Medical Marijuana: Who, When, and How

Dov Pickholtz, DO

Who is Cannabis for?

Indications - Really starts with therapeutic goals

- Pain / Inflammation
- Nausea
- Augment Current Therapies
- Responsible use (AKA “Recreational” - no one takes an acetaminophen recreationally)

Other Common Indications

Neuro: Epilepsy, Dravet syndrome, Tourettes, MS, Parkinsons, Alzheimer's, Neuropathy, Huntington's, ALS, Autism

Cardio: Afib, CHF

Endocrine: Diabetes, HTN

GI: Crohns, UC, IBS, Putz-Jegers, Hep C

Rheum: RA, Fibromyalgia

Psych: Anxiety, Depression, PTSD, ADHD, Sleep, OCD

Derm: Pruritus, skin cancers later

Oncology: to be discussed (briefly)

- Chemo associated nausea and vomiting
- Wasting syndrome/appetite stimulation

(Abrams DI, Guzman M. Cannabis in cancer care. Clin Pharmacol Ther. 2015;97:575-586.)
(Robson P. Therapeutic aspects of cannabis and cannabinoids. Br J Psychiatry. 2001;)

Eur J Intern Med. 2018 Mar;49:44-50. doi: 10.1016/j.ejim.2018.01.019.

Epidemiological characteristics, safety and efficacy of medical cannabis in the elderly

Ran Abuhasira [1], Lihi Bar-Lev Schleider [2], Raphael Mechoulam [3], Victor Novack [4]

Affiliations + expand

PMID: 29398248 DOI: 10.1016/j.ejim.2018.01.019

Abstract

Introduction: There is a substantial growth in the use of medical cannabis in recent years and with the aging of the population, medical cannabis is increasingly used by the elderly. We aimed to assess the characteristics of elderly people using medical cannabis and to evaluate the safety and efficacy of the treatment.

Methods: A prospective study that included all patients above 65 years of age who received medical cannabis from January 2015 to October 2017 in a specialized medical cannabis clinic and were willing to answer the initial questionnaire. Outcomes were pain intensity, quality of life and adverse events at six months.

Results: During the study period, 2736 patients above 65 years of age began cannabis treatment and answered the initial questionnaire. The mean age was 74.5 ± 7.5 years. The most common indications for cannabis treatment were pain (66.6%) and cancer (60.8%). After six months of treatment, 93.7% of the respondents reported improvement in their condition and the reported pain level was reduced from a median of 8 on a scale of 0-10 to a median of 4. Most common adverse events were: dizziness (9.7%) and dry mouth (7.1%). After six months, 18.1% stopped using opioid analgesics or reduced their dose.

Conclusion: Our study finds that the therapeutic use of cannabis is safe and efficacious in the elderly population. Cannabis use may decrease the use of other prescription medicines, including opioids. Gathering more evidence-based data, including data from double-blind randomized-controlled trials, in this special population is imperative.

Keywords: Aged; Elderly; Medical cannabis; Medical marijuana; Opioids.

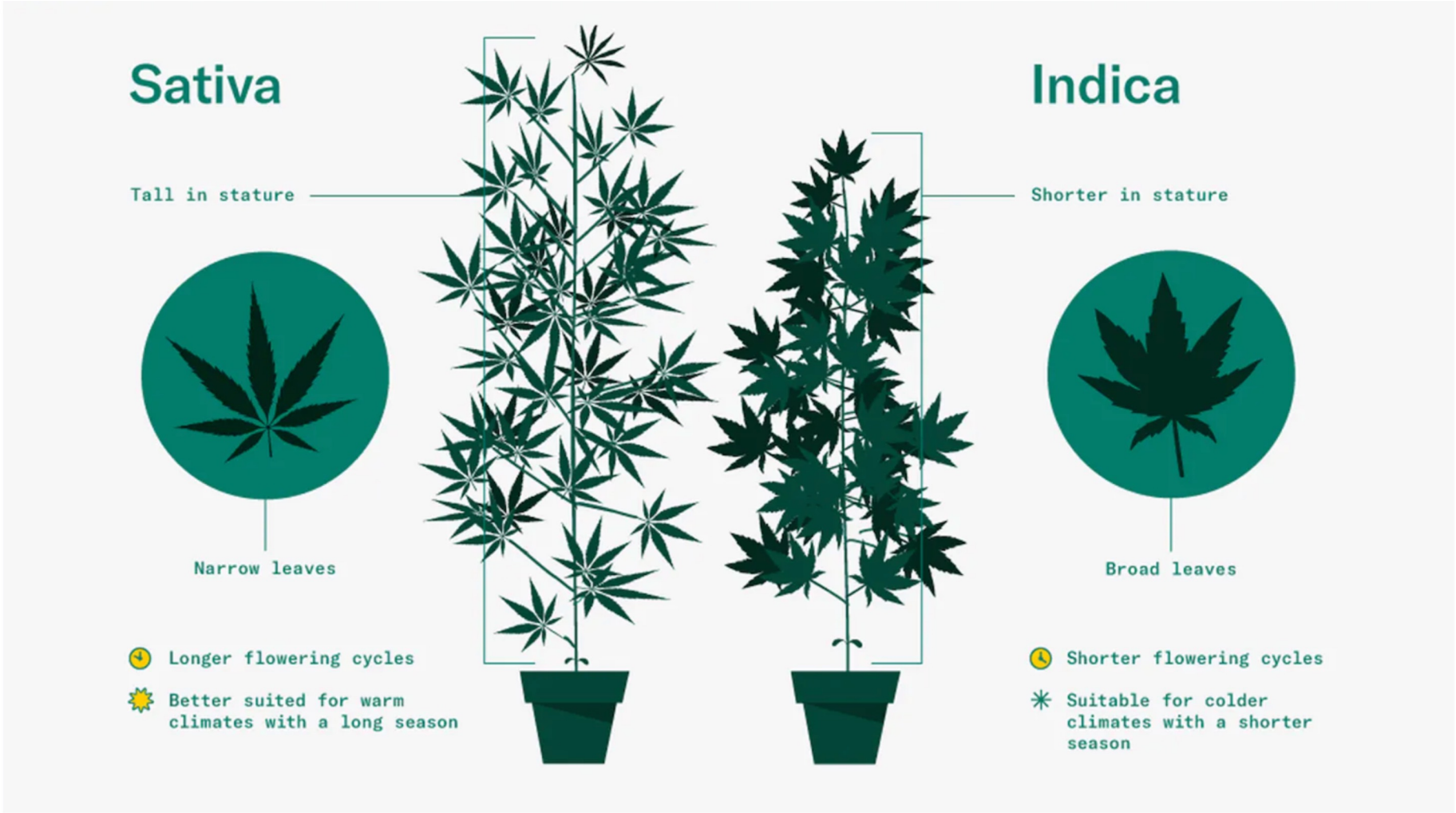
Similar articles

Effect of cannabis use in people with chronic non-cancer pain prescribed opioids:

What (exactly) is cannabis?

