More Reasons States Should Not Legalize Marijuana



Medical and Recreational Marijuana: Commentary and Review of the Literature

by Samuel T. Wilkinson, MD

Marijuana should undergo the same rigorous approval process as other medications prescribed by physicians, including randomized, placebo- and active-controlled trials to evaluate safety and efficacy, not by popular vote or state legislature.

Abstract

Recent years have seen substantial shifts in cultural attitudes towards marijuana for medical and recreational use. Potential problems with the approval, production, dispensation, route of administration, and negative health effects of medical and recreational marijuana are reviewed. Medical marijuana should be subject to the same rigorous approval process as other medications prescribed by physicians. Legalizing recreational marijuana may have negative public health effects.

Introduction

Recent years have seen a cultural shift in attitudes towards marijuana. At the time of this writing, medical marijuana is legal in 20 states and the District of Columbia; recreational marijuana is now legal in Washington and Colorado. A substantial and growing literature documents legalized marijuana may have adverse effects on individual and public health.

Medical Use of Marijuana

The term 'medical marijuana' implies that marijuana is like any other medication prescribed by a physician. Yet the ways in which medical marijuana has been approved, prescribed, and made available to the public are very different from other commercially available prescription drugs. These differences



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pose problems unrecognized by the public and by many physicians.

Lack of Evidence for Therapeutic Benefit

In the United States, commercially available drugs are subject to rigorous clinical trials to evaluate safety and efficacy. Data appraising the effectiveness of marijuana in conditions such as HIV/AIDS, epilepsy, and chemotherapyassociated vomiting is limited and often only anecdotal.^{1,2} To date, there has been only one randomized, double-blind, placebo- and active-controlled trial evaluating the efficacy of smoked marijuana for any of its potential indications, which showed that marijuana was superior to placebo but inferior to Ondansetron in treating nausea.³ Recent reviews by the Cochrane Collaboration find insufficient evidence to support the use of smoked marijuana for a number of potential indications, including pain related to rheumatoid arthritis,⁴ dementia,⁵ ataxia or tremor in multiple sclerosis,⁶ and cachexia and other symptoms in HIV/AIDS.² This does not mean, of course, that components of marijuana do not have potential therapeutic effects to alleviate onerous symptoms of these diseases; but, given the unfavorable side effect profile of marijuana, the evidence to justify use in these conditions is still lacking.

Contamination, Concentration & Route of Administration

Unlike any other prescription drug used for medical purposes, marijuana is not subject to central regulatory oversight. It is grown in dispensaries, which, depending on the state, have regulatory standards ranging from strict to almost non-existent. The crude marijuana plant and its products may be contaminated with fungus or mold.⁷ This is especially problematic for immunocompromised patients,8 including those with HIV/AIDS or cancer.9 Furthermore, crude marijuana contains over 60 active cannabinoids,10 few of which are well studied. Marijuana growers often breed their plants to alter the concentrations of different chemicals compounds. For instance, the concentration of tetrahydrocannabinol (THC), the principal psychoactive ingredient, is more than 20-fold more than in marijuana products used several decades ago. Without rigorous clinical trials, we have no way of knowing which combinations of cannabinoids may be therapeutic and which may be deleterious. As marijuana dispensaries experiment by breeding out different cannabinoids in order to increase the potency of THC, there may be unanticipated negative and lasting effects for individuals who smoke these strains.

Marijuana is the only 'medication' that is smoked, and, while still incompletely understood, there are legitimate concerns about long-term effects of marijuana smoke on the lungs.^{11,12} Compared with cigarette smoke, marijuana smoke can result in three times the amount of inhaled tar and four times the amount of inhaled carbon-monoxide.¹³ Further, smoking marijuana has been shown to be a risk factor for lung cancer in many^{14,15} but not all¹⁶ studies.

High Potential for Diversion

In some states, patients are permitted to grow their own marijuana. In addition to contributing to problems such as contamination and concentration as discussed above, this practice also invites drug diversion. Patients seeking to benefit financially may bypass local regulations of production and sell home-grown marijuana at prices lower than dispensaries. We do not allow patient to grow their own opium for treatment of chronic pain; the derivatives of opium, like marijuana, are highly addictive and thus stringently regulated.

