



Medical Marijuana

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Cancer Connections

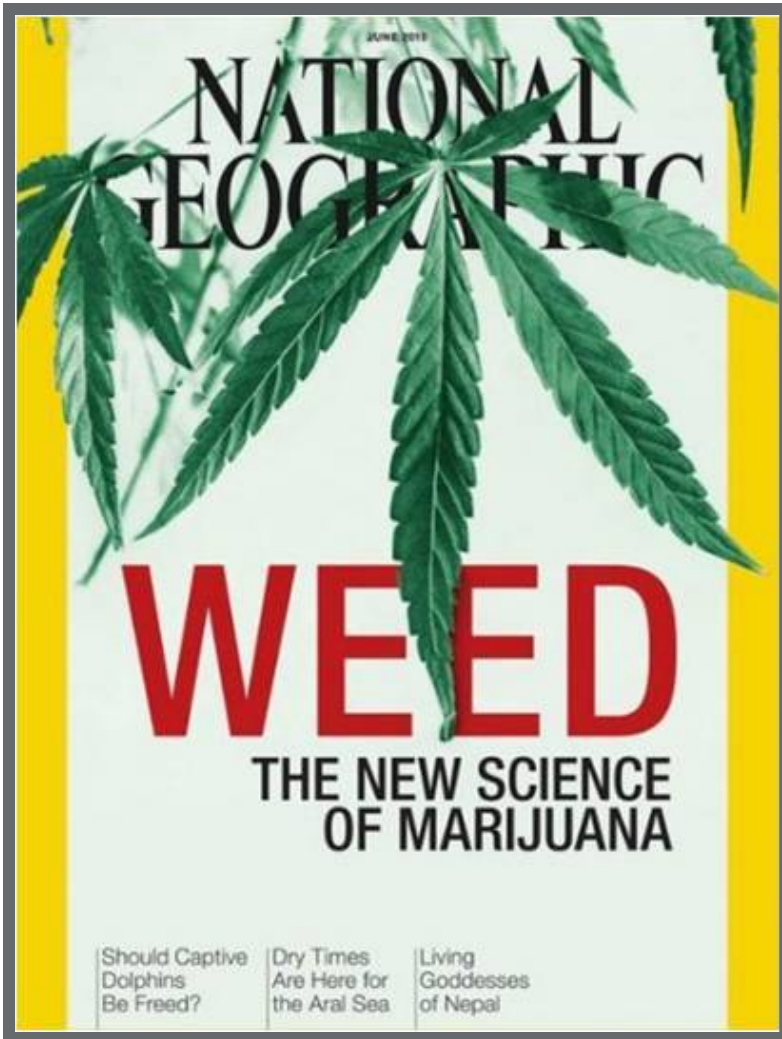
July 15, 2017

Medical Marijuana

Objectives

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





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
- 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





