Informed Consent: A Policy Prescription for Communicating Benefit and Risk in State Medical Marijuana Programs

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In creating medical marijuana laws, state governments signal to the public that marijuana can safely and effectively treat a wide range of diseases. In many cases, these state approvals overestimate the benefits of marijuana and understate the risks. After a comprehensive review of the medical literature, the National Academies of Sciences, Engineering, and Medicine identified six medical benefits from marijuana~~, which~~ were supported with at least a moderate level of medical evidence, and 14 potential health hazards. In contrast, the average state medical marijuana program lists 18 medical benefits, and 24 state medical marijuana program websites say nothing about possible risks. Medication approval processes through the federal government traditionally require independent analysis of data from well-designed clinical trials that measure the effectiveness and capture the risks of adverse effects from specific doses of the medicine. These considerations are generally missing from state approvals of medical marijuana. The power to declare something to be a legitimate medicine comes with the responsibility to provide information that people need to use the medicine wisely. The authors recommend that states that declare marijuana to be a medicine should inform the public about the quality of medical evidence behind each approved use and publicize all scientifically credible risks.

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Marijuana is an easily cultivated psychoactive plant that has been used ceremonially, recreationally, and medicinally for thousands of years. It has been essentially prohibited in the United States since 1937: first, by the Federal Marihuana Tax Act and then by placement in Schedule 1 of the federal Controlled Substances Act of 1970. Hobbled by federal restrictions, scientific research about marijuana has not kept pace with its popularity, which is surging. At a time when we most need high-quality data about marijuana's health effects, we find a scientific knowledge base far below modern standards.

Responding to favorable public opinion and well-financed political activity, many states have passed laws that permit the medical use of marijuana. However, in creating medical marijuana laws, states face the challenge of making sound policy about a substance with medical benefits that are currently unclear, with risks that are often contested, and in a setting where political pressures and financial motives may influence decisions.

This article offers suggestions for informing the public more effectively about the potential benefits and risks of marijuana in this challenging societal context.

UNDERSTANDING THE PROBLEM

Terminology

Cannabis is the botanical name for a genus of flowering plants. The genus contains three species (sativa, indica, and ruderalis) and hundreds of selectively bred strains. The plants produce about 100 chemicals unique to the genus, and these chemicals are collectively termed "cannabinoids." The most important cannabinoids are tetrahydrocannabinol

HIGHLIGHTS

- In creating medical marijuana programs, state governments send a strong message that marijuana is a beneficial medicine that can treat a wide array of illnesses.
- State medical marijuana programs have endorsed many medical benefits not supported by even moderate-quality scientific evidence, and many programs do not report any of marijuana's scientifically credible risks.
- State medical marijuana programs should use their program websites, marijuana packaging, and public service announcements to improve awareness of marijuana's plausible hazards and the limits of current medical evidence about its therapeutic benefits.

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(THC), which is intoxicating, and cannabidiol (CBD), which is biologically active but not intoxicating. Hemp refers to cannabis strains with negligible THC content. Marijuana is a colloquial term that refers to cannabis plants, or their dried leaves or flowers, which contain THC. Google Analytics suggests that more people speak of marijuana than cannabis, and the majority of state laws that have legalized cannabis have used the term "marijuana." Therefore, we use the term "marijuana" here to describe THC-containing plants, leaves, or flowers from any *Cannabis* species.

Legal definitions of marijuana in many states are considerably broader and may permit any cannabinoid at any concentration to be called "marijuana." Highly concentrated products such as vaping oils or solid concentrates (e.g., wax, budder, shatter) are often within the legal definition of marijuana in most states. In many cases, legalizing marijuana is equivalent to legalizing pure THC.

Marijuana policy reform has created distinctions between recreational use and medicinal use. Although issues related to the effects and potential harms apply to both medicinal and recreational use, there are important differences in the policy issues raised. Policy issues related to recreational use are outside the scope of this article.