The Stoner's Serenity Prayer:

Sativa to change the things I can.
Indica to accept the things I can't.
And Hybrid to know the difference.



Sativa vs. Indica illustration (Leafly)

All strains of cannabis derive from the Cannabaceae family of plants. Some experts consider that *Cannabis indica* and *Cannabis sativa* are the two main subspecies, although some people think they are separate species.

https://www.medicalnewstoday.com/articles/marijuana-strains#what-are-marijuana-strains

To create a strain, cultivators select a variety of traits to produce the effects they want. This is a similar process to how breeders create particular characteristics in dogs.

People often describe cannabis strains as being indica, sativa, or hybrid. Hybrid refers to a strain created by combining both indica and sativa strains.

Here are some examples of cannabis strains and the plant they derive from:

Strain name	Plant species
Kush	Pure *Cannabis indica* or *Cannabis indica* hybrid
Afghan Kush, Hindu Kush, Green Kush, Purple Kush	Pure *Cannabis indica*
Blueberry Kush, Golden Jamaican Kush	*Cannabis indica* hybrid
Diesel Haze	Pure *Cannabis sativa* or *Cannabis sativa* hybrid

Many producers crossbreed cannabis plants to develop new strains with specific characteristics. Experts suggest that there are over 700 strains of cannabis.

One of the most important characteristics of a cannabis strain is the THC content. Some rules exist on naming each strain, but many producers do not name their products according to these rules.

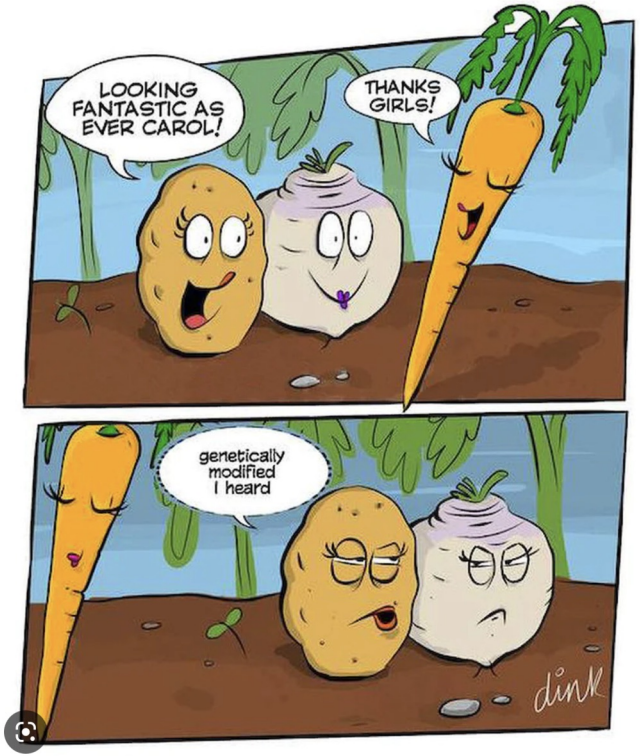
Despite these classifications, hybridization and crossbreeding has meant that people cannot tell exactly how much THC is in a particular plant by simply looking at its physical features.

Experts suggest it is impossible to guess the composition of a cannabis plant by looking at its height, branching, or leaf appearance.

We look at a COA

The only way to know the chemical composition of a cannabis-derived product is to analyze it in a biochemical assay.

Common Question: So, Synthetic Cannabis should be just as good as natural cannabis - or better



The experts' overall benefit assessments are already reported elsewhere (14). Figure 7 shows the user assessments. The strongest benefits/utilities were attributed to methadone, buprenorphine, and cannabis by the users. Synthetic cannabinoids were rated to have the smallest benefits (Figure 7).

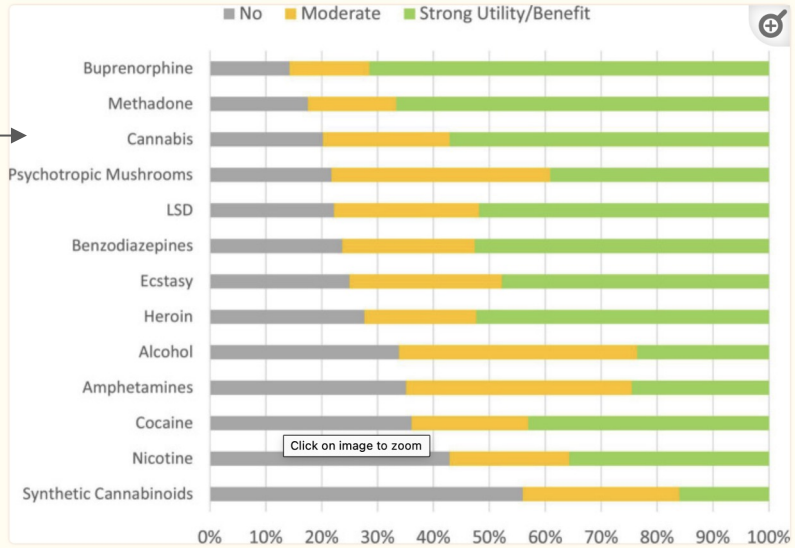


FIGURE 7

Distributions of benefits categories (cohort 1). The substances are ranked according to proportions of "no benefit" ratings. Supplementary Figure 21 shows also the ratings for the excluded substances.

Front Psychiatry. 2022; 13: 1041762.
Published online 2022 Nov 16. 10.3389/fpsyt.2022.1041762

Differences between users' and addiction medicine experts' harm and benefit assessments of licit and illicit psychoactive drugs: Input for psychoeducation and legalization/restriction debates

Udo Bonnet, 1 , 2 , * Michael Specka, 2 Ann-Kristin Kanti, 3 and Norbert Scherbaum 2

In 1998, Professors Raphael Mechoulam and Shimon Ben-Shabat posited that the endocannabinoid system demonstrated an "entourage effect" in which a variety of "inactive" metabolites and closely related molecules markedly increased the activity of the primary endogenous cannabinoids, anandamide and 2-arachidonoylglycerol (Ben-Shabat et al., 1998). They also postulated that this helped to explain how botanical drugs were often more efficacious than their isolated components (Mechoulam and Ben-Shabat, 1999). Although the single molecule synthesis remains the dominant model for pharmaceutical development (Bonn-Miller et al., 2018), the concept of botanical synergy has been amply demonstrated contemporaneously, invoking the pharmacological contributions of "minor cannabinoids" and Cannabis terpenoids to the plant's overall pharmacological effect (McPartland and Pruitt, 1999; McPartland and Mediavilla, 2001; McPartland and Russo, 2001, 2014; Russo and McPartland, 2003; Wilkinson et al., 2003; Russo, 2011). Several pertinent examples of the entourage effect in Cannabis are illustrative:

Front Plant Sci. 2018; 9: 1969.
Published online 2019 Jan 9. doi: 10.3389/fpls.2018.01969
PMCID: PMC6334252
PMID: 30687364

