

# Medical Marijuana: It's HIGH Time to Talk

ALISHA BENNER, MD  
PALLIATIVE MEDICINE



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## Overview

- > **History of medical marijuana**
- > Pharmacology
- > Physiology
- > Barriers to cannabis research
- > Current research on medical cannabis
- > Safety concerns and side effects
- > Current status

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## Herbal (Marijuana)

- > Most commonly used form in the US
- > Consists of the dried flowers, leaves and stems of the female cannabis plant where the active psychotropic substances are found
- > "Marijuana" is a slang term for the cannabis plant initially used by narcotic enforcement to scare potential users



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### History

- > Excavation in present day Afghanistan uncovered 120,000 y/o Paleolithic settlement
- > Several bodies buried with cannabis seeds and ashes



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### Japanese Neolithic cave drawings (~10,000 years old)



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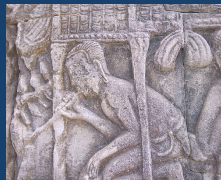
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### Ancient Greek and Roman Use



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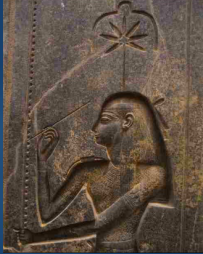
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### Egyptian Pharaohs and Priests



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2,500 year old mummified Siberian princess buried with cannabis found to have metastatic breast cancer



It is speculated she may have used cannabis palliatively

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### Rollercoaster History

- > **1800's**
  - > Hemp cultivated and used widely in US colonies for supplies like rope & cloth
- > **Late 19<sup>th</sup> century**
  - > Cannabis became a popular ingredient in many medicinal products and was sold openly in public pharmacies
- > **1850**
  - > US Physician's Pharmacopeia lists cannabis as "highly recommended" for a wide range of ailments including constipation, pain relief, muscle spasm, gout, neuropathy, insomnia and convulsions (seizures)
  - > Not removed until 1941
- > Sir William Osler had stated there was no greater medicine for migraine headaches

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### History

- **1920's-30's (Prohibition)**
  - Many commercially available cannabis-based medications
    - Eli-Lilly, Parke Davis, Merck
  - Studies linked marijuana to an increase in violence and crimes
  - By 1931- 29 states had outlawed marijuana
- **1940's**
  - Use of cannabis for any purpose, including medicinal, was criminalized in US
    - Against advice of the AMA
- **1960-70's**
  - More lax politics & cultural embrace of marijuana
  - New research (commissioned by Presidents JFK and Johnson) unlinked marijuana to crime
  - Increased drug use

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### History

- **1970's**
  - Marijuana listed as Schedule I Drug
    - No currently accepted medical use and a high potential for abuse
  - 1971 – Controlled Substances Act
    - Criminalized all recreational and medicinal use of cannabis

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### 1970's

- 1975 Journal of the National Cancer Institute
  - In mouse model demonstrated inhibition of lung cancer cells proliferation by THC and CBN, not by CBD
- 1976 Cancer Research
  - In vitro study demonstrated inhibition of DNA synthesis in lung cancer cells

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### History

- **1980's**
  - President Bush, the DEA and the National Institute on Drug Abuse (NIDA) start the 1980s "War on Drugs"  
Nationwide movement emerged of parent groups lobbying for stricter regulation of marijuana use by teenagers

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### 1990 ASCO Survey

- Random-sample, anonymous survey of ASCO members
- Conducted to measure the attitudes and experiences of U.S. oncologists concerning the use of marijuana for CINV
- 1035 respondents (43%) – not all oncologists answered each question
  - Data analysis extracted from total # of respondents answering each particular question
- 70% (n = 686) reported at least one of their patients was using medical marijuana and that they had discussed it with that patient
- 44% (n= 432) said they had recommended marijuana to at least one patient

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### 1990 ASCO Survey

- > 63% (n = 608) agreed with the statement affirming the efficacy of marijuana in the treatment of nausea and vomiting
  - > Only 77 respondents (8%) disagreed
- > 73% (n = 577) believed marijuana was both safe and efficacious
- > 53% (n = 599) favored making marijuana available by prescription

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### NIH 1997

"convened an Ad Hoc Group of Experts, which concluded that scientific evidence was insufficient to definitively assess marijuana's therapeutic potential and advised that the traditional scientific process should be allowed to evaluate the drug's use for certain disorders."

