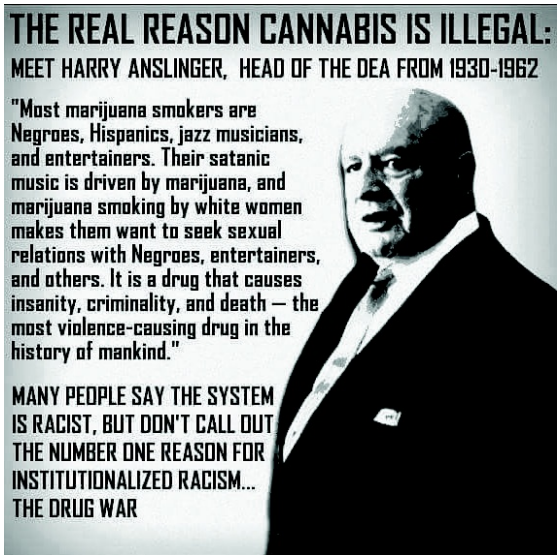
A PHYSICIAN'S GUIDE TO:

Oklahoma Cannabis LibertyAlliance

Your voice at the Capitol

Cannabis: The Basics



A Brief History of Cannabis Cannabis has been referenced in medical text for over five-thousand years. It has been part of Asian and Near-Eastern medicine throughout recorded history. Cannabis entered Western medicine in the mid-19th century (via British trade with India) and was used in the United States of America from the 1850s through 1937, when it became illegal due to economic and racially motivated agendas.

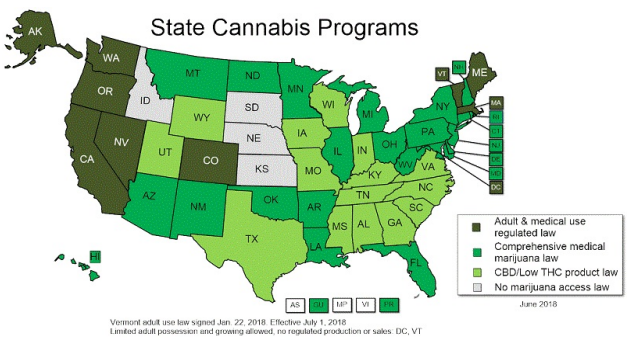
"The American Medical Association knows of no evidence that marijuana is a dangerous drug."

—Dr. William Woodward physician, attorney, chief AMA legal council during the 1937 Marihuana Tax Act hearings before the U.S. House of Representatives Ways and Means Committee

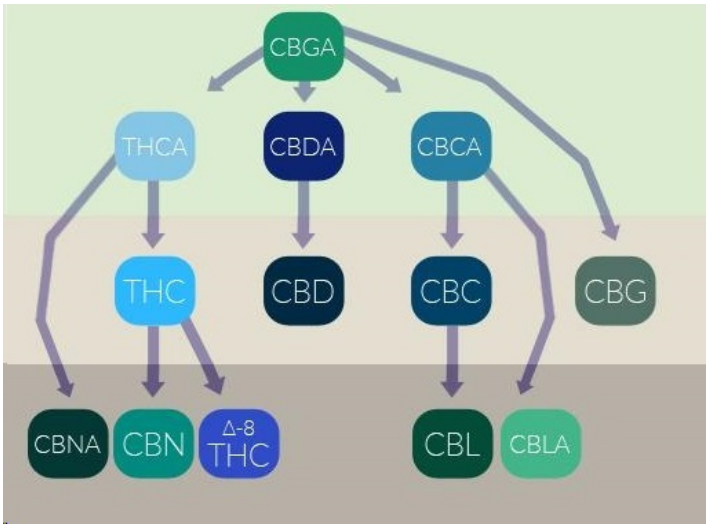
The American Medical Association vociferously objected to its ban, arguing for its ample medicinal benefits and comparative safety over opioids. William J. Woodward, the AMA's Director of Medicine at the time, warned that Congress's action will styme research for generations to come and in the end, ultimately hurt patients.

The US Pharmacopoeia recommended cannabis for indications including insomnia, pain, muscle spasms, seizures, and wasting. It was also characterized as safer than opioids with fewer side effects. The NIH funded research on Cannabis in Israel for these very same medical indications and as a result, it was legalized there in 1992. California followed suit four years later, and by 2000, eight states legalized it for medicinal purposes, by 2010 sixteen states, and now 31 states as well as the District of Columbia and thirty other nations around the world.