The Case for the Entourage Effect and Conventional Breeding of Clinical Cannabis: No "Strain," No Gain

Ethan B. Russo*

Author information · Article notes · Copyright and License information Disclaimer

Abstract

Go to:

The topic of Cannabis curries controversy in every sphere of influence, whether politics, pharmacology, applied therapeutics or even botanical taxonomy. Debate as to the speciation of Cannabis, or a lack thereof, has swirled for more than 250 years. Because all Cannabis types are eminently capable of cross-breeding to produce fertile progeny, it is unlikely that any clear winner will emerge between the "lumpers" vs. "splitters" in this taxonomical debate. This is compounded by the profusion of Cannabis varieties available through the black market and even the developing legal market. While labeled "strains" in common parlance, this term is acceptable with respect to bacteria and viruses, but not among Plantae. Given that such factors as plant height and leaflet width do not distinguish one Cannabis plant from another and similar difficulties in defining terms in Cannabis, the only reasonable solution is to characterize them by their biochemical/pharmacological characteristics. Thus, it is best to refer to Cannabis types as chemical varieties, or "chemovars." The current wave of excitement in Cannabis commerce has translated into a flurry of research on alternative sources, particularly yeasts, and complex systems for laboratory production have emerged, but these presuppose that single compounds are a desirable goal. Rather, the case for Cannabis synergy via the "entourage effect" is currently sufficiently strong as to suggest that one molecule is unlikely to match the therapeutic and even industrial potential of Cannabis itself as a phytochemical factory. The astounding plasticity of the Cannabis genome additionally obviates the need for genetic modification techniques.

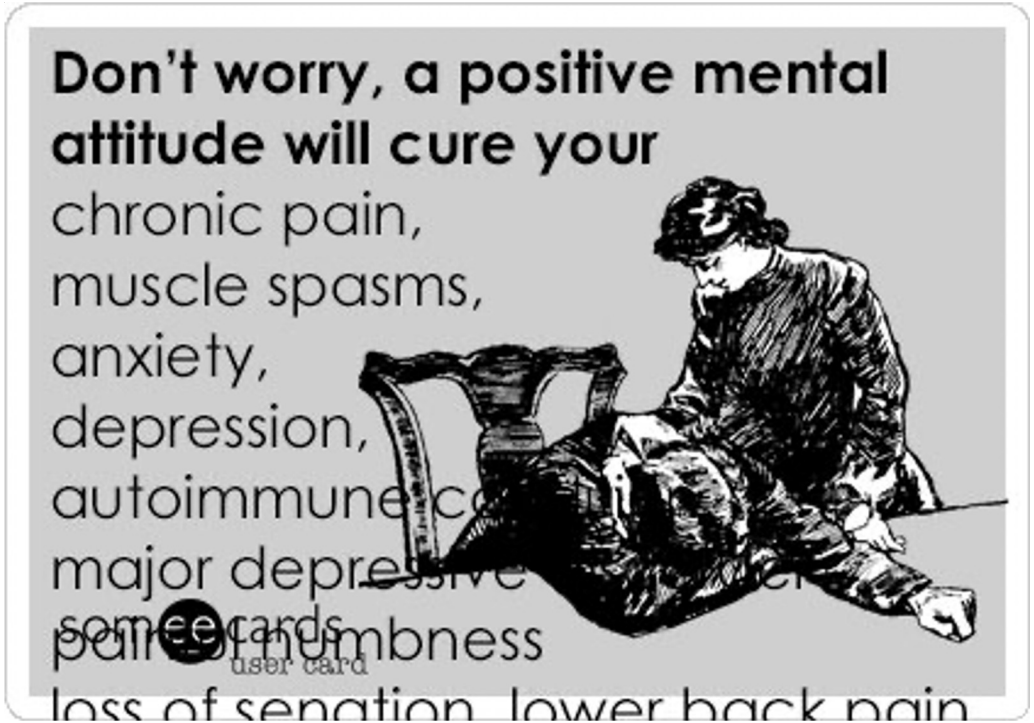
Keywords: cannabis, cannabinoid, marijuana, hemp, genomics, genetically modified organism, tetrahydrocannabinol, cannabidiol

Introduction: Defining Terms

Go to:

Earlier data on taxonomy of Cannabis was previously reviewed (Russo, 2007), which will be herein

What, then, can cannabis do?



Depends on **What's** in the Cannabis?

~489 Chemicals/Molecules

~113 Phytocannabinoids

*Terpenes

Flavonoids

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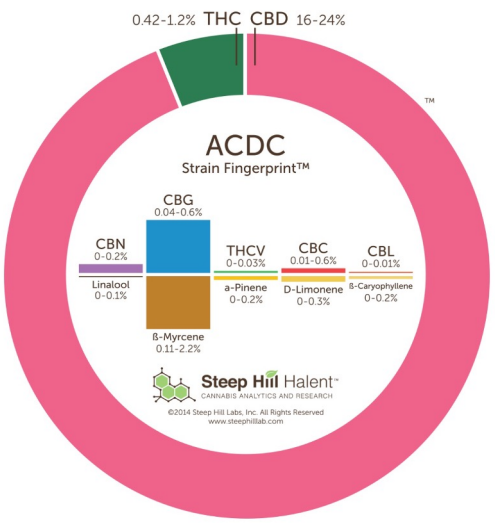
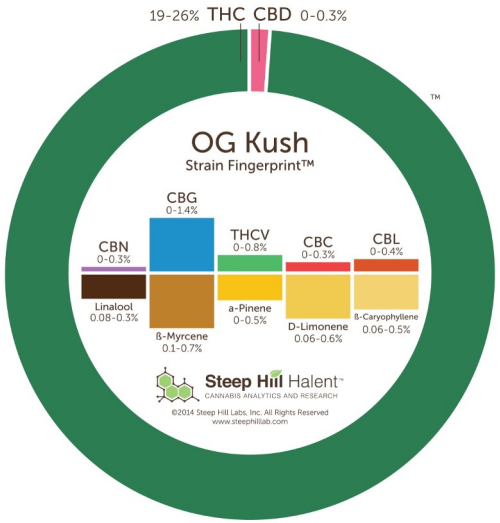
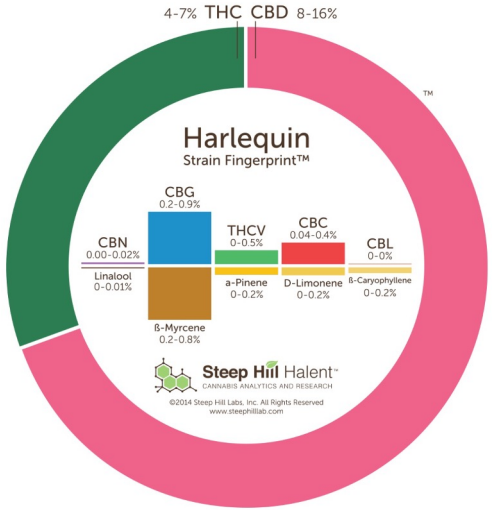
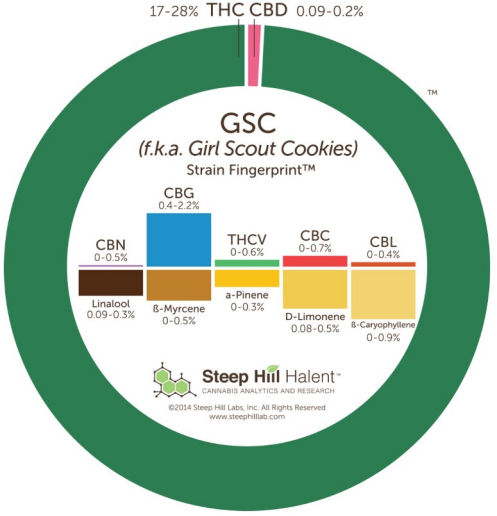