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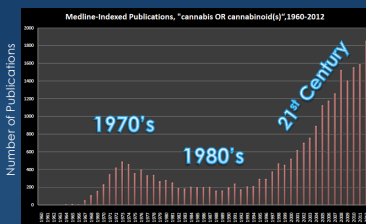
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Much of what has led to today's views on medicinal cannabis has been based on political and societal agendas rather than medical evidence



The medical literature follows political/social trends

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## THC

- Delta-9-tetrahydrocannabinol ( $\Delta$ -9-THC)
  - Primary psychoactive ingredient in cannabis but also has analgesic, anxiolytic and anti-inflammatory properties
- Cannabis plants contain the compound THC-A (non-psychoactive)
- Heating the cannabis causes hydroxylation of THC-A into psychoactive THC
- Marijuana's psychoactive "strength" is correlated to the % THC it contains
- The THC content in marijuana has been increasing since the 1970s due to selective breeding of the plant.
  - Average ~20% THC today vs. Average ~1-2% THC in 1970's

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## Other Cannabinoids

- **Cannabidiol (CBD)**
  - Mechanism of action is not entirely understood
  - Reported to relieve pain, seizures, inflammation, anxiety and nausea without psychoactive effects of THC
  - Appears to modulate and reduce the effects of THC
  - Main cannabinoid in low-THC cannabis strains
  - Modern breeders have been developing strains with greater CBD content for medical use without the "high"

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### CBD – Possible Anti-Epileptic Mechanisms

- Blocks the NMDA receptor
  - Similar mechanism of Felbamate
- Enhances GABA receptor
  - Felbamate, Depakote, Phenobarbital, Tegretol
- Stabilizes ion channels
  - Lamictal, Dilantin, Keppra, Trileptal

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### Charlotte Figi

- Dravet syndrome
- Frequent bouts of febrile and afebrile status epilepticus
- Failed multiple medications:
  - Levetiracetam, oxcarbazepine, topiramate, zonisamide, valproate, clobazam, clonazepam, and diazepam
- 5 y/o: had significant cognitive and motor delays, required a feeding tube, and needed full assistance with ADLs
- 50 generalized tonic-clonic seizures/day




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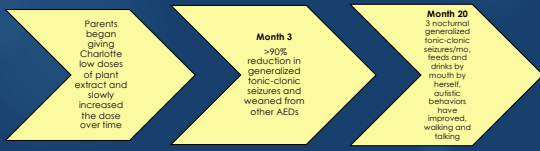
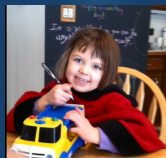
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### Charlotte's Web

- High concentration CBD:THC strain of cannabis
- Charlotte's Web, supplied by Realm of Caring in Colorado
- Families are relocating to attempt treatment




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## Other Cannabinoids

- **Cannabinol (CBN)**
  - Mildly psychoactive, decreases intraocular pressure and seizure occurrence
- **Cannabichromene (CBC)**
  - Promotes the analgesic effects of THC and has sedative effects
- **Cannabigerol (CBG)**
  - Has sedative effects and antimicrobial properties, and also lowers intraocular pressure
- **Tetrahydrocannibivarin (THCV)**
  - Showing promise for type 2 diabetes and other related metabolic disorders

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## “Entourage effect”

- Term coined by Dr. Ethan Russo in 2011
- Describes synergistic contributions of other compounds found in cannabis (483)
- Helps explain why Marinol (100% synthetic THC) is less effective than whole plant cannabis for side effects of chemotherapy
  - 2011 survey of 953 patients only 1.8% preferred synthetic THC pharmaceuticals

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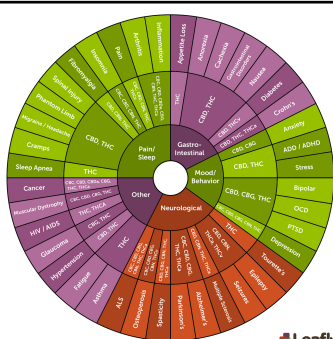
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Q: What do these two have in common?



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### A: The Endocannabinoid System

- > Term coined in 1990's
- > Discovery of membrane receptors for THC, the psychoactive principle component in *Cannabis*, and their endogenous ligands
- > "Highly conserved" from lower invertebrates (fly) to higher mammals (humans)
  - > Genes that are vital to the normal function of the organism
  - > Any major mutation likely result in extinction

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## Endocannabinoid System

- 1) The endocannabinoids: metabolites of arachidonic acid: anandamide and 2-AG
  - The molecules that binds to the cannabinoid receptors
- 2) Enzymes that synthesize and degrade the endocannabinoids
- 3) CB1 and CB2 receptors

The diagram illustrates the endocannabinoid system. On the left, it shows 'Plant-derived cannabinoid' (THC) and 'Endogenous cannabinoids' (AEA and 2-AG) with their chemical structures. On the right, it shows a 'Presynaptic neuron' and a 'Postsynaptic neuron'. The presynaptic neuron has CB1 receptors and is involved in neurotransmitter release. The postsynaptic neuron has CB1 and CB2 receptors. The diagram shows how endocannabinoids bind to these receptors, leading to an increase in activity (e.g.,  $Ca^{2+}$  concentration) in the postsynaptic neuron.

