



Controversies in Care: Cannabis

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Medical Cannabis

Objectives

- List the three types of cannabinoids and proposed mechanism of action
- Describe 3 routes of administration for medical marijuana
- Discuss at least two risks of medical marijuana use







SATIVA



INDICA



RUDERALIS

- Cannabis is a family of plants – sativa, indica and ruderalis
- Hemp is a member of Cannabis Sativa family – very little THC (0.2-0.3% legal)
- Marijuana comes from Cannabis Sativa, Indica and Ruderalis – much higher THC

Hemp vs Marijuana

The Difference Between Hemp and Marijuana

Type	Is it Cannabis?	Chemical Makeup	Psychoactive?	Cultivation	Applications
Hemp	Yes	Low THC (< 0.3%)	No	Requires minimal care. Adaptable to grow in most climates.	Automobiles, body care, clothing, construction, food, plastic, etc.
Marijuana	Yes	High THC (5%-35%)	Yes	Grown in carefully controlled atmosphere	Medical and recreational use

<https://ministryofhemp.com/hemp/not-marijuana/>

Medical Marijuana

Historical Perspectives – *Cannabis*

- Early use 5000+ years ago
 - Likely began in Central Asia
 - Spread to China, India, Persia, Egypt, Syria
- Was widely used medically, recreationally, spiritually
- Plant valued as strong rope – hemp – variety of cannabis sativa plant
- Fibers used to make paper
 - Declaration of Independence



Medical Marijuana

Historical Perspectives – *Cannabis*

- 1830's W.B. O'Shaughnessy – wrote paper “Indian Hemp”
 - Irish physician working in Calcutta
 - Recommended for:
 - Pain
 - Vomiting
 - Convulsions
 - Spasticity
- 1854 – listed in US Dispensatory
- Late 1800's - Cannabis tinctures, extracts, plasters, cigarettes common
 - Insomnia, headaches, anorexia, sexual dysfunction, pain, whooping cough, asthma



Medical Marijuana

Historical Perspectives – *Cannabis*

- 1906 – The Food and Drugs Act
- 1914 – Harrison Narcotic Act
 - Regulated opioids, opium based products, coca and cocaine
- 1937 – Marihuana Tax Act (opposed by AMA)
- 1970 - Controlled Substances Act (Schedule I)
- 1973 – Drug Enforcement Agency established