Phytocannabinoid Cell Targets

PROF of POT

THC vs. CBD

Cannabinoid System

THC		CBD
Partial Agonist	CB1	Negative Allo Modulator
Partial Agonist	CB2	Weak Antagonist
Not Tested	FAAH	Weak Inhibitor
Inhibitor	FABP	Inhibitor

Atypical Cannabinoid Receptors

Agonist	GPR18	Antagonist
Agonist	GPR55	Antagonist

Serotonin Receptors

No effect	5-HT1A	Full agonist
No effect	5-HT2A	Weak Partial Agonist
Negative Allo Modulator	5-HT3A	Negative Allo Modulator

Dopamine Receptors

Not Tested	D2High	Partial agonist

Opioid Receptors

Negative Allo Modulator	uOR	Negative Allo Modulator
Negative Allo Modulator	δOR	Negative Allo Modulator

Adenosine System

Inhibitor	ENT1	Inhibitor

Glycine Receptors

Positive Allo Modulator	GlyR	Positive Allo Modulator

GABA Receptors

Not Tested	GABA-A	Positive Allo Modulator

Acetylcholine Receptors

No Effect	α7-AChR	Negative Allo Modulator

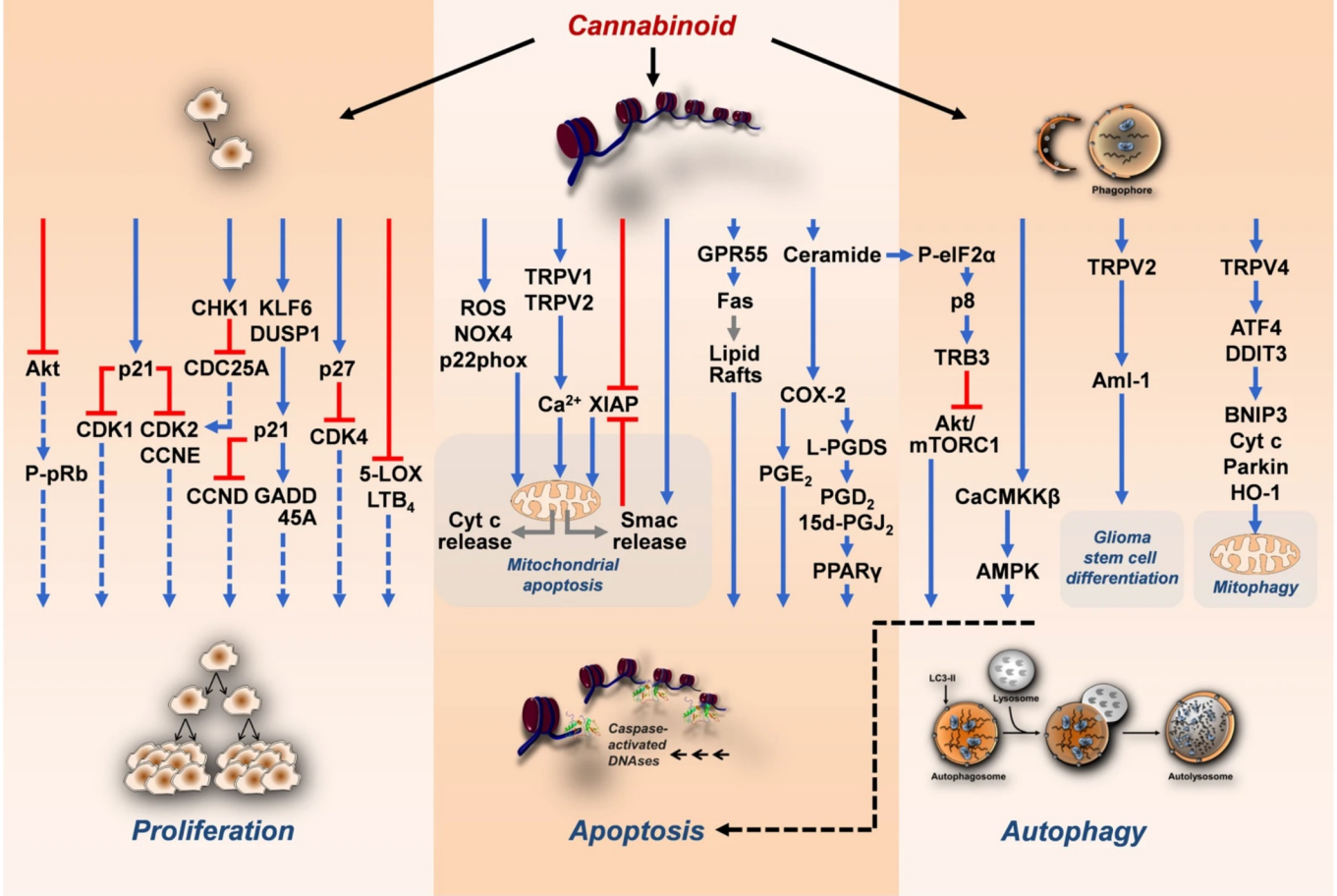
TRP Channels

No Effect	TRPV1	Agonist
Agonist	TRPV2	Agonist
Agonist	TRPV3	Agonist
Agonist	TRPV4	Agonist
Agonist	TRPA1	Agonist
Antagonist	TRPM8	Antagonist

Nuclear Receptors

Agonist	PPARγ	Agonist

	THC	CBD	CBG	CBN	CBC	THCv	CBGA	CGCA	CBCA	THCA	CBDA
Relieves pain Analgesic	●	●		●	●		●				
Suppresses appetite/Helps with weight loss Anorectic						●					
Kills or slows bacteria growth Antibacterial		●	●						●		
Reduces blood sugar levels Anti-diabetic		●									
Reduces vomiting and nausea Anti-emetic	●	●									
Reduces seizures and convulsion Anti-epileptic		●				●					
Treats fungal infection Antifungal									●		
Reduces inflammation Anti-inflammatory		●	●		●		●	●		●	●
Aids sleep Anti-insomnia				●							
Reduces risk of artery blockage Anti-ischemic		●									
Inhibits cell growth in tumors/cancer cells Anti-proliferative		●	●		●					●	●
Treats psoriasis Anti-psoriatic		●									
Tranquilizing, used to manage psychosis Antipsychotic		●									
Suppresses muscle spasms Antispasmodic	●	●		●						●	
Relieves anxiety Anxiolitic		●									
Simulates appetite Appetite Stimulant	●										
Promotes bone growth Bone Stimulant		●	●		●	●					
Reduces function in the immune system Immunosuppressive		●									
Reduces contractions in the small intestines Intestinal Anti-prokinetic		●									
Protects nervous system degeneration Neuroprotective		●									