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## Cannabinoid receptors

Receptors are found on cell surfaces

The diagram shows a human silhouette with blue dots representing cannabinoid receptors. Two circles on the left indicate the presence of CB1 (light blue) and CB2 (dark blue) receptors. The CB1 receptors are concentrated in the brain, while CB2 receptors are found throughout the body, including in the immune system.

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## Cannabinoid receptor type 1

- Found primarily in the brain, more specifically in the basal ganglia and in the limbic system
- CB1 receptors are absent in the medulla oblongata,
  - They do not affect respiratory/cardiovascular functions
- Activation of CB1 receptors is responsible for the psychoactive effects of cannabis (THC)
- CBD is an "inverse agonist" to CB1 receptors and blocks the psychoactive effects of THC
  - Induces the opposite effect of the agonist

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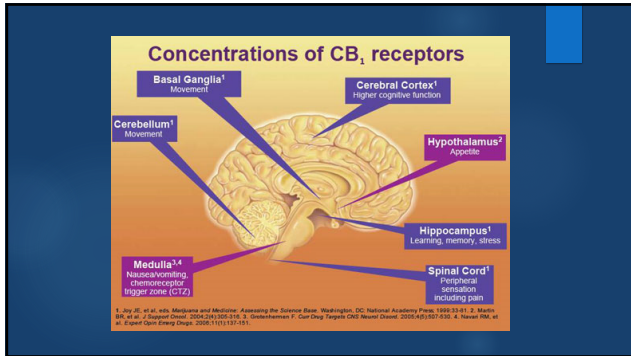
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### Cannabinoid receptor type 2

- Predominantly found in the immune system, or immune-derived cells with the greatest density in the spleen
- Found to be inducible in other tissues and organs including the CNS
- Appear to be responsible for the anti-inflammatory/immunosuppressive effects of cannabis
- CB2 agonists have been shown modulate and restore altered blood-brain barrier function during inflammatory conditions

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### Barriers to cannabis research

- Clinical researchers can get permission from the DEA to grow or create restricted compounds such as LSD, MDMA or psilocybin but not for cannabis
- To do cannabis research you need:
  - DEA license
  - Study approved by FDA
  - Research-grade marijuana must be obtained through the NIDA (National Institute on Drug Abuse)
    - University of Mississippi possesses sole DEA-approved license to grow cannabis for medical research
    - Canada has 30 licensed producers

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### National Academies of Science, Engineering and Medicine

- Report released January 12, 2017
- "In the United States, cannabis for research purposes is only available through the NIDA Drug Supply Program. The mission of the NIDA is to 'advance science on the causes and consequences of drug use and addiction and to apply that knowledge to improve individual and public health' rather than to pursue or support research into the potential therapeutic uses of cannabis or any other drugs... As a result of this emphasis, less than one-fifth of cannabis research funded by NIDA in the fiscal year 2015 concerns the therapeutic properties of cannabinoids"

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### Aug. 11, 2016 - DEA Declines to Reschedule Marijuana but Opens Door to Research

- "DEA [Drug Enforcement Administration] has denied two petitions to reschedule marijuana under the Controlled Substances Act (CSA)
  - DEA announced a policy change designed to foster research by expanding the number of DEA-registered marijuana manufacturers. This change should provide researchers with a more varied and robust supply of marijuana... This change illustrates DEA's commitment to working together with the FDA and NIDA to facilitate research concerning marijuana and its components."
- DEA.gov

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### PubMed 1990-2017

Drug as Treatment	# Clinical Trials
Cannabis (extract or whole plant)	67
Morphine	4745
Zofran	1186
Interferon (MS)	769
Seroquel	503
Abilify	381

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### 60 Peer-Reviewed Studies on Medical Marijuana

Medical Studies Involving Cannabis and Cannabis Extracts (1990 - 2014)

