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Comparative Analyses of "Medical Marijuana" Laws in the United States

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Abstract

The medical justification as to the risks and benefits associated with the use of marijuana for medical purposes is not supported by current medical research and state and federal laws in the United States. State endorsed "medical marijuana" currently take the form of a dried plant, *Cannabis sativa*. State laws in favor of legalizing marijuana for medical use fail to incorporate the general legal standards for medical practice and are created absent any uniformed guidelines. These attempts to circumvent federal law lack the support of the medical and legal community as they overlook the standards for safety and effectiveness established by the Food and Drug Administration for medical use. With a growing public demand for marijuana, states have merely attempted to bypass the federal government's current regulations on marijuana by legalizing such laws.

Keywords: Marijuana; Addictive disorders; Psychiatry; *Cannabis sativa*

Introduction

While the nation continues to witness a number of state laws establishing regulations in favor of "medical marijuana", medical literature and federal law have not demonstrated that marijuana is safe or effective to justify medical use in the United States [1-6]. In Report 3 of the Council on Science and Public Health (I-09) it states, "Because marijuana is a crude THC delivery system that also delivers harmful substances, smoked marijuana should generally not be recommended for medical use…[T]he purpose of clinical trials of smoked marijuana would not be to develop marijuana as a licensed drug but rather to serve as a first step toward the development of non-smoked rapid-onset cannabinoid delivery systems" [7]. Nonetheless, the desire to justify legalizing smoked, raw marijuana for "medical use" across the country continues to rise as a result of the growing demand for general use.

Unfortunately, state laws regulating "medical marijuana" generally do not provide guidelines or include legal standards accepted in medical practice. According to ProCon.org, it is estimated that there are a little over 2.6 million Americans that use "medical marijuana" in the US [8]. The question becomes can this use be regulated in order to secure a medication that abides by the Food and Drug Administration (FDA) standards or to pass laws to legalize marijuana as a drug, such as alcohol.

The Drug Approval Process

In the US, the Food and Drug Administration (FDA) was established in 1906 by the federal government following the Federal Food and Drug Act and was officially recognized by its present name in 1930 [7]. The FDA was appointed the task of regulating the procedures involved with manufacturing food and drug products and ensuring the safety of these products for public use [9]. According to the Federal Drug and Cosmetic Act, drugs are defined as "articles intended for use in the diagnosis, cure, mitigation, treatment, or prevention of disease" or "intended to affect the structure or any function of the body of man or other animal" [10]. One of the most important responsibilities of the FDA is to provide drug approval for prescription drugs sold in the marketplace for medical purposes [11]. In order to determine whether the "marijuana plant", in its natural form, qualifies as "safe and effective" by FDA standards, we must first examine the process by which a drug receives drug approval. The table below provides a summary of each stage in the FDA's drug approval process [12] (Table 1).

Stages in the Process	Explanation of each stage
Stage 1: Animal Testing	The drug sponsor must conduct animal testing in order to test for toxicity.
Stage 2: Investigational New Drug Application (IND)	The sponsor or pharmaceutical company must first fill out an Investigational New Drug Application (IND) and must submit the results of all preclinical testing of the drug to the FDA, along with a plan to test the drug on humans.
Stage 3: IND Review	The FDA, along with a local institutional review board (IRB), will determine whether it would be reasonably safe for the company to test the drug on humans by conducting clinical trials. The IRB approves the protocols for the