When a government declares something to be a medicine, there are responsibilities unique to medicines that a government needs to consider. Declaring something to be a medicine comes with duties to ensure that the claimed benefits are adequately supported by data and that consumers are informed about credible hazards. This article examines the policy implications of state government medical marijuana approvals and offers suggestions to better inform the public about marijuana's potential benefits and risks.

Medical Marijuana: Popular, Profitable, and Political

Despite federal prohibition, marijuana is widely used and increasingly accepted across the United States. Forty-five percent of U.S. adults have used marijuana, and between 7% and 12% are current users (1, 2). In comparison, about 14% of U.S. adults smoke tobacco cigarettes (3). The current number of marijuana users is the highest reported over the past decade (1). Support for legalizing marijuana has nearly quadrupled since 1990, to the point that 61% of U.S. adults favor it (4).

Public support for legalization is even stronger for medical uses of marijuana. More than 80% of Americans in a national survey reported that they believed that marijuana has at least one medicinal benefit, with pain management and treatment of epilepsy and multiple sclerosis being the most commonly assumed benefits (5). Seventy-three percent of U.S. voters supported medical marijuana in a 2010 Pew Research Center survey (6), and 86% of current marijuana supporters cite medical benefits as a reason why it should be legalized (7). Belief in the medical value of marijuana may be supported by the fact that each of marijuana's two most important cannabinoids, THC and CBD, have been approved for medical use by the U.S. Food and Drug Administration (FDA).

Legalizing marijuana also promises financial benefits for investors, businesses, and governments. About $30 billion is spent on marijuana every year in the United States (8), and many industry analysts predict double-digit annual growth (9). Marijuana-related businesses donate to both Republican and Democratic political campaigns in many states, and marijuana-related federal lobbying spending increased by 6,500% from 2014 to 2019 (10).

States Entering the Drug Approval Business Under Suboptimal Conditions

Responding to these incentives, 33 states and the District of Columbia have passed laws that legalize the cultivation, distribution, sale, or consumption of marijuana for medical use. These laws limit the medical use of marijuana to a set of diseases or symptoms deemed "qualifying conditions." (In Oklahoma's program, however, any medical condition may be treated with marijuana if a doctor feels that it would be useful.) Each state decides for itself what level of medical evidence is needed to categorize an illness as treatable with marijuana. States must also develop their own regulations for the cultivation, distribution, promotion, and sale of marijuana and determine the extent to which potential risks should be disclosed to citizens. In effect, individual states have taken on roles usually handled by larger, more experienced drug-regulatory agencies, such as the FDA. Although states have always had the right to regulate commerce and the practices of medicine and pharmacy within their borders, drug approval and regulation are specialized tasks that require resources and experience often unavailable to state governments.

Society has learned from earlier public health disasters (11) that government approvals of proposed medical treatments should be based on rigorous clinical studies and that approvals should be restricted to a limited range of specifically defined doses. We have also learned that financially or politically invested parties should not be involved in approval or regulatory decisions. Each of these basic principles of modern drug-approval ethics is radically compromised in state medical marijuana approval processes.

The gold-standard test of medication effectiveness and safety is the randomized, multisite, double-blind, placebo-controlled clinical trial. Drug regulators get the clearest possible picture of the true benefits and side-effect

risks of a proposed treatment by enrolling a large number of well-characterized volunteers; randomly assigning them to active-treatment or placebo-treatment groups, under conditions where neither patient nor investigator is biased by knowing the group assignment; and regularly scoring symptom severity and side-effect occurrence. However, largely because of marijuana's illegal status under federal law, such clinical studies are extraordinarily difficult to conduct. Placebo-controlled studies on marijuana are also limited by the fact that marijuana is intoxicating. Buzzed volunteers easily know whether they have been assigned to active-drug or placebo groups, compromising study integrity. Federal marijuana policies and the lack of adequate placebo controls make gold-standard medical evidence for marijuana scarce. State regulators are often forced to consider bodies of evidence that are more prone to ambiguous design or biased interpretation.