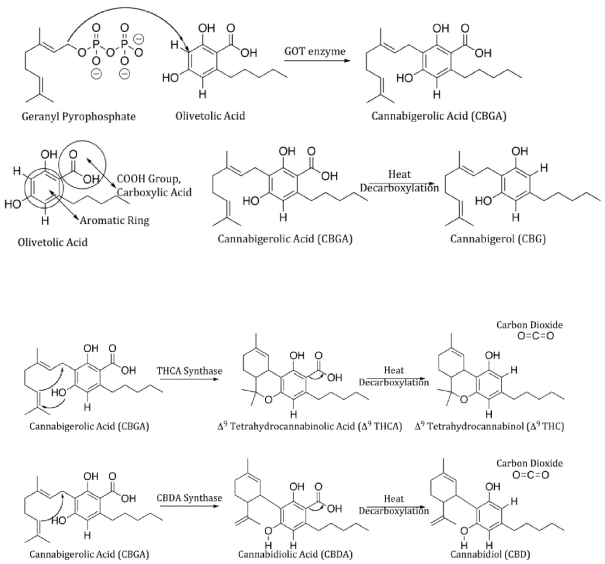
According to the New England Journal of Medicine (2013), 76% of physicians endorse its medical use. There are more than two million registered medical patients in the United States, leading to sizable reductions in opioid, antidepressant, benzodiazepine, and migraine medication use in states where it has been legalized (Journal of Psychopharmacology May 2017, 569-575).

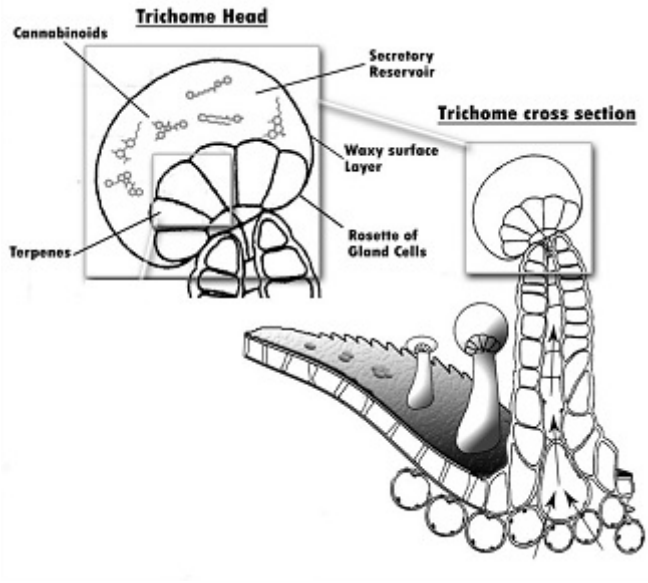


Cannabis: Not just a Delivery System for THC

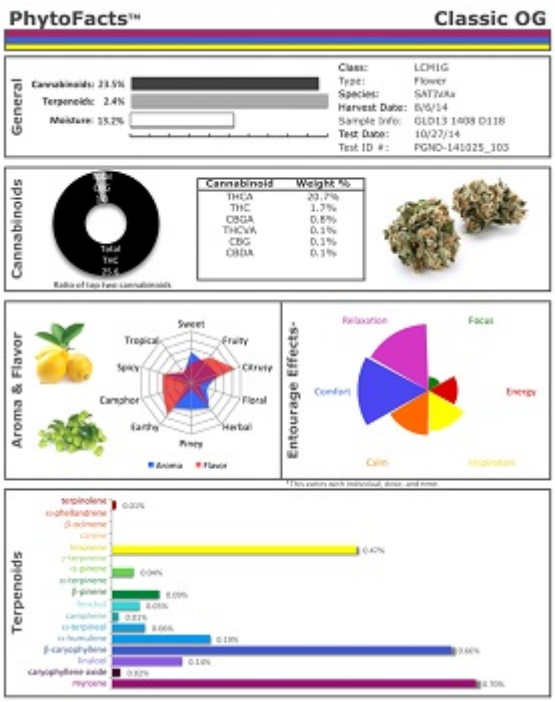


In addition to THC, cannabis contains many other medically active compounds, including further cannabinoids (e.g. CBD, CBG, CBN, CBC), as well as terpenoids such as myrcene, linalool, pinene, limonene, humelene, and caryophyllene. Both the psychoactive and medicinal benefits of cannabis are shaped by the combinatory effects of its cannabinoids and terpenes. Not only does THC have a far more narrow therapeutic window than whole-plant cannabis, but its psychoactivity is greatly reduced when consumed with its other naturally occurring compounds.