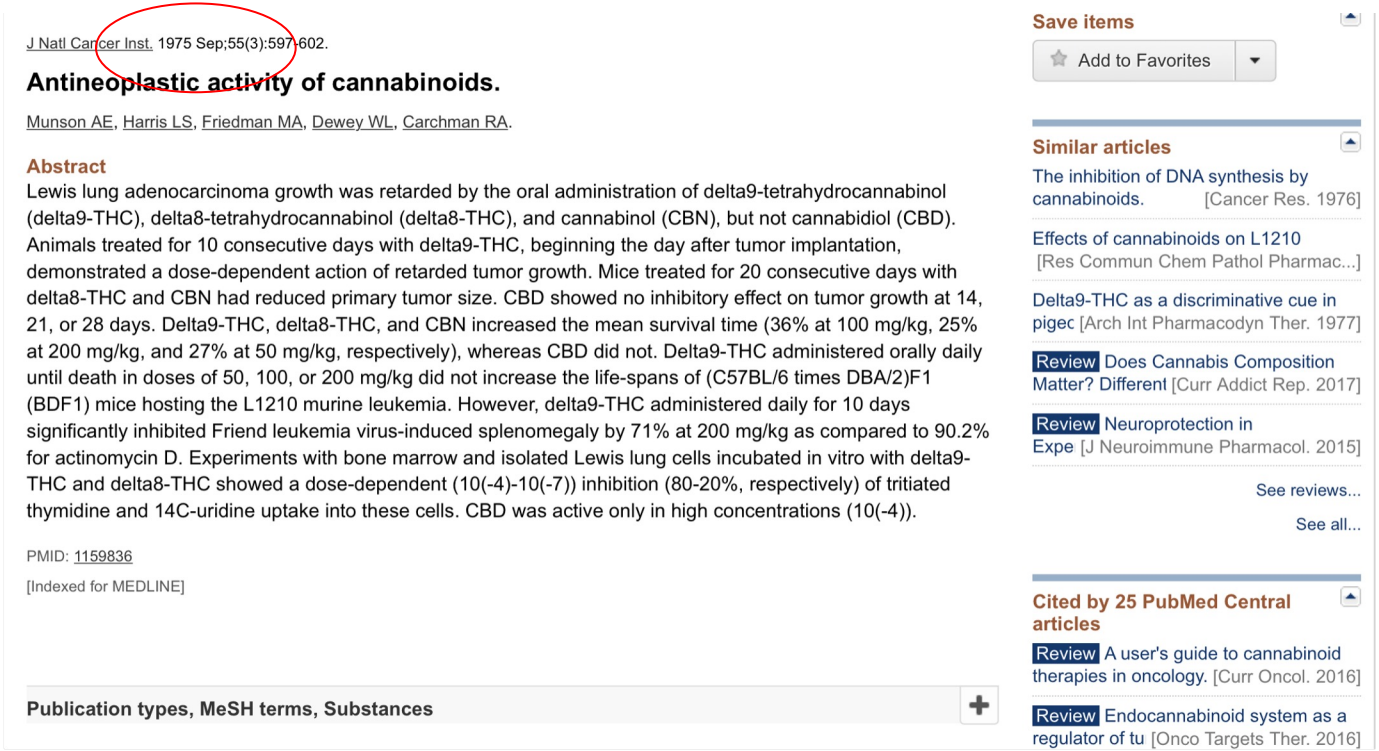


The black arrows emanating from the cannabinoid show the respective modulated structures or levels. Coloured arrows indicate inhibitory (red) and stimulatory (blue) effects of cannabinoids on the indicated targets. Blue dashed arrows indicate reduced stimulation of the respective effect by cannabinoid treatment. The grey arrows indicate a shift in a parameter. The black dashed arrow indicates a functional relationship between autophagy and apoptosis. All abbreviations are explained in the text.

Hinz, B., Ramer, R. Cannabinoids as anticancer drugs: current status of preclinical research. *Br J Cancer* 127, 1–13 (2022).

https://doi.org/10.1038/s41416-022-01727-4

How did this association with Cannabis and Cancer start?



J Natl Cancer Inst. 1975 Sep;55(3):597-602.

Antineoplastic activity of cannabinoids.

Munson AE, Harris LS, Friedman MA, Dewey WL, Carchman RA.

Abstract

Lewis lung adenocarcinoma growth was retarded by the oral administration of delta9-tetrahydrocannabinol (delta9-THC), delta8-tetrahydrocannabinol (delta8-THC), and cannabinol (CBN), but not cannabidiol (CBD). Animals treated for 10 consecutive days with delta9-THC, beginning the day after tumor implantation, demonstrated a dose-dependent action of retarded tumor growth. Mice treated for 20 consecutive days with delta8-THC and CBN had reduced primary tumor size. CBD showed no inhibitory effect on tumor growth at 14, 21, or 28 days. Delta9-THC, delta8-THC, and CBN increased the mean survival time (36% at 100 mg/kg, 25% at 200 mg/kg, and 27% at 50 mg/kg, respectively), whereas CBD did not. Delta9-THC administered orally daily until death in doses of 50, 100, or 200 mg/kg did not increase the life-spans of (C57BL/6 times DBA/2)F1 (BDF1) mice hosting the L1210 murine leukemia. However, delta9-THC administered daily for 10 days significantly inhibited Friend leukemia virus-induced splenomegaly by 71% at 200 mg/kg as compared to 90.2% for actinomycin D. Experiments with bone marrow and isolated Lewis lung cells incubated in vitro with delta9-THC and delta8-THC showed a dose-dependent (10(-4)-10(-7)) inhibition (80-20%, respectively) of tritiated thymidine and 14C-uridine uptake into these cells. CBD was active only in high concentrations (10(-4)).

PMID: 1159836

[Indexed for MEDLINE]

Publication types, MeSH terms, Substances

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Similar articles

The inhibition of DNA synthesis by cannabinoids. [Cancer Res. 1976]

Effects of cannabinoids on L1210 [Res Commun Chem Pathol Pharmac...]

Delta9-THC as a discriminative cue in pigec [Arch Int Pharmacodyn Ther. 1977]

Review Does Cannabis Composition Matter? Different [Curr Addict Rep. 2017]

Review Neuroprotection in Expe [J Neuroimmune Pharmacol. 2015]

See reviews...

See all...