The dose of a drug is critically important in predicting whether it will help or harm, yet the doses of active cannabinoids such as THC or CBD are rarely considered in state medical marijuana laws. In some cases, states may limit the amount of THC that can be purchased, but those limits can be high. Under Ohio's medical marijuana law, a "whole-day unit" of edible marijuana may contain up to 110 mg of THC, and a whole-day unit of vaping oil may contain up to 590 mg of THC (12). Consumers may not purchase more than a 70-day supply of medical marijuana under Florida law. However, Florida has not yet defined how much THC constitutes a day's supply. A rule-making advisory panel has recommended setting the daily edible THC product limit at 1,000 mg (13). For reference, the maximum recommended daily THC dose for FDA-approved use is 20 mg (14).

The potential benefits or risks of marijuana are also influenced by the ratio of the various cannabinoids within the marijuana product. A product with low THC and high CBD concentrations may have negligible intoxicating effects, but a variety with high THC and low CBD concentrations may be dangerously intoxicating. Most states do not address THC:CBD ratios in their definitions of medical marijuana and many states permit formulations that deliver THC at levels never found in nature.

The route of administration also influences the effects of marijuana. Inhalation of marijuana produces clinical effects within a few minutes but cannabinoids from edible marijuana products are absorbed over the course of hours and have longer-lasting effects. There is significantly greater risk for unpleasant psychiatric side effects from edible marijuana products (15). Many states make no regulatory distinction between inhaled, topical, or edible marijuana products. This inattention to therapeutic dosing is a major and potentially dangerous deviation from standard drug-regulatory practice.

Conflicts of Interest

Conflicts of interest can powerfully bias decision making. Modern drug regulation is designed so that decisions about medication approval and regulation are made by individuals who will not directly benefit from these decisions. Many state politicians receive campaign contributions from marijuana business interests, and state governments that legalize marijuana stand to generate tax revenue because of it. In cases in which state governments act as drug regulators, it is often unclear where the lines are drawn between the people who make decisions related to legalizing marijuana and the politicians who appoint them.

Objective Assessments of Marijuana's Benefits and Risks

In light of these conflict-of-interest concerns, it can be useful to rely on comprehensive analyses by neutral experts when assessing the medical benefits or risks of marijuana. The National Academies of Sciences, Engineering, and Medicine was asked in 2016 to conduct a comprehensive review of the scientific literature regarding the health effects of marijuana. The National Academies is a congressionally chartered organization tasked with providing objective analysis of complex problems, and the report is among the most comprehensive and most recent analyses of marijuana's potential benefits and risks (16).

In addition to describing benefits and risks, the report also considers the quality of scientific evidence supporting each finding. Box 1 lists the health benefits and risks supported by moderate evidence or better. "Moderate evidence" is defined as "several supportive findings from good- to fair-quality studies with very few or no credible opposing findings."

Public Misperceptions of Marijuana's Health Effects

Surveys suggest that the U.S. public has an overly optimistic view of marijuana's health effects. Aside from legal problems or the possibility of addiction, the majority of adults believe that marijuana has no significant risks, and 9% of adults believe that it has no risks at all (5). Among youths between ages 16 and 19, survey data demonstrate that almost two-thirds of them (65.4%) are not worried at all that marijuana use will damage their health (17). Meanwhile, a third of adults believe that eating, smoking, or vaping marijuana products will actually prevent health problems (5).

Inconsistent Messages About Marijuana's Medical Uses and Risks

All states with medical marijuana laws describe their programs on state websites. These public information portals represent official communication from state governments to citizens. However, the information they provide sends the public inconsistent and inaccurate messages about the benefits or risks of marijuana. We surveyed each of these government websites to assess the number of medical conditions that qualified for treatment with marijuana. We also searched each website to find whether, and to what extent, each state medical marijuana program described potential risks from marijuana treatment. The surveys were conducted in 2019, from July 15 to August 5, and included each

BOX 1. Health benefits and risks of marijuana use

Symptoms for which benefits are supported by conclusive evidence
- Chronic pain in adults
- Nausea or vomiting caused by chemotherapy
- Patient-reported muscle spasms from multiple sclerosis

