



Editorial

Cannabis Research and Therapeutics: An International Quasi-experiment in Cannabis Policy

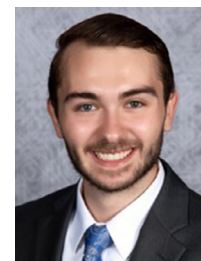
Interest in cannabis for its therapeutic potential is not new historically or worldwide; however, modern, post-prohibition policies have put a renewed spotlight on cannabis, its future in medicine, and the regulation of its use in adults. However, efforts to legalize cannabis use have been hampered by the complexity of cannabis regulations in balancing the host of potential and experienced effects of legalization. In this Specialty Update of *Clinical Therapeutics*, experts in research and policymaking discuss the complex history of cannabis to provide a better understanding of its potential in clinical therapeutics and the effects of modern-day cannabis legalization on other health- and society-related issues. These experts tackle a variety of key topics in this edition, including existing medicinal cannabis programs, use in adolescents, social equity, and social consumption, among many others.



Julie Johnson

LEGAL AND REGULATORY CONCERNS

There are challenges inherent in legalizing and regulating a quasi-regulated substance that is not yet well understood by scientists or policymakers. The legalization of medicinal- and adult-use cannabis raises societal concerns, such as clinical health effects, but also presents potential in clinical therapeutics, equity, and economics. The legalization policies, regulation, implementation, enforcement, and fidelity of implementation of cannabis use are different processes across states and countries, and these differences may affect outcomes. The outcomes of legalization may also change over time or be delayed, depending on delays in implementation¹; policy change/evolution²; and changes in price, potency,³ types of products,³ and social norms.^{1,3} Understanding and anticipating policy-related outcomes within the context of the interplay among social and environmental structures, such as the health care and criminal justice systems, are helpful to both counter adverse effects and maximize potential.



Alexander Colby

With many changes in the cannabis-legalization landscape in a short time across the globe, now is a crucial time to reflect, digest, and assess past policy and to proactively proceed with evidence-based policy and practices in the future. It is imperative that this issue include the perspectives and experiences of policymakers, regulators, and legal experts alike to help unite the historically separate silos of cannabis research and policy, as these stakeholders are experts in the writing, enactment, application, and enforcement of policies.

Kilmer and Davila⁴ discuss insights into modern 21st century cannabis legalization and policy gleaned after 10 years of policy implementation and digestion. The authors discuss the key policy issues of today; the wide array of products available, including high-potency products; and the need to change current methods of studying the effects of policy change.

In Schauer et al., state-level regulators across North America highlight the federal policy impeding on research and key gaps in scientific knowledge, and propose a research agenda that would address these phenomenon needed to regulate modern cannabis policies safely and effectively.⁵ Similarly, Massachusetts cannabis policymakers discuss balancing strong public demand for cannabis reform with the contemporary

lack of scientific consensus on key issues.⁶ Together, regulators and lawmakers argue for the need for research to establish a more evidence-based path forward, and include specific issues of acute concern, such as the medicinal use of cannabis and cannabinoids, standards for medical programs, product safety, consumer behaviors, cannabis impaired driving, and promotion of equity and reduction of health, social, and economic disparities.^{5,6}

MEDICINAL CANNABIS PROGRAMS

Unlike the conventional course of medical treatments and practices used today, in which research serves as the impetus for changes in policy and practice, cannabis-related policy and practice preceded much of the science; yet research is crucial for the safety and sustainability of medicinal cannabis programs. Johnson and Colby⁷ outline the complex history and evolution of medicinal cannabis, from ancient to modern society, discussing the scientific discovery and therapeutic potential of cannabinoids and the endocannabinoid system. Although a lack of research has stymied the available evidence base and training for medical practitioners overall, Australia has developed educational resources and clinical guidance, using the current scientific knowledge to address the gap in clinical information and to support the needs of health care professionals that recommend cannabis for treatment.⁸