	clinical trial, which includes information such as who may participate in the clinical trial, the schedule of tests and procedures, the medications and dosage to be studied, the length of the study, the overall objective of the study and a number of other considerations. These clinical trials usually take a number of years in order to complete and consist of three phases.
Stage 4: Clinical Trial - Phase 1	In Phase 1, the focus is on safety. The study may consist of a group made up of twenty to eighty healthy volunteers with the main objective of examining the side effects and to determine how the drug is metabolized or excreted.
Stage 5: Clinical Trial - Phase 2	Phase 2 will test for the effectiveness of the drug and whether the drug effectively works on people suffering from certain diseases or conditions. Data will be collected from a group with the size ranging from anywhere as small as a few dozen patients to as large as three hundred patients.
Stage 6: Clinical Trial-Phase 3	Following the determination of a drug's effectiveness in Phase 2, the FDA and sponsors will meet in order to decide on the size of the studies to be conducted in Phase 3. The size of the studies in this phase may consist of hundreds to thousands of individuals. The purpose of this phase is to collect more information on the safety and effectiveness of the drug by studying different populations, different dosages, and the results of using the drug with other drugs.
Stage 7: FDA Review	After gathering all this data from clinical trials, the FDA will meet with sponsors before a New Drug Application (NDA) is submitted.
Stage 8: New Drug Application (NDA)	The sponsor may file a New Drug Application (NDA) in order to request that the FDA consider approving a new drug for marketing in the United States by providing all animal and human data and analyses, the drug's behavior in the body, and how the drug is to be manufactured.
Stage 9: Application Reviewed	The FDA will review the application and will have up to 60 days - with a set goal to review priority drugs within 6 months - to consider whether or not to file the NDA. Once an application is approved for filing, the FDA review team will evaluate the drug's safety and effectiveness based on the research conducted by the sponsor or company.
Stage 10: Drug Labelling	The FDA will review the information found on the drug's label in order to ensure that healthcare professionals and consumers alike are being well informed about the drug.
Stage 11: Facility Inspection	The FDA will complete a thorough inspection of the facilities where these drugs will be manufactured.
Stage 12: FDA Drug Approval	If the FDA reviewers determine that the benefits of the drug outweigh the risks associated with it, then the application will be approved or a formal response letter will be issued.

Table 1: Summary of each stage in the FDA's drug approval process.

Ultimately, "this process provides important protections for patients, making medications available only when they: 1) are standardized by identity, purity, and quality; 2) are accompanied by adequate directions for use in the approved medical indication; and 3) have risk/benefits profiles that have been defined in well-controlled clinical trials"[7]. Once a drug is on the market, the FDA has methods in which to monitor the drug's performance [7]. One of these methods includes the FDA's Center for Drug Evaluation and Research (CDER), which helps regulate drugs found on the marketplace. Another method is the utilization of MedWatch, the FDA's reporting program, which is used to notify of any suspected side effects regarding a medication made known by a patient, physician or pharmaceutical company.

The FDA's position on "medical marijuana"

The most important factors in considering approval of a drug are determining the safety and effectiveness of the drug. While the FDA does support clinical trials testing the significance of marijuana in treating medical conditions, the FDA has yet to approve marijuana for medical use. One reason for this is that no product containing the natural form of marijuana has been proven by clinical trials to be safe or effective for the treatment of any disease or condition [7]. While states such as Florida, Georgia, Louisiana, New York and Pennsylvania, have shown interest in researching the effects of "medical marijuana" in order to develop their own state marijuana programs, a majority of the states that have legalized marijuana for medical use have failed to show interest in conducting medical research [10]. Thus, indicating the lack of medical support in justifying most states' decisions to legalize "medical marijuana" [13].

Manufacturing controlled substances

A drug is considered to be a controlled substance when it is "… illegal to possess or use without a doctor's prescription, specifically, any type of drug whose manufacture, possession, and use is regulated by law, including a narcotic, a stimulant, or a hallucinogen" [14]. Controlled substances can be divvied into five scheduled categories, as determined by the Controlled Substance Act, which indicate their restriction criteria as enforced by the Drug Enforcement Agency (DEA). The main argument surrounding the use of "medical marijuana" is regarding the restrictions imposed as a result of its schedule I placement. The below mentioned table describes schedules I and II as defined by the Controlled Substances Act (8) (Table 2).

Controlled Substances	Requirements
Schedule I	(A) The drug or other substance has a high potential for abuse.