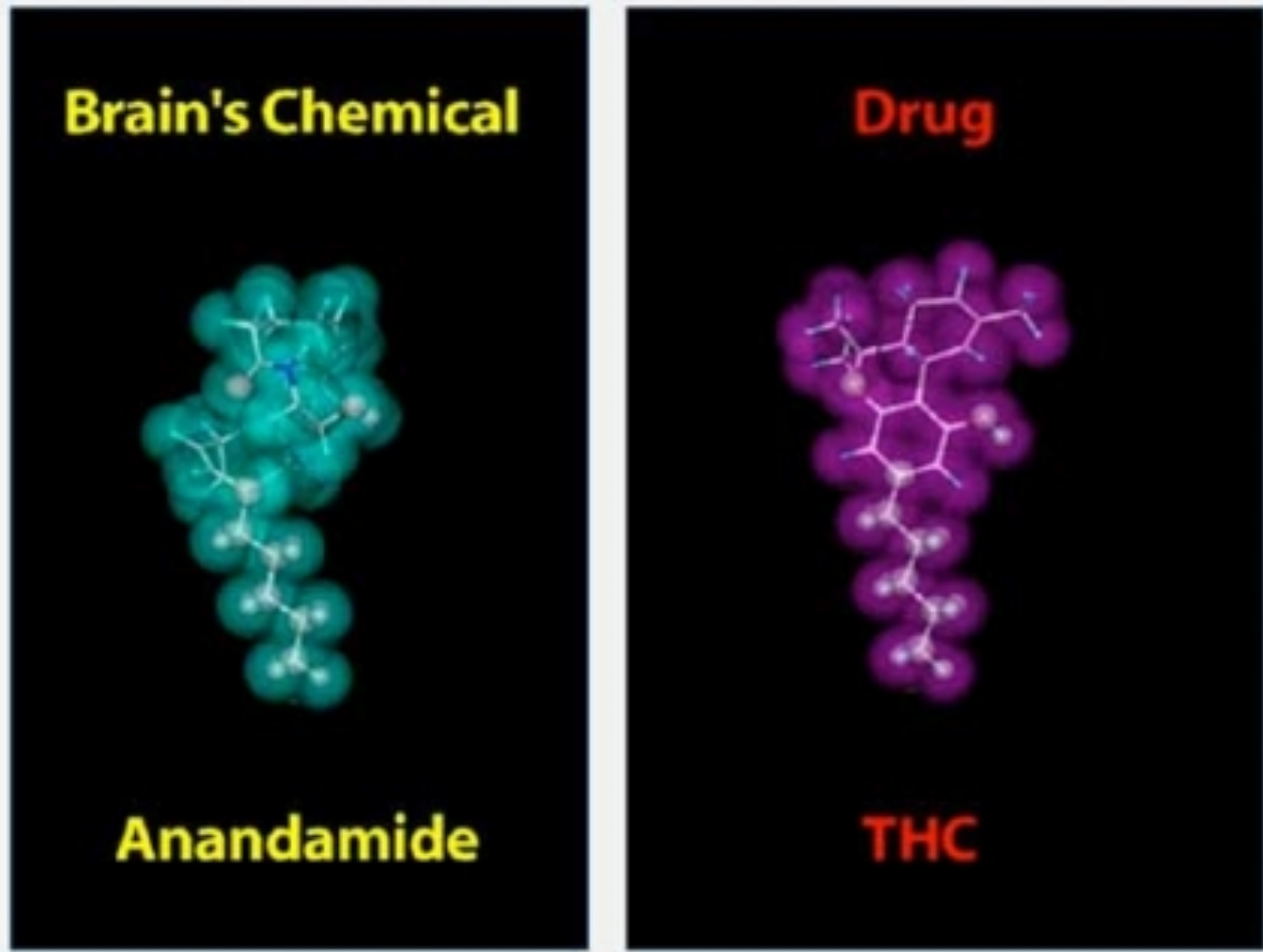
Three Types of Cannabinoids

Blurred Boundaries: The Therapeutics and Politics of Medical Marijuana

J. Michael Bostwick, MD

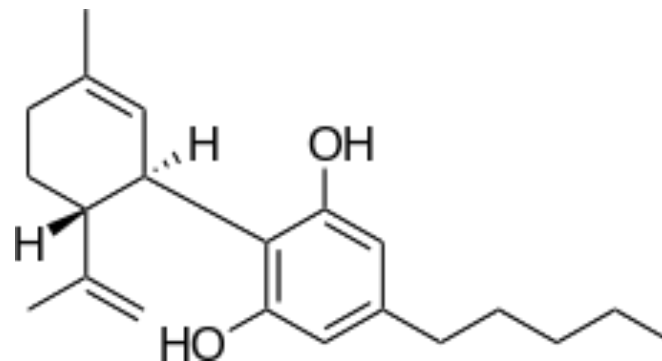
- Endocannabinoids
 - Endogenous neurotransmitters – arachidonic acid derivatives
 - E.g., Anandamide
- Phytocannabinoids (also called botanical cannabis)
 - Compounds found in cannabis plant (e.g., THC, CBD)
- Synthetic cannabinoids
 - Laboratory produced congeners of THC, CBD

Endocannabinoids



Endocannabinoids

- 1964 - δ -9-tetrahydrocannabinol (THC) isolated
- 1990 - Cannabinoid 1 (CB1) receptor cloned
 - Expressed primarily in CNS, lungs, liver, kidneys
- 1992 – Anandamide discovered (binds to CB1)
- 1993 – CB2 receptor cloned
 - Expressed primarily in immune, hematopoietic systems



Cannabidiol

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
 - Terpenes (found in sativa)

Synthetic Cannabinoids

- Dronabinol - CINV, anorexia due to HIV/AIDS
- Nabilone – CINV
- Nabiximols - neuropathic pain (not yet available in US)

