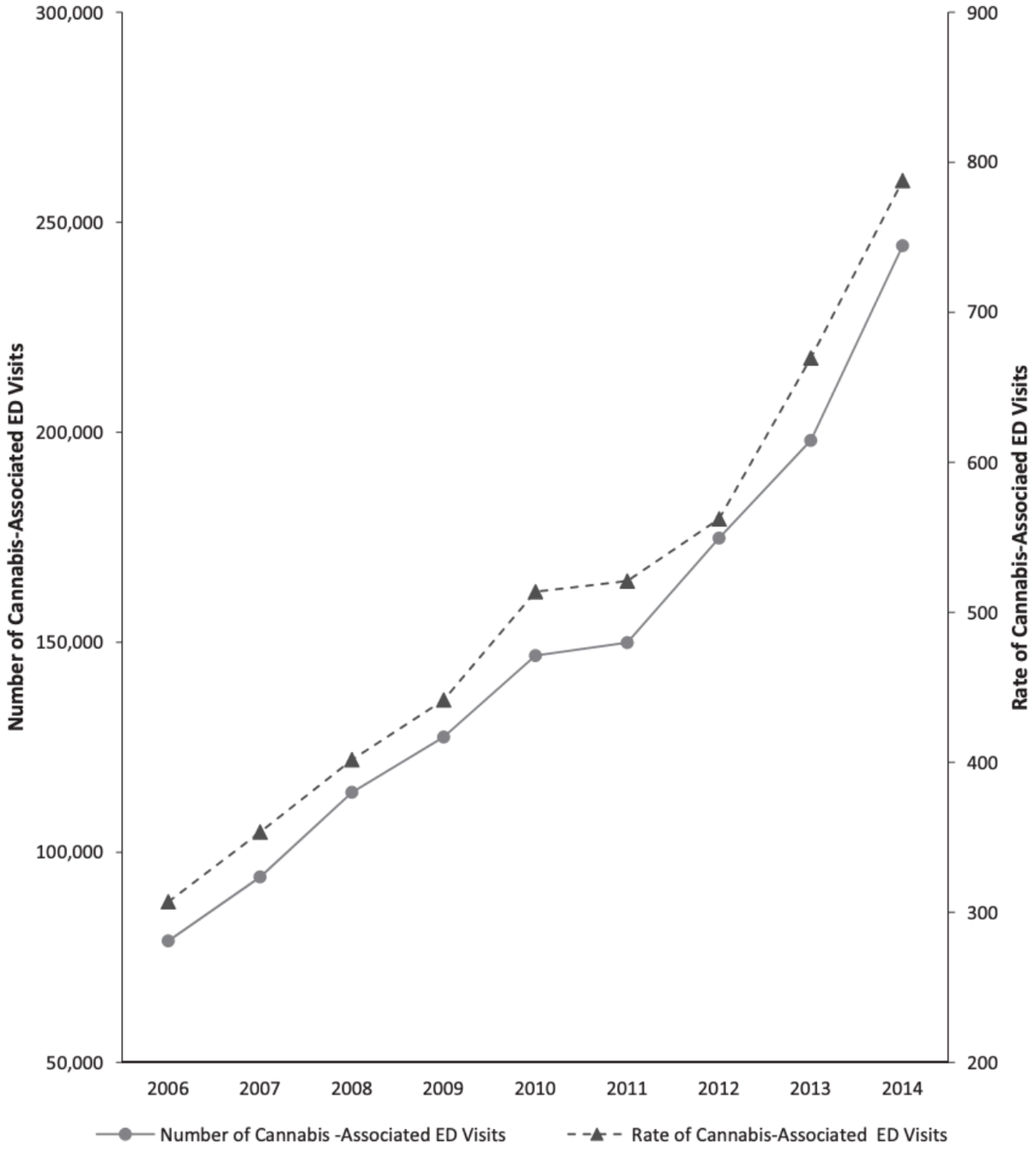
Stover CL et al. PNAS June 25, 2019 116 (26) 12624-12626; first published June 10, 2019
https://doi.org/10.1073/pnas.1903434116

ROAD TRAFFIC CRASHES AND CANNABIS

- After cannabis use:
  - Slower reaction time
  - Motor concentration problems
  - Poor judgment
- Evolving area of research
  - In jurisdictions with state-licensed medical marijuana dispensaries, the odds of marijuana-involved driving increased by 14% (Sevigny, 2018)
  - Significant positive association between cannabis use and road traffic crashes (Jorgenrud et al, 2018)

