

Problems With the Medicalization of Marijuana

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“Medical” marijuana is approved in 21 states and the District of Columbia for numerous conditions, including glaucoma, Crohn disease, posttraumatic stress disorder, epilepsy, Alzheimer disease, and chemotherapy-induced nausea and vomiting. Both the number of states and the number of approved indications for medical marijuana are expected to increase. Physicians will bear the responsibility of prescribing marijuana and thus have an obligation to understand the issues involved in its “medicalization.”

Medical marijuana differs significantly from other prescription medications. Evidence supporting its efficacy varies substantially and in general falls short of the standards required for approval of other drugs by the US Food and Drug Administration (FDA). Some evidence suggests that marijuana may have efficacy in chemotherapy-induced vomiting, cachexia in HIV/AIDS patients, spasticity associated with multiple sclerosis, and neuropathic pain. However, the evidence for use in other conditions—including posttraumatic stress disorder, glaucoma, Crohn disease, and Alzheimer disease—relies largely on testimonials instead of adequately powered, double-blind, placebo-controlled randomized clinical trials. For most of these conditions, medications that have been subjected to the rigorous approval process of the FDA already exist. Furthermore, the many conditions for which medical marijuana is approved have no common etiology, pathophysiology, or phenomenology, raising skepticism about a common mechanism of action.

There is no clear optimal dose of marijuana for its various approved conditions. The concentration of Δ^9 -tetrahydrocannabinol (THC) and other cannabinoids in each marijuana cigarette, the size of cigarettes, and the quantity of smoke inhaled by users can vary considerably. The relative lack of controlled clinical trial data makes finding the appropriate dose even more challenging. Furthermore, given that medical marijuana is approved for mostly chronic conditions that require long-term dosing, physicians must be aware of the development of tolerance and dependence (as evidenced by downregulation of the brain cannabinoid receptors), as well as withdrawal on discontinuation.

Prescription drugs are produced according to exacting standards to ensure uniformity and purity of active constituents and excipients. Because regulatory standards of the production process vary by state, the composition, purity, and concentration of the active constituents of marijuana are also likely to vary. This is especially problematic because unlike most other prescription medications that are single active compounds, marijuana contains more than 100 cannabinoids, terpenoids, and flavonoids that produce individual, interactive, and entourage effects. Although THC is believed to be the principal psychoactive constituent of marijuana, other cannabinoids present in marijuana may have important effects that may offset THC's negative effects. For

instance, cannabidiol has been shown to have anxiolytic and antipsychotic effects that might offset the anxiogenic and psychotogenic potential of THC. Yet cannabidiol is sometimes bred out to increase the THC potency of some medical marijuana strains.

Benefits notwithstanding, the potential harms associated with medical marijuana need to be carefully considered. No other prescription medication is smoked; concerns remain about the long-term risks of respiratory problems associated with smoking marijuana, which are a subject of active investigation. THC is already available in a pill approved by the FDA, yet this form seems to be less desirable to those seeking medical marijuana; this may in part be because its euphoric effects are not immediate and cannot be reliably controlled, unlike smoked marijuana. Furthermore, there is evidence that marijuana exposure is associated with an increased risk of psychotic disorders in vulnerable individuals. Clearly, some but not all individuals are at risk of psychosis with exposure to marijuana, but it is not possible to identify at-risk individuals. In individuals with established psychotic disorders, marijuana use has a negative effect on the course and expression of the illness. Furthermore, recent findings suggest that long-term marijuana exposure is associated with structural brain changes as well as a decline in IQ.

The current system of dispensing marijuana does not safeguard adequately against the potential for diversion and abuse. Many states, for instance, allow patients to grow their own marijuana. Furthermore, marijuana may be contaminated with pesticides, herbicides, or fungi, the latter being especially dangerous to immunocompromised individuals such as patients with HIV/AIDS or cancer. Central regulatory oversight by the FDA makes possible the recall of harmful drugs or contaminated batches and the dissemination of new information about drug safety. Is there sufficient oversight to monitor potential contamination of marijuana, especially when patients are permitted to grow it themselves?

A significant but largely overlooked problem with the medical marijuana movement is the message the public infers from its legalization and increasing prevalence. There is an increasing perception, paralleling trends in legalization, that marijuana is not associated with significant or lasting harm; data from 3 decades indicate that among adolescents, risk perception is inversely proportional to prevalence of cannabis use. As legalization has spread for medical or recreational purposes, it is possible that the perception of risk by adolescents will continue to decrease, with a subsequent increase in use. This is especially problematic given that many of the negative effects of marijuana are most pronounced in adolescents.

Projections of substantial revenue rather than evidence-based medicine may explain the eagerness of many states to legalize medical marijuana. Physicians have been invited to participate in the development of medical marijuana programs late in the process. In some instances (eg, Connecticut), legislators approved medical marijuana but consulted physicians with relevant expertise only afterward.

An unmet need remains for treatments of a number of debilitating medical conditions. Specific constituents of marijuana may have therapeutic promise for specific symptoms associated with these disorders. However, if marijuana is to be used for medical purposes, it should be subjected to the same evidence-based review and regulatory oversight as other medications prescribed by physicians. Potentially therapeutic compounds of marijuana should be purified and tested in

randomized, double-blind, placebo- and active-controlled clinical trials. Toward this end, the federal government should actively support research examining marijuana's potentially therapeutic compounds. These compounds should be approved by the FDA (not by popular vote or state legislature), produced according to good manufacturing practice standards, distributed by regulated pharmacies, and dispensed via a conventional and safe route of administration (such as oral pills or inhaled vaporization). Otherwise, states are essentially legalizing recreational marijuana but forcing physicians to act as gatekeepers for those who wish to obtain it.