Cited by 25 PubMed Central articles

Review A user's guide to cannabinoid therapies in oncology. [Curr Oncol. 2016]

Review Endocannabinoid system as a regulator of tu [Onco Targets Ther. 2016]

And then in 2003 there came along a man named Rick Simpson…

So **What** has been studied?

- Biliary tract cancer (cholangiocarcinoma)
- Breast carcinoma
- Cervical carcinoma
- Colorectal carcinoma
- Gastric adenocarcinoma
- Glioblastoma Multiforme**
- Leukemia cells
- Lymphomas
- Lung carcinoma
- Neuroblastoma
- Oral cancer
- Pancreatic adenocarcinoma
- Prostate carcinoma
- Skin carcinoma
- Thyroid epithelioma
- Urological cancers
- Uterus carcinoma

Getting Back to Cannabis: What options are out there

Route:

- Inhaled (Vape-pen; Flower - joint, bowl, bong, dry herb vaporizer)
- Oral (Capsules, Gummies, Brownies/Cookies)
- Sublingual/Tincture
- Topical
- (injectable)

Dose: ***Dosis sola facit venenum* - "The dose makes the poison"** (Paracelsus)

To be a Careful and Correct Conscientious Cannabis Consumer remember to Query the Quintessential Quattro Questions:

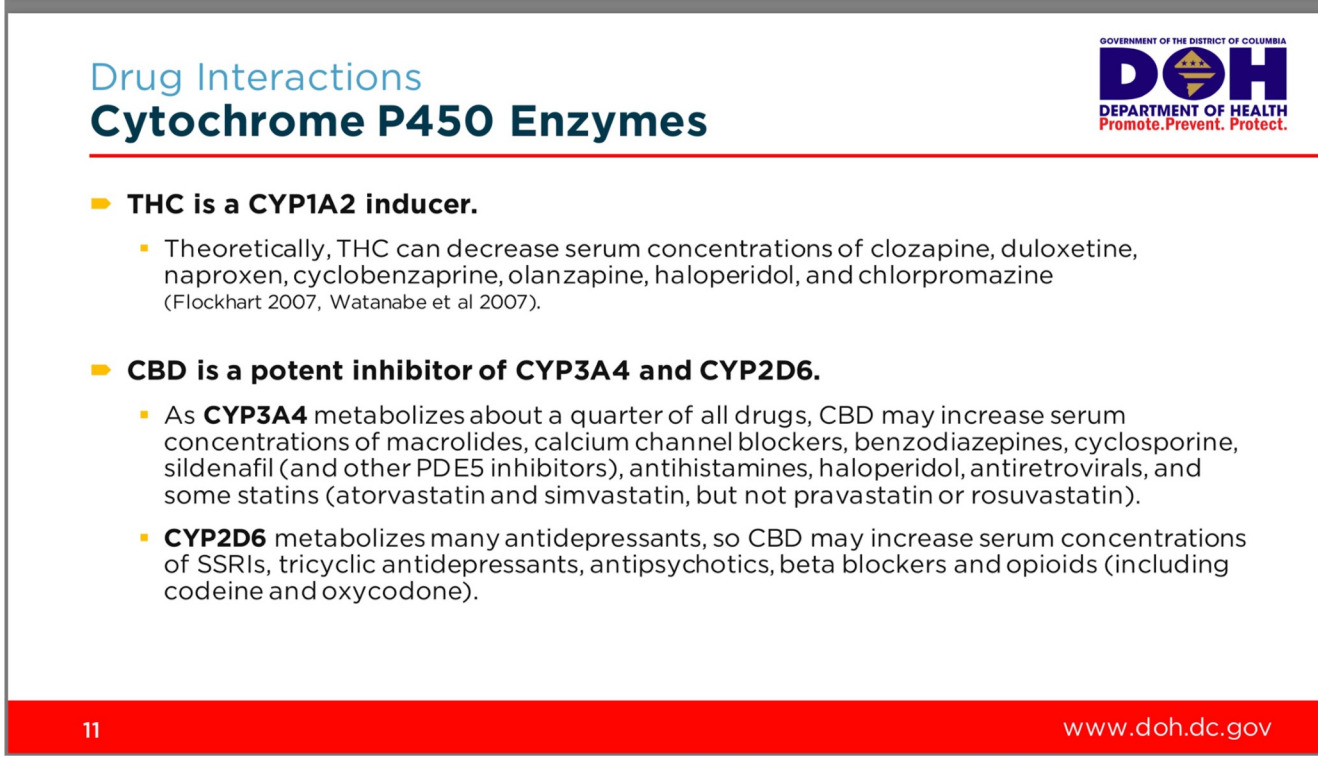
1. What is the treatment Goal?
   - (What are we aiming to treat/achieve?)
2. What is the right Strain?
   - (What are we treating it with?)
3. What is the right Route?
   - (How do we get “it” into you?)
   - (Stomach, Lung, Mucosa, Skin)
4. What is the right Dose?
   - (How much? How often?)

#CannabisIsComplicated #EducatedChoices

What are some negatives?

1) Side effects - Anticholenrgic, HYPEREUPHORIA,couch-lock
- Loose stools, hypotension,hyperphagia, gynecomastia
1) CYP450 interactions (Chemo/Immunomodulators/Warfarin/Statins)
2) Addiction?
3) Illegal???
4) Cannabis CAN be expensive