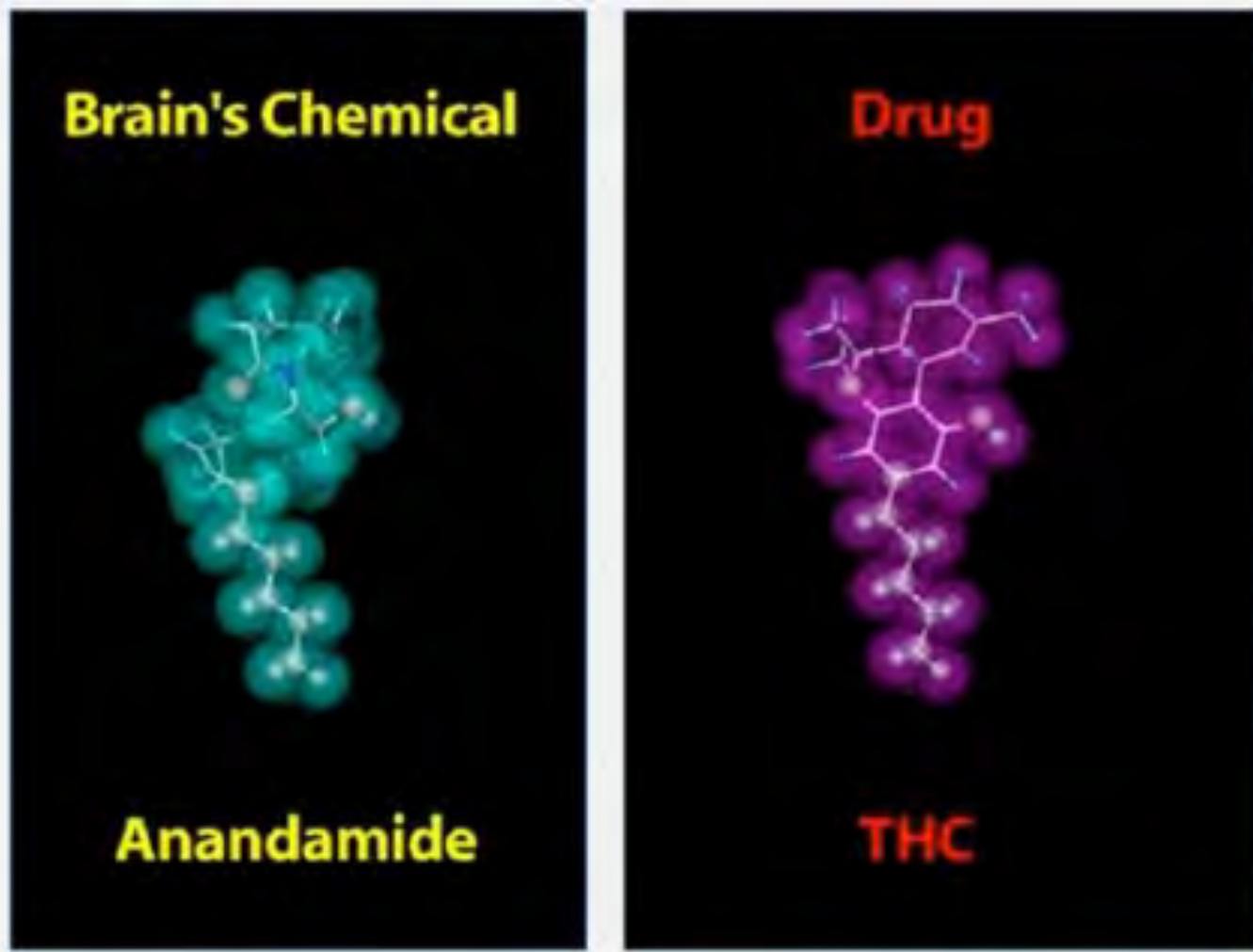
Three Types of Cannabinoids

Blurred Boundaries: The Therapeutics and Politics of Medical Marijuana

J. Michael Bostwick, MD

- Endocannabinoids
 - Endogenous neurotransmitters – arachidonic acid derivatives
 - E.g., Anandamide
- Phytocannabinoids (also called botanical cannabis)
 - Compounds found in cannabis plant (e.g., THC, CBD)
- Synthetic cannabinoids
 - Laboratory produced congeners of THC, CBD

Endocannabinoids



Endocannabinoids

CB1 receptors widely distributed throughout CNS

- Found in brain areas :
 - Pleasure, pain (frontal cortex)
 - Movement (basal ganglia, cerebellum)
 - Memory and learning (hippocampus)



Phytocannabinoids



- Cannabis indica
- Cannabis sativa
- Cannabis ruderalis

- 537+ constituents
 - THC
 - Cannabidiol (CBD)
 - Cannabinol (CBN)
 - Terpenes (found in sativa)

Synthetic Cannabinoids

- Marinol (dronabinol -THC) - CINV, anorexia due to HIV/AIDS
- Cecamet (nabilone -THC) – CINV
- Sativex (nabiximols -THC & CBD) - neuropathic pain & spasticity (not available in US)
- Epidiolex (cannabidiol) – for severe pediatric seizure disorders (Lennox-Gastaut and Dravet syndromes)



Routes of Administration

Phytocannabinoids

Routes of Administration

- Inhaled – smoked or **vaped**
- Food/ingested
- Topical/Oils



Marijuana - Inhaled

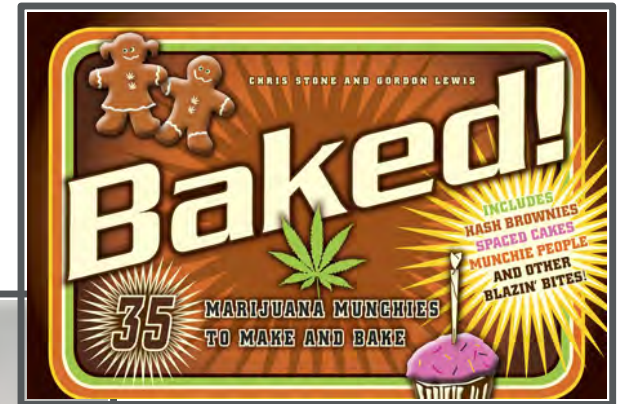
- High bioavailability
- Rapid and predictable onset
- Easy titration
- Most users experience:
 - Mild euphoria
 - Relaxation
 - Perceptual alterations
 - Intensification of ordinary experiences
- Some experience:
 - Dysphoria
 - Anxiety
 - Paranoia