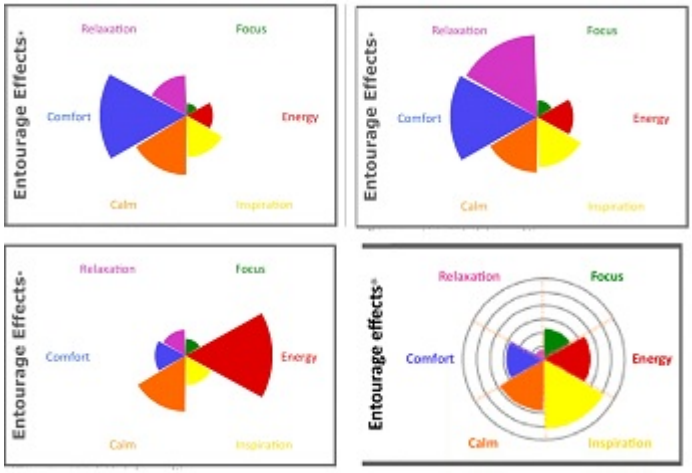


Most of the medically active compounds are not found in the primary plant material, but rather in glands known as trichomes which develop on it surface. Cannabigerol (CBG),or more precisely, its acylated precursor, Cannabigerolic Acid (CBGa) is converted through various enzymes into further cannabinoids, which along with its terpenes accumulate in surface trichomes.



Depending upon the plant's genetics and growing conditions, its CBG can be converted into other cannabinoids in different ratios, anywhere from <.1% THC to 30% CBD vs. <.1% CBD to 30% THC. Likewise, different plants will contain more or less CBN, CBC, mycene, linalool, pinene, etc.. Unfortunately, the strain of cannabis grown by the University of Mississippi under license from NIDA (National Institute of Drug Abuse) is notoriously low in CBD, terpenes, and other compounds found to be medically beneficial by way of the research conducted in Israel, Canada, Spain, and other countries where medical cannabis has been legalized for decades.

Nevertheless, many of the cannabis strains sold in legal states have been bred to have higher levels of CBD and terpenes, some reflecting the detailed strain-specific research which has been conducted in Israel since the 1990s. Patients thus are able to explore different THC:CBD ratios, the benefits of lesser cannabinoids such as CBN (which is sedative), and terpenes such as myrcene (which is an anti-inflammatory) or limonene (which is an anxiolytic).



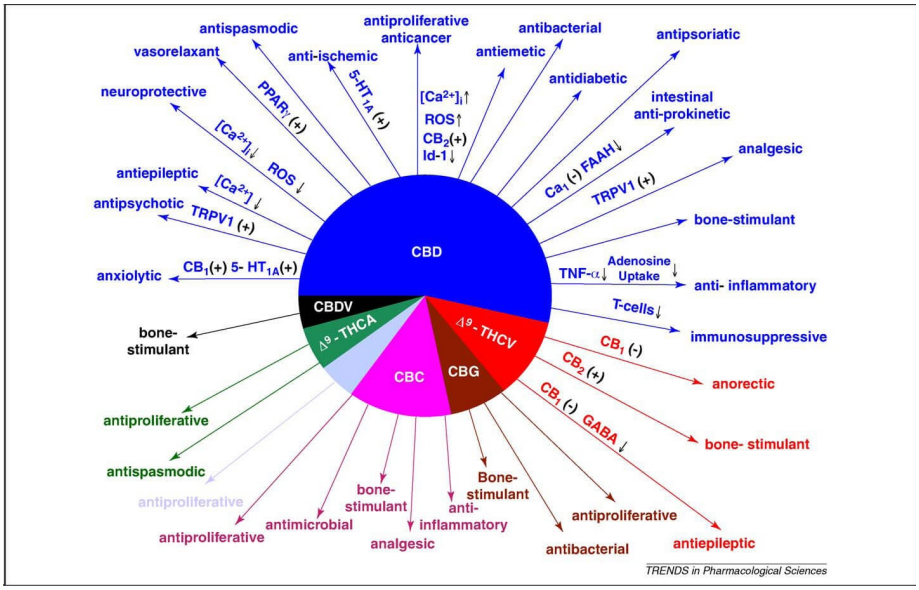
One of the main challenges faced by researchers is that, unlike pharmaceuticals which in most instances are isolated molecules, a sizable quantity of the medicial and psychoactive effects of cannabis arise out of the combinatory properties of its endogenous compounds.