Peer-reviewed studies on medical marijuana, listed by condition treated	# of studies		
	Pro	Con	Not Clearly Pro or Con
ALS	1	0	0
Bipolar Disorder	2	0	0
Cancer	5	1	1
General Use	2	0	0
Glaucoma	0	0	1
HIV/AIDS	5	1	2
Huntington's Disease	0	0	1
IBD/Crohn's	1	0	1
Multiple Sclerosis	11	3	5
Nausea	1	0	0
Pain	6	0	1
Parkinson's Disease	2	0	1
PTSD	1	0	0
Psychosis / Schizophrenia	1	0	1
Rheumatoid Arthritis	1	0	0
Tourette's Syndrome	2	0	0
<b>TOTALS</b>	<b>41</b>	<b>5</b>	<b>14</b>
	<b>68.3%</b>	<b>(8.3%)</b>	<b>(23.3%)</b>

Procon.org

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### Barriers to cannabis research

- Potency issues:
  - Highest available THC allowed – 12.4%
  - Only two NIH-funded clinical trials 2015 - 3.5% and 7.0%
  - Average sold in Colorado is 18.4%, some strains to 35%

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### William Utermohlen



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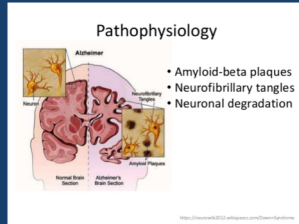
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### Alzheimer's disease

- One study demonstrated CB2 agonist drug induced removal of amyloid plaques by macrophages
- Effect was reversed by a CB2 selective antagonist
- Same CB2 agonists enhance amyloid protein phagocytosis
- Theorized by inhibition of release of proinflammatory cytokines
  - IL-1 and TNF- $\alpha$




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### Alzheimer's disease

- Prospective clinical trial conducted over 4 weeks
- 11 patients with AD
- Administered cannabis oil
- Significant reduction in
  - CGI severity score (6.5 to 5.7;  $p < 0.01$ )
  - NPI score (44.4 to 12.8;  $p < 0.01$ )
- NPI domains of significant decrease:
 

Delusions	Irritability
Agitation/aggression	Apathy
Sleep disturbance	Caregiver distress

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### Parkinson's disease

- 2014 open-label observational study
- 22 patients in motor disorder clinic at tertiary care hospital
- Evaluated symptoms at baseline and 30 minutes after inhaled cannabis use
- Significant improvement in:
 

Bradykinesia	Sleep
Tremor	Pain
Rigidity	Disease rating score
- No adverse effects

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### Parkinson's Disease



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### Multiple sclerosis

- Autoimmune disorder
- Activated cells lead to demyelination of nerve fibers in CNS leading to muscle spasms, tremor, ataxia, weakness or paralysis



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### Multiple sclerosis

- Cannabinoids protect against apoptosis of oligodendrocytes via CB1 and CB2 receptors
- 1994 survey of 112 MS patients self-medicating with cannabis in US and UK
  - Demonstrated improved symptoms including spasticity, pain, tremor and depression in > 90% of patients

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### Ischemic stroke

- Induced MCA stroke in mice
- Mice administered either CB2 agonist or antagonist
- Measured neuroblast migration and motor function
- CB2 antagonist caused
  - Decreased neuroblast migration towards stroke site
  - Lower number of new neurons
  - Worse sensorimotor function
- CB2 agonist
  - Increased migration of neuroblasts

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### Colitis

- Endocannabinoid system involved in many GI functions
  - N/V, visceral sensation, GI motility, intestinal inflammation
- Functional CB1 receptor is expressed in human ileum and colon
- Number of CB1-expressing cells is significantly increased after inflammation
- Studies which blocked CB1 or utilized genetically CB1-deficient mice demonstrated increased sensitivity to inflammatory insults or worse colitis

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### Crohn's disease

- 2011 retrospective observational study
- 30 patients with Crohn's (26 male)
- Evaluated disease activity (Harvey Bradsaw Index), use of medication, need for surgery and hospitalization before and after cannabis use
- 21 patients with significant improvement in disease activity\*, medication use\* and need for surgery

\*statistically significant

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### NCI - cannabis and cancer

- Mouse studies have shown that cannabinoids may inhibit tumor growth
- Cell death, blocking cell growth, and blocking angiogenesis
- Laboratory and animal studies have shown that cannabinoids may be able to kill cancer cells while protecting normal cells

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### NCI - cannabis and cancer

- THC in models of HCC had antitumor effects via acting on molecules also found in NSCLC and breast cancer cells
- THC treatment of mice with ALL cured approximately 25%
- Study of CBD in ER+ and ER- breast cancer cells demonstrated increased cancer cell death and little effect on normal breast cells
- Studies in mouse models of metastatic breast cancer showed that cannabinoids may lessen the growth, number and spread of tumors