Bostwick MJ, *Mayo Clin Proc* 87;172-186, 2012

Marijuana - Ingested

- Undergoes first-pass hepatic metabolism
- Slow and unpredictable onset
- More difficult to titrate to effect





Mary Jane's

HASH BROWNIES,
HOT POT, AND OTHER
MARIJUANA MUNCHIES

30 delectable ways with weed

DR HASH



Don't Harsh Our Mellow, Dude

JUNE 3, 2014

The New York Times



**Maureen
Dowd**

The caramel-chocolate flavored candy bar looked so innocent, like the Sky Bars I used to love as a child.

Sitting in my hotel room in Denver, I nibbled off the end and then, when nothing happened, nibbled some more. I figured if I was reporting on

Don't Harsh Our Mellow, Dude

JUNE 3, 2014



Maureen Dowd

SundayReview | Pot Rules

Pot Rules

JUNE 7, 2014

The New York Times

Maureen Dowd

WASHINGTON — IN the [last chapter](#), I covered how not to get high. In this one, I will cover how to get high.

After my admission that I did a foolish thing in Denver — failing to realize that consuming a single square, about

Topical



Potential Indications

Indications



Indications

- Glaucoma
 - Other standard treatments more effective
- Nausea
 - Suppresses nausea more than vomiting; can cause hyperemesis
- AIDS-associated anorexia and wasting
 - Data inconclusive
- Chronic pain
 - Various models of pain; dronabinol lower ratings on reward
- Inflammation
 - Induce apoptosis, inhibit cell proliferation, suppress cytokine (RA, Crohn's)
- Multiple sclerosis
 - Nabiximol – neuropathic pain, sleep, spasticity
- Epilepsy
 - Small survey positive, animal models positive, concern re: safety

Volkow ND, et al. *NEJM* 370;23:2219-27, 2014.

Kramer JL. *CA: A Cancer Journal for Clinicians* 15;16:109-122, 2015.

Marijuana

Risks

- Lifetime dependence
 - Marijuana – 9%
 - Nicotine – 32%
 - Heroin – 23 %
 - Cocaine – 17%
 - Alcohol – 15%
- Withdrawal
 - Irritability
 - Anxiety
 - Anorexia
 - Weight loss
 - Restlessness
 - Craving

The NEW ENGLAND JOURNAL of MEDICINE

REVIEW ARTICLE

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

Adverse Health Effects of Marijuana Use

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

Volkow ND, et al. Adverse health effects of marijuana use. *NEJM* 370;23:2219-27, 2014.



The NEW ENGLAND
JOURNAL of MEDICINE
ГОДНИКЪ МЕДИЦИНЕ

Volkow ND, et al.
Adverse health effects
of marijuana use. *NEJM*
370;23:2219-27, 2014.

Table 1. Adverse Effects of Short-Term Use and Long-Term or Heavy Use of Marijuana.

Effects of short-term use

Impaired short-term memory, making it difficult to learn and to retain information

Impaired motor coordination, interfering with driving skills and increasing the risk of injuries

Altered judgment, increasing the risk of sexual behaviors that facilitate the transmission of sexually transmitted diseases

In high doses, paranoia and psychosis

Effects of long-term or heavy use

Addiction (in about 9% of users overall, 17% of those who begin use in adolescence, and 25 to 50% of those who are daily users)*

Altered brain development*

Poor educational outcome, with increased likelihood of dropping out of school*

Cognitive impairment, with lower IQ among those who were frequent users during adolescence*

Diminished life satisfaction and achievement (determined on the basis of subjective and objective measures as compared with such ratings in the general population)*

Symptoms of chronic bronchitis

Increased risk of chronic psychosis disorders (including schizophrenia) in persons with a predisposition to such disorders

* The effect is strongly associated with initial marijuana use early in adolescence.