Synthetic Cannabinoids

Nabiximols

- Oromucosal spray – reduces first pass effect
- 2.7 mg THC and 2.5 mg CBD (1:1 ratio)
- Indications:
 - MS induced spasticity
 - Neuropathic pain
 - Cancer pain
- Approved/recommended for approval in 20+ countries: UK, Canada, Spain, Germany, Sweden, Czech Republic, Australia, Norway, Finland

Routes of Administration

Phytocannabinoids

Routes of Administration

- Inhaled – smoked or vaporized
- Food/ingested
- 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



Table 1. Pharmacologic Parameters Of Oral and Inhaled Marijuana

Pharmacologic Parameter	Oral	Inhaled
Bioavailability, %	6-20	10-40
Time to peak concentrations	1-6 hours	2-10 minutes
Maximal duration	2-3 hours	Dose-dependent; maximal psychotropic effects, 20 minutes; with rapid decline lasting 45-60 minutes
Distribution	90% plasma; protein-bound 10% red blood cells 1% in brain Crosses placenta and found in breast milk	

Sources: *Clin Pharmacol Ther* 2015;97(6):575-586;
Crit Rev Oncol Hematol 2012;83(1):1-10; *CA Cancer J Clin* 2015;65(2):109-122.



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



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

Potential 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.

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.

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

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



The NEW ENGLAND
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ГОУВНУГ ђ MEDICINE

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*

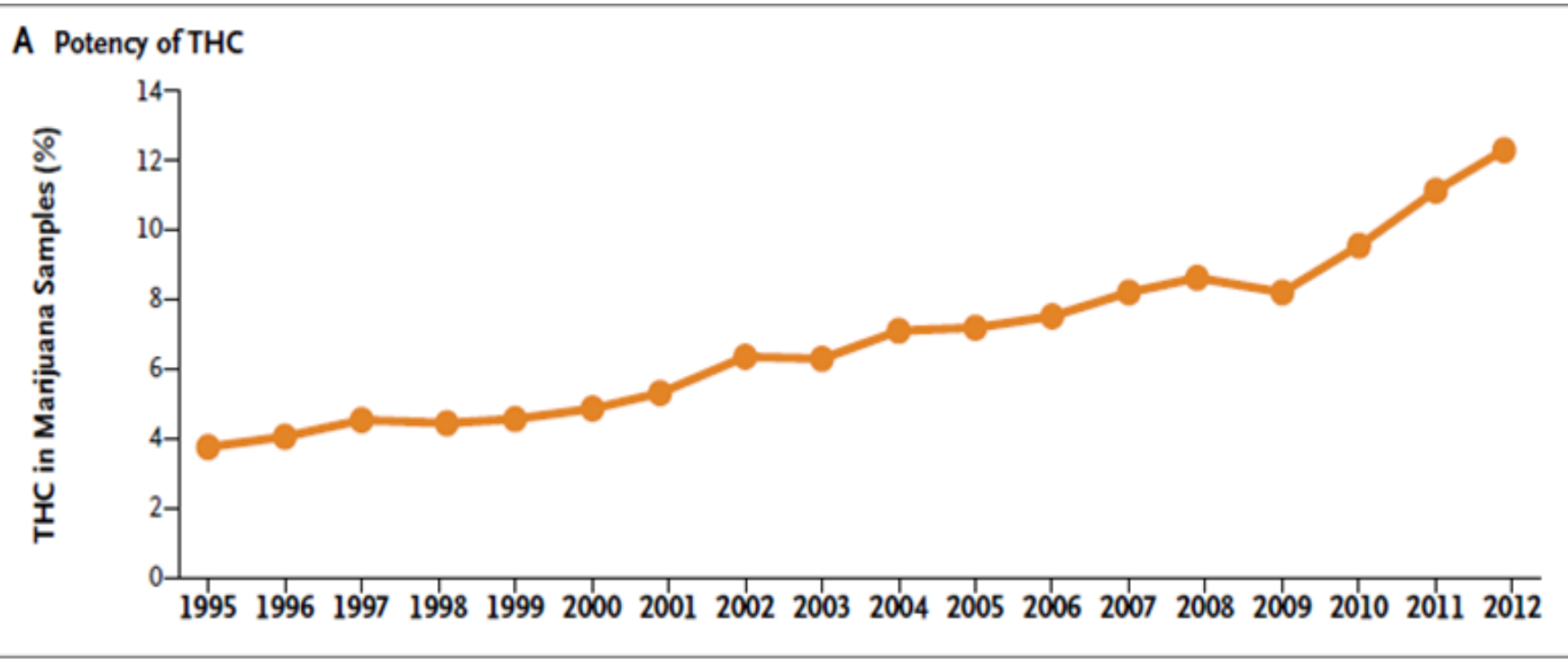
Diminished life satisfaction and achievement (determined on the basis of subjective and objective measures as compared with such ratings in the general population)*

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.