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### NCI - cannabis and cancer

- CBD given with chemotherapy in human glioma cells demonstrated possible increased efficacy of the chemotherapy without harming normal cells
- Studies in mouse models demonstrated that CBD given with THC may make chemotherapy such as temozolomide more effective

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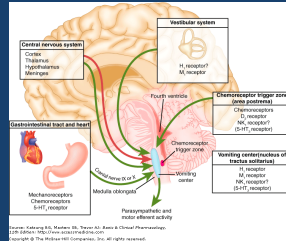
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### Cannabinoids for CINV

- Proposed that THC treats nausea via emetic reflex pathways
- THC reverses the effects of 5-HT3 receptor agonists which normally induce vomiting
- Anecdotally effective in suppressing anticipatory nausea even better than 5-HT3 receptor antagonists (Zofran)




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### NCI – cannabis and pain relief

- Two small clinical trials of oral THC demonstrated relief of cancer pain as well as relief from CINV and with better appetite
- A study of an extract of Cannabis which was sprayed under the tongue, found it was effective in patients with advanced cancer whose pain was not relieved by strong opioids alone
  - For some patients, control of their cancer-related pain continued without needing higher doses of spray or higher doses of their other pain medicines (no tolerance)

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### Rheumatoid arthritis

- Animal trial demonstrated CBD effectively blocked the progression of arthritis
  - Found that CBD protected joints against severe damage
  - Concluded that CBD offers a potent anti-arthritic effect
- One study found that cannabis-based medicine significantly improved pain during joint movement, pain while at rest, and quality of sleep in patients with rheumatoid arthritis
- Numerous preclinical studies confirmed cannabis' anti-inflammatory and pain-relieving effects in patients with arthritis




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## Osteoarthritis

- > Synthetic cannabinoids offer strong anti-inflammatory and immunosuppressive properties and reduce joint damage in mice with osteoarthritis
- > Cannabinoid treatments were found effective for reducing osteoarthritis-related cartilage breakdown

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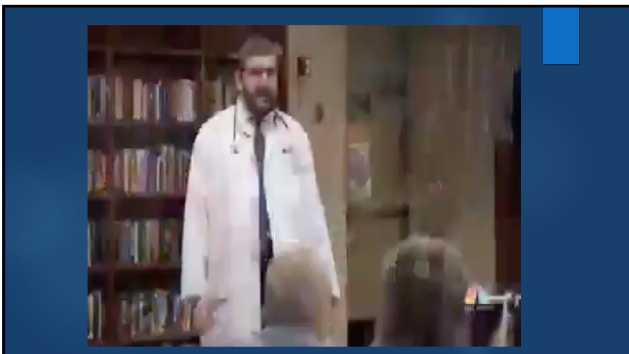
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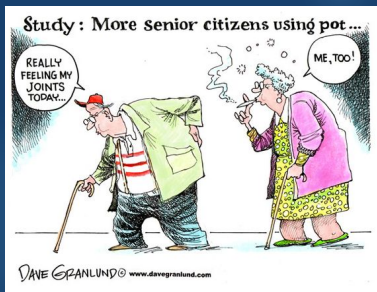
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### Cannabinoids and Pain

- In animal models, cannabinoids have been shown to relieve pain in "virtually every experimental pain paradigm"
- Supraspinal, spinal, and peripheral regions
- Involve both ascending and descending pain pathways



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### Cannabinoids and Pain - Mechanisms

- CB1 receptors found in high concentrations of areas of the brain involved in modulating nociceptive processing
  - Similar distribution to opioid receptors
- Role in inflammation
  - May act on mast cell receptors
  - Inhibit release of inflammatory substances
  - Enhance release of analgesic opioids to combat inflammation
- Role in neuropathic pain
  - Inhibit acute pain response in C-fibers
  - Inhibit "windup phenomenon" which contributes to hyperalgesia
- Believed to have synergistic effect with opiates via unknown mechanisms

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### Cannabis and Chronic Pain

- Studies show that chronic pain is the most common reason worldwide for patients to report the medicinal use of cannabis
- In CA one study reported 5% of people surveyed had used medical marijuana
  - 38.3 million (2014) = 1.92 million users
- Within chronic pain clinics
  - Estimates of the prevalence of use ranges from 12-15%
  - Fibromyalgia, OA, spinal cord injury & MS
- 2012 *The Clinical Journal of Pain*
  - Reviewed all available RCTs evaluating the use of cannabinoids for chronic pain
  - 71% were associated with adequate pain relief, with low adverse effects, and good tolerance