Effect of recreational marijuana sales on police-reported crashes in Colorado, Oregon, and Washington

October 2018

Samuel S. Monfort
Insurance Institute for Highway Safety

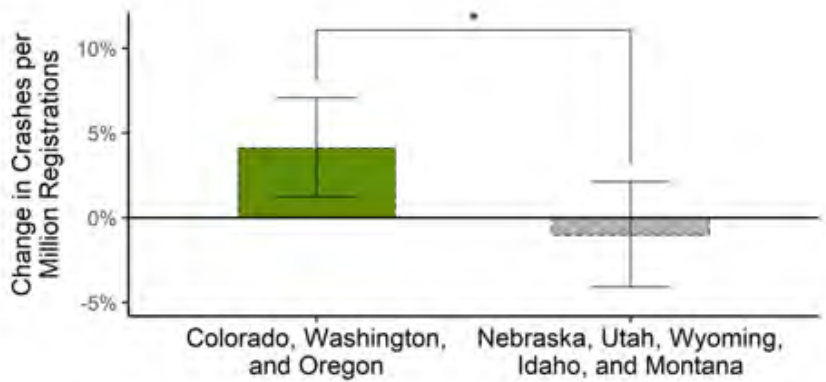
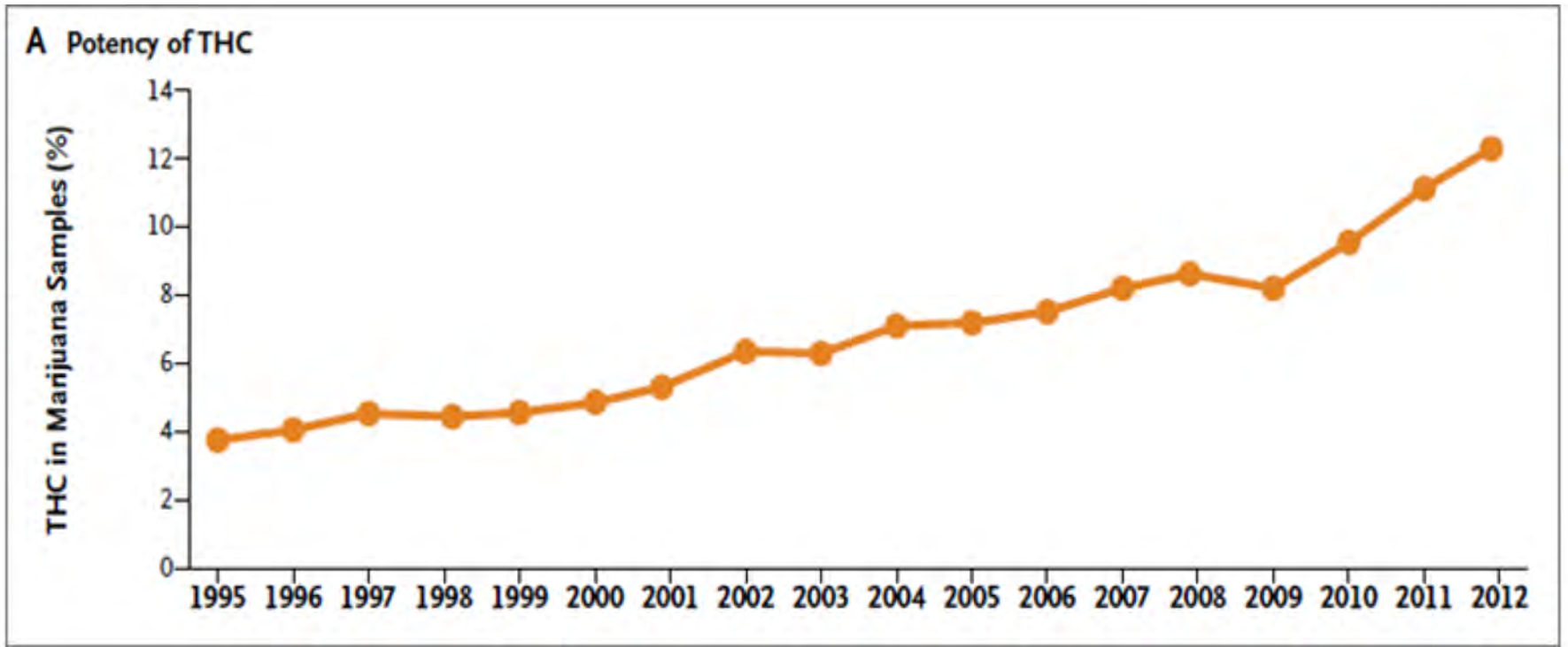


Figure 1. Estimated percent change in crash rates from pre- to post-legalization with covariates held constant. Error bars represent 95% confidence intervals.* = $p < .05$.