Sevigny EL. Accid Anal Prev. 2018 Sep; Jorgenrud B et al. Traffic Inj Prev. 2018;19(8):779-785.;118:57-65

FIGURE 1



Trends and Related Factors of Cannabis-Associated Emergency Department Visits in the United States: 2006–2014

Shen, Jay J.; Shan, Guogen; Kim, Pearl C.; Yoo, Ji Won; Dodge-Francis, Carolee; Lee, Yong-Jae

Journal of Addiction Medicine13(3):193-200, May/June 2019.
doi: 10.1097/ADM.0000000000000479

Trends in number and rate of cannabis-associated emergency department visits in United States, 2006–2014. ED, emergency department; rates, number of ED visits per 100,000 ED discharges. Source: NEDS, Nationwide Emergency Department Sample.

Vaping

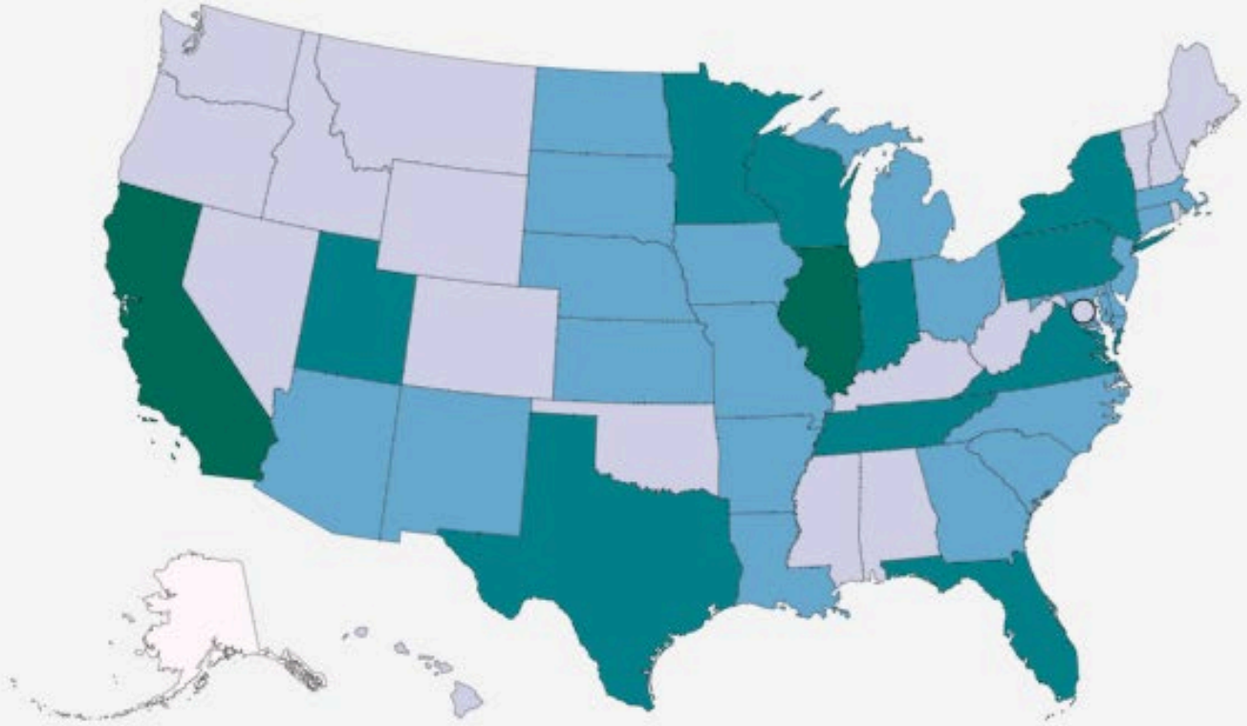
HEALTH
UNIVERSITY OF UTAH

OUTBREAK OF LUNG INJURY ASSOCIATED WITH E-CIGARETTE USE, OR VAPING

- As of October 15, 2019, 1,479* lung injury cases associated with the use of e-cigarette, or vaping, products have been reported to CDC from 49 states (all except Alaska), the District of Columbia, and 1 U.S. territory.
- Thirty-three deaths have been confirmed in 24 states.
- All patients have reported a history of using e-cigarette, or vaping, products.
- We do know that THC is present in most of the samples tested by FDA to date, and most patients report a history of using THC-containing products.
- The latest national and state findings suggest products containing THC, particularly those obtained off the street or from other informal sources (e.g. friends, family members, illicit dealers), are linked to most of the cases and play a major role in the outbreak.
- As such, we recommend that you should not use e-cigarette, or vaping, products that contain THC.
- Since the specific causes or causes of lung injury are not yet known, the only way to assure that you are not at risk while the investigation continues is to consider refraining from use of **all** e-cigarette, or vaping, products
- The use of e-cigarettes, or vaping, products is unsafe for all ages, including youth and young adults. Nicotine is highly addictive and can harm adolescent brain development, which continues into the early to mid-20s.