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## The Opioid Epidemic

- As the opioid overdose mortality rates continue to rise to epidemic levels in the US, there is an increasing need for new and safer modalities to treat chronic pain
- Important study findings
  - When used as an adjunct to opiates in palliative care, cannabis resulted in the use of lower doses of opiates with less side effects
  - States in the US with medical cannabis laws have significantly lower opioid overdose mortality rates than those without them

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### The Medical Necessity for Medicinal Cannabis: Prospective, Observational Study Evaluating the Treatment in Cancer Patients on Supportive or Palliative Care

Gil Bar-Sela, et al (2013 – Israel)

**Table 2:** Changes in degree of cancer-related symptoms or oncology treatment side effects among patients with continuous cannabis use.

	Grade	First interview	Second interview
Nausea	0	34 (32%)	73 (69%)
	1-2	69 (65%)	29 (27%)
	3-4	3 (3%)	4 (4%)
Vomiting	0	73 (69%)	98 (92%)
	1-2	33 (31%)	8 (8%)
	3-4	4 (4%)	4 (4%)
Mood disorders	0	78 (74%)	69 (64%)
	1-2	21 (20%)	9 (8%)
	3-4	3 (3%)	4 (4%)
Fatigue	0	43 (40%)	53 (50%)
	1-2	56 (53%)	3 (3%)
	3-4	35 (33%)	71 (67%)
Weight loss	0	66 (62%)	35 (33%)
	1-2	3 (3%)	0
	3-4	34 (32%)	72 (68%)
Anorexia	0	69 (65%)	29 (27%)
	1-2	3 (3%)	3 (3%)
	3-4	45 (42%)	71 (67%)
Constipation	0	54 (51%)	32 (30%)
	1-2	3 (3%)	3 (3%)
	3-4	26 (25%)	34 (32%)
Sexual function	0	30 (28%)	14 (13%)
	1-2	3 (3%)	3 (3%)
	3-4	23 (22%)	39 (36%)
Sleep disorders	0	74 (70%)	39 (36%)
	1-2	3 (3%)	3 (3%)
	3-4	11 (10%)	9 (8%)

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## Medical marijuana laws (MML) and prescription medication use in Medicare Part D

- University of Georgia Study
- Assessed relationship between MML and physician's prescribing patterns from 2010-2013 in 17 states
- Found significant decreases in prescriptions being filled for the conditions studied
- To ensure decrease in prescriptions filled were related to the marijuana laws they compared prescriptions being filled for 4 classes of drugs for which no evidence of benefit of medical marijuana
  - Blood thinners
  - Phosphorous stimulating agents
  - Antivirals for influenza
  - Antibiotics
- No change observed with these prescription classes

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**Exhibit 1**  
 Nine medical condition categories with at least one drug approved by the Food and Drug Administration for on-label use, and level of evidence for marijuana as a treatment for conditions in the category

Condition category	Anxiety		Depression		Glaucoma		Nausea		Pain		Psychosis		Seizures		Sleep disorders		Spasticity	
	Present	Inadequate	Present	Inadequate	Present	Inadequate	Present	Inadequate	Present	Inadequate	Present	Inadequate	Present	Inadequate	Present	Inadequate	Present	Inadequate
Clinical evidence of medical marijuana effect on conditions in each category																		
Institute of Medicine (2009) <sup>1</sup>	Present	Inadequate	Present	Inadequate	Present	Inadequate	Present	Inadequate	Present	Inadequate	Present	Inadequate	Present	Inadequate	Present	Inadequate	Present	Inadequate
Whiting et al. (2015) <sup>2</sup>	Very low	Very low	Low	Moderate	Low	Moderate	Low	Moderate	Low	Moderate	Low	Moderate	Low	Moderate	Low	Moderate	Low	Moderate
Drug classes with at least one on-label option for treating conditions in each category																		
Adrenal cortical steroids																		
Anesthetics																		
Antiarrhythmic agents																		
Anticonvulsants																		
Antidepressants																		
Antidiarrheal agents																		
Antiemetic or antiemetic agents																		
Antimicrobial agents																		
Antipsychotics																		
Antirheumatics																		
Anesthetics, sedatives, and hypnotics																		
Central nervous system stimulants																		
Functional bowel disorder agents																		
Immunostimulants																		
Muscle relaxants																		
Ophthalmic preparations																		
Proton pump inhibitors																		
Respiratory inhaled products																		
Sedatives and hypnotics																		
Smoking cessation agents																		