THC Potency



Volkow ND, et al. Adverse health effects of marijuana use. *NEJM* 370;23:2219-27, 2014.



Regulatory Issues



Marijuana in the US

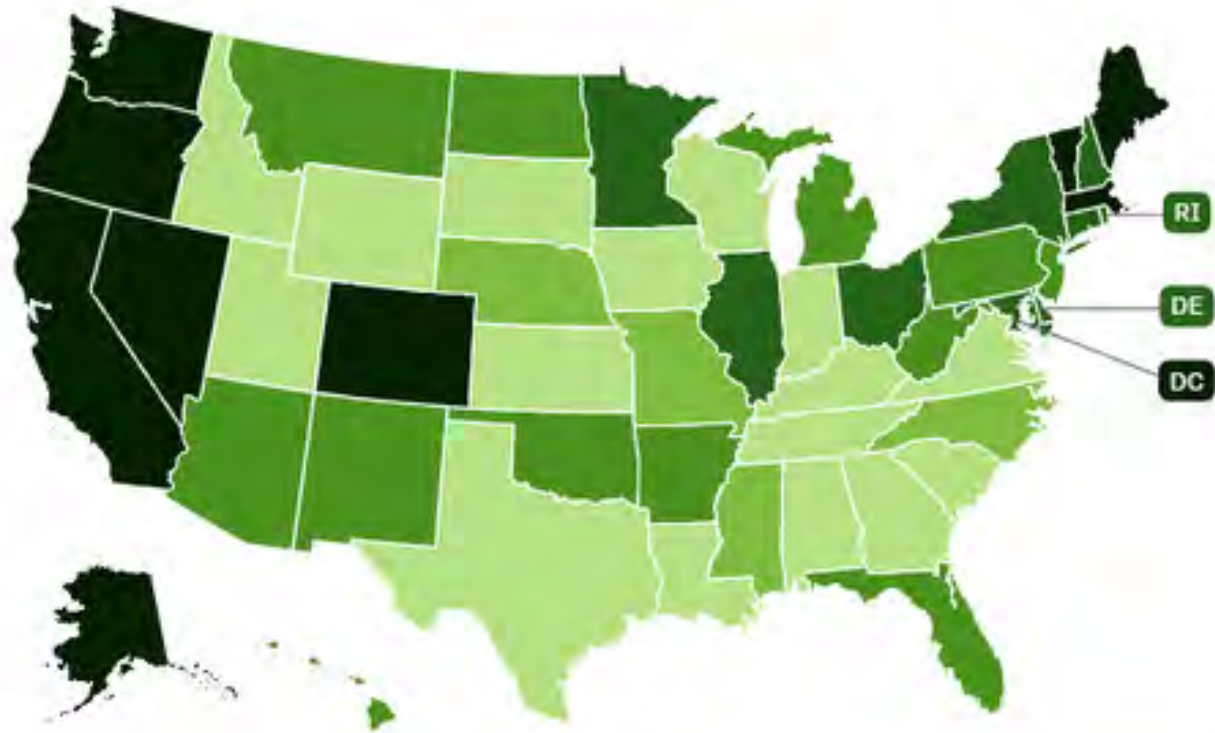
Evolving Legal Status



Marijuana laws in the US

Note: Vermont and Washington, DC, do not allow marijuana sales for recreational purposes.