https://www.cdc.gov/tobacco/basic_information/e-cigarettes/severe-lung-disease.html#map-cases
Update of October 17, 2019 at 1500 EDT

Number of Lung Injury Cases Reported to CDC as of October 15, 2019



Territories AS GU MH FM PW PR VI

Legend

Number of lung injury cases per state

- 0 cases
- 1-9 cases
- 10-49 cases
- 50-99 cases
- 100-149 cases

E-CIGARETTE USE, OR VAPING, PRACTICES AND CHARACTERISTICS AMONG PERSONS WITH ASSOCIATED LUNG INJURY — UTAH, APRIL–OCTOBER 2019

- **What is already known about this topic?**
- An outbreak of e-cigarette, or vaping, product use–associated lung injury (EVALI) of unknown source is ongoing in the United States.
- **What is added by this report?**
- Medical abstractions were completed for 79 Utah patients, 53 of whom were interviewed. Almost all patients reported using tetrahydrocannabinol (THC)-containing vaping cartridges. Most patients were hospitalized, half required breathing assistance, many reported preexisting respiratory and mental health conditions, and many identified as current or former smokers of combustible marijuana or tobacco. Most THC-containing products, acquired from six patients and, tested at Utah Public Health Laboratory, contained vitamin E acetate.
- **What are the implications for public health practice?**
- At present, persons should not use e-cigarette, or vaping, products containing THC. In addition, because the specific cause or causes of lung injury are not yet known and while the investigation continues, persons should consider refraining from use of all e-cigarette, or vaping, products.

At present, persons should not use e-cigarette, or vaping, products that contain THC. In addition, because the specific cause or causes of lung injury are not yet known and while the investigation continues, persons should consider refraining from use of all e-cigarette, or vaping, products (*10*).

https://www.cdc.gov/mmwr/volumes/68/wr/mm6842e1.htm?s_cid=mm6842e1_w

Recent Public Health Recommendations

HEALTH
UNIVERSITY OF UTAH

HEALTH EFFECTS OF MARIJUANA

- CDC:
  - https://www.cdc.gov/marijuana/index.htm
- CDC's Evidence-based review of Cannabis Effects on Health:
  - https://www.cdc.gov/marijuana/nas/index.html
- Marijuana and Pregnancy:
  - https://www.acog.org/Patients/FAQs/Marijuana-and-Pregnancy?IsMobileSet=false
- National Academies of Sciences, 2017:
  - http://nationalacademies.org/hmd/reports/2017/health-effects-of-cannabis-and-cannabinoids.aspx
- Info for Teens:
  - https://teens.drugabuse.gov/drug-facts/marijuana

THE HEALTH EFFECTS OF CANNABIS AND CANNABINOIDS

January 2017

In the report *The Health Effects of Cannabis and Cannabinoids: The Current State of Evidence and Recommendations for Research*, an expert, ad hoc committee of the National Academies of Sciences, Engineering, and Medicine presents nearly 100 conclusions related to the health effects of cannabis and cannabinoid use and makes recommendations for an agenda to help expand and improve cannabis research efforts and better inform future public health decisions.

The Chapter Highlights below provide broad overview statements of the report's chapters regarding certain prioritized health conditions. To read the committee's conclusions in detail, as well as the definitions of weights of evidence, please see the "Committee's Conclusions" document at nationalacademies.org/CannabisHealthEffects.

Each blue header below links to the corresponding chapter in the report, providing much more detail. To read the full report, please visit **nationalacademies.org/CannabisHealthEffects.**

tting cannabis smoking is likely to reduce chronic cough and phlegm production.

It is unclear whether cannabis use is associated with COPD, asthma, or worsened lung function.

IMMUNITY

There exists a paucity of data on the effects of cannabis or cannabinoid-based therapeutics on the human immune system.