For example, differing pain etiologies will respond differently to high THC/low CBD versus high CBD/low THC strains. Likewise, pure THC tends to cause anxiety, whereas in combination with CBD or certain terpenes, it does not. Because of this, the therapeutic window for THC is greatly increased in its natural form.

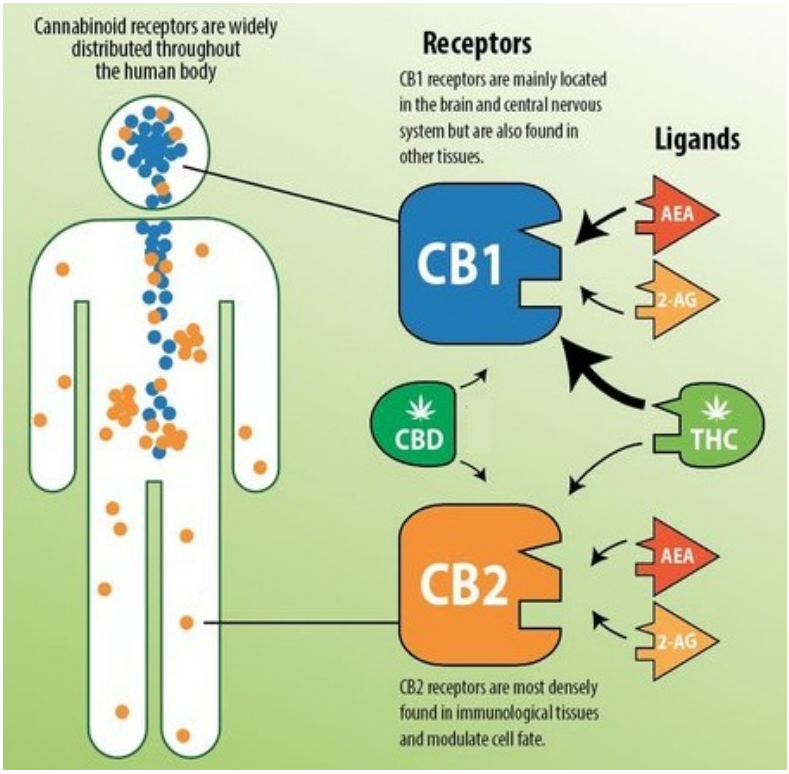
Researchers further believe that THC amplifies the effects of terpenes so that their common psychological effects (linalool as sedative, pinene as uplifing, etc) are all the greater when so combined. Such combinatory properties of cannabinoids and terpenes have come to be known as the "entourage effect," an effect which underlies much of the call for cannabis as a whole-plant medicinal rather than its reduction into isolated compounds.

The Endocannabinoid System: How and Why Cannabis Works

The Endocannabinoid System (ECS) consists of cannabinoid receptors, endocannabinoids, and metabolic enzymes. Two major cannabinoid receptors, CB1 and CB2, and two main endocannabinoids, anandamide (AEA) and 2-arachidonoyl-glycerol (2-AG), have been identified. Human endocannabinoids and plant cannabinoids, such as THC and CBD bind to cannabinoid receptors with great specificity, much like a lock and key. Activation of the cannabinoid receptors inhibits the release of neurotransmitters. The ECS plays a key role in homeostasis and regulates many physiological processes such as inflammation and pain perception, immunity, neuropathy and metabolism.

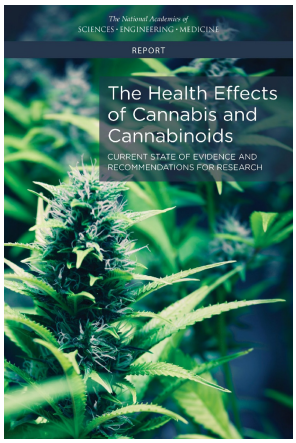


AEA binds to the CB1 receptor with greater affinity than CB2 whereas 2-AG binds to both receptors with equal affinity. THC binds to the CB1 receptor with greater affinity than to the Cb2 receptor, and it has been suggested that the binding effects of THC mimic AEA. It has been proposed that the binding effects of CBD are mimetic to 2-AG.