	(B) The drug or other substance has no currently accepted medical use in treatment in the United States.
	(C) There is a lack of accepted safety for use of the drug or other substance under medical supervision.
Schedule II	(A) The drug or other substance has a high potential for abuse.
	(B) The drug or other substance has a currently accepted medical use in treatment in the United States or a currently accepted medical use with severe restrictions.
	(C) Abuse of the drug or other substances may lead to severe psychological or physical dependence.

Table 2: Schedules I and II as defined by the controlled substances act [8].

The current classification for marijuana is a schedule I controlled substance due to being highly dangerous without legitimate medical use. For this reason, a prescription for such an agent from a licensed medical practitioner would be considered illegal under the controlled substances act enforced by the DEA [15,16]. In order to overcome this issue, states have allowed physicians to authorize the "certification" of their patients to attain licensure for possession of marijuana, rather than a direct prescription. The specifics of such licensure have been left up to state and local government regulations.

Dispensing Controlled Substances: The US Controlled Substance Act

The United States Controlled Substance Act further elaborates upon the roles of pharmacies in dispensing such agents as also being illegal based on lack of a valid prescription. Currently, not only are physicians barred from prescribing, pharmacists cannot dispense schedule I substances, such as marijuana. The primary factor that drives this decision is the lack of evidence-based medicine to support the validity of a specified indication for the use of marijuana, contributing to its schedule I designation. Much of the focus has been on producing literature to support marijuana's use in treating pain, specifically chronic pain of malignancy. If marijuana were found to be safe and effective to treat such chronic pain, changing marijuana's current classification as a schedule I controlled substance to a schedule II may be justified. Thus, allowing for it to be prescribed by physicians.

However, the major downfall with this indication is the availability of alternative options with the other FDA-approved controlled substances within schedules II-V (i.e., OxyContin, fentanyl, morphine, codeine, etc.) that are also highly addictive or dangerous. Not to mention, beyond a condition of chronic pain are a plethora of other indications for which marijuana licensed by states is currently being studied, including glaucoma, amyotrophic lateral sclerosis (ALS), Alzheimer's and schizophrenia [17]. Proof of marijuana's effectiveness in combatting each of these conditions by means of clinical studies alone is not enough. In order to ensure the safety of marijuana, a specific dose in which adequate treatment results may be met for each condition must also be determined. Even with a schedule II designation, smoked marijuana would still be limited by the inability to create a standardized dosing due to the 400+ chemicals contained within each plant. Further illustrating just why marijuana is a very toxic drug and therefore, fails to meet FDA's drug safety standards. The biocompatibility of each of these plants will need to be tested against one another and dosing regimens will need to be examined for each specific indication. In addition to overcoming toxicity, superiority over current alternative options in terms of safety and effectiveness would need to be examined in order to prove a benefit for making such an agent available.

Dispensing controlled substances: FDA's current good manufacturing practice (CGMP)

With the designation of a scheduled I drug comes the inability of marijuana to be compounded in a standardized fashion to be distributed and manufactured to various patient populations. However, in the event marijuana is reclassified as a schedule II controlled substance and is found to be both safe and effective by FDA standards, pharmaceutical companies must comply with the FDA's Current Good Manufacturing Practice (CGMP) [8]. By creating a process to manufacture the marijuana plant as a drug. The purpose of the CGMP is to ensure manufacturers provide strong quality management systems, apply high quality raw materials, establish operating procedures, identify any deviations in the quality of a product, and maintain testing laboratories [9]. In meeting these objectives, manufacturers are expected to utilize the most up to date technologies and systems in order to prevent errors. Pharmaceutical manufacturers who fail to comply with CGMP are said to produce "adulterated" drug products and may be penalized by having to voluntarily recall the product at FDA's request [18]. Failure to do so may lead to a public warning by the FDA followed by a seizure or injunction case brought against the manufacturer [18].

Dispensing controlled substances: Physician liability

The source of defiance of controlled substance laws by physicians can be traced to negative attitudes, inadequate education and training and current pressure to treat medical conditions of pain from political, regulatory, and professional organizations. A vivid illustration of the failure to observe admonishments from the controlled substance law is the attribution of addiction to marijuana as a myth. As such, positions taken by these bodies advocate ignoring, disregarding and pretending that addiction to marijuana does not exist when the intent is to treat pain. Further, rhetorical and unsubstantiated claims that addiction does not occur when marijuana is used to treat pain abound in government and medical recommendations for the management of pain [19].