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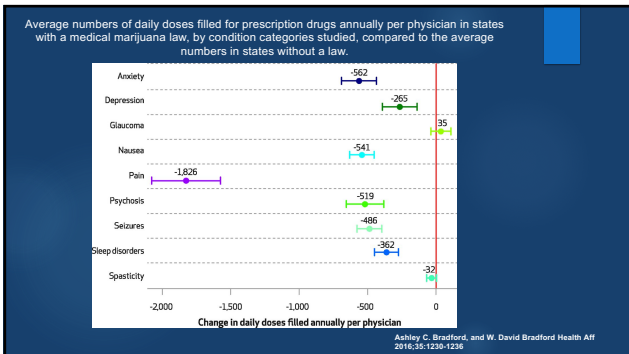
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**Physician perceptions**

- 2014 poll conducted by Medscape and WebMD found that more than three-quarters of U.S. physicians think cannabis provides real therapeutic benefits
- Those working with cancer patients were the strongest supporters
- 82% of oncologists agreed that cannabis should be offered as a treatment option

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"Marijuana is a wonder drug when it comes to the horrors of chemo"

Dr. Donald Abrams, UCSF Chief of Hematology-Oncology  
"A day doesn't go by where I don't see a cancer patient who has nausea, vomiting, loss of appetite, pain, depression and insomnia....(marijuana) is the only anti-nausea medicine that increases appetite."  
"It also helps patients sleep and elevates their mood—no easy feat when someone is facing a life-threatening illness. I could write six different prescriptions, all of which may interact with each other or the chemotherapy that the patient has been prescribed. Or I could just recommend trying one medicine."

Newsweek 7/22/15

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The American Cancer Society supports the need for more scientific research on cannabinoids for cancer patients, and recognizes the need for better and more effective therapies that can overcome the often debilitating side effects of cancer and its treatment. The Society also believes that the classification of marijuana as a Schedule I controlled substance by the US Drug Enforcement Administration imposes numerous conditions on researchers and deters scientific study of cannabinoids. Federal officials should examine options consistent with federal law for enabling more scientific study on marijuana.

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American College of Physicians

- "ACP urges review of marijuana's status as a schedule I controlled substance and its reclassification into a more appropriate schedule, given the scientific evidence regarding marijuana's safety and efficacy in some clinical conditions..."
- ACP strongly supports exemption from federal criminal prosecution; civil liability; or professional sanctioning, such as loss of licensure or credentialing, for physicians who prescribe or dispense medical marijuana in accordance with state law. Similarly, ACP strongly urges protection from criminal or civil penalties for patients who use medical marijuana as permitted under state laws."

"Supporting Research into the Therapeutic Role of Marijuana," [acponline.org](http://acponline.org)  
Confirmed as current position on Aug. 18, 2016

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### Overview

- > History of medical marijuana
- > Pharmacology
- > Physiology
- > Barriers to cannabis research
- > Current research on medical cannabis
- > **Safety concerns and side effects**
- > Current status

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### Pharmacology

- > Inhaled
  - > Rapid absorption into the bloodstream
  - > Peak concentration 2-10 minutes
  - > Rapidly declines over next 30 minutes
- > Oral (edibles, oils)
  - > Low bioavailability (4-20%)
  - > Peak plasma concentration after 1-6 hours
  - > Terminal t<sub>1/2</sub> of 20-30 hours

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### Dosing

- > Due to limited clinical studies, there is a lack of standardized dosing for medicinal cannabis and dosing will depend on several factors including THC:CBD ratio and route of administration (inhalation vs. oral)
- > Treatment is usually started in low doses and gradually titrated as tolerated to maximum benefit with minimum adverse events
- > Cannabis users should be advised not to drive for at least 3 to 4 hours after smoking, for at least 6 hours after oral ingestion, and for at least 8 hours if they experience a subjective "high"
- > The maximum recommended dose is 1 inhalation 4 times per day (approximately 400 mg per day) of dried cannabis containing 9% delta-9-tetrahydrocannabinol

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### Safety & Side Effects

- Side effects of marijuana use will be variable from person to person, depending upon strength and amount of marijuana used
- Psychologically addictive
  - 10% of first time users
  - Up to 25% for chronic users
- In 2009 marijuana was responsible for about 17% of all admissions to treatment facilities.
- Short term memory problems

According to the Substance Abuse and Mental Health Services Administration's (SAMHSA) National Survey on Drug Use and Health.