THC Potency



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

ARTICLE IN PRESS



RESEARCH
EDUCATION
TREATMENT
ADVOCACY



The Journal of Pain, Vol ■, No ■ (■), 2016: pp 1-15
Available online at www.jpain.org and www.sciencedirect.com

Focus Article

Cannabis in Pain Treatment: Clinical and Research Considerations

Seddon R. Savage,^{*,†} Alfonso Romero-Sandoval,[‡] Michael Schatman,[§] Mark Wallace,[¶]
Gilbert Fanciullo,^{*} Bill McCarberg,[¶] and Mark Ware^{||}

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[§]*U.S. Pain Foundation, Bellevue, Washington and Middletown, Connecticut.*

[¶]*University of California San Diego School of Medicine, La Jolla, California.*

^{||}*McGill University Faculty of Medicine, Montreal, Quebec, Canada.*

Table 1. Clinical Practice Recommendations for Care of Patients Using Cannabis as Therapy*

<i>ITEM</i>
Be aware of federal laws and prevailing interpretation and enforcement
Be aware of and work within state laws governing use of medical cannabis
Establish/learn the patient's goals for therapeutic use of cannabis
Screen for risk of misuse, addiction, and diversion
Counsel patients on individualized clinical risks and potential benefits of cannabis on the basis of their symptoms, conditions, and comorbidities
Advise on cannabis strains, cannabinoid medications, or extracts as possible, recognizing limitations due to lack of herbal/substance uniformity and regulatory oversight
Advise on routes of administration on the basis of current evidence
Be guided in all advising by available scientific evidence, not relying on messaging of commercial interests
Monitor similarly to opioids and other controlled substances:
<ul style="list-style-type: none"> ● Consider written informed consent and agreement to assure mutual understanding ● Review at regular intervals ● Assess control of targeted symptoms, functional status, pattern of use of cannabis or other substances, and medications ● Consider periodic UDTs for objective information on substance use
Continue or discontinue on the basis of observed outcomes:
<ul style="list-style-type: none"> ● Continue authorization if goals of treatment being met without harm ● Discontinue if not helpful in moving toward goals or if major intolerance or unsafe medication or substance use
Intervene through counseling or referral if harmful use or declining function apparent
Renew or recommend authorization/certification, or not, on the basis of observed outcomes:
<ul style="list-style-type: none"> ● Continuation if goals of treatment being met without harm ● Discontinuation if not helpful in moving toward goals or if unsafe medication or substance use