Politics aside, surveys of medical schools and residency training programs reveal significant and substantial deficiencies in educating medical students and residents in identifying, managing, and treating individuals with addictive diseases. Moreover, physicians woefully lack basic knowledge in the addicting properties of "medical marijuana" and skill in minimizing development of addiction in their patients. Although it is undisputed among physicians that marijuana provide humane and life-saving protection from pain in patient, only a minority of physicians understand and feel competent in preventing and treating complications from recommending "medical marijuana" or other addictions as well, including alcohol and other drugs [19].

What is needed is a weighing of the risks and benefits of recommending "medical marijuana" in the management of pain as delineated in the controlled substances laws. If necessary, vigorous litigation, legislation and regulations should be applied to physicians to hold them more diligently to a standard of preventing morbidity and mortality from their prescribing or recommending of addicting medications. Importantly, a marked change is urgently needed in the public policy for recommending "medical marijuana" in the management of pain [19].

Current State Laws on "Medical Marijuana"

Within the past few years alone, a number of states have redefined their positions regarding the legalization of marijuana by passing regulations in favor of "medical marijuana." The legal use of "medical marijuana" was first introduced by the state of California in 1996 [20]. Since then, a total of 23 states and the District of Columbia have approved its use, many of which, by establishing comprehensive "medical marijuana" programs in order to facilitate a process for dispensing the drug [21]. Prior to examining the state "medical marijuana" programs and the restrictions established by state laws that have legalized marijuana for medical use, one must consider the legal standards for medical practice and the role of the physician.

Legal standards for medical practice

The first standard in providing medical care requires the establishment of a patient-physician relationship. According to the American Medical Association, "[a] patient-physician relationship exists when a physician serves a patient's medical needs, generally by mutual consent between physician and patient" [21]. This relationship is built on trust and fosters the ethical obligations of the physician to see to it that the best interest of the patient is met by using sound medical judgment [21].

While a majority of the states' "medical marijuana" laws require physicians to establish a patient-physician relationship, there have been a number of situations where this requirement has not been met. For instance, based on a 2013 audit report conducted by the state of Colorado, one physician was found to have recommended marijuana to over 8,400 patients alone [21]. Earlier this year, the Chicago Tribune published an article identifying a case where a physician had recommended one-third of the 3,300 patients who applied for certification for "medical marijuana" in Illinois, suggesting that this was a result of a number of state physicians refusing to participate in the referral process [22]. In both these instances, it is highly doubtful that these physicians were able to establish a therapeutic and acceptable patient-physician relationship with each one of these patients.

In addition to creating a patient-physician relationship, a proper diagnosis is fundamental to the overall medical treatment of a patient and is the second standard in medical care. A diagnosis requires a physical examination of the patient and an assessment of the patient's medical history, including a patient's history of substance use/addictive disorders. In 2012, a Colorado physician was arrested and later convicted for improperly recommending marijuana to an undercover cop staged as a patient [23]. The physician identified "severe pain" as the debilitating medical condition, even though the patient was not suffering from such pain and had openly specified his intent to receive a recommendation in order to avoid resorting to the illegal use of marijuana [23]. Fraudulent representation is often the result of a physician's deliberate misdiagnosis and could lead to significant consequences for a patient who has a history of substance use/addiction.

The third standard for medical care requires a patient's informed consent. A patient must not only be informed of their physician's diagnosis, but also of their illness, course of treatment, and any other possible alternatives for treatment. Furthermore, patients should be informed of the lack of medical research associated with the risks and benefits of a given treatment, including high addiction potential and toxicity. The process of growing and distributing marijuana for medical use is completed outside the boundaries of the FDA and its standards. In its natural form, "medical marijuana" is derived from the plant *Cannabis sativa* and is being grown and purchased without consideration for its safety and effectiveness [24].