Widespread "Off-label" Use

FDA-approved forms of THC (Dronabinol) and a THC-analog (Nabilone), both available orally, already exist. Indications for these drugs are HIV/AIDS cachexia and chemotherapy-associated nausea and vomiting. Unlike smoked, crude marijuana, these medications have been subject to randomized, placebo-controlled, clinical trials. Yet despite these limited indications where marijuana compounds have a proven but modest effect in high-quality clinical trials, medical marijuana is used overwhelmingly for non-specific pain or muscle spasms. Recent data from Colorado show that 94% of patients with medical marijuana cards received them for treatment of "severe pain."¹⁷ Similar trends are evident in California.¹⁸ Evidence for the benefit of marijuana in neuropathic pain is seen in many¹⁹⁻²¹ but not all²² clinical trials. There is no high-quality evidence, however, that the drug reduces non-neuropathic pain; this remains an indication for which data sufficient to justify the risks of medical marijuana is lacking.4, 23-25

If marijuana is to be 'prescribed' by physicians and used as a medication, it should be subject to the same rigorous approval process that other commercially available drugs undergo. Potentially therapeutic components of marijuana should be investigated, but they should only be made available to the public after adequately powered, double-blind, placebo-controlled trials have demonstrated efficacy and acceptable safety profiles. Furthermore, these compounds should be administered in a way that poses

less risk than smoking and dispensed via standardized and FDA-regulated pharmacies to ensure purity and concentration. Bypassing the FDA and approving 'medicine' at the ballot box sets a dangerous precedent. Physicians should be discouraged from recommending medical marijuana. Alternatively, consideration can be given to prescribing FDA-approved medicines (Dronabinol or Cesamet) as the purity and concentration of these drugs are assured and their efficacy and side effect profiles have been well documented in rigorous clinical trials.

Recreational Marijuana

The question of recreational marijuana is a broader social policy consideration involving implications of the effects of legalization on international drug cartels, domestic criminal justice policy, and federal and state tax revenue in addition to public health. Yet physicians, with a responsibility for public health, are experts with a vested interest in this issue. Recent legislation, reflecting

changes in the public's attitudes towards marijuana, has permitted the recreational use of marijuana in Colorado and Washington. Unfortunately, the negative health consequences of the drug are not prominent in the debate over legalizing marijuana for recreational use. In many cases, these negative effects are more pronounced in adolescents. A compelling argument, based on these negative health effects in both adolescents and adults, can be made to abort the direction society is moving with regards to the legalization of recreational marijuana.

Myth: Marijuana is Not Addictive

A growing myth among the public is that marijuana is not an addictive substance. Data clearly show that about 10% of those who use cannabis become addicted; this number is higher among adolescents.²⁶ Users who seek treatment for marijuana addiction average 10 years of daily use.²⁷ A withdrawal syndrome has been described, consisting of anxiety, restlessness, insomnia, depression, and changes in appetite²⁸ and affects as many as 44% of frequent users,²⁹ contributing to the addictive potential of the drug.



There is some evidence that compounds naturally found in marijuana have therapeutic benefit for symptoms of diseases such as HIV/AIDS, multiple sclerosis, and cancer. If these compounds are to be used under the auspices of 'medical marijuana,' they should undergo the same rigorous approval process that other medications prescribed by physicians, including randomized, placebo- and active-controlled trials to evaluate safety and efficacy, not by popular vote or state legislature. This addictive potential may be less than that of opiates; but the belief, especially among adolescents, that the drug is not addictive is misguided.

Schizophrenia and Other Psychotic Disorders

Marijuana has been consistently shown to be a risk factor for schizophrenia and other psychotic disorders.³⁰⁻³² The association between marijuana and schizophrenia fulfills many, but not all, of the standard criteria for the epidemiological establishment of causation, including experimental evidence,33,34 temporal relationship,35-38 biological gradient,^{30,31,39} and biological plausibility.⁴⁰ Genetic variation may explain why marijuana use does not strongly fulfill remaining criteria, such as strength of association and specificity.41,42 As these genetic variants are explored and further characterized, marijuana use may be shown to cause or precipitate schizophrenia in a genetically

vulnerable population. The risk of psychotic disorder is more pronounced when marijuana is used at an earlier age.^{32,43}