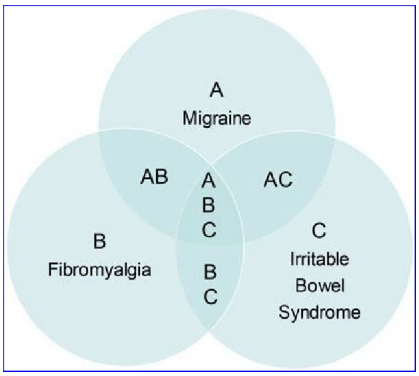


Medical Research and Clinical Use

Since the 1990s, with its legalization in various jurisdiction, there has been a marked increase in research on the medical benefits of Cannabis. From 1973 through 2000, an average of 200 studies were published per year. In 2010, nearly one thousand studies were published that year, and roughly two thousand studies have been published per year since 2016.



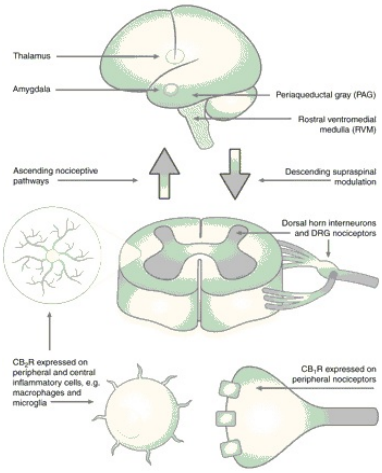
In 2017, the National Academies of the Sciences, Engineering, and Medicine published a comprehensive report on the current status of cannabis research, ranking the quality of evidence for its efficacy for such medical conditions as Multiple Sclerosis, Chemotherapy-Induced Nausea, HIV-wasting, Fibromyalgia, Chronic Pain, and obstructive sleep apnea. The report found conclusive to substantial evidence showing its efficacy for chronic pain, Chemotherapy-Induced Nausea, and multiple sclerosis spasticity. It further found evidence that it is effective for obstructive sleep apnea, HIV-wasting, PTSD, and a host of further conditions.



Further studies have shown its benefits for various IBS-type conditions including Crohn's Disease and Ulcerative Colitis, preventing the build-up of amyloid deposits associated with Alzheimer's Disease, Migraines, and even evidence showing that it can slow tumor growth.