Proper medical practice also requires that a physician conduct assessments at the various stages of the patient's treatment. The physician shall assess for any adverse effects or signs of marijuana or other expected drug addictions. With regards to "medical marijuana", this standard is most often not met. In some instances, state laws remain silent as to whether or not follow up sessions are required. In other instances, states have incorporated the follow up requirement as a factor in establishing a bona fide patient-physician relationship, but fail to clearly define what qualifies as a follow up [25]. Some "medical marijuana" clinics have opted to providing follow up surveys in place of in person observations in hopes of meeting state requirements. These surveys are typically vague and ask for the patient's name, date of birth, and whether the patient is experiencing any complications or side effects to treatment. Without an in person observation, these surveys should not be used to substitute a doctor's visit and likely do not satisfy legislators' intended definition of a "follow up".

The purpose of these legal standards is to ensure that patients are receiving adequate medical care. Although these standards are stated in most state "medical marijuana" laws, they are not clearly defined, implemented, or enforced appropriately, and do not correspond with usual medical practice. Most state "medical marijuana" laws provide guidelines for qualified illnesses, possession restrictions, caregiver limitations, and cultivation requirements. Below is a chart providing a brief summary of each category (Chart 1).

Comparison of the Current State "Medical Marijuana" Laws
Illnesses: The term "debilitating medical condition" is used in state "medical marijuana" laws to identify the various illnesses in which marijuana may be used by an individual for medical purposes. While no guidelines are provided to states in order to determine which medical conditions qualify as debilitating, the most commonly listed illnesses among the 23 states that have legalized "medical marijuana" include cancer, HIV/AIDS, epilepsy, glaucoma, and multiple sclerosis [18]. In states, such as Maine, patients suffering from illnesses such as Alzheimer's and post-traumatic stress disorder (PTSD) qualify for "medical marijuana" [19]. It is unclear as to how states determine which illnesses are debilitating medical conditions. Most states permit physicians to apply their own discretion in deciding if a patient's illness can be treated by "medical marijuana", regardless of whether or not the illness is listed as a debilitating medical condition by the state.

Possession: A state's limitation on the amount of marijuana a user may possess is found to lie somewhere between the one ounce restriction in Montana and the 24 ounces in Washington, with a majority of the states claiming a 2-2.5 ounces maximum [19]. In states such as Maryland, Massachusetts, Minnesota, and New York, possession limitations are determined as a 30 or 60 day supply [19]. While it is unknown how states reached these specific amounts, inconsistencies in "medical marijuana" possession illustrate a strong lack of medical guidance. Whereas physicians determine a specific dose of a medication to treat a patient's illness, all debilitating conditions treated by "medical marijuana" are provided the same amount, regardless of the illness as is set out by the state's laws. Thus, the amount of possession is not determined by a physician, but rather by legislators.
Caregiver: A licensed "medical marijuana" caregiver is a person who is responsible for the health and safety of a patient using "medical marijuana" to overcome a debilitating medical condition. In most states, caregivers are required to be of legal age (either 18 or 21 years of age) and cannot be a convicted felon. In states, such as California, a caregiver may grow, transport or cultivate marijuana [19].
Cultivation: States also restrict the number of plants that a single dispenser may grow at a given time. There are no safeguards or bases as to assess toxicity of "home grown" marijuana. While some states limit the number of licensed dispensaries within the state, others simply define strict requirements dispensers must satisfy. For example, in Colorado, dispensaries cannot be within 1,000 feet of a school or day-care centre. In California, all state-licensed dispensaries are to keep a distance of at least 600 ft from any schools and are restricted from operating for profit.

Chart 1: Brief summary of each category of "medical marijuana" laws.

These guidelines defined by state "medical marijuana" laws are not generated by the medical community. A majority of the state laws legalizing "medical marijuana" overlook the designated safety and effectiveness standards of the FDA and do not account for the FDA's current position on marijuana for medical use. Thus, these guidelines are not medically based. Furthermore, these state laws fail to incorporate the legal standards for medical practice and merely attempt to circumvent federal law in order to meet a growing public demand for marijuana.