Legalized Medical and decriminalized Medical Decriminalized Fully illegal



Source: Marijuana Policy Project
Credit: German Lopez

Vox

No Federal Oversight of Content

- Claims by Marketers
 - Chronic pain: Afghani #1 or Big Bud
 - Depression: Blueberry, OG-18
 - Glaucoma: Pluto OG
 - Headaches: White Gold, Super Lemon Haze
 - Insomnia: Northern Lights
 - Joint pain: Purple Kush
 - Multiple Sclerosis: Island Sweet Skunk, Sour Diesel
 - Nausea: Dutch Haze, Kandy Kush

Not covered by FDA

www.unitedpatientsgroup.com

The Compassionate Use of Medical Cannabis Pilot Program Act

Illinois Bill HB 0001 – became law January 1, 2014

- The physician provides a "written certification" - a document dated and signed by a physician, stating:
 - ~~(1) that in the physician's professional opinion the patient is likely to receive therapeutic or palliative benefit from the medical use of cannabis;~~
 - (2) specify the debilitating medical condition; and
 - (3) that the patient is under the physician's care for the debilitating medical condition.

This needs to be done during an in-person assessment, with documentation of medical history and a physical examination. Records need to be maintained – it is not yet clear if a note is sufficient or if a registry needs to be maintained.





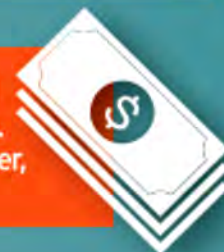
Top 10 Tips for Successfully Completing Your Medical Cannabis Patient Registry Application

- 1 Physician Written Certification Form** - Meet with your physician to discuss the use of medical cannabis for the treatment of your condition. This is an important first step in the application process. Your doctor must complete and mail this form to the Department. Your appointment must be within 90 days of submitting your application to the Department.



- 2 Complete and sign application** - Fill in all parts of the application, choose a medical cannabis dispensing organization and sign the last page. You may also fill out the optional demographic information. If you do not want to designate a caregiver, don't fill out that section of the application.

- 3 Application Fee** - Non-refundable fee of \$100 or reduced fee of \$50 for veterans or persons enrolled in federal Social Security Disability Income (SSDI) or Supplemental Security Income (SSI) disability program. Veterans, include a copy of your DD214. SSDI/SSI recipients, include a copy of your benefit verification letter, dated within the last year.



- 4 Photograph** - Do not send in a selfie! Provide a 2x2 inch passport-sized photo. Double check - are you by yourself, facing the camera, is your full face showing? Take the picture against a plain, white backdrop with absolutely nothing in the background or visit a local passport photo service.

- 5 Proof of residency** - You will need two items that prove you live in Illinois. The addresses on each of the documents must match the address on your application. Bank statements, utility bills, state ID, driver's license and voter ID cards are all acceptable. Check the application for a full list.





6 Proof of age and identity - Send us a copy of a valid, unexpired government issued photo ID.

7 Fingerprint Consent Form and Receipt from the livescan fingerprint vendor -

The form must be signed and include the Transaction Control Number (TCN). You must submit the completed form along with your application within 30 days of being fingerprinted.



8 Veterans - Send in a copy of your DD214 and the \$50 application fee. If you are receiving care at a Veterans Affairs (VA) facility, you may submit medical records from the VA about treatment for your qualifying debilitating medical condition from the past year, instead of a Physician Written Certification Form.

9 Caregiver application - Complete the entire caregiver application and send it with the \$25 caregiver fee and all supporting documents (photo, proof of residency, proof of age and identity, fingerprint consent form, caregiver's signature). The caregiver application should be sent with your patient application.



10 Call or email with questions - If you have a question, check with the Division of Medical Cannabis before sending your application. Call us at 855-636-3688 or send an email to DPH.MedicalCannabis@Illinois.gov. You may also view our Frequently Asked Questions.

[Animal Population Control](#)[Community Health Workers](#)[Epinephrine Auto-Injector and Anaphylaxis](#)[Immunization](#)[Injury & Violence Prevention](#)[Medical Cannabis](#)[Application Help \(FREE\)](#)[Debilitating Conditions](#)[Lost or Stolen Card](#)[Medical Cannabis Patient Application](#)[Minor Qualifying Patients](#)[Terminal Illness](#)[FEES](#)[Select a Medical Cannabis Dispensary](#)[Change Your Application Information](#)[Physician Information](#)[Petition to Add Debilitating Conditions](#)[Extending Your Registry Card](#)[Reports and Program Statistics](#)[Synthetic Cannabinoids](#)