There is insufficient data to draw overarching conclusions concerning the effects of cannabis smoke or cannabinoids on immune competence.

There is limited evidence to suggest that regular exposure to cannabis smoke may have anti-inflammatory activity.

There is insufficient evidence to support or refute a statistical association between cannabis or cannabinoid use and adverse effects on immune status in individuals with HIV.

PRENATAL, PERINATAL, AND NEONATAL 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

INJURY AND DEATH

Cannabis use prior to driving increases the risk of being involved in a motor vehicle accident.

In states where cannabis use is legal, there is increased risk of unintentional cannabis overdose injuries among children.

It is unclear whether and how cannabis use is associated with all-cause mortality or with occupational injury.

PSYCHOSOCIAL

Recent cannabis use impairs the performance in cognitive domains of learning, memory, and attention. Recent use may be defined as cannabis use within 24 hours of evaluation.

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.

The National Academies of
SCIENCES • ENGINEERING • MEDICINE

http://nationalacademies.org/hmd/reports/2017/health-effects-of-cannabis-and-cannabinoids.aspx

U.S. SURGEON GENERAL'S ADVISORY, 2019: MARIJUANA USE AND THE DEVELOPING BRAIN

- Advisory: https://www.hhs.gov/surgeongeneral/reports-and-publications/addiction-and-substance-misuse/advisory-on-marijuana-use-and-developing-brain/index.html
- Video: https://youtu.be/OYZvUDbzUk8

U.S. SURGEON GENERAL'S ADVISORY, 2019: MARIJUANA USE AND THE DEVELOPING BRAIN

- The human brain continues to develop from before birth into the mid-20s and is vulnerable to the effects of addictive substances.
- Frequent marijuana use during adolescence is associated with:
  - Changes in the areas of the brain involved in attention, memory, decision-making, and motivation. Impaired learning in adolescents.
  - Increased rates of school absence and drop-out, as well as suicide attempts.
  - Risk for and early onset of psychotic disorders, such as schizophrenia.
  - Other substance use.

https://www.hhs.gov/surgeongeneral/reports-and-publications/addiction-and-substance-misuse/advisory-on-marijuana-use-and-developing-brain/index.html

U.S. SURGEON GENERAL'S ADVISORY, 2019: MARIJUANA USE AND THE DEVELOPING BRAIN

- The American College of Obstetricians and Gynecologists holds that "[w]omen who are pregnant or contemplating pregnancy should be encouraged to discontinue marijuana use. Women reporting marijuana use should be counseled about concerns regarding potential adverse health consequences of continued use during pregnancy".
- In 2018, the American Academy of Pediatrics recommended that "…it is important to advise all adolescents and young women that if they become pregnant, marijuana should not be used during pregnancy".

https://www.hhs.gov/surgeongeneral/reports-and-publications/addiction-and-substance-misuse/advisory-on-marijuana-use-and-developing-brain/index.html

MARIJUANA USE DURING PREGNANCY CAN AFFECT THE DEVELOPING FETUS

- THC can enter the fetal brain from the mother's bloodstream.
- It may disrupt the endocannabinoid system, which is important for a healthy pregnancy and fetal brain development
- Studies have shown that marijuana use in pregnancy is associated with adverse outcomes, including lower birth weight
- The Colorado Pregnancy Risk Assessment Monitoring System reported that maternal marijuana use was associated with a 50% increased risk of low birth weight regardless of maternal age, race, ethnicity, education, and tobacco use

https://www.hhs.gov/surgeongeneral/reports-and-publications/addiction-and-substance-misuse/advisory-on-marijuana-use-and-developing-brain/index.html

Treatments?

Not a lot.

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BEHAVIORAL TREATMENTS FOR CUD

- Cognitive Behavioral Therapy
- Motivational Interviewing
- Contingency Management
- Group Therapy

- Cannabis Youth Treatment (CYT) study
  - Motivational Enhancement Therapy
  - Cognitive Behavioral Therapy
  - Adolescent Community Reinforcement Approach
  - Multidimensional Family Therapy

https://www.ncbi.nlm.nih.gov/pubmed/15501373

PHARMACOLOGIC TREATMENTS FOR CUD

- None FDA approved; ALL OFF-LABEL
- Evidence positive for:
  - N-acetyl cysteine 1200 mg BID, OTC reduced use and +UDS compared to placebo (Gray K, 2012)
  - Gabapentin 1800 mg daily decreased use, +UDS and withdrawal symptoms (Mason B, 2012)
  - Dronabinol 20 mg BID reduced withdrawal, not relapse; higher retention (Levin F, 2011)
  - Nabiximols reduced withdrawal; higher retention (Allsop D, 2014)
- Negative or high dropout studies:
  - Nefazodone, bupropion, buspirone
  - Rimonabant (CB1 partial agonist) not approved in US, removed from market in Europe due to increased SI