Enrollment process for state "medical marijuana" programs

An individual may be granted permission to enroll in a state "medical marijuana" program by completing the steps listed below:

- Scheduling a visit with a state licensed physician. Individuals may opt to schedule an appointment with a "medical marijuana" doctor, who "recommends" eligible patients to the program.
- The physician will determine whether or not an individual's illness qualifies the individual for enrollment in the states "medical marijuana" program and may recommend the individual for the program. This alters from state to state depending on the states' list of qualified illnesses, whether the physician may apply their own discretion, and whether the state requires additional information to grant approval.
- Following a physician's recommendation, an individual can apply for a state issued "medical marijuana" card so long as they have proof of state residence [26].
- Individuals who are approved for a "medical marijuana" card will be required to pay a fee, which varies from state to state. Most recommendations and "medical marijuana" cards are valid for up to one year before requiring renewal.

The Future of "Medical Marijuana"

Although the federal government has remained silent on states' decisions to legalize marijuana for medical use, recent proposals suggest that the government will soon solidify its position in favor of legalization at the federal level. Both the House and the Senate have proposed two different bills that will alter marijuana's current classification as a schedule I substance.

On February 20th, 2015, the House of Representatives introduced a bill, entitled "Regulate Marijuana like Alcohol Act of 2015" [27], proposing to eliminate marijuana as a controlled substance and to exempt it from all the schedules under the Controlled Substance Act. Under this bill, marijuana would be regulated, sold, and used similar to alcohol. Thus, granting marijuana "true legalization" in a sense. The bill also assigns the rights to regulate marijuana to the Food and Drug Administration (FDA); the Director of the Bureau of Alcohol, Tobacco, Firearms, and Explosives (ATF); and the Alcohol and Tobacco Tax and Trade Bureau [27].

Contrary to the House bill, the Senate proposes to amend the Controlled Substances Act by lessening the enforcement against individuals complying with state "medical marijuana" laws as is illustrated in the "Compassionate Access, Research Expansion, and Respect States Act" bill [28]. If passed, this bill would not only reclassify marijuana as a Schedule II controlled substance under the Controlled Substance Act, but would also establish certain effective and safe guards to legally prescribe marijuana [28].

The Houses' and Senates' bills provide the legalization of "medical marijuana" by taking two very different approaches. While the House plans to negate marijuana for medical purposes by treating it as a beverage, the Senate sanctifies marijuana for medical use by treating it as a prescription drug that would be required to satisfy the standards of the FDA. Under both bills, state "medical marijuana" laws and programs would be eliminated.

Alternative to reclassifying marijuana as a schedule II drug or a legal drug as alcohol is to retain its current classification as a schedule I drug. To enforce controlled substance laws as intended would likely result in lower addiction rates to marijuana and conserve adverse effects. These adverse effects to marijuana include, but are not limited to violence, disability, and death.

Conclusion

Current state regulations regarding "medical marijuana" are highly political and do not abide by medical practice in that these laws lack scrutiny. State "medical marijuana" laws are merely the result of legal manoeuvres in order to generate state tax revenues as well as to meet public demands for marijuana use and in doing so, intentionally circumvent the FDA's position on marijuana and its medical standards. These state laws will be replaced by federal marijuana regulations in search of uniformity as is illustrated by the current proposed bills by the House and the Senate.

The major criticism for changing the schedule of marijuana from I to II would be the repercussions on the use of other schedule I drugs. Marijuana could become a "gatekeeper" for other schedule I drugs being more accessible and thus, potentially lead to greater use or

prevalence for other addictive disorders from these agents. Critics have also pointed out that it would be improper to have marijuana regulated in the same manner as alcohol since it is highly dangerous and addictive. Hence, the best option would be to keep marijuana as a schedule I controlled substance and require greater medical scrutiny as a perquisite for state "medical marijuana" laws.

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