CYP450 interactions

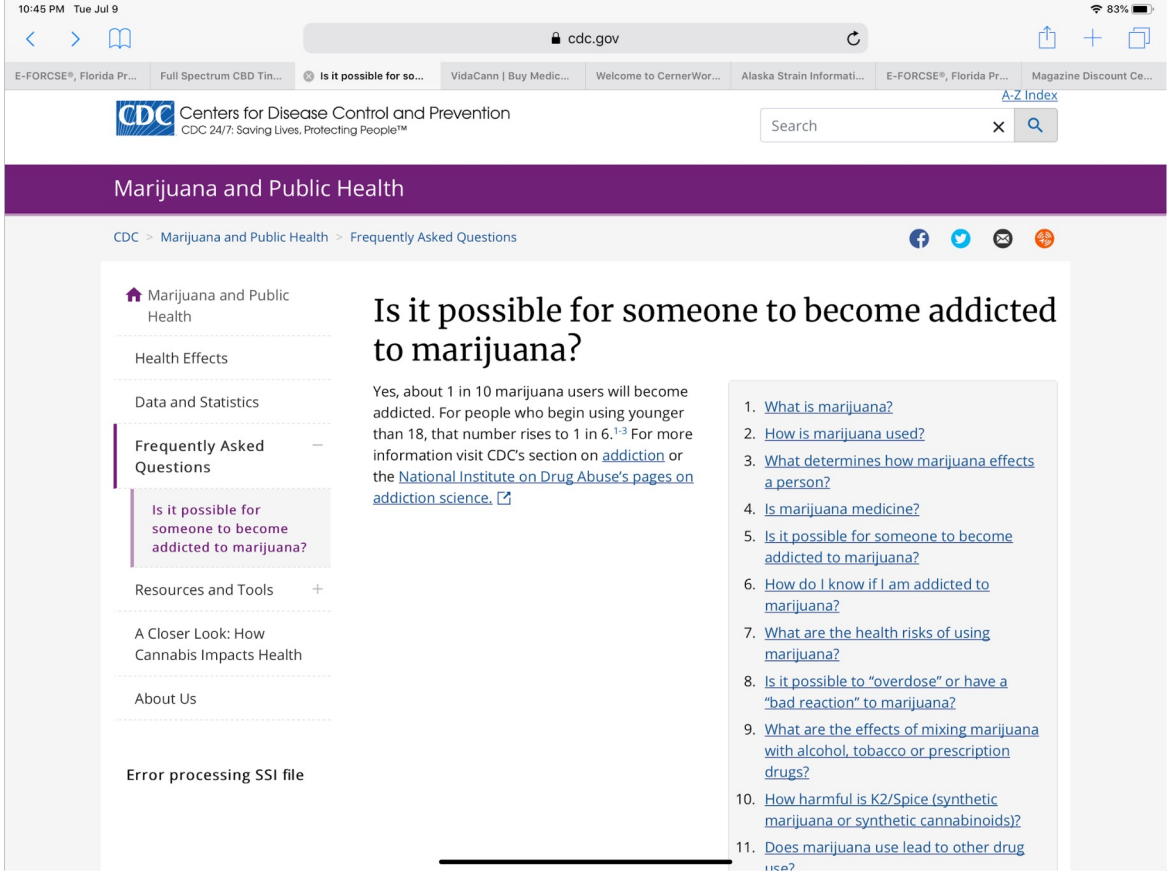


CBD

1. Studies in mice have shown that CBD inactivates cytochrome P450 isozymes in the short term, but can induce them after repeated administration.
2. Supraphysiologic doses used
3. CYP450-3A4 and A5 in particular, as well as 2C9(warfarin),

Who will get ADDICTED

In a study of cannabis research samples over time, the average delta-9 THC (the main form of THC in the cannabis plant) concentration almost doubled, from 9% in 2008 to 17% in 2017.[7] Products from dispensaries often offer much higher concentrations than seen in this study. In a study of products available in online dispensaries in 3 states with legal non-medical adult marijuana use, the average THC concentration was 22%, with a range of 0% to 45%.[8] In addition, some methods of using marijuana (for example, dabbing and vaping concentrates) may deliver very high levels of THC to the user.[6,9]



Addiction/Dependence:

After the first year of substance use onset the probability of transition to dependence was almost **2.0% for** nicotine, alcohol and **cannabis** users and 7.1% for cocaine users.

The probability estimates of transition to dependence **a decade after use** onset was 15.6% among nicotine users, 14.8% among cocaine users, 11.0% among alcohol users, and **5.9% among cannabis users**.

Lifetime cumulative probability estimates indicated that 67.5% of nicotine users, 22.7% of alcohol users, 20.9% of cocaine users, and **8.9% of cannabis users** would become dependent on those substances at some time in their life.

Half of the cases of nicotine, alcohol, cannabis and cocaine dependence were observed approximately 27, 13, **5** and 4 years after use onset, respectively

Lopez-Quintero C, Pérez de los Cobos J, Hasin DS, Okuda M, Wang S, Grant BF, Blanco C. Probability and predictors of transition from first use to dependence on nicotine, alcohol, cannabis, and cocaine: results of the National Epidemiologic Survey on Alcohol and Related Conditions (NESARC). Drug Alcohol Depend. 2011 May 1;115(1-2):120-30. doi: 10.1016/j.drugalcdep.2010.11.004. Epub 2010 Dec 8. PMID: 21145178; PMCID: PMC3069146.

This cohort study of New York State Prescription Monitoring Program data from 2017 to 2019 included patients receiving MC [Medical Cannabis] for chronic pain while also receiving opioid treatment. Of these, patients receiving LOT [long-term opioid therapy] prior to receiving MC were selected. Individuals were studied for 8 months after starting MC [medical cannabis]. … The daily MME [morphine milligram equivalent] for the last month of the follow-up period among patients receiving longer MC was **reduced by 48% in the lowest stratum, 47% in the middle stratum, and 51% in the highest stratum compared with the baseline dosages**. … In this cohort study of patients receiving LOT, receiving MC for a longer duration was associated with reductions in opioid dosages. … These findings contribute robust evidence for clinicians regarding the potential benefits of MC in reducing the opioid burden for patients receiving LOT and possibly reduce their risk for overdose.
Changes in prescribed opioid dosages among patients receiving medical cannabis for chronic pain, New York State, 2017-2019, JAMA Network Open, 2023

“Patients (n = 2,183) recruited from medical dispensaries across Florida completed a 66-item cross-sectional survey that included demographic, health, and medication usage items, along with items from the Medical Outcomes Survey to assess health functioning before and after cannabis initiation. … The majority of participants (79%) reported either cessation or reduction in pain medication use following initiation of medical cannabis.”
Medical cannabis patients report improvements in health functioning and reductions in opiate use, Substance Use & Misuse, 2022