Medical Cannabis Patient Registry Program

On August 28, 2018, the Opioid Alternative Pilot Program ([Public Act 100-1114](#)) became effective. While certain provisions can be implemented immediately, there is significant work which must be completed before the program starts. The Act requires IDPH and the other agencies involved in the program to adopt emergency administrative rules by December 1, 2018. IDPH will also have to make changes in the registration process to implement the Opioid Alternative Pilot Program. The provisions of P.A. 100-1114 which became effective immediately are:

- Patients and Designated Caregivers applying for a Medical Cannabis registry card do not need to submit fingerprints or consent to a background check as part of their application.
- No business or person may charge patients for help filling out applications. If a patient needs help with the application process, they visit a participating [local health department](#) for free help. Many medical cannabis dispensaries can also help a patient fill out the application at no charge.
- Certifying physicians are required to have a relationship with the patient established at a physician's office, hospital, or other healthcare facility and the physician must have an ongoing responsibility for the patient's assessment, care, and treatment.

Please watch this webpage or check the Statewide Medical Cannabis Program website www.mcpp.illinois.gov regularly for program updates as we work to implement this new initiative.

Please do not send any documents for the Opioid Alternative Pilot Program to the Department at this time. Do not use the current application to submit your registration for a registry card unless you are applying for the current Medical Cannabis Registry Program.

We do not offer onsite assistance, but we are able to answer your questions or process your requests via email at: DPH.medicalcannabis@illinois.gov

Medical Cannabis Program representatives are available by phone at 1-855-636-3688 Monday through Friday, 9:00 AM to 4:00 PM

Menu link:

RESOURCES

[Statewide Medical Cannabis Pilot Program](#)

LAWS & RULES

[Compassionate Use of Medical Cannabis Pilot Program](#)[Compassionate Use of Medical Cannabis Patient Registry Administrative Code](#)

PUBLICATIONS

[Tips for Successfully Applying for a Patient Registry Card](#)[Brochure - Medical Cannabis Infused Products](#)[Mind Your Meds - Basic Medication Safety Tips](#)[A Slippery Slope: The Dangers of Prescription Drug Misuse and Abuse](#)[Drug Facts - Marijuana](#)

Review

Medical Marijuana Use in Oncology A Review

Gianna Wilkie, BS; Bachir Sakr, MD; Tina Rizack, MD, MPH

IMPORTANCE Medicinal marijuana use is currently legal in 23 states and the District of Columbia. As more states approve marijuana use for medical indications, physicians will be asked by their patients for more information regarding the risks and benefits of use. This article reviews the history, adverse effects, and proposed mechanisms of action of marijuana and summarizes the available literature regarding symptom relief and therapeutic value in patients with cancer.

OBSERVATIONS Marijuana in oncology may have potential for use as an antiemetic, for refractory cancer pain, and as an antitumor agent. However, much of the data are based on animal data, small trials, or are outdated.

CONCLUSIONS AND RELEVANCE More research is needed in all areas related to the therapeutic use of marijuana in oncology.

JAMA Oncol. 2016;2(5):670-675. doi:10.1001/jamaoncol.2016.0155
Published online March 17, 2016.

+ CME Quiz at
jamanetworkcme.com and
CME Questions page 694

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Contents lists available at ScienceDirect

European Journal of Internal Medicine

journal homepage: www.elsevier.com/locate/ejim



Prospective analysis of safety and efficacy of medical cannabis in large unselected population of patients with cancer

Lihi Bar-Lev Schleider^{a,b}, Raphael Mechoulam^c, Violeta Lederman^b, Mario Hilou^b, Ori Lencovsky^a, Oded Betzalel^b, Liat Shbiro^a, Victor Novack^{a,*}

^a Clinical Cannabis Research Institute, Soroka University Medical Center and Faculty of Health Sciences, Ben-Gurion University of the Negev, Be'er-Sheva, Israel

^b Research Department, Tikun Olam LTD, Israel

^c Institute for Drug Research, School of Pharmacy, the Hebrew University of Jerusalem, Israel



Background: Cancer is a major public health problem as the leading cause of death. Palliative treatment aimed to alleviate pain and nausea in patients with advanced disease is a cornerstone of oncology. In 2007, the Israeli Ministry of Health began providing approvals for medical cannabis for the palliation of cancer symptoms. The aim of this study is to characterize the epidemiology of cancer patients receiving medical cannabis treatment and describe the safety and efficacy of this therapy.