Regulatory Issues

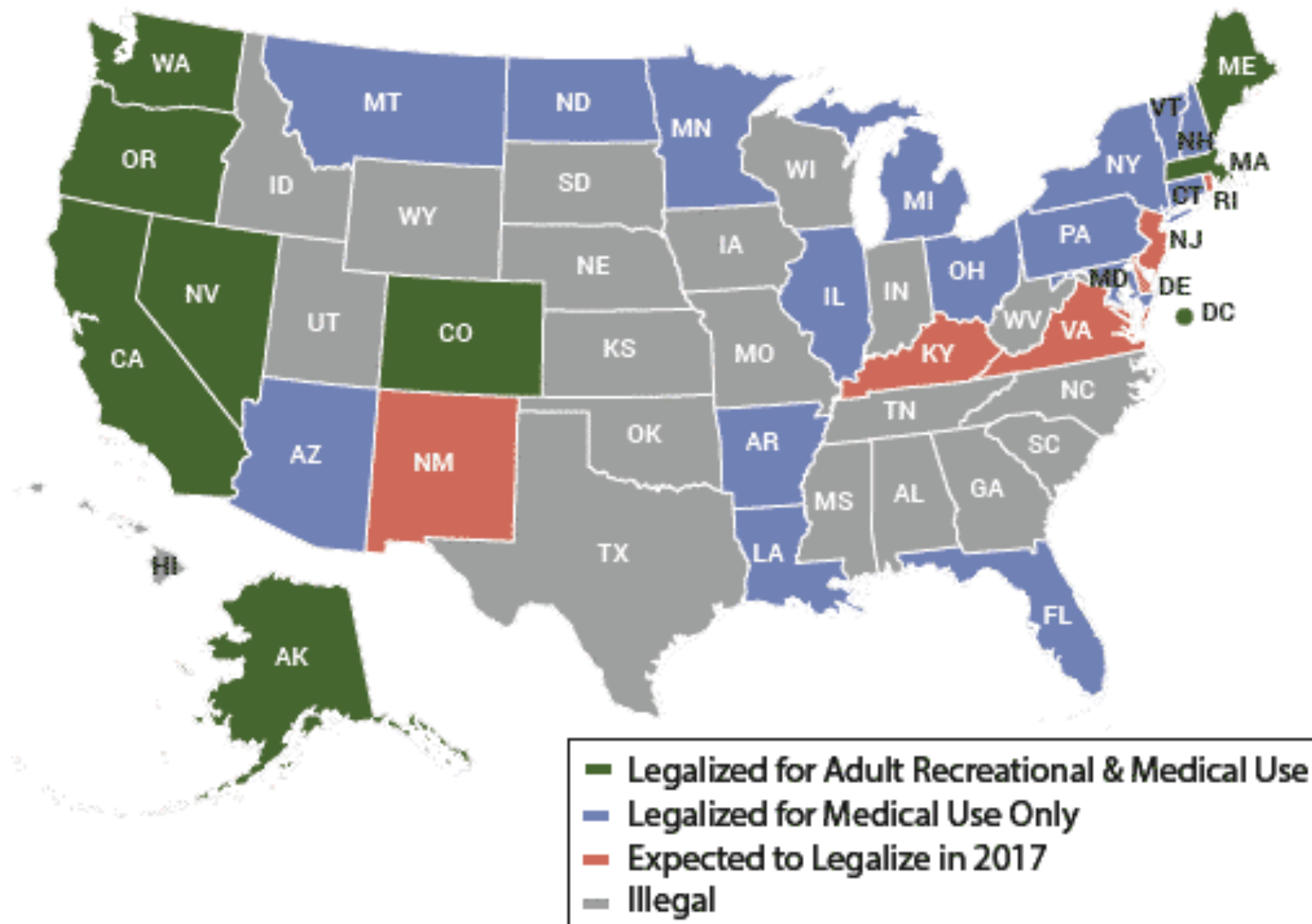
Marijuana in the US

Evolving Legal Status



States That Have Legalized Marijuana

After Nov. 8, these states now allow some form of legalized marijuana.



Sources: Money Morning Staff Research

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 (only MD or DO, not DDS or midlevel providers), 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 the 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.

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.

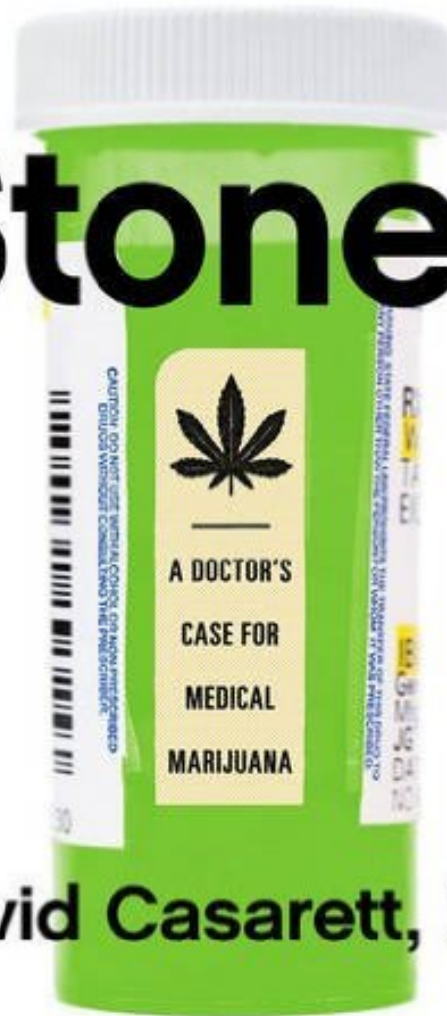
JAMA Oncol. 2016;2(5):670-675. doi:10.1001/jamaoncol.2016.0155
Published online March 17, 2016.

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

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Corresponding Author: Tina Rizack, MD, MPH, Program in Women's Oncology, Women and Infants' Hospital, Alpert Medical School of Brown University, 1 Blackstone Pl, Providence, RI 02905 (trizack@wihri.org).

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 

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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