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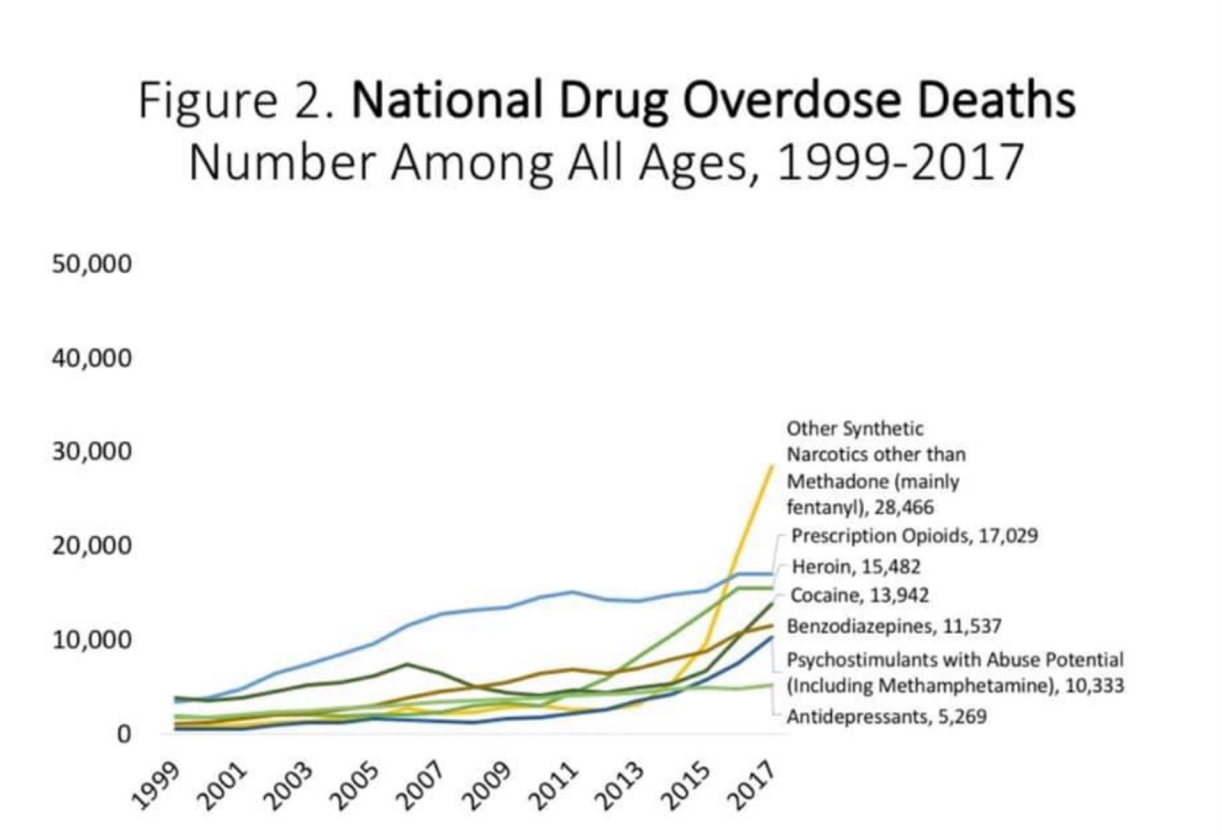
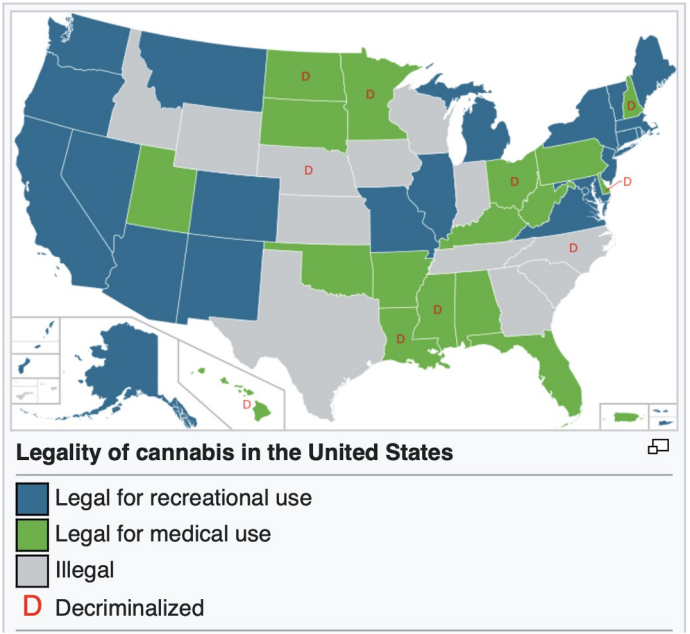
Cannabis made the list, see if you can find it....
....it's the grey line on the bottom, the 0.



NIH National Institute on Drug Abuse
Advancing Addiction Science

https://www.drugabuse.gov/related-topics/trends-statistics/overdose-death-rates

So if cannabis is potentially helpful, and has low to no mortality, why is it a schedule I drug….?



1988 - DEA Judge Francis Young

5...there are simply no credible medical reports to suggest that consuming marijuana has caused a single death.

6. By contrast aspirin, a commonly used, over-the-counter medicine, causes hundreds of deaths each year.

7. Drugs used in medicine are routinely given what is called an LD-50….

8. At present it is estimated that marijuana's LD-50 is around 1:20,000 or 1:40,000. **[one] would theoretically have to consume nearly 1,500 pounds of marijuana within about fifteen minutes to induce a lethal response.**

15. In strict medical terms marijuana is far safer than many foods we commonly consume. For example, eating ten raw potatoes can result in a toxic response. By comparison, it is physically impossible to eat enough marijuana to induce death.

16. Marijuana, in its natural form, is one of the safest therapeutically active substances known to man. By any measure of rational analysis marijuana can be safely used within a supervised routine of medical care."

Who should say something first: “My patients know about cannabis”

11:25 PM Mon Jul 1 — 7% — ncbi.nlm.nih.gov

Format: Abstract — Send to

Cancer. 2017 Nov 15;123(22):4488-4497. doi: 10.1002/cncr.30879. Epub 2017 Sep 25.

Cannabis use among patients at a comprehensive cancer center in a state with legalized medicinal and recreational use.

Pergam SA[1,2,3,4], Woodfield MC[1], Lee CM[5,6], Cheng GS[2,3], Baker KK[2], Marquis SR[1], Fann JR[2,5].

Author information

Abstract

BACKGROUND: Cannabis is purported to alleviate symptoms related to cancer treatment, although the patterns of use among cancer patients are not well known. This study was designed to determine the prevalence and methods of use among cancer patients, the perceived benefits, and the sources of information in a state with legalized cannabis.

METHODS: A cross-sectional, anonymous survey of adult cancer patients was performed at a National Cancer Institute-designated cancer center in Washington State. Random urine samples for tetrahydrocannabinol provided survey validation.

RESULTS: Nine hundred twenty-six of 2737 eligible patients (34%) completed the survey, and the median age was 58 years (interquartile range [IQR], 46-66 years). Most had a strong interest in learning about cannabis during treatment (6 on a 1-10 scale; IQR, 3-10) and wanted information from cancer providers (677 of 911 [74%]). Previous use was common (607 of 926 [66%]); 24% (222 of 926) used cannabis in the last year, and 21% (192 of 926) used cannabis in the last month. Random urine samples found similar percentages of users who reported weekly use (27 of 193 [14%] vs 164 of 926 [18%]). Active users inhaled (153 of 220 [70%]) or consumed edibles (154 of 220 [70%]); 89 (40%) used both modalities. Cannabis was used primarily for physical (165 of 219 [75%]) and neuropsychiatric symptoms (139 of 219 [63%]). Legalization significantly increased the likelihood of use in more than half of the respondents.

CONCLUSIONS: This study of cancer patients in a state with legalized cannabis found high rates of active use across broad subgroups, and legalization was reported to be important in patients' decision to use. Cancer patients desire but are not receiving information about cannabis use during their treatment from oncology providers. Cancer 2017;123:4488-97. © 2017 The Authors. Cancer published by Wiley Periodicals, Inc. on behalf of American Cancer Society. This is an open access article under the terms of the Creative Commons Attribution-NonCommercial-NoDerivs License, which permits use and distribution in any medium, provided the original work is properly cited, the use is non-commercial and no modifications or adaptations are made.

KEYWORDS: cancer; cannabis; marijuana; pain; supportive care

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Take Aways

- *Cannabis is Complex* and *Marijuana is NOT Magic*
- Goal, Strain, Route and Dose determine outcome

  - Nature did a better job than science with this one - synthetic isn't as good

- It's all about the receptors
- There are roles for cannabis to benefit basically any patient
- Cannabis can be addictive, (even if it has better numbers that tobacco, alcohol and cocaine)
- Your patients rely on you for direction.

Thanks

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