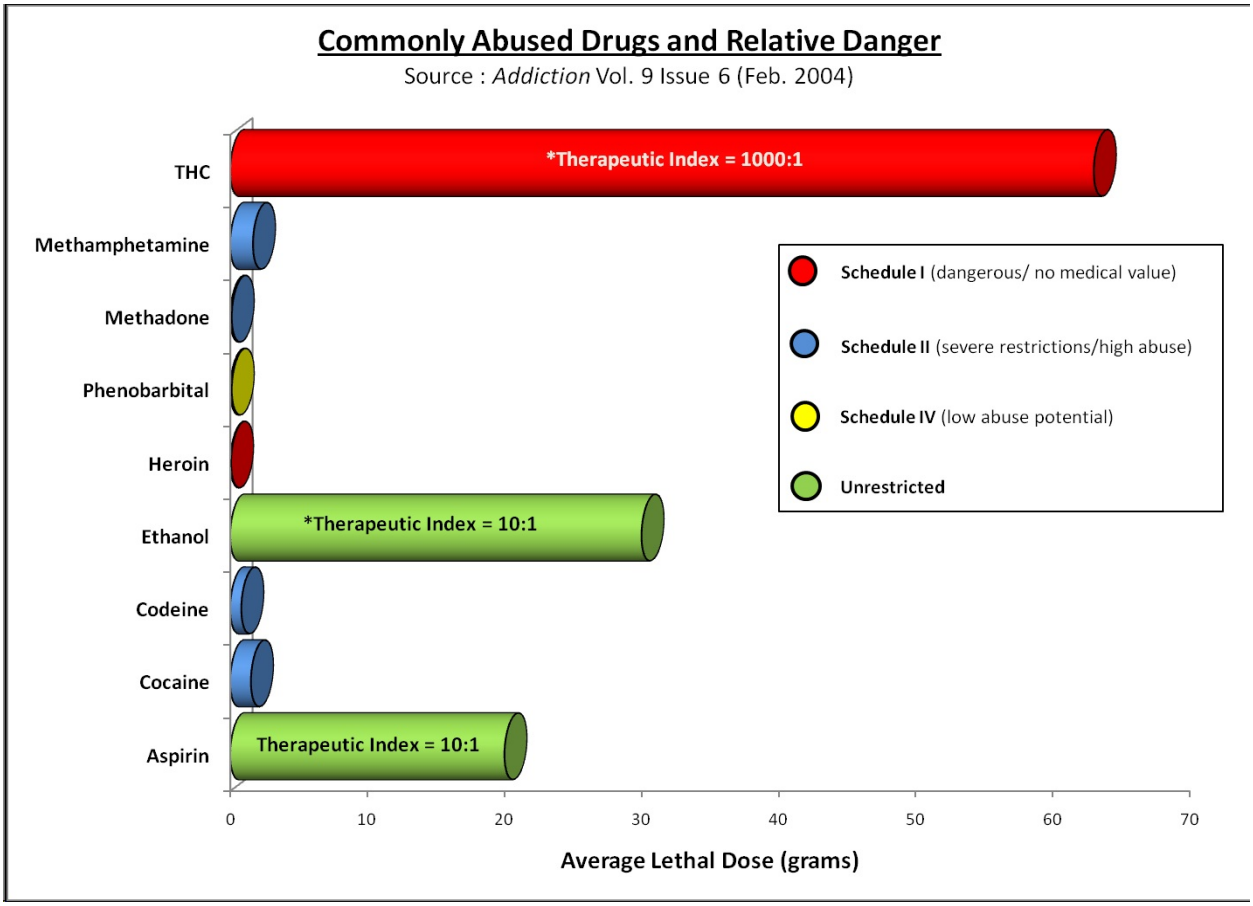
Recent research has in fact shown that a number of the medical conditions for which cannabis has been shown to be effective are due to a common underlying endocannabinoid deficiency. All humans have an underlying endocannabinoid tone that is a reflection of levels of the endocannabinoids, anandamide (arachidonylethanolamide), and 2-arachidonoylglycerol, their production, metabolism, and the relative abundance and state of cannabinoid receptors. In certain conditions, including migraines, fibromyalgia, and IBS, endocannabinoid tone becomes deficient and productive of pathophysiological syndromes. Exogenous cannabinoid treatment thus frequently provides symptomatic benefit for these conditions.

In addition to its ability to treat a variety of health conditions and symptoms, cannabis is most commonly used to alleviate chronic pain. Research has proven that both THC and CBD provide effective relief from pain and can be a safer choice than conventional medicine.



Agonist-activated cannabinoid receptors modulate nociceptive thresholds, inhibit release of pro-inflammatory molecules, and display synergistic effects with other systems that influence analgesia, including the endogenous opioid system. Anandamide,

and 2-AG are produced in injured tissues to suppress sensitization and inflammation by activation of cannabinoid (CB) receptors. Anandamide mobilizes in response to inflammation and nerve injury and modulates nociceptive signals by activating local CB receptors. 2-AG plays a prominent role in the descending modulation of pain during acute stress. Exogenous cannabinoids including THC and CBD are active on these receptors and thus in many ways offer more direct mechanisms of analgesia in comparison to opioids.



Cannabis also has a broader therapeutic window than opioids, in part because THC is not a respiratory depressant. As such, unlike opioids, cannabis can provide analgesia without risk of fatal overdose. Many physicians in jurisdictions with established medical Cannabis programs now integrate cannabis into pain management, reducing opioid, muscle relaxant and benzodiazepine dosages. Epidemiological data has shown that when cannabis is legalized, there is a marked decline in the number of prescriptions for these drugs as well as in overdose rates. Cannabis alone may not be sufficient for more severe pain, but pain management physicians report that the majority of their patients have successfully replaced long-acting opioid medications and/or reduced their breakthrough opioid dosages.

Medical Marijuana and the Law in Oklahoma

On June 26th, 2018 the people of Oklahoma voted in favor of State Question 788, which legalized medical marijuana. Some of the key provisions in the state question are as follows:

- There are no "qualifying conditions," recommendations are rather to be made "according to the accepted standards a reasonable and prudent physician would follow when recommending or approving any medication"
- Approved patients will receive a two-year license
- Recommendations have to come from an "Oklahoma Board certified physician"
- Recommendations to minors must have parent/guardian signatures and signatures of two physicians
- No physician may be unduly stigmatized or harassed for signing a medical marijuana license application
- Patients cannot be discriminated against solely for holding a medical marijuana license or as a licensee, for testing positive for its use
- This is not a prescription. It is a recommendation, and physicians are legally entitled to discuss marijuana as well as recommend its use.