Conditions and diseases for which benefits are supported by moderate evidence
- Sleep disturbances in people with obstructive sleep apnea syndrome
- Fibromyalgia, chronic pain
- Multiple sclerosis

Risks with substantial evidence of association with marijuana use
- Respiratory symptoms and bronchitis episodes, if smoked
- Increased risk of motor vehicle crashes
- Lower birth weight of babies whose mothers used marijuana during pregnancy
- The development of schizophrenia or other psychoses, with the highest risk among the most frequent users
- Problematic marijuana use, such as addiction

Risks with moderate evidence of association with marijuana use
- Increased risk of potentially serious overdose injuries among children living in marijuana-legal states
- Impairments of learning, memory, or attention
- Increased symptoms of mania or hypomania among people with bipolar disorders who regularly use marijuana
- Small increased risk of the development of depressive disorders
- Increased incidence of suicidal ideation and suicide attempts and suicide completion
- Increased incidence of social anxiety disorder among regular marijuana users
- Worsening of the negative symptoms of schizophrenia
- Development of a substance use disorder for alcohol, tobacco, or illicit drugs

of the 33 states with medical marijuana laws and the District of Columbia.

Each website (except Oklahoma's) lists the medical conditions eligible for treatment with marijuana. These medical approvals differ markedly across states. For instance, the District of Columbia, Maryland, and Florida recognize, respectively 8, 9, and 11 qualifying medical conditions, whereas Connecticut, North Dakota, and Illinois recognize 31, 32, and 40 conditions, respectively. The State of Oklahoma allows the use of marijuana to treat any medical condition that a physician feels would respond to marijuana treatment. For reference, the FDA has recognized two medical uses for THC and two medical uses for CBD.

Although there are technical differences between a state's designation of qualifying medical condition and the FDA's approval of a candidate drug for medical treatment, the average consumer will see them as roughly equivalent. This invites the public to overestimate the significance of state medical marijuana approvals.

Currently, no state medical marijuana program website informs visitors of the quality of medical evidence used to determine the medical effectiveness of marijuana for the listed qualifying medical conditions. This suggests to consumers that all medical conditions are equally likely to benefit from marijuana or that its many listed implied benefits are equally well supported by medical evidence.

Further, at least 24 of the nation's 34 medical marijuana program websites omit information about potential side effects or long-term risks from using medical marijuana. Meanwhile, risk information can be challenging to locate within the websites of state medical marijuana programs that do address risk. On the basis of the provided information, the average visitor to a medical marijuana program website may conclude that the risks are minimal or that medical marijuana is risk free. For reference, the manufacturers of prescription THC or CBD list more than 18 adverse reaction risks from each medication (14, 18)

RECOMMENDATIONS

Fully Disclose Limits of Knowledge About Medical Benefits

Thanks to modern drug regulation, the public has come to expect that approved medications are safe and effective and that approvals are based on clinical studies that meet modern standards of quality. Consumers and the public deserve to know that these standards do not apply to medical marijuana. Each state's medical marijuana program should disclose the quality of medical evidence underlying each approved use of marijuana. It should explain the rationale behind the approval of each qualifying condition as well as the limitations or caveats related to each approval. This will allow individuals considering the use of medical marijuana and their health care providers to discuss the limits of the current medical evidence regarding efficacy and risks, including paradoxical reactions.

Fully Disclose and Publicize Potential Risks

In creating medical marijuana laws and specifying qualifying medical conditions, states declare to the public that marijuana has medical benefits. In line with modern drug regulation ethics, they should also specify its risks. States should not offload the responsibility of risk education onto the shoulders of physicians or dispensary workers—these individuals did not confer the status of medicine on marijuana. Further, most physicians have not been educated about

marijuana risk and may actually be looking to the experts in their state's medical marijuana program for risk guidance.

We acknowledge that, like the evidence behind claims of marijuana's medical benefits, the risk data may not be up to accepted standards. However, imperfect data should not be misinterpreted as a safety signal; rather, such data call for even greater caution. Ethics dictate that the consumer has the right to know of scientifically credible concerns, and prudence demands that we err on the side of caution in matters of health and safety.