Patients have diverse needs that may be disparate from those of recreational cannabis users (hereafter, *adult use*), as patients use cannabis for the treatment of a variety of different ailments that must be considered. One cohort of patients that has drawn particular interest is military veterans, who face numerous barriers to accessing cannabis in the United States due to its Schedule I status.¹ Cannabis may be a substitute for potentially more harmful substances or pharmaceuticals. McNabb⁹ assesses cannabis as an alternative to prescription and over-the-counter medications used among US veterans. Although a spectrum of conditions, including chronic pain, post-traumatic stress disorder, anxiety, and depression, were prevalently reported by military veterans who were cannabis users, 91% of respondents across all conditions reported that cannabis provided a greater quality of life. Forty-five percent of respondents reported that medicinal cannabis reduced their use of other medications, notably prescription antidepressants and anti-inflammatories, and over-the-counter medications. These results demonstrate patients' different needs and indicate the importance of medicinal cannabis programs in meeting these diverse demands.

Adult-use cannabis programs alone may not be sufficient for meeting the needs of patients. Colby et al¹⁰ assessed medicinal cannabis programs in three US states after the implementation of adult-use cannabis programs, and found indicators of decreased utilization in two of the three states. Study results suggest the need for further evaluation of the policies and provisions of simultaneous adult-use and medicinal-use cannabis programs and their interactions, as policy design may be a crucial determinant of the sustainability of medicinal cannabis programs and of patient access to cannabis products in the long term.

TRADEOFFS TO CANNABIS LEGALIZATION

Jurisdictions with legalized cannabis use may experience a surplus of tax dollars in the short term, but legalization may also increase demands on health and public safety infrastructures in the long term, including an increased use of emergency and other health care services, as well as increased use of law-enforcement or criminal-justice services. Changes in the prevalence of use and norms that surround evolving cannabis policies might warrant different policy considerations, which in turn may have differential effects on various cohorts.¹¹ The legalization and regulation of the use of substances with the potential for dependence are often in juxtaposition with approaches to public health policy, given that the minority of heavy or dependent users often account for most of the consumption, which generates the tax revenue¹² as evidenced by the tobacco and alcohol industries.¹² Cannabis-related risks, including those for increased potency¹³ and cannabis-use disorder, remain a key concern with legalization, especially among youth cohorts.^{13–15} Greater ease of access to cannabis, and an increased prevalence of cannabis use, may also contribute to other adverse health concerns such as mental health disorders,^{16,17} cannabis-related health

conditions such as cannabinoid hyperemesis syndrome,^{18,19} and safety concerns, such as impaired driving^{20,21} or unintentional consumption.^{13,22,23} Youth, emerging adults, and persons with behavioral health disorders may be disproportionately at risk for adverse outcomes.^{24,25}

Potential adverse outcomes warrant the continued monitoring of cannabis-use behaviors by public health officials and policymakers alike. Multiple articles demonstrate key insights derived from monitoring public health data. Adverse outcomes may be different in youth and emerging adults, who are at disproportionately greater risk from cannabis use than are their adult counterparts. Ross and Levy²⁶ discuss the neurologic mechanisms of cannabis use in youth and the disproportionate risk due to the crucial period of brain neurodevelopment and premature activation of the reward pathway with early cannabis-use initiation. Another study explores the potential motivations for why adolescents and emerging adults may use cannabis at greater rates: English and Whitehill²⁷ theorize how legalization may change youths' perceptions of cannabis use among their social networks, and report that cannabis use by a parent, sibling, or best friend was associated with an increased risk for use in adolescents. This work highlights the role of the social network, including peers and family members, as an important determinant of cannabis use among youth.

The legalization of cannabis use merits ongoing public health monitoring, clinical and public education, and funding for evidence-based research to inform policies that will effectively counter potential adverse public health and clinical outcomes in youth specifically.