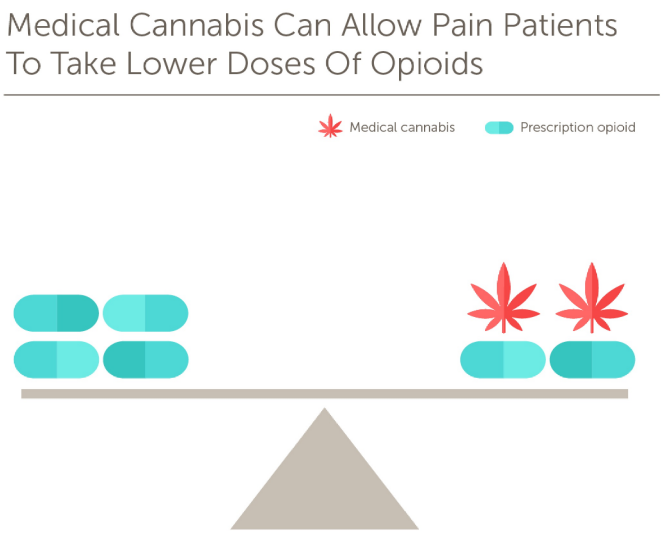
With the approval of State Question 788, its provisions have the force of law, and are engrossed into Title 63, Section 420A of Oklahoma statutes.

After the passage of the state question the board of health put in place more rules and regulations in order to provide further guidance to patients, physicians, and businesses. The initial rules were rescinded due to the Attorney General's opinion that they exceeded the Department of Health's statutory authority. A new set of rules were then approved with far more minimal regulations. The application portal for the program became active August 25th and roughly ten thousand patient licenses and fifteen hundred business licenses have been issued as of November 1st.

Although marijuana is still considered a Schedule One substance at the federal level, it is now legal in thirty-one states. California was the first to legalize in 1996, and in 2002 (Conat v. Walters), federal courts affirmed the right of physicians to recommend marijuana to their patients. In many states, with established medical marijuana programs, physicians have integrated cannabis into their medical practices, especially for pain management. This has come, in part, as a result of the national opioid crisis, and is reinforced through the Center For Disease Control (CDC), guidance that: "Clinicians should not test for substances for which results would not affect patient management or for which implications for patient management are unclear. For example, experts noted that there might be uncertainty about the clinical implications of a positive urine drug test for tetrahyrdocannabinol (THC)."

In October 2018, the Oklahoma Pain Society adopted an official policy statement on Medical Marijuana, which is as follows: "The Oklahoma Pain Society continues to investigate and evaluate therapies that may bring relief to patients suffering from chronic pain, including the use of medical marijuana.

Medical Marijuana is a scheduled therapy and should be treated with caution and education just as with any scheduled medication. It is important for OPS members and all providers who treat chronic pain to be educated on the benefits and risks of using medical marijuana to treat chronic pain as a stand-alone remedy or in conjunction with other prescribed medicines such as opioids.



We encourage healthcare professionals to review the American Pain Society's Guidance on Medical Marijuana for Pain that can be found at: http://americanpainsociety.org/about-us/press-room/american-pain-society-offers-guidance-on-medical-marijuana-for-pain".

Likewise, the Oklahoma Bureau of Narcotics' position is that it is within the physician's discretion as to how they treat patients who are medical marijuana patient licensees. The licensed use of medical marijuana does not disqualify patients from receiving other form of medical treatment, or from being prescribed scheduled medications, including opioids. In fact, the use of medical marijuana in order to help reduce patient opioid doses is one way for pain management physicians to be in compliance with Section 5.F.3. of S.B. 1446, which requires physicians to find ways for patients to reduce their opioid dosages. Physicians concerned about the legality of prescribing opioids to medical marijuana patient licensees may contact Mark Woodward, the OBN's Public Information officer, at 405-521-2885.

See also: http://omma.ok.gov/guidance-for-physicians

Suggested Further Reading

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(Kalin – can you get the bibliographic info for the citations below and format as above)
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