Mason B, 2012; Gray K, 2012; Levin F 2011; Allsop D, 2014

Harm reduction approaches

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LOWER RISK CANNABIS USE GUIDELINES (LRCUG) FROM CANADA

- From CRISM: the Canadian Research Initiative in Substance Misuse
- Evidence-based public health intervention tool, allowing cannabis users to modify and reduce their risks for health harms associated with cannabis use based on science-based recommendations.
- Developed to assess real world use and reduce harm
- Acknowledging risk with key strategies to modify this level of risk
- http://crismontario.ca/research-projects/lower-risk-cannabis-use-guidelines

KEY LRCUG RECOMMENDATIONS

- Early use of cannabis prior to age 16 → Poor prognostic factor for later mental health/dependence/learning issues
- When choosing cannabis products, go for lower THC or higher CBD levels
  - CBD can modify/lessen some of THC AEs
  - Using higher CBD/THC ratio products→ less health risk overall
  - ↑ THC levels or synthetic cannabinoids = ↑ health effects

http://crismontario.ca/research-projects/lower-risk-cannabis-use-guidelines

KEY LRCUG RECOMMENDATIONS

- Utilize non-smoked forms of cannabis such as edibles to prevent respiratory issues
  - Caution for cumulative, delayed effects
  - If smoking- avoid deep inhalation

- Frequency- daily or near daily users face ↑ health risks
  - One day/week or weekends if using

http://crismontario.ca/research-projects/lower-risk-cannabis-use-guidelines

KEY LRCUG RECOMMENDATIONS

- Do not operate heavy machinery/automobile while impaired
  - Wait at least 6 hours after use for Acute effects to dissipate
  - No safely established limits
  - Combination of alcohol and cannabis = synergistic effect
- Certain populations at higher risk for complications
  - Personal/1st degree family hx of mental illness
  - Pregnant

http://crismontario.ca/research-projects/lower-risk-cannabis-use-guidelines

Cannabis & Your Health

10 WAYS to Reduce Risks When Using

Cannabis use is now legal for adults, but it does have health risks.
If you use non-medically, you can make informed choices for safer use.

Delay using cannabis as late as possible in life, ideally not before adulthood.

Avoid using if you're pregnant, or if you or family members have a history of psychosis or substance use problems.

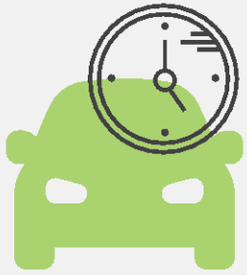
Choose low-potency products — those with low THC and/or high CBD content.

Use cannabis in ways that don't involve smoking — choose less risky methods of using like vaping or ingesting.

Stay away from synthetic cannabis products, such as K2 or Spice.

If you do smoke, avoid deep inhalation or breath-holding.

Occasional use, such as one day per week or less, is better than regular use.



Your actions add up. The more risks you take, the more likely you are to harm your health.

Don't operate a vehicle or machinery while impaired by cannabis. Wait at least 6 hours after using. Remember that combining alcohol and cannabis makes you more impaired.

Not using cannabis at all is still the best way to protect your health (unless you use with a medical recommendation).

http://crismontario.ca/Pages/LRCUG.PHAC.Poster.English.Final.pdf

When using cannabis, be considerate of the health and safety concerns of those around you. Don't hesitate to seek support from a health professional if you need help controlling your cannabis use, if you have withdrawal symptoms or if your use is affet ing your life

Public Health Agency of Canada | Agence de la santé publique du Canada | camh | CANADIAN RESEARCH INITIATIVE IN SUBSTANCE MISUSE

TAKE HOME POINTS

- Cannabis research is lacking on a large scale- partly due to legislative factors
- Cannabis has linked to several negative health factors that can put those with mental illness at risk
- Open conversations and harm reduction should be focus going forward

Thank you!

Additional Resources

http://learnaboutmarijuanawa.org/index.htm

THE REWARD CIRCUIT: HOW THE BRAIN RESPONDS TO MARIJUANA

- https://youtu.be/s27f7Jzy2k0
- Start at 1:41