SOCIAL EQUITY

The legalization of cannabis use offers a unique and crucial opportunity for societies to rectify past harms of people disproportionately affected by the inequitable enforcement of cannabis-prohibition policies (“War on Drugs”), another key objective of cannabis legalization. In 2020, the American Public Health Association issued a policy statement declaring racism as a long-standing issue in US and world history that permeates almost every institution, such as the health care and criminal justice systems, further stating that “Black and African Americans have suffered across multiple generations at the hands of the racist practices that plague each of these institutions.”²⁸ Legalization provides an opportunity to address past harms and provide economic opportunity among Black, Indigenous, and People of Color (BIPOC) communities. Social equity provisions imbedded in many legalization efforts focus on the economic social determinants related to structural racism and discrimination.²⁹

Achieving applied equity is multi-pronged and warrants multiple societal structures to create equity among different racial and ethnic groups in meaningful ways across society.³⁰ To achieve health equity, it is essential to address the institutional racism that creates inequities in clinical care.^{31,32} Similarly, economic equity requires work to address institutional racism in the economic systems that led to historical discrepancies in employment opportunities between racial groups.³³ A crucial aspect of achieving economic equity is understanding and rectifying the disproportionate rates of drug arrest and incarceration in BIPOC persons, which decrease employment and the opportunity to create generational wealth in BIPOC families and communities.³⁴

Underlining the systemic nature of racism in drug policy, Montgomery³⁵ outlines previous failures in drug policy that have affected BIPOC communities from the opium wars of the 19th century to the crack epidemic of the 1980s and 1990s. Montgomery³⁵ also highlights the ways in which policy historically was designed for extracting profits rather than for protecting public interest. The author discusses modern developments in the cannabis industry and highlights the potential of equity-related mandates in legalization efforts to prevent repeating this history of prejudicial treatment.

Furthermore, it is essential to determine the ways in which prejudicial drug policy and racial discrepancies in cannabis enforcement continue to cause harm today. To explore this occurrence in youth, Harris³⁶ studies the ways in which legalization affects the criminal justice system's referral of youth to treatment for cannabis use. Although Harris³⁶ find that racial/ethnic disparities in referral rates have declined in absolute terms, the relative extent of the disparities have increased in states with legalized use. The author did not find a significant difference between states with legalized and nonlegalized use.

Inequity persists despite a dedicated focus on reducing inequalities and inequities with cannabis legalization. In a second article, Belackova³⁷ discusses the utility of cannabis social clubs' advancing equity goals while simultaneously

preventing negative public health effects by removing profit as the principal driver of market expansion, and instead focusing on the welfare and advocacy of members. However, it remains to be seen whether these community-oriented supply mechanisms will have a future as the cannabis-legalization landscape evolves.

WHAT'S NEXT?

Cannabis legalization is complicated; there is no "one size fits all" policy or cannabinoid product profile for therapeutic efficacy. From public health to social equity to the concerns of patients, multiple different viewpoints need to be considered to effectively, safely, and equitably regulate cannabis use. To best maximize the benefits and minimize the risks of the legalization of cannabis and its therapeutic use, convening diverse stakeholders to guide policies and adhere to known best practices may optimize outcomes in jurisdictions and populations. For future success, it is crucial to both expand clinical and applied cannabis research, as well as bridge the silos between research and policy.

DECLARATION OF INTEREST

The authors have indicated that they have no conflicts of interest with regard to the content of this article.

ACKNOWLEDGMENTS

We gratefully acknowledge Shawn Collins, Massachusetts Cannabis Control Commission, Alisa Stack, Massachusetts Cannabis Control Commission, and Hailey Pensky, Massachusetts Cannabis Control Commission.

FUNDING

J.K. Johnson and A.M. Colby were supported by the Massachusetts Cannabis Control Commission, Commonwealth of Massachusetts. The content is solely the responsibility of the authors and does not necessarily represent the views of Massachusetts Cannabis Control Commission.

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