Methods: We analyzed the data routinely collected as part of the treatment program of 2970 cancer patients treated with medical cannabis between 2015 and 2017.

Results: The average age was 59.5 ± 16.3 years, 54.6% women and 26.7% of the patients reported previous experience with cannabis. The most frequent types of cancer were: breast (20.7%), lung (13.6%), pancreatic (8.1%) and colorectal (7.9%) with 51.2% being at stage 4. The main symptoms requiring therapy were: sleep problems (78.4%), pain (77.7%, median intensity 8/10), weakness (72.7%), nausea (64.6%) and lack of appetite (48.9%). After six months of follow up, 902 patients (24.9%) died and 682 (18.8%) stopped the treatment. Of the remaining, 1211 (60.6%) responded; 95.9% reported an improvement in their condition, 45 patients (3.7%) reported no change and four patients (0.3%) reported deterioration in their medical condition.

Conclusions: Cannabis as a palliative treatment for cancer patients seems to be well tolerated, effective and safe option to help patients cope with the malignancy related symptoms.

What Are you Really Getting?

- Accurate labeling in dispensaries in San Francisco, Los Angeles, Seattle
- < 17%
- CBD purchased over internet – most contain little or no active ingredient

Vandrey R, et al; JAMA 2015;313:2491-2493
2015 Warning Letters and Test Results for Cannabidiol-Related Products:
[www.fda.gov/NewsEvents/PublicHealth
Focus/ucm435591.htm](http://www.fda.gov/NewsEvents/PublicHealthFocus/ucm435591.htm). 2016

Pros and Cons

Pros

- Possible health benefits
 - Anxiolysis, sleep, pain, spasticity
- Possible reduction in opioid overdose and opioid misuse

Cons

- “Medical” may reduce perception of risk, especially among younger users
- Increased availability may increase access for non-medical use
- Increases in impaired driving
- Edible forms mistaken as candy by children and pets

Hasin DS, et al. JAMA Psychiatry April 26, 2017

Factoids

- Consider urine drug screens
- Pointers:
 - Do not bring to NM!!
 - Travel to states where it is not legal not advised (federal offense)
 - No use or growing on federal lands
 - No use by minors
 - Drugged driving

CORRESPONDENCE



Medical Marijuana Miscalculation

- 52 year old man anaplastic astrocytoma
- Acute delirium; unchanged CT head
- Liquid marijuana – 500 mg of 65.9% THC in 1 mL syringe
- Each 0.1 mL = 50 mg THC: 10-20 X recommended therapeutic dose (10 mg usual starting dose)



Figure 1. Liquid Marijuana Packaging and Syringe.

The liquid marijuana product used by the patient was obtained from a local medical marijuana dispensary. The syringe contains the amount remaining after 2 days of use.

Stoned



David Casarett, M.D.

ORIGINAL ARTICLE

“Zombie” Outbreak Caused by the Synthetic Cannabinoid AMB-FUBINACA in New York

Axel J. Adams, B.S., Samuel D. Banister, Ph.D., Lisandro Irizarry, M.D., Jordan Trecki, Ph.D., Michael Schwartz, M.D., M.P.H., and Roy Gerona, Ph.D.

December 14, 2016



DANGER:
FAKE WEED + U = ZOMBIE

The chemicals in fake weed cause hallucinations, paranoia and seizures.

DON'T RISK IT. www.K2ZombieDC.com

K2 ZOMBIE DC

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- Instagram us @ K2ZombieDC

This is a paid advertisement sponsored by DC Department of Health. The advertising space is a designated public forum and does not imply WMATA's endorsement of any views expressed.

D.C. DOH

FAAH-OUT

- No pain during childbirth
- Frequent trauma/surgery – no idea
- No anxiety
- Forgetful – losing items, train of thought midsentence
- Never felt adrenaline rush
- Elevated levels of anandamide – normally degraded by FAAH (fatty acid amide hydrolase)
- Enhanced endocannabinoid signalling



<https://www.nytimes.com/2019/03/28/health/woman-pain-anxiety.html>

Habib AM, et al. British Journal of Anaesthesia
doi: 10.1016/j.bja.2019.02.019



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“Never doubt that a small group of thoughtful, committed citizens can change the world. Indeed, it is the only thing that ever has”.

Margaret Mead