Independent and Transparent Assessment

The processes for recognizing qualifying medical conditions for medical marijuana use and the processes for identifying potential risks should be standardized and clearly stated to the public.

Financial or political conflicts of interest should be eliminated. Any committee that provides recommendations or makes decisions on legal uses of marijuana should be obligated to make a full disclosure of each member's affiliations. Those with potential conflicts of interest should be removed from the decision-making process. Additionally, in cases where committee members are political appointees, the public should be informed as to whether the appointing official has any affiliations with the marijuana industry or has received contributions from pro- or ~~antimarijuana~~ interests.

The work of identifying potential medical benefits or risks and assessing the quality of scientific evidence that supports each finding is specialized and time consuming. Such work demands continuous revision as new information becomes available. Given these considerations, such work may become burdensome and expensive for individual states. We suggest that this work could be undertaken by a central agency whose work could be jointly funded by the states. Forming such an agency would avoid duplicative processes in each state.

Implementation

States can use existing knowledge and infrastructure to more effectively communicate to the public the limits of medical knowledge about marijuana's proposed medical benefits, as well as its potential risks, and to show how they address financial or political conflicts of interest in their medical marijuana policies.

Independent comprehensive reviews of the evidence supporting medical uses of marijuana and of its potential risks already exist. The report from the National Academies of Sciences, Engineering, and Medicine is the most recent example (16). Its findings could serve as a starting point for informing the public about benefits and risks.

Dissemination infrastructure is also already in place. Every state with a medical marijuana program currently maintains its own website. Because these websites represent each state's most authoritative sources of information about its program, they are likely to be visited by people considering the use of medical marijuana. The state medical marijuana program website is a logical place for the state to fulfill its ethical duty to provide information that a patient may require to make an informed decision about using marijuana for treatment.

To provide accurate information about the likelihood for benefit, state medical marijuana program websites should be designed so that visitors can easily see the quality of medical evidence supporting the use of marijuana to treat each of the qualifying medical conditions that the state has identified. The websites should also remind visitors that not all diseases will respond equally well to marijuana, that some illnesses may be worsened by marijuana, and that the medical evidence supporting medical uses of marijuana is not up to modern standards of scientific quality.

Informed ~~decision making~~ about the medical use of marijuana also requires knowledge of its possible risks. State medical marijuana websites can and should be modified to effectively inform visitors of marijuana's scientifically credible risks. At a minimum, an easy-to-find, easy-to-understand list of the risks of marijuana use that are supported by at least moderate evidence must be made available to the public.

Warning labels should be included on marijuana product packaging, and public service announcement campaigns highlighting the known risks of marijuana use should be conducted. These measures have been effective in changing patterns of tobacco consumption and may reduce harm in vulnerable populations, such as pregnant women and adolescents (19).

Similarly, the issue of transparency needs to be addressed. State medical marijuana program websites should also provide information that allows the public to understand how decisions about marijuana uses and declarations are made, who makes the decisions, how they became decision makers, and whether they have financial or partisan ties.

CONCLUSIONS

There are good arguments for states to permit the medical use of marijuana. The ability of informed adults to act on their personal decisions is in line with the social value of freedom. Governments responding to the will of the majority is in line with the social value of democracy. Because some evidence suggests medical benefits from marijuana, making it available to relieve suffering is in line with the value of compassion. There are also good arguments for changing federal regulations to make it easier to study marijuana to learn how to better exploit its possible benefits while minimizing its risks.

On the other hand, we need to be aware of the limits of our current knowledge, and states with medical marijuana laws or considering them should proceed with great caution. Some legalization advocates will object that our recommendations are unfounded or unfairly burdensome. We concede that explaining marijuana's risks and the

uncertainties around its benefits will create more challenging policy making, but this is better than endorsing poorly documented benefits and letting people learn about risk through firsthand experience.

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AUTHOR QUERIES

AUTHOR PLEASE ANSWER ALL QUERIES

There are no queries in this article.