Effects on Cognition

Early studies suggested cognitive declines associated with marijuana (especially early and heavy use); these declines persisted long after the period of acute cannabis intoxication.44-46 Recently, Meier and colleagues analyzed data from a prospective study which followed subjects from birth to age 38; their findings yielded supportive evidence that cannabis use, when begun during adolescence, was associated with cognitive impairment in multiple areas, including executive functioning, processing speed, memory, perceptual reasoning, and verbal comprehension.⁴⁷ Rogeberg⁴⁸ criticized the study's methodology, claiming that the results were confounded by differences in socioeconomic status; this claim, however, was based on sub-analyses that used very small numbers. Additional sub-analyses⁴⁹ of the original study cohort showed that marijuana was just as prevalent in populations of higher

socioeconomic status, suggesting that socioeconomic status was not a confounding variable. Any epidemiological study is subject to confounding biases and future research will be needed to clarify and quantify the relationship between cognitive decline and adolescent marijuana use. However, the findings of the original study by Meier et al show there is indeed an independent relationship between loss of intelligence and adolescent marijuana use. This finding, moreover, is consistent with prior studies.⁴⁴

Other Negative Health Effects

Substantial evidence exists suggesting that marijuana is harmful to the respiratory system. It is associated with symptoms of obstructive and inflammatory lung disease,^{11,50} an increased risk of lung cancer,^{14,15} and it is suspected to be associated with reduced pulmonary function in heavy users.⁵¹ Further, its use has been associated with harmful effects to other organ systems, including the reproductive,⁵² gastrointestinal,⁵³ and immunologic^{10, 54} systems.

Social Safety Implications: Effects on Driving

Marijuana impairs the ability to judge time, distance, and speed; it slows reaction time and reduces ability to track moving objects.^{55,56} In many studies of drug-related motor vehicle fatalities, marijuana is the most common drug detected except for alcohol.^{57,58} Based on postmortem studies, Couch et al determined that marijuana was likely an impairing factor in as many fatal accidents as alcohol.⁵⁹ One study showed that in motor vehicle accidents where the driver was killed, recent marijuana use was detected in 12% of cases.⁵⁷ Other research confirms a significantly increased risk of motor vehicle fatalities in association with acute cannabis intoxication.⁶⁰

Risk Perception and Use in Adolescents

Marijuana use among adolescents has been increasing. Data that has tracked risk perception and use of marijuana among adolescents over decades clearly shows an inverse relationship; as adolescent risk perception wanes, marijuana use increases.⁶¹ As more states legalize medical and recreational marijuana, risk perception is expected to decrease, causing the prevalence of use among adolescent to continue to rise. This is among the most concerning of issues about the drug's legalization because so many of the negative effects of marijuana—including cognitive impairment and risk for short- and long-term psychosis are heightened when used during adolescence.



Marijuana and Madness Editors: David Castle, Robin M. Murray, Deepak Cyril D'Souza

BOOK REVIEW

A comprehensive overview of the psychiatry and neuroscience of Cannabis sativa (marijuana). It outlines the latest developments in understanding the human cannabinoid system, and links this knowledge to clinical and epidemiological facts about the impact of cannabis on mental health. Clinically focused chapters review not only the direct psychomimetic properties of cannabis, but also the impact



consumption has on the courses of evolving or established mental illnesses such as schizophrenia. Effects of cannabis on mood are reviewed, as are its effects on cognition. Source: Amazon.com / Hardcover: 252 pages / Publisher: Cambridge University Press; 2 edition ISBN-10: 1107000211 / ISBN-13: 978-1107000216

Conclusion

There is some evidence that compounds naturally found in marijuana have therapeutic benefit for symptoms of diseases such as HIV/AIDS, multiple sclerosis, and cancer. If these compounds are to be used under the auspices of 'medical marijuana,' they should undergo the same rigorous approval process that other medications prescribed by physicians, including randomized, placeboand active-controlled trials to evaluate safety and efficacy, not by popular vote or state legislature. Furthermore, these therapeutic compounds should be administered via a route that minimizes long-term health risk (i.e., via oral pill) and should be dispensed by centrally regulated pharmacies to ensure the purity and concentration of the drug and allow for the recall of contaminated batches.

Marijuana for recreational use will have many adverse health effects. The drug is addictive, with mounting evidence for the existence of a withdrawal syndrome. Furthermore, it has been shown to have adverse effects on mental health, intelligence (including irreversible declines in cognition), and the respiratory system. Driving while acutely intoxicated with marijuana greatly increases the risk of fatal motor vehicle collision. Legalization for recreational use may have theoretical (but still unproven) beneficial social effects regarding issues such as domestic criminal justice policy, but these effects will not come without substantial public health and social costs. Currently there is a lack of resources devoted to educating physicians about this most commonly used illicit substance. The potential

benefits and significant risks associated with marijuana use should be taught in medical schools and residency programs throughout the country.

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Disclosure

None reported.