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### Cannabinoid Hyperemesis Syndrome

Santineni criteria <sup>(2)</sup>	
<b>Essential</b>	Cannabis use for years Severe nausea and vomiting
<b>Major</b>	Vomiting that recurs in a cyclic pattern over months Resolution of symptoms after stopping cannabis use.
<b>Supportive</b>	Compulsive hot baths with symptom relief Colicky abdominal pain No evidence of gall bladder or pancreatic inflammation

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### Safety & Side Effects

- People who smoke marijuana have the same respiratory problems as cigarette smokers and are at increased risk of developing pneumonia and lung cancers
- Smoked cannabis has been found to contain Aspergillus
  - Canada offers irradiated cannabis to its cancer patients for this reason

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## Cannabis Use and Risk of Lung Cancer

- Case-controlled study of lung cancer in adults  $\leq 55$  yrs of age in New Zealand
- 79 cases of lung cancer and 324 controls
- Risk of lung cancer increased 8% for each joint-yr (1 joint/day for one year) of cannabis smoking after adjustment for confounding variables including tobacco
- Risk increased 7% for each pack-year tobacco
- "Long-term cannabis use increases risk of lung cancer in young adults"

Aldington et al. Eur Respir J. 2008;31:280-286

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## Unlike Opiates, Cannabis Has

- No constipation
- No nausea/vomiting
- No pruritus
- No drying of secretions
- No diminished appetite
- No respiratory suppression
- Less tolerance to effects & lower street value
- Withdrawal is extremely rare
- No severe physical withdrawal syndrome
- No end-organ damage (no need for routine labs)
- No lethal dose
- No one has ever died from an overdose of cannabis

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## Overview

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Qualifying Conditions

Conditions	PA	VT	MS, MO, NC, OK, SC, TN, TX, UT, WI, WY
Epilepsy	X	X	X
Cancer	X	X	
HIV/AIDS	X	X	
Chronic pain	X	X	
MS	X	X	
ALS	X		
Parkinson's	X		
SC injury with spasticity	X		
IBD	X		
Huntington's	X		
Sickle cell	X		
Glaucoma	X		
Autism	X		
"Terminally ill"	X		

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**North Carolina**

- On July 3, 2014 Governor Pat McCrory signed HB 1220 into law
- Allows universities to conduct clinical trials using CBD oil that is less than 0.3% THC and at least 10% CBD to be used only for the treatment of intractable epilepsy

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**Speaker Boehner 'has evolved' on marijuana**  
John Boehner is heading for the boardroom of a cannabis company, the former Speaker of the House announced Wednesday.  
CNN.COM

April 11, 2018 - Former Republican Speaker of the House tweeted: "I'm convinced de-scheduling the drug is needed so we can do research, help our veterans, and reverse the opioid epidemic ravaging our communities."

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**Schumer to introduce marijuana decriminalization legislation**  
By Sophie Tatum, CNN  
Updated 9:23 PM ET, Thu April 20, 2018

The legislation will include removing marijuana from the DEA controlled substance list

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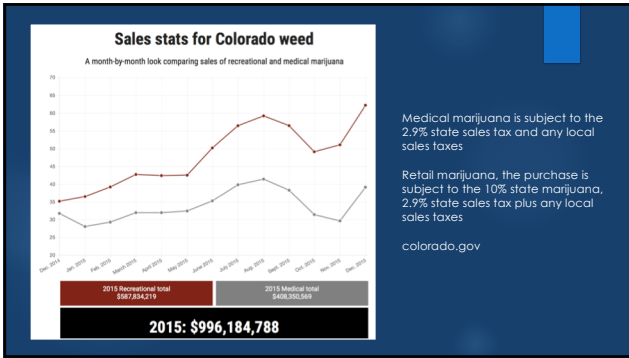
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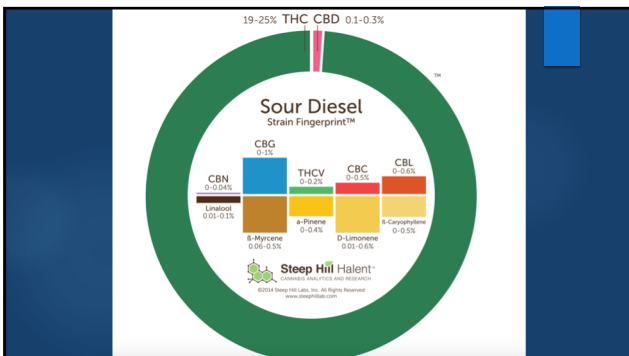
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